Scientific Report

2021

Partnership with:

Università della Svizzera italiana

List of frequently used abbreviations

AFRI	Area Formazione Accademica, Ricerca e Innovazione / Academic Education, Research, and Innovation Division
CHUV	Centre hospitalier universitaire vaudois
CTU-EOC	Clinical Trial Unit EOC
DAEICM	Dipartimento di Area Critica / Department of Anesthesiology, Emergency and Intensive Care Medicine
EOC	Ente Ospedaliero Cantonale
ICCT	Istituto Cardiocentro Ticino / Cardiocentro Ticino Institute
ICP	Istituto Cantonale di Patologia / Cantonal Institute of Pathology
ICT	Area Informatica e Tecnologia della Comunicazione / Information and Communications Technology Division
IIMSI	Istituto Imaging della Svizzera Italiana / Imaging Institute of Southern Switzerland
INSI	Istituto di Neuroscienze Cliniche della Svizzera Italiana / Institute of Clinical Neurosciences of Southern Switzerland
IOR	Institute of Oncology Research
IOSI	Istituto Oncologico della Svizzera Italiana / Oncology Institute of Southern Switzerland
IPSI	Istituto Pediatrico della Svizzera Italiana / Institute of Pediatrics of Southern Switzerland
IRB	Istituto di Ricerca in Biomedicina / Institute for Research in Biomedicine
ISFSI	Istituto di Scienze Farmacologiche della Svizzera Italiana / Institute of Pharmacological Sciences of Southern Switzerland
LRT	Laboratori di Ricerca Traslazionale / Laboratories for Translational Research
LRU	Local Research Unit
PI	Principal Investigator
RCT	Randomized controlled trial
SAKK	Swiss Group for Clinical Cancer research
SCTO	Swiss Clinical Trial Organization
SNSF	Swiss National Science Foundation
SUPSI	Scuola Universitaria Professionale della Svizzera italiana
USI	Università della Svizzera italiana

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Preface

The present annual scientific report summarizes the research activities at the Institutes and Departments of the Ente Ospedaliero Cantonale (EOC) and at the Università della Svizzera italiana (USI) in the field of medical research for the year 2021. This format reflects the increasing integration between research conducted at the two institutions following the creation of the USI Faculty of Biomedical Sciences and the signature of a research cooperation agreement in 2020. Despite the COVID-19 pandemic, EOC saw continued growth in research in 2021 – confirming the uptrend reported the previous year - with a significant increase of the scientific production. Several reasons can explain this finding: the positive influence of the USI Faculty of Biomedical Sciences, the integration of the Cardiocentro Ticino Institute in EOC but also the development of new research areas in all EOC Institutes and Departments (which singly showed an increased scientific production compared to the previous year). Beyond the great productivity, published scientific articles demonstrated also the breadth and the quality of the research being undertaken at the EOC. Furthermore, several research projects are underway involving multidisciplinary teams and collaborations with research groups worldwide. Collaborative efforts will further fuel the EOC research activities in the upcoming years. In 2021, the EOC Institutes and Departments, including both the clinical research groups and the laboratories for translational research (LRT-EOC), produced high-quality research attaining broad recognition at national and international level. Together with patient care and education, research is an essential part of EOC activities. Bringing research close to practice facilitates the development of clinical studies and the monitoring of the effectiveness of clinical interventions and care processes, guarantees the quality and safety of services provided to patients and ensures that patients benefit from innovative diagnostic methods and therapies. Furthermore, the steady growth in quantity and quality of research activities at EOC is paramount for the USI Faculty of Biomedical Sciences and is in line with the 2022-2025 EOC strategic plan for a cantonal hospital with mandate for academic education and research, that aspires to become a university hospital.

