



UNIVERSITA' CAMPUS BIO-MEDICO DI ROMA



RESEARCH YEARBOOK

2019



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On the Cover

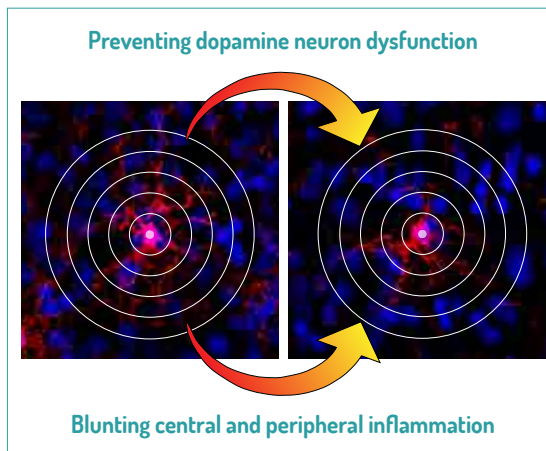
On the cover

Blunting Neuroinflammation with Resolvin D1 Prevents Early Pathology in a Rat Model of Parkinson's Disease

The ability of our immune system to respond to internal or external attacks is strictly related to the resolution of inflammation, the process by which the immune response terminates following the initial infection. For such a purpose our body produces small messenger molecules, including Resolvins, that act by resolving the immune response, to avoid the development of chronic inflammation.

A recent study has shown a direct link between malfunctions in the resolution of inflammation and Parkinson's disease, a devastating neurodegenerative motor disorder characterized by resting tremors, slow movements and rigidity. The main hallmark of Parkinson's disease is the loss of dopaminergic neurons in the substantia nigra, leading to impaired neuronal communication between the substantia nigra and the brain's motor control center of the striatum.

Neuroinflammation is another important aspect of Parkinson's Disease, yet the cause-effect relationship between the two has always been a mystery. In their study, published in *Nature Communications*, Krashia and collaborators used a validated rat model of Parkinson's disease to investigate the relationship between neuroinflammation and the malfunction of the nigrostriatal dopaminergic system. They found that the early neuronal and motor symptoms in these rats are associated with the early neuronal and motor symptoms in these rats are associated with central and peripheral inflammation, and also with deficits in Resolvin D1 levels. Importantly, administration of Resolvin D1 in the Parkinson rats could not only prevent inflammation, but could also prevent



On the cover

dopamine neuron dysfunction and motor deficits, thus seemingly also preventing Parkinson's.

Importantly, to validate in patients their data concerning deficits in Resolvin D1, the researchers analyzed blood and plasma samples from Parkinson's patients or control subjects and found that Resolvin D1 levels were significantly lower in patients, in a way that mirrors what occurs in old rats.

While we still lack answers on how the mechanisms of resolution are precisely affected in Parkinson's disease, this work proves the critical importance of Resolvins and highlights these molecules as important biomarkers and potential therapeutic agents, not only for Parkinson's but also for other neuroinflammatory and neurodegenerative diseases.

Krashia P., et al.

Blunting neuroinflammation with resolvin D1 prevents early pathology in a rat model of Parkinson's disease

Nature Communications 2019; 10(1): 3945.

Campus Bio-Medico University of Rome - Department of Science and Technology for Humans and the Environment - Research Unit of Molecular Neurosciences

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2019 Research Facts and Figures

2019 Research Facts and Figures

The research activities carried out in 2019 at the Campus Bio-Medico University of Rome have produced important outputs in terms of scientific publications, research projects, clinical trials and patents. More than 650 papers have been published, with 2900+ cumulative Impact Factor (I.F.), and 2900+ normalized I.F.. This represents, respectively, an increase of 28%, 47% and 36% with respect to 2018. About 64% of such publications appeared on journals belonging to the first quartile (Q1) of the Scopus/SCImago international periodicals ranking.

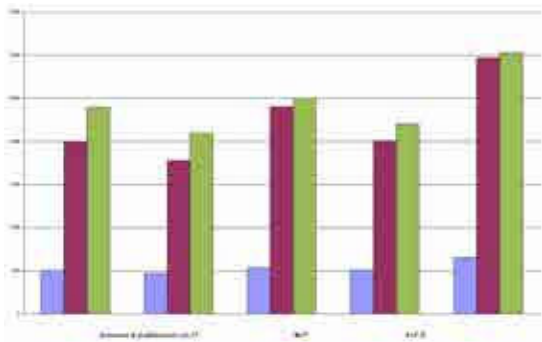


Figure 1 - Number of publications with I.F., total I.F. and total N.I.F. in the last five years

As shown in Figure 2 the number of publications per faculty member is about 4.5 and remained stable with respect to 2018; as well as the number of faculty members as shown in Figure 3.

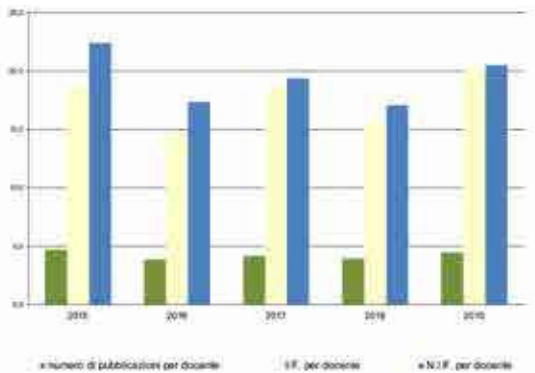


Figure 2 - Number of publications with I.F., total I.F. and total N.I.F. per faculty member in the last five years

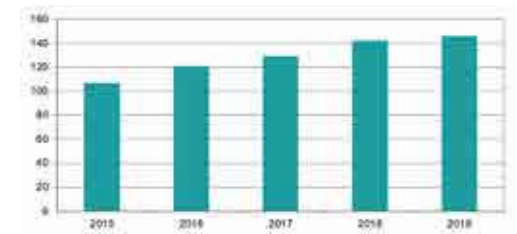


Figure 3 - Number of faculty members in the last five years

Figure 4 shows the overall scientific production in 2019 in terms of number of publications, Impact Factor (IF) and Normalized Impact Factor (NIF) for each of the 49 Research Units of the University.

There are several indicators, which provide objective evidence of the quality of the research carried out at the University such as, for example:

- Average of 4+ publications with Impact Factor per faculty member in 2019;
- 64% publications in the first quartile (Q1) according to SCImago ranking, which includes the top 25% journals in each subject category.

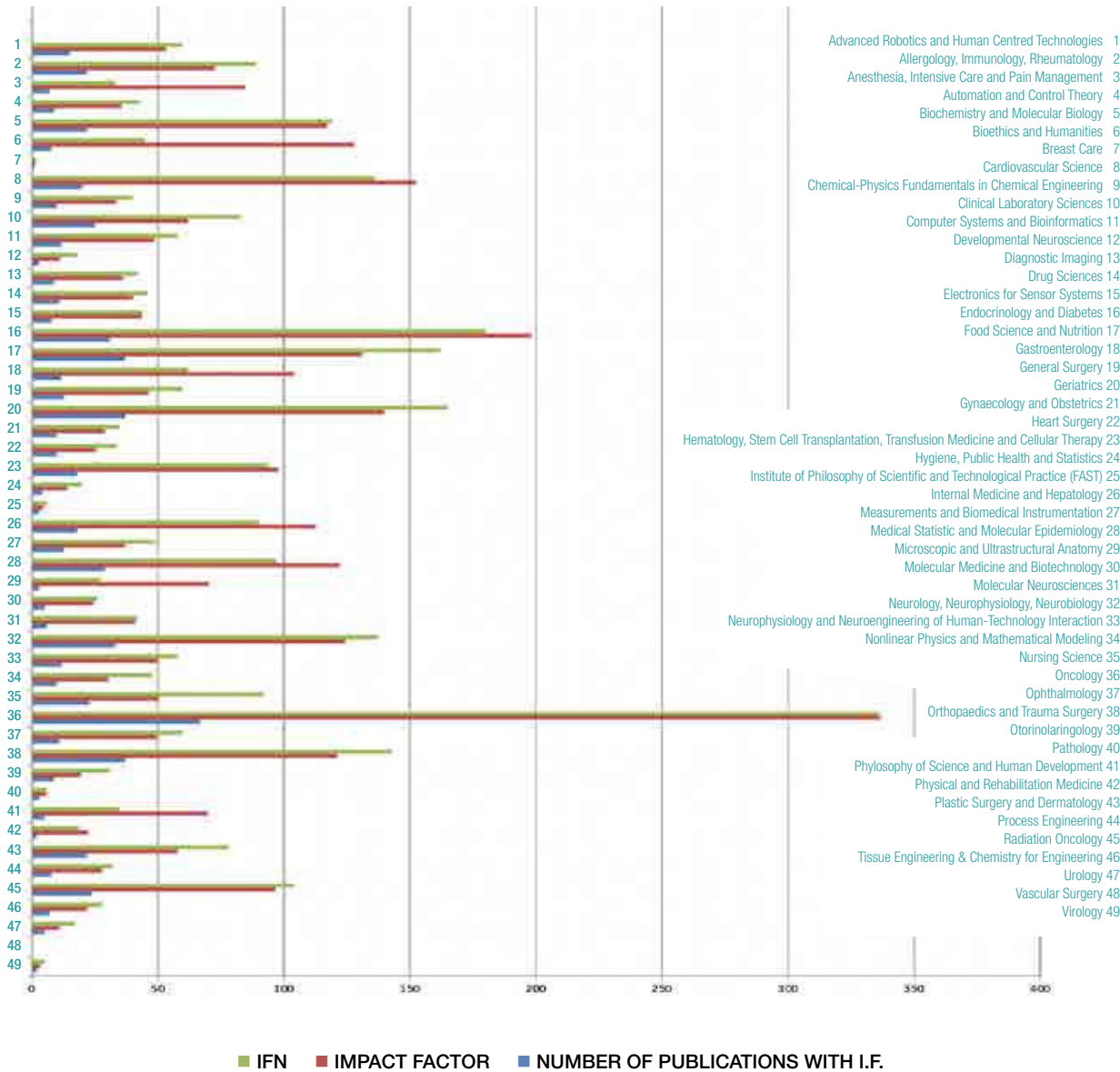


Figure 4 - Number of publications, Impact Factor (I.F.) and Normalized Impact Factor (N.I.F.) per Research Unit

In 2019, about 100 research projects, including clinical trials, were funded. The following figure illustrates the success rate on competitive calls during the period 2015-2019.

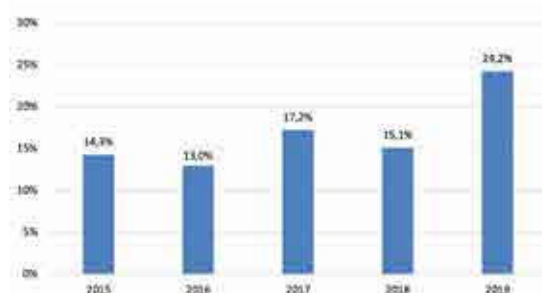


Figure 5 - Success rate on calls 2015-2019

The main funding bodies of 2019 ongoing projects were: European Commission, the National Institute for Insurance against Accidents at Work (INAIL), Italian Ministry of, University and Research, Italian Ministry of Health, Italian Ministry of Economic Development, Italian Space Agency, Lazio Regional Authority, Fondazione ANIA, European Foundation for the Study of Diabetes, Alzheimer's Association as well as several companies which have been supporting commissioned research and clinical trials; 65 internal clinical trials were also started.

As regards the activities related to exploitation of research results, in 2019, three applications for Italian patents, of which two co-owned with Italian organisations, were filed. UCBM received first royalties from a patented product licensed by UCBM to an Italian SME.

As of 31st December 2019, the patent portfolio owned or co-owned by the University includes 16 families of patents (with a total of 30 patents) in the fields of rehabilitation engineering, microengineering, regenerative medicine, biomedical instrumentation, cancer diagnostics, food analysis, etc.

In 2019 two new startups have been accredited as spin-off of the University, including the first one participated by UCBM, joining five spin-offs born in the previous years.

More detailed information on ongoing projects is available in the section "Research projects" of this Yearbook, whereas in the section "The University Third Mission" the activities related to commissioned research, clinical trials, University patents and University accredited spin-off companies are presented along with information about Public Engagement and other dissemination activities promoted by the University to enhance the impact on society of our research activities.



Research Quality Assurance Policies

Research Quality Assurance Policies

In accordance to relevant legislation and in conformity with the guidelines issued by the Italian National Agency for the Evaluation of the University and Research Systems (ANVUR), the Campus Bio-Medico University of Rome recognizes that quality is a fundamental value. Furthermore, it considers it its inspiring feature in the incessant effort to implement the University general mission as defined in its “Charter of the Aims”. The main UCBM source of reference for the quality assurance policy has been the “2014-2016 Strategic Guidelines” document. Its motto, “More Quality, More Person”, specifically identifies the strategic vision of combining the continuous improvement of all university activities with a systematic attention to the person, in teaching, research and healthcare.

The general principles guiding the quality assurance policy are:

- centrality of the person;
- special attention to the social impact and to the ethical implications of research;
- inseparable nature of teaching and research (or healthcare activities);
- efficient and effective use of resources;
- development of international cooperation activities and of research mobility programs;
- commitment to grant equal opportunities, to protect from discrimination and to remove barriers for the disabled;
- support to translational research to allow fast transfer of research results into medical practice and meaningful health outcomes;
- support to technological innovation and encouragement of socio-economic development, by promoting cooperation with local enterprises and institutions;
- support of University spin-off for the exploitation of research products.

Moreover, the University pursues systematic application of its “Charter of the Aims” and of its “Code of Ethics” to all research activities.

The Departments of Engineering, of Medicine and Surgery and of Science and Technology for Humans and Environment, supported by the Centre for Integrated Research, pursue continuous improvement of research activities paying special attention to the possible social impact of research outcomes by following

these general guidelines:

- improvement of key performance indicators in terms of quality and impact of scientific production. Faculty and research staff are assessed annually using criteria and parameters recognized by the scientific community of reference, specifically by indicators defined by ANVUR for assessing quality of research (Evaluation of Research Quality - VQR);
- multidisciplinary and transdisciplinary dimension of research: implementation of measures aimed at fostering collaboration among the various Research Units (RU), especially those within different Departments;
- international dimension of research: implementation of activities aimed at encouraging international programs of incoming and outgoing mobility. The University also aims at increasing its ability to attract external resources through participation in competitive calls, especially at a European level and at promoting cooperation with foreign centres of excellence including “visiting professors” programs which encourage the assignment of foreign scientists at our University for extended periods of research and teaching;
- policies for young researchers: the goal is to enhance the collaboration among researchers in an integration and skill enhancement logic. Furthermore, the University wishes to help to achieve outcomes and scientific growth of young researchers through promotion of participation in internally or externally funded competitive calls.
- policies for Ph.D courses: programs to be activated are selected according to scientific areas of excellence and scientific sectors active in the Departments; the University is implementing strategies to ensure an adequate number of Ph.D scholarships provided both by University funding, and by external sources of funding, i.e. research competitive grants. Furthermore, it prefers to focus resources on its strategic research lines and anyhow on sectors that demonstrate high quality standards and scientific self-sustainability and productivity; it also promotes consolidation of Ph.D programs on topics of interest in industrial activities by seeking external fund-

ing; it encourages the international dimension of Ph.D programs through participation in schools, conferences and visits to other universities or research centres featuring excellence in research;

- policies for the Third Mission: the University promotes initiatives to pursue its Third Mission through research, such as:
 - ▶ initiative to involve companies and other parties potentially interested in patents exploitation; measures to promote the incubation and acceleration of spin-off companies;
 - ▶ initiatives to improve diffusion and dissemination of scientific results;
 - ▶ fostering collaboration with public and private institutions, and companies, by publishing an annual report of its research activities, and by organizing a public engagement initiative, the Research Day with the aim of communicating the main research results.

The system for Quality Assurance in Research (QAR) intends to set research goals and objectives, to identify and plan what is required to achieve them, to monitor the regular course of each activity, as well as to verify the level of achievement of these objectives and propose corrective actions as appropriate.

Therefore, through the Quality Assurance in Research, the University implements its Quality Policy.

The boards and structures involved in the Quality Assurance in Research are:

- Quality Assurance Committee (Presidio di Qualità);
- Evaluation Committee (Nucleo di Valutazione);
- Academic Senate;
- Academic Research Board;
- Department Research Quality Assurance Groups;
- Department Councils;
- Department Boards.

The Academic Research Board plays a key role as the QAR main body, in tight cooperation with the university Quality Assurance Committee.

The background of the slide is a light gray pattern featuring various scientific and medical icons. These include DNA double helix structures, interlocking gears, stethoscopes, and stylized plant sprouts with leaves. The icons are scattered across the entire page, creating a thematic backdrop for the title.

Evaluation of Research Quality (VQR 2011-2014)

Evaluation of Research Quality (VQR 2011-2014)

The VQR (Valutazione della Qualità della Ricerca, Evaluation of Research Quality) is the Italian research assessment exercise that ANVUR (the National Agency for the Evaluation of the University and Research system) regularly carries out on behalf of the Italian Ministry of Education, University and Research (MIUR). On February 21, 2017, ANVUR presented the new VQR Report, which is referred to the period January 2011-December 2014 (www.anvur.org/rapporto-2016).

With more than 130 participant organizations, almost 65,000 contributors, and 118,000 research products having been evaluated, the VQR is by far the most important and comprehensive research evaluation exercise ever attempted in Italy. For the period 2011-2014, the VQR has ranked UCBM second in the area of Biological Sciences among all Italian universities. UCBM was ranked fourth in other two areas, namely Chemical Sciences and Industrial and Information Engineering Areas, and UCBM was ranked tenth in the area of Medical Sciences.

The VQR Report also shows that, as regards the single scientific disciplinary sectors, UCBM gained the first place (out of twenty-three universities) in Orthopaedics sector and the second place (out of thirty-two universities) in Neurology sector. Moreover, UCBM has been ranked third in Computer Systems, Diagnostic Imaging and Pathology sectors, out of fifty-three, thirty-seven and thirty-four universities respectively. These results are based on the very good UCBM performance as measured by the specific indicators used for this ANVUR assessment: UCBM stands well above the average performance of all other universities in terms of scientific products classified of “excellent” or “good” quality.

VQR results are presented in the table below, where also information about the separate ranking regarding only small universities is reported (i.e. dimensional range ranking) along with the percentage of UCBM scientific products classified in excellent and good classes.

Area	Overall ranking	Dimensional range ranking	% of publications in excellent and good levels
Area 03 Chemical Sciences	4° out of 56	4° out of 35	100%
Area 05 Biological Sciences	2° out of 62	2° out of 31	95,24%
Area 06 Medical Sciences	10° out of 52	8° out of 21	75,40%
Area 09 Industrial and Information Engineering	4° out of 63	4° out of 43	81,25%



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Research Organization and Services

Research Organization and Services

Centre for Integrated Research

The Centre for Integrated Research (CIR) provides support to the Department of Medicine and Surgery to the Department of Engineering and to Department of Science and Technology for Humans and the Environment for promotion, exploitation and administrative management of the research activities. It guarantees the proper management of funds for research activities, publications and scientific collaborations; it also ensures a correct execution of clinical trials according to relevant regulations, Good Clinical Practice and the Joint Commission International's standards. Amongst CIR's roles is the possibility of setting up and financing research units, groups and research programs open to the participation of scholars and researchers from national and international universities or research and cultural centres.

Academic Research Board

The Pro-Rector for Research chairs the Board, which is also composed of the Research Coordinators of the two UCBM Departments and of the Manager of Research Administrative Area. The Board ensures the necessary link between the three boards of the Departments, addressing and monitoring scientific research, and fostering their collaboration. The Board is primarily in charge of elaborating the University strategic plan for research development and of guiding the research quality assurance system (QAR).

Research Administrative Area

The Research Administrative Area promotes and fosters access to research funding sources, guarantees administrative management of research projects and of clinical trials, as well as exploitation of research results. The Research Administrative Area includes the following offices: Grant Office, Knowledge Transfer Office, Project Financial Management and Reporting Office. Activities of the offices are described below.

Grant Office

The Grant Office main objective is to assist researchers in finding the most appropriate funding sources, also carrying out internal scouting activities in order to promote and consolidate collaborations among differ-

ent UCBM Research Units. With this aim, the Office provides researchers with the support they need during the whole process of presenting research projects, from identification and notification of the most suitable financing opportunities to assistance in preparation and submission under national, European Commission and international competitive calls. It also offers support and follow up of project management in close synergy with the Project Financial Management and Reporting Office.

At the same time, the Office organizes seminars, workshops and informative events on competitive calls announcements.

The Office also provides technical-scientific support to activities of the Academic Research Board.

Knowledge Transfer Office

The Knowledge Transfer Office assists UCBM researchers in finding and assessing the best strategy to protect intellectual property and exploit research results, it manages the University patent portfolio in strict synergy with inventors, and promotes research results to SMEs and large companies with the aim to exploit research activities through licensing of patents and implementation of joint research projects.

Furthermore, the Office supports the promotion of joint laboratories with industries and spin-off research processes as well as incubation of spin-off companies. Finally, it organizes seminars and workshops on technology transfer issues.

Project Financial Management and Reporting Office

The Project Financial Management and Reporting Office assists the Research Units in the daily administrative management of the research projects.

It guarantees the proper post-award management of all grants, research contracts and clinical trials, analytical accounting management of research projects, expense analysis and monitoring. It also takes care of the projects periodic financial reports according to national and international regulations.

Furthermore, it assists Research Units in the accounting administrative auditing of projects carried out by external auditing companies.

The office manages also the Unique Code Project

a distinctive code for the identification of the project (Law 3/2003 art.11; Law 136/2010).

Finally, it also interacts with other administrative areas, such as Purchasing, Economics-Finance, Human Resources Areas and Management Secretary's Offices for an optimized administrative management of the research activities.

Clinical Innovation Office

The Clinical Innovation Office (CIO) promotes the quality system of the University's clinical research. This is an essential condition to make our University more and more competitive in the field of clinical research and, therefore, able to attract the main industrial players of pharmaceutical and biomedical sectors.

Objectives of the CIO are the improvement of the clinical trials' management conducted at Campus Bio-Medico of Rome according to Good Clinical Practices and the promotion of clinical research.

The CIO supports the investigators and sponsors providing a centralized point of contact for study budgets, contracts, regulatory affairs. The office is in charge of the preliminary feasibility analysis of the clinical studies, which is carried out in collaboration with the departments involved in the process of clinical trial authorization (University Hospital Board, Pharmacy, Clinical and Nursing Management, Research Administrative Area).

The CIO follows all the administrative and management steps of the study including the finalization of the formal contracts and agreements with the sponsoring partners. It also provides scientific and technical advice and offers support to the investigator during the start-up phase of the study, if required. During the execution of the clinical trials, the office carries out a regular reporting activity.

The office is also in charge of ensuring the full compliance with the quality standards established by the Joint Commission International (JCI) accreditation, including Principal Investigators training and updating on the best clinical research practices.

Core Facilities

In order to support the research programs of the various Faculties, the Campus Bio-Medico University offers facilities including work areas and the latest

generation tools. The facilities can be used by staff for their own research as well as research to be conducted in collaboration with other Institutions. Collaborators, in fact, are often invited to visit the University to work together on innovative projects with high scientific impact.

Work area provided:

- Cytometry
- Cell Imaging
- Cell culture room
- Molecular Biology
- Radioisotope Facility
- Clean Room
- Department of Engineering Facilities
- Department of Medicine and Surgery Facilities

Cytometry

The newly organized cytometry facility was created to support existing research lines at our University, to create new collaborations with other Institutes, and to promote flow cytometric methods in new areas of biomedical research and Engineering.

The Facility is equipped with cutting-edge tools and personnel available to collaborate with researchers in the design of the experimental panels, in the selection of the most suitable reagents and in the use of the instrumentation.

The area is equipped with:

- CytoFlex (BeckmanCoulter)



The Flow Cytometer Cytoflex is based on photodiode technology, it includes five channels of the 488 nm (Blue) laser, three of the 638 nm (Red) laser and two channels of the 405 nm (Violet) laser.

Optical Configuration:

Laser Blue 488nm	Laser Red 638nm	Laser Violet 405 nm
488\8SSC	660\20	450\45
525\40	712\25	525\40
585\42	780\60	
610\20		
690\50		
780\40		

MoFlo Astrios EQ (Beckman Coulter)

Our MoFloAstriosEQ is a cell sorter equipped with 2 lasers: 488 nm (Blue) and 640 nm (Red)

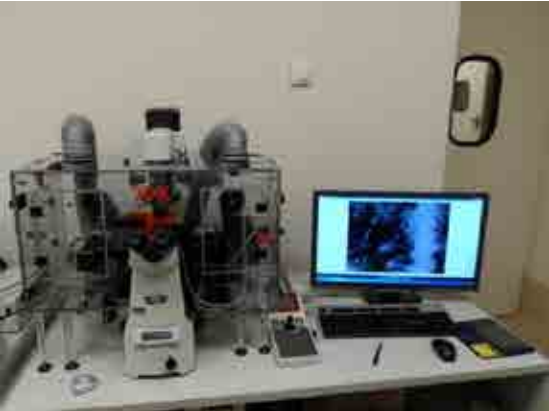


Technical features:

- jet-in-air system;
- temperature regulation for sampling and collection tubes;
- high-speed cell sorting (up to 70.000 cells/sec);
- nozzles available : 70µm, 100µm
- X-Y-Z stage for microplates, tubes (up to 6 populations can be separated at the same time) and slides.
- Sorting mode:
- purity;
- single cell (CLONING);
- enrichment.

CELL IMAGING

Fluorescent Microscope NIKON ECLIPSE Ti



The **Nikon Eclipse Ti** is a fluorescence microscope with a Nikon camera. It is equipped with a motorized system with high stability and solidity particularly suitable for micromanipulation and imaging applications. It can be used for different types of observation methods: light and dark field and phase contrast. It is also equipped with the **Okolab System**, that consist in a cage incubator for the inverted microscope complete of humidification system with external scrubber, CO2 control unit and temperature sensor (from 3 °C to 50 °C) for the study of cell culture. Thus allowing time-lapse acquisition on biologic samples.

Confocal Microscope NIKON ECLIPSE Ti2



The **Nikon A1+R Confocal Microscope** is equipped with a **4-channel detector** unit with high-sensitivity Gasp PMTs, allowing the acquisition of bright signals with minimal background noise, and a **spectral detector** for the simultaneous acquisition of 32-channel spectral images. Beside conventional galvano scanning mode, the microscope also features a **resonant scanner** for high speed scanning with minimal phototoxicity and photobleaching, ideal for live sample acquisition. The system is equipped with a **cage incubator** for prolonged observations of living cells.

TEM (Transmission Electron Microscope) Tecnai G2 Spirit –FEI Company



The FEI Tecnai Spirit 12G model can reach over 600,000 magnifications with high-contrast and high-resolution imaging, allowing it to work not only on cells but also on nano materials.

Critical point drying (CPD, Emitech K850)

This system allows preparing cell sample for SEM observation replacing intracellular water with alcohol, alcohol phase with liquid CO₂ first and then gaseous CO₂.

CELL CULTURE ROOM



This Facility is available to all researchers who need to prepare their animal or human cell culture on site.

This room is equipped with:

- laminar flow hoods,
- CO₂ incubators for cell culture,
- thermostatic bath,
- inverted microscope.

MOLECULAR BIOLOGY

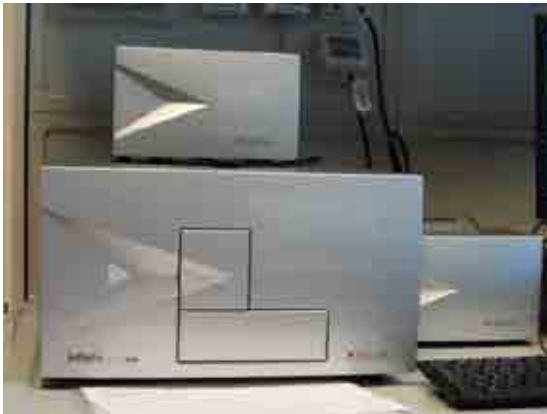
7900HT Fast Real –Time PCR System Applied Biosystem



The Fast Real-Time PCR System makes it possible to carry out Real-Time Quantitative polymerase chain

reaction. It can analyze 96 and 384 well plates and is compatible with the TaqMan system array also gives the possibility to work in Fast Real -Time PCR mode. The tool allows performing gene expression analysis (relative and absolute quantification) genotyping (mutation analysis) and methylation analysis.

Plate reader Tecan Infinite M200 PRO



Tecan Infinite 200Pro is a multimode plate reader equipped with monochromator optics, which allows the operator to select any wavelength, from UV to NIR, for absorbance, chemiluminescence and fluorescence readings on plates from 6 to 384 wells and on cuvettes. It is provided of two channels Te-Inject module that allows adding volumes of reagents starting from 1 μ l to 100 μ l.

This tool allows you to do:

- quantification of proteins and nucleic acids in a sample volumes as little as 2 μ l;
- enzymatic and immunochemical assays;
- ELISA tests;
- assays of gene expression

RADIOISOTOPE FACILITY



The Radioisotope facility is equipped with a fume hood and a biosafety cabinet to operate with beta-emitting radionuclides (^3H , ^{14}C). The laboratory is also equipped with basic equipment for cell biology and with an automated scintillation counter (Tricarb, Perkin Elmer).

CLEAN ROOM



Our Clean Room is Class 1000 facility and it is de-

signed to emit minimal levels of air contaminants and airborne particulates. It is used for controlled manufacturing process in a clean production environment. Our Clean Room is equipped with pure water, vacuum, clean compressed air, pure gas such as oxygen, nitrogen and argon.

Furthermore it is provided of:

- Chemical Hood;
- Plasma Cleaner (FEMTO, Diener Electronic);
- Spin coating system (Model P6700);
- Mask aligner (SUSS MicroTec);
- Sputter coater (Bal-Tec SCD500);
- Heating plates.

ENGINEERING DEPARTMENT FACILITIES

Our Engineering Department has tools that can be used for a wide range of research carried out by various laboratories:

- Freeze dryer Lio-5P (-55°C) (image);
- Oscilloscope;
- Voltage generator;
- Uniaxial testing machine (Instron 3365) (image);
- Computer Software license agreement (COM-SOL and Maple).



DEPARTMENT OF MEDICINE AND SURGERY FACILITIES

Set Up for electrophysiological recordings



The electrophysiology setup fully equipped with up-right microscope, camera, micromanipulators, recording amplifier, computer and acquisition software, is dedicated to performing field- and patch-clamp recordings from living neurons in brain slices or from cells in culture. The laboratory is also equipped with an electrode puller and a Vibratome for brain-slicing.

The Library

The Library mission is to provide comprehensive resources and services in support of the research, teaching, and learning needs. To fulfil this mission, the Library is committed to acquire, deliver and integrate information to support excellence in research, in education, and in patient care. The focus is to build broad print and e-resources collections, including access to specific databases and striving to make electronic content easily accessible to all users.

The concrete support given to research activities, with reference to the scientific productivity, deals with the use of research evaluation metrics and its application to the analysis of research systems.

Specifically it assists single users, departments or research units in the recovery of bibliometric indicators, such as the Impact Factor and the normalized Impact Factor, as well as the citation index data from Web of Science and Scopus.

Document supply service

The Library operates an advanced system for handling users' requests of documentation. The service allows registered users to request items, which are not available in the University Library.

The service is accessible on campus, upon registration through the online form available on the Library website.

Doctoral dissertations theses repository

The Library offers a storage and consultation service of doctoral dissertations repository. Full text doctoral dissertations theses are stored in the open access repository ILITHIA. The repository is indexed in OpenDOAR, an authoritative worldwide directory of academic open access repositories.



Contacts

Centre for Integrated Research (CIR)

Campus Bio-Medico University of Rome
Via Álvaro del Portillo, 21
00128 Roma

Tel. +39 0622541 9144

Fax +39 0622541 1947

E-mail cir@unicampus.it

Web site www.unicampus.it/ricerca

Pro-Rector for Research

Eugenio Guglielmelli

E-mail prorettorericerca@unicampus.it

Academic Research Board

Eugenio Guglielmelli, *Pro-Rector for Research*

Gianfilippo Capriotti, *Manager
of Research Administrative Area*

Vincenzo Di Lazzaro, *Research Coordinator
of the Department of Medicine and Surgery
(until October 31, 2020)*

Umile Giuseppe Longo, *Research Coordinator
of the Department of Medicine and Surgery
(since November 1, 2020)*

Marcella Trombetta, *Research Coordinator
of the Department of Engineering*

Marcello D'Amelio, *Research Coordinator
of the Department of Science and Technology
for Humans and the Environment*

Research Administrative Area

Gianfilippo Capriotti, *Manager*

Tel. +39 0622541 9146

E-mail g.capriotti@unicampus.it

Angela Aurora Pace

Tel. +39 0622541 9144

E-mail a.pace@unicampus.it

Mario Policastrì

Tel. +39 0622541 9147

E-mail m.policastrì@unicampus.it

Simona Virga

Tel. +39 0622541 9181

E-mail s.virga@unicampus.it

Grant Office

Antonella Benvenuto, *Head*

Tel. +39 0622541 9167

E-mail a.benvenuto@unicampus.it

Anna Lisa Ciano

Tel. +39 0622541 9186

E-mail a.ciano@unicampus.it

Project Financial Management and Reporting Office

Sara Buccioli

Tel. +39 0622541 9148

E-mail s.buccioli@unicampus.it

Valentina Cirulli

Tel. +39 0622541 9149

E-mail v.cirulli@unicampus.it

Ilenia Scaturchio

Tel. +39 0622541 9136

E-mail i.scaturchio@unicampus.it

Knowledge Transfer Office

Maria Carla De Maggio

Tel. +39 0622541 9126

E-mail m.demaggio@unicampus.it

Clinical Innovation Office

Francesco Rossi, *Scientific Board Chair*

Vincenzo Di Lazzaro, *Scientific Board Member*

Umile Giuseppe Longo, *Scientific Board Member
(since November 1, 2020)*

Giorgio Minotti, *Scientific Board Member
(until October 31, 2020)*

Tel. + 39 0622541 8710

E-mail cio@unicampus.it

Alice Zoccoli, *Executive Manager*

Tel. + 39 0622541 8710

E-mail a.zoccoli@unicampus.it

Iliana Iannaccone, *Clinical Contract Specialist*

Tel. + 39 0622541 8809

E-mail iliana.iannaccone@unicampus.it

Alessia Orasanu, *Billing Specialist*

Tel. + 39 0622541 9076

E-mail a.orasanu@unicampus.it

Flavia Salvadori, *Administrative Assistant*

Tel. + 39 0622541 8812

E-mail f.salvadori@unicampus.it

Chiara Cinnella, *Clinical Trial Specialist*

Tel. + 39 0622541 9412

E-mail c.cinnella@unicampus.it



The background of the slide is a light gray pattern featuring various medical and scientific icons. These include DNA double helix structures, interlocking gears, stethoscopes, and stylized plant sprouts with leaves. The icons are scattered across the entire page, creating a thematic backdrop for the text.

Ethics Committee

Ethics Committee

The Ethics Committee is an independent body whose tasks involve assessment, approval and monitoring of clinical trials, researcher training and consultancy services. The Ethics committee is composed of experts from the various fields of biomedical research, health care and safeguarding patients' rights. It protects and promotes respect for human life, from the moment of conception to natural death by taking inspiration from the Charters of Human Rights, recommendation from international bodies, medical deontology and, in particular, the Helsinki Declaration and Good Clinical Practice guidelines. The Ethics Committee meets once a month for the evaluation of the studies.

Technical-scientific secretariat of the Ethics Committee

The Technical-scientific secretariat of the Ethics Committee prepares all the needed documentation for Ethics Committee's assessment and assists the subsequent authorization steps, in accordance with the current regulation on the execution of clinical trials (Legislative Decree 211 / 2003 and ss) and the UCBM Ethics Committee Regulation. The office, within the scope of its responsibilities, also takes care of relationships with the Regulatory Authorities (Ministry of Health, Istituto Superiore Sanità, AIFA, EMA, FDA).

Technical-scientific secretariat of the Ethics Committee

Laura Santangelo, *Responsible of Scientific Secretariat*

Tel. + 39 0622541 8718

E-mail l.santangelo@unicampus.it

Daniela Marrocco, *Clinical Trial Specialist*

Tel. + 39 0622541 8873

E-mail d.marrocco@unicampus.it

Members of the Ethics Committee

Francesco Pallone, *Chair*

Raffaele Antonelli Incalzi, *Deputy Chair*

Daniele Santini, *Clinician*

Angelo Insola, *Clinician*

Giuseppe Perrone, *Clinician*

Stefano De Lillo, *Territorial General Practitioner*

Bruno Nobili, *Pediatrician*

Maurizio Genuardi, *Genetist*

Anita Paoletto, *Representative of Voluntary Associations*

Massimo Ciccozzi, *Biostatistician*

Pierantonio Menna, *Pharmacologist*

Domenica Ioele, *Pharmacist*

Alessandra Mecozzi, *Pharmacist*

Andrea Di Mattia, *Expert in Medical Devices*

Lorenzo Sommella, *Health Director*

Patrizio Rossi, *Expert in Legal and Insurance Matters*

Vittoradolfo Tambone, *Bioethicist*

Raffaella Gualandi, *Representative of Health Professions*

Sara Emerenziani, *Nutrition Expert*

Velio Macellari, *Clinical Engineer*

Bruno Beomonte Zobel, *Clinical Expert on New Diagnostic and Therapeutic Procedures*

Francesco Grigioni, *Clinician*

Dario Tuccinardi, *Clinician*

Giuseppe Umile Longo, *Clinician*

Pietro Ferrara, *Clinician*

The background of the slide is a light gray pattern featuring various scientific icons. These include DNA double helices, interlocking gears, and stylized plant sprouts with leaves and roots. The icons are scattered across the entire page, creating a thematic backdrop for the scientific content.

Research Units

overview and main 2019 scientific outputs

Advanced Robotics and Human Centred Technologies

Department of Engineering

**Head** L. Zollo**Faculty** F. Cordella, E. Guglielmelli, F. Taffoni, N.L. Tagliamonte**Other Personnel** F. Bentivoglio, A. L. Ciano (until May 2019), A. Demofonti, C. Gentile, E. Gruppioni, C. Lauretti, F. Leone, A. Longo, F. Mereu, L. Ricci, F. Salvadori (until May 2019), F. Scotto Di Luzio, M. Stefano, C. Tamantini

Description

CREO Lab (Advanced Robotics and Human-Centred Technologies) has the objective of pursuing advanced research in the fields of biomedical robotics, biorobotics and biomechatronics, by developing robotic and mechatronic technologies for human-robot interaction grounded on the analysis of user needs. The elective applications of CREO Lab research include (but are not limited to) collaborative robotics in domestic and hospital environment, assistive robotics, orthopedic/neurological rehabilitation and surgical robotics, neurodevelopmental and neural engineering. Biomimetic and bioinspired solutions for quality of life and sustainable development are also within the main mission of the Research Unit. Moreover, CREO Lab has a solid experience in data acquisition and interpretation of psychophysiological sensors, sensor-fusion algorithms and hardware/software integration. Main research areas are the following

- Collaborative Robotics
- Biomechanics and human ergo-

nomics

- Wearable Robotics
- Haptics and teleoperation
- Human-Machine Interfaces
- Systems for multimodal monitoring and assessment.

Main research activities

- PPRAS 1/3 – Control of hand prosthesis by invasive neural interfaces – funded by the National Institute for Insurance against Accidents at Work-2017-2020
- BRiC/RehabRobo@Work – Bio-cooperative robotic system for upper-limb rehabilitation in working contexts – funded by the National Institute for Insurance against Accidents at Work-2017-2019
- PCR 1/2 – New procedures to treat limb amputation for bionic prostheses – funded by National Institute for Insurance against Accidents at Work, 2017-2020
- SIRASI – Robotic system for upper- and lower-limb rehabilitation – funded by Regione Lazio - Bando INTESE, 2018-2019

- “Upper-limb bionic prostheses with personalized closed-loop interfaces for patients with macrolesions due to car accidents”, funded by National Association of Insurance Agencies (ANIA), 2018-2020
- PON/ARONA – Surgery Navigation assisted by Advanced Robotics – funded by Italian Ministry of Education, Universities and Research, 2018-2021
- FAM 2019 - Experimental Assessment of feeding skills in newborns: effect of different feeding bottles, research project supported by Artsana S.p.A.
- EXPERIENCE – Benchmarking Exoskeleton-Assisted Gait Based on Users' Subjective Perspective and Experience (FSTP-1 cascade funding del progetto europeo H2020-779963-EUROBENCH).
- BenchBalance – A device to apply well defined perturbations for benchmarking balance capabilities of wearable robots (FSTP-1 cascade funding del progetto europeo H2020-779963-EUROBENCH).
- SAFE-MOVER – a uSer-centred

Approach For improving both healthcare workers and patients conditions during patiEnt-handling MOVEMENTS (Bando University Strategic Projects, Topic: Healthcare 4.0), 2019-2021

- SENSE-RISC – Development of smart instrumented dresses for prevention and mitigation of risks for worker's safety (Bando BRIC 2019)

Main collaborations

- Applied Neurotechnology Laboratory, Department of Psychiatry and Psychotherapy, University Hospital of Tübingen, Tübingen, Germany

- Fetal Neonatal Neuroimaging and Developmental Science Center, Boston Children Hospital, US
- Fraunhofer IBMT, St. Ingbert, Germany
- INAIL Prosthetic Centre, Italy
- INAIL, Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, Italy
- Infant Communication Lab, University of Pittsburgh, US
- Institute of Cognitive Sciences and Technologies, National Research Council (CNR), Italy

- MASMEC SpA, Italy
- Pal Robotics, Spain
- Perelman School of Medicine, University of Pennsylvania, US
- Polytechnic University of Milan, Italy
- Sant'Anna School of Advanced Studies, Italy
- Santa Lucia Foundation, Italy
- Universidad Miguel Hernandez de Elche, Spain
- University College London, UK
- Complutense University of Madrid, Spain
- University of Twente, Netherland

Most important publications

Zollo L., Di Pino G., Ciancio A.L., Ranieri F., Cordella F., Gentile C., Noce E., Romeo R.A., Bellingegni A.D., Vadalà G., Miccinilli S., Mioli A., Diaz-Balzani L., Bravi M., Hoffmann K.P., Schneider A., Denaro L., Davalli A., Gruppioni E., Sacchetti R., Castellano S., Di Lazzaro V., Sterzi S., Denaro V., Guglielmelli E.

Restoring tactile sensations via neural interfaces for real-time force-and-slippage closed-loop control of bionic hands.

Sci Robot. 2019 May 21;4(27): eaau9924. PMID: 31620665. IF 19,4

Despite previous studies on the restoration of tactile sensation to the fingers and the hand, there are no examples of use of the routed sensory information to finely control a prosthetic hand in complex grasp and manipulation tasks. Here, it is shown that force and slippage sensations can be elicited in an amputee by means of biologically inspired slippage detection and encoding algorithms, supported by a stick-slip model of the performed grasp. A combination of cuff and intraneural electrodes was implanted for 11 weeks in a young woman with hand amputation and was shown to provide close-to-natural force and slippage sensations, paramount for substantially improving manipulative skills with the prosthesis. Evidence is provided about the improvement of the participant's grasping and manipulation capabilities over time resulting from neural feedback. The elicited tactile sensations enabled the successful fulfillment of fine grasp and manipulation tasks with increasing complexity. Grasp performance was quantitatively assessed by means of instrumented objects and a purposely developed metrics. Closed-loop control capabilities enabled by the neural feedback were compared with those achieved without feedback. Further, the work demonstrates that the described amelioration of motor performance in dexterous tasks had as central neurophysiological correlates changes in motor cortical plasticity and that such changes were not of purely motor origin, but were the effect of a strong and persistent drive of the sensory feedback.

Taffoni F., Focaroli V., Keller F., Iverson J.M.

Motor performance in a shape sorter task: a longitudinal study from 14 to 36 months of age in children with an older sibling ASD.

PLoS One. 2019 May 28;14(5): e0217416. PMID: 31136606. IF 2,776

During development, motor skills are fundamental in supporting interactions with the external world. The ability to plan actions is a particularly important aspect of motor skill since it is involved in many daily activities. In this work, we studied the development of motor planning longitudinally in children with an older sibling with Autism Spectrum Disorder (ASD) who are at heightened risk (HR) for the disorder and children with no such risk (low risk; LR) using a shape sorter task. Children were observed at 14, 18, 24 and 36 months. Three HR children with a later diagnosis of ASD (HR-ASD) were analyzed separately from the rest of the sample.

Behavioral and kinematic data indicated that precision demands significantly influenced children's actions, and that children's performance improved with age. No differences were found between the HR and LR groups, but a descriptive analysis of data from the three HR-ASD suggested differences in the variables describing children's action (as reaching time and acceleration) as well as variables describing children's performance (as the adjustment of the shapes).

Romeo R.A., Rongala U.B., Mazzoni A., Camboni D., Carrozza M.C., Guglielmelli E., Zollo L., Oddo C.M.

Identification of slippage on naturalistic surfaces via wavelet transform of tactile signals.

IEEE Sensors J. 2019; 19(4):1260-1268. DOI: 10.1109/JSEN.2018.2881831 IF 3,076

The effort toward replicating human skills into artificial systems is growing constantly. While artificial vision has reached a certain reliability, the sense of touch is still hard to introduce into robotic devices. Human manipulation comprises a sequence of static and dynamic actions, which may include unforeseen events, such as variation of object position, movement of the fingers, and modification of the object dimensions and shape (e.g., with soft objects) due to inappropriate force levels. These circumstances are likely to produce the slippage of the object being manipulated. Artificial manipulators are not yet able to be effective in dynamic environments. This paper intends to provide a method for the identification and prevention of slippage with tactile sensors. The method is based on filtering the tactile signals to extract slippage information. The filtering has been executed by means of the stationary wavelet transform that consists of recursive filtering operations. Then, the transformed signal has been rectified and its root mean square has been computed. Finally, an on/off signal has been generated according to a threshold logic. Eight natural surfaces, featuring diverse tactile properties, have been used with the aim of validating the ability of the method to be applied regardless the surface properties. To evaluate repeatability and generalization ability, a total of 2000 experiments have been performed, 250 per each stimulus, with a mechatronic platform: five velocities combined with five indentation force levels, repeating each combination 10 times. Results are provided in terms of true positive detection and of delay between onset of slippage and algorithm output.

Allergy, Immunology, Rheumatology

Department of Medicine and Surgery



Head A. Afeltra

Faculty D.P.E. Margiotta

Other Personnel L. Arcarese, I. Baglivo, A. Biaggi, D. Currado, S. Di Donato, P. Di Noi, S. Lorusso, M. Lo Vullo, A. Marino, L. Navarini, A. Rigon, M. Vadacca, A. Vernuccio

Description

The unit's research interests concern epidemiology, pathogenesis, diagnosis and therapy of the systemic autoimmune diseases. The most important research topics are Systemic Lupus Erythematosus, Rheumatoid Arthritis and Spondyloarthritis (Psoriatic Arthritis and Axial Spondyloarthritis). The unit's research methodology is based on the integration of clinical tools, diagnostic imaging (musculoskeletal ultrasonography and capillaroscopy) and laboratory methods (immunofluorescence, enzyme immunoassay, immunoblot).

Main research activities

- Quality of life in systemic lupus erythematosus (SLE), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and systemic sclerosis (SS) (collaboration: Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples): extensive evaluation of fatigue, sleep function, work disability and physical activity.
- Cardiovascular disease in psoriatic arthritis (PsA) and ankylosing spondylitis (AS) (collaboration: Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples; Rheumatology Unit, University Federico II of Naples): relationship between remission and cardiovascular disease in SLE; performance of cardiovascular risk algorithms in psoriatic arthritis and ankylosing spondylitis
- Machine Learning approach to cardiovascular risk prediction in psoriatic arthritis and ankylosing spondylitis (collaboration: Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples; Rheumatology Unit, University Federico II of Naples; PolitoBIOMed Lab, Department of Mechanical and Aerospace Engineering, Polytechnic University of Turin).
- Angiogenic and angiostatic factors in SS (collaboration: Scleroderma Unit, Sapienza University of Rome): relationship between VEGF/endostatin and parasympathetic activity, erectile dysfunction, microvascular damage and digital ulcers
- Lipid mediators in systemic au-

toimmune diseases (in collaboration with Biochemistry and Molecular Biology Unit, Campus Bio-Medico University, Rome): endocannabinoid system and resolving D1 in SLE.

Main collaborations

- PolitoBIOMed Lab, Department of Mechanical and Aerospace Engineering, Polytechnic University of Turin, Italy
- Rheumatology Unit, University Federico II of Naples, Italy
- Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples, Italy
- Scleroderma Unit, Sapienza University of Rome, Italy

Most important publications

Navarini L., Margiotta D.P.E., Costa L., Currado D., Tasso M., Angeletti S., Ciccozzi M., Scarpa R., Afeltra A., Caso F.

Performance and calibration of the algorithm ASSIGN in predicting cardiovascular disease in Italian patients with psoriatic arthritis.

Clin Rheumatol. 2019 Apr;38(4):971-976. PMID: 30680532. IF 2,293

The increased cardiovascular (CV) risk is one of the major challenges in the management of patients with psoriatic arthritis (PsA). Recently, EULAR suggested to adapt the already available CV risk algorithms with a 1.5 multiplication factor in all the patients with rheumatoid arthritis (RA), but it is still uncertain if this adaptation could also be applied to patients with PsA. This study aims to evaluate the performance and calibration of the CV risk algorithm ASSIGN and its adaptations for RA (ASSIGN-RA) and according to EULAR recommendations in a cohort of patients with PsA (ASSIGN*1.5). Prospectively, collected data from two Italian cohorts has been analyzed. The discriminatory ability for CV risk prediction was assessed using the areas under the ROC curves. Calibration between predicted and observed events was assessed by Hosmer-Lemeshow (HL) test and calibration plots. For each algorithm, sensitivity and specificity were calculated for low to high-risk cut-off (20%). One hundred fifty-five patients were enrolled with an observation of 1550 patient/years. Area under the ROC were 0.8179 (95% CI 0.72014 to 0.91558) for ASSIGN, 0.8160 (95% CI 0.71661 to 0.91529) for ASSIGN-RA, and 0.8179 (95% CI 0.72014 to 0.91558) for ASSIGN*1.5. HL tests did not demonstrate poor model fit for none of the algorithms. Discriminative ability and calibration were not improved by adaptation of the algorithms according to EULAR recommendations. Up to 20% of CV events occurred in patients at "low risk". No difference in performance has been observed between ASSIGN, Progetto CUORE, and QRISK2. ASSIGN could represent a useful tool in predicting CV risk in patients with PsA. Adaptation for RA or according to EULAR recommendations did not show any further improvement in performance and calibration.

Margiotta D.P.E., Laudisio A., Navarini L., Basta F., Mazzuca C., Angeletti S., Ciccozzi M., Incalzi R.A., Afeltra A.

Pattern of sleep dysfunction in systemic lupus erythematosus: a cluster analysis.

Clin Rheumatol. 2019 Jun;38(6):1561-1570. PMID: 30693395. IF 2,293

Objectives: To investigate how the different components of sleep dysfunction described in SLE patients combine together in sleep clusters.

Methods: We conducted a cross-sectional study on a perspective cohort of 79 SLE patients (mean age 8.2 ± 14.3 years). Sleep was evaluated using Pittsburgh Sleep Quality Index (PSQI). Clusters were defined using the single components of PSQI in a hierarchical clustering model. We used Beck Depression Inventory, Hamilton Anxiety Rating Scale, and Medical Outcomes Study Short Form 36 (SF36) to measure depressive symptoms, anxiety, and quality of life, respectively.

Results: Three sleep clusters were identified. The cluster 1 (N = 47) is characterized by the lowest values of PSQI total score. The cluster 2 (N = 21) presents higher values of sleep latency, but sleep duration similar to cluster 1. In cluster 3 (N = 11), we found sleep latency increased as in cluster 2, but the highest values of PSQI total score and reduced sleep duration. Scores of anxiety and sedentary time were higher in clusters 2 and 3 than in cluster 1. Cluster 3 presented the highest scores of depression and reduced mental and physical components of SF36.

Conclusions: The combination of different sleep components in SLE patients allowed us to identify three patterns of dysfunction: a first cluster with better sleep latency and duration, a second with increased sleep latency but conserved duration, and a third with impairment of both latency and duration. The stratification of sleep disorders in clusters might be useful for the personalization of therapy in relation to sleep cluster membership.

Laudisio A., Navarini L., Margiotta D.P.E., Fontana D.O., Chiarella I., Spitaleri D., Bandinelli S., Gemma A., Ferrucci L., Incalzi R.A.

The association of olfactory dysfunction, frailty, and mortality is mediated by inflammation: results from the InCHIANTI Study.

J Immunol Res. 2019 Feb 20; 2019:3128231. PMID: 30915369. IF 3,404

Objective: To evaluate the impact of duration of remission on the health-related quality of life (HRQoL) of patients with systemic lupus erythematosus (SLE).

Methods: We conducted a 5-year retrospective study on two Italian cohorts. Remission was defined as a continuative period of no clinical disease activity, according to the Systemic Lupus Erythematosus Disease Activity Index 2 K, and a permitted maximum prednisone dose of 5 mg/day. HRQoL was measured using the 36-Item Short-Form Health Survey (SF36) during the last visit.

Results: We enrolled 136 female SLE patients. During observation, 15 (11%) patients had been in remission for ≥ 1 and < 2 years, 15 (11%) for ≥ 2 and < 3 years, 19 (14%) for ≥ 3 and < 4 years, 9 (7%) for ≥ 4 and < 5 years, and 53 (39%) had been in prolonged remission for ≥ 5 years. In the multivariate model, considering depression and fatigue as covariates, patients in prolonged remission showed significantly better scores in the physical functioning ($p = 0.039$), role physical ($p = 0.029$), bodily pain ($p = 0.0057$), general health ($p = 0.0033$) and social functioning ($p = 0.0085$) components of the SF36, compared with those in remission < 5 years or unremitted. Subsequent mediation analyses found that these effects were partly influenced by depression.

Conclusion: Lupus remission could improve the HRQoL of SLE patients, particularly when associated with appropriate management of depression and fatigue.

Anesthesia, Intensive Care and Pain Management

Department of Medicine and Surgery



Head F.E. Agrò

Faculty M. Carassiti, R. Cataldo

Other Personnel F. Claps, F. Costa, F. Longo, M. Martuscelli, G. Pascarella, C. Piliego, E. Tomaselli

External members A. Del Buono

Description

The AIC&PM Research Unit works in different areas of research and applications concerning:

- Difficult airway management in Anesthesia and Intensive Care
- Tracheal intubation: advanced techniques
- Research on Extraglottic devices and oxygenation rescue techniques
- Forces and pressures during direct and video laryngoscopy
- Mechanical ventilation in Operating Theatre and ICU
- Pain therapy
- Loco-Regional Anesthesia and Ultra Sounds
- Advanced Loco-Regional Blocks
- Advanced Techniques for ultra-sounds vein catheterisation
- Good Clinical Pathways for Obese Patients
- Obstructive Sleep Apnea and Anesthesia

Main research activities

The AIC&PM Research Unit focuses its activities on:

- Anesthesia
 - ▶ Ultra Sounds and Loco-Regional anesthesia: advanced techniques and risks
 - ▶ Airway management in Emergency and Elective scenarios
 - ▶ Guidelines for Difficult Airway management
 - ▶ Airway management devices and innovations
 - ▶ Cardiac anesthesia and drugs
 - ▶ Obesity and perioperative safety
 - ▶ Obstructive Sleep Apnea and Anesthesia
 - ▶ Good Clinical Practice in Anesthesia
 - ▶ Pain management in perioperative medicine and serratus blocks
 - ▶ Multimodal care in pancreatic Surgery
 - ▶ "In vitro" airway management strategies simulation to improve patients safety
 - ▶ Cardiac surgery and controlled trial of volatile anesthetics

- Intensive therapy
 - ▶ Cardiac output: monitoring innovations in mechanically ventilated patients
 - ▶ Advanced pain control strategies in ICU
 - ▶ Ecocardiography in post cardio-surgical patients in ICU
- Pain Therapy
 - ▶ Pain Management and epidural space detection in vitro and in vivo FBSS (Patents development)
 - ▶ Post Herpetic pain and neurobiological modifications
 - ▶ Head of Clinical Integrated Life Project 2020 Heremos prot A0112-2016-13311 Financial Research 2018-2019.

Most important publications

Landoni G., Lomivorotov V.V., Nigro Neto C., Monaco F., Pasyuga V.V., Bradic N., Lembo R., Gazivoda G., Likhvantsev V.V., Lei C., Lozovskiy A., Di Tomasso N., Bukamal N.A.R., Silva F.S., Bautin A.E., Ma J., Crivellari M., Farag A.M.G.A., Uvaliev N.S., Carollo C., Pieri M., Kunstýř J., Wang C.Y., Belletti A., Hajjar L.A., Grigoryev E.V., Agrò F.E., Riha H., El-Tahan M.R., Scandroglio A.M., Elnakera A.M., Baiocchi M., Navalesi P., Shmyrev V.A., Severi L., Hegazy M.A., Crescenzi G., Ponomarev D.N., Brazzi L., Arnoni R., Tarasov D.G., Jovic M., Calabrò M.G., Bove T., Bellomo R., Zangrillo A.; MYRIAD Study Group.

Volatile anesthetics versus total intravenous anesthesia for cardiac surgery.

N Engl J Med. 2019 Mar 28; 380(13):1214-1225. PMID: 30888743. IF 70,67

A total of 5400 patients were randomly assigned: 2709 to the volatile anesthetics group and 2691 to the total intravenous anesthesia group. On-pump CABG was performed in 64% of patients, with a mean duration of cardiopulmonary bypass of 79 minutes. The two groups were similar with respect to demographic and clinical characteristics at baseline, the duration of cardiopulmonary bypass, and the number of grafts. At the time of the second interim analysis, the data and safety monitoring board advised that the trial should be stopped for futility. No significant difference between the groups with respect to deaths from any cause was seen at 1 year (2.8% in the volatile anesthetics group and 3.0% in the total intravenous anesthesia group; relative risk, 0.94; 95% confidence interval [CI], 0.69 to 1.29; $P = 0.71$), with data available for 5353 patients (99.1%), or at 30 days (1.4% and 1.3%, respectively; relative risk, 1.11; 95% CI, 0.70 to 1.76), with data available for 5398 patients (99.9%). There were no significant differences between the groups in any of the secondary outcomes or in the incidence of prespecified adverse events, including myocardial infarction.

Among patients undergoing elective CABG, anesthesia with a volatile agent did not result in significantly fewer deaths at 1 year than total intravenous anesthesia. (Funded by the Italian Ministry of Health; MYRIAD ClinicalTrials.gov number, NCT02105610.).

Longo F., Piliego C., Agrò F.E.

Ultrasound aided repositioning of misplaced guidewire during subclavian vein catheterisation.

J Vasc Access. 2019 Nov; 20(6):769-770. PMID: 30757941. IF 1,397

Catheter misplacement is a common complication during central vein catheterisation, and during subclavian vein catheterisation, one of the most common misplacements of the catheter is the ipsilateral internal jugular vein. Facing this type of misplacement, we tried to find an ultra-sound.

Carassiti M., De Filippis A., Palermo P., Valenti C., Costa F., Massaroni C., Schena E.

Injection pressures measuring for a safe peripheral nerve block.

Minerva Anesthesiol. 2019 Sep;85(9):1003-1013. PMID: 31124620. IF 2,84

The performance of a precise and safe peripheral nerve blockade (PNB) can currently rely on the aid of the ultrasounds and nerve stimulators. The injection pressure monitoring may be beneficial to perform a safer procedure. This review focuses on the pressures measured during PNB among studies conducted on animal, and human models. From a deep research among the PubMed/MEDLINE database for all reports published in English between January 2004 and November 2018, we selected 15 original papers. We excluded those that were reviews, case-reports, recommendations and correspondences, that did not match with object of our study. We highlighted the available systems for monitoring injection pressures and classified the reports on the basis of the model used for the respective study (animals, humans, in vitro). Intraneural injections were associated with lower pressures than perineural ones. High injection pressures registered at the needle tip were associated with an increased risk of nerve damage. To date, a precise cut-off pressure value has not yet emerged from the literature for a safe PNBs, but based on the recent literature, it can be stated that the threshold of 15 psi is an acceptable value under which a perineural injection can be performed during a PNB to achieve a safer procedure. So it is desirable to make further studies in order to assess them. In the future, the monitoring of the pressure could allow the use of a minimal quantity of anesthetic, empowering the safety of the nerve blocks. Moreover, the sensitive system should not be invasive and it should not hinder the job of the anesthetists.

Automation and Control Theory

Department of Engineering



Head R. Setola

Faculty G. Oliva, M. Papi, F. Smarrazzo

Other Personnel G. Assenza, L. Faramondi, M. Menci, S. Ott

Description

The Unit of Automation is marked by an innovative approach that combines theoretical research activities with practical technology solutions in a wide range of domains, such as automation technologies, industrial automation, control and robotics, biomedical engineering, computer science and, primarily, Critical Infrastructures. The activities of the Unit are focused on the development of innovative and strongly multidisciplinary methodologies, tools and technologies. Among others, the Unit provides both theoretical and applicative contributions in the fields of cyber-physical systems, optimization, sparse and distributed algorithms, data fusion, localization, and modelling and simulation of complex systems. In 2019, the group has been involved in 1 European research project and 6 national projects. The Unit jointly with University Campus Bio-Medico of Rome created in 2009 a Post Graduate Program (PGP) in Homeland Security, by now in its XII edition, that aims at training security experts able to cope with the actual socio-technological

threats of modern infrastructures and manage crisis situations.

Main research activities

- 4STER SAFERA: aimed to raise awareness and effectiveness of chemical industries and Seveso plants with respect to cyber-physical security threats and the work-related safety of employees
- SMARTBENCH: development of an innovative platform integrating mobile technology, web and IoT solutions, improving the awareness, and the safety of workers in dangerous zones
- RAFAEL: System for Risk Analysis and Forecast for Critical Infrastructure in the ApenninEs dorsaL Regions
- Collaboration with INAIL on the effect of cyber threats on the workers' safety and with Poste Italiane to design a holistic metric of cyber security readiness for SMEs
- Collaboration with the National Fire Department in the field of crowd management on modeling and simulation of pedestrian dynamics, with the aim

of establishing and improving safety measures for large-scale events

Main collaborations

- National Institute for Insurance against Accidents at Work (INAIL), Italy
- National Fire Department, Italy

Most important publications

Guarguaglini F. R., Papi M., Smarrazzo F.

Local and global solutions for a hyperbolic–elliptic model of chemotaxis on a network.