1. EOC
Institutes and multisite Departments

1.1 Oncology Institute of Southern Switzerland

Prof. Silke Gillessen Sommer, MD
Medical and scientific director

PD Anastasios Stathis, MD
Chair Clinical Research

The Oncology Institute of Southern Switzerland (IOSI) is one of the largest clinical cancer research centers in Switzerland with a long-standing experience in the conduct of clinical trials.
The IOSI clinics of Medical Oncology (Head: Prof. Dr. S. Gillessen), Haematology (Head: Prof. Dr. G. Stüssi), Radiation Oncology (Head: Dr. A. Richetti) and Palliative Care (Head: PD Dr. C. Gamondi) have their own clinical research activities and each team, based on its scientific interests, can propose trials to be activated or promote investigator-initiated trials.

The IOSI scientific research board composed of seven seniors, the head of research nurses, the head of the study coordinators and a finance representative, decides about the trials to be opened and is responsible for the strategy of the clinical research of the institute. To support investigators at IOSI and promote clinical research, a well-structured clinical research unit (CRU) is active within the IOSI and coordinates the research activities. The IOSI-CRU staff includes study coordinators and research nurses and provides the infrastructures and support for researchers of the institute. Finally, the New Drugs Development Unit (Head: PD Dr. A. Stathis) is taking care of the activation and conduct of early phase clinical trials including first-in-human phase I clinical trials.

The three main areas of clinical research of our institute comprise new drugs development, lymphoproliferative diseases (lymphoma and chronic lymphocytic leukaemia) and prostate cancer, but we have also started to strengthen our clinical research in additional specialties such as lung, breast and gastrointestinal cancer.

During 2021 twenty-three new trials (among them 18 interventional phase I-III clinical trials) were activated, which added to the already active, resulted in 57 open trials at the end of 2021, 47 of them being interventional phase I-III clinical trials. A particular mention should be made to “SAKK 38/19-Assessing a ctDNA and PET-oriented therapy in patients with DLBCL. A multicenter, open-label, phase II trial”, an international phase II study promoted by the SAKK (study chair: PD Dr. A. Stathis), which is prospectively assessing a new approach for treatment decisions, based on the combined results of PET/CT and circulating tumour DNA (ctDNA) in patients with diffuse large B-cell lymphoma. The idea was developed by IOSI investigators and the trial is being conducted in Switzerland and in Italy. All analyses of liquid biopsies for the detection of ctDNA are being performed at the laboratories of the IOR (Prof Dr. D. Rossi), while PET/CT scans are centrally reviewed by independent reviewers (coordinated by Prof. Dr. L. Ceriani).

Another important trial activated in 2021 is “ACTION: Phase I/II Trial of Abiraterone Acetate in Combination with Tildrakizumab (anti-IL23 targeting monoclonal antibody) in Men with Metastatic Castration-Resistant Prostate Cancer (mCRPC)”. This trial is based on preclinical work performed by Prof. Dr. A. Alimonti (IOR) on the tumor microenvironment and on myeloid-derived suppressor cells. The study is being conducted in collaboration with the Institute of Cancer Research (UK).

We also run several investigator-initiated trials assessing biomarkers in prostate, breast and haematological malignancies in collaboration with IOR.

The trials above reported highlight also the importance of collaborations in the field of research and the IOSI has an excellent history of collaborating with both the pharmaceutical industry and non-for-profit academic organizations. Of particular relevance are the collaborations with the IOR, the Institute for Research in Biomedicine (IRB), the International Extranodal Lymphoma Group

(IELSG), SAKK and the CTU-EOC. We have a central role in the USI Faculty of Biomedical Sciences and are also associated with ETH Zurich, University of Padua and University of Manchester.

The high volume of clinical research activity, despite the difficulties due to the pandemic, highlights the devotion of IOSI to clinical research, with an extensive publication record in a multitude of areas related to both solid tumours and hematological malignancies, that was maintained also in 2021 with high impact factor publications. Researchers from the IOSI present regularly results of their work, or are invited as speakers in major international conferences.

In 2021, two important awards were obtained from two physicians affiliated with the IOSI: Prof. Dr. D. Rossi was awarded with the very prestigious Robert Wenner Prize and Dr. A. Condoluci obtained the American Association for Hematology (ASH) Global Research Award. In addition, 4 EOC awards were obtained in 2021, one senior award to Prof. Dr. E. Zucca and 3 young investigator awards (Dr. I. Colombo, Dr. G. Pesola and Dr. R. Pereira Mestre). The training and career development of younger colleagues that will be the future principal investigators is an essential aspect as well as the training of international fellows through our international fellowship program with 2-3 fellows training each year in clinical research at the IOSI.

Finally, several grants were obtained by IOSI investigators, in particular, Dr. L. Rossi from Swiss Cancer league for clinical Trial SIESTA part Breast; PD Dr. S. De Dosso from Fondazione Ticinese per la ricerca sul Cancro and the Swiss Cancer League for the trial Fusometro-001 and Dr. S. Di Lascio from the Fondazione Ticinese per la ricerca sul Cancro for trial IOSI-IOR-CSSI.

For the years to come, the development of investigator-initiated trials represents a major objective of clinical research for the IOSI. For this reason, the IOSI is aiming to increase the number of investigator-initiated clinical trials over the next years in collaboration also with the CTU-EOC. Regular scientific brainstorming meetings with the IOR and the IRB (now Bios+) have been initiated in 2021 with many important topics, an initiative by Prof. S. Gillessen and Prof. D. Rossi together with the heads of the IOR and the IRB, as our main aim for the future is to bring the preclinical knowledge to the clinic and perform more translational research.

>> The list of publications of the Oncology Institute of Southern Switzerland is available on the EOC website at the following link.

1.2 Institute of Clinical Neurosciences of Southern Switzerland – Neurocenter (INSI)

Prof. Alain Kaelin, MD PhD
Medical and scientific director

The mission of the Institute of Clinical Neurosciences of Southern Switzeralnd (INSI) is offering the highest quality of cure to the patient with the application and promotion of an inter- and multidisciplinary approach. Translational and clinical research as well as educational activities are a priority of the INSI with a close interaction between research activities and patient care. Academic collaboration with the USI, SUPSI as well as other national and international universities are contributing to the success of the INSI. Also in 2021 there was an intense and successful research activity, and, for the first time in the history of the INSI, more than 100 peer-reviewed articles were published (PubMed).

Epilepsy research group (Dr. P. Agazzi, Dr. C. Prosperetti, Dr. M. Caporro)
Our group participates to a Swiss multicentre study on the evaluation of adult patients with a first seizure to find out electroencephalography (EEG) and brain magnetic resonance imaging (MRI) biomarkers of epilepsy. There is an industry sponsored ongoing study on the neuropsychological effects of a new anti-epileptic treatment in adult patients with epilepsy. We collaborate with the cardiological intensive care unit to study blood biomarkers of prognosis in cardiac arrest. Finally, we are studying the sex differences in typology and prognosis of brain tumours.

Headache research group (Prof. Dr. C. Zecca)
The research focuses on genetic and clinical predictors of efficacy of new migraine treatments, and exploring their safety profile in the post-marketing setting. Epidemiology and pathophysiology of migraine are also investigated. Our group currently participates in two industry sponsored observational studies in patients with migraine.

Movement disorders research group (PD Dr. S. Galati)
The priority of our clinical research relies on the influence of neuronal plasticity changes during sleep on movement disorders such as dystonia and dyskinesia in Parkinson´s disease. A longitudinal matched case-control research project aimed to corroborate the association between slow-wave sleep and levodopa-induced dyskinesia in Parkinson's disease patients is ongoing. We are performing a case-control study investigating the association between wake theta activity before and after sleep in patients with Parkinson's disease showing levodopa-induced dyskinesia. We are also conducting a study on the effect of sleep and medical therapy in patients with cervical dystonia by a dedicated transcranial magnetic stimulation (TMS) protocol. These projects will be of great interest for understanding fundamental pathophysiological features of Parkinson's disease and dystonia with expected benefit for the treatment.