Math Models Meth Appl Sci. 2019; 29(08): 1465-1509. DOI: 10.1142/S021820251950026X IF 3,127

In this paper, we study a hyperbolic–elliptic system on a network which arises in biological models involving chemotaxis. We also consider suitable transmission conditions at internal points of the graph which on one hand allow discontinuous density functions at nodes, and on the other guarantee the continuity of the fluxes at each node. Finally, we prove local and global existence of non-negative solutions - the latter in the case of small (in the L1-norm) initial data - as well as their uniqueness.

Oliva G., Rikos A. I., Hadjicostis C. N., Gasparri A.

Distributed flow network balancing with minimal effort.

IEEE Trans Autom Control. 2019;64(9):3529-3543. DOI: 10.1109/TAC.2019.2891443 IF 5,093

Flow balancing is crucial in several application domains, ranging from water and traffic networks to complex network synchronization and distributed adaptive networked control. In this paper, we focus on finding the solution for the flow network balancing problem that is optimal in a minimal effort sense. More specifically, we aim at modifying a given set of (unbalanced) flows so that we obtain a balanced solution. We assume that there is a (possibly heterogenous) cost associated to the unit variation of each flow, as well as lower and upper bounds on the per edge flows.

Oliva G., Scala A., Setola R., Dell’Olmo P.

Opinion-based optimal group formation.

Omega 2019; 89: 164-176. DOI: 10.1016/j.omega.2018.10.008 IF 5,341

Most of classical decision making processes aim at selecting the “best” alternative or at ranking alternatives based on the opinions of decision makers. In this paper, we investigate the conditions under which experts can be split into different sub-groups that share coherent and consistent opinions but are mutually in conflict in the ordering of the alternatives. We face this problem by presenting a non-linear integer programming model where each decision maker specifies incomplete preferences on pairs of alternatives and the objective is to obtain groups having the least possible degree of inconsistency. From a theoretical standpoint, we show that the proposed problem is non-convex and NP-Hard.

Biochemistry and Molecular Biology

Department of Medicine and Surgery



Head M. Maccarrone

Faculty V. Chiurchiù [until November 2019], A. Leuti

Other Personnel A. Calcaterra, E. Criscuolo, M. Fava, A.M. Sardanelli, D. Tortolani

External Members J. Dalli, J. Fernandez-Ruiz, J. A. French, D. Friedman, P. Pacher, M. van der Stelt

Description

The Research Unit has a long and widely recognized experience in biochemistry, epigenetics, immunology, medicinal chemistry, molecular biology, and pharmacology of lipid signalling, that is interrogated under health and disease conditions (most notably, neurodegenerative disorders [Alzheimer's disease (AD) and Multiple Sclerosis (MS)], and defective immune and reproductive events). In this context, up-to-date techniques are used to determine the drivers of signal transduction mediated by bioactive lipids like endocannabinoids (i.e., N-arachidonylethanolamine and 2-arachidonoylglycerol) and specialized pro-resolving mediators (i.e., resolvins and marins), through their specific receptor targets in several primary human and animal cells (immune and brain cells), as well as in in vivo animal models. In addition, metabolism of these ω -3 and ω -6 polyunsaturated fatty acid derivatives through multiple biosynthetic and degradative routes is studied by means of radiometric assays, in order to disclose the impact of metabolic regulation on the biolog-

ical activity of these compounds. The design of innovative drugs that selectively target metabolic enzymes and receptors of bioactive lipids, and the effect of food components on their tone and signalling pathways, are an additional focus of the Research Unit.

Main research activities

In the frame of the VITA mission of the Italian Space Agency (ASI), we addressed the problem of Space osteoporosis by using human blood-derived stem cells (BDSCs) as a suitable osteogenic differentiation model. We showed that osteogenic differentiation of BDSCs induced by rapamycin follows a coordinated pattern in protein expression and epigenetic arrangement, affected by microgravity. Moreover, in collaboration with Prof. Daniel Friedman and Prof. Jacqueline A. French (University of New York, US) we have critically assessed the potential benefits and threats to human health associated with cannabis (*Cannabis sativa* and *C. indica*) use, and with Prof. Mario van der Stelt (Leiden University, The Netherlands) we have characterized for

the first time selective inhibitors of the endocannabinoid-degrading enzyme ABHD2. Finally, we have demonstrated that the antiinflammatory agent bindarit acts as an unprecedented modulator of fatty acid-binding protein 4 in human monocytic cells.

Main collaborations

- Complutense University of Madrid, Spain
- Leiden University, The Netherlands
- National Institutes of Health, US
- New York University, US
- Queen Mary University of London, UK

Most important publications

Gambacurta A., Merlini G., Ruggiero C., Diedenhofen G., Battista N., Bari M., Balsamo M., Piccirillo S., Valentini G., Mascetti G., Maccarrone M.

Human osteogenic differentiation in space: proteomic and epigenetic clues to better understand osteoporosis.

Sci Rep. 2019 Jun 6; 9(1):8343. PMID: 31171801. IF 4,011

In the frame of the VITA mission of the Italian Space Agency (ASI), we addressed the problem of Space osteoporosis by using human blood-derived stem cells (BDSCs) as a suitable osteogenic differentiation model. In particular, we investigated proteomic and epigenetic changes in BDSCs during osteoblastic differentiation induced by rapamycin under microgravity conditions. A decrease in the expression of 4 embryonic markers (Sox2, Oct3/4, Nanog and E-cadherin) was found to occur to a larger extent on board the ISS than on Earth, along with an earlier activation of the differentiation process towards the osteogenic lineage. The changes in the expression of 4 transcription factors (Otx2, Snail, GATA4 and Sox17) engaged in osteogenesis supported these findings. We then ascertained whether osteogenic differentiation of BDSCs could depend on epigenetic regulation, and interrogated changes of histone H3 that is crucial in this type of gene control. Indeed, we found that H3K4me3, H3K27me2/3, H3K79me2/3 and H3K9me2/3 residues are engaged in cellular reprogramming that drives gene expression. Overall, we suggest that rapamycin induces transcriptional activation of BDSCs towards osteogenic differentiation, through increased GATA4 and Sox17 that modulate downstream transcription factors (like Runx2), critical for bone formation. Additional studies are warranted to ascertain the possible exploitation of these data to identify new biomarkers and therapeutic targets to treat osteoporosis, not only in Space but also on Earth.

Friedman D., French J.A., Maccarrone M.

Safety, efficacy, and mechanisms of action of cannabinoids in neurological disorders.

Lancet Neurol. 2019 May;18(5):504-512. PMID: 30910443. IF 28,755

In the past two decades, there has been an increasing interest in the therapeutic potential of cannabinoids for neurological disorders such as epilepsy, multiple sclerosis, pain, and neurodegenerative diseases. Cannabis-based treatments for pain and spasticity in patients with multiple sclerosis have been approved in some countries. Randomised controlled trials of plant-derived cannabidiol for treatment of Lennox-Gastaut syndrome and Dravet syndrome, two severe childhood-onset epilepsies, provide evidence of anti-seizure effects. However, small clinical trials of cannabinoids in other neurological disorders such as Huntington's disease, attention deficit hyperactivity disorder, and dementia, have not found any effect. Despite positive results in these two severe epilepsy syndromes, further studies are needed to determine if the anti-seizure effects of cannabidiol extend to other forms of epilepsy, to overcome pharmacokinetic challenges with oral cannabinoids, and to uncover the exact mechanisms by which cannabidiol or other exogenous and endogenous cannabinoids exert their therapeutic effects.

Baggelaar M.P., den Dulk H., Florea B.I., Fazio D., Bernabò N., Raspa M., Janssen A.P.A., Scavizzi F., Barboni B., Overkleeft H.S., Maccarrone M., van der Stelt M.

ABHD2 inhibitor identified by activity-based protein profiling reduces acrosome reaction.

ACS Chem Biol. 2019 Oct 18; 14(10):2295-2304. PMID: 31525885. IF 4,374

ABHD2 is a serine hydrolase that belongs to the subgroup of the α , β -hydrolase fold-containing proteins, which is involved in virus propagation, immune response, and fertilization. Chemical tools to selectively modulate the activity of ABHD2 in an acute setting are highly desired to investigate its biological role, but are currently lacking. Here, we report a library-versus-library screening using activity-based protein profiling (ABPP) to evaluate in parallel the selectivity and activity of a focused lipase inhibitor library against ABHD2 and a panel of closely related ABHD proteins. This screen resulted in the rapid identification of novel inhibitors for ABHD2. The selectivity of the inhibitor was further investigated in native mouse testis proteome by competitive ABPP, revealing a highly restricted off-target profile. The progesterone-induced acrosome reaction was reduced in a dosedependent manner by the newly identified inhibitor, which provides further support for the key-role of ABHD2 in the P4-stimulated acrosome reaction. On this basis, the ABHD2 inhibitor is an excellent starting point for further optimization of ABHD2 inhibitors that can modulate sperm fertility and may lead to novel contraceptives.

Bioethics and Humanities

Department of Medicine and Surgery



Head V. Tambone

Faculty R. Alloni, G. Ghilardi, G. La Monaca

Other Personnel M. Barone, L. Campanozzi, R. Esposito E. Midolo, G. Mottini, P. Pellegrino, A. Sisto

Secretary A. Lorusso

Main research activities

- “The Robot I wish”: survey on the desired robot as a clinical assistant. Building trust in social robotics: legal, medical and bioethical aspects in social robotics;
- Italian Humanities for medicine;
- Well done work ethics and end of life issues:
 - a) “Natural death protocol”;
 - b) “Protocol for continuous or intermittent terminal sedation for refractory respiratory distress”;
- Psychological resilience in healthcare personnel;
- Proposal for a new nosographic entity connected to the suffering caused by one's appearance: creation of an “App Pain”;
- Physiognomy applied to medicine;
- Logical-metaphysical foundations of clinical reasoning;
- Virtue of knowledge applied to scientific research.
- PRIN Project “Anthropology and the challenge of solidarity”

- PRIN Project “Exploring digital therapeutics”.

Laura Campanozzi: Trust in robotics compared with inter-human trust”, with Fondazione Mondo Digitale.

Giampaolo Ghilardi: Anthropology of scientific and technological practice: exploration of topics such as the educated scientist's epistemic virtue.

Giuseppe La Monaca: Analysis of the civil court of Rome judgments' upon medical malpractice.

Most important publications

Campanozzi L.L., Guglielmelli E., Cella E., Ghilardi G., Michilli M., Molina A., Ciccozzi M., Tambone V.

Building trust in social robotics: a pilot survey.

IEEE Technol Soc Mag. 2019;38(4): 45-54. DOI: 10.1109/MTS.2019.2948440 IF 1,002

This paper addresses people's attitudes towards the trust in robots in relation to the confidence among humans. It is based on the pilot survey "The robot I desire" involving 1640 Italian students and on an "ad hoc" online questionnaire, in order to explore the level of general trust of respondents and their preferences regarding some scenarios of advanced robotics. The results revealed the people's tendency to trust machines more than humans, preferring robots without an anthropomorphic appearance. Reliability emerged as one of the most important factors affecting robot trustworthiness. These findings support bottom-up recommendations to orient projects more focused on technical rather than relational machines.

Di Stefano N., Ghilardi G., Morini S.

The cerebral ventricles in Leonardo's anatomical drawings.

Lancet. 2019 Apr 6; 393(10179):1412. PMID: 30967209. IF 59,102

Fascinated with questions about the origin of life, Leonardo da Vinci (1452–1519) was captivated by the brain. The brain was perceived at that time to be the house of the principle of life (i.e., the soul was thought to reside at the geometrical centre of the brain). Evidence of the evolution of Leonardo's knowledge about the organization of the brain can be seen in the comparison of two drawings.

Marchetti D., Sgarbi I., Feola A., Marsella L.T., Caricato M., La Monaca G.

Il risarcimento della violazione del consenso informato nella giurisprudenza del Tribunale Civile di Roma (anni 2012-2016).

Rivista Italiana di Medicina Legale e del Diritto in Campo Sanitario. 2019; 2: 601-619.

Breast Care

Department of Medicine and Surgery



Head V. Altomare

Other Personnel A. Grasso, P. Orsaria

Description

Over the past years, the research activity related to breast cancer has significantly expanded. The research unit is actively enrolled in the field of tailored therapies, in order to individualize the treatment with an integrated approach, in the era of precision medicine. The mission of the Breast Care Unit is to provide the highest quality clinical service, research and education to guarantee the reduction of breast cancer mortality together with the quality of life improvement, in the context of a multidisciplinary setting with complex intellectual architecture. Specifically, Breast Cancer Surgeons are committed to:

- Providing the highest quality in all aspects of diagnosis, resection, reconstruction and clinical management.
- Achieving competence in a broad range of comprehensive oncological, radioguided and reconstructive procedures with structured educational supervision, assessment and feedback.
- Continuously increasing the

use of oncoplastic conserving procedures to offer solutions for challenging scenarios, while preserving the natural shape and appearance of the breast.

Main research activities

- New techniques of loco-regional anaesthesia performed by breast surgeon to improve surgical outcomes (pain control, opioid-free analgesia, prevention of chronic pain).
- Multicentric study "Prevention of the third millennium: liquid biopsy", to detect fragments of circulating DNA in peripheral blood. This approach considers breast cancer as a "moving target", a heterogeneous disease continuously evolving and changing.
- Management of B3 lesions (lesions of unknown biological potential) to investigate the role of possible new biomarkers for high risk patients
- International collaboration with Ministry of Health of Palestine to study the epidemiology of breast cancer in West Bank Area and the role of mini-invasive dia-

gnostic techniques to improve surgical outcome and quality of life.

- Oncoplastic breast surgery as an innovative approach that aims at the safe and effective treatment of the cancerous lesion while achieving the best possible aesthetic outcome, consisting of large lumpectomy and remodelling techniques such as breast-reshaping by therapeutic reduction mastopexy or volume replacement by local glandular flaps or regional/distant flaps.

Main collaborations

- Breast Surgical Oncology, Clinica Universidad de Navarra, Spain
- University at Groningen Medical Center, The Netherlands

Most important publications

Pallara T., Cagli B., Fortunato L., Altomare V., Loreti A., Grasso A., Manna E., Persichetti P.

Direct-to-implant and 2-stage breast reconstruction after nipple sparing mastectomy: results of a retrospective comparison.

Ann Plast Surg. 2019 Oct; 83(4):392-395. PMID: 31524730. IF 1,448

Breast reconstruction after nipple sparing mastectomy (NSM) plays, nowadays, a fundamental role in breast cancer management. There is no consensus on the best implant-based reconstruction technique, considering 2 stages (expander-prosthesis) or direct-to-implant (DTI). A retrospective review of consecutive adult female patients who underwent NSM with breast reconstruction over a 3-year period (January 2013 to December 2015) was performed. Patients were divided into 2 groups according to the type of reconstruction: expander/prosthesis (group A) and DTI (group B). Anamnestic data were collected. Number and type of procedures, complications and esthetic satisfaction were registered and compared. Fiftysix patients were included in group A (34.6%) and 106 in group B (65.4%). Complications associated with the 2 types of breast reconstruction were not different ($P = 0.2$). Patients in group A received a higher number of total surgical procedures (considering revisions, lipostructures and contralateral symmetrizations) than those in group B (2.5 ± 0.69 and 1.88 ± 1.02 , $P = 0.0001$). Satisfaction with breast reconstruction resulted higher in group A (7.5 ± 2.6 and 6 ± 1.9 , $P = 0.0004$). At the multivariate analysis, chemotherapy and radiotherapy were not correlated with complications, regardless of the group (odds ratio, 0.91 and 2.74, respectively). Radiotherapy and chemotherapy did not even influence the esthetic result, regardless of the group ($P = 0.816$ and $P = 0.521$, respectively). Prosthetic breast reconstructions, both in a single and in 2 stages, are welcomed by patients and have relatively low and almost equivalent complication rates, independent of other factors such as chemotherapy, radiotherapy, lymphadenectomy, smoking and age. In our experience, 2-stage breast reconstruction, although requiring more operations, is associated with a higher esthetic satisfaction. Patients who perform a DTI breast reconstruction after NSM should be informed of the high probability of surgical revision.

Cardiovascular Science

Department of Medicine and Surgery



Head F. Grigioni

Faculty F. Mangiacapra, R. Melfi, A. Nusca, G.P. Ussia

Other Personnel M.C. Bono, V. Calabrese, P. Gallo, C. Goffredo, S. Mega, M. Miglionico, D. Ricciardi, E. Ricottini, G. Salvati

Description

The Cardiovascular Science Research Unit comprises clinical cardiologists, interventional cardiologists, expert cardiologists in echocardiography and electrophysiology. Our Unit is involved in several national and international multicentre clinical trials, mainly focusing on new devices for percutaneous coronary and structural intervention and new drugs for management of patients with cardiovascular diseases. Moreover, we performed and are performing several prospective experimental studies on a wide range of clinical settings such as interventional pharmacology, glycaemic variability assessment, biological markers and cardiac electrophysiology.

Main research activities

The randomized RIVENDEL study, investigating the effects of Iva-bradine on vascular endothelial function, has been finalized and published; Substudies of the multicentre MATRIX study, comparing radial versus femoral approach in patients with acute coronary syndromes treated with PCI, have been published.

Ongoing research projects:

- Predictive role of a combined evaluation of carotid atherosclerosis and peripheral endothelial function on the presence and extent of coronary artery disease;
- Comparison of prasugrel and ticagrelor in protecting coronary microcirculation in patients with stable coronary artery disease undergoing PCI (PRO-MICRO 3 study);
- Impact of glycaemic variability assessed by a glucose continuous monitoring on platelet reactivity;
- Effects of ranolazine on glycaemic control in diabetic patients;
- Impact of micro-RNA evaluation

on cardiac resynchronization therapy outcome.

Enriquez-Sarano M., Michelena H.I., Grigioni F.

Treatment of functional mitral regurgitation.

Circulation. 2019 May 14;139(20):2289-2291. PMID: 31082291. IF 23,054

Functional mitral regurgitation (FMR) is a conundrum in terms of mechanism, assessment, and implications for outcome. FMR occurs on a structurally normal mitral valve as a result of annular enlargement/dysfunction and leaflet tenting/tethering caused mostly by left ventricular (LV) dysfunction (LVD).¹ FMR is generally low volume, often silent, and detected only by color Doppler imaging. FMR grading is difficult because Doppler echocardiographic signs of severe mitral regurgitation (MR) are rarely present and quantification is hindered by discordant guidelines. Most observational series showed independent association between effective regurgitant orifice (ERO) ≥ 20 mm² and excess mortality. However, whether FMR itself causes poor outcome or is a surrogate for advanced LVD remains uncertain. Confusion and doubts were amplified by discordant results of surgical and, more recently, percutaneous clinical trials of FMR treatment. <...>

Grigioni F., Benfari G., Vanoverschelde J.L., Tribouilloy C., Avierinos J.F., Bursi F., Suri R.M., Guerra F., Pasquet A., Rusinaru D., Marcelli E., Théron A., Barbieri A., Michelena H., Lazam S., Szymanski C., Nkomo V.T., Capucci A., Thapa P., Enriquez-Sarano M.; MIDA Investigators.

Long-term implications of atrial fibrillation in patients with degenerative mitral regurgitation.

J Am Coll Cardiol. 2019 Jan 29;73(3):264-274. PMID: 30678755. IF 18,639

Background: Scientific guidelines consider atrial fibrillation (AF) complicating degenerative mitral regurgitation (DMR) a debated indication for surgery. **Objectives:** This study analyzed the prognostic/therapeutic implications of AF at DMR diagnosis and long-term. **Methods:** Patients were enrolled in the MIDA (Mitral Regurgitation International Database) registry, which reported the consecutive, multicenter, international experience with DMR due to flail leaflets echocardiographically diagnosed. **Results:** Among 2,425 patients (age 67 ± 13 years; 71% male, 67% asymptomatic, ejection fraction $64 \pm 10\%$), 1,646 presented at diagnosis with sinus rhythm (SR), 317 with paroxysmal AD, and 462 with persistent AF. Underlying clinical/instrumental characteristics progressively worsened from SR to paroxysmal to persistent AF. During follow-up, paroxysmal and persistent AF were associated with excess mortality (10-year survival in SR and in paroxysmal and persistent AF was $74 \pm 1\%$, $59 \pm 3\%$, and $46 \pm 2\%$, respectively; $p < 0.0001$), that persisted 20 years post-diagnosis and independently of all baseline characteristics (p values < 0.0001). Surgery ($n = 1,889$, repair 88%) was associated with better survival versus medical management, regardless of all baseline characteristics and rhythm (adjusted hazard ratio: 0.26; 95% confidence interval: 0.23 to 0.30; $p < 0.0001$) but post-surgical outcome remained affected by AF (10-year post-surgical survival in SR and in paroxysmal and persistent AF was $82 \pm 1\%$, $70 \pm 4\%$, and $57 \pm 3\%$, respectively; $p < 0.0001$). **Conclusions:** AF is a frequent occurrence at DMR diagnosis. Although AF is associated with older age and more severe presentation of DMR, it is independently associated with excess mortality long-term after diagnosis. Surgery is followed by improved survival in each cardiac rhythm subset, but persistence of excess risk is observed for each type of AF. Our study indicates that detection of AF, even paroxysmal, should trigger prompt consideration for surgery.

Patti G., Rapacciuolo A., Segreti A., Ussia G.P., Goffredo C., Di Sciascio G.

Percutaneous left atrial appendage closure: acute effects on left atrial pressure in humans.

JACC Cardiovasc Interv. 2019 Jun 10;12(11):1089-1091. PMID: 31171286. IF 9,544

Percutaneous left atrial appendage (LAA) closure is effective for stroke prevention in patients with atrial fibrillation and contraindication to anticoagulant therapy (1), providing a permanent protection from thromboembolism without lifelong anticoagulation. To date, no experimental, in vivo data are available on acute consequences of percutaneous LAA closure on left atrial (LA) pressure. We explored such issue in 22 consecutive patients undergoing percutaneous implantation of the Amulet device (Abbott, Abbott Park, Illinois); this is constituted by an internal lobe occluding LAA at the level of the neck and a larger disk sealing the ostium. No patient had moderate-to-severe valvular heart disease or left ventricular ejection fraction $< 40\%$. The protocol was approved by the Ethic Committee of Campus Bio-Medico University. <...>

Chemical-Physics Fundamentals in Chemical Engineering

Department of Engineering



Head V. Piemonte

Faculty L. Di Paola

Other Personnel L. Marrelli, M. Cocchi, L. Mazzeo

Description

The Research Unit follows a methodology at the very basis of Process Engineering operative methods. To develop a new technology in the field, two steps are required:

- ▶ first, the theoretical elements characterizing the technology must be assessed, supported by purposed experimental campaigns;
- ▶ second, mathematical modeling, process simulation and economical assessment provide the essential framework to fully develop the technology.

Main research activities

- Biorefinery Processes: VFAs, Biogas and Compost production by anaerobic co-digestion of sludge and food waste (in collaboration with IRSA, Italy).
- In situ biological methanation: anaerobic digestion of food waste for the conversion of hydrogen in methane to storage electrical surplus, experimental and modelling (in collaboration with Sapienza University and ENEA Casaccia).
- Catalytic conversion: zeolite

catalyst from industrial waste for plastic pyrolysis process. Experimental lab-scale setup for catalyst testing and conversion yield measurement (in collaboration with ENEA Casaccia).

- Gastrointestinal system modelling for in silico trials of drug bioavailability (in collaboration with Unit of Gastroenterology and Unit of Elaboration Systems and Bioinformatics, Campus Bio-Medico University of Rome).
- Predictive models development for artificial pancreas (in collaboration with the Unit of Endocrinology and Diabetes and Unit of Elaboration Systems and Bioinformatics, Campus Bio-Medico University of Rome, Italy).
- Bioartificial liver optimization (in collaboration with Piaggio Research Centre, University of Pisa, Italy).
- Bioactive molecule extraction from solid matrix in the framework of the development of technological platforms for the valorization of agro-food chain waste.
- Computational biochemistry proteins as networks (in collaboration with National Institute of Health, Italy, National Research Council (CNR), Italy, University of Rome "Tor Vergata", Univer-

sity of Catania, Italy).

- Computational approach for developmental biology (in collaboration with Sapienza University of Rome, Italy, and John Innes Centre, UK);

Main collaborations

- Bio-P, gruppo Maire Technimont, Italy
- DLR – German Aerospace center, Koel, German
- DMT- Environmental technology, Joure, Netherland
- IRSA, Italy
- Italian National Agency for New Technologies, Energy and Sustainable Development - ENEA, Casaccia Research Centre, Rome, Italy
- John Innes Centre, UK
- National Institute of Health, Italy
- National Research Council (CNR), Italy
- Novamont, Italy
- Piaggio Research Centre, University of Pisa, Italy
- Polytechnic University of Milan, Italy
- Sapienza University of Rome, Italy
- University of Catania, Italy
- University of Rome Tor Vergata, Italy

Most important publications

Mazzelli A., Luzzi D. M., Buonanno G., Cicci A., Piemonte V., Iaquaniello G.

An optimized separation process of microalgal lipidic products by molecular distillation: techno-economic analysis.

Chem Eng Sci. 2019; 207:1187-1195. DOI: 10.1016/j.ces.2019.07.043 IF 3,372

Microalgae are a sustainable rich source of high-added value metabolites, as omega-3 and carotenoids, for their ability to grow and accumulate these compounds also in wastewaters or in seawaters. Molecular distillation is a valid technique respect to conventional distillation for fractionation of these thermosensitive products without affecting their nutritional and biological values. In this work a fractionation process using molecular distillation for separating fatty acids (in part omega-3) as esters and carotenoids from a microalgal lipidic extract, was designed and optimized. A Response Surface Method (RSM) analysis was carried out in order to find the optimal operative conditions of the molecular distiller in terms of temperature, pressure and purification ability. Furthermore, to complete the process scheme, also the design of the other equipments, including in particular the esterification reactor and the dewatering column, was done. In order to complete the feasibility study of the process, an estimation of the Operating Expense (OPEX) and Capital Expenditure (CAPEX), using the results of the simulations in terms of energy and utilities' consumption, was done. All of these informations, both technical and economical, will be the basis for future industrial implementations of the designed process.

Magliaro C., Mattei G., Iacoangeli F., Corti A., Piemonte V., Ahluwalia A.

Oxygen consumption characteristics in 3D constructs depend on cell density.

Front Bioeng Biotechnol. 2019 Oct 10; 7:251. PMID: 31649925. IF 5,122

Oxygen is not only crucial for cell survival but also a determinant for cell fate and function. However, the supply of oxygen and other nutrients as well as the removal of toxic waste products often limit cell viability in 3-dimensional (3D) engineered tissues. The aim of this study was to determine the oxygen consumption characteristics of 3D constructs as a function of their cell density. The oxygen concentration was measured at the base of hepatocyte laden constructs and a tightly controlled experimental and analytical framework was used to reduce the system geometry to a single coordinate and enable the precise identification of initial and boundary conditions. Then dynamic process modeling was used to fit the measured oxygen vs. time profiles to a reaction and diffusion model. We show that oxygen consumption rates are well-described by Michaelis-Menten kinetics. However, the reaction parameters are not literature constants but depend on the cell density. Moreover, the average cellular oxygen consumption rate (or OCR) also varies with density. We discuss why the OCR of cells is often misinterpreted and erroneously reported, particularly in the case of 3D tissues and scaffolds.

Montecchio D., Astals S., Di Castro V., Gallipoli A., Gianico A., Pagliaccia P., Piemonte V., Rossetti S., Tonanzi B., Braguglia C.M.

Anaerobic co-digestion of food waste and waste activated sludge: ADM1 modelling and microbial analysis to gain insights into the two substrates' synergistic effects.

Waste Manag. 2019 Sep; 97:27-37. PMID: 31447024. IF 5,431

The reasons for the acidification problem affecting Food Waste (FW) anaerobic digestion were explored, combining the outcomes of microbiological data (FISH and CARD-FISH) and process modelling, based on the Anaerobic Digestion Model n°1 (ADM1). Long term semi continuous experiments were carried out, both with sole FW and with Waste Activated Sludge (WAS) as a co-substrate, at varying operational conditions (0.8-2.2 g VS L⁻¹ d⁻¹) and FW / WAS ratios. Acidification was observed along FW mono-digestion, making it necessary to buffer the digesters; ADM1 modelling and experimental results suggested that this phenomenon was due to the methanogenic activity decline, most likely related to a deficiency in trace elements. WAS addition, even at proportions as low as 10% of the organic load, settled the acidification issue; this ability was related to the promotion of the methanogenic activity and the consequent enhancement of acetate consumption, rather than to WAS buffering capacity. The ability of the ADM1 to model processes affected by low microbial activity, such as FW mono-digestion, was also assessed. It was observed that the ADM1 was only adequate for digestions with a high activity level for both bacteria and methanogens (FISH/CARD-FISH ratio preferably >0.8) and, under these conditions, the model was able to correctly predict the relative abundance of both microbial populations, extrapolated from FISH analysis.

Clinical Laboratory Sciences

Department of Medicine and Surgery



Head S. Angeletti

Faculty G. Gherardi

Other Personnel M. De Cesaris, L. De Florio, E. Ferraro, M. Fogolari, A. Lai

Description

The research unit is actively interested in research studies aimed to investigate biomolecular markers involved in the diagnosis and prognosis of important disease such as chronic disease or sepsis. Further fields of research included the molecular evolution of microorganisms causing important epidemic in Italy as well as worldwide and the antimicrobial resistant microorganisms circulating in different settings, especially in nosocomial. Furthermore, the activity of the research unit was extended also to the evaluation of interesting clinical case diagnosed at the Internal medicine Department of the University Campus Bio-Medico in terms of prompt diagnosis and treatment.

Main research activities

In the year 2019, the most important activities developed by the research unit have been in the areas of infectious disease, antibiotic resistance and their pathogenesis. Different collaboration were established with several department of internal medicine, surgery and geriatrics of the university hospital campus bio-medico. Furthermore, the research unit by a scientific agreement with the extraordinary reception center for migrants and refugees "Mondo Migliore" at Rocca di Papa in Rome continued the collaboration began in the year 2017. By this agreement, a protocol for migrant's surveillance was developed and results of the surveillance reported in some publication on international peer-reviewed scientific journals. Other important agreement have been continued since 2016 with the Public Health Institute in Podgorica (Montenegro), the Public Health Institute of Sofia (Bulgaria) and with the department of pathology and laboratory medicine of the University of Florida, Gainesville, USA. By these agreements, several scientific publications on international

and peer-reviewed journals have been published and new scientific collaborations are ongoing. The research unit actively collaborate with other research units of the University Campus Bio-Medico.

Main collaborations

- Public Health Institute, Bulgaria
- Public Health Institute, Montenegro
- University of Florida, Gainesville, US

Most important publications

Vita S., Sinopoli M.T., Fontanelli Sulekova L., Morucci L., Lopalco M., Spaziante M., Pacifici L.E., Bazzardi R., Angeletti S., Ciccozzi M., Ceccarelli G.

Vaccination campaign strategies in recently arrived migrants: experience of an Italian reception centre.

J Infect Dev Ctries. 2019 Dec 31;13(12):1159-1164. PMID: 32088704. IF 1,175

Introduction: Control of vaccine preventable diseases, while constituting a priority of European health policies, is challenged by migrations from countries with suboptimal levels of immunization coverage. We report here two different types of vaccination campaign strategy in one of the bigger Italian asylum seekers' centres. The vaccination service staff of the local national health institute came monthly during the first three years of observation, while in the last year, the vaccinations were offered directly upon arrival of migrants in the asylum seekers' centre. **Methodology:** we performed a descriptive cross-sectional study that analysed data collected from the database of the internal healthcare facility and ARVA Target tool, regarding vaccinations performed from 2013 to 2017 in the asylum seekers' centre. **Results:** In the four years of observation period the asylum seekers centre hosted 3941 migrants. Among them, 85% were vaccinated during their stay, for a total of 4252 vaccinations administered, covering 95% of minors and 85% of adults. During the study period, there was an important increase from an average of 10.5% of migrants vaccinated in the first three years to 66% in the last year, when vaccines were delivered directly upon arrival in the centre. **Conclusions:** To improve the rate of immunization in migrants, the first requirement is a strong collaboration with the local vaccine services and the second, vaccinations must be carried out when migrants arrive at the asylum seekers' centre, avoiding any delay

Angeletti S, Ciccozzi M.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry in clinical microbiology: an updating review.

Infect Genet Evol. 2019 Dec; 76:104063. PMID: 31618693. IF 2,927

In the last years, Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry gained the attribute of gold-standard method for microbial identification. A rich scientific literature has been produced to evaluate its performance in gram-positive, gram-negative, anaerobic bacteria, and also difficult and exigent pathogens identification, included mycobacteria, yeasts, and molds. Typing in PubMed "MALDI-TOF mass spectrometry" at the date of August 1st 2019, about 14.468 articles can be found. Typing "MALDI-TOF identification" or "MALDI-TOF and microbiology" or "MALDI-TOF and infection" the number of articles is reduced to 5747, 3720 and 1746, respectively. In this review, an update of the most important findings reported during last ten years has been provided, confirming the central role of this technology in microbiology.

Cesareo R., Palermo A., Benvenuto D., Cella E., Pasqualini V., Bernardi S., Stacul F., Angeletti S., Mauri G., Cicciozzi M., Trimboli P.

Efficacy of radiofrequency ablation in autonomous functioning thyroid nodules. A systematic review and meta-analysis.

Rev Endocr Metab Disord. 2019 Mar;20(1):37-44. PMID: 30887407. IF 5,516

Whether thermal ablation is effective to treat toxic thyroid nodules (TTN) is still unknown. Aim of this review was to achieve more robust evidence on the efficacy of radiofrequency ablation (RFA) in treating TTN in terms of TSH normalization, thyroid scintiscan, and volume reduction rate (VRR). A comprehensive literature search of PubMed/Medline and Scopus was performed in November 2018 to retrieve published studies. Original papers reporting TTN treated by RFA and later followed-up were eligible. Excluded were: articles not within this field, articles with unclear data, overlapping series, case/series reports. Discordances were solved in a final collegial meeting. Information was collected concerning population features, treatment procedure, follow-up, cases with TSH normalization, cases with scintiscan normalization, VRR of nodules. Pooled prevalence of patients with TSH or scintiscan normalization, and pooled VRR over time were calculated. For statistical analysis, the random-effects model was used. Eight articles published between 2008 and 2018 were included. The overall number of AFTN treated by RFA was 205. Five studies used a single session of treatment. The time of follow-up ranged from six to 24 months. The pooled rate of patients with TSH normalization was 57%. The pooled rate of patients with scintigraphically proven optimal response was 60%. The pooled VRR at 1 year was 79%. Baseline nodules volume was associated with the rate of TSH normalization. In conclusion, a moderate efficacy of RFA in treating TTN was found, and this can represent a solid starting point in this field.

Computer Systems and Bioinformatics

Department of Engineering



Head G. Iannello

Faculty F. Cacace, P. Soda, L. Vollero

Other Personnel P. Afferni, L. Ardito, E. Cordelli, M. Merone, R. Sicilia, R. Valenti

Description

The research activities of the Computer Science and Bioinformatics (CoSBI) Research Unit are focused on the analysis of data, signals, and images with a special attention to biomedical applications. The Unit has also experience on high performance computing, machine learning and data analytics, computer networks with special focus on wireless networks, modeling dynamic stochastic system, and innovation management.

Main research activities

- CAD systems for automatic analysis of Indirect Immunofluorescence images.
- Decision Support Systems for clinical applications, even for fragile patients.
- Radiomics and pathomics, that is decoding tumour phenotypes by non-invasive quantitative imaging.
- Social media analysis
- Algorithms for the analysis of EEG and EEG-TMS signals, and of fMRI images.
- Computer Networks and Wireless Systems.
- Control and estimation theory for stochastic, distributed and time-delayed systems, and control and systems technology for health-care applications: artificial pancreas, control of tumor growth.
- Patent analysis and evaluation of innovation value, digital innovation.

Main collaborations

- Catholic University of the Sacred Heart, Italy
- Centro Diagnostico Italiano SpA, Italy
- Bracco Imaging, for Radiomics Research, Italy
- Departments of Information and Electrical Engineering, L'Aquila, Italy
- Informatics and Automation, Sapienza University, Rome, Italy
- IASI-CNR, Italy
- Eindhoven University of Technology, The Netherlands
- BPCOMedia srl, Italy
- Centre for Enterprise, Innovation and Growth, Birmingham City University, UK

Most important publications

Merone M., Sansone C., Soda P.

A computer-aided diagnosis system for HEp-2 fluorescence intensity classification.

Artif Intell Med. 2019 Jun; 97:71-78. PMID: 30503016. IF 3,574

The indirect immunofluorescence (IIF) on HEp-2 cells is the recommended technique for the detection of antinuclear antibodies. However, it is burdened by some limitations, as it is time consuming and subjective, and it requires trained personnel. To alleviate IIF limitations, this paper presents a computer-aided diagnosis (CAD) system classifying HEp-2 fluorescence intensity: it represents each image using an Invariant Scattering Convolutional Network (Scatnet). The proposed CAD is tested on a new dataset of 1771 images annotated by three independent medical centers. The performances achieved by our CAD in recognizing positive, weak positive and negative samples are also compared against those obtained by other two approaches presented so far in the literature. The results confirm the effectiveness of our proposal, also revealing that it achieves the same performance as medical experts.

Cacace F.

Comments on “Distributed information-weighted Kalman consensus filter for sensor net-works”.

Automatica. 2019;109:108552. DOI: 10.1016/j.automatica.2019.108552 IF 6,355

A recent paper proposes a novel distributed information-weighted Kalman consensus filter called IKCF for linear systems in a continuous-time setting. In this note we highlight the reasons for which IKCF is in general not locally optimal and in some cases may not attain consensus.

Faramondi L., Oliva G., Setola R., Vollero L.

IIoT in the hospital scenario: Hospital 4.0, blockchain and robust data management.

In: Alcaraz C. (Eds) Security and privacy trends in the industrial internet of things. Advanced sciences and technologies for security applications. Springer, 2019. ISBN: 978-3-030-12329-1 DOI: 10.1007/978-3-030-12330-7_13

Blockchain is an emerging technology for the management of data that may avoid or mitigate the impact of threats related to data storage and management, in general, and to the administration, in particular, of healthcare records. The paper discusses the application of blockchain technologies in the context of Hospital records.

Developmental Neuroscience

Department of Medicine and Surgery

**Head** F. Keller**Other Personnel** V. Focaroli, R. Marino

Description

The Developmental Neuroscience unit investigates developmental mechanisms at the molecular, cellular and systemic levels, both in animal models and in human infants. One major focus of the lab has been the interaction between reelin, a protein of the extracellular matrix and environmental factors, in particular gonadal hormones, during brain development. The reelin gene is a candidate gene for autism, a pervasive developmental disorder that is more frequent in males. The other major focus of the lab is the role of motor development and other embodied functions for development of cognitive functions and mental processes. Specifically, we are investigating early motor signs of autism risk in high-risk babies, who have an older sibling affected by this disorder. A new research focus of the lab is the investigation of embodied music perception in children.

Main collaborations

- G. B. Bietti Foundation for Study and Research in Ophthalmology, Italy
- University of Pittsburgh, US

Most important publications

Dettin M., Sieni E., Zamuner A., Marino R., Sgarbossa P., Lucibello M., Tosi A.L., Keller F., Campana L.G., Signori E.

A novel 3D scaffold for cell growth to asses electroporation efficacy.

Cells. 2019 Nov 19;8(11): E1470. PMID: 31752448. IF 5,656

Tumor electroporation (EP) refers to the permeabilization of the cell membrane by means of short electric pulses thus allowing the potentiation of chemotherapeutic drugs. Standard plate adhesion 2D cell cultures can simulate the in vivo environment only partially due to lack of cell-cell interaction and extracellular matrix (ECM). In this study, we assessed a novel 3D scaffold for cell cultures based on hyaluronic acid and ionic-complementary self-assembling peptides (SAPs), by studying the growth patterns of two different breast carcinoma cell lines (HCC1569 and MDA-MB231). This 3D scaffold modulates cell shape and induces extracellular matrix deposit around cells. In the MDA-MB 231 cell line, it allows three-dimensional growth of structures known as spheroids, while in HCC1569 it achieves a cell organization similar to that observed in vivo. Interestingly, we were able to visualize the electroporation effect on the cells seeded in the new scaffold by means of standard propidium iodide assay and fluorescence microscopy. Thanks to the presence of cell-cell and cell-ECM interactions, the new 3D scaffold may represent a more reliable support for EP studies than 2D cancer cell cultures and may be used to test new EP-delivered drugs and novel EP protocols.

Taffoni F., Focaroli V., Keller F., Iverson J.M.

Motor performance in a shape sorter task: a longitudinal study from 14 to 36 months of age in children with an older sibling ASD.

PLoS One. 2019 May 28;14(5): e0217416. PMID: 31136606. IF 2,776

During development, motor skills are fundamental in supporting interactions with the external world. The ability to plan actions is a particularly important aspect of motor skill since it is involved in many daily activities. In this work, we studied the development of motor planning longitudinally in children with an older sibling with Autism Spectrum Disorder (ASD) who are at heightened risk (HR) for the disorder and children with no such risk (low risk; LR) using a shape sorter task. Children were observed at 14, 18, 24 and 36 months. Three HR children with a later diagnosis of ASD (HR-ASD) were analyzed separately from the rest of the sample. Behavioral and kinematic data indicated that precision demands significantly influenced children's actions, and that children's performance improved with age. No differences were found between the HR and LR groups, but a descriptive analysis of data from the three HR-ASD suggested differences in the variables describing children's action (as reaching time and acceleration) as well as variables describing children's performance (as the adjustment of the shapes).

Balzamino B.O., Esposito G., Marino R., Keller F., Micera A.

Changes in vitreal protein profile and retina mRNAs in Reeler mice: NGF, IL33 and Müller cell activation.

PLoS One. 2019 Feb 27;14(2): e0212732. PMID: 30811468. IF 2,776

A possible link between Nerve Growth Factor (NGF) and Reelin might take place during impaired retinal development occurring in the Reelin deficient mouse model (Reeler). To better characterize NGF and retina impairments at the Reeler retina, vitreous and retina were investigated by means of protein expression and glial cell activation. Reeler (n = 9; RELN^{-/-}) and WT (n = 9; wild-type RELN^{+/-}, B6C3Fe) mice were analyzed at 14, 21 and 28 postnatal days (p). Retinas and vitreous were subjected to confocal analysis and protein array, followed by conventional analysis. A significant increase of NGF, IL33 and TIMP1, a trend to a decrease of IL12 and IL6, as well as a significant decrease of NT3 were detected in Reeler vitreous, particularly at p28 (p<0.05). MIP3 β mRNA was decreased while IL33mRNA was significantly upregulated in Reeler retina. Increased number of GFAP⁺ and Nestin⁺ cells as well as upregulation of Glutamine Synthetase and Nestin mRNAs were observed in Reeler retinas (p<0.05). These findings extend our previous studies on Reeler retina showing a selective Müller cell activation. NGF and IL33 release into vitreous would suggest a local activation of Müller cells, in addition to retinal ganglion and accessory cells. Overall, the data from this experimental study would strength the potential neuroprotective role played by activated Muller cells through NGF release.

Diagnostic Imaging

Department of Medicine and Surgery



Head B. Beomonte Zobel

Faculty E. Faiella, R.F. Grasso, C.C. Quattrocchi

Other Personnel V. Cirimele, G. Frauenfelder, S. Gaudio, C. A. Mallio, D. Santucci

Description

Research is carried out following different lines, in cooperation with other research units, both inside and outside our University:

- Neuroimaging, that is the correlation of MRI with diagnosis, treatment or rehabilitation of different acute and chronic diseases;
- Interventional Radiology, how radiologists use small invasive approaches and specific technologies for diagnosis and treatment of several diseases;
- Image based navigations systems, that use mechatronics and images acquired directly from the patients to guide diagnostic and therapeutic procedures in Medicine;
- Elderly Imaging, how senescence processes can modify the functionality and the morphology of different organs and tissues;
- Oncologic Imaging, how radiologists can improve the diagnosis, the treatment and the follow-up of oncologic patients;

- Radiomics, that is the correlation between some imaging biomarkers and genetic characteristics of different diseases;
- Artificial Intelligence and Machine Learning in Imaging, how neural networks can be trained and used to increase the value, efficiency and accuracy of radiologists.

patients with prostatic carcinoma.

Main research activities

- Contrast media, evaluating in vivo Gadolinium pharmacokinetics and dynamics of linear MRI contrast agents.
- Interventional Radiology, suggesting the percutaneous management of bone metastases and evaluating the clinical efficacy of augmented reality navigation systems.
- Neuroimaging, evaluating specific aspects of functional connectivity and of brain circuitry in patients affected by eating disorders.
- Oncologic imaging, assessing clinical and radiological features driving diagnosis and performing of percutaneous biopsies in

Most important publications

Santucci D., Faiella E., Calabrese A., Favale L., Zobel B.B., de Felice C.

Our radiological experience on B3 lesions: correlation between mammographic and MRI findings with histologic definitive result.

Clin Breast Cancer. 2019 Oct;19(5): e643-e653. PMID: 31377083. IF 2,762

Introduction: The purpose of this study was to evaluate mammographic and magnetic resonance imaging (MRI) features in B3 lesions. **Patients and methods:** From 2011 to 2018, 139 patients with histologically proven B3 lesions who underwent mammography or/and MRI, were retrospectively reviewed. B3 lesions were classified in: atypical ductal hyperplasia (ADH), lobular neoplasia (LN), papillary lesion (PL), radial scar (RS), flat epithelial atypia (FEA), phyllodes tumor (PT), or mesenchymal lesion. Imaging features evaluated were: the presence of microcalcifications, mass and architectural distortions on mammograms and type of margins (circumscribed, irregular, spiculate), enhancement (mass-like, non-mass-like), size (≤ 15 mm, > 15 mm), and kinetics curves (I, II, III) on MRI. The definitive histologic results confirmed benign lesion or were upgraded to malignancy, and the positive predictive value was calculated. **Results:** Histologic classification of B3 lesions counted 45 (32.37%) ADH, 12 (8.63%) LN, 25 (17.99%) PL, 5 (3.61%) RS, 31 (22.31%) FEA, 20 (14.39%) PT, and 1 (0.70%) mesenchymal lesion. One hundred seven patients had mammography, and 38 had MRI. In 90 (65%) cases, the histologic diagnosis confirmed B3, in 15 (11%) cases, benign lesion, and in 34 (24%) cases, malignancies were found, with best positive predictive value for mesenchymal tumor (1), ADH (0.36), and FEA (0.4). Significant correlations comparing core needle biopsy groups and microcalcifications ($P = .016$) and presence of mass ($P = .002$) and comparing definitive histology with the presence of mass ($P = .023$), were found. Regarding MRI, the morphology correlated with core needle biopsy groups ($P = .038$); morphology ($P = .024$), dimension ($P = .040$), and kinetic curve ($P = .005$) correlated with malignancy. **Conclusions:** The B3 category includes different entities, with various risk of malignancy; their heterogeneity is associated with specific mammographic and MRI features, although further confirmations are needed.

Gaudio S., Carducci F., Piervincenzi C., Olivo G., Schiöth HB.

Altered thalamo-cortical and occipital-parietal-temporal-frontal white matter connections in patients with anorexia and bulimia nervosa: a systematic review of diffusion tensor imaging studies.

J Psychiatry Neurosci. 2019 Sep 1;44(5):324-339. PMID: 30994310 IF 4,988

Background: Anorexia nervosa and bulimia nervosa are complex mental disorders, and their etiology is still not fully understood. This paper reviews the literature on diffusion tensor imaging studies in patients with anorexia nervosa and bulimia nervosa to explore the usefulness of white matter microstructural analysis in understanding the pathophysiology of eating disorders. **Methods:** We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to identify diffusion tensor imaging studies that compared patients with an eating disorder to control groups. We searched relevant databases for studies published from database inception to August 2018, using combinations of select keywords. We categorized white matter tracts according to their 3 main classes: projection (i.e., thalamo-cortical), association (i.e., occipital-parietal-temporal-frontal) and commissural (e.g., corpus callosum). **Results:** We included 19 papers that investigated a total of 427 participants with current or previous eating disorders and 444 controls. Overall, the studies used different diffusion tensor imaging approaches and showed widespread white matter abnormalities in patients with eating disorders. Despite differences among the studies, patients with anorexia nervosa showed mainly white matter microstructural abnormalities of thalamo-cortical tracts (i.e., corona radiata, thalamic radiations) and occipital-parietal-temporal-frontal tracts (i.e., left superior longitudinal and inferior fronto-occipital fasciculi). It was less clear whether white matter alterations persist after recovery from anorexia nervosa. Available data on bulimia nervosa were partially similar to those for anorexia nervosa. **Limitations:** Study sample composition and diffusion tensor imaging analysis techniques were heterogeneous. The number of studies on bulimia nervosa was too limited to be conclusive. **Conclusion:** White matter microstructure appears to be affected in anorexia nervosa, and these alterations may play a role in the pathophysiology of this eating disorder. Although we found white matter alterations in bulimia nervosa that were similar to those in anorexia nervosa, white matter changes in bulimia nervosa remain poorly investigated, and these findings were less conclusive. Further studies with longitudinal designs and multi-approach analyses are needed to better understand the role of white matter changes in eating disorders.

Parillo M., Sapienza M., Arpaia F., Magnani F., Mallio C.A., D'Alessio P., Quattrocchi C.C.

A structured survey on adverse events occurring within 24 hours after intravenous exposure to gadodiamide or gadoterate meglumine: a controlled prospective comparison study.

Invest Radiol. 2019 Apr;54(4):191-197. PMID: 30379729. IF 6,091

Objective: This study compares the incidence of new-onset symptoms within 24 hours after enhanced magnetic resonance imaging (eMRI) with intravenous administration of gadodiamide or gadoterate meglumine compared with a control group undergoing unenhanced MRI (uMRI). **Materials and methods:** A prospective cohort study ($n = 1088$ patients) was designed to assess the incidence of symptoms within 24 hours after administration of gadodiamide or gadoterate meglumine. The participants underwent a structured questionnaire by phone call before and 24 hours after the MRI scan to check for symptoms that were not present before the scan. The questionnaire included a list of active questions aimed to test the prevalence of symptoms that have been proposed in the debated definition of gadolinium deposition disease (GDD) and that we recorded in this study as GDD-like. In particular, the following symptoms and signs were tested: central torso pain, arm or leg pain, bone pain, headache, skin redness (any site of the body), fatigue, and mental confusion. Fisher exact test was used to test differences between groups with significance threshold set at $P < 0.05$. **Results:** Within the 24 hours after the MRI scan, 8.3% of patients reported at least one new-onset symptom in the uMRI group versus 17.4% in the gadodiamide eMRI versus 17.8% in the gadoterate meglumine eMRI group. The difference between the eMRI and the uMRI group was statistically significant ($P < 0.001$ for gadodiamide and $P < 0.001$ for gadoterate meglumine). There was not a different incidence of symptoms between the gadodiamide and the gadoterate meglumine eMRI groups. For gadodiamide, fatigue ($P < 0.05$) and dizziness ($P < 0.05$) were symptoms significantly more frequent than uMRI group; for gadoterate meglumine, fatigue ($P < 0.01$), mental confusion ($P < 0.01$), and diarrhea ($P < 0.01$) were significantly more frequent than uMRI group. **Conclusions:** We found that the onset of new symptoms within 24 hours after exposure to gadolinium-based contrast agent was more frequent than after uMRI. Among GDD-like symptoms, fatigue and mental confusion were the most frequent symptoms reported after eMRI. The other GDD-like symptoms were not overreported after eMRI versus uMRI. Thus, these results are questioning the term GDD.

Drug Sciences

Department of Medicine and Surgery

**Head** G. Minotti**Faculty** E. Salvatorelli**Other Personnel** P. Menna

Description

This Research Unit is committed to elucidating pharmacological foundations and clinical correlates of cardiovascular liability of antitumor drugs. It designs and performs clinical studies and preclinical experiments (molecular modelling, cell biology, ex vivo human tissue biopsies, optical and mass spectrometry techniques).

Main research activities

- Recalculation of cumulative anthracycline doses associated with 5% risk of heart failure.
- Clinical trajectories of cardio-oncology
- Clinical phenotypes of cardiovascular toxicity from tyrosine kinase inhibitors
- Clinical characterization of early diastolic dysfunction induced by anthracyclines and nonanthracycline chemotherapeutics
- Clinical pharmacology of hemodynamic effects of natriuretic peptides in patients treated by cancer drugs

Most important publications

Minotti G., Menna P., Calabrese V., Greco C., Armento G., Annibali O., Marchesi F., Salvatorelli E., Reggiardo G.

Pharmacology of Ranolazine versus common cardiovascular drugs in patients with early diastolic dysfunction induced by anthracyclines or nonanthracycline chemotherapeutics: a phase 2b Minitrial.

J Pharmacol Exp Ther. 2019 Aug;370(2):197-205. PMID: 31101682. IF 3,615

We have reported that anthracyclines and nonanthracycline chemotherapeutics caused diastolic dysfunction in cancer patients without cardiovascular risk factors. Diastolic dysfunction occurred as early as 1 week after the last chemotherapy cycle and manifested as impaired myocardial relaxation at echocardiography or persistent elevations of B-type natriuretic peptide (BNP) or troponin. The antianginal drug ranolazine shows cardiac relaxant effects that we considered of value to treat early diastolic dysfunction induced by cancer drugs; therefore, 24 low-risk patients with post-chemotherapy diastolic dysfunction were randomized (1:1) to ranolazine or the investigator's choice of common cardiovascular drugs, such as β -blockers and/or angiotensin-converting enzyme inhibitors or loop diuretics (best standard therapy, BST). After 5 weeks, 12 of 12 patients on ranolazine recovered from diastolic dysfunction, whereas 3 of 12 patients on BST did not improve; however, adverse events (not serious) were apparently more frequent for ranolazine than for BST (4/12 vs. 1/12). Ranolazine did not lower blood pressure, whereas BST reduced systolic pressure and caused a trend toward a reduced diastolic pressure. Most patients at randomization showed tachycardia resulting from chemotherapy-related anemia. Hemoglobin recovery contributed to normalizing heart rate in these patients; however, some patients in the ranolazine arm developed tachycardia through chronotropic effects of high BNP levels and returned to a normal heart rate through the effects of ranolazine on decreasing BNP levels. This minitrial describes the potential effects of ranolazine on relieving chemotherapy-related diastolic dysfunction; however, clinical implications of these findings need to be characterized by studies with an adequate sample size. SIGNIFICANCE STATEMENT: The antianginal drug ranolazine causes cardiac relaxant effects that might relieve diastolic dysfunction. In a clinical pharmacology study, 24 patients were randomized (1:1) to receive ranolazine or common cardiovascular drugs to treat early diastolic dysfunction induced by anthracycline-based or nonanthracycline chemotherapy. Ranolazine relieved diastolic dysfunction in these patients. The safety profile of ranolazine in cancer patients is similar to that of the general population. Compared with common cardiovascular drugs, ranolazine relieved diastolic dysfunction without lowering blood pressure. The sample size of this study was nonetheless too small to permit considerations about the potential clinical value of ranolazine for oncologic patients with early diastolic dysfunction induced by anthracyclines or nonanthracycline chemotherapeutics. This information should be obtained by studies with an adequate sample size.

Marchesi F., Salvatorelli E., Renzi D., Mengarelli A., Minotti G., Menna P.

Efficacy and safety of low dose ponatinib in a case of Ph-positive acute lymphoblastic leukaemia.

Br J Haematol. 2019 Oct;187(1): e15-e17. PMID: 31368155. IF 5,206

Ponatinib is a kinase inhibitor indicated for the treatment of adult patients with Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) or chronic phase, accelerated phase or blast phase chronic myeloid leukaemia (CML) that is resistant or intolerant to da-satinib or nilotinib and for which imatinib is not clinically appropriate. Ponatinib shows a unique activity in patients with T315I-mutated BCR-ABL1. Unfortunately, the clinical use of ponatinib is limited by the possible occurrence of cardiovascular side effects, primarily arterial and venous thrombosis (Moslehi & Deininger, 2015).<....>

Dent S.F., Suter T.M., López-Fernández T., Opolski G., Menna P., Minotti G.

Cardio-oncology in clinical studies and real life.

Semin Oncol. 2019 Dec;46(6):421-425. PMID: 31767270. IF 3,606

Session V of the Colloquium was chaired by Professors Teresa López-Fernández of Spain and Grzegorz Opolski of Poland. The 3 speakers addressed cardio-oncology issues as they relate to both clinical studies and real life situations. Professor Susan Dent discussed cardio-oncology networks for patients, emphasizing the importance of establishing a framework where the expertise of the cardiology consultant can supplement and reinforce the goals of optimal cancer therapy. Professor Thomas Suter moved the discussion further, sharing his insight into cardiac monitoring in clinical trials, emphasizing the lack of uniform criteria and lack of consensus regarding reversibility of cardiac events and long-term implications of modest declines in systolic function frequently found in clinical trials for which long-term follow-up may not be a component of the trial. Professor Giorgio Minotti added important considerations to the discussion of clinical trials. He emphasized that the usual reporting of cardiac systolic function omits important diastolic dysfunction data generated but often ignored during the routine cardiac exams. The inclusion of cardiac biomarker changes would also help to broaden the perspective of cardiac effects and events seen in patients enrolled in clinical trials.

Electronics for Sensor Systems

Department of Engineering



Head G. Pennazza

Faculty: M. Santonico

Other Personnel A. Sabatini, A. Zompanti

External Members S. Grasso

Description

The Unit of Electronics for Sensor Systems (ESS) has a long experience in the study, design, development and test of sensors and electronic interfaces for sensor systems, especially for medical applications and food monitoring. Its main characteristic is the multidisciplinary approach: designing sensors and electronic interfaces is the core activity, and it is addressed to specific issues in the biomedical context or coming from food-industry. ESS staff includes Electronic Engineers, Biomedical Engineers and a Biotechnologist. This unit is able to cover many steps of the development process of innovative technologies, starting from the basic research on electronic circuits and on new sensing materials. ESS transforms this research in a new technology concept and it is also able to integrate a prototype system in an engineered version, and to test them in the lab and in a relevant environment. This unit also applies multivariate data analysis techniques for the elaboration of the data.

Main research activities

In 2019 the project AUDIO (Acoustic Upgraded Diagnostics In-Orbit) (started in 2018 and funded by the Italian Space Agency) achieved the result of testing the device developed for measuring Oto Acoustic Emissions in orbit, on the International Space Station, in the frame of the Mission named Beyond, lead by the Italian astronaut Luca Parmitano.

In the frame of a FLAG-ERA project (Convergence) this unit tested in relevant environment a low-power and wireless CO₂ sensor.

The study conducted with CNR Institute of Biomedicine and Molecular Immunology of Palermo for the monitoring of paediatric asthma was published in 2019 on the Journal of Breath Research.

In 2019, in the frame of the project COMETA (Quality testing of organoleptic properties of COffee blends via genetic and METAbolic fingerprinting, coordinated by Danesi caffè SpA) this unit developed a non-destructive sensor system for the characterization of coffee blend during the roasting process.

Main collaborations

- CNR Institute of Biomedicine and Molecular Immunology, Palermo, Italy
- Danesi caffè SpA, Italy
- Italian Space Agency, Italy

Most important publications

Brinkman P., Wagener A.H., Hekking P.P., Bansal A.T., Maitland-van der Zee A.H., Wang Y., Weda H., Knobel H.H., Vink T.J., Rattray N.J., D'Amico A., Pennazza G., Santonico M., Lefaudeux D., De Meulder B., Auffray C., Bakke P.S., Caruso M., Chanez P., Chung K.F., Corfield J., Dahlén S.E., Djukanovic R., Geiser T., Horvath I., Krug N., Musial J., Sun K., Riley J.H., Shaw D.E., Sandström T., Sousa A.R., Montuschi P., Fowler S.J., Sterk P.J.; U-BIOPRED Study Group.

Identification and prospective stability of electronic nose (eNose)-derived inflammatory phenotypes in patients with severe asthma.

J Allergy Clin Immunol. 2019 May;143(5):1811-1820.e7. PMID: 30529449. IF 14,11

Background: Severe asthma is a heterogeneous condition, as shown by independent cluster analyses based on demographic, clinical, and inflammatory characteristics. A next step is to identify molecularly driven phenotypes using "omics" technologies. Molecular fingerprints of exhaled breath are associated with inflammation and can qualify as noninvasive assessment of severe asthma phenotypes.

Objectives: We aimed (1) to identify severe asthma phenotypes using exhaled metabolomic fingerprints obtained from a composite of electronic noses (eNoses) and (2) to assess the stability of eNose-derived phenotypes in relation to within-patient clinical and inflammatory changes. **Methods:** In this longitudinal multicenter study exhaled breath samples were taken from an unselected subset of adults with severe asthma from the U-BIOPRED cohort. Exhaled metabolites were analyzed centrally by using an assembly of eNoses. Unsupervised Ward clustering enhanced by similarity profile analysis together with K-means clustering was performed. For internal validation, partitioning around medoids and topological data analysis were applied. Samples at 12 to 18 months of prospective follow-up were used to assess longitudinal within-patient stability. **Results:** Data were available for 78 subjects (age, 55 years [interquartile range, 45-64 years]; 41% male). Three eNose-driven clusters ($n = 26/33/19$) were revealed, showing differences in circulating eosinophil ($P = .045$) and neutrophil ($P = .017$) percentages and ratios of patients using oral corticosteroids ($P = .035$). Longitudinal within-patient cluster stability was associated with changes in sputum eosinophil percentages ($P = .045$). **Conclusions:** We have identified and followed up exhaled molecular phenotypes of severe asthma, which were associated with changing inflammatory profile and oral steroid use. This suggests that breath analysis can contribute to the management of severe asthma.

D'Amico A., Santonico M., Lundstrom I.

The getter effect in the Langmuir regime.

J Applied Physics. 2019;126(2):025304. DOI: 10.1063/1.5099627 IF 2,328

The concentration of an analyte in a closed test chamber containing a chemical sensor is affected by the adsorption-desorption processes acting on the sensor surface. This phenomenon is called the "getter" whose effect has been known for many decades to occur in, e.g., vacuum tubes even if its mathematical expression has not been elaborated upon so far for affinity based chemical sensors. In this paper, we describe the "getter" equation and its consequences for affinity based chemical sensors in both the gas phase and the liquid phase with the starting point in the standard kinetic equation leading to Langmuir-like adsorption isotherms. More specifically, we calculate the "getter" isotherm and compare it with the Langmuir isotherm. The getter phenomenon is shown to be important at sufficiently small analyte concentrations (partial pressure in the gas phase or molecular concentration in the liquid phase) and in test chambers or sample cells of small volumes. A simple rule of thumb is given when the "getter" effect may be important. As an example, for a sample cell with a volume of 1 ml and a sensor surface area of 1 cm² without a constant flow of analyte through it, the "getter" phenomenon may occur around parts per million levels for a gas sensor and around submicromolar concentrations for a sensor in a liquid. Experimental examples from the literature where the "getter" effect is observed will be given. We also show a more general electric equivalent circuit which accounts also for the getter effect by using a coverage dependent series resistance in the equivalent circuit previously suggested for Langmuir adsorption under constant partial pressure/concentration in the test chamber.