Multiple sclerosis research group (Prof. Dr. C. Gobbi, Prof. Dr. C. Zecca)
The research focuses on diagnosis and treatment, exploring new MRI techniques, understanding better risks associated with new multiple sclerosis (MS) therapies in aged MS patients and in the context of the COVID-19 pandemic, and searching for innovative neuromodulation treatments of overactive bladder. We also participate in a nationwide investigator-initiated project on MS epidemiology. Our center is also a recognized study site for several industry sponsored international clinical trials.

Neurodegeneration research group (Prof. Dr. P. Paganetti)
Our research is focused on proteins involved in aberrant cellular mechanisms associated to aging-related human disorders, neurodegeneration and cancer, as well as other rare proteinopathies. Currently we are mainly investigating Tau as model protein to address two unanswered questions: the putative role of Tau in the management of a lesion to the DNA or in the epigenetic regulation of DNA transcription and the identification of the cellular organelle where toxic forms of Tau propagate during disease progression. Our recent data clarify, among other, the molecular mechanisms utilized by Tau to regulate the stability and activity of p53, as well as the epigenetic repression of gene expression and cell senescence induction. In cells exposed to pathogenic forms of Tau, e.g. when included in extracellular vesicles, we observed for the first time the molecular encounter of internalized toxic Tau with endogenous normal Tau in lysosomes. We are also interested to study the role of lysosomal dysfunction as it occurs in rare pediatric diseases or in the aging brain. As a Tau-independent project, we are searching natural compounds able to increase the expression of breast cancer-associated proteins with the goal to de-risk cancer in families carrying BRCA1/2 mutations.
See also section 3: **Laboratories for Translational Research (LRT) of EOC**

Neuropsychology and behavioural neurology research group (Dr. L. Sacco, PD Dr. G.C. Riccitelli)
This research group conducts research projects to identify, prevent, and improve cognitive and behavioural dysfunctions related to acquired brain damages and diseases. The scientific projects are focused on the application of multidisciplinary approaches to understanding brain mechanisms responsible for the onset of cognitive alterations, and to identify new rehabilitative-therapeutic strategies to limit cognitive disturbances. In this context, researchers' work is currently focused on investigating the effect of TMS on social cognition abilities in patients with mild cognitive impairment to improve cognitive skills. At the same time the researchers are developing new tests, in collaboration with the Universitäre Altersmedizin (Basel), for the detection of social cognition deficits. Currently, this research group is actively involved as co-investigator site in the following multicentric clinical trials: 1) the EMBARK study (to evaluate the efficacy and safety of Aducanumab in subjects with early symptomatic Alzheimer's disease); 2) the EORTC 1635 trial (to investigate cognitive profiles in patients with lower grade glioma

following resection); 3) The MoCA-DCI study (to assess the impact of delayed cerebral ischemia on neuropsychological outcome after subarachnoid haemorrhage).

Neuroradiology research group (Prof. Dr. A. Cianfoni, PD Dr. E. Pravatà)
The Neuroradiology Service of the INSI provides high-level morphological and functional advanced diagnostic neuroimaging, image-guided spine interventions, as well as endovascular diagnostic and therapeutic procedures. During 2021, the neuroradiology team capitalized on the experience of the previous years in the fields of MRI dedicated to the optic pathways, and of treatment of unstable osteoporotic vertebral fractures. These include the 3D-STIR-ZOOMit MRI technique, and the "stent-screw-assisted internal fixation - SAIF" percutaneous technique, respectively. Several other studies in both diagnostic and interventional areas were performed in close collaboration with other research groups of INSI and IIMSI. Among others, the diagnostic Neuroradiology took part in the "Swiss Cohort" multiple sclerosis project, sponsored by the University of Basel, the "IMAGINE" study, a Swiss multicenter project sponsored and coordinated by the University of Zurich, focusing on glioblastoma radiomics, with the aim of standardizing patients' imaging data acquisition, and continued the cooperation with the multicenter prospective clinical trial "GelStix Study" sponsored by PD Dr. P. Maino. On the interventional site, results of the "Post-marketing non-inferiority study comparing Triojection to Discectomy for Lumbar Disc Herniation" multicenter international clinical trial, comparing minimally-invasive disc herniation treatment with surgery, have been published. The INSI interventional neuroradiology, along with the Stroke Center, has also participated in the international multicenter SWIFT-DIRECT randomized stroke trial. Other active collaborations with the Inselspital of Bern, the University of Chieti in the field of MRI brain tumor research, and with the University of Genoa in the field of multiple sclerosis, were also carried on.