Zompanti A., Sabatini A., Santonico M., Grasso S., Gianfelici A., Donatucci B., Di Castro A., Pennazza G.

A Sensor platform for athletes' training supervision: a proof of concept study.

Sensors (Basel). 2019 Sep 12;19(18): 3948. PMID: 31547403. IF 3,031

One of the basic needs of professional athletes is the real-time and non-invasive monitoring of their activities. The use of these kind of data is necessary to develop strategies for specific tailored training in order to improve performances. The sensor system presented in this work has the aim to adopt a novel approach for the monitoring of physiological parameters, and athletes' performances, during their training. The anaerobic threshold is herein identified with the monitoring of the lactate concentration and the respiratory parameters. The data collected by the sensor are used to build a model using a supervised method (based on the partial least squares method, PLS) to predict the values of the parameters of interest. The sensor is able to measure the lactate concentration from a sample of saliva and it can estimate a respiratory parameter, such as maximal oxygen consumption, maximal carbon dioxide production and respiratory rate from a sample of exhaled breath. The main advantages of the device are the low power; the wireless communication; and the non-invasive sampling method, which allow its use in a real context of sport practice.

Endocrinology and Diabetes

Department of Medicine and Surgery

Head P. Pozzilli

Faculty S. Manfrini, N. Napoli

Other Personnel S.I. Briganti, F. Cannata, I. Cavallari, G. Defeudis, R. Del Toro, A. Di Mauro, S. Fallucca, E. Fioriti, G. Leanza, S. Kyanvash, E. Maddaloni, D. Maggi, L. Monte, A. Naciu, A. Palermo, A. Piccoli, S. Peralice, G. Rossini, A. Soare, R. Strollo, G. Tabacco, F. Tramontana, D. Tuccinardi, C. Vinci

Lab Technician L. Valente **Scientific Secretary** S. Miglietta, D.J.R. Petrelli
Secretary A. Suppa



Description

Unit of Endocrinology and Diabetes has a long-standing expertise in diabetes, metabolic diseases and bone metabolism. Prof Pozzilli currently leads the Unit and is a worldwide known expert in diabetes. Campus Bio-Medico is now a center for excellence for Diabetes with one of the largest clinical and research facilities in Italy. Since 2007, it has also emerged as one of the leading Centers for translational and clinical studies of bone metabolism, with studies focused on bone health in T1D and T2D. Our research focuses primarily on T1 and T2D, their prevention and care, by means of new therapies and novel insulin administration systems. Research is also carried out on thyroid and calcium metabolism diseases. Our group works closely with scientific communities and governmental and non-governmental organizations on joint research programs. Specific attention is paid to phase II and III clinical trials (spontaneous studies and trials in collaboration with major pharmaceutical industries).

Main research activities

- Pathogenesis and immunotherapy of Type 1 diabetes
- Biomarkers of T1D prediction, progression, vascular and bone complications (OxIDIA): Anti-bodies to oxidized insulin as biomarkers of T1D.
- Latent Autoimmune Diabetes in Adults (LADA)
- Research activity on bone metabolism: Risk factors for bone fragility in patients with osteoporosis, T1D, T2D.
- Diabetes and cardiovascular complications: Early markers of autonomic cardioneuropathy.
- Technology and diabetes: Novel insulin pumps and non-invasive glucose monitoring systems.
- Mineral Metabolism: Mineral metabolism in post-surgical chronic hypoparathyroidism and normocalcemic primitive hyperparathyroidism.
- Thyroid diseases: Novel diagnostic methods for diagnosis of thyroid cancer, core biopsy and Raman technology.

Main collaborations

- Harvard University- Boston, US
- Sapienza University of Rome, Rome, Italy
- St. Bartholomew's and The London School of Medicine, University of London, UK
- University of Rome Foro Italico, Rome, Italy
- Washington University, St. Louis, US

Most important publications

Strollo R., Vinci C., Napoli N., Fioriti E., Maddaloni E., Åkerman L., Casas R., Pozzilli P., Ludvigsson J., Nissim A.

Antibodies to oxidized insulin improve prediction of type 1 diabetes in children with positive standard islet autoantibodies.

Diabetes Metab Res Rev. 2019;35(4): e3132. PMID: 30693639. IF 4,758

We tested whether our newly developed biomarker of type 1 diabetes (T1D), circulating antibodies to modified insulin (oxPTM-INS-Ab), improves disease prediction compared to unmodified insulin autoantibodies (IAA). In children with other standard autoantibodies (AAB+: GADA, IAA, IA2A), accuracy of oxPTM-INS-Ab was higher than GADA and IAA ($p \leq 0.017$). T1D risk was higher among multiple AAB+ who were also oxPTM-INS-Ab+ (vs. oxPTM-INS-Ab-). When replacing IAA with oxPTM-INS-Ab, T1D risk increased to 100% in combination with GADA and IA-2A, compared to 84.37% in those with IAA/GADA/IA2A ($p=0.04$). Compared to IAA, oxPTM-INS-Ab improve T1D risk assessment and prediction accuracy in AAB+ children.

Leanza G., Maddaloni E., Pitocco D., Conte C., Palermo A., Maurizi A.R., Pantano A.L., Suraci C., Altomare M., Strollo R., Manfrini S., Pozzilli P., Schwartz A.V., Napoli N.

Risk factors for fragility fractures in type 1 diabetes.

Bone. 2019 Aug;125: 194-199. PMID: 31059862. IF 4,36

Fracture rate is disproportionately high in type 1 diabetes (T1D) relative to modestly reduced bone mass. We aimed to determine clinical diabetes-related risk factors for fragility fractures in T1D. We analyzed data from 600 T1D adults with 5 years of follow-up data and no history of secondary causes of osteoporosis. Within the cohort, 111 participants sustained at least 1 fracture (18.5%), with 29 of those patients reporting at least 2 fractures. We found that kidney function and neuropathy were associated with an increased risk of fracture. In addition, long disease duration and HbA1c of at least 7.9% were independent risk factors for sustaining multiple fractures among adults with T1D.

Napoli N., Conte C., Pedone C., Strotmeyer E.S., Barbour K.E., Black D.M., Samelson E.J., Schwartz A.V.

Effect of insulin resistance on BMD and fracture risk in older adults.

J Clin Endocrinol Metab. 2019 Aug 1;104(8):3303-3310. PMID: 30802282. IF 5,605

Objective: To investigate in 2398 nondiabetic older adults the relationship among IR HOMA-IR, BMD, and fractures risk (FR).

Results: Cut-off values for HOMA-IR quartiles were 1.05, 1.54, and 2.33. Total hip BMD was 0.104 g/cm² higher in the fourth vs the first HOMA-IR quartile. This difference was attenuated after adjustment for BMI. In unadjusted models, FR was lower in those with higher HOMA-IR. After adjustment for BMD and BMI, FR was higher in the third quartile and increased in the fourth quartile vs the first quartile.

Conclusions: Greater IR is associated with higher BMD. We did not find consistent evidence that greater IR is associated with increased FR after adjustment for BMI and BMD

Food Science and Nutrition

Department of Science and Technology for Humans and the Environment



Head L. De Gara

Faculty L. Dugo, C. Fanali, V. Locato, M. Russo

External Members E. Marconi, L. Mondello

Description

Research unit interests:

- Metabolism in plants and characterization of bio-active phytochemicals with particular attention to antioxidants, oligo- and saccharides;
- Chemical characterization of bioactive compounds in foods employing liquid and gas chromatography techniques.
- Set up of green chemistry techniques for the extraction characterization and purification of bioactive molecule from food and food waste
- Validation of multisensorial platform based on electronic sensors for its use on shelf life monitoring and food quality assessment;
- In vitro and ex vivo tests evaluating nutritional / health value of food matrixes and nutraceutical compounds;
- Climate change effects on plant growth and productivity - plant signalling in the responses to environmental stresses.

- Food education and scientific divulgation related to food and nutrition
- Research unit expertise:
 - Plant molecular biology and biochemistry, plant and animal cell cultures, analytical chemistry of metabolites with traditional and omics approaches, food chemistry, plant and food biotechnology.

Main research activities

- Prof. Fanali, PI; Dugo and De Gara Participant – project granted by AGER2 “VIOLIN –
- Valorization of Italian Olive products through Innovative analytical tools”;
- Prof. De Gara, PI; Locato Participant – Project granted by MIUR – PRIN “Adattamento e tolleranza delle piante agli stress abiotici in condizioni ambientali mutevoli”.
- Prof De Gara, PI – Project granted by Nestlé Italy “Nutripiatto” a tool of nutritional education for children between 4 to 12 years old

- Prof. De Gara PI, Fanali Participant - Cometa– Project granted by Regione Lazio; KETs – tecnologie abilitanti
- Prof. De Gara PI, Locato Participant. InnovalV Gamma Project granted by Regione Lazio;
- Prof. De Gara PI, Dugo and Fanali participants’ project granted by Soremartec - Ferrero

Most important publications

Sabetta W., Vandelle E., Locato V., Costa A., Cimini S., Bittencourt Moura A., Luoni L., Graf A., Viggiano L., De Gara L., Bellin D., Blanco E., de Pinto M.C.

Genetic buffering of cyclic AMP in *Arabidopsis thaliana* compromises the plant immune response triggered by an avirulent strain of *Pseudomonas syringae* pv. tomato.

Plant J. 2019 May;98(4):590-606. PMID: 30735606. IF 5,726

Cyclic AMP plays important roles in different physiological processes, including plant defence responses. However, as little information is known on plant enzymes responsible for cAMP production/degradation, studies of cAMP functions have relied, to date, on non-specific pharmacological approaches. We therefore developed a more reliable approach, producing transgenic *Arabidopsis thaliana* lines overexpressing the 'cAMP-sponge' (cAS), a genetic tool that specifically buffers cAMP levels. In response to an avirulent strain of *Pseudomonas syringae* pv. tomato (PstAvrB), cAS plants showed a higher bacterial growth and a reduced hypersensitive cell death in comparison with wild-type (WT) plants. The low cAMP availability after pathogen infection delayed cytosolic calcium elevation, as well as hydrogen peroxide increase and induction of redox systems. The proteomic analysis, performed 24 h post-infection, indicated that a core of 49 proteins was modulated in both genotypes, while 16 and 42 proteins were uniquely modulated in WT and cAS lines, respectively. The involvement of these proteins in the impairment of defence response in cAS plants is discussed in this paper. Moreover, in silico analysis revealed that the promoter regions of the genes coding for proteins uniquely accumulating in WT plants shared the CGCG motif, a target of the calcium-calmodulin binding transcription factor AtSR1 (*Arabidopsis thaliana* signal responsive1). Therefore, following pathogen perception, the low free cAMP content, altering timing and levels of defence signals, and likely acting in part through the misregulation of AtSR1 activity, affected the speed and strength of the immune response.

Gentili A., Dal Bosco C., Fanali S., Fanali C.

Large-scale profiling of carotenoids by using non aqueous reversed phase liquid chromatography - photodiode array detection - triple quadrupole linear ion trap mass spectrometry: Application to some varieties of sweet pepper (*Capsicum annuum* L.).

J Pharm Biomed Anal. 2019 Feb 5;164: 759-767. PMID: 30481639. IF 2,983

Analysis of carotenoids is very complex and demanding in terms of both separation and detection. In this article, an analytical strategy relying on high-performance liquid chromatography-photodiode array detection-tandem mass spectrometry (HPLC-PAD-MS/MS) is presented for the large-scale screening of these phytochemicals. Separation was realized by means of Non-Aqueous Reversed Phase (NARP) chromatography on a triacetyl stationary phase kept at subambient temperature, using a mobile phase compatible with atmospheric pressure chemical ionization (APCI). The standards of 14 analytes were used to optimize the method and to predict the chromatographic behaviour of untargeted carotenoids. MS and MS/MS data, obtained during Information Dependent Acquisition (IDA) experiments, were utilized to set up a sensitive HPLC- selected reaction monitoring (SRM) method. Relative abundance between SRM ion currents (ion ratio) allowed the MS distinction of structural isomers (for example, bicyclic, monocyclic and acyclic isomers), while the identification of geometrical isomers was based on Q ratio and fine structure, as calculated from UV-vis spectra. The comparison of LC-PAD- SRM chromatograms, acquired after applying two different extraction procedures (matrix solid-phase dispersion and overnight cold saponification), allowed verifying that sweet peppers are a good source of xanthophylls, prevalently occurring as esterified forms. The overall strategy could identify more than 40 carotenoids in some sweet pepper varieties (Jolly, horn and sweet chili pepper) available on the Italian and European food market.

Gionfriddo M, De Gara L, Loreto F.

Directed evolution of plant processes: towards a green (r)evolution?

Trends Plant Sci. 2019 Nov; 24(11):999-1007. PMID: 31604600. IF 14,006

Directed Evolution is a powerful approach for generating proteins with new chemical and physical properties. It mimics the principles of Darwinian evolution by imposing selective pressure on a large population of molecules inducing random genetic variation in DNA, so that sequences with specific desirable properties are generated and selected. We propose that combining Directed Evolution and Genome Editing (named DE-GE) technologies poses a powerful tool to effectively discover and integrate new traits into plants for agronomic and biotechnological gain. DE-GE has the potential to deliver a new Green (r)Evolution research platform that can provide novel solutions to major trait delivery aspirations around sustainable agriculture, climateresilient crops, improved food security and nutritional quality.

Gastroenterology

Department of Medicine and Surgery



Head M. Cicala

Faculty S. Emerenziani, M.P.L. Guarino

Other Personnel A. Altomare, P. Balestrieri, M. Ribolsi, L. Trillo, A. Tullio

External members R. Farrè, L. Putignani, S. Roman

Description

The Research Unit carries out basic and translational research projects through molecular biology analysis and electrophysiological study of mucosal integrity and of muscle contraction with dedicated devices (Ussing Chamber System for measuring epithelial membrane properties and Radnoti organ bath system).

The Gastrointestinal Laboratory collaborates with several Research Units of the University, such as Food Sciences and Human Nutrition Unit, Nonlinear Physics and Mathematical Modeling Laboratory and Biochemical Laboratory. Through the employment of high-quality instruments (high-resolution manometry and pH-impedance measuring), the GI Unit also conducts clinical research protocols, both spontaneous and sponsored, for the study of pathophysiology and diagnosis of gastroesophageal reflux disease and esophageal motility disorders. Therefore the GI Unit is exploring the role of intestinal microbiome in GI disorders, through a collaboration with the Microbiology Unit of OPBG (Rome).

Main research activities

The GI laboratory focuses on the following research topics: immunomodulation of intestinal motility, modulation of microbiota and effect of prebiotics and probiotics in Health and Gastrointestinal diseases, physio-pathological mechanisms of Inflammatory and functional gastrointestinal disorders (Inflammatory Bowel Disease, Irritable Bowel Syndrome and chronic constipation).

The Clinical Nutrition Unit carries out the following projects: Impact of preoperative nutritional status on surgical outcome in cancer patients and on nutritional therapy in Inflammatory Bowel Disease patients.

Moreover, the Research Unit carries on several phase II and III clinical trials to test new biological and small molecule agents for the treatment of Crohn disease and Ulcerative Colitis (IBD), and esophageal and ano-rectal motility study with High Resolution manometry in patients affected by Achalasia, Eosinophilic Esophagitis and ano-rectal motor disorders.

Main collaborations

- Centre Hospitalier Universitaire Edouard-Henriot de Lyon, Lyon, France
- Human Microbiome Unit, Bambino Gesù Paediatric Hospital, Italy
- Leuven University, Belgium

Most important publications

Pauwels A., Boecxstaens V., Andrews C.N., Attwood S.E., Berrisford R., Bisschops R., Boeckxstaens G.E., Bor S., Bredenoord A.J., Cicala M., Corsetti M., Fornari F., Gyawali C.P., Hatlebakk J., Johnson S.B., Lerut T., Lundell L., Mattioli S., Miwa H., Naftoux P., Omari T., Pandolfino J., Penagini R., Rice T.W., Roelandt P., Rommel N., Savarino V., Sifrim D., Suzuki H., Tutuian R., Vanuytsel T., Vela M.F., Watson D.I., Zerbib F., Tack J.

How to select patients for antireflux surgery? The ICARUS guidelines (international consensus regarding preoperative examinations and clinical characteristics assessment to select adult patients for antireflux surgery).

Gut. 2019 Nov;68(11):1928-1941. PMID: 31375601. IF 17,943

This study aimed at generating key recommendations in the selection of patients for antireflux surgery, including 35 international experts in a Delphi process and developing 37 statements that were revised by the Consensus Group. Through this work, the ICARUS guidelines established that patients with heartburn with a satisfactory response to PPIs, patients with a hiatal hernia (HH), patients with oesophagitis Los Angeles (LA) grade B or higher and patients with Barrett's oesophagus are good candidates for antireflux surgery. The guidelines have also indicated what procedures are mandatory in order to select patients for antireflux surgery.

Lo Presti A., Zorzi F., Del Chierico F., Altomare A., Cocca S., Avola A., De Biasio F., Russo A., Cella E., Reddel S., Calabrese E., Biancone L., Monteleone G., Cicala M., Angeletti S., Ciccozzi M., Putignani L., Guarino M.P.L.

Fecal and mucosal microbiota profiling in irritable bowel syndrome and inflammatory bowel disease.

Front Microbiol. 2019 Jul 17;10: 1655. PMID: 31379797. IF 4,259

In this prospective study, we investigated whether inflammatory bowel diseases (IBD) and irritable bowel syndrome (IBS) patients exhibit specific changes in richness and distribution of fecal and mucosal-associated microbiota. The results have shown that, in fecal and mucosal samples, the microbiota richness was characterized by a microbial diversity reduction, going from CTRLs to IBS to IBD. Based upon the LEfSe data, the Anaerostipes and Ruminococcaceae were identified as the most differentially abundant bacterial taxa in CTRLs. Erysipelotrichi was identified as potential biomarker for IBS, while Gammaproteobacteria, Enterococcus, and Enterococcaceae for IBD.

Tambone V., Lauri G., Guarino M.P.L., Campanozzi L.L., Ciccozzi M.

Leonardo's folio 730 recto: lessons for the medical humanities.

Lancet. 2019 Apr 6;393(10179): 1411-1412. PMID: 30967207. IF 59,102

This manuscript shows the relevance of Leonardo da Vinci's genius for the field of medical education. Specifically, through the consideration of the still little known Folio 730 Recto of the Codex Atlanticus of Leonardo, we highlight three key points for the Medical Humanities, which could be a valuable tool for nurturing the humanistic skills necessary for medical doctors. As such, this paper addresses a topic of great relevance in the current field of medicine, with the aim to outline a core curriculum proposal for Medical Humanities in view of a better clinical practice.

General Surgery

Department of Medicine and Surgery



Head R. Coppola

Faculty R. Alloni, D. Borzomati, D. Caputo, M. Caricato, P. Crucitti, V. Ripetti

Other Personnel V. Bruni, G. Capolupo, V. La Vaccara, S. Valeri

Description

Surgical Oncology represents the main topic of research of the Unit. Pancreatic, colorectal and lung cancer are the most important investigated diseases. The Unit carries out its activity in the field of both basic and clinical research of the above-mentioned neoplastic conditions. Thyroid endocrine dysfunction of surgical interest is also studied.

Main research activities

- Exploitation of nanoparticle blood interaction for early diagnosis of pancreatic and colorectal cancer.
- AIRC project "Nanoparticle-enabled blood test for pancreatic cancer detection".
- Diagnosis, treatment and control of infections in pancreatic and colorectal cancer.
- Management of surgical drains after pancreaticoduodenectomy
- Minimally invasive pancreatic cancer surgery
- Indications, technique and outcome of TaTME,
- Raman spectroscopy for the diagnosis of cancer.
- Anastomotic leak in colorectal surgery: economic analysis of the in-hospital impact.
- Breathprinting and early diagnosis of lung cancer.

Main collaborations

- Amsterdam Universitair Medische Center, The Netherlands
- Harvard Medical School, Boston MA, US
- National Research Council (CNR), Rome, Italy
- Pelican Cancer Foundation, UK
- University of Hamburg, Germany
- University of Roma Tre, Rome, Italy
- Department of Molecular Medicine, Sapienza University, Rome, Italy

Most important publications

Capretti G., Boggi U., Salvia R., Belli G., Coppola R., Falconi M., Valeri A., Zerbi A.

Application of minimally invasive pancreatic surgery: an Italian survey.

Updates Surg. 2019 Mar;71(1):97-103. PMID: 29770922. IF 2,476

The value of minimally invasive pancreatic surgery (MIPS) is still debated. To assess the diffusion of MIPS in Italy and identify the barriers preventing wider implementation, a questionnaire was developed under the auspices of three Scientific Societies (AISP, It-IHPBA, SICE) and was sent to the largest possible number of Italian surgeons also using the mailing list of the two main Italian Surgical Societies (SIC and ACOI). The questionnaire consisted of 25 questions assessing: centre characteristics, facilities and technologies, type of MIPS performed, surgical techniques employed and opinions on the present and future value of MIPS. Only one reply per unit was considered. Fifty-five units answered the questionnaire. While 54 units (98.2%) declared to perform MIPS, the majority of responders were not dedicated to pancreatic surgery. Twenty-five units (45.5%) performed < 20 pancreatic resections/year and 39 (70.9%) < 10 MIPS per year. Forty-nine units (89.1%) performed at least one minimally invasive (MI) distal pancreatectomy (DP), and 10 (18.2%) at least one MI pancreatoduodenectomy (PD). Robotic assistance was used in 18 units (31.7%) (14 DP, 7 PD). The major constraints limiting the diffusion of MIPS were the intrinsic difficulty of the technique and the lack of specific training. The overall value of MIPS was highly rated. Our survey illustrates the current diffusion of MIPS in Italy and underlines the great interest for this approach. Further diffusion of MIPS requires the implementation of standardized protocols of training. Creation of a prospective National Registry should also be considered. © 2018, Italian Society of Surgery (SIC).

Caracciolo G., Safavi-Sohi R., Malekzadeh R., Poustchi H., Vasighi M., Zenezini Chiozzi R., Capriotti A.L., Laganà A., Hajipour M., Di Domenico M., Di Carlo A., Caputo D., Aghaverdi H., Papi M., Palmieri V., Santoni A., Palchetti S., Digiacomo L., Pozzi D., Suslick K.S., Mahmoudi M.

Disease-specific protein corona sensor arrays may have disease detection capacity.

Nanoscale Horiz. 2019; 4(5):1063-1076. DOI: 10.1039/c9nh00097f IF 9,095

The earlier any catastrophic disease (e.g., cancer) is diagnosed, the more likely it can be treated, providing improved patient prognosis, extended survival and better quality of life. In early 2014, we revealed that various types of disease can substantially affect the composition/profile of protein corona (i.e., a layer of biomolecules that forms at the surface of nanoparticles upon their interactions with biological fluids). Here, by combining the concepts of disease-specific protein corona and sensor array technology we developed a platform with disease detection capacity using blood plasma. Our sensor array consists of three cross-reactive liposomes, with distinct lipid composition and surface charge. Rather than detecting a specific biomarker, the sensor array provides pattern recognition of the corona protein composition adsorbed on the liposomes. As a feasibility study, sensor array validation was performed using plasma samples obtained from patients diagnosed with five different cancer types (i.e. lung cancer, glioblastoma, meningioma, myeloma, and pancreatic cancer) and a control group of healthy donors. Although no single corona composition is specific for any one cancer type, overlapping but distinct patterns of the corona composition constitutes a unique "fingerprint" for each type of cancer (with a high classification accuracy, i.e. 99.4%). To finally probe the capacity of this sensor array for early detection of cancers, we used cohort plasma obtained from healthy people who were subsequently diagnosed several years after plasma collection with lung, brain, and pancreatic cancers. Our results suggest that the disease-specific protein corona sensor array will not only be instrumental in the screening, detection, and identification of diseases, but may also help identify novel protein pattern markers whose role in disease development and/or disease biology has not been appreciated so far.

Palchetti S., Caputo D., Digiacoimo L., Capriotti A.L., Coppola R., Pozzi D., Caracciolo G.

Protein corona fingerprints of liposomes: new opportunities for targeted drug delivery and early detection in pancreatic cancer.

Pharmaceutics. 2019 Jan 15;11(1):31. PMID: 30650541. IF 4,773

Pancreatic ductal adenocarcinoma (PDAC) is the fourth cause of cancer-related mortality in the Western world and is envisaged to become the second cause by 2030. Although our knowledge about the molecular biology of PDAC is continuously increasing, this progress has not been translated into better patients' outcome. Liposomes have been used to circumvent concerns associated with the low efficiency of anticancer drugs such as severe side effects and damage of healthy tissues, but they have not resulted in improved efficacy as yet. Recently, the concept is emerging that the limited success of liposomal drugs in clinical practice is due to our poor knowledge of the nanobio interactions experienced by liposomes in vivo. After systemic administration, lipid vesicles are covered by plasma proteins forming a biomolecular coating, referred to as the protein corona (PC). Recent studies have clarified that just a minor fraction of the hundreds of bound plasma proteins, referred to as "PC fingerprints" (PCFs), enhance liposome association with cancer cells, triggering efficient particle internalization. In this study, we synthesized a library of 10 liposomal formulations with systematic changes in lipid composition and exposed them to human plasma (HP). Size, zeta potential, and corona composition of the resulting liposome-protein complexes were thoroughly characterized by dynamic light scattering (DLS), micro-electrophoresis, and nano-liquid chromatography tandem mass spectrometry (nano-LC MS/MS). According to the recent literature, enrichment in PCFs was used to predict the targeting ability of synthesized liposomal formulations. Here we show that the predicted targeting capability of liposome-protein complexes clearly correlate with cellular uptake in pancreatic adenocarcinoma (PANC-1) and insulinoma (INS-1) cells as quantified by flow-assisted cell sorting (FACS). Of note, cellular uptake of the liposomal formulation with the highest abundance of PCFs was much larger than that of Onivyde®, an Irinotecan liposomal drug approved by the Food and Drug Administration in 2015 for the treatment of metastatic PDAC. Given the urgent need of efficient nanocarriers for the treatment of PDAC, we envision that our results will pave the way for the development of more efficient PC-based targeted nanomaterials. Here we also show that some BCs are enriched with plasma proteins that are associated with the onset and progression of PDAC (e.g., sex hormone-binding globulin, Ficolin-3, plasma protease C1 inhibitor, etc.). This could open the intriguing possibility to identify novel biomarkers.

Geriatrics

Department of Medicine and Surgery



Head R. Antonelli Incalzi

Faculty C. Pedone, S. Scarlata

Other Personnel A. Bertini, A. Cavalli, C. Celesti, I. Chiarella, L. Cortese, L. Costanzo, E. Falanga, A. Ferrini, P. Finamore, D. Fontana, F. Galdi, A. Laudisio, D. Lelli, E. Lo Greco, M. Ludovisi, C. Rivera, C. Peccenini, G. Perri, D. Spitaleri, A. Zito

Description

This Unit is made up by researcher and clinicians that bring together their skills to produce cutting-edge scientific evidences and provide the best available care for older people. About 60% of the research is based on the clinical activities carried on by the Unit, while the remaining includes analysis of data from epidemiological studies (such as the InCHIANTI and the SARA study) and systematic reviews and meta-analysis.

Main research activities

The lines of research currently ongoing are:

- Evaluation of health status and frailty;
- Evaluation of respiratory function with special focus on the interpretation of spirometric results;
- Evaluation of the diagnostic/prognostic properties of volatile organic compounds (VOCs) in different chronic and acute diseases;
- Development and implementation of system for remote tele-monitoring of chronic diseases;
- Evaluation of nutritional intake as a determinant of the health status;
- Assessing the biological bases of and risk.

Most important publications

Veronese N., Stubbs B., Punzi L., Soysal P., Incalzi R.A., Saller A., Maggi S.

Effect of nutritional supplementations on physical performance and muscle strength parameters in older people: A systematic review and meta-analysis.

Ageing Res Rev. 2019 May; 51:48-54. PMID: 30826500. IF 10,39

Malnutrition plays a role in the development of poor physical performance, frailty and sarcopenia. The use of nutritional supplementations for improving physical performance and muscle strength parameters in older people is unclear. We therefore aimed to summarize the effect of nutritional supplementations compared to placebo on physical performance (i.e. tests more investigating physical function, utilising aerobic capacity & muscle power) and muscle strength (i.e. tests depending on muscle power) outcomes in older people in randomized controlled trials (RCTs). A literature search in major databases was undertaken until the 01st September 2018. Eligible studies were RCTs investigating the effect of nutritional supplementations vs. placebo in older people (people having an age >60 years). Standardized mean differences (SMD) and 95% confidence intervals (CIs) were used through a random effect model. Over 4007 potentially eligible articles, 32 RCTs for a total of 4137 older participants (2097 treated and 2040 placebo) (mean age: 76.3 years; 65% females) were included. Compared to placebo, multi-nutrient supplementations significantly improved chair rise time ($n = 3$; SMD = -0.90; 95%CI: -1.46 to -0.33; $I^2 = 87\%$). Multi-nutrients significantly improved handgrip strength when compared to placebo ($n = 6$; 780 participants; SMD = 0.41; 95%CI: 0.06 to 0.76; $I^2 = 79\%$), as did nutritional supplementations including protein ($n = 7$; 535 participants; SMD = 0.24; 95%CI: 0.07 to 0.41; $I^2 = 16\%$). Nutritional supplementations also led to a significant improvement in chair rise time and in handgrip strength in participants affected by frailty/sarcopenia and in those affected by medical conditions. In conclusion, nutritional supplementation can improve a number of physical performance outcomes in older people, particularly when they include multi-nutrients and in people already affected by specific medical conditions, or by frailty/sarcopenia.

Di Pasquale M.F., Sotgiu G., Gramegna A., Radovanovic D., Terraneo S., Reyes L.F., Rupp J., González Del Castillo J., Blasi F., Aliberti S., Restrepo MI; [Scarlati S.] GLIMP Investigators.

Prevalence and etiology of community-acquired pneumonia in immunocompromised patients.

Clin Infect Dis. 2019 Apr 24;68(9):1482-1493. PMID: 31222287. IF 9,055

Background: The correct management of immunocompromised patients with pneumonia is debated. We evaluated the prevalence, risk factors, and characteristics of immunocompromised patients coming from the community with pneumonia. **Methods:** We conducted a secondary analysis of an international, multicenter study enrolling adult patients coming from the community with pneumonia and hospitalized in 222 hospitals in 54 countries worldwide. Risk factors for immunocompromise included AIDS, aplastic anemia, asplenia, hematological cancer, chemotherapy, neutropenia, biological drug use, lung transplantation, chronic steroid use, and solid tumor. **Results:** At least 1 risk factor for immunocompromise was recorded in 18% of the 3702 patients enrolled. The prevalences of risk factors significantly differed across continents and countries, with chronic steroid use (45%), hematological cancer (25%), and chemotherapy (22%) the most common. Among immunocompromised patients, community-acquired pneumonia (CAP) pathogens were the most frequently identified, and prevalences did not differ from those in immunocompetent patients. Risk factors for immunocompromise were independently associated with neither *Pseudomonas aeruginosa* nor non-community-acquired bacteria. Specific risk factors were independently associated with fungal infections (odds ratio for AIDS and hematological cancer, 15.10 and 4.65, respectively; both $P = .001$), mycobacterial infections (AIDS; $P = .006$), and viral infections other than influenza (hematological cancer, 5.49; $P < .001$). **Conclusions:** Our findings could be considered by clinicians in prescribing empiric antibiotic therapy for CAP in immunocompromised patients. Patients with AIDS and hematological cancer admitted with CAP may have higher prevalences of fungi, mycobacteria, and noninfluenza viruses.

Chiurchiù V., Leuti A., Saracini S., Fontana D., Finamore P., Giua R., Padovini L., Incalzi R.A., Maccarrone M.

Resolution of inflammation is altered in chronic heart failure and entails a dysfunctional responsiveness of T lymphocytes.

FASEB J. 2019 Jan;33(1):909-916. PMID: 30052486. IF 5,391

Chronic heart failure (CHF) is characterized by an ongoing nonresolving inflammatory status, where T lymphocytes seem critical. It has been recently recognized that transition from acute to chronic inflammation could be caused by defects in resolving inflammation, the resolution of which is mediated by a novel family of ω -3-derived specialized proresolving lipid mediators such as resolvins. We analyzed 27 elderly patients with CHF and 23 healthy age-matched control subjects, and we reported significantly lower levels of D-series resolvins (RvD)1 in plasma of patients with CHF that were associated with a reduced ability of their leukocytes to produce this lipid via its biosynthetic enzyme 15-lipoxygenase and that correlated with gas exchange dysfunction. Furthermore, when pretreating ex vivo peripheral blood mononuclear cells of patients with CHF with RvD1 or RvD2, we found that neither of them was able to modulate the immune response of CD8+ and CD4+ T cells in terms of proinflammatory cytokine production, namely TNF- α , IFN- γ , IL-17, and IL-2. Such impaired T-cell responsiveness in patients with CHF was associated with a significant reduction in mRNA and protein expression of RvD1 receptor GPR32, suggesting a defective signaling in the proresolving pathway. We conclude that patients with CHF show alterations in producing proresolving mediator RvD1 and a failure of adaptive immune cells in responding to the anti-inflammatory actions of RvDs that may contribute to the progression of chronic inflammation. Thus, the proresolution pathway might be a potential candidate to design better treatments for CHF aimed at reducing T cell-mediated chronic inflammation. -Chiurchiù, V., Leuti, A., Saracini, S., Fontana, D., Finamore, P., Giua, R., Padovini, L., Incalzi, R. A., Maccarrone, M. Resolution of inflammation is altered in chronic heart failure and entails a dysfunctional responsiveness of T lymphocytes.

Gynaecology and Obstetrics

Department of Medicine and Surgery



Head R. Angioli

Faculty C. De Cicco Nardone, F. Plotti, C. Terranova

Other Personnel C. Battista, R. Montera, G.B. Serra

Description

The Unit's work is mainly focused on gynecologic oncology, gynecological surgery for both benign and malignant diseases, endoscopy (laparoscopy and hysteroscopy), endometriosis and uro-gynecology.

Main research activities

Our research activity is focused on the identification of biomarkers for the early diagnosis and prognosis of endometrial cancer, on the evaluation of the quality of life of patients affected by gynecological cancers and on the different chemotherapy schemes for cervical cancer. In collaboration with Yale University, we synthesized and characterized polylactico-glycolic-acid (PLGA) nanoparticles (NPs) modified with the carboxy-terminal-binding domain of CPE (c-CPE-NP) for the delivery of suicide gene therapy to chemotherapy-resistant ovarian cancer cells. Besides, with the George Mason University and the University of Arizona Cancer Center we explored the kinase-driven metabolic signalling in early and advanced epithelial ovarian cancers, and its role in tumor progression and response to carboplatin-paclitaxel treatment.

Main collaborations

- George Mason University, US
- University of Arizona Cancer Center, US

Most important publications

Luvero D., Plotti F., Aloisia A., Montera R., Terranova C., Carlo De Cicco Nardone, Scaletta G., Lopez S., Miranda A., Capriglione S., Gatti A., Pierluigi Benedetti Panici, Angioli R.

Ovarian cancer relapse: from the latest scientific evidence to the best practice.

Crit Rev Oncol Hematol. 2019 Aug;140: 28-38. PMID: 31176270. IF 5,012

Ovarian cancer (OC) is the fifth most common cause of cancer death in women worldwide. Despite treatment options have continued to improve in recent years, the recurrence rate is still high; in fact around 80% of patients relapses within 18 months. Recently, the scientific landscape is agree in asserting that the ovarian cancer is not a single disease but the outcome of patients depends from the molecular and biological characterization of tumor tissue. In this scenario, molecular targeted therapy given alone or in combination with chemotherapy is showing significant results. We review the different options for the treatment of ovarian cancer recurrence, including the role of surgery, in order to try outlining a possible treatment algorithm evaluating the recent scientific literature and the most important trials.

Zammataro L., Lopez S., Bellone S., Pettinella F., Bonazzoli E., Perrone E., Zhao S., Menderes G., Altwerger G., Han C., Zeybek B., Bianchi A., Manzano A., Manara P., Cocco E., Buza N., Hui P., Wong S., Ravaggi A., Bignotti E., Romani C., Todeschini P., Zanotti L., Odicino F., Pecorelli S., Donzelli C., Ardighieri L., Angioli R., Raspagliesi F., Scambia G., Choi J., Dong W., Bilguvar K., Aexandrov L.B., Silasi D.A., Huang G.S., Ratner E., Azodi M., Schwartz P.E., Pirazzoli V., Stiegler A.L., Boggon T.J., Lifton R.P., Schlessinger J., Santin A.D.

Whole-exome sequencing of cervical carcinomas identifies activating ERBB2 and PIK3CA mutations as targets for combination therapy.

Proc Natl Acad Sci U S A. 2019 Nov 5;116(45):22730-22736. PMID: 31624127. IF 9,58

The prognosis of advanced/recurrent cervical cancer patients remains poor. We analyzed 54 fresh-frozen and 15 primary cervical cancer cell lines, along with matched-normal DNA, by whole-exome sequencing (WES), most of which harboring Human-Papillomavirus-type-16/18. We found recurrent somatic missense mutations in 22 genes (including PIK3CA, ERBB2, and GNAS) and a widespread APOBEC cytidine deaminase mutagenesis pattern (TCW motif) in both adenocarcinoma (ACC) and squamous cell carcinomas (SCCs). Somatic copy number variants (CNVs) identified 12 copy number gains and 40 losses, occurring more often than expected by chance, with the most frequent events in pathways similar to those found from analysis of single nucleotide variants (SNVs), including the ERBB2/PI3K/AKT/mTOR, apoptosis, chromatin remodeling, and cell cycle. To validate specific SNVs as targets, we took advantage of primary cervical tumor cell lines and xenografts to preclinically evaluate the activity of pan-HER (afatinib and neratinib) and PIK3CA (copanlisib) inhibitors, alone and in combination, against tumors harboring alterations in the ERBB2/PI3K/AKT/mTOR pathway (71%). Tumors harboring ERBB2 (5.8%) domain mutations were significantly more sensitive to single agents afatinib or neratinib when compared to wild-type tumors in preclinical in vitro and in vivo models ($P = 0.001$). In contrast, pan-HER and PIK3CA inhibitors demonstrated limited in vitro activity and were only transiently effective in controlling in vivo growth of PIK3CA-mutated cervical cancer xenografts. Importantly, combinations of copanlisib and neratinib were highly synergistic, inducing long-lasting regression of tumors harboring alterations in the ERBB2/PI3K/AKT/mTOR pathway. These findings define the genetic landscape of cervical cancer, suggesting that a large subset of cervical tumors might benefit from existing ERBB2/PIK3CA/AKT/mTOR-targeted drugs.

Plotti F., Guzzo F., Schirò T., Terranova C., De Cicco Nardone C., Montera R., Luvero D., Scaletta G., Lopez S., Capriglione S., Benedetti Panici P., Angioli R.

Role of human epididymis protein 4 (HE4) in detecting recurrence in CA125 negative ovarian cancer patients.

Int J Gynecol Cancer. 2019 Apr 16. pii:ijgc-2019-000211. PMID: 30992329. IF 1,746

Objective: There are no current guidelines regarding evaluation of patients with normal CA125 at initial diagnosis during routine surveillance after completion of treatment. Thus, the purpose of this study was to evaluate the role of human epididymis protein 4 (HE4) in the detection of recurrence in patients with ovarian cancer and a negative CA125 at diagnosis. **Methods:** All patients with ovarian cancer with a negative CA125 referred to the Division of Gynecologic Oncology of the University Campus Bio-Medico of Rome were included in the study. Inclusion criteria were: age between 18 and 70 years old, diagnosis of epithelial ovarian cancer, optimal primary surgery (residual tumor <1 cm), and normal CA125 at initial diagnosis. Patients with other malignancies or chronic diseases were excluded from the study. Statistical analysis was based on the calculation of percentages, means, medians, and ranges of the values. **Results:** A total of eight patients were included in the study. The median age was 53 years (range 40-75). All patients had a normal CA125 at initial diagnosis while seven (87.5%) patients had abnormal HE4 levels at diagnosis. The International Federation of Gynecology and Obstetrics (FIGO) stages at enrollment varied from IC to IIIC (IB (1), IC (3), IIC (1), IIIC (3)). The most common histologic subtype was serous (62.5%). Seven patients recurred and had abnormal HE4 and normal CA125 values. The median HE4 at recurrence was 107 pmol/L. The median disease-free interval was 55 months (range 5-108) and all the patients underwent optimal cytoreductive surgery. **Conclusions:** HE4 levels may serve as a marker for recurrence in patients with a normal CA125 at initial diagnosis. Future studies are needed to evaluate the role of HE4 levels in earlier detection of recurrent ovarian cancer.

Heart Surgery

Department of Medicine and Surgery



Head M. Chello

Faculty M. Lusini

External Members F. Nappi, C. Spadaccio

Description

This research unit focuses both on clinical research and on basic, translational and surgical research in the field of cardiac surgery. Current and future research focuses on the clinical evaluation of patients undergoing adult cardiac surgery procedures, with regards to preoperative strategies to reduce complications. Also, intra-operative research on myocardial protection and early postoperative care play a pivotal role in the surgical outcomes and are under continuous development. The preclinical field of research, experienced in aging and in the development of bioresorbable scaffolds and biomaterials, offers parallelism with the clinical research by means of an introduction of materials and methods of research in the surgical scenario. A new area of research has been achieved in the field of safety during cardiac surgery. It is geared to develop a model for analysing and preventing the risk of electric microshock.

Main research activities

Research results focused on the effect of statin in postoperative atrial fibrillation and bleeding (unpublished results), development of an experimental model of the Ross operation and the effect of aging in conduction system. Collaborations with other departments within the institution, such as the Biomaterials and Bioengineering Dept., or other departments in other institutions (Centre Cardiologique du Nord, Golden Jubilee National Hospital) set the basis for ongoing researches. Current project include the evaluation of the heart rate variability in postoperative cardiac surgery patients to prevent atrial fibrillation and complications (submitted for PRIN), effect of statins in postoperative bleeding, degeneration of native and prosthetic aortic valve and their connections with pharmacologic approaches, the role of advanced glycation end products in aging and potential therapeutic approaches in cardiac surgery. In addition, myocardial protection with a detailed cardioplegia protocol comparison and intraoperative bleeding depending on preoperative treatment with newer anti-

platelet agents are currently under investigation. In the field of safety during cardiac surgery a study has been carried out that produced an interesting increase of knowledge, in partnership with Dept. of Astronautics, Electrical and Energetics Engineering of Sapienza University of Rome, Italy, and with the Dept. of Technological Innovations and Safety of Power Plants, Apparatus and Human Settlements of INAIL, Italy. The study provides a scientific method, based on quantitative data obtained by models, measurements and literature reviews, to assess the microshock risk during a real surgical intervention.

Main collaborations

- Dept. of Astronautics, Electrical and Energetics Engineering, Sapienza University of Rome, Rome, Italy
- Dept. of Technological Innovations and Safety of Power Plants, Apparatus and Human Settlements, INAIL, Italy

Most important publications

Nappi F., Lusini M., Avtaar Singh S.S., Santana O., Chello M., Mihos C.G.

Risk of ischemic mitral regurgitation recurrence after combined valvular and subvalvular repair.

Ann Thorac Surg. 2019 Aug;108(2):536-543. PMID: 30684477. IF 3,919

Background: Mitral valve repair (MVR) combined with papillary muscle approximation (PMA) may improve repair durability in severe ischemic mitral regurgitation (MR), when compared with MVR alone. We sought to identify preoperative transthoracic echocardiographic markers associated with MR recurrence after MVR with PMA. **Methods:** A post-hoc analysis was performed on patients with severe ischemic MR who underwent coronary artery bypass graft surgery with MVR with PMA in the papillary muscle approximation randomized trial. The PMA was performed utilizing a 4-mm polytetrafluoroethylene graft placed around the papillary muscles. Linear regression analyses and receiver-operating characteristic curves were used to identify echocardiographic variables and diagnostic models associated with recurrent MR. **Results:** There were 48 patients with a mean age of 63 ± 7 years, a left ventricular ejection fraction of $35\% \pm 5\%$, and a left ventricular end-diastolic diameter of 63 ± 3 mm. Of these, 37 patients had baseline and 5-year follow-up echocardiograms, with moderate-to-severe MR recurring in 27%. Linear regression analyses revealed associations between preoperative pulmonary artery systolic pressure (standardized beta coefficient, $\beta = 0.49/\text{mm Hg}$, $p = 0.002$), MV tenting area ($\beta = 0.47/\text{cm}^2$, $p = 0.004$), a symmetric MV tethering pattern ($\beta = 0.44$, $p = 0.007$), and left ventricular end-diastolic diameter ($\beta = 0.37/\text{mm}$, $p = 0.02$) with follow-up MR grade. The presence of both MV tenting area 3.1 cm^2 or greater (area under the curve 0.822) and left ventricular end-diastolic diameter of 64 mm or greater (area under the curve 0.801) was the most robust discriminative model for moderate-to-severe MR recurrence (specificity 92%, sensitivity 69%, area under the curve 0.804, $p = 0.003$). **Conclusions:** In patients undergoing coronary artery bypass graft surgery with MVR plus PMA, the extent of baseline MV apparatus and left ventricle geometric remodeling identifies patients at increased risk for MR recurrence.

Nappi F., Singh S.S.A., Lusini M., Nenna A., Gambardella I., Chello M.

The use of allogenic and autologous tissue to treat aortic valve endocarditis.

Ann Transl Med. 2019 Sep;7(18):491. PMID: 31700927 IF 3,689

The surgical treatment of aortic valve endocarditis (AVE) is generally performed using conventional mechanical or biological xenograft prosthesis, with limited use of aortic homograft (Ao-Homo) or pulmonary autograft (PA). Clinical evidence has demonstrated a clear contradiction between the proven benefits of Ao-Homo and PA in the context of infection and the very limited use of allogenic or autologous tissue in everyday clinical practice. This review aims to summarize the most recent and relevant literature in order to foster the scientific debate on the use of the use of allogenic and autologous tissue to treat AVE. The decisional process of the Heart Team should also include the preferences of the patient, his/her family, the general cardiologist or primary care physician. The use of allogenic or autologous valve substitute is beneficial if there is a high risk of recurrence of infection, avoiding extensive adhesiolysis and debridement of synthetic material. In any case, those procedures should be performed by highly trained centers to optimize outcomes.

Mastroianni C., Nenna A., Lebreton G., D'Alessandro C., Greco S.M., Lusini M., Leprince P., Chello M.

Extracorporeal membrane oxygenation as treatment of graft failure after heart transplantation.

Ann Cardiothorac Surg. 2019 Jan;8(1):99-108. PMID: 30854318. IF 2,895

Heart transplantation (HTx) is a valuable option in eligible patients with end-stage heart failure. The most significant complication in the immediate post-operative period is early graft failure (EGF), with a mean incidence of 20-25%. EGF is a major risk factor for death and accounts for 40-50% of early mortality after HTx. Despite the use of inotropes, EGF may persist and require temporary mechanical circulatory support. Extracorporeal membrane oxygenation (ECMO) has been investigated over the years and has proved to be a reliable strategy in patients with EGF after HTx. This study aims to review the contemporary literature on this topic. Considering short-term outcomes, 45-80% of patients were discharged alive from hospital. Duration of support is variable, with a mean duration of 4-8 days. Cannulation strategy and device selection have no differences with respect to short-term outcomes. The main causes of death are multi-organ failure, bleeding, heart failure, stroke and sepsis. Considering long-term outcomes, ECMO survivors appear to have similar survival rates to HTx patients who did not experience EGF. Also, ECMO-treated EGF, among survivors, has no detrimental effect for graft function. In conclusion, ECMO is a reliable therapeutic option to support patients with severe graft failure after HTx, providing adequate support with either central or peripheral arteriovenous cannulation. Further studies will be needed to establish the correct threshold for ECMO support and to provide long-term results.

Hematology, Stem Cell Transplantation, Transfusion Medicine and Cellular Therapy

Department of Medicine and Surgery



Head G. Avisati

Faculty M.C. Tirindelli, O. Annibali

Other Personnel L. Antonelli, D. Armiento, E. Cerchiara, E. Circhetta, M. De Muro, M. Di Cerbo, S. Ferraro, B. Giannetti, C. Gregorj, F. Landi, A.M. Morgia, C. Nobile, A. Pagano, S. Paolasini, C. Sarlo, A. Scardocci, S. Spurio, M.A. Tafari, V. Tomarchio

Description

The research unit is involved in several trials on the treatments of adult lymphoproliferative and myeloproliferative disorders and their main complications. Laboratory's Instrumentations to perform research activities are located in the University Hospital Blood Bank.

Main research activities

The unit participates in several clinical Trials, proposed by the following National and International cooperative Groups: FIL, IELSG, GIMEMA and SEIFEM. Moreover, as member of the Rome transplant network (RTN), performs autologous hematopoietic stem cells transplantation (HSC) and, in collaboration with the Urology Unit, has a leading national position in the treatment of severe resistant hemorrhagic cystitis, which may appear in these patients. Furthermore, in cooperation with the Orthopaedic and Trauma Surgery Unit, performs research studies on the use of platelet rich plasma in degenerative articular pathologies. In addition, the unit is deeply involved in the study of the kinetics of CECs in patients with Multiple Myeloma undergoing HSC and in collaboration with the Pathology Unit is involved in the study of new immune checkpoints pathway like TIGIT in Hodgkin Lymphoma. The Unit collaborates with the Computer Systems and Bioinformatics of this University to develop a mobile App for monitoring the side effects of treatments. The

head of the Unit has a leading international role in the treatment of acute promyelocytic leukemia and from January 2008 to December 2013 has served as a member of the editorial board of Blood (official journal of the American Society of Hematology).

Most important publications

Annibaldi O., Hohaus S., Marchesi F., Cantonetti M., Di Rocco A., Tomarchio V., Di Napoli A., Pelliccia S., Battistini R., Anticoli Borza P., Abruzzese E., Cenfra N., Andriani A., Tesei C., Alma E., Palombi F., Pupo L., Petrucci L., Becilli M., Maiolo E., Bellesi S., Cuccaro A, D'Alò F, Cox MC.

The neutrophil/lymphocyte ratio ≥ 3.5 is a prognostic marker in diffuse large B-cell lymphoma: a retrospective analysis from the database of the Italian regional network 'Rete Ematologica del Lazio per i Linfomi' (RELLI).

Leuk Lymphoma. 2019 Dec;60(14):3386-3394. PMID: 31259651. IF 2,674

In solid tumors and lymphomas, the neutrophil/lymphocyte (N/L) ratio at diagnosis has been shown to be a prognostic factor. The aim of our study was to validate the originally reported N/L ratio cut-point of 3.5 in patients with diffuse large B-cell lymphoma (DLBCL) registered in an Italian real-life database. The prognostic role of the N/L ratio at diagnosis on event-free survival (EFS) and overall survival (OS) was assessed in 505 patients with DLBCL. Patients with an N/L ratio < 3.5 ($n = 249$) had a 4-year EFS probability of 76% and OS probability of 86%, significantly higher than the 4 year EFS rate of 48% and OS rate of 64% in patients with N/L ratio ≥ 3.5 ($n = 256$, both $p < .0001$). The N/L ratio was an independent prognostic factor in the multivariate analysis including the IPI score, and could separate patients with a low/intermediate risk IPI (IPI < 3).

Sanz M.A., Fenaux P., Tallman M.S., Estey E.H., Löwenberg B., Naoe T., Lengfelder E., Döhner H., Burnett A.K., Chen S.J., Mathews V., Iland H., Rego E., Kantarjian H., Adès L., Avvisati G., Montesinos P., Platzbecker U., Ravandi F., Russell N.H., Lo-Coco F.

Management of acute promyelocytic leukemia: updated recommendations from an expert panel of the European LeukemiaNet.

Blood. 2019 Apr 11;133(15):1630-1643. PMID: 30803991. IF 16,601

Since the comprehensive recommendations for the management of acute promyelocytic leukemia (APL) reported in 2009, several studies have provided important insights, particularly regarding the role of arsenic trioxide (ATO) in frontline therapy. Ten years later, a European LeukemiaNet expert panel has reviewed the recent advances in the management of APL in both frontline and relapse settings in order to develop updated evidence- and expert opinion-based recommendations on the management of this disease. Together with providing current indications on genetic diagnosis, modern risk-adapted frontline therapy, and salvage treatment, the review contains specific recommendations for the identification and management of the most important complications such as the bleeding disorder APL differentiation syndrome, QT prolongation, and other all-trans retinoic acid- and ATO-related toxicities, as well as recommendations for molecular assessment of the response to treatment. Finally, the approach to special situations is also discussed, including management of APL in children, elderly patients, and pregnant women. The most important challenges remaining in APL include early death, which still occurs before and during induction therapy, and optimizing treatment in patients with high-risk disease.

Bove P., Iacovelli V., Tirindelli M.C., Bianchi D., Flammia G.P., Cipriani C., Ferraro A.S., Ferro M., Arcese W., Ingrosso G., Vespasiani G., Finazzi Agrò E.

Endoscopic intravesical fibrin glue application in the treatment of refractory hemorrhagic radiation cystitis: a single cohort pilot study.

J Endourol. 2019 Feb;33(2):93-98. PMID: 30280911. IF 2,267

Objective: To evaluate the clinical value of endoscopic fibrin glue (FG) application therapy in treating hemorrhagic radiation cystitis (HRC). **Patients and methods:** This is a single-cohort, prospective pilot study. We collected data from patients with HRC who were treated at our urology unit from May 2014 to December 2016. Patients with grade ≥ 2 HRC for whom conventional therapy and transurethral endoscopic electrocoagulation had failed were treated with endoscopic intravesical FG. The mean follow-up was 26.2 ± 9.78 months. Our analysis included data on patient demographics, pelvic malignancies, radiotherapy regimens, total dose of radiation received, time of onset and severity of hematuria, and previous intravesical management. Following FG intervention, patients' clinical status was defined as: (1) clinical response; absence of dysuria, urgency, and frequency; discontinuation of analgesic medication; and Foley catheter removal, but with ongoing hematuria grade < 2 ; (2) complete response, clinical response, and no further hematuria; or (3) no response, no clinical response, and sustained hematuria. **Results:** A total of 20 patients (12 women and 8 men; mean age, 69 ± 7.5 years) were treated with 12 mL FG intravesically, using endoscopic application. Of the 20 patients, 16 (80%) had a complete response and 4 (20%) had a clinical response. In the case of four patients (20%), treatment was carried out twice. Mean hospital stay was 6 ± 2.5 days. The intervention showed good tolerability in all patients. No major adverse events were reported. Bladder spasms were the only minor adverse events reported in six patients (30%). **Conclusion:** Application of FG is an effective, practical, affordable, and repeatable procedure for the treatment of grade ≥ 2 HRC.

Hygiene, Public Health and Statistics

Department of Medicine and Surgery



Head T. Petitti

Faculty A. Ianni

External Members A. Picchia (Fondazione don Carlo Gnocchi ONLUS)

Main research activities

Main research interests include:

- Methodological and operational support to the research units of the Faculty of Medicine and other national research institutions for the definition of the research protocol activities, collection and organization of data, analysis and presentation of results;
- Models data scouting and data analysis of hospital current database (management and clinical) with the objective of identifying useful indicators to management and clinicians.
- Evaluation of outcomes of innovative rehabilitative pathways (both in technological and organizational terms) in the field of subacute and chronic disability.

Main collaborations

- Department of Public Health, Section of Hygiene, Catholic University of the Sacred Heart, Italy
- Cattedra di Igiene, Cassino University, Italy

Most important publications

Mastroianni C., Ramon Codina M., D'Angelo D., Petitti T., Latina R., Casale G., Turrziani A., Piredda M., De Marinis M.G.

Palliative care education in undergraduate nursing curriculum in Italy.

J Hosp Palliat Nurs. 2019 Feb;*21*(1):96-103. PMID: 30608363. IF 0,708

Worldwide, more than 19 million people require palliative care because of an advanced stage of disease. Undergraduate nursing education should include palliative care as the European consensus suggests. In 2004, the European Society of Palliative Care issued a guide for the development of palliative nurse education in Europe. This study aims to describe the extension and characteristics of palliative care education within all of the nursing degree curricula in Italy, as well as to what extent their topics match the European Society of Palliative Care guide. A descriptive study was conducted through the universities web pages. For each degree, the curricula of the academic years from 2010 to 2014 were analyzed. Sixty percent of the curricula had formal education in palliative care, heterogeneously distributed in different courses and provided few compulsory and mandatory teaching hours. Data on clinical training suggested that education was essentially theoretical, with poor theory and practice integration. The increasing need for palliative care in different settings corresponds to increasing attention to nursing education in palliative care from the undergraduate level. The inclusion of palliative care teaching in universities at all levels of education and research development represent the future challenges for this discipline.

Ferrara P., Sannicandro V., Ianniello F., Quattrocchi E., Sbordone A., Petitti T., Mariotti P.

Attention-deficit/hyperactivity disorder and enuresis: a study about effectiveness of treatment with methylphenidate or desmopressin in a pediatric population.

Minerva Pediatr. 2019 Apr;*71*(2):135-138. PMID: 28260347. IF 0,832

Background: The aim of this study was to evaluate the effectiveness of treatment with methylphenidate or desmopressin (dDAVP) in patients with comorbid attention-deficit/hyperactivity disorder (ADHD) and enuresis. **Methods:** We enrolled 103 patients affected by ADHD and 125 patients with monosymptomatic nocturnal enuresis (NE). Data were collected between January 2014 and December 2015. The study was carried out in compliance with the Helsinki Declaration. **Results:** About children with ADHD, 9/103 (8.7%) were also suffering from NE; of those 8/9 followed treatment with methylphenidate and cognitive behavioral therapy. After 3 months 2/8 (25%, CI 95%: 8-65%) showed improvements, remaining 75% has been increased dosage of methylphenidate. After 6 months a response was achieved in 6/8 (75%, CI 95%: 35-96%) children and 1/8 was lost to follow-up. Furthermore the drug withdrawal showed a recurrence of symptoms both ADHD and NE in 1/7 (14.3%, CI 95%: 0.3-57%) vs. 6/7 (85.7%, CI 95%: 42-99%) that not presented recurrences. About children with NE enrolled at Campus Bio-Medico University it was found that 4/125 (3.8%) children were also suffering from ADHD; 3/4 (75%) treated with dDAVP and motivational therapy, of those 2/3 (66.7%, CI 95%: 9-99%) showed no improvements of symptoms vs. 1/3 (33.3%, CI 95%: 0.8-90%) that showed partial response with a reduction of wetnights. **Conclusions:** It is important the service of recruitment of patients with NE. In fact considering NE in a Child Neuropsychiatry Service where patients belong to a diagnosis of ADHD and NE is an incidental finding, this one is not considered as the addressee of treatment, but the therapy is directed to the neuro-behavioral problem using specific drugs and therapies, which are resolute in the enuretic disorder.

Nappo G., Capretti G.L., Petitti T., Gavazzi F., Ridolfi C., Cereda M., Montorsi M., Zerbi A.

The evolution of post-operative pancreatic fistula (POPF) classification: a single-center experience.

Pancreatology. 2019 Apr;19(3):449-455. PMID: 30890308. IF 3,241

Background: The ISGPS classification of post-operative pancreatic fistula (POPF) was recently revised, introducing the concept of biochemical leak (BL) which replaced grade A POPF. More recently, an additional distinction on three different subclasses for grade B (B1-B3) POPF was proposed. The aim of this study was to evaluate the impact of these modifications in clinical practice. **Methods:** All pancreatico-duodenectomies (PD) and distal pancreatectomies (DP) performed between 2010 and 2016 were retrospectively evaluated. Incidence and grade of POPF using the old and new ISGPS classification were evaluated. Three grade B subclasses (B1: maintenance of abdominal drain >3 weeks; B2: adoption of specific medical treatments for POPF; B3: use of radiological procedures) were evaluated for clinical severity. **Results:** A total of 716 patients (502 PD, 214 DP) were evaluated. The new ISGPS classification reduced the reported rate of POPF (30.7% vs 35.2% for PD, $p > 0.05$; 28% vs 44.9% for DP, $p < 0.05$), due to the abolition of grade A POPF. Grade B1, B2 and B3 rates were 3.1%, 73.8% and 23.1% in PD and 12.3%, 47.4% and 40.3% in DP, respectively. Passing from B1 to B3, significant increases in wound infection (0-40%), mean length of stay in PD (14.7-22.5 days; $p < 0.05$) and readmission rate in DP (0-39.1%) were observed. **Conclusions:** The new ISGPS classification significantly reduces the reported rate of POPF, particularly after DP. The three different grade B subclasses (B1-B3) better discriminate the severity of post-operative course, especially after PD.

Institute of Philosophy of Scientific and Technological Practice (FAST)

Department of Medicine and Surgery



Head L. Borghi

Other Personnel A. Marchetti, G. Mottini, M. Pennacchini

Board F. Keller, G. Tanzella-Nitti

Description

The Institute coordinates the University's Educational and research activities in the Humanities: Anthropology, Ethics, Aesthetics, Professional Ethics, General Bioethics, Clinical Bioethics, Moral Philosophy, Logic and Philosophy of Science, Forensic Medicine, History of Medicine, History of Science and Technology, Social Psychology and Social Medicine.

FAST's education and research are conducted via interdisciplinary work, carried out both within the borders of the Campus Bio-Medico University and in collaboration with other Institutions, aiming to foster the dialogue among philosophers, researchers and teachers of the various scientific and technological disciplines.

Main research activities

Luca Borghi

- Historical research on William Osler's relationship with Italy and Italian medicine.

Most important publications

Borghi L.

Osler and Italy. An intermittent love story.

Amazon KDP, 2019, pp. 190, ISBN: 9781701243002

William Osler (1849-1919) can be considered the 'noble father' of contemporary American medicine. As unquestioned leader of the early medical school at Johns Hopkins University in Baltimore, as author of one of the most appreciated and long-selling textbooks of internal medicine, *The Principles and Practice of Medicine*, and, through this book, the inspirer of the Rockefeller Institute for Medical Research in New York, his influence on twentieth century healthcare can hardly be exaggerated. This book explores, for the first time, William Osler's relationship with Italy and with Italian people - not only those in the medical field - from his early medical, scientific and literary connections with Italians to the three trips he made to the Bel Paese in the last years of his life. Even if Osler's esteem for Italian medicine in his times was somehow 'intermittent', he came to appreciate Italy more and more as time gave him the opportunity to experience the country and its inhabitants directly.