Neurosurgery research group (PD Dr. T. Robert, PD Dr. P. Scarone)
Research topics concerned cranial pathologies as much as spinal pathologies and principally concerned clinical studies. Clinical research in spinal neurosurgery (lead: PD Dr. P. Scarone) is focused on new intraoperative imaging and navigation technologies in complex spinal surgery. The TRIBECA study (in collaboration with the Maastricht University and the Zuyderland Medisch Centrum in Herleen, The Netherlands) is the first multicentric randomized controlled trial (RCT) that evaluates the impact of a psychological preoperative intervention in patients at risk for chronic pain after lumbar fusion. The ATTR screening study (in collaboration with IOSI) explores the prevalence of amyloidosis in patients with lumbar spinal stenosis. The Neurosurgery research group is also active in clinical research about cranial neurosurgery (lead: PD Dr. T. Robert). The largest part of this activity is dedicated to vascular neurosurgery and oncological neurosurgery. Among other, the Neurosurgery research group participates in multicentric national and international studies as the Swiss SOS (for intracranial aneurysms), the Swiss Meningioma Network and the International ReSurge Glioma Network. Local prospective studies about the use of neuro-monitoring in aneurysmal microsurgery and about the importance of biomolecular study in glioblastomas are also important ongoing projects.

Pain management research group (PD Dr. P. Maino, PhD; PD Dr. E. Koetsier, PhD)
Our research group is conducting and coordinating several international, multicenter RCTs, with a focus on neuromodulation, minimal-invasive spinal interventions, and psychological factors that have an impact on the outcome of pain treatments. These are studies regarding for example dorsal root ganglion stimulation, spinal cord stimulation, and intra-discal interventions for discogenic pain. Additionally, we conduct multidisciplinary research projects, like the TRIBECA trial with the neurosurgery department that assesses the impact of a psychological treatment on the outcome after lumbar spinal fusion surgery. Our research group has also a close academic cooperation with the University of Maastricht (Dr. S. van Kuijk, PhD) and with SUPSI (Prof. M. Barbero).

Parkinson's disease research group (PD Dr. G. Melli, Prof. Dr. A. Kaelin)
Our research group aims to set-up novel biomarkers for Parkinson's disease by analyzing skin biopsy and peripheral fluids like plasma and cerebrospinal fluid using advanced new biotechnology. In 2021 our lab hosted three master students for master thesis internship and a PhD student in Neuroscience USI. We mainly work on the development of a novel diagnostic model based on plasma-derived extracellular vesicles for Parkinson's disease.
See also section 3: **Laboratories for Translational Research (LRT) of EOC**

Peripheral nerves research group (PD Dr. G. Melli, Dr. P. Ripellino)
One of the main research project of Dr. P. Ripellino was the NEUROCAVE study, exploring the neurological complications of hepatitis E. Moreover, we coordinated in Switzerland the NERVES study, focusing on neuropathies related to hepatitis E. We also continued ongoing collaborations to describe neuroimaging findings of neuralgic amyotrophy, for the characterization of T cells in Guillain-Barré syndrome (with the ETH Zurich), and to identify genetic determinants of hepatitis E course (with the CHUV in Lausanne). We also explored the role of SARS-COV-2 infection as potential trigger. The unit also includes the "skin biopsy laboratory" for the diagnosis of small fiber neuropathy (lead: PD Dr. G. Melli). We also participate to clinical trials studies sponsored by the industry for developing new drugs for treating pain in small fiber neuropathies and for developing a dorsal root ganglion stimulation for the management of intractable painful polyneuropathy in collaboration with the Pain management research group. Finally, we collaborated with IOSI (PD Dr B. Gerber) for an observational study on early identification of patients with wild type transthyretin amyloidosis. Furthermore, we actively participate in the Swiss Register of neuromuscular diseases.