Creta A., Arigliani M., di Gioia G., Lapenna R., Quintarelli F., Fittipaldi M., Antinolfi V., Bettini R., Costanzo D., Cruciani A., Di Berardino S., Giorgino R., Satriano U., Mangiameli G., Sut D., Caricato M., Cogo P., Proclemer A., Mottini G., Lambiase P.D., Providência R.

Impact of ethnicity on the prevalence of early repolarization pattern in children: comparison between Caucasian and African populations.

Pediatr Cardiol. 2019 Dec;40(8):1553-1558. PMID: 31446474. 1,413

The patterns and prevalence of early repolarization pattern (ER) in pediatric populations from ethnic backgrounds other than Caucasian have not been determined. Black African children (ages 4-12) from north-west Madagascar were prospectively recruited and their ECGs compared with those of age- and sex-matched Caucasian ethnicity individuals. ER was defined by ≥ 0.1 mV J-point elevation in at least two contiguous inferior and/or lateral ECG leads. A total of 616 children were included. There was a trend toward a higher frequency of ER in the Africans compared to the Caucasians (23.3% vs. 17.1%, respectively, $p = 0.053$). The subtype (slurred vs. notched) and location of ER (lateral, inferior, or inferior-lateral) were significantly different in the two groups ($p < 0.001$ and $p = 0.020$, respectively). There was no significant difference in the number of high-risk ECG features of ERP (i.e., horizontal/descendent pattern, inferior or inferior-lateral location or J-waves ≥ 2 mm) between African and Caucasian children. On the multivariate analysis, African ethnicity was an independent predictive factor of ER (OR 3.57, 95% CI 2.04-6.25, $p < 0.001$). African children have an increased risk of ER compared to Caucasian counterparts. Future studies should clarify the clinical and prognostic significance of ER in the pediatric population, and whether ethnicity has an impact on the outcomes.

Borghi L.

Il Codice Lauri nella storia del "Trattato della Pittura".

In: Ghilardi G., Morini S., Tambone V. (a cura di) Codice Lauri. Apografo del Trattato della Pittura di Leonardo da Vinci. Edizioni LSWR, 2019. ISBN 978-88-6895-783-4

Internal Medicine and Hepatology

Department of Medicine and Surgery



Head A. Picardi

Faculty U. Vespasiani Gentilucci

Other Personnel A. De Vincentis, G. Galati, P. Gallo

Description

Independent and collaborative studies embody the main interests of our clinical research Unit. Poly-pathology and therapy, together with drug interactions are main issues in the ongoing collaborative REPOSI study, promoted and coordinated by the Italian Society of Internal Medicine (SIMI). Liver diseases due to metabolic derangements - namely non-alcoholic steatohepatitis (NASH) - or primary biliary cholangitis (PBC) are the purpose of international controlled trials on innovative drug treatments. Other collaborations are set with the Italian society for liver disease (AISF) and with the Club of the Hospital Hepatologist (CLEO), a scientific society with a wide national diffusion. Main scientific collaborations involve other Units from our University; the Department of Molecular and Clinical Medicine, University of Gothenburg, Sweden; the University of Navarra, Spain; IRCCS Bambino Gesù Paediatric Hospital, Italy, and the University of Rome "Tor Vergata", Italy.

Main research activities

Main research results of our Unit regard the demonstration of the efficacy of obeticholic acid in the treatment of NASH, from the interim analysis of an international phase 3 trial. In a cohort study, we highlighted drug interactions that may affect frail elders admitted in internal medicine units and that concern drugs - mainly cardiovascular - of very common use. Finally, the analysis of clinical studies published by other groups allowed us to express an expert opinion on the incidence of HCC in patients with chronic HCV liver disease treated with the new direct antiviral drugs, denying an alarm raised on the increased incidence of HCC in patients recovered from viral infection. Another study on HCC in metabolic liver disease in patients treated or not with metformin stressed the involvement of SIRT-3 and p-mTOR in metabolic dysfunctions occurring in these patients, suggesting SIRT-3 and HIF-1 α as predictors of prognosis, and p-mTOR as target for the treatment of advanced HCC.

Most important publications

Younossi Z.M., Ratziu V., Loomba R., Rinella M., Anstee Q.M., Goodman Z., Bedossa P., Geier A., Beckebaum S., Newsome P.N., Sheridan D., Sheikh M.Y., Trotter J., Knapp W., Lawitz E., Abdelmalek M.F., Kowdley K.V., Montano-Loza A.J., Boursier J., Mathurin P., Bugianesi E., Mazzella G., Oliveira A., Cortez-Pinto H., Graupera I., Orr D., Gluud L.L., Dufour J.F., Shapiro D., Campagna J., Zaru L., MacConell L., Shringarpure R., Harrison S., Sanyal A.J.; [Vespasiani-Gentilucci U.] REGENERATE Study Investigators.

Obeticholic acid for the treatment of non-alcoholic steatohepatitis: interim analysis from a multicentre, randomised, placebo-controlled phase 3 trial.

Lancet. 2019 Dec 14;394(10215):2184-2196. PMID: 31813633. IF 59,102

Non-alcoholic steatohepatitis (NASH) is a chronic liver disease that can lead to cirrhosis. Obeticholic acid, a farnesoid X receptor agonist, has been shown to improve the histological features of NASH. Here we report results from a planned interim analysis of a phase 3 study of obeticholic acid for NASH. The fibrosis improvement endpoint was achieved by 37 (12%) patients in the placebo group, 55 (18%) in the obeticholic acid 10 mg group ($p=0.045$), and 71 (23%) in the obeticholic acid 25 mg group ($p=0.0002$). The overall safety profile was similar to that in previous studies. Obeticholic acid 25 mg significantly improved fibrosis and key components of NASH disease activity among patients with NASH.

Gallo P., De Vincentis A., Pedone C., Nobili A., Tettamanti M., Vespasiani Gentilucci U., Picardi A., Mannucci P.M., Incalzi R.A.; REPOSI Investigators.

Drug-drug interactions involving CYP3A4 and p-glycoprotein in hospitalized elderly patients.

Eur J Intern Med. 2019 Jul; 65:51-57. PMID: 31084979. IF 3,66

Polypharmacy is common and could associate with drug interactions. Cytochrome P450 (notably 3A4 subtype) is a key enzyme in most drug metabolism; P-glycoprotein (P-gp) is a transporter influencing drug distribution & bioavailability. We assessed prevalence and patterns of interactions in a hospitalized elder's cohort (REPOSI) exposed to at least two interacting drugs at admission, during hospitalization and at discharge. The most frequent interactions were amiodarone-statin for CYP3A4 and atorvastatin-verapamil-diltiazem for P-gp. Hospital admission is associated with an increased prevalence of drug interaction. Educational strategies and appropriate use of dedicated software seem desirable.

Galati G., Muley M., Viganò M., Iavarone M., Vitale A., Dell'Unto C., Lai Q., Cabibbo G., Sacco R., Villa E., Trevisani F.

Occurrence of hepatocellular carcinoma after direct-acting antiviral therapy for hepatitis C virus infection: literature review and risk analysis.

Expert Opin Drug Saf. 2019 Jul;18(7):603-610. PMID: 31067134. IF 3,22

Concerns raised on a high occurrence of HCC after successful treatment of CHC by direct-acting antivirals (DAAs). The introduction of all-oral DAAs has substantially changed the scenario of CHC, achieving a sustained virological response in >90% of cases. Concerns raised about an increasing incidence of HCC post-DAAs were flawed by heterogeneity, limited number of well-designed prospective studies and inclusion of patients with advanced liver disease (excluded from interferon-based studies). Actually, current data on DAAs have shown a lower risk of HCC development; even if unable to identify patients at greater risk for HCC after SVR. Surveillance strategy is mandatory in these patients.

Measurements and Biomedical Instrumentation

Department of Engineering

**Head** S. Silvestri**Faculty** C. Massaroni, E. Schena**Other Personnel** A. Carnevale, J. Di Tocco, D. Lo Presti, R. Sabbadini, M. Zaltieri

Description

The Research Unit scientific activity is mainly focused on measurements and measurement systems for clinical diagnostics and applied to human wellbeing.

In particular, the research activity focuses on the development of novel sensors and measurement systems for measuring forces, gas flow-rate, cardiac output, temperature, human motion, optical absorption and respiratory parameters. The research unit realized instruments for the respiratory simulation and performance testing of artificial ventilators and optoelectronic systems dedicated to respiratory mechanics along with uncertainty evaluation. Researches are carried out on novel modalities and procedures to obtain measurements and/or information from physio-pathological processes, opto-mechanical variables, wearable system for vital signs monitoring, flexible sensors, performance assessment and quality evaluation of medical instruments and their clinical efficacy with a particular emphasis on non-invasive processes.

Main research activities

The research activity has been focused on innovative methods to obtain a temperature map of organs by means of invasive and contactless methods, innovative MR-compatible optical fibre sensors for medical applications, wearable systems for vital signs monitoring and experimental estimation of tissue optical properties for modelling laser-tissue interaction. During the last two years, five research projects have been funded by national and international agencies.

Most important publications

Massaroni C., Di Tocco J., Lo Presti D., Longo U.G., Miccinilli S., Sterzi S., Formica D., Saccomandi P., Schena E.

Smart textile based on piezoresistive sensing elements for respiratory monitoring.

IEEE Sensors J. 2019;19(17):7718-7725. DOI: 10.1109/JSEN.2019.2917617 IF 3,076

Wearable systems are gaining large interest in applications related to the monitoring of physiological parameters. Piezoresistive strain sensors are a valid option to develop wearables for several medical applications. Among them, respiratory monitoring can be performed by recording chest movements. The aim of this paper is threefold: 1) the experimental assessment of elastic piezoresistive textile; 2) the influence of length and width on piezoresistive response; and 3) the use of these elements to develop a smart textile (ST) for respiratory monitoring. The ST consists of six piezoresistive elements. The static calibration and the hysteresis analysis were carried out to assess the characteristics of the piezoresistive elements. The feasibility assessment of the ST for respiratory monitoring was performed on four healthy volunteers under two conditions (i.e., quiet breathing and tachypnea). Respiratory frequency values were estimated by the ST and compared with the ones gathered by means of a reference system (i.e., a motion capture system). Length and width influence both the sensitivity and hysteresis of the piezoresistive element. Regarding the ST performance, good agreement with data provided by the reference system was found. Indeed, results obtained by considering the output of single sensing elements and their sum were promising: The difference between the average respiratory frequency was always lower than 1% and 4% during quiet breathing and tachypnea, respectively. The proposed ST seems to be suitable for respiratory frequency monitoring in a wide range of values, where unobtrusiveness is of great value.

Carnevale A., Longo U.G., Schena E., Massaroni C., Lo Presti D., Berton A., Candela V., Denaro V.

Wearable systems for shoulder kinematics assessment: a systematic review.

BMC Musculoskelet Disord. 2019 Nov 15;20(1):546. PMID: 31731893. IF 2,002

Background: Wearable sensors are acquiring more and more influence in diagnostic and rehabilitation field to assess motor abilities of people with neurological or musculoskeletal impairments. The aim of this systematic literature review is to analyze the wearable systems for monitoring shoulder kinematics and their applicability in clinical settings and rehabilitation. **Methods:** A comprehensive search of PubMed, Medline, Google Scholar and IEEE Xplore was performed and results were included up to July 2019. All studies concerning wearable sensors to assess shoulder kinematics were retrieved. **Results:** Seventy-three studies were included because they have fulfilled the inclusion criteria. The results showed that magneto and/or inertial sensors are the most used. Wearable sensors measuring upper limb and/or shoulder kinematics have been proposed to be applied in patients with different pathological conditions such as stroke, multiple sclerosis, osteoarthritis, rotator cuff tear. Sensors placement and method of attachment were broadly heterogeneous among the examined studies. **Conclusions:** Wearable systems are a promising solution to provide quantitative and meaningful clinical information about progress in a rehabilitation pathway and to extrapolate meaningful parameters in the diagnosis of shoulder pathologies. There is a strong need for development of this novel technologies which undeniably serves in shoulder evaluation and therapy.

Massaroni C., Lo Presti D., Formica D., Silvestri S., Schena E.

Non-contact monitoring of breathing pattern and respiratory rate via RGB signal measurement.

Sensors (Basel). 2019 Jun 19;19(12):2758. PMID: 31248200. IF 3,031

Among all the vital signs, respiratory rate remains the least measured in several scenarios, mainly due to the intrusiveness of the sensors usually adopted. For this reason, all contactless monitoring systems are gaining increasing attention in this field. In this paper, we present a measuring system for contactless measurement of the respiratory pattern and the extraction of breath-by-breath respiratory rate. The system consists of a laptop's built-in RGB camera and an algorithm for post-processing of acquired video data. From the recording of the chest movements of a subject, the analysis of the pixel intensity changes yields a waveform indicating respiratory pattern. The proposed system has been tested on 12 volunteers, both males and females seated in front of the webcam, wearing both slim-fit and loose-fit t-shirts. The pressure-drop signal recorded at the level of nostrils with a head-mounted wearable device was used as reference respiratory pattern. The two methods have been compared in terms of mean of absolute error, standard error, and percentage error. Additionally, a Bland–Altman plot was used to investigate the bias between methods. Results show the ability of the system to record accurate values of respiratory rate, with both slim-fit and loose-fit clothing. The measuring system shows better performance on females. Bland–Altman analysis showed a bias of -0.01 breaths·min $^{-1}$, with respiratory rate values between 10 and 43 breaths·min $^{-1}$. Promising performance has been found in the preliminary tests simulating tachypnea.

Medical Statistics and Molecular Epidemiology

Department of Medicine and Surgery



Head M. Ciccozzi

Faculty C. Leuter,

Other Personnel S. Fabris, M. Giovanetti, L. Navarini, M. Testi

External Members I. Alexiev, M. Baimakova, R. Bazzardi, F. Benedetti, A. Borsetti, G. Ceccarelli, A. B. Demir, R.C. Gallo, B. Mugosa, C. Sagnelli, M. Salemi, G. el Sawaf, D. Zella

Description

The research unit is actively interested in research studies aimed to investigate epidemics and nosocomial infection biomarkers involved in the diagnosis and prognosis of communicable and non-communicable disease. Further fields of research included the molecular evolution of microorganisms causing important epidemic in Italy as well as worldwide (pandemic) and the antimicrobial resistant microorganisms circulating in nosocomial setting. Furthermore, the activity of the research unit was extended also to the evaluation of public health in migrants subjects. The statistical analysis is also extended to different research groups in Italy in different studies. Mathematical Model studies on infectious diseases (epidemic and pandemic) are also one of the topics of this unit.

Main research activities

In the year 2019, the most important activities developed by the research unit have been in the areas of evolution of infectious disease and antibiotic resistance. Statistical collaboration and epidemiology has been established with several Unit of Internal medicine, Surgery and Geriatrics of the University Hospital Campus Bio-Medico. Migrants has been an important chapter for epidemiological research, developing epidemiological surveillance system in different center for Migrants where agreement has been signed (CARA Centre of Castelnuovo di Porto and Rocca di Papa). The results of the surveillance reported in some publication on international peer-reviewed scientific journals. The unit have been also participate in resolving epidemics in Italy (Chikungunya) so as worldwide as reported in some publications. Other important agreement have been continued since 2015 with the Public Health Institute of Montenegro, the Public Institute of Bulgaria (Sofia) and with the Department of Pathology and Laboratory medicine of the University

of Florida, Gainesville, USA. By these agreements, several scientific publications on international and peer-reviewed journals have been published and new scientific collaborations are ongoing. Moreover we are also consultant for WHO for nosocomial surveillance system in Montenegro. We are also finalized scientific agreement with the University of Izmir (Turkey) and of Alessandria of Egypt for study epidemics and nosocomial infection. The unit published in 2019 about 30 articles in international journals. This Unit started to follow in 2019 December the Sars Cov2 pandemic and at the end of August published more than 25 articles on this issue (53 in total in seven months).

Main collaborations

- Human Virology Institute of Baltimore, US
- Public Health Institute of Montenegro
- Public Institute of Bulgaria, Sofia, Bulgaria
- University of Alessandria, Egypt
- University of Florida, Gainesville, US
- University of Izmir, Turkey

Most important publications

Ciotti M., Angeletti S., Minieri M., Giovannetti M., Benvenuto D., Pascarella S., Sagnelli C., Bianchi M., Bernardini S., Ciccozzi M.

COVID-19 outbreak: an overview.

Chemotherapy. 2019; 64(5-6):215-223. PMID: 32259829 IF 1,571

In late December 2019, Chinese health authorities reported an outbreak of pneumonia of unknown origin in Wuhan, Hubei Province. A few days later, the genome of a novel coronavirus was released (<http://virological.org/t/novel-2019-coronavirus-genome/319>; Wuhan-Hu-1, GenBank accession No. MN908947) and made publicly available to the scientific community. This novel coronavirus was provisionally named 2019-nCoV, now SARS-CoV-2 according to the Coronavirus Study Group of the International Committee on Taxonomy of Viruses. SARS-CoV-2 belongs to the Coronaviridae family, Betacoronavirus genus, subgenus Sarbecovirus. Since its discovery, the virus has spread globally, causing thousands of deaths and having an enormous impact on our health systems and economies. In this review, we summarize the current knowledge about the epidemiology, phylogenesis, homology modeling, and molecular diagnostics of SARS-CoV-2. Phylogenetic analysis is essential to understand viral evolution, whereas homology modeling is important for vaccine strategies and therapies. Highly sensitive and specific diagnostic assays are key to case identification, contact tracing, identification of the animal source, and implementation of control measures.

Lo Presti A., Zorzi F., Del Chierico F., Altomare A., Cocca S., Avola A., De Biasio F., Russo A., Cella E., Reddel S., Calabrese E., Biancone L., Monteleone G., Cicala M., Angeletti S., Ciccozzi M., Putignani L., Guarino M.P.L.

Fecal and mucosal microbiota profiling in irritable bowel syndrome and inflammatory bowel disease.

Front Microbiol. 2019 Jul 17;10: 1655. PMID: 31379797. IF 4,259

An imbalance in the bacterial species resulting in the loss of intestinal homeostasis has been described in inflammatory bowel diseases (IBD) and irritable bowel syndrome (IBS). In this prospective study, we investigated whether IBD and IBS patients exhibit specific changes in richness and distribution of fecal and mucosal-associated microbiota. Additionally, we assessed potential 16S rRNA gene amplicons biomarkers for IBD, IBS, and controls (CTRLs) by comparison of taxonomic composition. The relative abundance of bacteria, at phylum and genus/species levels, and the bacterial diversity were determined through 16S rRNA sequence-based fecal and mucosal microbiota analysis. Linear discriminant analysis effect size (LEfSe) was used for biomarker discovery associated to IBD and IBS as compared to CTRLs. In fecal and mucosal samples, the microbiota richness was characterized by a microbial diversity reduction, going from CTRLs to IBS to IBD. β -diversity analysis showed a clear separation between IBD and CTRLs and between IBD and IBS with no significant separation between IBS and CTRLs. β -diversity showed a clear separation between mucosa and stool samples in all the groups. In IBD, there was no difference between inflamed and not inflamed mucosa. Based upon the LEfSe data, the Anaerostipes and Ruminococcaceae were identified as the most differentially abundant bacterial taxa in CTRLs. Erysipelotrichi was identified as potential biomarker for IBS, while Gammaproteobacteria, Enterococcus, and Enterococcaceae for IBD. This study provides an overview of the alterations of microbiota and may aid in identifying potential 16S rRNA gene amplicons mucosal biomarkers for IBD and IBS.

Lo Presti A., Del Chierico F., Altomare A., Zorzi F., Cella E., Putignani L., Guarino M.P.L., Monteleone G., Cicala M., Angeletti S., Ciccozzi M.

Exploring the genetic diversity of the 16S rRNA gene of *Akkermansia muciniphila* in IBD and IBS.

Future Microbiol. 2019 Nov; 14:1497-1509. PMID: 31850811. IF 2,746

Aim: The human gastrointestinal tract harbors diverse, abundant microbiota and *Akkermansia muciniphila* is involved in this community. The aim of this study is to characterize 16 new *A. muciniphila* 16S ribosomal RNA sequences selected from a metagenomic database from stools of patients with irritable bowel syndrome (IBS), inflammatory bowel diseases and control (CTRLs) subjects by a phylogenetic approach. **Materials & methods:** A phylogenetic approach was used to study the genetic diversity and SNPs in 16 *A. muciniphila* 16S ribosomal RNA sequences from stools of 107 individuals, 36 of which were patients affected by IBS, 30 by inflammatory bowel disease and 41 were CTRLs. **Results:** Phylogenetic analysis confirmed the subdivision into different supported clusters. An increase of variability in IBS has been identified. **Conclusion:** The genetic variation combined to the relative abundance, contribute to the protective role of *A. muciniphila*. Phylogenesis represent an additional approach to investigate genetic variability.

Microscopic and Ultrastructural Anatomy

Department of Medicine and Surgery



Head S. Morini

Faculty S. Carotti, F. Zalfa

Other Personnel M. Francesconi, V. Panasiti, L. Sancillo, M. Zingariello

External Members F. Cimini

Description

The Microscopic and Ultrastructural Anatomy Unit applies techniques for morphological and molecular analysis of cells and tissues with particular reference to the digestive system and blood. The main research fields are the study of the liver diseases, focusing on the morphological features and molecular mechanisms of hepatic fibrogenesis and carcinogenesis. Structural and ultrastructural features, gene expression and post-transcriptional regulation mechanisms are investigated using advanced technologies. Also, the history of anatomical illustration and its relevance for the history of medicine was addressed by the research unit.

Main research activities

Histo-morphology of liver tissue, biochemical serological parameters, cellular and molecular biology techniques and the genetic signatures have been used in order to identify factors connecting liver inflammation and fibrosis during non-tumoral liver diseases. The effects of disease-associated variants at different loci to multiply the risk of NAFLD and NASH-cirrhosis have been evaluated.

By applying immunohistochemistry and immunofluorescence on specimens from patients with blood malignancies, the role of neo-angiogenesis, fibrosis and differentiation factors in bone medullary tissue have been investigated.

Most important publications

Eran Z., Zingariello M., Bochicchio M.T., Bardelli C., Migliaccio A.R.

Novel strategies for the treatment of myelofibrosis driven by recent advances in understanding the role of the microenvironment in its etiology.

F1000Res. 2019 Sep 19;8. pii: F1000 Faculty Rev-1662. PubMed PMID: 31583083.

Myelofibrosis is the advanced stage of the Philadelphia chromosome-negative myeloproliferative neoplasms (MPNs), characterized by systemic inflammation, hematopoietic failure in the bone marrow, and development of extramedullary hematopoiesis, mainly in the spleen. The only potentially curative therapy for this disease is hematopoietic stem cell transplantation, an option that may be offered only to those patients with a compatible donor and with an age and functional status that may face its toxicity. By contrast, with the Philadelphia-positive MPNs that can be dramatically modified by inhibitors of the novel BCR-ABL fusion-protein generated by its genetic lesion, the identification of the molecular lesions that lead to the development of myelofibrosis has not yet translated into a treatment that can modify the natural history of the disease. Therefore, the cure of myelofibrosis remains an unmet clinical need. However, the excitement raised by the discovery of the genetic lesions has inspired additional studies aimed at elucidating the mechanisms driving these neoplasms towards their final stage. These studies have generated the feeling that the cure of myelofibrosis will require targeting both the malignant stem cell clone and its supportive microenvironment. We will summarize here some of the biochemical alterations recently identified in MPNs and the novel therapeutic approaches currently under investigation inspired by these discoveries.

Zingariello M., Bardelli C., Sancillo L., Ciaffoni F., Genova M.L., Girelli G., Migliaccio A.R.

Dexamethasone predisposes human erythroblasts toward impaired lipid metabolism and renders their ex vivo expansion highly dependent on plasma lipoproteins.

Front Physiol. 2019 Apr 4; 10:281. PubMed PMID: 31019464. IF 3,201

Cultures of stem cells from discarded sources supplemented with dexamethasone, a synthetic glucocorticoid receptor agonist, generate cultured red blood cells (cRBCs) in numbers sufficient for transfusion. According to the literature, however, erythroblasts generated with dexamethasone exhibit low enucleation rates giving rise to cRBCs that survive poorly in vivo. The knowledge that the glucocorticoid receptor regulates lipid metabolism and that lipid composition dictates the fragility of the plasma membrane suggests that insufficient lipid bioavailability restrains generation of cRBCs. To test this hypothesis, we first compared the expression profiling of erythroblasts generated with or without dexamethasone. This analysis revealed differences in expression of 55 genes, 6 of which encoding proteins involved in lipid metabolism. These were represented by genes encoding the mitochondrial proteins 3-Hydroxymethyl-3-Methylglutaryl-CoA lyase, upregulated, and 3-Oxoacid CoA-Transferase1 and glycerol-3-phosphate acyltransferase1, both downregulated, and the proteins ATP-binding cassette transporter1 and Hydroxysteroid-17-Beta-Dehydrogenase7, upregulated, and cAMP-dependent protein kinase catalytic subunit beta, downregulated. This profiling predicts that dexamethasone, possibly by interfering with mitochondrial functions, impairs the intrinsic lipid metabolism making the synthesis of the plasma membrane of erythroid cells depend on lipid-uptake from external sources. Optical and electron microscopy analyses confirmed that the mitochondria of erythroblasts generated with dexamethasone are abnormal and that their plasma membranes present pebbles associated with membrane ruptures releasing exosomes and microvesicles. These results indicate that the lipid supplements of media currently available are not adequate for cRBCs. To identify better lipid supplements, we determined the number of erythroblasts generated in synthetic media supplemented with either currently used liposomes or with lipoproteins purified from human plasma [the total lipoprotein fraction (TL) or its high (HDL), low (LDL) and very low (VLDL) density lipoprotein components]. Both LDL and VLDL generated numbers of erythroid cells 3-2-fold greater than that observed in controls. These greater numbers were associated with 2-3-fold greater amplification of erythroid cells due both to increased proliferation and to resistance to stress-induced death. In conclusion, dexamethasone impairs lipid metabolism making ex vivo expansion of erythroid cells highly dependent on lipid absorbed from external sources and the use of LDL and VLDL as lipid supplements improves the generation of cRBCs.

Di Stefano N., Ghilardi G., Morini S.

The cerebral ventricles in Leonardo's anatomical drawings.

Lancet. 2019 Apr 6;393(10179):1412. PubMed PMID: 30967209. IF 59,102

Fascinated with questions about the origin of life, Leonardo da Vinci (1452–1519) was captivated by the brain. The brain was perceived at that time to be the house of the principle of life (ie, the soul was thought to reside at the geometrical centre of the brain). Evidence of the evolution of Leonardo's knowledge about the organisation of the brain can be seen in the comparison of two drawings.

Molecular Medicine and Biotechnology

Department of Medicine and Surgery



Head V.M. Fazio

Other Personnel M. Costantini, F. Picardo, S. Virga

External Members M. De Robertis, M.L. Poeta, E. Signori

Description

The permanent staff is composed only by VM Fazio and S Virga. Researchers from other University (MLP) and CNR (ES, MD) actively cooperate both on research projects and the didactic activities.

Residents (Scuola di Specializzazione in Patologia Clinica e Biochimica Clinica): Angela Pantalone, Marta Fogolari, Marco Vicari, Maria Francesconi, Annamaria Puglielli, Francesco Romano, Maria Carmina Manzorra.

Main research activities

The specific competences of the RU are focused on molecular genetics and epigenetics; development of in vitro and in vivo cancer models; in vitro and in vivo gene transfer; histopathology technologies; cytofluorimetric analysis and cell sorting; bioinformatics and biostatistics studies in collaboration with leading groups.

Three main projects are in development:

- Study of the leading epigenetic and genetic mechanisms that control the reprogramming of stem cells during the first phases of carcinogenesis and the cancer progression, in the two-way connection with the microenvironment, including exosomes and circulating nucleic acids;
- Intra- and inter- tumor heterogeneity, tumor cell subpopulations, phylogenetics evolution of tumor in the course of cancer progression;
- Study of genetic and epigenetic biomarkers for the development of multilevel genomics-based

cancer taxonomy, prediction of cancer progression, response to therapy and metastasization (renal, colorectal, lung, breast tumors).

Most important publications

Muscarella L.A., Fabrizio F.P., De Bonis M., Mancini M.T., Balsamo T., Graziano P., Centra F., Sparaneo A., Trombetta D., Bonfitto A., Scagliusi V., Larizza P., Capoluongo E.D., Fazio V.M.

Automated workflow for somatic and germline next generation sequencing analysis in routine clinical cancer diagnostics.

Cancers (Basel). 2019 Oct 30;11(11):1691. PMID: 31671666. IF 6,162

Thanks to personalized medicine trends and collaborations between industry, clinical research groups and regulatory agencies, next generation sequencing (NGS) is turning into a common practice faster than one could have originally expected. When considering clinical applications of NGS in oncology, a rapid workflow for DNA extraction from formalin-fixed paraffin-embedded (FFPE) tissue samples, as well as producing high quality library preparation, can be real challenges. Here we consider these targets and how applying effective automation technology to NGS workflows may help improve yield, timing and quality-control. We firstly evaluated DNA recovery from archived FFPE blocks from three different manual extraction methods and two automated extraction workstations. The workflow was then implemented to somatic (lung/colon panel) and germline (BRCA1/2) library preparation for NGS analysis exploiting two automated workstations. All commercial kits gave good results in terms of DNA yield and quality. On the other hand, the automated workstation workflow has been proven to be a valid automatic extraction system to obtain high quality DNA suitable for NGS analysis (lung/colon Ampli-seq panel). Moreover, it can be efficiently integrated with an open liquid handling platform to provide high-quality libraries from germline DNA with more reproducibility and high coverage for targeted sequences in less time (BRCA1/2). The introduction of automation in routine workflow leads to an improvement of NGS standardization and increased scale up of sample preparations, reducing labor and timing, with optimization of reagents and management.

Picardo F., Romanelli A., Muinelo-Romay L., Mazza T., Fusilli C., Parrella P., Barbazán J., Lopez-López R., Barbano R., De Robertis M., Taffon C., Bordoni V., Agrati C., Costantini M., Ricci F., Graziano P., Maiello E., Muscarella L.A., Fazio V.M., Poeta M.L.

Diagnostic and prognostic value of b4galt1 hypermethylation and its clinical significance as a novel circulating cell-free DNA biomarker in colorectal cancer.

Cancers (Basel). 2019 Oct 19;11(10):1598. PMID: 31635093. IF 6,162

Epigenetic modifications of glyco-genes have been documented in different types of cancer and are tightly linked to proliferation, invasiveness, metastasis, and drug resistance. This study aims to investigate the diagnostic, prognostic, and therapy-response predictive value of the glyco-gene B4GALT1 in colorectal cancer (CRC) patients. A Kaplan-Meier analysis was conducted in 1418 CRC patients (GEO and TCGA datasets) to assess the prognostic and therapy-response predictive values of the aberrant expression and methylation status of B4GALT1. Quantitative methylation-specific PCR (QMSP) and droplet digital quantitative methylation-specific PCR (dd-QMSP) were respectively used to detect hypermethylated B4GALT1 in metastasis and plasma in four cohorts of metastatic CRC cases (mCRC). Both the downregulated expression and promoter hypermethylation of B4GALT1 have a negative prognostic impact on CRC. Interestingly a low expression level of B4GALT1 was significantly associated with poor cetuximab response (progression-free survival (PFS) $p = 0.01$) particularly in wild-type (WT)-KRAS patients ($p = 0.03$). B4GALT1 promoter was aberrantly methylated in liver and lung metastases. The detection of hypermethylated B4GALT1 in plasma of mCRC patients showed a highly discriminative receiver operating characteristic (ROC) curve profile (area under curve (AUC) value 0.750; 95% CI: 0.592-0.908, $p = 0.008$), clearly distinguishing mCRC patients from healthy controls. Based on an optimal cut-off value defined by the ROC analysis, B4GALT1 yield a 100% specificity and a 50% sensitivity. These data support the potential value of B4GALT1 as an additional novel biomarker for the prediction of cetuximab response, and as a specific and sensitive diagnostic circulating biomarker that can be detected in CRC.

Fabrizio F.P., Sparaneo A., Centra F., Trombetta D., Storlazzi C.T., Graziano P., Maiello E., Fazio V.M., Muscarella L.A.

Methylation density pattern of KEAP1 gene in lung cancer cell lines detected by quantitative methylation specific PCR and pyrosequencing.

Int J Mol Sci. 2019 May 31;20(11):2697. PMID: 31159323. IF 4, 183

Background: The KEAP1/NRF2 pathway is the key regulator of antioxidants and cellular stress responses, and is implicated in neoplastic progression and resistance of tumors to treatment. KEAP1 silencing by promoter methylation is widely reported in solid tumors as part of the complex regulation of the KEAP1/NRF2 axis, but its prognostic role remains to be addressed in lung cancer.

Methods: We performed a detailed methylation density map of 13 CpGs located into the KEAP1 promoter region by analyzing a set of 25 cell lines from different histologies of lung cancer. The methylation status was assessed using quantitative methylation specific PCR (QMSP) and pyrosequencing, and the performance of the two assays was compared. **Results:** Hypermethylation at the promoter region of the KEAP1 was detected in one third of cell lines and its effect on the modulation KEAP1 mRNA levels was also confirmed by in vitro 5-Azacytidine treatment on lung carcinoid, small lung cancer and adenocarcinoma cell lines. QMSP and pyrosequencing showed a high rate of concordant results, even if pyrosequencing revealed two different promoter CpGs sub-islands (P1a and P1b) with a different methylation density pattern. **Conclusions:** Our results confirm the effect of methylation on KEAP1 transcription control across multiple histologies of lung cancer and suggest pyrosequencing as the best approach to investigate the pattern of CpGs methylation in the promoter region of KEAP1. The validation of this approach on lung cancer patient cohorts is mandatory to clarify the prognostic value of the epigenetic deregulation of KEAP1 in lung tumors.

Molecular Neurosciences

Department of Medicine and Surgery



Head M. D'Amelio

Other Personnel A. Cordella, A. Nobili

External Members P. Krashia, L. La Barbera

Description

The Molecular Neurosciences Unit focuses on neurodegenerative diseases and other neuropsychiatric conditions by means of the application of biologic techniques. We have a particular interest in the pathogenesis of β -amyloid neurodegenerative disorders such as Alzheimer's disease (AD). We use cell and transgenic mouse models to gain an understanding of the pathogenesis of the disorder, and also to assist in the development of novel therapeutic techniques. We have applied similar techniques for the study of Parkinson's disease (PD) and spinal muscular atrophy (SMA). We have identified several novel proteins involved in the pathogenesis of AD, and we have cell and mouse models of the disease. We are also applying similar techniques to psychiatric conditions such as autism and schizophrenia. The laboratory offers research opportunities to undergraduates, graduate students, postdoctoral fellows and other interested scientists.

Main research activities

During last year, the Molecular Neurosciences Unit consolidated scientific collaborations with national and international partners. In particular, the Laboratory collaborated with the National Research Council (CNR) of Rome, "Roma Tre" University of Rome, Sapienza University of Rome, Université Libre de Bruxelles, Center of Excellence for Biomedical Research, University of Genova and University of Perugia. The aforementioned collaborations involve the study of neuronal function alterations in several models of human neurological disease. During last year, the Molecular Neurosciences Unit published several papers in the field of neurodegenerative disorders. Among these, a Nature Communication paper disclosing the crucial role of dopaminergic brain stem in early phase of Alzheimer's disease by using a validated model of the disease.

Main collaborations

- Center of Excellence for Biomedical Research, University of Genova, Italy
- Center of Excellence for Biomedical Research, University of Perugia, Italy
- Roma Tre University of Rome, Rome, Italy
- Sapienza University of Rome, Rome, Italy
- Université Libre de Bruxelles, Belgium
- National Research Council (CNR) of Rome, Italy

Most important publications

Krashia P., Cordella A., Nobili A., La Barbera L., Federici M., Leuti A., Campanelli F., Natale G., Marino G., Calabrese V., Vedele F., Ghiglieri V., Picconi B., Di Lazzaro G., Schirinzi T., Sancesario G., Casadei N., Riess O., Bernardini S., Pisani A., Calabresi P., Viscomi M.T., Serhan C.N., Chiurchiù V., D'Amelio M., Mercuri N.B.

Blunting neuroinflammation with resolvin D1 prevents early pathology in a rat model of Parkinson's disease.

Nat Commun. 2019 Sep 2;10(1):3945. 2019 Oct 14;10(1):4725. PMID: 31477726. IF 11,878

Neuroinflammation is one of the hallmarks of Parkinson's disease (PD) and may contribute to midbrain dopamine (DA) neuron degeneration. Recent studies link chronic inflammation with failure to resolve early inflammation, a process operated by specialized pro-resolving mediators, including resolvins. However, the effects of stimulating the resolution of inflammation in PD - to modulate disease progression - still remain unexplored. Here we show that rats overexpressing human α -synuclein (Syn) display altered DA neuron properties, reduced striatal DA outflow and motor deficits prior to nigral degeneration. These early alterations are coupled with microglia activation and perturbations of inflammatory and pro-resolving mediators, namely IFN- γ and resolvin D1 (RvD1). Chronic and early RvD1 administration in Syn rats prevents central and peripheral inflammation, as well as neuronal dysfunction and motor deficits. We also show that endogenous RvD1 is decreased in human patients with early-PD. Our results suggest there is an imbalance between neuroinflammatory and pro-resolving processes in PD.

Bonsi P., Ponterio G., Vanni V., Tassone A., Sciamanna G., Migliarini S., Martella G., Meringolo M., Dehay B., Doudnikoff E., Zachariou V., Goodchild R.E., Mercuri N.B., D'Amelio M., Pasqualetti M., Bezard E., Pisani A.

RGS9-2 rescues dopamine D2 receptor levels and signaling in DYT1 dystonia mouse models.

EMBO Mol Med. 2019 Jan;11(1): e9283. PMID: 30552094. IF 10,624

Dopamine D2 receptor signaling is central for striatal function and movement, while abnormal activity is associated with neurological disorders including the severe early-onset DYT1 dystonia. Nevertheless, the mechanisms that regulate D2 receptor signaling in health and disease remain poorly understood. Here, we identify a reduced D2 receptor binding, paralleled by an abrupt reduction in receptor protein level, in the striatum of juvenile Dyt1 mice. This occurs through increased lysosomal degradation, controlled by competition between β -arrestin 2 and D2 receptor binding proteins. Accordingly, we found lower levels of striatal RGS9-2 and spinophilin. Further, we show that genetic depletion of RGS9-2 mimics the D2 receptor loss of DYT1 dystonia striatum, whereas RGS9-2 overexpression rescues both receptor levels and electrophysiological responses in Dyt1 striatal neurons. This work uncovers the molecular mechanism underlying D2 receptor downregulation in Dyt1 mice and in turn explains why dopaminergic drugs lack efficacy in DYT1 patients despite significant evidence for striatal D2 receptor dysfunction. Our data also open up novel avenues for disease-modifying therapeutics to this incurable neurological disorder.

Romoli M., Krashia P., Sen A., Franciotta D., Gastaldi M., Nobili A., Mancini A., Nardi Cesarini E., Nigro P., Tambasco N., Mercuri N.B., Parnetti L., Di Filippo M., D'Amelio M., Irani S.R., Costa C., Calabresi P.

Hippocampal epileptogenesis in autoimmune encephalitis.

Ann Clin Transl Neurol. 2019 Nov;6(11):2261-2269. PMID: 31617317. IF 4,656

Objective: Autoantibody-mediated forms of encephalitis (AE) include neurological disorders characterized by subacute memory loss, movement disorders, and, often, frequent, focal epileptic seizures. Yet, the electrophysiological effects of these autoantibodies on neuronal function have received little attention. In this study, we assessed the effects of CSF containing autoantibodies on intrinsic and extrinsic properties of hippocampal neurons, to define their epileptogenic potential. **Methods:** We compared the effects of CSF containing leucine-rich glioma inactivated 1 (LGI1), contactin-associated protein-like 2 (CASPR2), and γ -aminobutyric acid receptor B (GABAB R) antibodies on ex vivo electrophysiological parameters after stereotactic hippocampal inoculation into mice. Whole-cell patch-clamp and extracellular recordings from CA1 pyramidal neurons and CA3-CA1 field recordings in ex vivo murine brain slices were used to study neuronal function. **Results:** By comparison to control CSF, AE CSFs increased the probability of glutamate re-lease from CA3 neurons. In addition, LGI1- and CASPR2 antibodies containing CSFs induced epileptiform activity at a population level following Schaffer collateral stimulation. CASPR2 an-tibody containing CSF was also associated with higher spontaneous firing of CA1 pyramidal neurons. On the contrary, GABAB R antibody containing CSF did not elicit changes in intrinsic neuronal activity and field potentials. **Interpretation:** Using patient CSF, we have demonstrated that the AE-associated antibodies against LGI1 and CASPR2 are able to increase hippocampal CA1 neuron excitability, facilitating epileptiform activity. These findings provide in vivo pathogenic insights into neuronal dysfunction in these conditions.

Neurology, Neurophysiology, Neurobiology

Department of Medicine and Surgery



Head V. Di Lazzaro

Faculty G. Assenza, F. Capone, M. Tombini, F. Vernieri

Other Personnel C. Altamura, M. Boscarino, N. Brunelli, ML. Caminiti, A. Cascio Rizzo, G. Cecchi, G. Corrao, C. Costa, L. Di Biase, A. Di Santo, A. De Liso, E. Falato, A. Fallacara, M. Ferrante, J. Lanzone, M. Marano, F. Motolese, F. Ranieri, L. Ricci, MG. Rossi, M. Ulivi, F. Ursini, C. Vico

Description

The main area of research of the Research Unit is the study of the pathophysiology of a variety of neurological disorders, including stroke, degenerative diseases (dementias, Parkinson's disease, tremor, amyotrophic lateral sclerosis), inflammatory diseases of the central nervous system (multiple sclerosis), spinal cord diseases, epilepsy, and headache. Another relevant area of interest is the use of electrophysiological techniques (EEG, EMG, evoked potentials), non-invasive brain stimulation (TMS, tDCS, tACS, vagal stimulation) and neurosonology (cerebral hemodynamics evaluation, functional TCD, TCD with bubble test), for the diagnosis of neurological disorders, and for the evaluation of the effects of drugs on the intact human brain and the study of human brain plasticity.

Main research activities

The research Unit has provided a relevant contribution in understanding of the physiological bases of non-invasive human brain stimulation and in the development of innovative methods of neuromodulation aimed at enhancing human brain plasticity. Significant results were obtained in the study of brain connectivity in epileptic patients and in the field of deep brain stimulation in movement disorders. Other relevant scientific contributions were provided in the field of rare neurodegenerative disorders such as Huntington Disease. Research activity involving patients with migraine led to the publication of relevant studies on the diagnosis (cerebral hemodynamic evaluation) and on the innovative treatment (monoclonal antibodies), of this neurological disorder.

Most important publications

Marano M., Naranian T., di Biase L., Di Santo A., Poon Y.Y., Arca R., Cossu G., Marano P., Di Lazzaro V., Fasano A.

Complex dyskinesias in Parkinson patients on levodopa/carbidopa intestinal gel.

Parkinsonism Relat Disord. 2019 Dec; 69:140-146. PMID: 31759188. IF 4,36

Background: Levodopa-carbidopa intestinal infusion is an effective treatment for motor fluctuations in Parkinson's disease. However, it has been recently associated with emergent complex/atypical dyskinesias. We sought to characterize patients who developed these dyskinesias after levodopa infusion initiation, and to compare these patients to a control population with conventional motor fluctuations.

Methods: 208 Parkinson's disease patients, treated with levodopa intestinal infusion due to motor fluctuations, were screened for onset and/or worsening of dyskinesias after initiation of levodopa infusion, resistant to the routine titration, and presenting with atypical or unexpected patterns. Patients with extensive follow-up data were enrolled for a longitudinal analysis. Cases were compared to a control sample with conventional motor fluctuations in order to investigate predisposing factors, difference in dyskinesia phenotype, management strategies and dropouts. **Results:** Thirty patients out of 208 (14.4%) reported atypical (i.e. long-lasting) biphasic, biphasic-like (i.e. continuous) or mixed (peak-dose and continuous biphasic) dyskinesias after levodopa infusion. They were compared at baseline and follow-up to a sample of 49 patients with conventional motor fluctuations on levodopa infusion. Both groups had similar demographic and clinical features, except the former having higher prevalence of biphasic dyskinesias while on oral therapy. Biphasic-like dyskinesias in nearly half the number of cases improved with increasing the dopaminergic load, while mixed dyskinesias had the worst outcome and highest dropout rate (58%). **Conclusions:** Atypical biphasic, biphasic-like and complex dyskinesias could hinder the course of patients treated with levodopa infusion. This study further informs the selection process of advanced therapies, particularly in dyskinetic patients.

Guerra A., Suppa A., Ascì F., De Marco G., D'Onofrio V., Bologna M., Di Lazzaro V., Berardelli A.

LTD-like plasticity of the human primary motor cortex can be reversed by γ -tACS.

Brain Stimul. 2019 Nov - Dec; 12(6):1490-1499. PMID: 31289014. IF 6,919

Background: Cortical oscillatory activities play a role in regulating several brain functions in humans. However, whether motor resonant oscillations (i.e. β and γ) modulate long-term depression (LTD)-like plasticity of the primary motor cortex (M1) is still unclear. **Objective:** To address this issue, we combined transcranial alternating current stimulation (tACS), a technique able to entrain cortical oscillations, with continuous theta burst stimulation (cTBS), a transcranial magnetic stimulation (TMS) protocol commonly used to induce LTD-like plasticity in M1. **Methods:** Motor evoked potentials (MEPs) elicited by single-pulse TMS, short-interval intracortical inhibition (SICI) and intracortical facilitation (ICF) were evaluated before and 5, 15 and 30 min after cTBS alone or cTBS delivered during β -tACS (cTBS- β) or γ -tACS (cTBS- γ). Moreover, we tested the effects of β -tACS (alone) on short-latency afferent inhibition (SAI) and γ -tACS on SICI in order to verify whether tACS-related interneuronal modulation contributes to the effects of tACS-cTBS co-stimulation. **Results:** cTBS- γ turned the expected after-effects of cTBS from inhibition to facilitation. By contrast, responses to cTBS- β were similar to those induced by cTBS alone. β - and γ -tACS did not change MEPs evoked by single-pulse TMS. β -tACS reduced SAI and γ -tACS reduced SI-CI. However, the degree of γ -tACS-induced modulation of SICI did not correlate with the effects of cTBS- γ . **Conclusion:** γ -tACS reverses cTBS-induced plasticity of the human M1. γ -oscillations may therefore regulate LTD-like plasticity mechanisms.

Insola A., Di Lazzaro V., Assenza G.

Cortical inhibitory dysfunction in epilepsy partialis continua: a high frequency oscillation somatosensory evoked potential study.

Clin Neurophysiol. 2019 Apr;130(4):439-444. PMID: 30769270. IF 3,675

Objective: The pathophysiology of epilepsy partialis continua (EPC) is still unclear, a thalamo-cortical circuit dysfunction has been hypothesized. The aim of present study is the functional evaluation of the thalamo-cortical network in EPC by means of the study of low- and high-frequency somatosensory evoked potentials (LF-SEP and HF-SEP). **Methods:** Median LF-SEP and HF-SEP were recorded in 3 patients with EPC and in 2 patients with rolandic lesions without EPC (non-EPC). Recording electrodes were placed on P3, C3, F3 and P4, C4, F4 of scalp regions. HF-SEP were obtained by an offline 400-800 Hz filtering of P3-F3 and P4-F4 traces. **Results:** In EPC patients, we found a significant suppression of post-synaptic HF-SEP burst and an amplitude reduction of the P24 wave of the LF-SEPs. Both these components are related to cortical inhibitory interneuron activity. HF-SEP and LF-SEP were normal in non-EPC patients. **Conclusion:** The different results obtained in patients with a rolandic lesion with and without EPC supports the hypothesis that EPC might be correlated to a dysfunction of gabaergic interneurons of a cortical sensory-motor network. **Significance:** Our results might contribute to the understanding of the physiological basis of the cortical dysfunction causing epilepsy partialis continua.

Neurophysiology and Neuroengineering of Human-Technology Interaction

Department of Medicine and Surgery



Head G. Di Pino

Faculty D. Formica

Other Personnel M. D'Alonzo, E. Falato, F. Le Jeune, A. Mioli, G. Musumeci, A. Nocco, V. Piombino, L. Raiano

Description

The Research Unit investigates the neurophysiological processes underlying complex interaction between the human nervous system and technological artifacts.

Today, more and more often, the man is part of artificial/organic mixed complex, interacting with devices, robots, or with tool for functional replacement (e.g. prostheses). From a neuroscience perspective, this may strongly impact on well-known concepts, such as sensory feedback, motor control, biomechanics, learning, functional recovery.

The Unit object of study is no longer humans as such, but modern humans in the era of the confluence with the technology, both in their physiological and pathological manifestations.

Furthermore, the Research Unit aims to investigate classical themes of neurophysiology of systems (motor control, body representation) using typical neuroengineering tools (e.g. modeling, objectification, automation).

Its multidisciplinary flavor favors direct applications on the healthy subjects and patients.

Main research activities

- Design and development of Hardware and Software Systems of virtual and augmented reality, and of cognitive studies that integrate VR-AR stimuli, external stimulations (e.g. tDCS, TMS) and the recording and processing of biological signals (EEG, fMRI, EMG).
- Development of a robot aided transcranial magnetic stimulation guided by artificial vision.
- Identification of the physiological parameters correlated to the embodiment of a limb
- Investigation protocols to neuro-modulated ownership during the rubber hand illusion paradigm.
- Experiments with healthy participants performed in order to extend current knowledge on supernumerary limb embodiment.
- Investigation of embodiment and sensorimotor performance in amputees underwent surgical procedures to control the prosthesis.
- Clinical trial of implanted intraneural electrodes.

Most important publications

D'Alonzo M., Mioli A., Formica D., Vollero L., Di Pino G.

Different level of virtualization of sight and touch produces the uncanny valley of avatar's hand embodiment.

Sci Rep. 2019 Dec 13;9(1):19030. PMID: 31836765. IF 4,011

Humans increasingly often act through virtual and robotic avatars. How virtualization of sensory inputs affects avatar self-attribution is a key question for understanding nowadays human behavior. We assessed the relative weight of the virtualization of sight (Real, Robotic, Virtual) and of touch (Real, Virtual) on artificial hand embodiment in experiments fashioned after the rubber hand illusion. Virtualization decreased embodiment, but lowest embodiment was found when only one sense was virtual. Discordant levels of virtualization of sight and touch elicited revulsion, extending the concept of the uncanny valley to avatar embodiment. Besides timing, spatial constraints and realism of feedback, a matched degree of virtualization of seen and felt stimuli is a further constraint in building the representation of the body.

Zangrandi A., Mioli A., D'Alonzo M., Formica D., Pellegrino G., Di Pino G.

Conditioning transcranial magnetic stimulation of ventral premotor cortex shortens simple reaction time.

Cortex. 2019 Dec; 121:322-331. PMID: 31670027. IF 4,275

The ventral premotor cortex (PMv) is a key area of the sensorimotor control loop, it subtends complex motor sequences. To investigate the role of PMv in simple motor response to sensory cue, we used transcranial magnetic stimulation (TMS) to interfere with its function during a simple reaction time task. We ran two experiments where participants were required to respond as fast as possible to a median nerve stimulation (go-signal), while sub-M1-threshold single pulse TMS was delivered either on left PMv or right PMv, 5–65ms after the go-signal. TMS delivered on either PMv up to 25ms after the go-signal shortened reaction time, as if conditioning before sensory afferences arrive lower the threshold needed to release the pre-planned motor program to the primary motor cortex.

Ranieri F., Coppola G., Musumeci G., Capone F., Di Pino G., Parisi V., Di Lazzaro V.

Evidence for associative plasticity in the human visual cortex.

Brain Stimul. 2019 May - Jun;12(3):705-713. PMID: 30773491. IF 6,919

Background: Repetitive convergent inputs to a single post-synaptic neuron can induce long-term potentiation (LTP) or depression (LTD) of synaptic activity in a spike timing-dependent manner. **Objective:** Here we set a protocol of visual paired associative stimulation (vPAS) of the primary visual cortex (V1) in humans to induce persistent changes in the excitatory properties of V1 with a spike timing rule. **Methods:** We provided convergent inputs to V1 by coupling transcranial magnetic stimulation (TMS) pulses of the occipital cortex with peripheral visual inputs, at four interstimulus intervals of -50/-25/+25/+50 ms relative to the visual evoked potential (VEP) P1 latency. We analysed VEP amplitude and delayed habituation before and up to 10 min after each vPAS protocol. **Results:** VEP amplitude was reduced after vPAS+25. Delayed VEP habituation was increased after vPAS-25 while it was reduced after vPAS+25. **Conclusions:** We provide evidence that associative bidirectional synaptic plasticity is a feature not only of the sensorimotor but also of the human visual system.

Nonlinear Physics and Mathematical Modeling

Department of Engineering



Head S. Filippi

Faculty C. Cherubini, L. Chiodo, A. Gizzi, M. Inguscio, A. Loppini

Other Personnel A. Barone, M. Nicoletti

External Members F. H. Fenton, R. Ruiz-Baier

Description

The Nonlinear Physics and Mathematical Modelling Research Unit investigates different problems belonging to Physics, Mathematics, Engineering, Biology and Medicine. Theoretical, analytical and numerical tools in union with experimental studies are applied to investigate complex dynamics underlying biological systems as well as astrophysics and classical and quantum mechanics, with particular attention to fluid dynamics, nonlinear solid mechanics, condensed matter physics and stellar and black hole dynamics. Regarding biophysics, research activities focus on animal and human physiopathology of cardiac, intestine, neural, endocrine systems through the derivation and solution of mathematical models calibrated on experiments. To this aim, advanced tools of numerical calculus, atomistic simulations, biomedical imaging as well as data analysis are implemented with the aim of obtaining predictive information regarding complex systems. The Unit moreover extends its skills through national and international networks of collaborations.

Main research activities

In 2019 Prof. Massimo Inguscio has joined the Research Unit, considerably enriching its research lines with relevant results on experimental Quantum Mechanics. Moreover, within the framework of a scientific agreement between UCBM and the Italian Institute for Technology (IIT), the Unit has been working at a neuroscience project focused on computational and experimental investigation of physiological neural networks. The Unit also contributed into the scientific organization of special sessions at: 1) PLACE Conference, "Experiment, Modeling and Simulation in Cardiac Physio-Pathology", Rome (IT); 2) ESB-ITA 2019, Italian Chapter of the European Society of Biomechanics, Bologna (IT). Moreover, some members of the Unit have continued their long-lasting collaboration with the International Center for Relativistic Astrophysics Network (ICRANet) on the research lines "Interdisciplinary Complex Systems: Theoretical Physics Methods in Systems Biology" and "Self Gravitating Systems, Galactic Structures and Galactic Dynamics".

Most important publications

Loppini A., Gizzi A., Cherubini C., Cherry E.M., Fenton F.H., Filippi S.

Spatiotemporal correlation uncovers characteristic lengths in cardiac tissue.

Phys Rev E. 2019 Aug;100(2-1):020201. PMID: 31574686. IF 2,353

Spatiotemporal patterns of action potential duration have been shown to occur in many mammalian hearts due to period-doubling bifurcations. Through high-resolution optical mapping experiments and mathematical modeling, we introduce a characteristic spatial length of cardiac activity in canine ventricular wedges via a spatiotemporal correlation analysis, at different stimulation frequencies and during fibrillation. We show that the characteristic length ranges from 40 to 20 cm during one-to-one responses and it decreases to a specific value of about 3 cm at the transition from period-doubling bifurcation to fibrillation. We further show that during fibrillation, the characteristic length is about 1 cm. Another significant outcome of our analysis is the finding of a constitutive phenomenological law obtained from a nonlinear fitting of experimental data which relates the conduction velocity restitution curve with the characteristic length of the system. The fractional exponent of $3/2$ in our phenomenological law is in agreement with the domain size remapping required to reproduce experimental fibrillation dynamics within a realistic cardiac domain via accurate mathematical models.

Nicoletti M., Loppini A., Chiodo L., Folli V., Ruocco G., Filippi S.

Biophysical modeling of *C. elegans* neurons: single ion currents and whole-cell dynamics of AWCon and RMD.

PLoS One. 2019 Jul 1;14(7): e0218738. PMID: 31260485. IF 2,776

C. elegans neuronal system constitutes the ideal framework for studying simple, yet realistic, neuronal activity, since the whole nervous system is fully characterized with respect to the exact number of neurons and the neuronal connections. Most recent efforts are devoted to investigate and clarify the signal processing and functional connectivity, which are at the basis of sensing mechanisms, signal transmission, and motor control. In this framework, a refined model of whole neuron dynamics constitutes a key ingredient to describe the electrophysiological processes, both at the cellular and at the network scale. In this work, we present Hodgkin-Huxley-based models of ion channels dynamics, built on data available both from *C. elegans* and from other organisms, expressing homologous channels. We combine these channel models to simulate the electrical activity of two among the most studied neurons in *C. elegans*, which display prototypical dynamics of neuronal activation, the chemosensory AWCON and the motor neuron RMD. Our model properly describes the regenerative responses of the two cells. We analyze in detail the role of ion currents, both in wild type and in *in silico* knockout neurons. Moreover, we specifically investigate the behavior of RMD, identifying a heterogeneous dynamical response which includes bistable regimes and sustained oscillations. We are able to assess the critical role of T-type calcium currents, carried by CCA-1 channels, and leakage currents in the regulation of RMD response. Overall, our results provide new insights in the activity of key *C. elegans* neurons. The developed mathematical framework constitutes a basis for single-cell and neuronal networks analyses, opening new scenarios in the *in silico* modeling of *C. elegans* neuronal system.

Wengerowsky S., Joshi S.K., Steinlechner F., Zichi J.R., Dobrovolskiy S.M., van der Molen R., Los J.W.N., Zwiller V., Versteegh M.A.M., Mura A., Calonico D., Inguscio M., Hübel H., Bo L., Scheidl T., Zeilinger A., Xuereb A., Ursin R.

Entanglement distribution over a 96-km-long submarine optical fiber.

Proc Natl Acad Sci U S A. 2019 Apr 2;116(14):6684-6688. PMID: 30872476. IF 9,580

Background: Quantum entanglement is one of the most extraordinary effects in quantum physics, with many applications in the emerging field of quantum information science. In particular, it provides the foundation for quantum key distribution (QKD), which promises a conceptual leap in information security. Entanglement-based QKD holds great promise for future applications owing to the possibility of device-independent security and the potential of establishing global-scale quantum repeater networks. While other approaches to QKD have already reached the level of maturity required for operation in absence of typical laboratory infrastructure, comparable field demonstrations of entanglement-based QKD have not been performed so far. Here, we report on the successful distribution of polarization-entangled photon pairs between Malta and Sicily over 96 km of submarine optical telecommunications fiber. We observe around 257 photon pairs per second, with a polarization visibility above 90%. Our results show that QKD based on polarization entanglement is now indeed viable in long-distance fiber links. This field demonstration marks the longest-distance distribution of entanglement in a deployed telecommunications network and demonstrates an international submarine quantum communication channel. This opens up myriad possibilities for future experiments and technological applications using existing infrastructure.

Nursing Science

Department of Medicine and Surgery



Head M.G. De Marinis

Faculty M. Matarese, M. Piredda, D. Tartaglini

Other Personnel G. Facchinetti, M. Lommi, A. Marchetti

Description

The Unit investigates topics within clinical, pedagogical and organizational areas using quantitative and qualitative methods. Clinical areas include nursing in palliative care and chronic diseases, geriatrics, cancer nursing and peripheral venous access. Palliative care topics include pressure ulcers, patient's transition, adolescents losing a parent. Chronic disease topics comprise self-care in patients with COPD and multiple chronic conditions and the contribution to self-care of family caregivers. Geriatric topics include self-care, discharge process, continuity of care, and ageism. Cancer topics include protective isolation in hematology and nursing care dependence. Pedagogical topics focus on hidden curriculum in nursing education, palliative care education, students' career preferences, stakeholders' engagement in nursing curriculum, students' caring behaviours. Organizational topics include missed nursing care, use of mobile technology in healthcare, and hospital patient flow.

Main research activities

Ongoing multicenter projects include:

- Design of a robotic device for patient-handling (SAFE-MOVER);
- Self-care experiences of people with COPD;
- Mindfulness based stress reduction Intervention in patients with COPD and their caregivers (MIND study) ;
- The contribution of the patient/caregiver dyad on self-care in COPD (RESPYRO study) ;
- Self-care and quality of life in older adults with chronic diseases;
- Self-care Of patient and caregiver DyAd in chronic conditions: a Longitudinal study (SODALITY study) ;
- RCT of a polyurethane foam dressing for pressure injuries (MULTISCHIUME study) ;
- Measure of cancer patients' perception of care dependency;
- Epidemiology of pressure ulcers in hospice inpatients (PRELUdiHO) ;
- Discharge of elderly with chronic diseases;
- Alliance between generations: ageism ;
- Nursing decision-making in artificial nutrition and hydration of patient with cancer at end-of-life;
- Nurses' compliance with standard precautions ;
- Care complexity in nurses' views.

Most important publications

Matarese M., Lommi M., Piredda M., Marchetti A., De Marinis M.G.

"Where would I prefer to work after graduation?" Career preferences of students attending Italian nursing schools.

Nurse Educ Today. 2019 Dec; 83:104204. PMID: 31521011. IF 2,442

Cross sectional study conducted in 14 Italian undergraduate nursing schools to identify students' career preferences and influencing factors. A multivariate binary logistic regression was used to identify the factors influencing choices. Participants were 1534 nursing students who, consistently in all the three years and in line with international literature, preferred working in paediatrics, critical care and operating theatres, and disregarded psychiatry and geriatrics. Age, gender, nationality, and university attended predicted students' preferences. Nursing formal and hidden curricula and internships need to be reviewed to enable students to understand the value present in all areas of practice.

Facchinetti G., Ianni A., Piredda M., Marchetti A., D'Angelo D., Dhurata I., Matarese M., De Marinis M.G.

Discharge of older patients with chronic diseases: what nurses do and what they record. An observational study.

J Clin Nurs. 2019 May;28(9-10):1719-1727. PMID: 30653788. IF 1,757

Structured nonparticipant observation of 1224 nursing activities performed during discharge of 102 older patients with chronic diseases and retrospective audit of nursing records were conducted to describe the nursing activities actually performed and their consistency with those documented. The number of activities was not related to patients' age, gender and educational level, nor to nurses' postgraduate education. Statistically significant correlations emerged between the number of activities observed and the nurses' work experience. A discharge plan guiding nurses' activities would enable them to better respond to care needs of elderly patients.

D'Angelo D., Mastroianni C., Artico M., Biagioli V., Latina R., Guarda M., Piredda M., De Marinis M.G.

Validity and reliability of the Palliative Care Transition Measure for Caregivers (PCTM-C).

Palliat Support Care. 2019; 17(2):202-207. PMID: 29352818. IF 1,965

The Care Transition Measure, developed to evaluate care transitions experienced by the elderly, was modified and psychometrically tested with 272 family caregivers of patients in palliative care through confirmatory factor analysis. The content validity index for each of the items was higher than 0.80, whereas that for the scale was 0.95. The model tested with confirmatory factor analysis fitted the data well and confirmed that the transition measures referred to communication, integrated care and a trusting-relationship, and therefore the core dimensions of continuity according to existing conceptual models. The internal consistency was high (Cronbach's $\alpha = 0.94$). Significance of results. The PCTM-C proved to be a suitable measure of the quality of such transitions. It may be used in clinical practice as a continuity quality indicator and has the potential to guide interventions to enhance family caregivers' experience of care continuity.

Oncology

Department of Medicine and Surgery

Head G. Tonini

Faculty F. Pantano, D. Santini, B. Vincenzi

Other Personnel C. Anesi, G. Armento, F. Citarella, M.C. Cursano, G. D'Onofrio, E. Dell'Aquila, I. Fioroni, S. Foderaro, C. Fulgenzi, A. Galletti, C. Grilli, M. Iuliani, A. La Cesa, E. Marrucci, A. Mazzocca, A. Minelli, A. Napolitano, A. Onorato, V. Ricoszi, G. Ribelli, M. Russano, M. Silletta, M. Spalato Ceruso, S. Simonetti, M. Stellato, L. Stumbo, A. Terenzio, V. Virzi, T. Zeppola

Data Manager T. Grassani, T. Pignatelli, C. Potestà



Description

The Oncology Research Unit is a multidisciplinary group of clinicians and scientists with expertise across the fields of clinical medicine, cancer care, epidemiology, bioinformatics and statistics, cell and molecular biology and immunology.

A key aim of the Department of Oncology is the optimal translation of fundamental research into patient benefit. Our Translational Laboratory is physically closely located with the hospital and our strategy is to promote a tight interaction between basic scientists and clinicians. Research activities are mainly focused on diagnosis, treatment and prevention of cancers and can be divided into two broad disciplines: Translational and Clinical Research. Teaching is one of our principal mission promoted by training and education activities including PhD and Resident-Specialty programs in Medical Oncology.

Main research activities

Translational research is focused on:

- Identification of cellular and molecular profiles to predict immunotherapy response in advanced solid tumors
- Evaluation of the effects of new molecular target therapies for renal carcinoma on the bone tumor microenvironment
- Analyses of the effects of cyclin-dependent kinase inhibitors (CDK4/6) on pre-clinical models of bone metastases from breast cancer
- Identification of new therapeutic targets in castration-resistant prostate cancer
- Study of new biomarkers involved in tumor progression and resistance to anticancer treatments in patients affected by soft tissue sarcomas
- Use of novel non-invasive approaches to identify biomarkers of response to immunotherapy in non-small cell lung cancer
- Clinical Trial Unit focuses on:

breast, prostate, renal, colorectal and lung cancers, but it also run trials in other rarer cancer types, including sarcoma. The unit is specialized in phase II exploratory and phase III randomized trials of new treatments

Most important publications

Cremolini C., Rossini D., Dell'Aquila E., Lonardi S., Conca E., Del Re M., Busico A., Pietrantonio F., Danesi R., Aprile G., Tamburini E., Barone C., Masi G., Pantano F., Pucci F., Corsi D.C., Pella N., Bergamo F., Rofi E., Barbara C., Falcone A., Santini D.

Rechallenge for patients with RAS and BRAF wild-type metastatic colorectal cancer with acquired resistance to first-line Cetuximab and Irinotecan: a phase 2 single-arm clinical trial.

JAMA Oncol. 2019 Mar 1; 5(3):343-350. PMID: 30476968. IF 22,416

We prospectively assess the activity of cetuximab plus irinotecan as third-line treatment for patients with RAS and BRAF wild-type metastatic colorectal cancer (mCRC) who were initially sensitive to and then resistant to first-line irinotecan- and cetuximab-based therapy. We demonstrated that patients with RAS wild-type ctDNA had significantly longer progression-free survival than those with RAS mutated ctDNA. This is the first prospective demonstration that a rechallenge strategy with cetuximab and irinotecan may be active in patients with RAS and BRAF wild-type mCRC with acquired resistance to first-line irinotecan- and cetuximab-based therapy.

André F., Ciruelos E., Rubovszky G., Campone M., Loibl S., Rugo H.S., Iwata H., Conte P., Mayer I.A., Kaufman B., Yamashita T., Lu Y.S., Inoue K., Takahashi M., Pápai Z., Longin A.S., Mills D., Wilke C., Hirawat S., Juric D.; SOLAR-1 Study Group [Tonini G.].

Alpelisib for PIK3CA-mutated, hormone receptor-positive advanced breast cancer.

N Engl J Med. 2019 May 16;380(20):1929-1940. PMID: 31091374. IF IF 70,67

In a randomized, phase 3 trial, we compared alpelisib (at a dose of 300 mg per day) plus fulvestrant (at a dose of 500 mg every 28 days and once on day 15) with placebo plus fulvestrant in patients with HR-positive, HER2-negative advanced breast cancer who had received endocrine therapy previously. We demonstrated that treatment with alpelisib–fulvestrant prolonged progression-free survival among patients with PIK3CA-mutated, HR-positive, HER2-negative advanced breast cancer who had received endocrine therapy previously.

von Minckwitz G., Huang C.S., Mano M.S., Loibl S., Mamounas E.P., Untch M., Wolmark N., Rastogi P., Schneeweiss A., Redondo A., Fischer H.H., Jacot W., Conlin A.K., Arce-Salinas C., Wapnir I.L., Jackisch C., DiGiovanna M.P., Fasching P.A., Crown J.P., Wülfing P., Shao Z., Rota Caremoli E., Wu H., Lam L.H., Tesarowski D., Smitt M., Douthwaite H., Singel S.M., Geyer C.E. Jr; KATHERINE Investigators[Tonini G.].

Trastuzumab emtansine for residual invasive HER2-positive breast cancer.

N Engl J Med. 2019 Feb 14;380(7):617-628. PMID: 30516102. IF 70,67

We conducted a phase 3, open-label trial involving patients with HER2-positive early breast cancer who were found to have residual invasive disease in the breast or axilla at surgery after receiving neoadjuvant therapy containing a taxane (with or without anthracycline) and trastuzumab. Patients were randomly assigned to receive adjuvant T-DM1 or trastuzumab for 14 cycles. We demonstrated that among patients with HER2-positive early breast cancer who had residual invasive disease after completion of neoadjuvant therapy, the risk of recurrence of invasive breast cancer or death was 50% lower with adjuvant T-DM1 than with trastuzumab alone.

Ophthalmology

Department of Medicine and Surgery



Head S. Bonini

Faculty M. Coassin, A. Di Zazzo

Other Personnel G. Cupo, C. Giusti, R. Sgrulletta

External Members A. Micera

Description

The Ophthalmology area with its diagnostic and research laboratory of Ocular surface performs diagnostic activities focused on the eye surface, corneal, conjunctival dealing with an extremely peculiar eye section. Moreover, several research studies are investigating clinical and molecular aspects of retinal diseases; such age-related macular degeneration, diabetic retinopathy and vitreoretinal interface abnormalities.

Main research activities

The research activities of the Ophthalmology Unit has been significant since many years, being among the top teams in the national landscape. An advanced research lab is part of this area, allowing to mix the most innovative techniques and discoveries of basic research in daily clinical activity.

The research areas are developed in various fields:

- Pathogenesis of allergic eye diseases;
- Pathogenesis and therapy of dryeye disease;
- Corneal transplants, indications and treatment;
- Immunological Management of Graft-Versus Host Disease (GVHD) and related complications;
- Neuromediators and Nerve Growth Factor (NGF) at ocular surface;
- Endocrine system effect at ocular surface.

The clinical and chirurgic team has a very pronounced international

background that still offers educational, clinical and research exchanges with the major national and international institutions such as the one below.

Most important publications

Di Zazzo A., Micera A., De Piano M., Cortes M., Bonini S.

Tears and ocular surface disorders: usefulness of biomarkers.

J Cell Physiol. 2019 Jul;234(7):9982-9993. PMID: 30515814. IF 4,522

Corroborating data suggest that the analysis of tear fluid might represent an additional tool in the ophthalmological practice. Areas covered: The purpose of this review was to sum up the tear protein profiles in healthy and diseased ocular surface and to highlight biomarker usefulness in the early diagnosis as well as at follow-up. This analysis encompasses a deep examination of the protein profile ex-pression under physiological and pathological conditions. Tear protein profile analysis will allow in the near future discriminating between different grades of inflammation, from acute trauma toward immune-, endocrine-, and nervous-related disorders of the ocular surface. Concluding remarks: The review provides an overview of old and recent findings about inflammatory mediators identified at the ocular surface, under physiological and pathological conditions. To date, the analysis of tear fluid represents a new additional approach for diagnosis and management of ocular surface diseases. Understanding the pathophysiological mechanism could also offer significant advantages to develop strategies addressed to better clarify some complex ocular surface disorders. To sum up, the possibility to provide selective biomarkers as a future target of specific diseases should be considered for supporting diagnosis and management of ocular surface diseases.

Di Zazzo A., Micera A., De Piano M., Coassin M., Sharma S., Bonini S., Fernandes M.

Adult vernal keratoconjunctivitis: clinical and biochemical profile of a rare disease.

Ocul Surf. 2019 Oct;17(4):737-742. PMID: 31276829. IF 9,108

Vernal keratoconjunctivitis (VKC) is a chronic bilateral ocular allergic disease mainly affecting the pediatric population. Although it is considered a long-term disease, with an average duration of 4–8 years, it usually recovers spontaneously after puberty. Moreover similar to other atopic conditions, VKC has a different prevalence between males and females with two to four times greater preponderance in males. Therefore a close relationship between sex hormones, sexual development and ocular surface conditions such allergic diseases particularly VKC, has been proposed. A variable incidence of VKC has been noted in endemic tropical regions, between 3 and 10%, amongst school age children in Cameroon, Turkey, Israel and South East Asia probably due to humidity and warmer temperatures, while the prevalence is 3.2 per 10000 inhabitants in Western Europe.

Di Zazzo A., Coassin M., Varacalli G., Galvagno E., De Vincentis A., Bonini S.

Neurotrophic keratopathy: pros and cons of current treatments.

Ocul Surf. 2019 Oct;17(4):619-623. PMID: 31526824. IF 9,108

Background: Several therapeutics have been proposed for neurotrophic keratitis, but no direct comparison among different approaches is available. **Objective:** To compare treatment-related problems and outcomes of both traditional and novel therapeutics for neurotrophic keratopathy, focusing on resolution rate, healing time, and recurrence rate. **Data sources:** Literature search of published studies between 1980 and 2019 on neurotrophic keratopathy available on PubMed was made without any language constraints but limited to human study participants. **Study selection:** All published peer-reviewed open, blinded and randomized clinical trials, case series and case reports, divided according to evidence level, were reviewed and resolution rate, healing time, relapses of the disease, and visual outcomes were evaluated. **Data extraction and synthesis:** Single observer data extraction. **MAIN OUTCOMES AND MEASURES:** resolution rate, healing time, recurrence rate. **Results:** Human recombinant Nerve Growth Factor eye drops, Serum Tears and Substance P showed comparable resolution rate in patients with neurotrophic keratopathy. Amniotic membrane transplantation and Nerve Growth Factor eye drops are associated with a faster healing time among available treatments. Nerve Growth Factor eye drops clinical trial are the only study with evidence level 1, hence randomized and controlled. **Conclusions and relevance:** Several new treatment options are available for patients with neurotrophic keratitis with adequate safety.

Orthopaedic and Trauma Surgery

Department of Medicine and Surgery

Head R. Papalia

Faculty F. Franceschi, U.G. Longo, A. Marinozzi, G. Vadalà

Other Personnel E. Albo, A. Alifano, C. Amato, A. Baldari, A. Berton, L. Binci, F. Buschini, S. Campi, F. Cancilleri, V. Candela, M. Ciuffreda, G. Cortina, V. Denaro, L. Diaz, C. De Andreis, G. De Angelis, S. De Salvatore, C. Di Naro, G. Di Giacomo, F. Franceschetti, A. Gambineri, A. Guarnieri, G. Marineo, M. Paciotti, A. Palumbo, N. Papapietro, A. Perrino, F. Pollara, G. Rizzello, F. Russo, G. Salvatore, S. Santini, G. Stelitano, G. Torre, S. Vasta, F. Vorini, B. Zampogna



Description

The UCBM Research Unit of Orthopaedic Surgery and Trauma Surgery is devoted to the study of new surgical and biological strategies for the treatment of degenerative and traumatic diseases of the musculoskeletal system, in particular upper and lower limbs and spine. The research topics are related to the use of Adult Stem Cells and Platelet Rich Plasma for the treatment cartilage, disc, bone and tendon regeneration. Moreover, research on bone tumors and sport related trauma with the use of finite elements models are also being investigated. As part of the Centre of Integrated Research, research is approached with a multidisciplinary view in order to get new cutting age hypothesis and objectives to achieve the best results for the patients.

The Research Unit is also equipped with a Laboratory of Regenerative Orthopaedic where basic and pre-clinical researches are performed. Two full time biologist with cell and molecular biology expertise as well as histology work in the laboratory. Preclinical studies have been

carried out for several years at the Animal Facility of Tor Vergata University of Rome and in collaboration with the Veterinary Hospital at University of Padua.

Main research activities

- Development of a multidisciplinary and integrated approach, for the management of work affected by degenerative pathologies of the spine: study of occupational aspects and innovative regenerative treatment of the intervertebral disc to favour the return to work (ACTIVE);
- Intra-articular injection of Irisin combined with Hyaluronic Acid can promote Cartilage Regeneration in a Murine Model of Osteoarthritis;
- Efficacy of intradiscal injection of allogeneic mesenchymal stem cells from bone marrow in subjects with low back pain caused by degenerative intervertebral disc disease not responsive to conventional therapy (RESPINE);
- Advanced injectable nanocomposite biomaterials with therapeutic-regenerative activity for the treatment of bone metastases (ACTION);

ses (ACTION);

- Intervertebral disc regeneration mediated by intradiscal injection of autologous mesenchymal stem cells: phase IIB randomized clinical trial;
- Impending fracture of the metastatic lumbar spine: identification of prognostic factors and optimization of preventive vertebroplasty;
- Development of a computer model to study shoulder instability;
- Induced Pluripotent Stem Cells for Vertebral Regeneration (iP-Spine);
- Isolated reconstruction of the medial patello-femoral ligament in patients with patellofemoral instability;
- Reverse shoulder arthroplasty: the role of the teres minor and the humeral version in the performance of daily activities;
- Clinical controlled study on the use of computer-assisted navigation for the total knee arthroplasty: clinical and radiological evaluation;
- Improving accuracy in reverse shoulder prosthesis: new frontiers of computer navigation

- Enhancing the osteo-chondrogenic regenerative properties of a three-dimensional matrix: a multiphase study;
- Periprosthetic infections: get the diagnosis quickly and with low-cost techniques;
- Evaluation of the outcomes of the trapezoid-metacarpal prosthesis for the treatment of rhizoarthrosis compared to trapeziectomy and suspension tenoplasty. Randomized prospective clinical trial;
- Effect of lateralization in the reverse shoulder prosthesis: where lateralize improves outcomes. Correlation between the variations of the pre and post-operative morphological angles with ROM improvement and pre and postoperative functional scores;
- Role of patellar prosthesis in knee arthroplasty. Randomized prospective clinical trial on the influence of patellar replacement in anterior post-operative pain and functional scores in knee arthroplasty;
- Volumetric analysis of the bony edema of the knee in case of anterior cruciate ligament injury and correlation with ligamentous stability parameters before and after intervention of reconstruction;
- Medial pivot vs postero-stabilized type knee replacement: clinical and radiological evaluation and analysis of patient satisfaction;
- Clinical and radiological study for the evaluation of the clinical outcomes of Cotton Osteotomy.

Most important publications

Svantesson E., Hamrin Senorski E., Baldari A., Ayeni O.R., Engebretsen L., Franceschi F., Karlsson J., Samuelsson K.

Factors associated with additional anterior cruciate ligament reconstruction and register comparison: a systematic review on the Scandinavian knee ligament registers.

Br J Sports Med. 2019 Apr;53(7):418-425. PMID: 30018121. IF 11,645

Objective: To present an overview of the Scandinavian knee ligament registers with regard to factors associated with additional ACL reconstruction, and studies comparing the Scandinavian registers with other knee ligament registers. **Design:** Systematic review. **Data sources:** Four electronic databases: PubMed, EMBASE, the Cochrane Library and AMED were searched, and 157 studies were identified. Two reviewers independently screened titles, abstracts and full-text studies for eligibility. A modified version of the Downs and Black checklist was applied for quality appraisal. **Eligibility criteria for selecting studies:** Eligible studies were those published since the establishment of the Scandinavian registers in 2004, which reported factors associated with additional ACL reconstruction and compared data from other registers. **Results:** Thirty-one studies met the inclusion criteria and generally displayed good reporting quality. Adolescent age (<20 years) was the most common factor associated with additional ACL reconstruction. The choice of hamstring tendon graft compared with patella tendon, transportal femoral tunnel drilling, smaller graft diameter and utilisation of suspensory fixation devices were associated with additional ACL reconstruction. Concomitant cartilage injury decreased the likelihood of additional ACL reconstruction. Patient sex alone did not influence the likelihood. The demographics of patients undergoing ACL reconstruction in the Scandinavian registers are comparable to registers in other geographical settings. However, there are differences in surgical factors including the presence of intra-articular pathology and graft choice. **Summary:** The studies published from the Scandinavian registers in general have a high reporting quality when regarded as cohort studies. Several factors are associated with undergoing additional ACL reconstruction. The results from the registers may help facilitate treatment decisions.

Hamrin Senorski E., Svantesson E., Baldari A., Ayeni O.R., Engebretsen L., Franceschi F., Karlsson J., Samuelsson K.

Factors that affect patient reported outcome after anterior cruciate ligament reconstruction-a systematic review of the Scandinavian knee ligament registers. *Br J Sports Med.* 2019

Apr;53(7):410-417. PMID: 30030283. IF 11,645

Objective: To perform a systematic review of findings from the Scandinavian knee ligament registers with regard to factors that affect patient reported outcome after anterior cruciate ligament (ACL) reconstruction. **Design:** Systematic review. **Data sources:** Four electronic databases: PubMed, EMBASE, the Cochrane Library and AMED were searched, and 157 studies were identified. Two reviewers independently screened the titles, abstracts and full text articles for eligibility. A modified version of the Downs and Black checklist was applied for quality appraisal. **Eligibility criteria for selecting studies:** Studies published from the Scandinavian registers from their establishment in 2004 and onwards that documented patient reported outcome and provided information on concomitant injuries were eligible. **Results:** A total of 35 studies were included. Younger age at ACL reconstruction, male sex, not smoking and receiving a hamstring tendon autograft positively influenced patient reported outcome. Patients with concomitant cartilage and meniscal injuries reported inferior subjective knee function compared with patients with an isolated ACL tear. One study reported that patients treated non-reconstructively reported inferior knee function compared with patients who had ACL reconstruction. **Conclusion:** Younger age, male sex, not smoking, receiving a hamstring tendon autograft and the absence of concomitant injuries were associated with superior patient reported outcomes after ACL reconstruction.

Papalia R., Torre G., Maffulli N., Denaro V.

Hip fractures in children and adolescents.

Br Med Bull. 2019 Mar 1;129(1):117-128. PMID: 30753305. IF 2,804

Background: Femoral neck fractures account for <1% of the fractures in children, and are produced by high energy trauma. The most commonly accepted treatment for such fractures is gentle manual anatomical reduction and internal fixation, yielding a healing rate between 80% and 90%. **Sources of data:** Electronic search through major web databases (Medline, Cochrane and Google Scholar). All types of article were eligible for inclusion, except for reviews, systematic reviews, meta-analyses and case reports. The methodological quality of the studies was assessed using the Methodological Index for Non-Randomized Studies (MINORS). **Areas of agreement:** Both open reduction and internal fixation (ORIF) and closed reduction and internal fixation (CRIF) can be used to manage hip fractures in paediatric patients. ORIF is more accurate in reducing and fixing the fracture, with better clinical and functional outcomes, and lower complication rate. Delayed fixation decreases the rate of acceptable outcome and increases the rate of complications. **Areas of controversy:** The methodological quality of the included studies is average-low, and the published evidence is not of sufficient quality to allow to draw final conclusion on the topic. **Growing points:** Good results were reported for both ORIF and CRIF techniques, but are not supported by scientific evidence of adequate quality. More and better studies, including randomized trials, should be carried out to provide more scientifically evidence based conclusions.

Otolaryngology

Department of Medicine and Surgery



Head F. Salvinelli

Faculty M. Casale

Other Personnel V. Frari, F. Greco, P. Tarantino, M. Trivelli

Description

The research unit has been working for years in the design of new devices for topical therapy of upper airway, we are studying the endothelial dysfunction and the potential role of Nerve growth factor (NGF) and the inner ear disorders. We are working on new hearing aids and new methods of nasal breathing evaluation and innovative techniques for vertigo and sinus-nasal diseases.

Main research activities

- New devices for topical therapy for upper airway;
- Development of hearing aids “transparent” to maintain the spectral characteristics of the sound;
- New surgical techniques for the treatment of Meniere disease. Prospective study;
- Otologic disorders, temporo-mandibular dysfunction and serotonergic pattern;
- Endothelial dysfunction and inner ear disorders;
- New device to evaluate nasal breathing;
- The level of NGF and the expression of NGF receptors in nasal cavity and in the olfactory bulb and the role of Resveratrol in nasale breathing

Most important publications

Rinaldi V., Costantino A., Moffa A., Cassano M., Mantovani M., Casale M., Pignataro L.

Postoperative pain and wound healing after coblation-assisted barbed anterior pharyngoplasty (CABAPh): an observational study.

Indian J Otolaryngol Head Neck Surg. 2019 Nov;71(Suppl 2):1157-1162. PMID: 31750142.

Despite the numerous progresses in the palatal surgery, one of the critical aspect of snoring and OSA surgery is the postoperative pain. Over the last decades several surgical palatal procedures have been proposed. Our aim was to evaluate the tolerability of the coblation-assisted barbed anterior pharyngoplasty (CABAPh) in terms of postoperative pain and wound healing, compared with bipolar assisted barbed anterior pharyngoplasty (BAPh). An observational study on 20 patients with simple snoring was conducted. The outcomes measured to assessing pain were a 10 cm visual analog scale (VAS) and the dose of paracetamol + codeine administrated postoperatively. The wound healing was evaluated using a 3-point scale. The other parameters indicative of both pain and surgical repair were food intake and weight loss postoperatively. The mean overall pain (VAS scale) was significantly less in the CABAPh group (M 3.7; CI 3.34-4.06) compared with the BAPh (M 4.73; CI 4.28-5.19) with a $P=0.003$. The mean wound healing after 4 weeks was significantly less in CABAPh group (M 2.7; CI 3.12-2.28) compared with the BAPh (M 2.1; CI 2.45-1.75) with a $P=0.02$. There were no statistically significant difference with regard to food intake ($P=0.09$) and weight loss ($P=0.94$). The CABAPh was able to achieve a greater pain reduction and a faster wound healing compared with bipolar forceps.

Casale M., Costantino A., Sabatino L., Cassano M., Moffa A., Rinaldi V.

Image-guided endoscopic marsupialization technique for frontal sinus mucocele with orbital extension: a case report.

Int J Surg Case Rep. 2019;61: 259-262. PMID: 31398667.

Introduction: Frontal sinus mucocele with intra-orbital extension represents a rare benign cyst-like lesion. Surgical management could be summarized in an open approach, an endoscopic marsupialization or a combined procedure. The present study reports a case of frontal mucocele with wide intra-orbital invasion treated with endoscopic marsupialization assisted by an image-guided navigation system. **Presentation of case:** A 34-year-old African male was referred to the otolaryngology clinic for unilateral supraorbital swelling and post-nasal drip. A clinical ophthalmic assessment showed normal ocular movement, the absence of diplopia and normal visual acuity. CT scan showed a large soft tissue density lesion originating from the right frontal sinus with a supero-medial orbital erosion. The mass invaded the orbital cavity compressing and dislocating the eyeball forward and laterally. An image-guided ESS was performed according to Draft type IIa. Frontal mucocele's inferior wall was open in order to drain muco-purulent content. No complications were detected and the patient was completely recovered with open frontal sinus drainage at 4 months follow-up visit. **Discussion:** We have successfully treated a wide intra-orbital frontal mucocele with an endoscopic marsupialization thanks to image-guided navigation system support. This technology prevented an external approach with associated morbidity and longer hospitalization. **Conclusion:** Navigated assisted endoscopic approach with marsupialization can be considered a safe treatment for FM with orbital extension. In particular, the image-guided system could be useful if bony landmarks are missing, if orbital erosion is present, and to completely drain lateral and multi-cystic lesions.

Rinaldi V., Casale M., Moffa A., Mancini G., Carioli D., Portmann D., Cassano M., Pignataro L.

New low-cost magnifying device for temporal bone laboratory.

J Otol. 2019 Jun;14(2):73-75. PMID: 31223305.

Temporal bone dissection has important role in educating and training oto and skull base surgeons. Mounting of a temporal bone laboratory is expensive. A dedicated magnifying system, such as a surgical microscope or an endoscopic equipment, represents one of the most significant costs. The aim of this study is to test and demonstrate the utility of a commercial USB as a low-cost solution to equip the laboratory with a good magnifying system and illumination

Pathology

Department of Medicine and Surgery



Head G. Perrone

Faculty A. Onetti Muda, C. Rabitti

Other Personnel N. Orlando

Description

The Anatomic Pathology Lab is dedicated to medical diagnosis and scientific research activities. The latter is in turn divided into two main operative fields: development of research lines that are specific to the area, and collaboration within research lines in other areas. Over the years, the laboratory has been furnished with a wide range of technologically advanced equipment, which allows it to better implement activities. Currently, procedures include:

- Histopathology and cytopathology;
- Histochemistry;
- Immunohistochemistry;
- APERIO Digital Pathology Slide Scanner;
- Fluorescence microscope with FISH equipment;
- Pyrosequencing station;
- Real-time PCR equipment;
- Idylla station, for fully-automated real-time PCR;
- N-Counter Nanostring for gene expression profiling.

Main research activities

Research topics:

- Morphological and molecular technologies for cancer characterization and correlation with disease progression/treatment outcome;
- Breast cancer – morphological and molecular characterization of breast cancer supporting innovative medical and surgical procedures;
- Gastrointestinal neoplasms – histological and immunohistochemical subtyping; validation of preoperative molecular analysis as an additional mutodiagnostic tool for cancer;
- Neoplastic, metabolic and inflammatory liver diseases: morphological characterization and correlation with disease progression.

Funded projects:

- Extension of the RealQuant® Lung Fusion Genes kit validation to cytological specimens (OSLO) - Principal Investigator: G. Perrone;
- Utility of molecular sub-typing (PAM50) of breast cancer in

clinical practice Principal Investigator: G. Perrone; Francesca Zalfa;

- Identification of new cancer biomarker in ovarian serous carcinoma (PAO65). Principal Investigator: G. Perrone; Francesca Zalfa;
- Colorectal cancer KRAS mutation status in liquid biopsies and tumor tissue (LIQUID36). -Principal Investigator: G. Perrone.

Main collaborations

- Medical Oncology Department, Hospital Clínic. Universitat de Barcelona, Barcelona, Spain
- Dept. of Pathology. Harvard University School of Medicine, Boston, US
- Dept. of Fundamental Neuroscience, Faculty of Biology and Medicine. University of Lausanne, Switzerland
- Dept. of Clinical and Experimental Medicine. University of Florence, Italy
- Dept. of Pharmacy – Pharmaceutical Sciences. University of Bari Aldo Moro Italy

Most important publications

Fiore M., Trecca P., Perrone G., Amato M., Righi D., Trodella L., D'Angelillo R.M., Ramella S.

Histologic transformation to small-cell lung cancer following gefitinib and radiotherapy in a patient with pulmonary adenocarcinoma.

Tumori J. 2019 Dec;105(6):NP12-NP16. PMID: 30799776. IF 1,234

Introduction: Targeted therapies against epidermal growth factor receptor (EGFR) have revolutionized the treatment of a subset of lung adenocarcinomas that have EGFR-activating mutations; however, all patients treated with EGFR tyrosine kinase inhibitors (TKIs) ultimately develop resistance. Histologic transformation of EGFR-mutant adenocarcinoma to small cell lung cancer (SCLC) is a resistance mechanism rarely reported in the literature. **Case presentation:** We describe the case of a woman with metastatic lung cancer adenocarcinoma with mutated EGFR with an initial response to gefitinib and radiation therapy, who progressed after 18 months due to the development of a resistance mechanism. The new biopsy performed after progression highlighted histologic transformation to SCLC, while maintaining the original EGFR mutation. **Conclusions:** To better identify patients who progress after TKIs and radiation therapy, it is important to perform tumor rebiopsy and collect data to study mechanisms of acquired EGFR TKI resistance.

Pascual T., Martin M., Fernández-Martínez A., Paré L., Alba E., Rodríguez-Lescure Á., Perrone G., Cortés J., Morales S., Lluch A., Urruticoechea A., González-Farré B., Galván P., Jares P., Rodríguez A., Chic N., Righi D., Cejalvo J.M., Tonini G., Adamo B., Vidal M., Villagrasa P., Muñoz M., Prat A.

A pathology-based combined model to identify PAM50 non-luminal intrinsic disease in hormone receptor-positive HER2-negative breast cancer.

Front Oncol. 2019 Apr 26; 9:303. PMID: 31106144. IF 4,137

Background: In hormone receptor-positive (HR+)/HER2-negative breast cancer, the HER2-enriched and Basal-like intrinsic subtypes are associated with poor outcome, low response to anti-estrogen therapy and high response to chemotherapy. To date, no validated biomarker exists to identify both molecular entities other than gene expression. **Methods:** PAM50 subtyping and immunohistochemical data were obtained from 8 independent studies of 1,416 HR+/HER2-negative early breast tumors. A non-luminal disease score (NOLUS) from 0 to 100, based on percentage of estrogen receptor (ER), progesterone receptor (PR) and Ki67 tumor cells, was derived in a combined cohort of 5 studies (training dataset) and tested in a combined cohort of 3 studies. The performance of NOLUS was estimated using Area Under the ROC Curve (AUC). **Results:** In the training dataset (n = 903) and compared to luminal disease, non-luminal disease had lower percentage of ER-positive cells (median 65.2 vs. 86.2%, $p < 0.01$) and PR-positive cells (33.2 vs. 56.4%, $p < 0.01$) and higher percentage of Ki67-positive cells (18.2 vs. 13.1%, $p = 0.01$). A NOLUS formula was derived: $-0.45 \cdot \text{ER} - 0.28 \cdot \text{PR} + 0.27 \cdot \text{Ki67} + 73.02$. The proportion of non-luminal tumors in NOLUS-positive (≥ 51.38) and NOLUS-negative (< 51.38) groups was 52.6 and 8.7%, respectively. In the testing dataset (n = 514), NOLUS was found significantly associated with non-luminal disease ($p < 0.01$) with an AUC 0.902. The proportion of non-luminal tumors in NOLUS-positive and NOLUS-negative groups was 76.9% (56.4-91.0%) and 2.6% (1.4-4.5%), respectively. The sensitivity and specificity of the pre-specified cutoff was 59.3 and 98.7%, respectively. **Conclusions:** In the absence of gene expression data, NOLUS can help identify non-luminal disease within HR+/HER2-negative breast cancer.

Papini E., Pacella C.M., Solbiati L.A., Achille G., Barbaro D., Bernardi S., Cantisani V., Cesareo R., Chiti A., Cozzaglio L., Crescenzi A., De Cobelli F., Deandrea M., Fugazzola L., Gambelunghe G., Garberoglio R., Giugliano G., Luzzi L., Negro R., Persani L., Raggiunti B., Sardanelli F., Seregni E., Sollini M., Spiezia S., Stacul F., Van Doorne D., Sconfienza L.M., Mauri G.

Minimally-invasive treatments for benign thyroid nodules: a Delphi-based consensus statement from the Italian minimally-invasive treatments of the thyroid (MITT) group.

Int J Hyperthermia. 2019;36(1):376-382. PMID: 30909759. IF 3,589

Benign thyroid nodules are a common clinical occurrence and usually do not require treatment unless symptomatic. During the last years, ultrasound-guided minimally invasive treatments (MIT) gained an increasing role in the management of nodules causing local symptoms. In February 2018, the Italian MIT Thyroid Group was founded to create a permanent cooperation between Italian and international physicians dedicated to clinical research and assistance on MIT for thyroid nodules. The group drafted this list of statements based on literature review and consensus opinion of interdisciplinary experts to facilitate the diffusion and the appropriate use of MIT of thyroid nodules in clinical practice. (#1) Predominantly cystic/cystic symptomatic nodules should first undergo US-guided aspiration; ethanol injection should be performed if relapsing (level of evidence [LoE]: ethanol is superior to simple aspiration = 2); (#2) In symptomatic cystic nodules, thermal ablation is an option when symptoms persist after ethanol ablation (LoE = 4); (#3) Double cytological benignity confirmation is needed before thermal ablation (LoE = 2); (#4) Single cytological sample is adequate in ultrasound low risk (EU-TIRADS ≤ 3) and in autonomously functioning nodules (LoE = 2); (#5) Thermal ablation may be proposed as first-line treatment for solid, symptomatic, nonfunctioning, benign nodules (LoE = 2); (#6) Thermal ablation may be used for dominant lesions in nonfunctioning multinodular goiter in patients refusing/not eligible for surgery (LoE = 5); (#7) Clinical and ultrasound follow-up is appropriate after thermal ablation (LoE = 2); (#8) Nodule retreatment can be considered when symptoms relapse or partially resolve (LoE = 2); (#9) In case of nodule regrowth, a new cytological assessment is suggested before second ablation (LoE = 5); (#10) Thermal ablation is an option for autonomously functioning nodules in patients refusing/not eligible for radioiodine or surgery (LoE = 2); (#11) Small autonomously functioning nodules can be treated with thermal ablation when thyroid tissue sparing is a priority and $\geq 80\%$ nodule volume ablation is expected (LoE = 3).

Philosophy of Science and Human Development

Department of Science and Technology for Humans and the Environment



Head M. Bertolaso

Other Personnel C. Beneduce, N. Di Stefano, M. R. Brizi, L. Corti, S. Melino, A. Pensotti, F. Sterpetti

Description

The Research Unit of Philosophy of Science and Human Development is mainly interested in philosophical and epistemological aspect of the dynamics (development, growth, crisis, etc.) of complex systems and their functional integration. We currently focus on the contemporary digital transitions especially when applied to social and educational systems in global scenarios. Expertise from social sciences, economics, law and ethics integrate through collaboration our competences and fields of research activity.

Main research activities

- **Laura Corti** mainly works on the human-machine interaction from a philosophical point of view. Her research interests are Post-phenomenology, Epistemology of AI, Robotics, and Philosophy of science. Currently, she is studying the concept of human-centric AI.
- **Chiara Beneduce** mainly works on the concept of "personalized medicine", in its historical background and philosophical implications.
- **M. Rosaria Brizzi's** research is on Social Sustainability.
- **Andrea Pensotti** mainly deals with the notion of complex systems in biology and medicine. His current interest is mainly related to tumor reversion processes with regards to the experimental models and pharmacological therapies.

Most important publications

Bizzarri M., Giuliani A., Pensotti A., Ratti E., Bertolaso M.

Co-emergence and collapse: the mesoscopic approach for conceptualizing and investigating the functional integration of organisms.

Front Physiol. 2019 Jul 26;10: 924. PMID: 31427981. IF 3,021

The fall of reductionist approaches to explanation leaves biology with an unescapable challenge: how to decipher complex systems. This entails a number of very critical questions, the most basic ones being: “What do we mean by ‘complex’?” and “What is the system we should look for?” In complex systems, constraints belong to a higher level than the molecular one and their effect reduces and constrains the manifold of the accessible internal states of the system itself. Function is related but not deterministically imposed by the underlying structure. It is quite unlikely that such kind of complexity could be grasped by current approaches focusing on a single organization scale. The natural co-emergence of systems, parts and properties can be adopted as a hypothesis-free conceptual framework to understand functional integration of organisms, including their hierarchical or multilevel patterns, and including the way scientific practice proceeds in approaching such complexity. External, “driving” factors – order parameters and control parameters provided by the surrounding microenvironment – are always required to “push” the components’ fate into well-defined developmental directions. In the negative, we see that in pathological processes such as cancer, organizational fluidity, collapse of levels and dynamic heterogeneity make it hard to even find a level of observation for a stable explanandum to persist in scientific practice. Parts and the system both lose their properties once the system is destabilized. The mesoscopic approach is our proposal to conceptualizing, investigating and explaining in biology. “Mesoscopic way of thinking” is increasingly popular in the epistemology of biology and corresponds to looking for an explanation (and possibly a prediction) where “non-trivial determinism is maximal”: the “most microscopic” level of organization is not necessarily the place where “the most relevant facts do happen.” A fundamental re-thinking of the concept of causality is also due for order parameters to be carefully and correctly identified. In the biological realm, entities have relational properties only, as they depend ontologically on the context they happen to be in. The basic idea of a relational ontology is that, in our inventory of the world, relations are somehow prior to the relata (i.e., entities).

Beneduce C.

Personalized medicine and complexio. ‘What is Human?’ as a medical question.

Etica & Politica/Ethics & Politics 2019; XXI(2):89-98.

In this paper, I show the parallelism between the Galenic concept of “complexion” (complexio, in Latin) as it was used in the medieval medical and natural-philosophical texts and the current concept of “personalized medicine”. In this way, I point out to what extent the parallelism between personalized medicine and the medieval notion of “complexion” is nowadays relevant to inquire the proprium of the “human” in a bio-medical framework. For, the medieval notion of “complexion” as “substantial quality” optimally worked as to deal with the problem of reconciling the “case-by-case” approach of medicine with the need of a unified bio-medical account of the “human”. Against the background of this reasoning, I further suggest that a mesoscopic perspective on the living organisms, as the one entailed by the concept of “complexion” and used in current scenarios of Systems Biology, could be advantageous to the bio-medical investigations on “what is human”.

Bertolaso M.

Artificialmente e umanamente: epistemologie a confronto.

Paradoxa. 2019; XIII(2):137-149.

Our relationship with artificial entities is legitimately felt as increasingly closer: the replacement of human activities and the confrontation with the abilities of Artificial Intelligence in the industrial, medical, political or social fields are evident. The performance of new AI technologies is evolving beyond our ability to control their internal procedural systems as part of what can be called a 'digital transition': the ethical guidelines proposed by a digital world management are still inadequate and unsatisfactory, since there is no data value theory that allows us to deal with the increasing amount of digital information and of its value. In this paper, it is discussed how the difficulty in managing technological, socio-cultural and ethical transitions of emerging technologies is largely linked to a notion of experience and knowledge inherited from much of the philosophy of contemporary science, in close connection with a reductionist and mechanist and mechanist vision of the natural world but also of scientific work itself. In other words, contemporary man has inherited a very narrow concept of his own agent nature, to the point of making his comparison with machines plausible both on an epistemic and axiological level.

Physical and Rehabilitation Medicine

Department of Medicine and Surgery



Head S. Sterzi

Faculty F. Bressi

Other Personnel M. Bravi, M. Maselli, S. Miccinilli, M. Morrone, F. Santacaterina

Description

Research Unit members are Doctors and Rehabilitation professionals referring to the Department of Physical Medicine and Rehabilitation. The Department is equipped with Motion Capture System and a movement analysis laboratory for optoelectronic plethysmography of the chest wall, gait analysis and analysis of the upper limb kinematics. The Research Unit is also equipped with the hand rehabilitation glove Gloreha, that provides computer-controlled, repetitive, passive and active assisted mobilization of the fingers with multi-sensory feedback, which is used for clinical trials involving hand functional recovery after stroke. An instrumented treadmill, the Walker View, is available for real time gait analysis and gait treatment since it is equipped with a 3D camera and a sensorized tape with load cells. An instrumented balance board is available for balance disorders diagnosis and treatment.

Main research activities

- Analysis of gait disorders in neurologic and musculoskeletal pathologies and development of treatment strategies
- Development of wearable systems for respiratory monitoring and analysis of the kinematics of the chest wall
- Assessment of treatment strategies for upper limb recovery after stroke by means of robotic platforms
- Development of bio-cooperative robotic systems for the rehabilitation of work-related musculoskeletal pathologies of the upper extremities.
- Restoring tactile sensation in upper limb amputees by implantation of neural invasive interfaces for the bidirectional control of an upper limb cybernetic prosthesis

Main collaborations

- Don Carlo Gnocchi Foundation of Rome, Italy
- IRCCS Bambino Gesù Paediatric Hospital, Italy

Most important publications

Massaroni C., Di Tocco J., Lo Presti D., Longo U.G., Miccinilli S., Sterzi S., Formica D., Saccomandi P., Schena E.

Smart textile based on piezoresistive sensing elements for respiratory monitoring.

IEEE Sensors J. 2019;19(17):7718-7725. DOI: 10.1109/JSEN.2019.2917617 IF 3,076

Respiratory monitoring can be performed by recording chest movements. Aim of this study was the development of a smart wearable textile (ST) for respiratory monitoring by means of piezoresistive elements. The feasibility assessment of the ST for respiratory monitoring was performed on four healthy volunteers under two conditions (quiet breathing and tachypnea). The proposed ST resulted suitable for respiratory frequency monitoring in a wide range of values, where unobtrusiveness is of great value.

Plastic Surgery and Dermatology

Department of Medicine and Surgery



Head P. Persichetti

Faculty C. Dianzani, G.F. Marangi, S. Tenna

Other Personnel B. Brunetti, A. Cagli, B. Cogliandro, V. Panasiti, P. Simone

Description

Fields of interests and research:

- Reconstructive surgery following neoplasms, malformations or trauma of:
 - ▶ head and neck
 - ▶ upper and lower limb
 - ▶ thorax
 - ▶ abdomen
 - ▶ perineum
- Screening, diagnosis and treatment of skin cancer
- Breast reconstruction (Implants, Flap, Lipofilling)
- Treatment of ulcers:
 - ▶ vascular
 - ▶ diabetes
 - ▶ pressure sore
- Application of regenerative medicine with autologous fat plus Platelet Rich Plasma (PRP)
- Burns
- Body contouring procedures after bariatric surgery
- Cosmetic surgery and aesthetic medicine:
 - ▶ Head and neck (rhinoplasty, blepharoplasty, face lift, otoplasty)
 - ▶ Breast (augmentation, mas-

topexy, reduction mammoplasty)

- ▶ Abdomen (abdominoplasty, liposuction)
- ▶ Upper and lower limb (thigh lift, brachioplasty, liposuction)
- ▶ Filler
- ▶ Botulinum toxin
- Application of regenerative medicine in skin rejuvenation
- Application of regenerative medicine in the treatment of acne scars
- Lasers treatment of:
 - ▶ Hemangiomas
 - ▶ Scars
 - ▶ Cutaneous lesions
 - ▶ Photoaging
 - ▶ Hypertrichosis

Main research activities

- Application of regenerative medicine in treatment of atrophic acne scars: nanofat plus PRP infiltration and fractional CO2 laser resurfacing
- The use of PRP in breast implant capsule contracture.
- Treatment of venous ulcers with different combinations of fat graft and platelet rich plasma: a prospective comparative evaluation
- Quality of life in patients affected

by breast cancer treated with reconstructive procedures: application of the BREAST-Q questionnaire

- Evaluation of the posteromedial scar brachioplasty technique associated to lipoaspiration in the post-bariatric arm remodeling.
- Platelet-rich plasma in breast implant capsule contracture.
- IPL in the treatment of posterior blepharitis.
- The use of regenerative devices in chronic wounds: a prospective randomized control trial
- Bioelectrochemical sensor to detect antibiotic-resistant *Pseudomonas Aeruginosa*
- Evaluation of the periprosthetic breast capsule in patients subjected to breast reconstruction with tissue expanders with different surfaces
- Association of human papilloma virus infection and keratoacanthoma clinal evolution.
- Correlation with dysfunction of the thyroid gland and skin pathology.
- Association of human papilloma virus infection and aktinic chertosis.



- CDKN2A involvement in melanoma and mesothelioma susceptibility in rare familial cancer syndromes.
- Clinical evaluation of topical treatment in papulo cystic acne.

In the 2017 creation of a Multidisciplinary Research Group: "To be and to appear, objective indication to Plastic Surgery" of Campus Bio-Medico University of Rome, Italy.

Main collaborations

- Kansai Medical University Department of Plastic and Reconstructive Surgery - Osaka, Japan
- Singapore Centre for Environmental Life Sciences Engineering, Nanyang Technological University, Singapore

Most important publications

Brunetti B., Tenna S., Barone M., Cassotta G., Casale M., Persichetti P.

Bipaddle chimaeric forehead flap: a new technique for simultaneous lining and cutaneous reconstruction in case of full thickness defects of the nose.

Microsurgery. 2019 Feb;39(2):124-130. PMID: 30221388. IF 1,945

Introduction: Many techniques have been described to treat full thickness nasal defects. The authors introduce the bipaddle chimaeric forehead flap (BCFF), a new alternative technique to achieve simultaneous lining and cutaneous reconstruction in case of full thickness hemi-nasal defects, presenting surgical details and applications for its clinical use. **Patients and methods:** From June 2015 to April 2017, 10 patients presenting with oncological full thickness defects involving nasal sidewall and/or nasal ala were reconstructed with the BCFF technique. Mean age was 69.4 years. The chimaeric flap was composed of 2 paddles (cutaneous and periosteal), nourished by a single supratrochlear pedicle, which were used to independently reconstruct the deficient cutaneous and mucosal layers of the nose. Cartilage grafts were used in 8/10 patients. **Results:** Mean surgical time was 114 minutes. An intermediate thinning operation was performed in 3 out of 10 patients. All the flaps survived with no partial necrosis or cartilage exposure observed. Viability and mucosalization of the periosteal paddle was documented both intra-operatively (during the 2nd stage of the operation) and postoperatively (with fiberoptic rhinoscopy performed 3 months after the procedure). Clinical follow-up period ranged from 4 to 24 months postoperatively. The final result was judged sufficient, good and excellent in 1, 5, and 4 cases, respectively. **Conclusions:** The BCFF technique may be a new alternative approach to address full thickness hemi-nasal defects with no extra donor site morbidity, allowing primary placement of structural cartilage grafts and immediate definition of the nasal subunits to be reconstructed.

Segreto F., Marangi G.F., Signoretti M., Cazzato V., Giorgino R., Alessandri-Bonetti M., Persichetti P.

The use of botulinum toxin in flap surgery: a review of the literature.

Surg Innov. 2019 Aug;26(4):478-484. PMID: 30734634. IF 1,472

Botulinum neurotoxin-A and botulinum neurotoxin-B have been shown to play a potential role in improving flap survival in animal models. The aim of this study is to review indications as well as to study injection timing, technique, and doses of botulinum neurotoxin-A and botulinum neurotoxin-B in animal models. Seventeen articles describe a total of 266 animals that underwent botulinum toxin injections before or during flap harvesting or vascular anastomosis procedure. All the studies demonstrated a beneficial effect of botulinum toxin administration in flap surgery or vascular anastomosis. Botulinum neurotoxin-A injection was shown to be a reliable approach in reducing vascular complications rate and increasing survival of flaps in animal models. The main conclusions drawn from the study include the following: perivascular injections targeting each vascular pedicle are preferred in cases of free flaps or axial flaps; subdermal injections are favorable in cases of random pattern skin flaps; and injections should be performed 7 days before flap elevation.

Barone M., Cogliandro A., Salzillo R., Colapietra A., Alessandri Bonetti M., Morelli Coppola M., List E., Ciarrocchi S., Tenna S., Persichetti P.

Role of spreader flaps in rhinoplasty: analysis of patients undergoing correction for severe septal deviation with long-term follow-up.

Aesthetic Plast Surg. 2019 Aug;43(4):1006-1013. PMID: 30868305. IF 1,399

Introduction: The aim of this randomized controlled study was to analyze the long-term results of patients undergoing rhinoplasty because of severe septal deviation and to evaluate the stability of results. **Materials and Methods:** The study was performed with a randomized design. Patients were randomly divided into four groups: group 1, spreader flaps were used in combination with spreader grafts; group 2, spreader flaps were used alone; group 3, spreader grafts were used alone; and group 4, neither spreader flaps nor grafts flaps were used. Patients answered the Italian version of the FACE-Q rhinoplasty module. Anthropometric measurements were performed by AutoCAD for MAC. We determined the angle of deviation, and we compared the pre- and postoperative angles and compared patient satisfaction in the four groups using the Chi-squared test for unpaired data. Two plastic surgeons reviewed all the postoperative photographs of the study patients and rated the photographs on a scale of 1 to 5. **Results:** A total of 264 patients who underwent primary rhinoplasty between January 2010 and September 2016 satisfied the inclusion criteria and were finally enrolled in this study. Anthropometric measurements revealed statistically significant differences ($P < 0.01$) between the preoperative and postoperative values for the angle of septal deviation in group 1 versus the other groups. Over the long-term follow-up, group 1 maintained an angle close to 180 degrees ($P < 0.01$). Group 1 and group 3 were more satisfied compared with groups 2 and 4 ($P < 0.01$). According to evaluations by the 2 reviewers, group 1 and group 3 were the most satisfactory outcomes ($P < 0.01$). **Conclusions:** This was the first randomized study to show that the combined use of the spreader flap and spreader graft is the best choice for a good long-term outcome and durable correction of septal deviation.

Process Engineering

Department of Engineering



Head M. De Falco

Faculty M. Capocelli

Other Personnel D. Barba, A. Germanà, N. Greco

Description

In the Research Unit, academic figures and business leaders (lecturers of the Master of Chemical Engineering for the Sustainable Development) work in close synergy with the objective to develop new technologies of industrial interest, aimed at increasing the compatibility of production systems with safeguarding the environment and human health. The scientific and technological approach derives from the belief that every production system should be equipped with advanced technologies able to improve the performance but, at the same time, reducing the pollutants emissions into the environment at the minimum values allowed by the state of technological knowledge.

Main research activities

- Analysis of CO₂ utilization processes, such as methanation and ethers production, in collaboration with NextChem (Maire Tecnimont group).
- Process analysis of a humidification-dehumidification-adsorption (HDHA) desalination method for the production of clean water from renewable energies, in collaboration with the University of Naples "Federico II".
- Microfluidic bioreactors, in collaboration with the Sapienza University of Rome, Rome.
- Thermal energy storage, in collaboration with ENEA.

Main collaborations

- Maire Tecnimont, Rome, Italy;
- Sapienza University, Rome, Italy;
- University of Naples "Federico II", Italy.

Most important publications

Capocelli M., Prisciandaro M., Piemonte V., Barba D.

A technical-economical approach to promote the water treatment & reuse processes.

J Clean Prod. 2019; 207:85-96. DOI: 10.1016/j.jclepro.2018.09.135 IF 6,395

Despite the emergency of water scarcity, the man's choices have always been directed towards the mismanagement of this vital resource; drinking water is far from being a right for everyone and is rather scarce and poorly distributed in many areas of the world. The aim of this work is to set up a water cost evaluation methodology based on the energetic equivalence among all the possible treatment strategies, water sources and water end-uses. An economic incentive is proposed on the basis of the thermodynamic and process analysis of a Wastewater Treatment & Reuse (WWTR) Plant. The analysis extends our previous approach to the whole panorama of the water-cycle related technologies. The energy use intensity of different (in-series) process of a water reuse project has been addressed: from the COD and nutrient removal, to the energy harvesting and to the separation of dissolved ions. The incentive is able to reward the processes having the goal of low energy consumption and low carbon emissions. The methodology has been applied to WWTR projects at different scales. The results showed that it is possible to obtain an acceptable Return of Investment (ROI), even for a low plant productivity (around 200 m³/day). Moreover, based on the profitability of the WWTR Project, the calculation of the "true value" of the "water source" has been presented. An acceptable price of waster (as a commodity) is evaluated for both wastewater and sea-water by varying the potentiality of the water reclamation plant. This calculation could be implemented to evaluate the economic benefit of public investment as well as to reduce the use of water from non-renewable sources.

Bellocchi S., De Falco M., Gambini M., Manno M., Stilo T., Vellini M.

Opportunities for power-to-Gas and Power-to-liquid in CO₂-reduced energy scenarios: the Italian case.

Energy 2019; 175: 847-861. DOI: 10.1016/j.energy.2019.03.116 IF 5,537

Integration of renewable energy in the electricity market poses significant challenges on power grid management due to the volatility of these sources. In fact, the mismatch between renewable power generation and load curves, along with the need for grid stability, may lead to substantial curtailments when potential electricity supply exceeds demand. In this respect, the surplus from renewable energies can be conveniently exploited to produce hydrogen via electrolysis. This concept can be referred to as "Power-to-Gas" and "Power-to-Liquid" when synthetic grid gas and liquid fuels are respectively produced via syngas hydrogenation processes and is rapidly emerging as a promising measure in support of renewable energy penetration, leading to the decarbonisation of energy generation without affecting grid reliability. This study evaluates the impact of Power-to-Gas and Power-to-Liquid systems on future CO₂-reduced scenarios, characterised by increasing shares of renewable energies and electric vehicles under a holistic Smart Energy System perspective. Results show potential synergies among crucial energy sectors in terms of CO₂ emissions, curtailments and costs. Among the proposed options, synthetic grid gas produced by biomass gasification, and subsequent hydrogenation, leads to the best techno-economic scenario with a reduction of CO₂ emission of 30% with negligible change in yearly total costs.

Capocelli M., Luberti M., Inno S., D'Antonio F., Di Natale F., Lancia A.

Post-combustion CO₂ capture by RVPSA in a large-scale steam reforming plant.

J CO₂ Util. 2019;32:53-65. DOI: 10.1016/j.jcou.2019.02.012 IF 5,189

Steam reforming (SR) of natural gas is the most widespread process to produce hydrogen. This paper presents a comprehensive simulation of an industrial plant for hydrogen production for the internal use in a refinery industrial complex based on the SR of different feedstocks. The reference plant is a 42,000 Nm³/h hydrogen production unit located in the South of Italy in the Refinery of Milazzo, Sicily. Hydrogen is produced from light gaseous hydrocarbons and purified by means of pressure swing adsorption technology. In the present work, a process simulation has been built on scientific basis and validated against field data at different feedstocks and operating conditions. The model correctly predicts the effect of relevant process parameters such as reformer feed pressure and temperature, steam to carbon ratio and plant load.

In addition, the paper proposes the design of an industrial-scale rapid vacuum pressure swing adsorption (RVPSA) unit which was designed and simulated to capture carbon dioxide from the flue gas exiting the steam reformer. The RVPSA unit was integrated in the current plant enabling the concentration of CO₂ with a purity of 96.64%, an overall recovery of 90.84% and a specific energy consumption of 628.93 kJ/kgCO₂, thus meeting the requirements for transportation and geological storage. An energetic efficiency calculation was introduced to quantify the effectiveness of the hydrogen conversion process and to predict the effect of CO₂ capture and some process parameters to the overall H₂ production efficiency.

Radiation Oncology

Department of Medicine and Surgery

**Head** S. Ramella**Faculty** R.M. D'Angelillo (until November 2019), M. Fiore, E. Ippolito**Other Personnel** A. Carnevale, A. Di Donato, B. Floreno, C. Greco, A. Iurato, P. Matteucci, E. Molfese, C. G. Rinaldi, S. Silipigni, L.E. Trodella, L. Trodella

Description

The Radiation Oncology Research Unit's strategy focuses on the association between radiotherapy and systemic agents and on radiobiological and technical issues. In particular, combination of radiation and target agents, chemotherapy and immunotherapy in clinical and multidisciplinary setting is investigated. Special efforts are about combined treatment of lung cancer, prostate cancer, pancreatic cancer and rectal cancer. In addition, modern breast irradiation technique is explored in order to optimize dose distribution to the target and to the organs at risk. Special techniques such as stereotactic treatment, volumetric arc therapy and respiratory gating are implemented in radiation research protocols and in clinical practice. A novel interest of the research group involves radiomics which revealed itself as the needed bridge between medical imaging and personalized medicine. Moreover, new tools to monitor patients' quality of life are being developed.

Main research activities

In the era of personalized medicine, the main topic developed has been exploiting radiopathomics data in NSCLC, in order to develop a RadioPathomics-based Decision Support Systems (RPDSSs) to predict the progression free survival (PFS), best response and pulmonary toxicity during chemoradiation. In castration resistant prostate cancer, a national project about the role of radiation therapy with new hormonal drugs is ongoing. In addition, the research unit is involved in three multicentric randomized interventional studies regarding second line treatment of refractory SCLC, adjuvant immunotherapy in locally advanced NSCLC treated with chemoradiation and the combination between immunotherapy and stereotactic radiotherapy in stage I NSCLC. Multidisciplinary treatment protocols in gastrointestinal cancer are also ongoing.

Most important publications

Dingemans A.C., Hendriks L.E.L., Berghmans T., Levy A., Hasan B., Faivre-Finn C., Giaj-Levra M., Giaj-Levra N., Girard N., Greillier L., Lantuéjoul S., Edwards J., O'Brien M., Reck M., Smit E.F., Van Schil P., Postmus P.E., Ramella S., et al.

Definition of synchronous oligometastatic non-small cell lung cancer-a consensus report.

J Thorac Oncol. 2019 Dec;14(12):2109-2119. PMID: 31398540. IF 12,46

Introduction: Improved outcome has been shown in patients with synchronous oligometastatic (sOM) NSCLC when treated with radical intent. As a uniform definition of sOM NSCLC is lacking, we developed a definition and diagnostic criteria by a consensus process. **Methods:** A pan-European multidisciplinary consensus group was established. Consensus questions were built on the basis of current controversies, and definitions were extracted from a survey, cases and a systematic review. This statement was formulated during a consensus meeting. **Results:** It was determined that definition of sOM NSCLC is relevant when a radical treatment that may modify the disease course (leading to long-term disease control) is technically feasible for all tumor sites with acceptable toxicity. On the basis of the review, a maximum of five metastases and three organs was proposed. Mediastinal lymph node involvement was not counted as a metastatic site. Fludeoxyglucose F 18 positron emission tomography-computed tomography and brain imaging were considered mandatory. A dedicated liver magnetic resonance imaging scan was advised for a solitary liver metastasis, and thoracoscopy and biopsies of distant ipsilateral pleural sites were recommended for a solitary pleural metastasis. For mediastinal staging, fludeoxyglucose F 18 positron emission tomography-computed tomography was deemed the minimum requirement, with pathological confirmation recommended if this influences the treatment strategy. Biopsy of a solitary metastatic location was mandated unless the multidisciplinary team is of the opinion that the risks outweigh the benefits. **Conclusion:** A multidisciplinary consensus statement on the definition and staging of sOM NSCLC has been formulated. This statement will help to standardize inclusion criteria in future clinical trials.

Lapini A., Caffo O., Pappagallo G., Iacovelli R., D'Angelillo RM., Vavassori V., Ceccarelli R., Bracarda S., Jereczek-Fossa BA., Da Pozzo L., Conti GN.

Monitoring patients with metastatic hormone-sensitive and metastatic castration-resistant prostate cancer: a multidisciplinary consensus document.

Cancers (Basel). 2019 Dec 1;11(12):1908. PMID: 31805687. IF 6,162

Background: The availability of a number of agents that are efficacious in patients with metastatic prostate cancer (mPC) has led to them being used sequentially, and this has prolonged patient survival. However, in order to maximize their efficacy, clinicians need to be able to obtain a reliable picture of disease evolution by means of monitoring procedures. **Methods:** As the intensive monitoring protocols used in pivotal trials cannot be adopted in everyday clinical practice and there is no agreement among the available guidelines, a multi-disciplinary panel of Italian experts met to develop recommendations for monitoring mPC patients using a modified Delphi method. **Results:** The consensus project considered methods of clinically, radiographically, and bio-chemically monitoring patients with metastatic hormone-sensitive and metastatic castration-resistant prostate cancer undergoing chemotherapy and/or hormonal treatment. The panelists also considered the methods and timing of monitoring castration levels, bone health, and the metabolic syndrome during androgen deprivation therapy. **Conclusions:** The recommendations, which were drawn up by experts following a formal and validated consensus procedure, will help clinicians face the everyday challenges of monitoring metastatic prostate cancer patients.

Putora P.M., Glatzer M., Belderbos J., Besse B., Blackhall F., Califano R., Cappuzzo F., de Marinis F., Dziadziuszko R., Felip E., Faivre-Finn C., Früh M., Garrido P., Le Pechoux C., McDonald F., Nestle U., Novello S., O'Brien M., Paz Ares L., Peeters S., Pöttgen C., Ramella S., Reck M., Slotman B., Troost E.G.C., Van Houtte P., Westeel V., Widder J., Mornex F., De Ruyscher D.

Prophylactic cranial irradiation in stage IV small cell lung cancer: selection of patients amongst European IASLC and ESTRO experts.

Radiother Oncol. 2019 Apr; 133:163-166. PMID: 30935574. IF 5,252

Background: Due to conflicting results between major trials the role of prophylactic cranial irradiation (PCI) in stage IV small cell lung cancer (SCLC) is controversial. **Methods:** We obtained a list of 13 European experts from both the European Society for Therapeutic Radiation Oncology (ESTRO) and the International Association for the Study of Lung Cancer (IASLC). The strategies in decision making for PCI in stage IV SCLC were collected. Decision trees were created representing these strategies. Analysis of consensus was performed with the objective consensus methodology. **Results:** The factors associated with the recommendation for the use of PCI included the fitness of the patient, young age and good response to chemotherapy. PCI was recommended by the majority of experts for non-elderly fit patients who had at least a partial response (PR) to chemotherapy (for complete remission (CR) 85% of radiation oncologists and 69% of medical oncologists, for PR: 85% of radiation oncologists and 54% of medical oncologists). For patients with stable disease after chemotherapy, PCI was recommended by 6 out of 13 (46%) radiation oncologists and only 3 out of 13 medical oncologists (23%). For elderly fit patients with CR, a majority recommended PCI (62%) and no consensus was reached for patients with PR. **Conclusion:** European radiation and medical oncologists specializing in lung cancer recommend PCI in selected patients and restrict its use primarily to fit, non-elderly patients who responded to chemotherapy.

Tissue Engineering & Chemistry for Engineering

Department of Engineering



Head M. Trombetta

Faculty F. Basoli, A. Rainer, S.M. Giannitelli, E. Mauri

Other Personnel F. Abbruzzese, M. Gori

Description

The Tissue Engineering and Chemistry for Engineering Research Unit works mainly on the following fields:

Tissue engineering: the Unit works on the synthesis and functionalization of biomaterials and manufacturing of scaffolds for regenerative medicine application. The Unit also develops advanced in vitro tissue and organ models for drug discovery and morphogenesis/pathogenesis studies. In particular, one of the most promising research lines is focused on the integration of micro-manufacturing technologies with tissue engineering ones, designed to miniaturize organ models to be combined with advanced imaging and spectroscopy techniques (organ-on-chip approach). At present, the Research Unit is involved in a Joint Laboratory for Nanotechnologies for the Life Sciences (nano4life), together with the Institute of Photonics and Nanotechnologies, National Research Council of Rome.

Nanomaterials for energy: sulphur, carbon and re-oxidation tolerant Solid Oxide Fuel Cells (SOFC) an-

odes.

Food crime: development of e-learning platforms to train Europol officers on food crime.

Critical Infrastructure Protection: creating added-value, decision-support capabilities with consequence analysis for national and multi-nation emergency management and CI owners

Main research activities

Dr. Alberto Rainer has been awarded a research grant in the framework of the Internal Grant Program for the project "GUT2.0 - A multi-cellular 'gut-on-chip' technology for predictive human safety testing: an integrated experimental and modeling approach". GUT 2.0 foresees the application of an organ-on-chip model in the field of predictive safety. The approach proposed by the present method represents a significant advance in the field of in vitro models, as we foresee to recapitulate, within the 'chip' footprint, a multicellular gut environment. This approach represents an increased level of complexity if compared with the in vitro toxicological models for the

intestine. Hence, its development should provide the necessary degree of interplay among different cell populations for a robust safety testing model. Prof. Marcella Trombetta is National Coordinator of a PRIN2012 project entitled "aCTIoN - Cells-on-chip technologies for the study of the endocannabinoid system in an in vitro model of tumor/immune system interaction". The project aims to develop advanced models for the in vitro study of cellular interactions, taking advantage from 3D co-culture technologies within microfluidic devices. In particular, the on-chip technologies will be applied to a model of tumor stem compartment to study its interaction with immune system cells) to investigate the role of the endocannabinoid system in the cross-talk between the two populations.

Prof. Marcella Trombetta is Scientific Coordinator and Leader of the Operational Activity 4.10 "BACCUS Class: an e-learning platform for training law enforcement officers to combat food crime" of the Europol project coordinated by Carabinieri NAS "ASKLEPIOS-Actions on food Supplements, fake genuine (not) food exhibition, e-Learning platform, action

on Pesticides, operation “In Our Sites” and JAD” funded by EU Commission- Europol for the EM-PACT activities under the OAP Counterfeit Goods. Prof. Marcella Trombetta is partner of the project CIPR-Net, Critical Infrastructure

Research and Resilience Network Co-funded by EU FP7. CIPRNet establishes a Network of Excellence in Critical Infrastructure Protection (CIP). CIPRNet performs research and development that addresses a wide range of stake-

holders including (multi) national emergency management, critical infrastructure operators, policy makers, and the society.

Most important publications

Nocita E., Del Giovane A., Tiberi M., Boccuni L., Fiorelli D., Sposato C., Romano E., Basoli F., Trombetta M., Rainer A., Traversa E., Ragnini-Wilson A.

EGFR/ErbB inhibition promotes OPC maturation up to axon engagement by co-regulating PIP2 and MBP.

Cells. 2019 Aug 6;8(8):844. PMID: 31390799. IF 5,656

Remyelination in the adult brain relies on the reactivation of the Neuronal Precursor Cell (NPC) niche and differentiation into Oligodendrocyte Precursor Cells (OPCs) as well as on OPC maturation into myelinating oligodendrocytes (OLs). These two distinct phases in OL development are defined by transcriptional and morphological changes. How this differentiation program is controlled remains unclear. We used two drugs that stimulate myelin basic protein (MBP) expression (Clobetasol and Gefitinib) alone or combined with epidermal growth factor receptor (EGFR) or Retinoid X Receptor gamma (RXR γ) gene silencing to decode the receptor signaling required for OPC differentiation in myelinating OLs. Electrospun polystyrene (PS) microfibers were used as synthetic axons to study drug efficacy on fiber engagement. We show that EGFR inhibition per se stimulates MBP expression and increases Clobetasol efficacy in OPC differentiation. Consistent with this, Clobetasol and Gefitinib co-treatment, by co-regulating RXR γ , MBP and phosphatidylinositol 4,5-bisphosphate (PIP2) levels, maximizes synthetic axon engagement. Conversely, RXR γ gene silencing reduces the ability of the drugs to promote MBP expression. This work provides a view of how EGFR/ErbB inhibition controls OPC differentiation and indicates the combination of Clobetasol and Gefitinib as a potent remyelination-enhancing treatment.

Mauri E., Naso D., Rossetti A., Borghi E., Ottaviano E., Griffini G., Masi M., Sacchetti A., Rossi F.

Design of polymer-based antimicrobial hydrogels through physico-chemical transition.

Mater Sci Eng C Mater Biol Appl. 2019 Oct;103: 109791. PMID: 31349504. IF 4,959

The antimicrobial activity represents a cornerstone in the development of biomaterials: it is a leading request in many areas, including biology, medicine, environment and industry. Over the years, different polymeric scaffolds are proposed as solutions, based on the encapsulation of metal ions/particles, antibacterial agents or antibiotics. However, the compliance with the biocompatibility criteria and the concentration of the active principles to avoid under- and over-dosing are being debated. In this work, we propose the synthesis of a versatile hydrogel using branched polyacrylic acid (carbomer 974P) and aliphatic polyetherdiamine (elastamine®) through physico-chemical transition, able to show its ability to counteract the bacterial growth and infections thanks to the polymers used, that are not subjected to further chemical modifications. In particular, the antimicrobial activity is clearly demonstrated against *Staphylococcus aureus* and *Candida albicans*, two well-known opportunistic pathogens. Moreover, we discuss the hydrogel use as drug carrier to design a unique device able to combine the antibacterial/antimicrobial properties to the controlled drug delivery, as a promising tool for a wide range of biomedical applications.

Campana P.T., Marletta A., Piovesan E., Francisco K.J.M., Neto F.V.R., Petrini L. Jr., Silva T.R., Machado D., Basoli F., Oliveira O.N. Jr., Licoccia S., Traversa E.

Pulsatile discharge from polymeric scaffolds: a novel method for modulated drug release.

Bull Chem Soc Jpn. 2019;92(7):1237-1244. DOI: 10.1246/bcsj.20180403 IF 4,431

Controlled drug release holds promise to revolutionize medicine, particularly if short-term and long-term release can be combined in a single system. We present here a new pulsatile release system, in which the pulses were achieved using 3D scaffolds of poly(L-lactic acid), PLLA. From a morphological characterization of the scaffold's surfaces, before and after releasing experiments at distinct pHs, we infer that release is governed by electrostatic interactions and the fractal geometry of the scaffolds. Furthermore, the scaffold can present short-term (within hours) or long-term (several days long) releasing profiles by varying the pH, which opens the way for unprecedented drug release control. We introduce a new pulsatile release system, using PLLA 3D scaffolds and performing release experiments at distinct pH. We infer that release is governed by electrostatic interactions and the scaffolds' fractal geometry. Furthermore, the scaffold can present short-term (within hours) or long-term (several days long) releasing profiles by varying the pH, which opens the way for unprecedented drug release control.

Urology

Department of Medicine and Surgery

**Head** R. M. Scarpa**Faculty** M. Buscarini, R. Papalia**Other Personnel** F. Esperto

Description

The research unit of Urology is focused on surgical innovations and clinical researches. The main fields of interest are: modern diagnostic tools and markers for prostate cancer, the study of radiomics for the prediction of prostate cancer aggressiveness and new approaches for the treatment of urinary tract stones.

Main research activities

Our group was invited to write an Editorial Comment on Supracostal Upper Pole Endoscopic-Guided Prone Tubeless "maxi-Percutaneous Nephrolithotomy" on the Journal of Endourology.

We evaluated Urotensin II receptor expression in prostate cancer patients as a new possible marker and published results on The Prostate.

We also cooperated for a multicentric study on 1,119 patients on elastic fusion biopsy versus systematic biopsy for prostate cancer detection and published results on Actas Urological Espanolas.

Our retrospective analysis on effectiveness of transurethral prostate procedures at enabling urologic medication discontinuation has been published on Urology.

Our cooperation with other institutions allowed to publish a multicentric study on prostate cancer grading accuracy with systematic and MRI/US fusion targeted biopsies on World Journal of Urology.

Most important publications

Scarpa R.M., Papalia R.

Re: Giusti et al., Editorial comment on: Supracostal upper pole endoscopic-guided prone tubeless "maxi-percutaneous nephrolithotomy": a contemporary evaluation of complications by Altschuler et al. (From: Giusti G., Proietti S., Rodríguez-Socarrás M.E. J Endourol 2019; 33:279-280; DOI: 10.1089/end.2018.0856).

J Endourol. 2019 Apr;33(4): 281-282. PMID: 30760023. IF 2,267

Objective: To develop a contemporary complication profile for supracostal upper pole endoscopic-guided prone tubeless "maxi-PCNL" to evaluate the need for change. **Materials/Methods:** We identified patients undergoing supracostal upper pole percutaneous nephrolithotomy (PCNL) by a single surgeon at a high volume tertiary care stone center between October 2010 and April 2017. Access was obtained with ureteroscopic guidance. The tract was dilated to 30F through radial balloon dilation. All cases were tubeless with ureteral stent for 5-7 days. Preoperative, operative, and postoperative variables were recorded. We recorded need for blood transfusion, angioembolization, thoracentesis and/or chest tube insertion, intensive care unit (ICU) admission, and 30-day readmission. **Results:** A total of 375 patients were included. Mean age was 57 years and 59% were women. Mean body mass index was 33 kg/m². Mean stone burden was 35 mm. The mean operative time was 99 minutes. Median stay was 1 day. There were no complications because of prone position. Postoperative complications included pleural drain (4%), transfusion (6.7%), and angioembolization (0.5%). Transfusion rates were higher in patients with preoperative hemoglobin <10 mg/dL (28% vs 5.1%, $p < 0.00001$). Rate of ICU admission and readmission was 4.5% and 7.5%, respectively. Transfusion ($p \leq 0.001$), pleural drain ($p = 0.0002$), and readmission ($p = 0.030$) were associated with ICU admission. Male gender was associated with readmission (10.3% vs 5.5%, odds ratio = 3.1, $p = 0.012$). **Conclusions:** In supracostal upper pole endoscopic-guided prone tubeless Maxi-PCNL, pulmonary complication rate was lower than previously reported and bleeding complications were comparable with mini-PCNL series. Establishing contemporary complication rates will help to assess the need for evolution to mini-PCNL or lower pole supine PCNL.

Scarpa R.M., Papalia R.

Editorial comment on: Comparative effectiveness of transurethral prostate procedures at enabling urologic medication discontinuation: a retrospective analysis.

Urology. 2019 Dec; 134:197-198. PMID: 31789179. IF 1,861

Objectives: To test the hypothesis that transurethral prostate procedures (TUPPs) eliminating tissue result in greater medication discontinuation and lower de novo initiation rates than procedures inducing tissue necrosis. **Methods:** Retrospective review of all men undergoing first time TUPPs at a large tertiary center from 2001 to 2016 was completed. Procedure type and urologic medication use before, 3-12 months after, and greater than 12 months after TUPP were analyzed with simple open prostatectomy as a comparator. Tissue-eliminating TUPPs included transurethral resection of the prostate and laser prostatectomy. Tissue-necrosing procedures included microwave therapy (transurethral microwave therapy) and radiofrequency ablation (transurethral needle ablation), which were grouped in analyses. Medication types were 5-alpha reductase inhibitors (5ARI), alpha blockers, anticholinergics, and beta-3 agonists (B3A). **Results:** A total 5150 TUPPs were analyzed. Preoperative medication uses significantly varied across TUPPs for 5ARI ($P < .01$), alpha-blockers ($P .01$), and anticholinergics ($P .047$), but not B3A ($P .476$). Transurethral resection of the prostate and laser prostatectomy were associated with significantly higher medication discontinuation rates and lower resumption and initiation rates compared to tissue-necrosing procedures. Relative to TUPPs, simple prostatectomy had significantly higher medication discontinuation, as well as the lowest resumption and initiation rates. **Conclusion:** Tissue-eliminating benign prostatic hyperplasia procedures were associated with better medication discontinuation, resumption, and de novo initiation rates compared to tissue-necrosing benign prostatic hyperplasia procedures.

Diamand R., Oderda M., Al Hajj Obeid W., Albisinni S., Van Velthoven R., Fasolis G., Simone G., Ferriero M., Roche J.B., Piechaud T., Pastore A., Carbone A., Fiard G., Descotes J.L., Marra G., Gontero P., Altobelli E., Papalia R., Kumar P., Eldred-Evans D., Giacobbe A., Muto G., Lacetera V., Beatrice V., Roumeguere T., Peltier A.

A multicentric study on accurate grading of prostate cancer with systematic and MRI/US fusion targeted biopsies: comparison with final histopathology after radical prostatectomy.

World J Urol. 2019 Oct;37(10):2109-2117. PMID: 30652213. IF 2,761

Objective: To evaluate the accuracy in histologic grading of MRI/US image fusion biopsy by comparing histopathology between systematic biopsies (SB), targeted biopsies (TB) and the combination of both (SB+TB) with the final histopathologic outcomes of radical prostatectomy specimens. **Materials and Methods:** Retrospective, multicentric study of 443 patients who underwent SB and TB using MRI/US fusion technique (Urostation® and Trinity®) prior to radical prostatectomy between 2010 and 2017. Cochran's Q test and McNemar test were conducted as a post hoc test. Uni-multivariable analyses were performed on several clinic-pathological variables to analyze factors predicting histopathological concordance for targeted biopsies. **Results:** Concordance in ISUP (International Society of Urological Pathology) grade between SB, TB and SB+TB with final histopathology was 49.4%, 51.2%, and 63.2% for overall prostate cancer and 41.2%, 48.3%, and 56.7% for significant prostate cancer (ISUP grade ≥ 2), respectively. Significant difference in terms of concordance, downgrading and upgrading was found between SB and TB (ISUP grade ≥ 2 only), SB and SB+TB, TB and SB+TB (overall ISUP grade and ISUP grade ≥ 2) ($p < 0.001$). Total number of cores and previous biopsies were significant independent predictive factors for concordance with TB technique. **Conclusion:** In this retrospective study, combination of SB and TB significantly increased concordance with final histopathology despite a limited additional number of cores needed.

Vascular Surgery

Department of Medicine and Surgery



Head F. Spinelli

Faculty F. Stilo

Other Personnel V. Catanese, N. Montelione

Description

Our interests focus on all the aspects of arterial surgery, from the carotid artery endarterectomy/bypass for prevention of cerebral ischemia, down to the plantar revascularization for limb salvage, through all the diseases of the aorta. When endovascular treatment is the best choice for the patient, it strictly follows the Instructions for Use from the manufacturer. Large vessels reconstruction after tumor resection is one of our specific interest.

Decision making impacts on survival in Critical Limb Ischemia

We already showed that the Endovascular technique and open bypass are complementary in treatment of CLI, as these apply to different patterns of disease. While the majority of patients with rest pain can be successfully treated by endovascular techniques despite the TASC II class, those with advanced necrosis and tissue loss are best treated by an open bypass whenever possible. In the last year we could update our series and refine our ultrasound-based decision algorithm. The significant

improvement of late survival of our patients, compared to most of the current series, confirmed the value of this approach

EVAR: Role of open conversion

EV treatment of endoleaks is not always possible, and an open conversion is occasionally needed. In the case of suprarenal grafts this can be a hazardous procedure. Following the principle of minimally invasive laparotomic aneurysm repair, we propose a technique to make open conversion safer, avoiding the removal of the whole suprarenal graft.

Restenosis after CEA: indications to the treatment

Restenosis after CEA is currently treated by CAS. Late reports have shown suboptimal late results.

We already reported our series of carotid restenosis treated by a carotid vein graft in patients with a longlife expectancy. We have updated our series with the late controls favoring this option versus CAS.

Recently we have participated to an international review regarding this concern.

Also, we will study the histologi-

cal component of atherosclerotic plaque associated of plasma level of proinflammatory factors.

Endovascular and Open treatment of aortic embolism causing distal disease

Critical limb ischemia due to aortic athero embolism is not as rare as it is currently believed. This is an insidious disease and if unrecognized can be at the origin of failures of treatment and bad outcomes. An endovascular aortic coverage, coupled with a femoral to popliteal or tibial graft seems to be a durable solution. We reviewed our series of such hybrid procedures, and described the diagnostic workout, technique and results.

Main collaborations

- Sapienza University of Rome, Italy
- St. Thomas Hospital, University of London, UK
- University of Messina, Italy
- University of Oxford, UK
- Vall d'Hebron Hospital, Barcelona, Spain

Most important publications

Stilo F., Montelione N., Vigliotti R. C., Spinelli F.

Transaxillary decompression of thoracic outlet syndrome.

It J Vasc Endovasc Surg. 2019; 26(1):6-9. DOI: 10.23736/S1824-4777.18.01394-3

Background: The thoracic outlet syndrome (TOS) is a defined clinical and etiologically disorder characterized by the compression of the neurovascular bundle in the thoracic outlet with an estimated incidence of 0.3% to 2% in the general population. The most frequent is the neurogenic TOS, while the arterial and the venous TOSs are relatively uncommon. The diagnosis is essentially clinic, supported by imaging. The aim of this study was to present our experience in surgical decompression of TOS through transaxillary approach.

Methods: A retrospective study was conducted on a prospectively compiled, computerized database between May 2014 and June 2018 including patients affected by TOS surgically treated in our center. We obtained diagnosis firstly considering clinical presentation and physical examination; then performing chest radiography, computed tomography angiography and/or magnetic resonance imaging, which can exclude other cause for patient's symptoms.

Results: Of the 16 patients, 14 were women (87.5%) and 2 were man (12.5%). Median age was 37.4 ± 10.6 . Clinical presentation was neurological in 10 patients (62.5%), venous in 3 (18.7%) and arterial in 1 patient (6.25%). In two patients (12.5%) both neurological and venous symptoms were present. Two patients (12.5%) had bilateral TOS. Technical success was achieved in all cases. The main perioperative complication was pneumothorax in 8 patients (50%). Neurological complications or nerve injury were null. Symptoms recurrence was 6.25%. **Conclusions:** In our experience transaxillary approach is a safe and feasible procedure associated with an acceptable rate of perioperative morbidity and satisfactory long-term relief of symptoms.

Virology

Department of Medicine and Surgery



Head E. Riva

Other Personnel F. Antonelli, C. Concato, L. Piccioni

Description

The Virology Research Unit is involved in both basic and clinical virology.

The main topics concern host's and viral factors able to predict the outcome and the treatment response of persistent viral infections such as HCV infection (in terms of Progression and treatment response), CMV infection (in terms of reactivation and clinical progression in transplanted recipients) and HPV infections (in terms of HPV-related dysplasia progression).

Based on the past and the more recent experience, the Virology research staff is mainly involved in the field of molecular virology and in assays useful in identifying and monitoring viral infections other than specific Single nucleotide polymorphisms (SNPs) such as Real Time PCR, Melting and Pyrosequencing analysis and Syndromic molecular panels.

Main research activities

The specific SNPs that have been under study are mainly rs12979860, rs8099917, ss46945590 TT/delta G SNPs in Interferon lamda III-IV region. These SNP are mainly involved in host's innate immunity and in treatment response in chronic infectious diseases.

The Unit has been also involved in the comparison and validation of molecular methods applied for persistent virus (CMV, HCV, EBV and parvovirus) and emergent/acute infections (Chikungunya, respiratory viruses).

All these topics are addressed in ongoing studies which involve different areas of Campus Bio-Medico University Hospital.

The team Acts also in the contest of the project "Migrant and Health" aimed to prevent and monitoring infectious diseases in Migrants and in the implementation and validation of molecular syndromic panels (respiratory, CNS, sexual transmitted and enteric diseases). Recent interest involves the relevance of respiratory infections in pediatric/adult immunodepressed. The Virology Unit is also in close

collaboration with the Department of Molecular Medicine -Virology section- Sapienza University of Rome, AIFA/EMA and with the Virology Lab of IRCCS Bambino Gesù Paediatric Hospital of Rome, Italy.

Main collaborations

- Department of Molecular Medicine -Virology section- "Sapienza" University of Rome, Italy;
- Virology Lab, IRCCS Bambino Gesù Paediatric Hospital, Italy.

Most important publications

Spoto S., Valeriani E., Locorriere L., Anguissola G.B., Pantano A.L., Terracciani F., Riva E., Ciccozzi M., Costantino S., Angeletti S.

Influenza B virus infection complicated by life-threatening pericarditis: a unique case-report and literature review.

BMC Infect Dis. 2019 Jan 10;19(1):40. PMID: 30630424. IF 2,565

Background: Acute pericarditis may occur frequently after viral infections. To our knowledge, influenza B virus infection complicated by pericarditis without myocardial involvement has never been reported. We report the first case of life-threatening pericarditis caused by influenza B virus infection. **Case presentation:** A 48-years-old woman with trisomy 21 and ostium primum atrial septal defect was transferred from Cardiology to our Internal Medicine Department for severe pericardial effusion unresponsive to ibuprofen and colchicine. Based on the recent patient history of flu-like syndrome, and presence of pleuro-pericardial effusion, a viral etiology was suspected. Laboratory evaluation and molecular assay of tracheal aspirate identified influenza B virus. Therefore, the ongoing metilprednisolone and colchicine therapy was implemented with oseltamivir with progressive patient improvement and no evidence of pericardial effusion recurrence during follow-up. **Conclusions:** Especially in autumn and winter periods, clinicians should include Influenza B virus infection on differential diagnosis of pericarditis with large pericardial effusion.

Ceccarelli G., Cella E., Vita S., Lai A., Ebranati E., Zehender G., Fogolari M., Antonelli F., Luca Guarino M.P., Riva E., Angeletti S., Ciccozzi M.

A case of hepatitis B virus infection in Eritrean Diciotti migrant: phylogenetic analysis and 'mirror effect'.

Future Virol. 2019; 14(8):509-514. DOI: 10.2217/fvl-2019-0034 IF 0,730

A case of hepatitis B virus (HBV) infection in an Eritrean migrant was described to provide an epidemiological approach based on phylogenetic analysis useful in developing countries with lacking information. Migrant, positive for HBsAg and HBeAg, carried HBV at high copy number. A sequence of HBV HBsAg region was used for phylogenetic relationships and genetic variability investigation. In the phylogenetic tree, the sequence corresponded to D2 HBV genotype and the cluster root dated 7 years ago. These data compared with the date of landing in Italy, suggest that he was infected at least 7 years before his arrival. This approach by 'mirror effect' allows the reconstruction of HBV epidemiology in the country of origin, analyzing the migrant population in the host country.

The background of the slide is a light gray field filled with a repeating pattern of small, stylized scientific icons. These icons include DNA double helix structures, interlocking gears, and sprouting plants with leaves and roots. The icons are scattered across the entire page, creating a textured, scientific aesthetic.

Research Projects

Grants from Competitive Calls

EUROPEAN COMMISSION

RESHAPE

Restoring the Self with Embodiable Hand Prostheses

Principal Investigator: Prof. Giovanni Di Pino, Campus Bio-Medico University of Rome

Funding under: ERC-StG-2015 - ERC Starting Grant
End: 31/08/2021

Contacts: Giovanni Di Pino (g.dipino@unicampus.it), Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction

RESHAPE aims to study prosthesis embodiment, identify what makes a hand prosthesis easily embodyable, and test non-invasive brain stimulation to facilitate the embodiment.

The first of three phases develops the enabling technology and defines the embodiment protocol.

The following phase evaluates thirty myoelectric-prosthesis users and the first of two amputees implanted with peripheral neural electrodes, for functional ability, prosthesis embodiment and acceptability and for phantom limb pain (PLP), before and after neuro-modulation.

In the last phase, a neuro-controlled prosthesis is optimized in line with the specifications defined in the previous phase and tested in the second implanted amputee.

Patients are stimulated with a homeostatic plasticity-based rTMS either on premotor cortex or on intraparietal sulcus. A robot-aided TMS compensates head-coil relative displacement, allowing the subject to operate the prosthesis during the stimulation.

RESPINE

Regenerative therapy of intervertebral disc: a double blind phase 2b trial of intradiscal injection of mesenchymal stromal cells in degenerative disc disease of the lumbar spine unresponsive to conventional therapy

Coordinator: Centre Hospitalier Universitaire Montpellier

Partners: Campus Bio-Medico University of Rome, Universidad De Navarra, Universidad De Valladolid, Univercell-Biosolutions, National University Of Ireland, Galway, Citospin S.L., Institut De Terapia Regenerativa Tisular SI, Assistance Publique - Hôpitaux De Paris, Centre Hospitalier Universitaire De Nantes, Centre National De La Recherche Scientifique (CNRS), Ecrin European Clinical Research Infrastructure Network, Bg Klinikum Bergmannstrost Halle Ggmbh, Universite De Montpellier

Funding under: H2020-SC1-2016-RTD

End: 31/12/2022

Contacts: Gianluca Vadalà (g.vadala@unicampus.it), Research Unit of Orthopaedic and Trauma Surgery

The World Health Organisation (WHO) has included low back pain in its list of twelve priority diseases. Notably, Degenerative disc disease (DDD) presents a large, unmet medical need that results in a disabling loss of mechanical function. To develop the world's first rigorously proven, effective treatment of DDD, RESPINE aims to assess, via a multicentre, randomized, controlled, phase 2b clinical trial including 112 patients with DDD, the efficacy of an allogenic intervertebral mesenchymal stem cell (MSC)-based therapy. This innovative therapy aims to rapidly (within 3 months) and sustainably (at least 24 months) reduce pain and disability. In addition, the consortium aims to provide new knowledge on immune response & safety associated with allogeneic BM-MSC intradiscal injection. This simple procedure would be cost-effective, minimally invasive, and standardised.

CONVERGENCE

Frictionless Energy Efficient Convergent Wearables for Healthcare and Lifestyle Applications

Url: <https://www.convergence-era.org/>

Coordinator: Ecole Polytechnique Fédérale de Lausanne (EPFL)

Partners: Campus Bio-Medico University of Rome, CEA LETI – Laboratoire d'Electronique et de Technologie de l'Information, Elektronikas un datorzinatnu instituts/Signal Processing Lab, Italian National Agency for New Technologies, Energy and Sustainable

Economic (ENEA), ETHZ Eidgenössische Technische Hochschule Zürich / Department of Mechanical and Process Engineering, Institut Polytechnique de Grenoble, Hirslanden Clinic Cecil/Cardiovascular Center, Consorzio Nazionale Interuniversitario Per La Nanoelettronica (IUNET), Middle East Technical University, National Institute for R&D in Microtechnologies/Laboratory of Microsystems for Biomedical & Environmental Applications, ST Microelectronics, TAGLIAFERRI Società Responsabilità Limitata, Tallinn University of Technology / Thomas Johann Seebeck Department of Electronics, Unit of Electronics for Sensor Systems, Department of Engineering, Università degli Studi di Cagliari/Department of Electrical and Electronic Engineering, Universitatea Transilvania din Brasov/Department of Automation and Information Technology, Université catholique de Louvain.

Funding under: JTC2016-PILOTS

End: 28/02/2022

Contacts: Marco Santonico (m.santonico@unicampus.it), Research Unit of Electronics for Sensor Systems

The project adopts a focused strategy centred on proofs-of-concepts related to energy efficient sensor networks for future wearables exploiting the convergence of multi-parameter biosensors and environmental sensors on an autonomous system technology platform, serving data fusion for preventive life-style and healthcare. We connect solidly a critical mass of research institutions in-between and to some end user, to set the foundation of future emerging research project in this field, at European level by connecting national competences and resources.

DETOP

Dexterous Transradial Osseointegrated Prosthesis with neural control and sensory feedback

Coordinator: Scuola Superiore Sant'Anna di Pisa

Partners: Campus Bio-Medico University of Rome, Goeteborgs Universitet, Prensilia Srl, Integrum ab, Lunds Universitet, CSEM Centre Suisse d'Electronique ed de Microelectronique, University of Essex, Istituto Nazionale Assicurazione Infortuni sul Lavoro, Istituto Ortopedico Rizzoli

Funding under: H2020-ICT-2015

End: 28/02/2020

Contacts: Vincenzo Denaro (denaro@unicampus.it), Research Unit of Orthopaedic and Trauma Surgery

This project addresses the problem of recovery of hand function after amputation. Amputees continue to use technology for powered prostheses developed over 40 years ago. These devices do not purposely provide sensory feedback and are known for their poor functionality, controllability and sensory feedback.

The consortium has pioneered the use of osseointegration as a long-term stable solution for the direct skeletal attachment of limb prostheses. This technology aside from providing an efficient mechanical coupling can also be used as a bidirectional communication interface between implanted electrodes and the prosthetic arm. The goal of the DeTOP project is to push the boundaries of this technology to the next TRL and to make it clinically available to the largest population of upper limb amputees, namely transradial amputees.

IPSPINE

Induced pluripotent stem cell-based therapy for spinal regeneration

Coordinator: Universiteit Utrecht

Partners: Campus Bio-Medico University of Rome, Universite de Nantes, Ecole Nationale Veterinaire Agroalimentaire et de l'Alimentation Nantes Atlantique, Universitair Medisch Centrum Utrecht, National University of Ireland Galway, Universitaet Ulm, Universitaet Bern, Institut National De la Sante ed de la Recherche Medicale, Naturwissenschaftliches und Medizinisches Institut an der Universitaet Tuebingen, Ao-Forschungsinstitut Davos, Scheffield Hallam University, Ntrans Technologies bv, Universite de Montpellier, University of Miami, Spineserv GMBH & Co.Kg, The University of Hong Kong, Pharmalex GMBH, Catalyze B.V., Sticing Nationaal Reumafonds

Funding under: H2020-SC1-BHC-2018-2020

End: 31/12/2023

Contacts: Gianluca Vadalà (g.vadala@unicampus.it), Research Unit of Orthopaedic and Trauma Surgery

Low back pain (LBP) is a leading cause of disability and morbidity worldwide. It is widely accepted that a major contributor to LBP is intervertebral disc degeneration (IDD). These patients receive conservative treatment (e.g. pain relief medication and physiother-

apy). To date, no treatments halt or reverse IDD. The aim of the iPSpine team is to investigate and develop a new advanced therapy medicinal product (ATMP) of the future, based on a novel developmental biology-based therapeutic strategy employing pluripotent stem cells (iPSC) and smart biomaterials. The iPSpine consortium will develop and demonstrate Proof-of-concept with the aid of novel and extended knowledge, tools and technology platforms.

CONBOTS

CONnected through roBOTS: physically coupling humans to boost handwriting and music learning

Coordinator: Campus Bio-Medico University of Rome

Partners: Imperial College of Science Technology and Medicine, Sant'Anna School of Advanced Studies, Arvrtch Doo Novi Sad, Universiteit Gent, Iuvo Srl, IBM Israel – Science and Technology Ltd

Funding under: H2020-ICT-2018-20/H2020-ICT-2019-2

End: 30/06/2023

Contacts: Domenico Formica (d.formica@unicampus.it), Research Unit of Neurophysiology and Neuro-engineering of Human-Technology Interaction

From a parent coordinating movements to help a child learn to walk, to a violinist training a concerto, humans rely on physical interaction to learn from each other and from the environment. Building on a strongly multidisciplinary foundation with an integrated approach, CONBOTS proposes a paradigm shift that aims to augment hand-writing and music learning through robotics, by creating a physically interacting robotic platform connecting humans in order to facilitate the learning of complex sensorimotor tasks.

The newly designed platform will combine four enabling technologies: i) compact robotic haptic devices to gently interact with upper limbs; ii) an interactive controller yielding physical communication, integrating differential Game Theory (GT) and an algorithm to identify the partner's control; iii) a bi-directional user interface encompassing AR-based application-driven serious games, and a set of wearable sensors and instrumented objects; iv) Machine learning algorithms for tailoring learning exercises to the user physical,

emotional, and mental state

CONBOTS is building on recent neuroscientific findings that showed the benefits of physical interaction to performing motor tasks together, where the human central nervous system understands a partner motor control and can use it to improve task performance and motor learning. This will be implemented on innovative robotic technology, wearable sensors and machine learning techniques to give rise to novel human-human and human-robot interaction paradigms applied in two different learning contexts: i) training graphomotor skills in children learning handwriting; ii) augmenting learning performance in beginner musicians.

Using its neuroscience-driven unifying approach to motor learning and physical communication CONBOTS will expand the impact and the application of robotics to the education industry.

FIDELIO

Training network for research into bone Fragility In Diabetes in Europe – towards a person-aLised medicine apprOach

Coordinator: Technische Universitaet Dresden

Partners: Campus Bio-Medico University of Rome, Syddansk Universitet, Universitaetsklinikum Hamburg-Eppendorf, Universite de Geneve, Eidgenoesische Technische Hochschule Zuerich, The University of Sheffield, Erasmus Universitair Medisch Centrum Rotterdam, Tamirna GMBH

Funding under: H2020-MSCA-ITN-2019

End: 30/09/2023

Contacts: Nicola Napoli (n.napoli@unicampus.it), Research Unit of Endocrinology and Diabetes

Diabetes is characterized by chronic inflammation and dysregulation of Wnt pathway and thus may contribute to diabetic bone complication. In our study we aim to test the effect of fiber-rich diet (FEHC) on improving bone and muscle health in type 2 diabetes (T2D) through a positive effect on inflammation and Wnt pathway. We will enroll elderly T2D women undergoing hip replacement. Inflammation, Wnt markers and bone quality will be assessed before and after intervention from serum, fat, muscle and bone tissues. Our study may improve the understanding of the molecular mechanisms and therapeutic approach of T2D related bone and muscle fragility.

EXPERIENCE

Benchmarking Exoskeleton-Assisted Gait Based on Users' Subjective Perspective and Experience

Coordinator: Santa Lucia Foundation

Partners: Campus Bio-Medico University of Rome

Funding under: Eurobench FSTP-1 Open Call – Sub-projects Grant Agreement

End: 09/12/2020

Contacts: Nevio Tagliamonte (n.tagliamonte@uni-campus.it), Research Unit of Advanced Robotics and Human Centred Technologies

The objective of the EXPERIENCE project is to provide developers of lower-limb exoskeletons and clinical experimenters with a benchmarking method capable of catching the subjective experience of end-users, which goes beyond both quantitative biomechanical metrics and qualitative clinical scales inasmuch as it centrally includes the personal opinion of the user, who is considered to be the main actor and the most important source of information during human-robot interaction. The project will devise a benchmarking method for the user-centered assessment of exoskeleton-assisted gait including a novel purposely developed multifactor questionnaire and a set of indicators estimating the user's psychophysiological state starting from physiological signals. Data including questionnaire results and psychophysiological indicators are collected during pilot experiments with stroke, spinal cord injury and healthy subjects interacting with treadmill-based and overground exoskeletons. The project includes Università Campus Bio-Medico di Roma and Santa Lucia Foundation (coordinator).

BENCHBALANCE

BenchBalance: a device to apply well defined perturbations for benchmarking balance capabilities of wearable robots

Coordinator: Agencia Estatal Consejo Superior de Investigaciones Científicas

Partners: Universiteit Twente, Polytechnic University of Madrid, Campus Bio-Medico University of Rome

Funding under: Eurobench FSTP-1 Open Call – Sub-projects Grant Agreement

End: 10/02/2021

Contacts: Nevio Tagliamonte (n.tagliamonte@uni-campus.it), Research Unit of Advanced Robotics and Human Centred Technologies

BenchBalance project aims at developing a benchmarking solution to conduct reproducible assessments of balance in different conditions, mainly focused on wearable lower-limb exoskeletons but also applicable to humans not wearing them. The main objective is to design and develop a novel and low-cost testbed capable of measuring well-defined external perturbations, manually provided by an experimenter, in terms of magnitude, orientation and location. To approach this goal, BenchBalance integrates two key elements: (1) a portable perturbator equipped with a force sensor, which can provide and quantify the applied perturbations; (2) a smart garment, which determines the location of the generated disturbance on the human body. The information provided by the developed testbed is merged and synchronized with the data provided by the tested exoskeleton and/or by a conventional motion capture system, and subsequently analysed to derive metrics (body sway and recovery time) to assess the balance capabilities of the user-exoskeleton compound system.

The project includes Università Campus Bio-Medico, Polytechnic University of Madrid and University of Twente (coordinator).

ITALIAN MINISTRY OF EDUCATION, UNIVERSITY AND RESEARCH

PRIN (Research Projects of National Interest) 2015

Adaptation and tolerance of plants to climate change-dependent abiotic stresses

Coordinator: Università di Milano

Partners: Research Unit of Food Science and Nutrition (UCBM), Università degli studi di Padova, Scuola Superiore di Studi Universitari e Perfezionamento Sant'Anna

Endocannabinoid Signaling in Alzheimer's Disease: A Novel Target for Mechanistic Understanding and Potential Therapeutics

Coordinator: Mauro Maccarrone - Research Unit of biochemistry and molecular biology (UCBM)

Partners: Consiglio Nazionale delle Ricerche, Università degli Studi di Roma "La Sapienza", Università degli Studi di Roma "Tor Vergata" Università degli Studi di Teramo

Pancreatic β -cell identity, glucose sensing and the control of insulin secretion

Coordinator: Paolo Pozzilli - Research Unit of endocrinology and diabetes

Partners: Università degli Studi di Verona, Università degli Studi di Catania, Università degli Studi di Parma, Università degli Studi di Roma "La Sapienza", Università Cattolica del Sacro Cuore, Università degli Studi di Siena, Università di PISA, Università degli Studi di Roma "Tor Vergata", Libera Università "Vita Salute S. Raffaele" Milano

PRIN (Research Projects of National Interest) 2017

Advanced injectable nano-composite biomaterials with dual therapeutic/regenerative behaviors for bone cancer (ACTION)

Coordinator: National Research Council (CNR)

Partners: Research Unit of Orthopaedic and Trauma Surgery (UCBM), Polytechnic University of Milan

Molecular and pathophysiological heterogeneity of autoimmune diabetes: implications for precision medicine

Coordinator: Sapienza University of Rome

Partners: Research Unit of allergology, immunology, rheumatology (UCBM), University of Siena, Vita Salute San Raffaele University, National Research Council (CNR), University of Pisa

Novel therapeutic strategies to reduce coronary microvascular obstruction and to OPTimize non-culprit stenosis revascularization in ST-Elevation acute Myocardial Infarction (OPTI-STEMI project)

Coordinator: University of Naples "Federico II"

Partners: Research Unit of Cardiovascular Science (UCBM), Catholic University of the Sacred Heart, Sapienza University of Rome, University of Verona

3D Muscle-Tendon Unit modelling for unravelling tissue crosstalk in muscular dystrophies and aging (3D-MTU)

Coordinator: Università degli Studi di Padova

Partners: Research Unit of Orthopaedic and Trauma Surgery (UCBM), University of Milan, University of Bologna, University of Rome "Tor Vergata", National Research Council (CNR)

FARE ERC

ENABLE - Empowering Novel Augmentation of Limb Embodiment

Principal Investigator: Dr. Giovanni Di Pino, Campus Bio-Medico University of Rome

PON (National Operational Program)

ARONA (Advanced Robotic-Assisted Surgical Navigation)

Coordinator: Masmec S.p.A.

Partners: Research Unit of Advanced Robotics and Human Centred Technologies (UCBM), Research Unit of Diagnostic Imaging (UCBM), Research Unit of Automation and Control Theory (UCBM), Research Unit of Computer Systems and Bioinformatics (UCBM),



Scuola Superiore Sant'Anna di Pisa, Istituto Tumori Giovanni Paolo II di Bari, USL Toscana Nord Ovest

RAFAEL

System for Risk Analysis and Forecast for Critical Infrastructure in the Apennines dorsal Regions

Coordinator: Energy and Sustainable Economic (ENEA)

Partners: Research Unit of Automation and Control Theory (UCBM), INGV, ANAS SpA, TIM SpA, e-Distribuzione SpA, Centro Ricerche Elettro-Ottiche, GORI SpA, Università di Ferrara, Università dell'Aquila, Consorzio CUEIM, Consorzio MEDIS, Nuvap Srl, Tointech Srl, G&A Engineering Srl, Ylichron Srl, GEO-K Srl, Himet Srl

ITALIAN MINISTRY OF HEALTH FINALISED RESEARCH

NET – Network Project 2013

Italian autism spectrum disorders network: filling the gaps in the National Health Care System

Coordinator: Italian National Institute of Health

Partners: Research Unit of Molecular Psychiatry and Neurogenetics (UCBM), IRCCS Eugenio Medea – Associazione La Nostra Famiglia, Fondazione Stella Maris, Bambino Gesù Paediatric Hospital

CO Industrial Co-Financing 2013

Extremely low frequency magnetic field (ELF-MF) stimulation as a neuroprotective treatment in acute ischemic stroke

Coordinator: Campus Bio-Medico University of Rome

Partners: Research Unit of Neurology, Neurophysiology, Neurobiology (UCBM), IGEA S.p.A.

GR Ordinary 2013

Cerebellar-cortical circuits in Autism Spectrum Disorders: new perspectives for treatment implementation.

Coordinator: Santa Lucia Foundation

Partners: Research Unit of Neurology, Neurophysiology, Neurobiology (UCBM), Sapienza University, Rome

PE – Italian researcher abroad 2016

Surgical versus conservative management for patients with rotator cuff tears: a randomized controlled trial

Coordinator: UCBM (Research Unit of Orthopaedic and Trauma Surgery)

Partners: Co-Funding: BIDMC (Beth Israel Deaconess Medical Center - Harvard Medical School Teaching Hospital)

RF – Ordinary 2018

Raman spectroscopy as an innovative tool to improve diagnosis of thyroid cancer and reduce unnecessary surgery

Coordinator: UCBM (UOC Pathology)

Partners: Research Unit of Endocrinology and Diabetes (UCBM), "Roma Tre" University of Rome, Dipartimento di Scienze

CO – Industrial Co-financing 2016

Effects of fiber enriched diet on bone and muscle health in elderly obese subjects

Coordinator: UCBM (Research Unit of Endocrinology and Diabetes)

Partners: IRCCS Istituto Ortopedico Galeazzi, Santa Lucia Foundation

GR – Young Researcher 2018

Intervertebral disc regeneration mediated by autologous mesenchymal stem/stromal cells intradiscal injection: a phase IIB randomized clinical trial

Coordinator: UCBM (UOC Pathology)

Partners: Research Unit of Orthopaedic and Trauma Surgery (UCBM), Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milano

GR – Young Researcher 2018

Role of post-translational insulin modifications in the pathogenesis, staging and therapy of type 1 diabetes

Coordinator: UCBM (Research Unit of Endocrinology and Diabetes)

Partners: University of Campania "Luigi Vanvitelli", Naples

ITALIAN MINISTRY OF ECONOMIC DEVELOPMENT

B³- Bioscience, Patents and Business – Exploitation of research in the bioscience sector through knowledge transfer, human resources development and industrial properties transfer.

Coordinator: UCBM

INAIL BRIC

Bio-cooperative robotic system for upper-limb rehabilitation in working contexts

Funding Body: INAIL

PI: Research Unit of Advanced Robotics and Human Centred Technologies (UCBM)

SmartBench – Smart Industrial Safety Workbench

Funding Body: INAIL

PI: University of Rome "Tor Vergata"

Partner: Research Unit of Automation and Control Theory (UCBM), University of Salento, University of Bologna, University of Messina

Active-Development of a multidisciplinary and integrated approach, for the management of the worker affected by degenerative pathologies of the spine: study of the occupational aspects and an innovative regenerative treatment of the intervertebral disc to favor the return to work

Coordinator: Research Unit of Orthopaedic and Trauma Surgery (UCBM)

Partners: University of Helsinki; IRCCS Foundation Ca' Granda Maggiore Hospital Milan

SENSE-RISC – Development of wearable smart systems for improving worker safety

Coordinator: Sapienza University of Rome, Astronautical Engineering Department Electricity and Energy (DIAEE)

Partners: Research Unit of Measurements and Biomedical Instrumentation (UCBM); University of Pisa - Department of Chemistry and Industrial Chemistry (UP-DCCI); Sapienza University of Rome - Charles Darwin Biology and Biotechnology Department (UR-DBBCD); Sant'Anna Institute of Biorobotics (SSSA); Technological Pole, IRCCS Don Carlo Gnocchi Foundation (FDG); University of Pisa - Centro E. Piaggio (UP-CP).

INAIL – Centro per la sperimentazione ed applicazione di protesi e presidi ortopedici di Vigorso di Budrio (BO)

3D-AID – Low Cost Hand Prostheses and Exoskeletal Robotic Aids

Coordinator: Research Unit of Advanced Robotics and Human Centred Technologies (UCBM)

Partners: Research Unit of Physical and Rehabilitation Medicine, Neurophysiology and Neuroengineering of Human-Technology Interaction, Neurology, Neurophysiology, Neurobiology, Orthopaedic and Trauma Surgery (UCBM)

LAZIO REGIONAL AUTHORITY

INTESE – Innovation and Technology transfer to support exploitation of research results

Coordinator: UCBM

HEREMOS – HEalth REmote MONitoring System

Coordinator: RDSLAB srl

Partners: Research Unit of Measurements and Bio-medical Instrumentation (UCBM)

COMETA – Quality testing of organoleptic properties of COffee blends via genetic and METAbolic fingerprinting

Coordinator: Danesi Caffè S.p.A.

Partners: Research Unit of Food Science and Nutrition (UCBM), Genechron s.r.l.; Energy and Sustainable Economic (ENEA).

WINGED: WIne GrEen Distillery

Coordinator: Sire srl

Partners: Research Unit of Chemical-Physics Fundamentals in Chemical Engineering (UCBM), Sire Srl, Processi Innovativi srl, Sapienza University of Rome, Gotto D'Oro s.c.

OTHER GRANTS

VIOLIN – Valorization of Italian products deriving from Oliva through innovative analytical techniques

Funding Body: Fondazione Cariplo

Coordinator: University of Messina

Partners: Research Unit of Food and science and nutrition (UCBM), University of Rome La Sapienza, Alma Mater Studiorum University of Bologna, University of Turin, Edmund Mach Foundation, University of Sanio, university of Tuscia, University of Genoa, University of Bari, University of Verona.

SERISM: Role of the endocannabinoid system in reprogramming human pluripotent stem cells under microgravity

Funding Body: ASI – Italian Space Agency

Partners: Research Unit of Biochemistry and Molecular Biology (UCBM)

Interdisciplinary complex systems: theoretical physics methods in systems biology; Self-gravitating systems, galactic structures and galactic dynamics

Funding Body: ICRANet

Partners: Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM), ICRA

Continuity of care for terminally ill patients: Data collection-Observation-Sperimentation (CA-IOS)

Funding Body: ENPAPI

Partners: Research Unit of Nursing Science (UCBM)

Artificial Intelligence and Society: Between Innovation and Common Good

Funding Body: Fondazione Cattolica Assicurazioni

Partners: Philosophy of Science and Human Development

Antibodies to post-translationally modified insulin as biomarker of type 1 diabetes

Funding Body: EFSD (European Foundation for the Study of Diabetes), JDRF and Lilly

Partner: Research Unit of Endocrinology and Diabetes (UCBM)

PI: Rocky Strollo (Endocrinology and Diabetes, UCBM); **CoPI:** Ahuva Nissim (Queen Mary University of London);

CoPI: Paolo Pozzilli (Endocrinology and Diabetes, UCBM)

EFSD Mentorship Programme supported by AstraZeneca

Funding Body: EASD (European Association for the Study of Diabetes e V.)

Partner: Research Unit of Endocrinology and Diabetes (UCBM)

Evaluation of bone fragility in type 1 diabetes

Funding Body: SIOMMMS (Società Italiana dell'Osteoporosi, del Metabolismo Minerale e delle Malattie dello Scheletro)

Partner: Research Unit of Endocrinology and Diabetes (UCBM)

PI (Young investigator): Rocky Strollo

Supervisor: Nicola Napoli (Endocrinology and Diabetes, UCBM)

Specialized pro-resolving lipid mediators as a novel strategy to "resolve" the altered adaptive immuneresponses in multiple sclerosis

Funding Body: FISM

Partners: Research Unit of Biochemistry and Molecular Biology (UCBM)

PI: Dr. Valerio Chiurchiù

Other Research Units involved: Santa Lucia Foundation of Rome, Policlinico Tor Vergata of Rome

Future leaders mentorship programme for clinical diabetologists

Funding Body: European Foundation for the Study of Diabetes

Partner: Research Unit of Endocrinology and Diabetes (UCBM); Cardiff University

PI: Dr. Rocky Strollo

Acoustic Upgraded Diagnostics In-Orbit

Funding Body: Agenzia Spaziale Italiana (ASI)

Partners: Research Unit of Electronics for Sensor Systems (UCBM); University of Rome "Tor Vergata"

AARG-18-566270 - Targeting dopamine neuronal loss in a model of Alzheimer's Disease.

Funding Body: Alzheimer's Association

PI: Dr. D'Amelio Marcello, Research Unit of Molecular Neurosciences (UCBM)

Bone material strength and fracture risk in subjects with end stage chronic kidney disease on dialysis

Funding Body: Amgen Inc.

PI: Dr. Andrea Palermo Research Unit of Endocrinology and Diabetes (UCBM)

Other Research Units involved: Research Unit of Geriatrics (UCBM), Sapienza University of Rome

BIOC02 - CCS-CCU Technology For Carbon Footprint Reduction Using Bio-Adsorbent

Funding Body: Polish National Agency for Academic Exchange

Coordinator: Czestochowa University of Technology

Partners: Research Unit of Process Engineering (UCBM), Instituto Nacional del Carbón, Instituto di Tecnologie Avanzate per l'Energia "Nicola Giordano, Instituto Superior Técnico Universidade de Lisboa

SAFERA - Integrated Management of Safety and Security Synergies in Seveso Plants_OLIVA

Funding Body: INAIL, Research Unit of Automation and Control Theory (UCBM)

Precision medicine: implementation of a network of laboratories to improve the diagnosis of communicable diseases and the treatment of infection diseases

Coordinator: Istituto Superiore di Sanità

Partners: Research Unit of medical statistic and molecular epidemiology and Research Unit of Clinical Laboratory Sciences (UCBM)

MONREAB - Platform for the rehabilitation process monitoring

Funding Body: Fondazione Giovan Battista Baroni, Research Unit of Measurements and Biomedical Instrumentation (UCBM)

Project agreement on biocidal products

Funding Body: Istituto Superiore di Sanità, Research Unit of Food Science and Nutrition (UCBM)

New molecular approaches in the field of food safety: application and harmonisation of massive sequencing methods Whole Genome Sequencing WGS for the characterization of pathogens causing zoonoses – ZOOPROPHYLACTIC

Funding Body: Istituto Zooprofilattico Sperimentale della Sardegna, Research Unit of medical statistic and molecular epidemiology (UCBM)

Progetto di Supercalcolo, ISCRA-classe C - Italia, "SLEAN - Spatial Localization of Excitons in Anatase Nanostructures"

Funding Body: ISCRA-CINECA (National HPC Italian Center)

PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

Progetto di Supercalcolo, ISCRA-classe C - Italia, "PILSENER - Post processing operations for the analysis of Electronic properties of titanium dioxide nanowires"

Funding Body: ISCRA-CINECA (National HPC Italian Center)

PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

Progetto di Supercalcolo, ISCRA-classe C - Italia, "ExMoxC - EXcited state properties of Metal OXynitrides for photocatalysis via Many Body Perturbation Theory - HP10CMVPR7"

Funding Body: ISCRA-CINECA (National HPC Italian Center)

PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

"Towards realistic NANOsized TiO2 particles: Electronic and Optical properties Many Body study (NanoEIOp) - HP10B41C1L", 9.5M CPU hours, 2018-19

Funding Body: ISCRA- CINECA (National HPC Italian Center)

PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

"Thermodynamics and Kinetic of single ion permeation in human alpha 7 nicotinic receptor bound to partial agonist lobeline" (IONLOB) - HP10CKX019", 100k CPU hours, 2018-19, PI G. Cottone

Funding Body: ISCRA-CINECA (National HPC Italian Center)

PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

CLIPSIS – ExCited states of metal oxynitrides for Photocatalysis, 30 M standardised CPU hours, Marconi – Marconi 100, 2019-2020,

Funding body: PRACE Project Access-18th.

PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

NEWTONS – NEW photocatalyst materials:

Transition metal OxyNitrides Sheets

codice HP10BHGARA, budget di 750000

standard hours, 1.5 M CPU hours, Marconi100, 2019-2020.

Funding Body: ISCRA-CINECA (National HPC Italian Center)

PI: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

ANCIENT_ROME – study of mANy body exCitations in dEffective titanium dioxide maTeRials by ab-initiO Methods, 30 M standardised CPU hours, Marconi100, 2019-2020.

Funding body: PRACE Project Access-19th

PI: C. Cardoso, CNR NANO, Modena.

Co-investigator: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

Botulinium Neuro Toxins structure-function-dynamics: a computational study, 3.8 M CPU hours, 2019-2020.

Funding body: DARI-CINES-GENCI (Grand Equipement National de Calcul Intensif), France

PI: T. Malliavin, Institut Pasteur and CNRS, Paris, France Co-investigator: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

SENT_TO_NY – Study of covEred and functioN-alized TiO2 nanostrucTures: the role Of maNy-bodyY, 30 M standardised CPU hours, 2018-2019

Funding body: PRACE Project Access-17th

PI: I. Marri, Univ. Modena e Reggio Emilia

Co-investigator: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

COMBINER – COmputational Modelling of Neuronal Effective netwoRks, 280K CPU hours, Marconi A2, 2019.

Funding body: ISCRA-CINECA (National HPC Italian Center)

PI: A. Loppini, Research Unit of Nonlinear Physics and Mathematical Modeling.

Co-investigator: Letizia Chiodo, Research Unit of Nonlinear Physics and Mathematical Modeling (UCBM)

University Strategic Projects 2018

A competitive call has been launched in 2018 in order to fund projects of strategic interest to be developed at the internal research facilities and to enhance the capabilities of the Research Units to oversee and participate in the international, national and regional research programs. Two different strategic topics have been individuated, namely:

- 1) **“Healthcare 4.0”**, related to a new hospital model, distributed over the territory, exploiting all emerging technologies (high efficiency miniaturized sensors, wearable devices, advanced computational tools for modeling complex systems, for the analysis of big data and for artificial intelligence, internet of things, cloud computing, automation, advanced robotics and additive manufacturing, etc.) to improve the effectiveness, efficiency, safety and sustainability of personal care services in acute and chronic conditions, but also for prevention towards a healthy life and active aging.
- 2) **“Biomarkers for precision medicine”**, with the aim to promote research on precision medicine, and hence, on genetic, epigenetic, quantitative functional signal- and image-based biomarkers that improve appropriateness, efficacy, sustainability and safety of therapies.

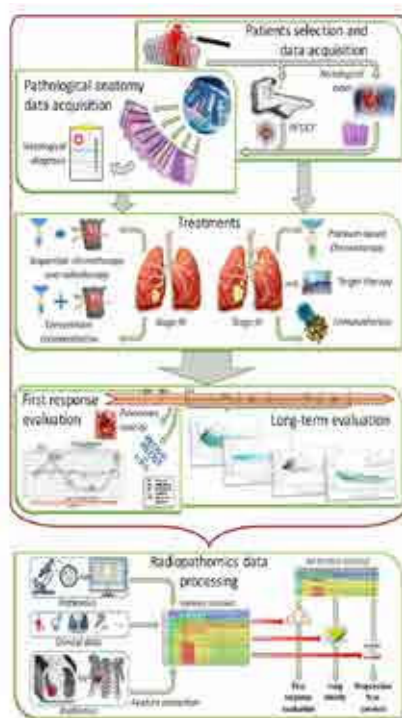
Four projects lasting 2 years have been funded (total funding: 500 KEuro) and started in April 2018. All the projects passed interim review, performed by qualified external reviewers, with good results.

CLARO: a CoLIABorative multi-sources Radio-pathomics approach for personalized Oncology in non-small cell lung cancer

PI: Prof. Sara Ramella, Research Unit of Radiation Oncology

Other Research Units involved: Computer Systems and Bioinformatics, Oncology, Diagnostic Imaging, Pathology

CLARO is focused on non-small cell lung cancer, often diagnosed in an advanced stage and characterized by a wide prognostic variability. This study aims to identify outcome prediction factors for patients with stage III and IV non-small cell lung cancer through customized image analysis models (Radio-Pathomic). The goal is to convert radiological and histopathological medical images, associated with other clinical information of the patient into a single group of biomarkers: in this way it will be possible to provide the right therapy to the right patient. One year after the beginning of the project, 148 patients out of the 150 planned were enrolled. In order to test the radiomic predictive model in reference to overall survival, a retrospective analysis was performed on 100 stage III NSCLC patients showing an accuracy of 83.5%. The pathomic analysis was also able to differentiate responders vs non-responders to the radiation treatment with an accuracy of 82%. Furthermore, the main volume of interest for the features extraction was found to be the Clinical Target Volume, consisting primarily of the neoplasm but also of the immediately adjacent tissues.



Experimental pipeline of CLARO project

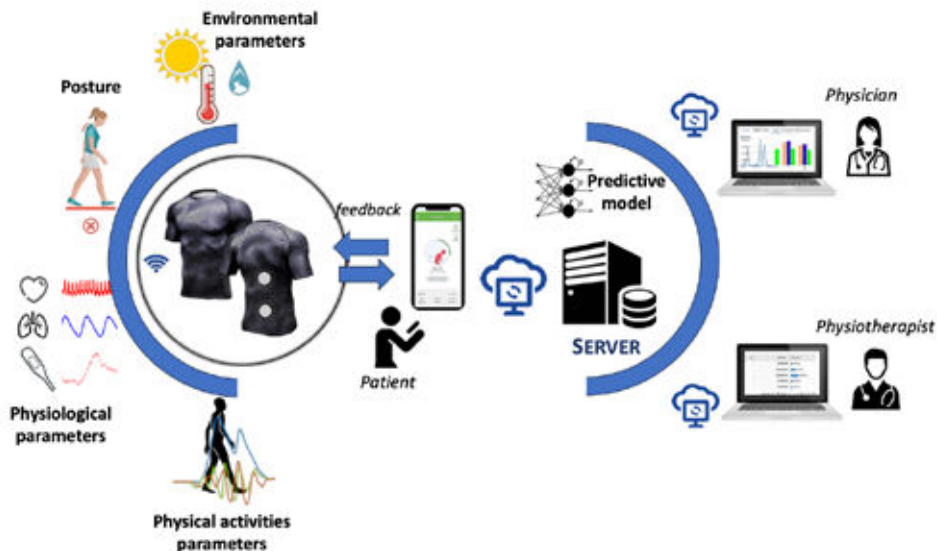
HOPE: H0spital to the PatiEnt

PI: Prof. Emiliano Schena, Research Unit of Measurements and Biomedical Instrumentation

Other Research Units involved: Bioethics and Humanities, Neurophysiology and Neuroengineering of Human-Technology Interaction, Physical and Rehabilitation Medicine, Orthopaedic and Trauma Surgery, Anesthesia, Intensive Care and Pain Management, Computers Systems and Bioinformatics, Automation and Control Theory.

According to the Global Burden of Disease study (2017), low back pain (LBP) is the leading cause of disability and work absence in industrialized countries, causing a high economic burden.

HOPE is a patient-oriented project whose goal is changing the way chronic LBP patients are monitored and managed. The innovative paradigm is based on the development of an easy-to-use unobtrusive technological platform for tailoring LBP treatment on each patient. The HOPE technology consists of a wearable system for the continuous monitoring of patient-related and surrounding environmental parameters, a tool for real-time data collection and storage, and Physician-Patient human-computer interfaces. HOPE will provide a valid alternative/complement to conventional therapies by providing patient-specific and personalized solutions for LBP patients, will cut health expenditures and costs by optimizing the number of follow-up visits, and will improve the quality of life and personal wellness.



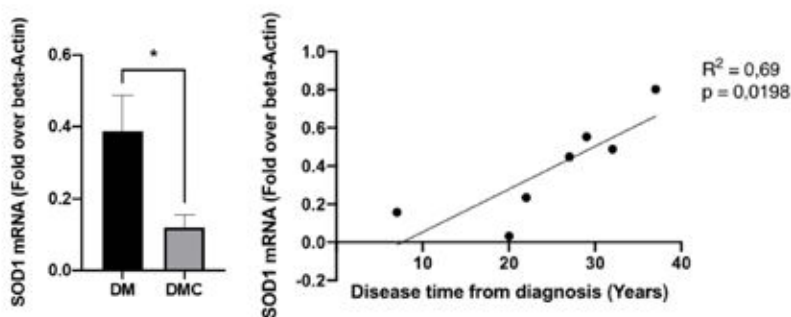
Concept of the HOPE Platform

OXIDIA: Oxidative post-translational modifications of Insulin as biomarkers of type 1 DIAbetes prediction, progression and complications

PI: Prof. Nicola Napoli, Research Unit of Endocrinology and Diabetes

Other Research Units involved: Biochemistry and Molecular Biology, Cardiovascular Sciences, Geriatrics, Diagnostic Imaging, Electronics for Sensor Systems

Detection of biomarkers able to improve early diagnosis of Type 1 diabetes (T1D) and chronic complications is an important unmet clinical need. The overall objective of this study across aims was to test the potential of oxPTM-INS-Ab as biomarker of T1D along the continuum of the disease natural history (prediction, progression and complications). During the first year, we identified from the IMDIAB cohort a total of 51 subjects and we collected sera, clinical data and assessed diabetic vascular complications and bone fragility. Specifically, fracture prevalence, Bone mineral density (BMD) and Trabecular bone score (TBS) by DXA. We also evaluated metabolic risk factors for cardiovascular disease (CVD) and we performed imaging analysis for carotid intima media thickness (CIMT). Finally, we started collecting blood samples of the different groups specified for peripheral blood mononuclear cells (PBMCs) isolation, which allowed us to perform RNA and DNA extraction that will be used for oxidative stress gene expression and epigenetic analysis.



A: mRNA expression levels of SOD1 measured in PBMCs isolated from Type 1 diabetic patients with complications (DMC) and without complications (DM). T test ($p < 0.05$). **B:** Analysis of correlation of SOD1 mRNA levels and disease duration. Pearson test (Coefficient of correlation 0.69; $p = 0.0198$)

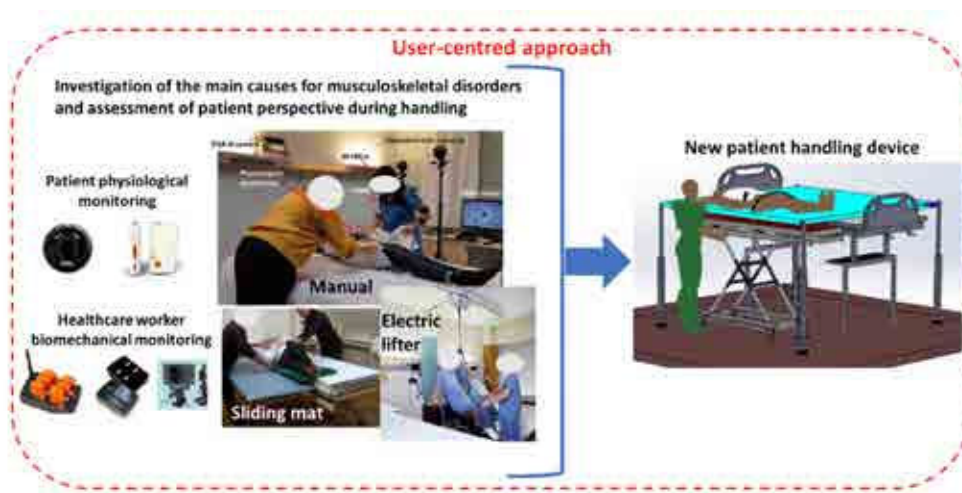
SAFE MOVER: User-centred design of a robotic device for improving working conditions and user subjective perspective during patient-handling movements)

PI: Prof. Loredana Zollo, Advanced Robotics and Human Centred Technologies,

Other Research Units involved: Physical Medicine and Rehabilitation, Nursing Sciences

About 50 per cent of the reported injuries and illnesses among healthcare workers (nurses, caregivers and nursing support staff) are musculoskeletal disorders, affecting mostly the lower back. They are mainly due to the repetitive and heavy tasks that health workers are required to perform every day, such as handling the patients for lifting, pushing or pulling, and cause a number of drawbacks in terms of quality of life, and job satisfaction, and high costs resulting from lost workdays. On the other hand, the market already offers technological devices for helping perform such tasks, but they are scarcely used by the healthcare workers and scarcely accepted by the patients.

The SAFE-MOVER project has the ambition to in-depth analyse the movements performed during patient handling and the inter-action modalities between healthcare workers and patients during manual handling in order to: (i) investigate the main causes for musculoskeletal disorders, (ii) extract gesture descriptors for reproducing the correct movement with a robotic device, (iii) assess user subjective perspective, and (iv) design a new technology based on a user-centred approach for significantly reducing the risk and prevent the onset of such disorders while taking care of the patients' perspective and their need for physical and social interaction with human operators. The new technology will be progressively validated healthy subjects, simulated patients, and at least 1 temporarily non-cooperative patient (who suffers from temporary motor impairment), in an application scenario arranged in the facilities of UCBM hospital. Performance of the overall SAFE-MOVER platform will be assessed by means of quantitative indicators and semi-qualitative tools aimed at evaluating the system effectiveness, functionality, safety and acceptability by the healthy subjects and patients.



Concept of the SAFE-MOVER project

The background of the slide is a light gray pattern featuring various scientific and technological icons. These include DNA double helices, interlocking gears, and stylized plant sprouts with leaves and roots. The icons are scattered across the entire page, creating a thematic backdrop for the text.

Research and the “Third Mission” of the University

Impact of Research on Society

Impact of Research on Society

The key factor of UCBM policy for Third Mission activities is the centrality of human being to foster society innovation. According to its main mission for healthy living and improvement of quality of life, UCBM systematically pursues the activities related to third mission with the aim of transferring both knowledge and technology in order to enhance the socio-economic development at local and national level.

The activities are mainly devoted to strengthen competitiveness by promoting process and product innovation and by networking mainly with local SMEs but also with national and international companies with a twofold aim: placement of students and exploitation of the research activities of the Research Units of Engineering, Medicine and Surgery and Science and Technology for Human and Environment Departments.

Thanks to the co-financing by the Italian Ministry of Economic Development for strengthening the technology transfer offices of Italian universities and research organisations, the UCBM Knowledge Transfer Office started in 2019 an initiative with Italian SMEs consisting in a free diagnostic service of patents portfolio proposing methods and strategies for improving exploitation.

Moreover, specific attention is also devoted to ethical and anthropological issues in order to enhance the social impact of research results.

In the last years, UCBM joined different National networks such as NETVAL (Italian Network of Technology Transfer Offices of Universities and Public Research Organizations), PNIcube (Italian Association of University Incubators and Local Business Plan Competitions), Fondazione R&I (Italian foundation for research and entrepreneurship) for technology transfer and ALMALAUREA for placement, and created a University-Enterprise Committee with the aim of collaborating with companies not only for technology transfer, but also for defining education and research strategies.

Third mission activities, in particular commissioned research, clinical trials, UCBM patent portfolio, UCBM spin-off companies, and public engagement activities, are briefly reported below.

COMMISSIONED RESEARCH

INAIL - CENTRO PER LA SPERIMENTAZIONE ED APPLICAZIONE DI PROTESI E PRESIDII ORTOPEDICI DI VIGORSO DI BUDRIO (BO)

PCR 1/2 Project New methods in the treatment of limb amputation for the application of bionic prostheses

Client: INAIL-Centro per la Sperimentazione ed Applicazione di Protesi e Presidi Ortopedici di Vigorso di Budrio (BO)

Contractor: Research Unit of Orthopaedic and Trauma Surgery

Research Units involved: Research Unit of Advanced Robotics and Human Centred Technologies; Research Unit of Physical and Rehabilitation Medicine; Research Unit of Neurology, Neurophysiology, Neurobiology; Research Unit of Neurophysiology and Neuroengineering of human-technology interaction.

PPR AS 1/3 Project Implantable system for the control of upper-limb prosthesis with invasive neural interfaces and wireless communication

Client: INAIL-Centro per la Sperimentazione ed Applicazione di Protesi e Presidi Ortopedici di Vigorso di Budrio (BO)

Contractor: Research Unit of Advanced Robotics and Human Centred Technologies

Other Research Units involved: Research Unit of Physical Medicine and Rehabilitation, Research Unit of Orthopaedic and Trauma Surgery, Research Unit of Neurology, Neurophysiology, Neurobiology, Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction

FONDAZIONE ANIA

Development of an algorithm to calculate the risk of stroke and to adopt strategies capable of substantially reducing it by intervening on modifiable factors

Client: Fondazione ANIA

Contractor: Research Unit of Neurology, Neurophysiology, Neurobiology

Development of upper limb bionic prostheses with personalized interface and sensory feedback for patients with amputation due to road accident

Client: Fondazione ANIA

Contractor: Research Unit of Advanced Robotics and Human Centred Technologies

Other Research Units involved: Research Unit of Physical and Rehabilitation Medicine, Research Unit of Neurology, Neurophysiology, Neurobiology, Research Unit of Neurophysiology and Neuroengineering of Human-Technology Interaction

Remote multiparameter telemonitoring for the management of chronic pathologies in the elderly

Client: Fondazione ANIA

Contractor: Research Unit of Geriatrics

Other Research Units involved: Research Unit of Computer Systems and Bioinformatics

Assessment of predictive molecular biomarkers, in response to antitumor therapy with "targeted" drugs used in normal clinical practice

Client: Diatech Pharmacogenetics srl

Contractor: Research Unit of Pathology

Biochemical profiling of new chemical entities with therapeutic potential

Client: F. Hoffmann-La Roche Ltd

Contractor: Research Unit of Biochemistry and Molecular Biology

Biological effects of cyclin-dependent kinase drugs ribociclib, palbociclib and abemaciclib on breast cancer bone microenvironment

Client: Novartis Farma SpA

Contractor: Research Unit of Oncology

Blockchain for food supply chain

Client: Poste Italiane SpA

Contractor: Research Unit of Automation and Control Theory

Design and development of an electronic differential sensor system for water characterization

Client: Puretech srl

Contractor: Research Unit of Electronics for Sensor Systems

Development and validation of a new quantitative analytical method of ponatinib in human plasma and CSF using LC-MS/MS

Client: Incyte Biosciences International s.a.r.l.

Contractor: Research Unit of Drug Sciences

Development of a Finite Element Method (FEM)-based computation model to study the distribution of mechanical stresses on the Rotator Cuff Tendon Patch

Client: Anika Therapeutics srl

Contractor: Research Unit of Nonlinear Physics and Mathematical Modeling

Development of a Model Comparison Tool for Cyber Insurance

Client: Business Integration Partners SpA

Contractor: Research Unit of Automation and Control Theory

Efficacy of remote multiparametric monitoring based on selected sensors and a mini-invasive electronic device for the care of type 2 diabetes mellitus: a randomized controlled trial

Client: Laboratori di Informatica Applicata (L.I.A.)

Contractor: Research Unit of Geriatrics

Genotyping and analysis of the origin and evolutionary history of introduced and distributed HIV-1 strains in Bulgaria

Client: Bulgaria National Center for Infectious and Parasitic Diseases (NCIPD)

Contractor: Research Unit of Medical Statistics and Molecular Epidemiology

GL01 as novel potential target to overcome Trabectedin resistance in soft tissue sarcomas

Client: Pharma Mar S.A.

Contractor: Research Unit of Oncology

IEEE Editorial Services Agreement

Client: The Institute of Electrical and Electronics Engineers, Incorporated ("IEEE")

Contractor: Center for Integrated Research

Impact of InMed compounds on the endocannabinoid system of human keratinocytes and on biological activities thereof

Client: InMed Pharmaceuticals Inc.

Contractor: Research Unit of Biochemistry and Molecular Biology

In vitro profiling of MAGL inhibitors

Client: F. Hoffmann-La Roche Ltd

Contractor: Research Unit of Biochemistry and Molecular Biology

In-vitro study of the activity of polyphenols on cell damage caused by "AGE" (advanced glycation end-products)

Client: Soremartec Italia srl

Contractor: Research Unit of Food Science and Nutrition

Let's sensor technology data acquisition, comparison and validation

Client: Let's Wearable Solutions srl

Contractor: Research Unit of Measurements and Biomedical Instrumentation

Markers of the endocannabinoid system in inflammation

Client: Vetagro SpA

Contractor: Research Unit of Biochemistry and Molecular Biology

Mindfulness-based stress reduction intervention in patients with chronic obstructive pulmonary disease and their caregivers

Client: OPI – CECRI (Ordine delle Professioni Infermieristiche – Centro di Eccellenza per la Cultura e la Ricerca Infermieristica)

Contractor: Research Unit of Nursing Science

Multicenter prospective trial on pressure sores in hospice patients: prevalence, incidence, and associated factors

Client: OPI – CECRI (Ordine delle Professioni Infermieristiche – Centro di Eccellenza per la Cultura e la Ricerca Infermieristica)

Contractor: Research Unit of Nursing Science

Nutrition education project “Nutripiatto”

Client: Nestlé Italiana SpA

Contractor: Research Unit of Food Science and Nutrition

Production of CytoMatrix samples for demonstration and validation purposes

Client: SGM Diagnostics srl

Contractor: Research Unit of Tissue Engineering & Chemistry for Engineering

SIB-ECG: Biometric Identification System through ECG

Client: Laboratori di Informatica Applicata (L.I.A.)

Contractor: Research Unit of Computer Systems and Bioinformatics

Smart Patient's Security

Client: Proge-Software srl

Contractor: Research Unit of Automation and Control Theory

Study and validation of functional specifications for the development of augmented reality surgical navigation systems equipped with advanced interfaces

Client: MASMEC S.p.A.

Contractor: Research Unit of Diagnostic Imaging

Support for the technical contents of the web portal www.oil-gasportal.com

Client: Serintel S.r.l.

Contractor: Research Unit of Process Engineering

Technical services for field experiments

Client: Laboratori di Informatica Applicata (L.I.A.)

Contractor: Research Unit of Computer Systems and Bioinformatics

The hospital discharge of the elderly patient with chronic disease: development of a nursing discharge plan

Client: OPI – CECRI (Ordine delle Professioni Infermieristiche – Centro di Eccellenza per la Cultura e la Ricerca Infermieristica)

Contractor: Research Unit of Nursing Science

TraiNurse: innovative app for exploiting the skills of the nursing profession

Client: Artmediamix

Contractor: Research Unit of Nursing Science

CLINICAL TRIALS

During the year 2019, 165 studies have been approved by the independent Ethics Committee of the UCBM. 79 (47,9%) and 86 (52,1%) of these projects were interventional or observational studies, respectively (Figure 1). The distribution of studies among the different Research Units is summarized in Figure 2. The very majority of the interventional trials is of Phase 2 or 3.

Out of a total of 165 studies approved in 2019, UCBM promoted 59 (35,75% of the total), 64 projects were promoted by non profit institutions/research networks, and 42 projects were sponsored by Companies (pharmaceutical or developing medical devices) (Figure 3)

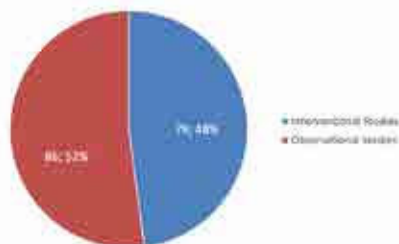
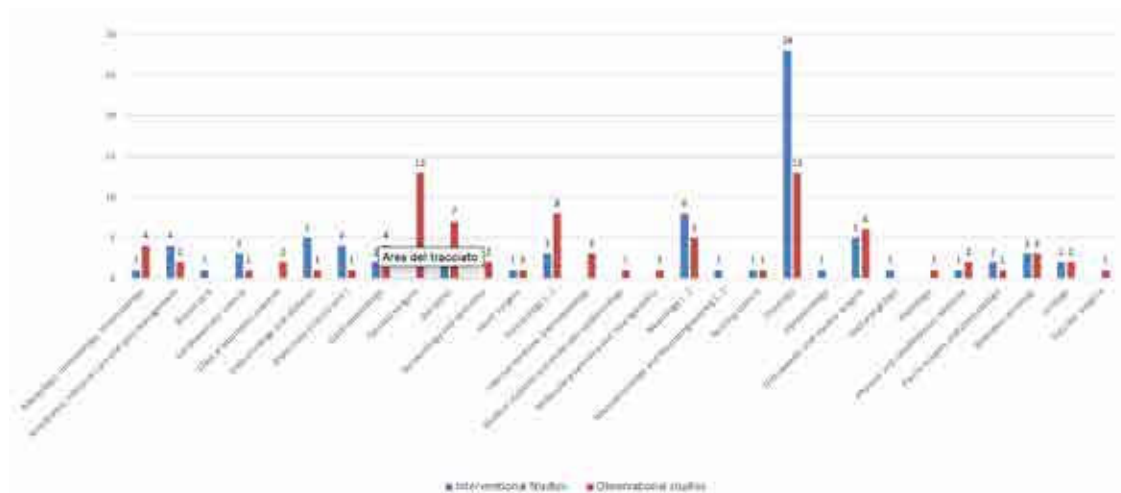


Figure 1 - Ethics Committee Evaluations 2019



Figure 3 - Profit and no profit studies 2019

Figure 2 - Distribution of clinical trials among the different Research Units 2019



RESEARCH EXPLOITATION

Patent portfolio owned/co-owned by UCBM

- **A bioactive material for the regeneration of cartilage and process for the obtainment thereof (Italian patent);** Inventors: M. Centola, V. Denaro, A. Marsano, I. Martini, A. Rainer, M. Trombetta, G. Vadalà. Co-owner: Universitätsspital Basel.
- **Adipose tissue purification technique to obtain high concentration of adipose stem cells (Italian patent);** Inventors: C. Gregorj, G. F. Marangi, F. Pantano, P. Persichetti, F. Segreto, M.C. Tirindelli.
- **Apparatus and method for videorhinohygmometric (vri) measures (USA patent);** Inventors: M. Casale, V. Cusimano, F. Salvinelli, R. Setola, P. Soda.
- **A tactile sensor device (Italian patent application);** Inventors: J. D'Abbraccio, L. Massari, C. M. Oddo, E. Palermo, E. Schena, E. Sinibaldi, G. Terruso, M. Zaltieri. Co-owners: Sant'Anna School of Advanced Studies, Sapienza University of Rome, University of Venice Ca' Foscari, Istituto Italiano di Tecnologia.
- **Device for sampling food products (Italian patent);** Inventors: M. Dachà, A. D'Amico, G. Pennazza, M. Santonico, A. Zompanti.
- **Device for the sampling of the eye surface by imprinting (Italian patent, European and USA patent applications);** Inventors: B. Balzamino, I. Ghezzi, A. Micera, R. Sgrulletta, L. Zollo. Co-owner: Fondazione G. B. Bietti.
- **Gradual compression medical device for supporting and optimizing the cutaneous scar (Italian patent);** Inventors: C. Falcinelli, S. Filippi, A. Gizzi, G.F. Marangi, P. Persichetti, F. Segreto.
- **Innovative functionalization on liquid phase sensors for the detection of bioactive lipids (Italian patent application);** Inventors: T. Bisogno, S. Grasso, M. Maccarrone, G. Pennazza, M. Santonico. Co-owner: CNR
- **Method for measuring the slipping between two surfaces (Italian patent);** Inventors: E. Guglielmelli, R. Romeo, L. Zollo, Co-owner: INAIL
- **Method for positioning receptors for sensory stimuli, a device obtained by said method and apparatuses comprising said device (Italian patent application);** Inventors: L. Beccai, M.C. Carrozza E. Guglielmelli, C. Oddo, R. Romeo, L. Zollo, . Co-owners: Scuola Superiore Sant'Anna, Istituto Italiano di Tecnologia.
- **Method for the early diagnosis of the pancreatic adenocarcinoma (Italian patent application);** Inventors: D. Caputo, G. Caracciolo, R. Coppola, L. Digiaco, S. Palchetti, D. Pozzi. Co-owner: Sapienza Università di Roma.
- **Pneumopipe – Auxiliary device for collection and sampling of exhaled air (Italian, French, German, UK, Austrian and Dutch patents);** Inventors: R. Antonelli Incalzi, A. D'Amico, G. Pennazza, M. Petriaggi, M. Santonico .
- **Porous material for the inclusion of cytologic preparations, process for obtaining the same and its use. (Italian and international PCT patent applications);** Inventors: M. Costantini, A. Crescenzi, P. Mozetic, A. Rainer, A. Santoro, C. Taffon, M. Trombetta. Co-owner: UCS Diagnostic srl.
- **Predictive analysis of endometrial cancer risk (Italian patent application);** Inventors: R. Angioli, S. Capriglione, C. De Cicco, D. Luvero, R. Montera, F. Plotti, C. Terranova.
- **Robotic device for assistance and rehabilitation of lower limbs (Italian, French, German and UK patents);** Inventors: D. Accoto, G. Carpino, M. Di Palo, S. Galzerano, E. Guglielmelli, F. Sergi, N. L. Tagliamonte.
- **Robotic joint for prosthetic articulation (Italian patent application);** Inventors: L. Bramato, G. Carpi, D. Simonetti, L. Zollo. Co-owner: INAIL.
- **Statistical methods for the identification of regions of the genome that are highly representative of the tumor mutational burden (Italian patent application);** Inventors: P. Manca, A. Napolitano, F. Pantano, D. Santini, G. Tonini.

UCBM spin-off companies



Bio Health Lab

BHL – Bio Health Lab srl

BHL designs, develops and markets mobile app and software solutions related to healthcare sector. The solutions, with high innovative contents, are the result of research activities in several fields such as diagnostics, hospital organization and physician-patient communication.

Website: www.biohealthlab.it



Biomedical Research in Otolaryngology srl (B.R.I.O.)

BRIO produces and distributes innovative biomedical devices for the healthcare sector. In particular, the company is involved in the distribution of an innovative device for otolaryngology, manually operable, dispensing substances in the form of aerosol.



BPCO media srl

BPCO media deals with telemedicine and medical diagnostics research. Its innovative medical device allows patients to monitor their health state and detect the onset of flare-ups and critical clinical situations. It highlights prognostic symptoms that patients are not able to perceive and prompts them to contact their doctor in order to receive an early treatment and avoid potential dangerous situations before symptoms appear.

Website: www.bpcomedia.com



Brain Innovations srl

In Parkinson's disease management, today there are 3 main problems: misdiagnosis, symptoms monitoring and therapy management. The solution proposed by Brain Innovations is a complete solution that addresses all the needs of Parkinson's disease patients with the following instruments:

- Answer to PD - Diagnosis device
- Answer to PD - Symptoms monitoring device
- PD Assistant - Oral Therapy device
- PD Assistant - Infusional Therapy device

Website: www.braininnovations.eu



Epiclick srl

Epiclick aims at contributing to the prevention of melanoma by using modern technologies: by exploiting the immediacy of the information technology and through the joint use of epiluminescence and the best telematic tools, it allows early remote diagnosis of melanoma, avoiding long waiting lists of public service.

Website: www.epiclick.it



ICan Robotics srl

ICan Robotics is an innovative start-up company, founded in September 2014, active in the field of biomedical robotics, developing technologies for rehabilitation and physical assistance for patients with neurological, orthopedic or age-induced conditions. ICan robotics develops innovative and user-friendly products, which can be used not only in healthcare facilities, but also at patients' abodes, for the benefit of the quality of life of patients and their caregivers. Heaxel was founded in 2018 as part of a financing operation by a VC on ICan robotics. Heaxel inherited the product, the business project and the team.

Website: www.heaxel.com



Winged srl

WINGED proposes to create technological platforms for the recycling of food waste, in the logic of integrated biorefinery for the production of energy, biofuels and organic compounds for fine chemicals. The project giving it its name (WINE GrEen Distillery) concerns the realization of a technological system for the valorization of wine processing waste in order to produce high added value products, such as fine chemicals and nutraceuticals, and green energy.

Public engagement activities

One of the priorities for the Campus Bio-Medico University of Rome is to design specific public engagement activities to meet special social needs. Projects for the protection of health are carried out regularly as for example, lung cancer prevention campaigns for smokers and former smokers, prevention days and screening of thyroid cancer, information days on osteoporosis and rheumatoid arthritis. Furthermore, a counselling service for relatives of chronic degenerative disease patient has been active since 2011.

Guidance programs and interaction with high school students take place regularly. Undergraduate Open Days, the “Salone dello studente” and the RomeCup annual event, are great opportunities to get information or get to visit the University. The University publishes the magazine “Lettere dal Campus” accessible on line as well, which typically includes a section focused on ongoing research activities, latest achievements and news from the UCBM research community. Finally, the University is also active on social media (Facebook, Twitter, YouTube, Google+, Flickr, LinkedIn, Pinterest) having 30,000 users and a pool of 8 million annual contacts.

Below a list of the main public engagement activities carried out at UCBM in 2019 is reported.

Rome, 9 January 2019

HPV: Facts and fakenews

Discussant: Prof. Aldo Venuti, Head HPV unit, UOSD Tumor Immunology and Immunotherapy RIDAT Dept. Seminar promoted by IRCCS Regina Elena National Cancer Institute – Rome.

Rome, 9 January 2019

Entrepreneurship in medical technology

Discussant: Prof. Robert S. Langer, Massachusetts Institute of Technology, Campus Bio-Medico University.

Rome, 22 January 2019

Research in healthcare management: open topics and methodological approaches

Discussants: Prof. Davide Aloini, Pisa University, prof. Erica Mazzola, Palermo University, prof. Elisabetta

Benevento, Pisa University and Tor Vergata University, prof. Alessandro Stefanini, Pisa University.

Seminar promoted by the Faculty of Engineering, Campus Bio-Medico University.

Rome, 23 January 2019

Objective and scientific data on BI-ALCL

Discussant: dr. Luana Clerico, Clinical and Medical Affairs Director POLYTECH Health & Aesthetics, and Genoa University.

Seminar promoted by the Plastic Surgery and Dermatology Unit, Campus Bio-Medico University.

Rome, 4 February 2019

CytoMatrix: the new frontier of fine needle aspiration

The workshop is an activity of the project “INTESE: INnovazione e Trasferimento tEcnologico per Sostenere la fruizione dei risultati della ricerca sul tErritorio” co-financed by Lazio Region.

Seminar promoted by Centre for Integrated Research (CIR), Campus Bio-Medico University.

Rome, 4 February 2019

Human-Robot collaboration: intuitive interaction and mate systems

Discussant: dr. Valeria Villani, DISMI - Department of Science and Methods for Engineering, University of Modena and Reggio Emilia.

Seminar promoted by Advanced Robotics and Human Centred Technologies Unit, Campus Bio-Medico University.

Rome, 6 February 2019

Osteoporosis: clodronate yesterday, today and tomorrow

Discussant: dr. Sergio Rosini, expert in osteoporosis therapies.

Seminar promoted by Physical and Rehabilitation Medicine Graduate School, Campus Bio-Medico University.

Rome, 8 February 2019

Mucosal integrity: evaluation and impact on gastro-intestinal diseases

Discussant: prof. Ricard Farré, Leuven University.

Seminar promoted by the Gastroenterology Unit, Campus Bio-Medico University.

Rome, 12 February 2019**Neural stem cells: physiology, pathophysiology and experimental therapies**

Discussant: Prof. Angelo Vescovi, Scientific Director IRCCS Casa Sollievo della Sofferenza.

Seminar promoted by the Neurology, Neurophysiology, Neurobiology Unit, Campus Bio-Medico University.

Rome, 14 February 2019**International on understanding complexity in life sciences**

Workshop promoted by FAST, Campus Bio-Medico University, in collaboration with Bicocca University, Milan, and CNR, Naples.

Rome, 21 February 2019**Bionic hand. From the origins of research to experiments on amputees**

Accademia dei Lincei

Discussants: Prof. Eugenio Guglielmelli Campus Bio-Medico University, Prof. Silvestro Micera, École polytechnique fédérale de Lausanne and Sant'Anna School of Advanced Studies, Pisa, Prof. Paolo Maria Rossini, Catholic University of the Sacred Heart, Italy and Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rinaldo Sacchetti Protheses Centre INAIL and Giulia Grillo Health Ministry.

Congress promoted in collaboration with: Inail, École polytechnique fédérale de Lausanne, Sant'Anna School of Advanced Studies, Catholic University of the Sacred Heart, Italy and University Hospital Agostino Gemelli.

Rome, 25 February 2019**Operational use of clinical simulation to reduce harm and improve efficiency in endovascular interventions: the Mentice project**

Discussants: Prof. David Ballard, President of Mentice Inc.

Seminar promoted by CardioCenter, Campus Bio-Medico University.

Rome, 26 February 2019**Brain/neural-machine interfaces for restoration of brain function**

Discussant: Surjo R. Soekadar, MD, Einstein Professor of Clinical Neurotechnology at the Charité - University Medicine Berlin (Germany).

Seminar promoted by Advanced Robotics and Human Centred Technologies Unit, Campus Bio-Medico University.

Rome, 1 March 2019**Activities of the Universidad Miguel Hernandez in the field of rehabilitation robotics**

Discussant: Prof. Nicolas Garcia Aracil, Biomedical Neuroengineering, Departamento de Ingeniería de Sistemas y Automática Universidad Miguel Hernandez de Elche.

Seminar promoted by Advanced Robotics and Human Centred Technologies Unit, Campus Bio-Medico University.

Rome, 20 March 2019**Gut microbiome and obesity**

Discussant: dr. Mario Marani, expert in Human Nutrition.

Seminar promoted by the Plastic Surgery and Dermatology Unit, Campus Bio-Medico University.

Rome, 25 March 2019**Flow cytometry: technological aspects, quality control, problems and troubleshooting**

Discussant: dr. Massimo Sanchez, head of Cytometry Service and Core Facilities at the National Institute of Health, Italy.

Seminar promoted by Centre for Integrated Research (CIR), Campus Bio-Medico University.

Rome, 3 April 2019**BioSpine7: 7th International congress on biotechnologies for spinal surgery**

Honorary Chair: prof. Vincenzo Denaro; Congress Chair: dr. Gianluca Vadalà.

Seminar promoted by the Orthopaedic and Trauma Surgery Unit, Campus Bio-Medico University of Rome.

Rome, 4 April 2019**Sports sensors: what should we measure, why and how?**

Discussant: Andrea Nicolò, PhD, Department of Movement Human and Health Sciences, University of Rome "Foro Italico".

Rome, 10 April 2019**Recent trends on the integration of experimental**

testing and simulations for materials design

Discussant: Prof. Marco Paggi, Full Professor of Structural Mechanics, Director's Delegate for Research, IMT School for Advanced Studies Lucca. Seminar promoted by Nonlinear Physics and Mathematical Modeling Unit, Campus Bio-Medico University.

Rome, 16 April 2019

A new proposed algorithm in the treatment of amputated patients

Discussant: Dr. Paolo Sassu, Dept. of Hand Surgery, Sahlgrenska University Hospital, Goteborg, Sweden. Seminar promoted by Neurophysiology and Neuro-engineering of Human-Technology Interaction (NEXT), Campus Bio-Medico University.

Rome, 7 May 2019

Drugs from basic research to therapy

Congress promoted by Campus Bio-Medico University and FarmaIndustria.

Rome, 24 May 2019

IoT: challenges and trends

Discussant: Oscar Martinez-Bonastre, Professor of Advanced Distributed Systems, Universidad Miguel Hernández de Elche (Elche, Spain).

Seminar promoted by Centre for Integrated Research (CIR), Campus Bio-Medico University.

Rome, 31 May 2019

Bioinspired robots: the evolution of a new species?

Discussant: Barbara Mazzolai, Center for Micro-BioRobotics (CMBR) Istituto Italiano di Tecnologia (IIT). Seminar promoted by the Master's Degree Course in Biomedical Engineering and by Bachelor's Degree Course in Food Science and Human Nutrition, Campus Bio-Medico University.

Rome, 8 June 2019

Self-care in Italian and international research

Promoted by the Campus Bio-Medico University, Tor Vergata University, Sapienza University and Catholic University of the Sacred Heart, Rome.

Rome, 10 June 2019

Kick-off meeting active

Promoted by INAIL (National Institute for Insurance

against Accidents at Work), Foundation IRCSS Ca'Granda Hospital, University of Helsinki.

Rome, 10 June 2019

Finite-time distributed algorithms for balancing and consensus

Discussant: Dr. Apostolos I. Rikos, KIOS Research and Innovation, Centre of Excellence, University of Cyprus.

Rome, 14 June 2019

Design thinking

Discussant: Prof. Alessandra Talamo, Sapienza University.

Promoted by PhD Course in Science and Engineering for Humans and the Environment and by Institute of Philosophy of Scientific and Technological Practice (FAST), Campus Bio-Medico University.

Rome, 17 June 2019

A dry ECG recording system for the ambulatory monitoring of the human electrocardiogram

Discussant: Prof. Soumyajyoti Maji, Trinity College Dublin.

Seminar promoted by the Faculty of Engineering, Campus Bio-Medico University.

Rome, 20 June 2019

The need for the revision of the IEC 60601 standards pertaining to electrocardiography

Seminar promoted by the Faculty of Engineering, Campus Bio-Medico University.

Rome, 27 June 2019

Slowing down ALS with electroceuticals

Launch of the new experimental non-pharmacological home therapy funded by the Nicola Irti Foundation and carried out by the Campus Bio-Medico University of Rome and the Italian Auxological Institute IRCCS. Discussants: Prof. Vincenzo Silani, Italian Auxological Institute IRCCS, University of Milan; Prof. Vincenzo Di Lazzaro, Campus Bio-Medico University.

Rome, 11-12 July 2019

The anastomotic failure

Congress promoted and organized by Campus Bio-Medico University.

Rome, 17 July 2019

Integrated Dynamics: rethinking our understanding of biological organization patterns and healthcare with a relational perspective

Discussants: Maria Sophia Aguirre, Catholic University of America.

Rome, 4 September 2019

Minimally invasive thermal techniques for cancer removal: a journey through state-of-the-art, research and clinical application

Discussants: prof. Paola Saccomandi, Politecnico di Milano, Milan, prof. Emiliano Schena, dr. Francesco M. Di Matteo, dr. Serena Stigliano, prof. Carlo Masaroni, Campus Bio-Medico University; Haim Azhari, Technion - Israel Institute of Technology, Haifa, Israel, Iris Weitz, ORT Braude College, Karmiel, Israel.

Seminar promoted by the Faculty of Engineering, Campus Bio-Medico University.

Rome, 18 September 2019

47th National Congress of the Italian Society of Microbiology

Promoted by

Sapienza University, Tor Vergata University, Catholic University of the Sacred Heart, Rome, Campus Bio-Medico University, and the National Institute of Health (ISS), Spallanzani Institute of Hospitalization and Care, S. Lucia Foundation IRCCS.

Rome, 19 September 2019

Improving the quality of life in paralysis: brain/neural robotics for assistance and rehabilitation

Discussants: Prof. Surjo Soekadar, MD, Einstein Professor of Clinical Neurotechnology at the Charité - University Medicine Berlin (Germany).

Seminar promoted by Advanced Robotics and Human Centred Technologies Unit, Campus Bio-Medico University.

Rome, 25 September 2019

Rare Disease Hackathon 2019

Discussants: Prof. Giulio Iannello, Campus Bio-Medico University, Dr. Vito Colella – Regional Access Lead – Italy Shire Italia Spa (part of Takeda), dr. Ernesto Borrelli - Associazione Emofilici Lazio.

Seminar promoted by the Faculty of Engineering, Campus Bio-Medico University.

Rome, 25 September 2019**Research Day 2018**

Organized by the Centre for Integrated Research (CIR), Campus Bio-Medico University of Rome.

Rome, 26 September 2019**Proprioception: where are we now**

Discussant: Prof. Simon Gandevia, Deputy Director and Foundation Scientist, NeuRA Senior Principal Research Fellow, NHMRC Conjoint Prof, UNSW, Honorary Prof, USyd and UQld Neuroscience Research Australia.

Seminar promoted by Neurophysiology and Neuro-engineering of Human-Technology Interaction (NEXT Lab), Campus Bio-Medico University of Rome.

Rome, 10 October 2019**Reprocessing and microbiological surveillance: an unbreakable tandem**

Promoted by dr. Francesco M. Di Matte, University Hospital Campus Bio-Medico of Rome.

Rome, 18 October 2019**Soft and self healing actuators for human robot interaction in health and manufacturing**

Discussant: Prof. Bram Vanderborght, Department of Mechanical Engineering, Faculty of Applied Sciences, Vrije Universiteit Brussel.

Seminar promoted by the Faculty of Engineering, Campus Bio-Medico University.

Rome, 24 October 2019**Towards development of theranostic platforms to investigate and modulate neuroinflammation in neurodegenerative diseases... and beyond**

Discussants: Dr. Marco Peviani, PhD, Lab. Cellular and Molecular Neuropharmacology, Dpt. Biology and Biotechnology, Università degli Studi di Pavia - Harvard Medical School, Dana Farber/Boston Children's Cancer and Blood disorders Center, Boston, MA.

Seminar promoted by Tissue Engineering & Chemistry for Engineering Lab, Campus Bio-Medico University.

Rome, 25 October 2019**CBM Cardio 2019**

Congress promoted by the Cardiovascular Science Unit, Campus Bio-Medico University.

Rome, 27 November 2019**Kick-off meeting European Grant Fidelio: Not only smart grid: the many links between electronics, software and power systems**

Seminar promoted by the Faculty of Engineering, Campus Bio-Medico University.

Rome, 2 December 2019**Graduate School – shared education platform**

Promoted by the Board for Ph.D programs and supported by the Centre for Integrated Research (CIR), Campus Bio-Medico University.

Rome, 3 December 2019**Workshop "Bionic technologies and disabilities: the challenges of limb prosthetics"**

Promoted by INAIL (National Institute for Insurance against Accidents at Work Sant'Anna School of Advanced Studies, Pisa, Campus Bio-Medico University for the International Day of Disabled Persons.

Rome, 4 December 2019**Post Rio Review: IGCS Update**

Promoted by the International Gynecologic Cancer Society (IGCS) and Campus Bio-Medico University, Rome.

The background of the slide is a light gray with a repeating pattern of small, stylized icons. These icons include DNA double helices, interlocking gears, and sprouting leaves, all rendered in a light gray color. The icons are scattered across the entire page, creating a scientific and technological theme.

Research Agreements and Collaborations

Research Agreements and Collaborations

National agreements and collaborations

Bio-P, gruppo Maire Technimont, Italy

BPCOMedia srl, Italy

Bracco Imaging, for Radiomics Research, Italy

Casaccia Research Centre, Rome, Italy

Cassino University, Italy

Catholic University of the Sacred Heart, Italy

Center of Excellence for Biomedical Research, University of Genova, Italy

Center of Excellence for Biomedical Research, University of Perugia, Italy

Centro Diagnostico Italiano SpA, Italy

Danesi caffè SpA, Italy

Department of Molecular Medicine, Sapienza University, Rome, Italy

Department of Public Health, Section of Hygiene, Catholic University of the Sacred Heart, Italy

Departments of Information and Electrical Engineering, L'Aquila, Italy

Dept. of Astronautics, Electrical and Energetics Engineering, Sapienza University, Rome, Italy

Dept. of Clinical and Experimental Medicine. University of Florence, Italy

Dept. of Pharmacy – Pharmaceutical Sciences. University of Bari Aldo Moro Italy

Dept. of Technological Innovations and Safety of Power Plants, Apparatus and Human Settlements, INAIL, Italy

Don Carlo Gnocchi Foundation of Rome, Italy

G. B. Bietti Foundation for Study and Research in Ophthalmology, Italy

Human Microbiome Unit, Bambino Gesù Children's Hospital and Research Institute, Rome, Italy

IASI-CNR, Italy

INAIL, Centro per la sperimentazione ed applicazione di protesi e presidi ortopedici di Vigorso di Budrio, Italy

INAIL, Department of Medicine, Epidemiology, Workplace and Environmental Hygiene

Informatics and Automation, Sapienza University of Rome, Rome, Italy

Institute of Cognitive Sciences and Technologies, National Research Council (CNR), Italy

IRSA, Italy

IRCCS Bambino Gesù Paediatric Hospital

Italian National Agency for New Technologies, Energy and Sustainable Development - ENEA,

Italian Space Agency, Italy

Maire Technimont, Rome, Italy

MASMEC SpA, Italy

National Fire Department, Italy

National Institute for Insurance against Accidents at Work (INAIL), Italy

National Institute of Health, Italy

National Research Council (CNR), Italy

Novamont, Italy

Piaggio Research Centre, University of Pisa, Italy

PolitoBIOMed Lab, Department of Mechanical and Aerospace Engineering, Polytechnic University of Turin, Italy

Polytechnic University of Milan, Italy

Rheumatology Unit, University of Naples "Federico II", Italy

Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples, Italy

Sant'Anna School of Advanced Studies, Italy

Santa Lucia Foundation, Italy

Sapienza University of Rome, Italy

Scleroderma Unit, Sapienza University of Rome, Italy

University of Catania, Italy

University of Messina, Italy

University of Naples "Federico II", Italy

University of Rome Foro Italico, Italy

University of Rome "Roma Tre", Italy

University of Rome "Tor Vergata", Italy

Virology Lab, IRCCS Bambino Gesù Paediatric Hospital, Italy

International agreements and collaborations

Amsterdam Universitair Medische Center, The Netherlands

Applied Neurotechnology Laboratory, Department of Psychiatry and Psychotherapy, University Hospital of Tübingen, Tübingen,

Germany

Breast Surgical Oncology, Clinica Universidad de Navarra, Spain

Centre for Enterprise, Innovation and Growth, Birmingham City University, UK.

Centre Hospitalier Universitaire Edouard-Henriot de Lyon, Lyon, France

Complutense University of Madrid, Spain

Dept. of Fundamental Neuroscience, Faculty of Biology and Medicine. University of Lausanne, Switzerland

Dept. of Pathology. Harvard University School of Medicine, Boston, US

DLR – German Aerospace center, Koel, Germany

DMT- Environmental technology, Joure, Netherland

Eindhoven University of Technology, The Netherlands

Fetal Neonatal Neuroimaging and Developmental Science Center. Boston Children Hospital, US

Fraunhofer IBMT, St. Ingbert, Germany

George Mason University, US

Harvard Medical School, Boston MA, US

Harvard University- Boston, US

Human Virology Institute of Baltimore, US

Infant Communication Lab, University of Pittsburgh, US

John Innes Centre, UK

Kansai Medical University Department of Plastic and Reconstructive Surgery - Osaka, Japan

Leiden University, The Netherlands

Leuven University, Belgium

Medical Oncology Department, Hospital Clínic. Universitat de Barcelona, Spain

National Institutes of Health, US

New York University, US

Pal Robotics, Spain

Pelican Cancer Foundation, UK

Perelman School of Medicine, University of Pennsylvania, US

Public Health Institute of Montenegro

Public Health Institute, Bulgaria

Public Institute of Bulgaria, Sofia, Bulgaria

Queen Mary University of London, UK

Singapore Centre for Environmental Life Sciences Engineering, Nanyang Technological University, Singapore

St. Bartholomew's and The London School of Medicine, University of London, UK

St. Thomas Hospital, University of London, UK

Universidad Miguel Hernandez de Elche, Spain

Université Libre de Bruxelles, Belgium

University at Groningen Medical Center, The Netherlands

University College London, UK

University of Alessandria, Egypt

University of Arizona Cancer Center, US

University of Florida, Gainesville, US

University of Hamburg, Germany

University of Izmir, Turkey

University of Oxford, UK

University of Pittsburgh, US

University of Twente, Netherland

Vall d'Hebron Hospital, Barcelona, Spain Washington University, St. Louis,



Editorial board membership

Editorial board membership

Agrò F.	La Clinica Terapeutica
Angeletti S.	Disease Marker EC Microbiology
Angioli R.	Minerva Ginecologica Oncology Reports
Antonelli Incalzi R.	Advances in Respiratory Medicine Aging Clinical and Experimental Research Journal of Frailty and Aging
Avvisati G.	La Clinica Terapeutica
Bertolaso M.	Bioethics Update Current Bioinformatics Filosofia e Saperi MEDIC - Metodologia didattica e innovazione clinica Medicina e Storia Organisms – An International Journal of Biological Sciences Per la Filosofia Scienze e Ricerche Springer Series Human Perspectives in Health Sciences and Technology
Bonini S.	Ocular Surface
Borghi L.	ISHM (International Society for the History of Medicine) Newsletter
Cacace F.	Mathematical Problems in Engineering
Caputo D.	Austin Digestive Sistema Gastroenterology Research GSL Journal of Clinical Pathology International Journal of Surgery & Surgical Procedures SM Journal of Minimally Invasive Surgery
Carassiti M.	Minerva Anestesiologica
Carotti S.	Journal of Digestive Disease and Hepatology
Casale M.	Austin Otolaryngology Global Journal of Otolaryngology
Cataldo R.	BMC Anesthesiology

Cicala M.	Alimentary Pharmacology & Therapeutics (Reviewer editor) European Medical Journal (Reviewer editor) Faculty Member of F1000, section Disorders of Neurogastroenterology & Motility (Reviewer editor) Frontiers in Neuroscience (Reviewer editor) Gut (Reviewer editor) Journal of Digestive Diseases and Hepatolog (Editorial board) Journal of Gastroenterology and Hepatology (Reviewer editor) MEDIC: Metodologia e Didattica Clinica (Editorial board) Neurogastroenterology and Motility Journal (Reviewer editor) UNIGASTRO Manuale di Gastroenterologia Ed. 2019-2022, (Editorial board) World Journal Gastroenterology (Editorial board)
Ciccozzi M.	PLoS One, sections: Biostatistics and methods, Economics Health economics Public health and epidemiology
Coppola R.	International Journal of Surgery International Journal of Surgery Case Reports Pancreatology PLoS One, sections: General Surgery Gastrointestinal Surgery
Crucitti P.	Journal of Thoracic disease
Di Lazzaro V.	Brain Stimulation Case Reports in Medicine, section: Clinical Neurology Neurology Research International
Di Paola L.	Advances in Systems Biology International Journal of Biochemistry Research and Review (Editor in Chief) International Journal of Medical Biotechnology & Genetics (IJMBG) Journal of Physical Chemistry and Biophysics
Di Stefano N.	De Musica International Lexicon of Aesthetics (ILAe) Lebenswelt. Aesthetics and Philosophy of Experience Sensibilia. Colloquium on Perception and Experience
De Gara L.	Experimental Plant Biology Plant Cell and Environment
Emerenziani S.	EC Nutrition
Fanali C.	Advances in Food Analysis - Editor of the Special Issue Journal Current Analytical Chemistry Journal Electrophoresis Journal Open Chemistry - Analytical Chemistry section Journal Recent Advancement in Food Science and Nutrition Research
Filippi S.	Frontiers in Physics - Optics and Photonics

Faramondi L.	IEEE SMC Technical Committee on Homeland Security (TCH)
Formica D.	Guest Editor of the Special Issue "Fiber optic sensors for biomedical Applications" Guest Editor of the Special Issue "Smart Sensors for Healthcare and Medical Applications" Sensors (MDPI)
Gizzi A.	International Journal of Cutaneous Disorders & Medicine International Journal of Mathematical Physics JSM Head and Face Medicine Mathematical Problems in Engineering
Ghilardi G.	Collana: Biblioteca di Filosofia e Scienze Umane - Bonomi Editore MEDIC: Metodologia e Didattica Clinica Quaderni Europei sul Nuovo Welfare
Guarino M.P.L.	Journal of Digestive Diseases and Hepatology
Guglielmelli E.	Applied Bionics and Biomechanics IEEE Robotics & Automation Society (Vice-President for Publications Activities) Springer Series on Biosystems and Biorobotics (Editor in Chief) Springer Series Human Perspectives in Health Sciences and Technology
Ippolito E.	Musculoskeletal Surgery
Laudisio A.	Frontiers in Geriatric Medicine
Locato V.	Atmosphere Frontiers in Plant Science Plant Cell and Environment Plant Science: Current Research
Longo U.G.	BMC musculoskeletal disorder
Maccarrone M.	Anti-Allergy and Anti-Inflammatory Agents in Medicinal Chemistry BioFactors Cannabis and Cannabinoid Research Cardiovascular Psychiatry and Neurology Current Medicinal Chemistry Current Neurovascular Research Frontiers in Endocrinology Frontiers in Molecular Neuroscience Frontiers in Neuroscience Lipids in Health and Disease Molecules The Open Journal of Neuroscience
Mangiacapra F.	Journal of Cardiovascular Translational Research
Marinozzi A.	Applied Bionics and Biomechanics

Margiotta D.P.E.	PLoS One, sections: General Endocrinology Diabetes and Obesity
Massaroni C.	Advance Research in Textile Engineering Annals of Advanced Biomedical Sciences Archive of Biomedical Science and Engineering eHealth - Innovazione e Tecnologia in Ospedale Sensors (MDPI) The Open Biomedical Engineering Journal Special Issue "Smart Sensors for Healthcare and Medical Applications"
Menna P.	Cardio-Oncology Chemotherapy
Minotti G.	Cardio-Oncology (Deputy Editor) Chemotherapy (Editor in Chief) Italian Journal of Medicine Journal of Pharmacology and Experimental Therapeutics (Editorial Advisory Board) Springer Series Human Perspectives in Health Sciences and Technology
Morini S.	Journal of Digestive Diseases and Hepatology
Napoli N.	Bone Endocrine (Associate editor) Journal of Bone and Mineral Research Osteoporosis International
Navarini L.	Journal of clinical endocrinology and metabolism PLoS One sections: Biochemistry - Lipids Glycobiology Immunology – Autoimmune diseases Rheumatology
Nusca A.	PLoS One, sections: Cardiovascular science and medicine Basic cardiovascular research
Oliva G.	Control Systems Society of the Institute of Electrical & Electronic Engineers
Palermo A.	International Journal of Endocrinology Biomedicines
Papalia R.	Musculoskeletal Surgery
Pedone C.	Advances in Respiratory Medicine (Vice Editor in Chief)
Perrone G.	Archives of Clinical Hepatitis Research International Journal of Clinical and Experimental Pathology

Pennazza G.	Journal of Sensors Sensors (MDPI) Special Issue "Smart Sensors for Healthcare and Medical Applications" World Journal of Respiriology
Persichetti P.	European journal of plastic surgery (Editor in Chief)
Petitti T.	European Journal of Plastic Surgery
Piemonte V.	Artificial Organs Journal of Sustainable Energy Engineering Journal of Technology Innovations in Renewable Energy
Picardi A.	World Journal of Gastroenterology
Pozzilli P.	Diabetes Metabolism Research & Reviews (DMRR) (Editor in Chief) La Clinica Terapeutica
Salvatorelli E.	Cardio-Oncology Chemotherapy
Santini D.	Clinical Medicine Insights: Oncology Critical Review in Oncology and Haematology Expert Opinion on Biological Therapy Expert Opinion on Emerging Drugs Expert Opinion on Therapeutic Targets (Editor in Chief) Journal of Chemotherapy MEDIC: Metodologia e Didattica Clinica Oncotarget PLoS One
Schena E.	Acta Imeko Advance Research in Textile Engineering Guest Editor of the Special Issue "Smart Sensors for Healthcare and Medical Applications" International Journal of Measurement Technologies and Instrumentation Engineering International Journal of Radiology Journal of Healthcare Engineering Sensors (MDPI)
Setola R.	International Journal of Critical Infrastructure Protection International Journal of System of Systems Engineering (IJSSE)
Silvestri S.	The Open Biomedical Engineering Journal
Soda P.	Proceedings of the 41st Annual International Conference of the IEEE Engineering in Medicine & Biology Society (Associate Editor) The Open Medical Devices Journal

Spinelli F.

Annals of Vascular Surgery
 BMJ Case Reports
 Brain Injury
 Catheterization and Cardiovascular Interventions
 Computers and Fluids
 International Angiology
 Italian Journal of Vascular and Endovascular Surgery
 Journal of Cancer and Clinical Oncology
 Journal of Cardiovascular Surgery
 Journal of Emergency Medicine and Intensive Care
 Journal of Infection and Public Health Diseases
 Journal of International Medical Research
 Journal of Neurology and Neurosurgery
 Journal of Neuroscience and Neuropsychology
 Journal of Vascular Medicine and Surgery
 Minerva Chirurgica
 Neurology Research International
 Sage Open Medical Case Reports

Sterzi S.

Giornale Italiano di Ortopedia e Traumatologia

Taffoni F.

EC Paediatrics journal
 Journal of Healthcare Engineering

Tambone V.

La Clinica Terapeutica
 MEDIC: Metodologia e Didattica Clinica

Tenna S.

European Journal of Plastic Surgery

Tonini G.

Colorectal Cancer
 Expert Opinion on Investigational Drugs (Editor-In-Chief)
 Expert Opinion on Pharmacotherapy
 Expert Review of Anticancer Therapy
 Future Oncology
 Hepatic Oncology
 Journal of Cancer Therapy
 La Clinica Terapeutica

Vadalà G.

Journal of Functional Morphology and Kinesiology
 Journal of Stem Cells and Clinical Practice

Vincenzi B.

Cancer Breaking News
 Clinical Medicine Insights: Oncology
 Current Drug Therapy
 Expert Opinion on Emerging Drugs
 International Journal of Molecular Sciences
 Journal of Oncology
 Scientific Reports

Vollero L.

Journal of Sensors

Zollo L.	Applied Bionics and Biomechanics IEEE Transactions on Computational Intelligence and AI in Games International Journal of Advanced Robotic Systems IEEE Transactions on Medical Robotics and Bionics Journal of Healthcare Engineering (Editor in Chief) Springer Series on Biosystems and Biorobotics
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The background of the slide is a light gray with a repeating pattern of small, stylized scientific icons. These icons include DNA double helices, interlocking gears, and sprouting leaves with stems, all rendered in a light gray color that blends with the background.

PhD Courses and XXXI cycle theses (2017-2019)

Ph.D Courses

The Campus Bio-Medico University of Rome offers Ph.D courses to students motivated to gain autonomy and rigor in scientific research. Courses aim to provide doctoral students a scientific culture, methodological tools and advanced technical skills, thereby contributing to the growth of research and scholarship in Italy and internationally.

The primary purpose of Ph.D study is the preparation and presentation of a substantial piece of original research designed to be completed within three years of study.

Full text Ph.D dissertations are deposited in the open access repository ILITHIA. The repository is indexed in OpenDOAR, an authoritative worldwide directory of academic open access repositories. Link: <<http://ilithia.unicampus.it/ilithia/Default.asp>>.

Authors hold copyright of dissertation in accordance with current legislation (Law 633/1941) and subsequent amendments and additions. The dissertations present in the University repository are a guarantee for the author, certifying and dating intellectual property. The repository helps to ensure a high level of visibility of Ph.D dissertations increasing significantly their impact, for the benefiting of both researchers and Campus Bio-Medico University itself.

PH.D IN INTEGRATED BIOMEDICAL SCIENCES AND BIOETHICS

Duration 3 years

Coordinator Prof. Paolo Pozzilli

Students enrolled

XXXIII Cycle (2017/2018): M.M.C. Amato, M. Barone, A. Berton, A. Creta, M. Del Fabbro Arcopinto, R. Del Toro, S. Della Posta, L.A. Diaz Balzani, I. D'Onofrio, G. Franchi, V. Giacinti, S. La Padula, F. Leone, D. Lo Presti, D. Liuvero, B. Marigliano, G. Manascià, M. Naciu Anda, M. Nicoletti, F. Picardo, M. Pinardi, L. Raiano, F. Russo, A. Sabatini, G. Salvatore, M. Stefano, S. Vasta, B. Zampogna, A. Zangrandi

XXXIV Cycle (2018/2019): F. Cannata, A. De Vincentis, M. Donati, Emma. Falato, M. Giuffreda, A. Guarnieri, M. Marano, G. Musumeci, M. Paolucci, M. Russano, F. Tramontana

XXXIV Cycle (2019/2020): G. Albergo, G. Alhamar, N. Brunelli, V. Candela, M.C. Cursano, A. Di Santo, M.I. Faraj, E. Gianni, P. Luffarelli, C. Madaudo, A. Nenna, V. Piombino, G. Tabacco, F. Tavaglione, V. Tilotta

Learning outcomes

The structure of the Ph.D in Integrated Biomedical Sciences and Bioethics is designed to produce graduates who have a thorough knowledge of the literature and comprehensive understanding of scientific methods and techniques applicable to their own research. This particular Ph.D focuses its attention in integration of the broader fields of biomedical research with a more philosophical approach, which include further study in anthropology, ethics, aesthetics, epistemology, and bioethics.

Research fields

The Ph.D in Integrated Biomedical Sciences and Bioethics is divided in various tracks:

- **Endocrinology:** MED/13, MED/09, MED/08, BIO/10, MED/16, MED/18
- **Bioethics:** MED/43, BIO/14, MED/26, BIO/16
- **Osteo-Oncology Pathology:** MED/06, MED/04, BIO/10, MED/15, MED/40, MED/16
- **Ageing Sciences and of Tissue Regeneration:** MED/09, MED/19, MED/26, MED/15

PH.D IN BIOENGINEERING AND BIOSCIENCES

Duration 3 years

Coordinator Prof. Giulio Iannello

Students enrolled

XXXII Cycle (2016/2017): S. Cocca, C. Gentile, E. Gruppioni, M. Langone, M. Menci, A. Nocco, F. Scotto Di Luzio, R. Sicilia, A. Vilmercati

Learning outcomes

The structure of the Ph.D in Bioengineering and Biosciences is designed to produce graduates with rigorous research and analytical skills, who are exceptionally well-equipped to carry out research in academic, industry, or government positions. The program is divided in two tracks: one oriented to biomedical engineering applications the other to Science and food technology and nutrition.

Ph.D program allows graduates to:

- develop new methods, instruments and systems, for biomedical engineering and for food sciences and nutrition;
- describe, plan, coordinate and carry out research programs developing technical and medical-biological skills;
- integrate traditional formation in the biomedicine, with knowledge such as maths and technology which can face the increasing complexity of “bioinspired” research fields.

Research fields

The main fields of study are:

- **Bioengineering:** study, design and development of new methods, systems and medical devices, medical and biological research, development of bioinspired medical technologies;
- **Material science and nanotechnology:** study, development and testing of materials for industrial applications with a particular consideration to medical and food applications;
- **Modelling:** study and use of complex systems models for applications in biology and medicine;
- **Food chemistry and plant physiology:** study and development of new knowledge and protocols for the characterization of bioactive molecules and their metabolism. Use of new technologies for the nutritional enhancement of traditional and innovative foods;
- **Nutrition:** use of advanced technological for the study of nutritional parameters and their impact in the prevention of diseases; Experimentation protocols and procedures applied to clinical nutrition.

PH.D IN SCIENCE AND ENGINEERING FOR HUMANS AND THE ENVIRONMENT

Duration 3 years

Coordinator Prof. Giulio Iannello

Students enrolled

XXXIII Cycle (2017/2018): M. Del Fabbro Arcopinto, S. Della Posta, G. Franchi, V. Giacinti, F. Leone, D. Lo Presti, M. Nicoletti, L. Raiano, A. Sabatini, M. Stefano

XXXIV Cycle (2018/2019): A. Carnevale, L. Corti, N.C. D'Amico, A. Demofonti, B. Di Sero, M. Gionfriddo, G. Lattanzi, F. Le Jeune, V. Madiati, F. Mereu, A. Pensotti, A. Salvati, M. Torre, A. Vaccaro

XXXIV Cycle (2019/2020): L. Bacco, M. Cocchi, F. D'Antoni, C. Di Rosa, J. Di Tocco, T. Falcone, A.B. Leone, M. Lombardi, S. Melino, E. Possemato, D. Santucci, L. Spagnuolo, C. Tamantini, M. Zaltieri

Learning outcomes

The Ph.D in Science and Engineering for Humans and the Environment aims at training experts capable of carrying out research activities for the care of the individual and the environment. The Ph.D is divided into courses that offer the development of complementary skills in engineering, as well as different scientific and technological fields, but likewise focused on improving the quality of life for individuals with reference to the environment they live in.

This goal is pursued thanks to the presence in the Academic Board of researchers from different macro-areas of study and having a long-standing commitment to the subject matter of the Ph.D course. The training courses also aim at stimulating doctoral students with a multi-disciplinary approach to problems regarding man and the environment.

Ph.D program allows graduates to:

- develop new methods, instruments and systems to promote health, well-being and personal safety, through the care of environment and also supported by the most up-to-date research results
- describe, plan, coordinate and carry out research programs in order to develop technical and multidisciplinary research combining different technical and scientific skills
- integrate the traditional type of education in biomedicine, with knowledge such as maths and technology which can help to face the increasing complexity of “bioinspired” research fields.

Research fields

The main fields of study are:

- study, design and development of new methods, systems and devices for biomedical applications, with particular reference to biorobotics, biomedical instrumentation, biomaterials, and tissue engineering;
- study and use complex systems models for applications in biology, medicine and environmental science;
- study and development of new knowledge and protocols for the characterization of bioactive molecules and their metabolism, their nutritional parameters and impact on diseases prevention, as well as experimentation of protocols and procedures applied to clinical nutrition;
- study, design and development of new methods, systems and devices based on information technology, with particular reference to the analysis of large amounts of data.

Graduate School – shared education platform

The Coordinating Board for Ph.D programs, formed by Doctoral program Coordinators and supported by the Centre for Integrated Research, in the academic year 2013/14 created a training event called 'Graduate School – a shared education platform'. Its goal was to offer a training course in Scientific Research, cutting across individual Degree Program, to investigate issues of common interest. The event is organized with a series of short lectures that address specific issues identified by Doctoral program Coordinators.

Monday 2 December 2019

09:30-10:00	Institutional greetings and introduction to 'Graduate School – a shared education platform' 2019.
10:00-11:15	Critical and Design Thinking: Human dimension between technique and art – Part One Introduces and moderates: Marta Bertolaso, Department of Sciences and Technologies for Human and Environment, Campus Bio-Medico University of Rome. Speakers: Robert Alexander, IBM, Italy; Archaeologist Ambrogio Risari, Dubini Risari and Melzi d'Eril Associati Architecture office, Milano
	Coffee break
11:30-13:00	Critical and Design Thinking: Human dimension between technique and art – Part Two Welcome lunch
14:30-15:30	Leadership model – virtues – underlying competencies Livio Anfossi, Human Resources and Personnel Policies, Campus Bio-Medico University of Rome.
15:30-16:30	Riddle of relevance Marco Magheri, Communication and Brand Management Area, Campus Bio-Medico University of Rome.

Tuesday 3 December 2019

10.00-11.15	Course of European design with cas studies and working groups Marta Calderaro, APRE
	Coffee break
11.30-13.00	Course of European design with case studies and working groups Marta Calderaro, APRE
	Lunch break
13.45-16.15	Course of European design with case studies and working groups Marta Calderaro, APRE
16.15-16.30	Grant Office for proposals presentation Antonella Benvenuto, Anna Lisa Ciancio, Grant Office, Campus Bio-Medico University of Rome

16.30-17.00	The Conbots project Domenico Formica, Department of Engineering, Campus Bio-Medico University of Rome
17.00-17.30	Q&As

Wednesday 4 December 2019

10.00-13.00	Submission of reports for Ph.D students of XXXIII, XXXIV and XXXV cycle Ph.D Courses in Science and Engineering for Human and Environment
09.30-13.30	Submission of reports for Ph.D students of XXXIII, XXXIV and XXXV cycle Ph.D Course in Integrated Bi-omedical Sciences and Bioethics
	Lunch break
14.30-17.00	Submission of reports for Ph.D students of XXXIII, XXXIV and XXXV cycle Ph.D Courses in Science and Engineering for Human and Environment
14.30-17.30	Submission of reports for Ph.D students of XXXIII, XXXIV and XXXV cycle Ph.D Course in Integrated Bi-omedical Sciences and Bioethics

Thursday 5 December 2019

09.30-10.30	Scientific publications: From the scientific to the academic impact Paolo Pozzilli, Editor in Chief Diabetes Metabolism Research and Review, Department of Medicine and Surgery, Campus Bio-Medico University of Rome.
10.30-11.00	How to write a funding request for a research project Rocky Strollo, Campus Bio-Medico University of Rome.
	Coffee break
11.15-11.45	Ethical aspects and scientific publications Nicola Napoli, Department of Medicine and Surgery, Campus Bio-Medico University of Rome.
11.45-12.15	The importance of statistics knowledge for the PhD Massimo Ciccozzi, Department of Medicine and Surgery, Campus Bio-Medico University of Rome
12.15-13.00	PhD role in industry Cesar Libanati, Medical Director Global di UCB S.A., Bruxelles
	Lunch break

14.00-14.15	Library role at Internet time Maria Dora Morgante, Chief librarian, Campus Bio-Medico University of Rome
14.15-14.45	How to present your scientific work results (Presentation at conferences) Francesco Pantano, Campus Bio-Medico University of Rome
14.45-15.15	Bibliometrics and its impact on academic life Andrea Palermo, Campus Bio-Medico University of Rome
15.15-15.45	How to write a scientific work Giovanni Di Pino, Department of Medicine and Surgery, Campus Bio-Medico University of Rome
15.45-17.00	The potential of intellectual property protection Sara Manna, S.p.A. Brevetti Italian Society
17.00-17.45	How to fill in a patent application Giorgio Pennazza, Department of Engineering, Campus Bio-Medico University of Rome
17.45-18.00	Knowledge Transfer Office: Services supporting researchers Maria Carla De Maggio, Knowledge Transfer Office, Campus Bio-Medico University of Rome

Friday 6 December 2019

09.30-11.00	The new epidemiological-molecular monitoring system in the public healthcare Massimo Ciccozzi, Department of Medicine and Surgery, Campus Bio-Medico University of Rome
	Coffee break
11.30-12.30	The informative sources and the monitoring systems for workers' health and security. What is the impact and the prospect of the public healthcare in the Big Data era Sergio Iavicoli, INAIL
12.30-13.00	Brain Innovation spin-off experience Lazzaro Di Biase, Campus Bio-Medico University of Rome
13.00-13.15	Conclusions and works closing

Ph.D dissertations defended in 2019-2020

*Link to full text dissertations: <http://ilithia.unicampus.it/ilithia/Default.asp>

A MEDITERRANEAN-PATTERN MEAL INCREASES GLP-1 AND OXYNTOMODULIN MORE THAN AN ENERGY-MATCHED HIGH FIBER PLANT-BASED MEAL IN TYPE-2 DIABETES PATIENTS: A CROSSOVER, RANDOMIZED, CONTROLLED INPATIENT PHYSIOLOGY STUDY

Ph.D Antonio Di Mauro

Tutor Paolo Pozzilli

Background. Type-2 diabetes (T2D) is a multifactorial metabolic burden whose metabolic features include alterations in GLP-1 secretion and ultimately hunger/satiety circuit derangement. Manipulating the composition of the diet in order to promote GLP-1 secretion may represent a promising lifestyle strategy for obesity and T2D management. **Aims.** The objective of this study was to assess the post-prandial profile of appetite regulating hormones and assessing the post-prandial appetite ratings using a Visual Analogue Scale (VAS), as well as measuring the fasting and post-prandial glucose/insulin responses in overweight and/or obese, well controlled patients with T2D. **Materials and methods.** Twelve T2D patients (M:F = 7:5) aged 63.1 ± 8.5 years were enrolled in a randomized, controlled, crossover trial. Subjects consumed on two different days, at one-week interval, an experimental High Fiber Vegetarian meal (HFV) rich in dietary carbohydrate and fiber in comparison with a standard, Mediterranean-like meal (MED). The two meals were isocaloric. Appetite ratings, glucose/insulin and gastrointestinal hormone responses were assessed either at fasting and every 30' until 210' for GLP-1 and Oxyntomodulin and 240' for glucose and insulin after the ingestion of the meal. Subjects consuming the MED meal exhibited significant and higher levels of GLP-1 and oxyntomodulin across the 210' compared to the HFV group ($p < .05$ one-sided for both the hormones). The 210'-GLP-1 and Oxyntomodulin AUC were significantly increased in the MED group ($P < .022$ and $P < .023$, respectively). Both the MED and HFV meals consumption induced a biphasic shaped secretion pattern over time but the MED consumption produced a significant delayed second GLP-1 peak at 150' compared to the HFV meal (56 ± 21 pg/mL Vs 44 ± 18 pg/mL, respectively $P < .05$), delaying the second peak one hour and half after the HFV-M group. The MED group maintained significant and consistent decreased levels of plasma over time compared to the HFV group ($P < .039$) and the 240-minute glycemic AUC was significantly higher in the HFV compared to the MED meal, even after the adjustment for age and gender, BMI and HbA1c ($P < .006$). In addition, the 240-minute glycemic iAUC was significantly higher in the MED meal ($P < .002$). No major significant changes in VAS and postprandial insulin profile between the two groups were assessed. **Conclusions.** A Mediterranean type of meal is more effective in increasing postprandial secretion of GLP-1 and oxyntomodulin and reducing postprandial plasma glucose levels in overweight/obese T2D patients. These changes did not influence the appetite ratings evaluated through the visual analogue scale. These findings suggest that, in acute, diet-related endocrine release may not be related to changes in self-rated hunger/satiety, possibly because of T2D metabolic features. Either on short and long term, diet influences gut hormone levels in T2D.

ARTIFICIAL INTELLIGENCE MEETS DIABETES AT THE MICRO-SCALE: FORECASTING COMPLICATIONS AND QUANTITATIVELY MINING INSULIN GRANULES MOTIONS

Ph.D student Ermanno Cordelli

Tutor Paolo Soda

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose, which leads over time to serious complications. Unfortunately, no cure exists and the only way to tackle the disease consists in constantly monitoring the blood sugar concentration and furnishing insulin via periodic injections in type 1 diabetes and only in prevention in type 2. The thesis presents innovative applications of Artificial Intelligence to two key issues in diabetes. In a first part, it presents a decision support system that analyses red blood cells fluidity to diagnose diabetes and diabetes with complications. In the second part, it investigates the insulin granules' dynamic inside the b-cells, assessing their motion in presence of different environmental glucose concentration with a clustering analysis.

HUMAN-INSPIRED CONTROL STRATEGY FOR HAND PROSTHETICS

Ph.D student Cosimo Gentile

Tutor Loredana Zollo

The hand is the human body part that has always fascinated researchers: several studies have been conducted to understand and explain its perfect mechanism. The hand is used to learn and to interact with the environment and it is clear that hand loss involves irreparable damage for a person. Besides having suffered hand loss, monolateral amputee subjects need to learn how to perform everyday life actions with only one hand. To overcome this problem, since the ancient Egypt, prostheses have been used for both cosmetic and functional purposes. The functioning of an active prosthetic hand is guaranteed by a mechatronic device, a decoding system to decode human biological signals in gestures and a control law that translates all the inputs (from the hand and from the user) in the desired movement. The ambition of this thesis is to design and develop a control strategy able to improve grasp and manipulation capabilities of prosthesis based on the tactile sensorization and on the use of this information in the control strategy. The proposed strategy is divided into 3 levels: low-level to regulate force and slippage during the whole grasp, middle-level, to manage the pre-shaping and the fingers reaching to the object, high-level, to decode the biological human signals in movements and force levels. The greatest limitation for an amputee subject who uses a prosthesis having no sensory feedback is the difficulty to manage unexpected events in an autonomous way. In grasp and manipulation tasks, the possibility of the object slippage is high. For this reason, it is necessary to detect the beginning of the slippage and provide control with a fast contrast action. The first contribution of this thesis is the development of a touch-and-slippage detection algorithm for effective grasp control of a prosthetic hand embedding monoaxial, low-cost sensors is proposed. One of the main problems in the prosthetic hand design is to provide the hand with a reliable system for force and slippage control. To decrease the attention level and the cognitive burden for the user during grasp tasks, an automatic strategy is necessary. The second contribution of this thesis is to propose a force-and-slippage control strategy able to i) regulate the grasping force, ii) prevent the slippage events, iii) coordinate fingers for replicating a human-like behaviour on the prosthetic system. Real-time reaction to slippage events and finger coordination has been achieved by means of i) a force control with inner position loop, ii) a sensorization system giving information about the applied normal forces, and iii) an approach for controlling the fingers in a coordina-

ted manner on the basis of the virtual finger concept. The middle-level is managed with a proportional position control where the user can actively close or open the hand. The high-level proposed in this thesis consists of a hierarchical classification system used to simultaneously discriminate hand/wrist gestures and desired force levels. Moreover, a system composed of software for the EMG signals management and virtual reality were ad-hoc developed for upper limb amputees underwent the Targeted Muscle Reinnervation (TMR) to train them to control multiple prosthetic modules in a coordinated manner in a safe environment. Dexterity and manipulations skills in humans are allowed by complex biomechanics of the hand and a control loop based on a bidirectional communication with the brain, thanks to a sophisticated sensory system. This thesis has contributed to show the possibility to enable real-time closed-loop control of bionic hands in tasks of fine grasp and manipulation. Force and slippage sensations were elicited in an amputee by means of biologically inspired slippage detection and encoding algorithms, supported by an extended stick-slip model of the performed grasp. Closed-loop control capabilities enabled by the neural feedback were compared with those achieved without feedback.

FROM POLY-ARTICULAR TO SUPER-ARTICULAR PROSTHESES AND ROBOTIC MANIPULATORS

Ph.D student Emanuele Gruppioni

Tutor Eugenio Guglielmelli

The external limb prosthetic sector is experiencing years of profound change, as the research carried out over the past two decades has been progressively shifting, finding concrete application in patients who have undergone an amputation. Bionics, understood as a stable bi-directional man-machine connection that integrates the man at the machine and the machine at the man, it is the frontier on which research is spending its main energies and whose findings mostly affects the world of disability, with consequent transversal effects in society. Upper limb prostheses are among the most popular applications that benefit from such research, in view of the large distance, still existing, between the devices normally in use and the functionality of a natural limb. Despite the most recent discoveries, this distance remains, however, they are looking for solutions to make a significant reduction this distance.

The evolutionary thrust of bionics derives on the one hand from the complexity that these areas of research requires, on the other hand, the awareness that the ever-greater contribution of knowledge and studies transversal to various disciplines should be integrated into the projects of research from their earliest stages. Based on these principles, the doctoral work was carried out within the INAIL Prosthesis Center, where there is a high experience within the field of limb prostheses, as well as the expertise of Campus Bio-Medico on the surgical, rehabilitation and front engineering; this combination has made it possible to reach relatively quickly results both of great scientific and technical/application relevance and of great impact for patients who, by participating in the challenges of research, were able to benefit from solutions that are improving their well-being and their quality of life. In particular, the doctorate was carried out on two potentially convergent activities: the development of a bionic system of the upper limb and the development of a prototype of bilateral grip manipulator. The first topic is part of a project in progress between INAIL Prosthesis Center and Campus Bio-Medico University, aimed at exploring functional surgery for the application of new bionic prostheses. The second line of research opens the way to the development of not strictly anthropomorphic devices: in the field of prosthetics, these may in the future be able to compensate some limits of current hand prostheses, while in the field of robotics they could optimize gripping and handling tasks.

Numerous others have also been followed, supported and developed during the PhD research in the field of bioengineering, in addition to those described above. With these premises, the present paper has been divided

into two sections: the first on core activities (bionic arm and bilateral hand) and the second on further activities research. The first chapter begins with a synthetic but rational treatment of standard prosthetics, to provide the basis for better understanding the meaning of subsequent activities. The activities described in the second chapter, related to the development of the bionic prosthesis of the upper limb, which were made with the collaboration of engineering students of the University of Bologna and the Campus Bio-Medico University, with reference to work done for the degree thesis. The third chapter relates to the prototype development activities of the ABILHA hand (Artificial BiLateral HAnd), carried out with the collaboration of engineering students of the University of Genoa. The first section concludes with the fourth chapter, which reports the discussion of the results obtained and future development prospects. The second section schematically reports the further study topics addressed during the PhD course alongside the main objectives, aimed at completing the activity of research.

ADULTS WITH AUTOIMMUNE DIABETES: VASCULAR RISK, EMERGING COMPLICATIONS AND NOVEL DISEASE PATHWAYS

Ph.D student Ernesto Maddaloni

Tutor Raffaella Buzzetti

Background. The population of adults with autoimmune diabetes has grown world-wide. This is largely the result of better care and increased longevity of people with young-onset type 1 diabetes (T1D), but also of the increased number of latent autoimmune diabetes of the adult (LADA) diagnoses. Adults with autoimmune diabetes differ from those with type 2 diabetes (T2D), with challenges and uncertainties about the impact of aging in people with autoimmune diabetes. In the immediate future, we will have to face complications of autoimmune diabetes in the context of aging and long exposure to the disease, but a paucity of data is available in this regard. Therefore, studies elucidating the pathophysiology, epidemiology and clinical features of autoimmune diabetes in adults and elderly people, both those with T1D and LADA, are needed. **Hypothesis.** We hypothesized that clinical features and risk of diabetic chronic complications may differ in adults with different forms of diabetes. Therefore, we also hypothesize that the study of vascular and bone disorders in adults with autoimmune diabetes may unveil novel risk factors and pathways of chronic complications. **Aims and methods.** The overall aim of this project was to investigate the pathophysiology and clinical features of autoimmune diabetes and its complications during the adulthood and the senescence. More specifically we aimed to: 1. Evaluate whether rates and risk factors for vascular complications differ between LADA and T2D. To this aim data from the UK Prospective Diabetes Study (UKPDS) have been retrieved and analyzed. Diabetes autoantibodies (AAb) were measured in 5,062 UKPDS participants. The incidence of major adverse CV events (MACE), defined as CV death, nonfatal myocardial infarction or nonfatal stroke, was compared in those with LADA (>/- 1 AAb test positive) with those without LADA (AAb negative). 2. Evaluate bone health and its relationship with vascular complications in adults and aging people with autoimmune diabetes. To this aim adults with T1D followed in the centers of the IMDIAB group and elderly people enrolled in the 50-Years Joslin Medalist Study were fully characterized in terms of history of metabolic control, chronic complications and bone fractures. Bone mineral density was measured by DEXA in a subgroup of these subjects. Risk factors for impaired bone health and the relationship between bone fragility and vascular complications were investigated in both young adults and elderly with long standing type 1 diabetes. 3. To investigate circulating osteoprogenitors as a new mechanism of vascular complication in type 1 diabetes Osteocalcin (OCN) + monocytes were studied in a unique population with ≥ 50 years of T1D, the 50-Year Joslin Medalists. CD45 bright/CD14+/OCN+ cells in the circulating mononuclear blood cell fraction were quantified by flow cytometry in and reported as percentage of CD45 bright cells. Mechanisms were studied by inducing OCN expression in human monocytes in vitro. **Results.** Specific aim 1.

There were 567 participants with LADA (11.2%). Compared with T2D, they were younger, with higher mean HbA1c and HDL-cholesterol values but lower body mass index, total cholesterol and systolic blood pressure values (all $p < 0.01$). After median (25th – 75th percentile) 17.3 (12.6–20.7) years follow-up, MACE occurred in 157 (17.4 per 1000 person-years) LADA and 1544 (23.5 per 1000 person-years) T2D participants respectively (HR 0.73, 95% Confidence Interval [CI] 0.62–0.86, $p < 0.001$). However, after adjustment for confounders, this difference was no longer significant (HRadj 0.90, 95% CI 0.76–1.07, $p = 0.22$).

Specific aim 2. Among 600 adult subjects with T1D (age: 41.9 ± 12.8 years, disease duration: 19.9 ± 12.0 years; BMI: 24.4 ± 3.7 kg/m²; 5-year average HbA1c: $7.6 \pm 1.0\%$), 18.5% experienced at least one fragility fracture (73.8% had only one and 26.2% had more than one fracture). In this population, increased risk for ≥ 2 fractures was found in subjects in the highest tertile of HbA1c ($\geq 7.9\%$) compared with the lowest tertile ($< 5.7\%$) (RRR 7.59 [1.60–35.98], $p = 0.01$). The presence of neuropathy increased the risk of single fracture (RRR adj: 2.57 [95%CI: 1.21–5.46]), and multiple fractures (p -value for the difference of the effect on outcomes: 0.99). Differently, in a selected population of elderly T1D subjects (age: 66.0 ± 7.6 years) with an extreme disease duration (> 50 years) we found a lower prevalence of fragility fractures (1.12%). Because of the low prevalence of chronic complications in this population (cardiovascular disease: 39.9%; retinopathy: 46.4%; nephropathy: 12.5%), we hypothesized an association between vascular complications and bone health. This was confirmed by a significant association found between history of cardiovascular disease and low bone mass at the femoral neck (RR: 4.6 [1.2–18.1], $p = 0.03$).

Specific aim 3. Subjects without history of CVD ($n = 16$) showed lower levels of OCN+ monocytes than subjects with CVD ($n = 14$) ($13.1 \pm 8.4\%$ vs $19.9 \pm 6.4\%$, $p = 0.02$). OCN+ monocytes level was inversely related to total high-density lipoprotein (HDL) cholesterol levels ($r = -0.424$, $p = 0.02$), large ($r = -0.413$, $p = 0.02$) and intermediate ($r = -0.445$, $p = 0.01$) HDL sub-fractions, but not to small HDL. In vitro, incubation with oxidized low-density lipoprotein (OxLDL) significantly increased the number of OCN+ monocytes ($p < 0.01$). This action of OxLDL was significantly reduced by the addition of HDL in a concentration dependent manner ($p < 0.001$). Inhibition of the scavenger receptor B1 (SR-B1) reduced the effects of both OxLDL and HDL ($p < 0.05$).

Conclusions. This project evaluated in depth the risk of cardiovascular disease, bone fragility and their intimate relationship in adult and elderly subjects with autoimmune diabetes. Our data show that the healthier cardiometabolic profile of subjects with LADA compared with T2D translates in a lower incidence of major cardiovascular events, which is mostly explained by traditional cardiovascular risk factors, including age, lipids and blood pressure. This highlights the importance of aggressively tackling these cardiovascular risk factors in autoimmune diabetes to keep the lower risk of CVD. On the other hand, we are showing an alarming increased risk of bone fractures in adults with T1D. As bone fragility fractures are among the most important causes of reduced life expectancy in elderly and because of the ageing of T1D population, our data claim for immediate action to tackle this emerging complication. Of note, we are showing a close relationship between bone fragility and chronic complications of diabetes, which has been confirmed also in a special population of elderly subjects with T1D protected from vascular complications. This might suggest that strategies to prevent vascular complications may also aid in preventing fragility fractures in T1D. Furthermore, this led to the hypothesis that common mechanisms of disease are shared between bone and vascular complications. This was explored by looking at the role of circulating osteoprogenitors in CVD, which were found lower in T1D subjects protected from CVD. Results regarding the regulation of OCN expression on monocytes by OxLDL and HDL through SR-B1 and its relationship with CVD provide new information on vascular pathophysiology specifically in T1D. In-deed, these findings may provide new insights on the mechanism of HDL-mediated cardiovascular protection in autoimmune diabetes and promote advances in therapeutic strategies in this population.

ANALYTICAL FOUNDATIONS OF A CLASS OF HYBRID MODELS WITH APPLICATIONS TO COLLECTIVE DYNAMICS

Ph.D student Marta Menci

Tutor Marco Papi

The thesis as a whole focus on mathematical models describing collective dynamics of agents in different contexts. In the first part of this work, we study a distinct type of systems of differential equations, arising from mathematical models that combine discrete and continuum approaches, known as hybrid or discrete-continuum models. In the last years, these kind of models has gained interest in those biological phenomena involving cell-cell interactions and cell-matrix interaction, specifically chemotactic ones. The terminology hybrid thus refers to the presence of different scales within the same model: while cells are treated as discrete units, the chemo-tactic signal influencing their dynamics is represented as a continuum. The great variety of applications of these kind of models does not correspond to a relevant literature published elsewhere concerning theoretical fundamentals. From a mathematical point of view, the general structure of the investigated models combines ordinary and partial differential equations. There are at least two main aspects that differentiate our formulation from those available in the current state of the art concerning analytical results for coupled systems. Part I of the thesis is devoted to analytical results concerning existence and uniqueness of the solution of hybrid systems. In a first published work, we propose well-posedness theorems for the solutions in \mathbb{R}^N assuming, between others, the source term g and the initial data f continuous functions. This contribution has been extended in a paper, where we investigated the case of a source term with less regularity properties. In fact, the present literature exhibits models with discontinuous source term, in order to differentiate regions from which a signal arises from the others. In an ongoing work, we further generalize the above structure of hybrid system, assuming in particular $f \in H^1(\mathbb{R}^N)$ and $g \in \text{Lip}(\mathbb{R}^N \times \mathbb{R}^N; L^2(\mathbb{R}^N))$. In this work we are going to introduce a different technique, based on a preliminary study concerning well-posedness of a pseudo-parabolic approximation problem, in order to prove existence and uniqueness of the solution. Another crucial investigated aspect concerns the asymptotic behavior of the solution. In a more applied and numerical oriented work, we consider an alignment and chemotaxis mechanism, whose evolution in time is modeled by a parabolic equation with constant coefficient, acting on a system of interacting particles, and initial null concentration of chemical. The proposed model is studied both from an analytical and a numerical point of view. From the analytic point of view, we proved existence and uniqueness of the solution. Then, the asymptotic behavior of a linearised version of the system is investigated. We proved that the migrating aggregate exponentially converges to a state in which all the particles have a same position with zero velocity. Theoretical results were compared with numerical simulations, based on finite difference schemes, concerning the behavior of the full nonlinear system. Part II of the thesis introduces a different approach to collective dynamics of agents. The research started with a published book chapter focused on robustness and control of distributed systems. In order to provide evidence of the robustness of distributed biological systems, we considered a case study describing chemotaxis processes for a colony of *E. Coli* bacteria. Afterwards, distributed systems of agents have been investigated in a decision-making perspective. The research in this area has led to two contributions. In a first work, we aimed at finding effective distributed algorithms to solve the Sparse Analytic Hierarchy Process problem, where a set of networked agents (e.g., wireless sensors, mobile robots or IoT devices) need to be ranked based on their utility/importance. However, instead of knowing their absolute importance, the agents know their relative utility/importance with respect to their neighbors. Moreover, such a relative information is perturbed due to errors, subjective biases or incorrect information. The aim of this paper is to provide a numerical comparison of the performances of four methods over networks with different characteristics. In the second contribution, we considered a scenario where a set of agents, interconnected by a network topology, aim at computing an estimate of their own utility, based on pairwise relative information having hybrid nature. In greater detail, the agents are able to measure the difference between their value and the value of some of their neighbors, or have an estimate of the ratio between their value and the value of the remaining neighbors. The "hybrid" scenario represents the novelty with respect to previous work in literature, where the

two types of information are treated separately. Specifically, we developed a distributed algorithm that lets each agent asymptotically compute a utility value. To this end, we first characterized the task at hand in terms of a least-squares minimum problem, providing a necessary and sufficient condition for the existence of a unique global minimum. Moreover, we proved that the proposed algorithm asymptotically converges to the global minimum.

SMART TOOLS FOR ORTHOPAEDIC SURGERY WITH SENSING CAPABILITY: A NOVEL APPROACH

Ph.D student Iacopo Portaccio

Tutor Dino Accoto

Low back pain is a very common and unsolved health problem and a major cause of disability, affecting work performances and general well-being. It is estimated that it affects roughly 60–80% of the adult population in the US. The strategies for treating this pathology range from conservative management to surgery. Novel biological technologies, such as regenerative medicine and bio-artificial organs, are already being tested in human pilot clinical trials. These approaches are an emerging and promising therapeutic tool that might stop, delay or reverse intervertebral disc degeneration. All the above surgical procedures are commonly delivered by injections into the nucleus pulposus through the annulus fibrosus route. However, even small needle annulus fibrosus punctures (25 gauge) may affect intervertebral disc biomechanics, cellularity and biosynthesis. An alternative approach to the annulus fibrosus route, namely the transpedicular route, has been developed and tested: it allows to preserve the annulus fibrosus intact, while the nucleus pulposus is reached via the endplate route. For this purpose, it is necessary to create a deep hole into the verte-bra along the transpedicular trajectory. Generally, rotative drills are used, which can cause intraoperative complications: damaging of surrounding soft tissues and over-heating of adjacent tissues up to necrosis are not uncommon. Moreover, the procedure is manually performed: the surgeon dexterity and experience, in fact, play a crucial role in maintaining the route toward the end plate of the vertebra during drilling. The accurate and safe creation of a single transpedicular bone hole to access to intervertebral disc space represents therefore an engineering challenge in the new transpedicular procedure. With this aim, a novel system has been developed for guiding surgical tools used for intervertebral access creation. The proposed positioning system (PS) allows to enhance the positional accuracy of drilling task. The PS allows the manual advancement of the drilling tool constrained along a fixed trajectory, in order to preserve the natural haptic perception of the surgeon, who remains in charge of modulating the drilling force and the feeding rate according to the position of the drill bit in the bone. Furthermore, a trajectory planning algorithm has been implanted for guiding the insertion towards the intervertebral space based only on the acquisition of a few fluoroscopic images. The insertion orientation, and therefore the regulation of the system joints configuration, can be planned by a software based on two perpendicular C-arm fluoroscopic images and starting from the identification of the insertion point and of the insertion direction drawn on the images by the surgeon. The system has been dimensioned so to be compatible with the size of C-arm workspace and to minimally interfere with the surgical procedure and with the work of the medical staff. Furthermore, in order to enhance the safety of the procedure, ultrasonic technology has been adopted for developing a new ultrasonic drill for deep hole creation. Ultrasonic bone cutting has advantages in controlling tissue damages because it selectively cuts only mineralized tissues, avoiding damages to soft tissues for frequencies in the range of 25 - 35kHz. In this work a development process for bone ultrasonic drill has been proposed. The whole ultrasonic drill has been designed in COMSOL Multiphysics environment, exploiting the multi-domain tools for simulation. After the manufacturing, the ultrasonic drill has been characterized in terms of vibration properties. The experimental results are in agreement with the simulations. The safety issues in spinal transpedicular procedures cannot be solely exhausted by taking into account the aforementioned solutions. Generally, the accuracy problem in bone drilling consists in finding the right drill termination moment to guarantee that the rear hole will not

be widened. Different hardware and software solutions have been developed in order to estimate the drill position during drilling for detecting the bone layers breakthrough. Nevertheless, the main disadvantage of these techniques is the use of the pushing force generating drill bit advancement as effective signal to discriminate among different bone tissues when the feed rate is constant. Therefore, the adoption of these methods is ineffective in the proposed surgical positioning system, where the surgeon can manually control the advancement of the drill bit, thus preserving the haptic feedback that she/he receives from the interaction between the tool and the bone tissues. To address the problem of tissue characterization while leaving the surgeon in complete control of the transpedicular procedure, the average impedance parameter has been introduced. A custom drill, embedded with force and position sensors, which allows the evaluation this new parameter, has been developed. In this work the average impedance estimation results on porcine models are discussed. In addition, the average impedance results obtained on human vertebrae drilling tests are presented and compared with bone mineral density evaluated from CT scans. Finally, in this work it is shown the feasibility to use the ultrasonic drill in the process for the bone layers breakthrough detection, thanks to its capability of sensing of the thrust force applied during bone drilling. This represents a huge advantage, since: i) all the advantages of the ultrasonic cutting, already described, are assured; ii) a single device allows cutting and sensing features simultaneously.

A BIO-COOPERATIVE APPROACH FOR UPPER LIMB ROBOT-AIDED REHABILITATION

Ph.D student Francesco Scotto Di Luzio

Tutor Loredana Zollo

The design of patient-tailored rehabilitative protocols has a crucial role both in the clinical and research fields. Moreover, the inclusion of the patient in the robot control loop and a control strategy adaptable to the user's requirements are expected to significantly improve functional recovery in robot-aided rehabilitation. Ambition of this thesis is to design and develop of a bio-cooperative platform for upper limb robot-aided rehabilitation based on human-in-the-loop approach. The proposed platform is composed of an end-effector robot arm, a purposely developed arm-weight support of patient limb and a multimodal interface to constantly monitor patient status. It is equipped with sensors that allow recording kinematic, kinetic and physiological data both during the evaluation phase of the patient and during the rehabilitation treatment. It is capable of adapting therapy characteristics to specific patient needs, thanks to biomechanical and physiological measurements, and thus closing the subject in the control loop. The level of arm-weight support and the level of the assistance provided by the end-effector robot are varied on the basis of muscular fatigue and biomechanical indicators. An assistance-as-needed approach is applied to provide the appropriate amount of assistance. An overview of the validated tools for patient evaluation, used both in the clinical setting and in research, was presented. In addition, sensory systems, such as position/force, magneto-inertial (M-IMU) and electromyographic (EMG) sensors, and indicators extracted from these signals, presented in the state-of-the-art, were analyzed. Among these, muscular hand synergies in chronic stroke patients have been investigated in combination with robot-aided rehabilitation. The results show a good similarity of muscle patterns between the affected and the healthy hand of the same subject. Furthermore, following the robot-mediated rehabilitation, the muscular synergies of the affected hand they tend to look like those of the healthy limb. Muscle synergies can also be a useful tool for assessing the patient's status, especially in patients with mild and moderate impairment. The platform and the adopted control strategy have been tested on 8 healthy subjects performing point-to-point 3D movements. The trajectory executed by the forearm support has been monitored to assess the performance of the chosen control approach. Moreover, a questionnaire based on the Likert rating scale has been submitted to the subjects to evaluate the overall platform. Preliminary results showed that the proposed control algorithm allowed to follow the arm movement in 3D space with a reduced position error. Moreover, the subjects felt their arm completely supported, free to move in any direction of the space and judged the platform easy to use. The proposed bio-cooperative approach has been experimentally validated on 10 healthy subjects;

they performed 3D point-to-point tasks in two different conditions, i.e., with and without assistance-as-needed. The results have demonstrated the capability of the proposed system to properly adapt to real needs of the patients. Moreover, the provided assistance was shown to reduce the muscular fatigue without negatively influencing motion execution. Repetitive and intensive exercises are the main features of robot-aided rehabilitation, but they may expose patients to inappropriate and unsafe postures. The introduction of a sensory feedback can help the subject to perform the rehabilitation task with an ergonomic posture. A preliminary evaluation on eight healthy subjects shows that the use of the proposed platform allowed subjects to execute highly controlled movements while maintaining an ergonomic posture able to limit the trunk compensatory movements during reaching. The introduction of visual and vibrotactile feedback in the proposed robotic platform for upper limb rehabilitation has been proposed to ensure ergonomic posture during rehabilitation. The two feedback modalities have been used to provide information about incorrect neck and trunk posture. Ten healthy subjects have been involved in this study. Each of them performed 3D reaching movements with the aid of the robotic platform in three different conditions, i.e. without feedback, with visual feedback and with vibrotactile feedback, and a comparative analysis has been carried out to evaluate feedback effectiveness, acceptance and performance. Experimental results show that in case of no feedback the subjects reach and maintain configurations that can lead to incorrect neck and trunk configurations and therefore, if repeated, to musculoskeletal disorders. Conversely, with visual or vibrotactile feedback, the subjects tend to correct inappropriate posture with both trunk and head during task performing. The proposed bio-cooperative platform is currently adopted in a clinical trial on 10 workers suffering from humerus fracture and subjects in aftermath of surgical repair of rotator cuff injury. The objective is to verify the efficacy of the proposed platform for robot-aided rehabilitation of the upper limb in workers affected by musculoskeletal pathologies.

MICRO-LEVEL RUMOUR DETECTION ON TWITTER

Ph.D student Rosa Sicilia

Tutor Paolo Soda

Recent years have witnessed a drastic change in information diffusion that has become more and more immediate and effortless thanks to social media, allowing not only certified and professional press practitioners but also common end users to share news contents at a little to no cost. Despite the clear advantages of this phenomenon, the absence of systematic control and moderation on these platforms easily leads to spread unreliable information. This is usually referred to as rumour, an unverified and instrumentally relevant statement in circulation. To prevent treacherous information to have social consequences, researchers have been directing considerable effort in studying automatic systems able to recognize rumours. Most of the work focuses on macro-level analyses, i.e. the detection system considers as rumour news carried by a set of microblog posts rather than by an individual post. However, a micro-level analysis that considers the individual posts, could be of major interest in specific domains, such as health, where a finer investigation is often needed. On these grounds, in this thesis we investigate machine learning methods to detect rumours at the micro-level, and we apply our research on two real-world test cases. To this goal, we investigated four main directions: the collection and the annotation of two datasets, the design of the feature set, the introduction of a novel feature selection approach and the investigation of how the knowledge can be transferred among different topics. First, we present two Twitter datasets on health trending topics, manually labeled in three classes, namely rumour, nonrumour, i.e. referenced news, and unknowns, i.e. posts that do not belong to rumours and nonrumours classes. Second, we design a novel feature set, accounting both descriptors based on the literature and newly conceived for the micro-level task, describing influence potential and network characteristics. Third, we explore the feature selection influence on the specific problem, proposing a novel filter algorithm, relying on a rule-based topology framework which characterizes the feature space aiming at reducing samples in unreliable configurations. Testing this third approach on two health datasets, we are able to obtain promising results, reaching even an accuracy of 96.8%. As a further step in micro-level research, we also tackle

the problem of knowledge transfer among different topic domains. To this end, we present a novel hybrid transfer learning approach that exploits the rule-based topology framework used for feature selection. Comparing this novel method with state-of-the-art techniques over our two datasets we are able to provide interesting results, showing the validity of the method and the potential of transfer learning for rumour detection.

BIOINFORMATIC APPROACH FOR THE INTEGRATION OF ARRAY-CGH AND GENOME WIDE EXPRESSION DATA FOR A MOLECULAR DIAGNOSIS AND A PERSONALIZED OF THE AUTISM SPECTRUM DISORDER

Ph.D student Pasquale Tomaiuolo

Tutor Antonio Maria Persico

Autism Spectrum Disorders (ASDs) are neurodevelopmental disorders characterized by a deficit in social interactions, communication difficulties, and the presence of restricted and stereotypical behaviors or interests. The National and International guidelines recommend the array-CGH as a first level test for people with neurodevelopmental disorders, particularly with autism. Otherwise, both phenotypes and gene expression can be influenced by CNVs through different mechanisms. The type of CNVs (dup/del) and the degree of overlap with the coding portion of the gene and its promoter, control the appearance of new candidate genes and the remapping of gene location. To evaluate the consequences established by a CNV, it may be useful to examine the gene expression profile in the same subject, in addition to a genomic study. The study of gene expression throughout the genome provides a measure in a specific tissue or cell type, often white blood cells. The amount of mRNA transcribed for each gene present in the entire genome may be used to identify groups of hyper- or hypo-expressed genes.

This work aims to:

- Define a pipeline that carries out a complete transcriptomic study.
- Produce a script that correlates data from CNV genomic studies with expression data from Rna-seq.
- Test the scripts on a well-defined group of subjects suffering from idiopathic autism and their siblings paired by gender and age. It is important to explain the impact of CNVs on gene expression to them.

The developed pipeline is very complex. However, it helps the user quickly, clearly and automatically, to perform the analysis and interpretation of the RNA-seq data. It requires user intervention in just a few stages.

The CGH array was confirmed as a first level test ("gold standard") in the genetic diagnosis of Autism Spectrum Disorder. Differential expression analysis instead showed the significant influence of drug treatment and puberty. The proposed correlation model represents a way of describing and interpreting the complex interaction between genotype and phenotype. These results, globally, confirm that CNVs have an impact on gene expression, however, the interpretation of CNV pathogenicity is challenging and influenced by genetic, epigenetic, and environmental factors. Gene Ontology and GSEA have confirmed that different pathways are associated with ASD, others are not yet revealed and their potential role in etiology needed to be studied.

DETERMINATION AND EVALUATION OF THE ANTIOXIDANT ACTIVITY OF ITALIAN EXTRA-VIRGIN OLIVE OILS BY CHEMICAL AND CELLULAR AS-SAYS

Ph.D student Alessandra Vilmercati

Tutor Laura Dugo

Italy is the first country in Europe in terms of number of Protected Designation of Origin (PDO) extra-virgin olive oils (EVOOs). Extra-Virgin Olive Oils (EVOOs) contains a variety of phenolic molecules that are highly valuable to the quality of the oil with regard to sensory and health characteristics. Its composition greatly varies with genetic, agronomic and environmental factors. The analysis of olive oil minor components, such as polyphenols, could be used for the discrimination on a geographical basis and could be useful in the prevention of frauds and false declarations. Therefore, the goal of this study was to investigate the difference in total phenolic content and antioxidant activity of 293 samples of monovarietal and multivarietal EVOOs samples, including PDO oils, from different Italian geographic areas. The analysis of total concentration of phenolic compounds in extra virgin olive oils was determined through Folin-Ciocalteu method, while antioxidant activity was evaluated by four different assays based on different reaction mechanisms and substrates. The final aim of the project will be to create a composition data bank with a great number of Italian EVOO samples. Results showed that Total Phenolic Contents values ranged from 50 to 680 mg gallic acid equivalents/Kg of oil and antioxidants activity values ranged from 0.94 to 12.43 $\mu\text{mol Trolox eq./g}$ of oil, from 0.15 to 2.72 $\mu\text{mol Trolox eq./g}$ of oil, 0.27 to 3.82 $\mu\text{mol Trolox eq./g}$ of oil and 1.09 to 21.37 $\mu\text{mol Trolox eq./g}$ of oil for ABTS, DPPH, FRAP and ORAC assays, respectively. Macrophage function as control switches of the immune system, maintaining the balance between pro and anti-inflammatory activities. Classic polarization (M1) and activation of macrophages into pro-inflammatory cells is characterized by generation of reactive oxygen and nitrogen species (ROS/RNS) and pro-inflammatory cytokines, including TNF- α and IL-1 β . Alternative activation profile (M2) is characterized by secretion of anti-inflammatory cytokines. Bioactive food components, such as polyphenols, have gained attention for their anti-inflammatory properties. EVOO, a polyphenol rich food, has many beneficial effects on human health, including anti-inflammatory effects. Moreover, we evaluated the antioxidant activity of bioactive molecules extracted from dried olive leaves and vegetation water through an in vitro cell culture system. In this study, we investigated the hypothesis that EVOO polyphenol extracts has anti-inflammatory effects on macrophage phenotype favoring an anti-inflammatory state. Macrophages deriving from THP-1 cells were cultured at a starting density of 2×10^4 cells per well for 24h. Cells were then activated for an additional 24h with either LPS ($1 \mu\text{g/ml}$). Specific cytokines were detected and quantified by ELISA assay. In vitro, EVOO polyphenolic extracts attenuated inflammatory with significantly decreased macrophage response to M1 activation. This was evidenced by a significant decrease of pro-inflammatory cytokines secretion (TNF- α , IL-1 β) after stimulation with LPS $1 \mu\text{g/ml}$. Data showed a significant decrease of ROS production and MDA level, while cell vitality increased.

The background of the slide is a light gray surface covered with a repeating pattern of small, stylized icons. These icons include DNA double helices, interlocking gears, and sprouting leaves with small stems, all rendered in a muted teal or sage green color. The icons are scattered across the entire page, creating a scientific and organic aesthetic.

Awards

Awards

Marta Bertolaso

Expanded Reason Award 3rd Edition, Research Category by the University Francisco de Vitoria (Madrid, Spain), for her work: Philosophy of cancer – A dynamic and relational view. Published in the Springer Series “History, Philosophy and Theory of the Life Sciences” (2016).

Alessandra Berton

Patellofemoral Research Excellence Award 2019

Carotti S., Valentini F., **Zingariello M.**, Francesconi M., Lettieri-Barbato D., Aquilano K., **Zalfa F.**, **Perrone G.**, **Vespasiani-Gentilucci U.**, **Morini S.**

Histological and molecular features of lipophagy impairment in non-alcoholic fatty liver disease.

Best Poster Award at the 73rd Congress of the Italian Society of Anatomy and Histology, 2019.

Laura De Gara

Elected Vice President of the Italian Society of Plant Biology (SIBV) for the period 2020-21 and President for the period 2022-23

Alessio Gizzi

GNFM-INdAM, Young Researcher Grant, awarded for the project: Constitutive modeling of active fiber-distributed media.

National Science Foundation (NSF), grant awarded for the project: Novel data assimilation techniques in mathematical cardiology-development, analysis and validation (Collaborative research prof. A. Veneziani).

Alessandro Loppini

Cover Page PTRSA, Vol. 377 Issue. 2144 (March) 20190090 (2019) Phyl. Trans. Roy. Soc. A.

Nonlinear Physics and Mathematical Modeling

Mobility GNFM-INdAM grants awarded by the ESB University of Vienna (AU) and the RCM Leibniz University Hannover (DE).

Andrea Palermo

National Competitive Grant program in Nephrology (2019). Grant awarded by the Italian Society of Nephrology (SIN) for the project: Bone material strength, Fractures and CKD.MBD.

Best abstract at the National congress SIOMMMS 2019 (Bologna, Italy). Award for: Influence of phosphate metabolism on bone health.

Paolo Soda

Best paper at 18th IEEE International Conference on Cognitive Informatics & Cognitive Computing, 2018, Milano, Italy.

Wang Y., Plataniotis K.N., Kwong S., Leung H., Yanushkevich S., Karray F., Hou M., Howard N., Fiorini R.A., Soda P., Tunstel E., Wang J., Patel S.

On autonomous systems: from reflexive, imperative and adaptive intelligence to autonomous and cognitive intelligence.

IEEE 18th International Conference on Cognitive Informatics & Cognitive Computing (ICCI*CC), Milan, Italy, 2019. ISBN: 978-1-7281-0496-6 DOI: 10.1109/ICCICC46617.2019.9146038.

Rocky Strollo

Life Science Young Researchers. Awarded by Salerno Medical Association at the “Giornate della Scuola Medica Salernitana”.

International Professional Award “Rocca D’Oro” Europa Leader; Serrone (FR), Italia

Flavia Tramontana

2019 Travel Grant awarded by the European Association for the Study of Diabetes (EASD).

2019 Research papers awarded by Department of Medicine and Surgery as “UCBM Paper of the month”

January

Annibali O., Giacomelli R., Afeltra A., Alunno A., Bartoloni-Bocci E., Berardicurti O., Bombardieri M., Bor-toluzzi A., Caporali R., Caso F., Cervera R., Chimenti M.S., Cipriani P., Coloma E., Conti F., D'Angelo S., De Vita S., Di Bartolo-meo S., Distler O., Doria A., Feist E., Fisher B.A., Gerosa M., Gilio M., Guggino G., Liakouli V., Margiotta D.P.E., Meroni P., Moroncini G., Perosa F., Prete M., Priori R., Rebuffi C., Ruscitti P., Scarpa R., Shoenfeld Y., Todoerti M., Ursini F., Valesini G., Vettori S., Vitali C., Tzioufas A.G.

Guidelines for biomarkers in autoimmune rheumatic diseases - evidence based analysis.

Autoimmun Rev. 2019 Jan;18(1):93-106.PMID: 30408582. IF 7,716

February

Ivziku D., Clari M., Piredda M., De Marinis M.G., Matarese M.

Anxiety, depression and quality of life in chronic obstructive pulmonary disease patients and caregivers: an actor-partner interdependence model analysis.

Qual Life Res. 2019 Feb;28(2):461-472. PMID: 30341578. IF 2,488

De Maria M., Vellone E., Ausili D., Alvaro R., Di Mauro S., Piredda M., De Marinis M., Matarese M.

Self-care of patient and caregiver Dy-Ads in multiple chronic conditions: A Longitudinal study (SO-DALITY) protocol.

J Adv Nurs. 2019 Feb;75(2):461-471. PMID: 30168154. IF 2,376

Arcangeli S., Jereczek-Fossa B.A., Alongi F., Aristei C., Becherini C., Belgioia L., Buglione M., Caravatta L., D'Angelillo R.M., Filippi A.R., Fiore M., Genovesi D., Greco C., Livi L., Magrini S.M., Marvaso G., Maz-zola R., Meattini I., Merlotti A., Palumbo I., Pergolizzi S., Ramella S., Ricardi U., Russi E., Trovò M., Sindoni

A., Valentini V., Corvò R.

Combination of novel systemic agents and radiotherapy for solid tumors - Part II: An AIRO (Italian association of radiotherapy and clinical oncology) overview focused on treatment toxicity.

Crit Rev Oncol Hematol. 2019 Feb;134: 104-119. PMID: 30658887. IF 5,012

Amadori S., Arcese W., Avvisati G., Gale RP, Lo-Coco F.
Prof. Franco Mandelli leukaemia visionary. May 12, 1931- July 15, 2018.

Leukemia. 2019 Feb;33(2):285-286. PMID: 30635628. IF 9,944

Cortellini A., Bersanelli M., Buti S., Cannita K., Santini D., Perrone F., Giusti R., Tiseo M., Michiara M., Di Marino P., Tinari N., De Tursi M., Zoratto F., Veltri E., Marconcini R., Malorgio F., Russano M., Anesi C., Zeppola T., Filetti M., Marchetti P., Botticelli A., Antonini Cappellini G.C., De Galitiis F., Vitale M.G., Rastelli F., Pergolesi F., Berardi R., Rinaldi S., Tudini M., Silva R.R., Piredda A., Atzori F., Chiari R., Ricciuti B., De Giglio A., Iacono D., Gelibter A., Occhipinti M.A., Parisi A., Porzio G., Fargnoli M.C., Ascierto P.A., Ficorella C., Natoli C.

A multicenter study of body mass index in cancer patients treated with anti-PD-1/PD-L1 immune checkpoint inhibitors: when overweight becomes favorable.

J Immunother Cancer. 2019 Feb 27; 7(1):57. PMID: 30813970. IF 8,728

Lelli D., Antonelli Incalzi R., Ferrucci L., Bandinelli S., Pedone C.

Association between PUFA intake and serum concentration and mortality in older adults: a cohort study.

Clin Nutr. 2020 Feb;39(2):510-515. PMID: 30850268. IF 5,496

March

Pozzilli P., Signore A.

The reconstructed natural history of type 1 diabetes mellitus.

Nat Rev Endocrinol. 2019 May;15(5):256-257. PMID: 30858529. IF 24,646

Lattanzi S., Brigo F., Trinka E., Vernieri F., Corradetti T., Dobran M., Silvestrini M.

Erenumab for preventive treatment of migraine: a systematic review and meta-analysis of efficacy and safety.

Drugs. 2019 Mar;79(4):417-431. PMID: 30793254. IF 4,993

Biagioli V., Piredda M., Annibali O., Tirindelli M.C., Pignatelli A., Marchesi F., Mauroni M.R., Soave S., Del Giudice E., Ponticelli E., Clari M., Cavallero S., Monni P., Ottani L., Sica S., Cioce M., Cappuccinati L., Boni-fazi F., Alvaro R., De Marinis M.G., Gargiulo G.

Development and initial validation of a questionnaire to assess patients' perception of protective isolation follow-ing haematopoietic stem cell transplantation.

Eur J Cancer Care (Engl). 2019 Mar;28(2): e12955. PMID: 30357945. IF 2,421

Cesareo R., Palermo A., Benvenuto D., Cella E., Pasqualini V., Bernardi S., Stacul F., Angeletti S., Mauri G., Ciccozzi M., Trimboli P.

Efficacy of radiofrequency ablation in autonomous functioning thyroid nodules. A systematic review and meta-analysis.

Rev Endocr Metab Disord. 2019 Mar;20(1):37-44. PMID: 30887407. IF 5,516

Fanali C., D'Orazio G., Gentili A., Fanali S.

Analysis of enantiomers in products of food interest.

Molecules. 2019 Mar 21;24(6):1119. PMID: 30901832. IF 3,06

Rachiglio A.M., Fenizia F., Piccirillo M.C., Galetta D., Crinò L., Vincenzi B., Barletta E., Pinto C., Ferraù F., Lambiase M., Montanino A., Roma C., Ludovini V., Montagna E.S., De Luca A., Rocco G., Botti G., Perrone F., Morabito A., Normanno N.

The presence of concomitant mutations affects the activity of EGFR tyrosine kinase inhibitors in EGFR-Mutant Non-Small Cell Lung Cancer (NSCLC) patients.

Cancers(Basel). 2019 Mar 10;11(3): E341. PMID: 30857358. IF 6,162

April

Di Stefano N., Ghilardi G., Morini S.

The cerebral ventricles in Leonardo's anatomical drawings.

Lancet. 2019 Apr 6; 393(10179):1412. PMID: 30967209. IF 59,102

June

Gonella S., Basso I., De Marinis M.G., Campagna S., Di Giulio P.

Good end-of-life care in nursing home according to the family carers' perspective: a systematic review of qualitative findings.

Palliat Med. 2019 Jun;33(6):589-606. PMID: 30969160. IF 4,956

July

Rimbaş M., Pizzicanella M., Larghi A.

EUS-guided treatment of WON using lumen-apposing metal stents: protocol standardisation based on the occurrence of natural healing processes.

Gut. 2019 Jul;68(7):1334-1335. PMID: 30030302. IF 17,943

De Plato F., Fontana C., Gherardi G., Privitera G.P., Puro V., Rigoli R., Viaggi B., Viale P.

Collection, transport and storage procedures for blood culture specimens in adult patients: recommendations from a board of Italian experts.

Clin Chem Lab Med. 2019 Oct 25;57(11):1680-1689. PMID: 31348753. IF 3,368

Cortellini A., Chiari R., Ricciuti B., Metro G., Perrone F., Tiseo M., Bersanelli M., Bordi P., Santini D., Giusti R., Grassadonia A., Di Marino P., Tinari N., De Tursi M., Zoratto F., Veltri E., Malorgio F., Garufi C., Russa-no M., Anesi C., Zeppola T., Filetti M., Marchetti P., Berardi R., Rinaldi S., Tudini M., Silva R.R., Pireddu A., Atzori F., Iacono D., Migliorino M.R., Porzio G., Cannita K., Ficorella C., Buti S.

Correlations between the immune-related adverse events spectrum and efficacy of anti-pd1 immunotherapy in NSCLC patients.

Clin Lung Cancer. 2019 Jul;20(4):237-247.e1. PMID: 30885550. IF 2,441

August

Napoli N., Conte C., Pedone C., Strotmeyer E.S., Barbour K.E., Black D.M., Samelson E.J., Schwartz A.V.

Effect of insulin resistance on BMD and fracture risk in older adults.

J Clin Endocrinol Metab. 2019 Aug 1;104(8):3303-3310. PMID: 30802282. IF 5,605

September

Luminari S., Merli M., Rattotti S., Tarantino V., Marcheselli L., Cavallo F., Varettoni M., Bianchi B., Merli F., Tedeschi A., Cabras G., Re F., Visco C., Torresan Delamain M., Cencini E., Spina M., Ferrero S., Ferrari A., Deodato M., Mannina D., Annibali O., Rago A., Orsucci L., DeFrancesco I., Frigeni M., Cesaretti M., Arcaini L.

Early progression as a predictor of survival in marginal zone lymphomas: an analysis from the FIL-NF10 study.

Blood. 2019 Sep 5;134(10):798-801. PMID: 31292118. IF 16,601

October

Mangieri A., Montalto C., Poletti E., Sticchi A., Crimi G., Giannini F., Latib A., Capodanno D., Colombo A.

Thrombotic versus bleeding risk after transcatheter aortic valve replacement: JACC review topic of the week.

J Am Coll Cardiol. 2019 Oct 22;74(16):2088-2101. PMID: 31623768. IF 18,369

Cicconi L., Platzbecker U., Avisati G., Paoloni F., Thiede C., Vignetti M., Fazi P., Ferrara F., Divona M., Albano F., Efficace F., Sborgia M., Di Bona E., Breccia M., Borlenghi E., Cairoli R., Rambaldi A., Melillo L., La Nasa G., Fiedler W., Brossart P., Hertenstein B., Salih H.R., Annibali O., Wattad M., Lubbert M., Brandts C.H., Hanel M., Rolig C., Schmitz N., Link H., Frairia C., Fozza C., Maria D'Arco A., Di Renzo N., Cortelezzi A., Fabbiano F., Dohner K., Ganser A., Dohner H., Amadori S., Mandelli F., Voso M.T., Ehninger G., Schlenk RF., Lo-Coco F.

Long-term results of all-trans retinoic acid and arsenic trioxide in non-high-risk acute promyelo-

cytic leukemia: update of the APL0406 Italian-German randomized trial.

Leukemia. 2020 Mar;34(3):914-918. PMID: 31611624.

Tsachev I., Baymakova M., Ciccozzi M., Pepovich R., Kundurzhiev T., Marutsov P., Dimitrov K.K., Gospodinova K., Pishmisheva M., Pekova L.

Seroprevalence of hepatitis E virus infection in pigs from Southern Bulgaria.

Vector Borne Zoonotic Dis. 2019 Oct;19(10):767-772. PMID: 31017536. IF 1,939

Di Gregorio L.M., Zambrotta E., Di Guardo F., Gulino F.A., Musmeci G., Capriglione S., Angioli R., Palumbo M.

Effects of body mass index and bio-chemical lipid levels on reproductive outcomes during an intracytoplasmic sperm injection: a retrospective study.

Int J Fertil Steril. 2019 Oct;13(3):190-195. PMID: 31310072. IF 0,471

Masetti M., Grigioni F.

LVAD and electrical capacity: do we know how it works and what to do?

Eur J Prev Cardiol. 2019 Nov;26(17):1803-1805. PMID: 31412715. IF 5,64

Ceccarini M.R., Tasegian A., Franzago M., Patria FF., Albi E., Codini M., Conte C., Bertelli M., Dalla Ragione L., Stuppia L., Beccari T.

5-HT2AR and BDNF gene variants in eating disorders susceptibility.

Am J Med Genet B Neuropsychiatr Genet. 2020 Apr;183(3):155-163. PMID: 31746551. IF 3,123

November

Russo M., Bonaccorsi I.L., Arigò A., Cacciola F., De Gara L., Dugo P., Mondello L.

Blood orange (*Citrus sinensis*) as a rich source of nutraceuticals: investigation of bioactive compounds in different parts of the fruit by HPLC-PDA/MS.

Nat Prod Res. 2019 Nov 29:1-5. PMID: 31782660. IF 1,999

Sisto A., Vicinanza F., Campanozzi L., Ricci G., Tartaglino D., Tambone V.

Towards a transversal definition of psychological resilience: a literature review.

Medicina (Kaunas). 2019 Nov 16; 55(11):745. PMID: 31744109. IF 1,467

December

Fischer S., Tandstad T., Cohn-Cedermark G., Thibault C., Vincenzi B., Klingbiel D., Albany C., Necchi A., Terbuch A., Lorch A., Aparicio J., Heidenreich A., Hentrich M., Wheeler M., Langberg CW., Ståhl O., Fankhauser CD., Hamid AA., Koutsoukos K., Shamas J., White J., Bokemeyer C., Beyer J., Gillessen S.; Global Germ-Cell CancerGroup.

Outcome of men with relapses after adjuvant bleomycin, etoposide, and cisplatin for clinical stage I nonseminoma.

J Clin Oncol. 2020 Apr 20;38(12):1322-1331 EPMID: 31877087. IF 28,245

The background of the page is a light gray pattern featuring various scientific and biological motifs. These include DNA double helices, interlocking gears, and stylized leaves or vines. The motifs are scattered across the entire page, creating a textured, scientific aesthetic.

2019 Publications

Full List

ADVANCED ROBOTICS AND HUMAN CENTRED TECHNOLOGIES

Head L. Zollo

Articles

Rybarczyk Y., Carvalho D.G., Cordella F.
Bioinspired implementation and assessment of a remote-controlled robot.

Appl Bionics Biomech. 2019 Sep 11; 2019:8575607. PMID: 31611928. IF 1,525

Petrini F.M., Mazzoni A., Rigosa J., Giambattistelli F., Granata G., Barra B., Pampaloni A., Guglielmelli E., Zollo L., Capogrosso M., Micera S., Raspovic S.
Microneurography as a tool to develop decoding algorithms for peripheral neuro-controlled hand prostheses.

Biomed Eng Online. 2019 Apr 8;18(1):44. PMID: 30961620. IF 2,013

Tagliamonte N.L., Valentini S., Sudano A., Portaccio I., De Leonardis C., Formica D., Accoto D.
Switching assistance for exoskeletons during cyclic motions.

Front Neurobot. 2019 Jun 19; 13:41. PMID: 31275130. IF 3

Leone F., Gentile C., Ciancio A.L., Gruppioni E., Davalli A., Sacchetti R., Guglielmelli E., Zollo L.
Simultaneous sEMG classification of hand/wrist gestures and forces.

Front Neurobot. 2019 Jun 19; 13:42. PMID: 31275131. IF 3,00

Romeo R.A., Rongala U.B., Mazzoni A., Camboni D., Carrozza M.C., Guglielmelli E., Zollo L., Oddo C.M.
Identification of slippage on naturalistic surfaces via wavelet transform of tactile signals.

IEEE Sensors J. 2019; 19(4):1260-1268. DOI: 10.1109/JSEN.2018.2881831 IF 3,076

Tosi J., Taffoni F., Santacatterina M., Sannino R., Formica D.

Throughput analysis of BLE sensor network for motion tracking of human movements.

IEEE Sensors J. 2019; 19(1):370-377. DOI: 10.1109/JSEN.2018.2877102 IF 3,076

Massaroni C., Nicolo A., Girardi M., La Camera A., Schena E., Sacchetti M., Silvestri S., Taffoni F.

Validation of a wearable device and an algorithm for respiratory monitoring during exercise

IEEE Sensors J. 2019;19(12): 4652-4659. DOI: 10.1109/JSEN.2019.2899658 IF 3,076

Campanozzi L.L., Guglielmelli E., Cella E., Ghilardi G., Michilli M., Molina A., Ciccozzi M., Tambone V.

Building trust in social robotics: a pilot survey.

IEEE Technol Soc Mag. 2019;38(4): 45-54. DOI: 10.1109/MTS.2019.2948440 IF 1,002

Lauretti C., Cordella F., Zollo L.

A hybrid joint/Cartesian DMP-based approach for obstacle avoidance of anthropomorphic assistive robots.

Int J Soc Robot. 2019; 11(5):783-796. DOI: 10.1007/s12369-019-00597-w IF 2,296

Carpino G., Pezzola A., Urbano M., Guglielmelli E.

Response to: Comment on "Assessing effectiveness and costs in robot-mediated lower limbs rehabilitation: a meta-analysis and state of the art".

J Healthc Eng. 2019 Sep 24;2019: 9693801. PMID: 31662835. IF 1,295

Noce E., Dellacasa Bellingegni A., Ciancio A.L., Sacchetti R., Davalli A., Guglielmelli E., Zollo L.

EMG and ENG-envelope pattern recognition for prosthetic hand control.

J Neurosci Methods. 2019 Jan 1; 311:38-46. PMID: 30316891. IF 2,785

Tamilia E., Parker M.S., Rocchi M., Taffoni F., Hansen A., Grant P.E., Papadelis C.

Nutritive sucking abnormalities and brain microstructural abnormalities in infants with established brain injury: a pilot study.

J Perinatol. 2019 Nov;39(11):1498-1508. PMID: 31462720. IF 2,046

Taffoni F., Focaroli V., Keller F., Iverson J.M.

Motor performance in a shape sorter task: a longitudinal study from 14 to 36 months of age in children with an older sibling ASD.

PLoS One. 2019 May 28;14(5): e0217416. PMID: 31136606. IF 2,776

Zollo L., Di Pino G., Ciancio A.L., Ranieri F., Cordella F., Gentile C., Noce E., Romeo R.A., Bellingegni A.D., Vadalà G., Miccinilli S., Mioli A., Diaz-Balzani L., Bravi M., Hoffmann K.P., Schneider A., Denaro L., Davalli A., Gruppioni E., Sacchetti R., Castellano S., Di Lazzaro V., Sterzi S., Denaro V., Guglielmelli E.

Restoring tactile sensations via neural interfaces for real-time force-and-slippage closed-loop control of bionic hands.

Sci Robot. 2019 May 21;4(27): eaau9924. PMID: 31620665. IF 19,4

Badesa F.J., Diez J.A., Catalan J.M., Trigili E., Cordella F., Nann M., Crea S., Soekadar S.R., Zollo L., Vitiello N., Garcia-Aracil N.

Physiological responses during hybrid BNCI control of an upper-limb exoskeleton.

Sensors (Basel). 2019 Nov 12;19(22):4931. PMID: 31726745. IF 3,031

Conference Proceedings

Scotto Di Luzio F., Cordella F., Lauretti C., Simonetti D., Sterzi S., Draicchio F., Zollo L.

A bio-cooperative robotic system to ensure ergonomic postures during upper limb rehabilitation in occupational contexts.

20th Congress of the International Ergonomics Association, Florence, 26-30 August 2018. ISBN 978-172810429-4

In: *Adv Intell Syst Comput* 2019;826:327-336. DOI: 10.1007/978-3-319-96065-4_37

Cordella F., Scotto Di Luzio F., Lauretti C., Draicchio F., Zollo L.

A biofeedback-based posture correction system for working environments.

2019 IEEE International Workshop on Metrology for Industry 4.0 and IoT, Naples, 4-6 June 2019. ISBN 978-1-7281-0429-4 DOI: 10.1109/ME-TROI4.2019.8792920

Chericoni A., Tosi J., Visco A.M., Lubrano R., Taffoni F.

Assessment of feeding teats: an experimental study.

41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBS), Berlin, 23-27 July 2019. ISBN 978-1-5386-1311-5

DOI: 10.1109/EMBC.2019.8857796

Tosi J., Taffoni F., Hussain A., Campolo D., Formica D.

Methodology for the evaluation of magneto-inertial orientation filters in SO(3)

2019 IEEE International Workshop on Metrology for Industry 4.0 and IoT, Naples, 4-6 June 2019. ISBN 978-1-7281-0429-4 DOI: 10.1109/ME-TROI4.2019.8792914

Di Santo A., Di Biase L., Tosi J., Marano M., Rizzo A.C., Fallacara A., Taffoni F., Formica D., Di Pino G., Tombini M., Di Lazzaro, V.

Quantitative sit-to-stand task analysis, in Parkinson's disease.

5th Congress of the European Academy of Neurology, Oslo, 29 June-2 July 2019.

In: *Eur J Neurol* 2019;26(Suppl 1):459.

Book Chapters

Cordella F., Ciancio A.L., Zollo L.

Robot-assisted post-surgery rehabilitation.

XXXVIII Bioengineering School in advanced bioengineering methods, technologies and tools in surgery and therapy. Patron Editore, 2019.

Scotto Di Luzio F., Cordella F., Lauretti C., Draicchio F., Zollo L.

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ALLERGOLOGY, IMMUNOLOGY, RHEUMATOLOGY

Head A. Afeltra

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ANESTHESIA, INTENSIVE CARE AND PAIN MANAGEMENT

Head F.E. Agrò

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AUTOMATION AND CONTROL THEORY

Head R. Setola

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BIOCHEMISTRY AND MOLECULAR BIOLOGY

Head M. Maccarrone

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Head F. Keller

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Head G. Pennazza

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Head P. Pozzilli

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Head L. De Gara

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GASTROENTEROLOGY

Head M. Cicala

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Head R. Coppola

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Head R. Angioli

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Head M. Chello

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HEMATOLOGY, STEM CELL TRANSPLANTATION, TRANSFUSION MEDICINE AND CELLULAR THERAPY

Head G. Avvisati

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Head S. Silvestri

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Head: M. Ciccozzi

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Head S. Morini

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NEUROLOGY, NEUROPHYSIOLOGY, NEUROBIOLOGY

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NEUROPHYSIOLOGY AND NEUROENGINEERING OF HUMAN-TECHNOLOGY INTERACTION

Head G. Di Pino

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NONLINEAR PHYSICS AND MATHEMATICAL MODELING

Head S. Filippi

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NURSING SCIENCE

Head M.G. De Marinis

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Head G. Tonini

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Head S. Bonini

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Head R. Papalia

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Head G. Perrone

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Head S. Sterzi

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Head P. Persichetti

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Head M. De Falco

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RADIATION ONCOLOGY

Head S. Ramella

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TISSUE ENGINEERING & CHEMISTRY FOR ENGINEERING

Head M. Trombetta

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UROLOGY

Head R. M. Scarpa

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The background of the page is a light gray with a repeating pattern of stylized icons. These icons include DNA double helices, interlocking gears, and small leaves on stems, all rendered in a light gray color. The icons are scattered across the entire page, creating a scientific and naturalistic theme.

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