Sleep research group (Prof. Dr. M. Manconi)
The research mission of the Sleep Medicine is to explore brain function during sleep and sleep-related disorders mainly by using electrophysiological innovative approaches. The main field of interest of our research are sleep related movement disorders such as restless legs syndrome and periodic limb movements. In 2021 our group produced the highest number of publications so far, included an article in Nature Prime Disease. We are also continuing in coaching two PhD students. These results have been obtained thanks to consolidated local and external collaborations, and thanks to the financial support of two competitive grants from the Swiss National Science Foundation (SNSF). New therapies are under investigation for restless legs syndrome: a phase 2b trial with anti-glutamatergic compound and a study on the effect of electrical spinal stimulation. In recent years, we developed a strong expertise in using High-Density EEG. Other sleep related fields are also represented, among others, by projects on: sleep and pregnancy, sleep and stroke, sleep and attention deficit hyperactive disorder, and infraslow oscillation. Two important local collaboration have been consolidated, one with the IOSI to evaluate the impact of hormonal treatment on sleep in patients with prostate cancer, and the second on REM sleep behavior disorders in Parkinson's Disease. In collaboration with the University of Bern, the post-doc Master in Sleep and Consciousness successfully progressed from diploma for advanced studies into a master of advanced studies.

Stroke research group (PD Dr. C. Cereda, Dr. G. Bianco)
Our research activities focus on patient-oriented clinical research: we are principally interested in understanding the role of multimodal advanced neuroimaging (perfusion imaging) for the diagnosis and selection of best treatment for acute ischemic stroke patients together with the Neuroradiology research group. We are currently leading studies addressed to the role of multimodal imaging in patients with ischemic stroke in the posterior circulation (basilar artery stroke), in gender differences in acute stroke treatment and stroke related to small vessel disease. We are also especially interested in recognizing new serum biomarkers in order to optimize the diagnostic process of transient ischemic attack (TIA). We also offer a platform for industry promoted international trials, promote several other clinical studies, and participate to numerous national and international projects mainly dedicated to acute stroke management, stroke prevention and stroke treatment.

>> The list of publications of the Institute of Clinical Neurosciences of Southern Switzerland available on the EOC website at the following link.

1.3 Cardiocentro Ticino Institute (ICCT)

Prof. Stefanos Demertzis, MD
Scientific director

Prof. Marco Valgimigli, MD PhD
Chair Clinical Research

Scientific work and research areas reflect the focus of the Cardiocentro Ticino Institute (ICCT) on providing better care to its patients through science and research. The main research areas per Department are as follows:

1) Cardiology

Clinical Electrophysiology (Prof. Dr. A. Auricchio)
The Clinical Electrophysiology research group is focused on cardiac disorder diagnosis and management including atrial fibrillation, cardiac implantable devices, management of lead and device issues, remote patient monitoring, computer modelling, and advanced signal processing. The group collaborates with Fondazione Ticino Cuore, the InterDisciplinary Institute of Data Science at USI (Prof. A. Mira) and MeteoSwiss; a research cluster on out of-hospital cardiac arrest (OHCA) has been established. The project makes use of advanced spatial statistics methods to identify patterns of temporal-spatial distribution of cardiac arrests in Canton Ticino. This project is supported by SNSF. Furthermore, additional research activities on OHCA in Switzerland have been successfully carried out in collaboration with the Swiss “Interverband für Rettungswesen” Association. Finally, the The Clinical Electrophysiology research group has a longstanding research partnership with EULER Institute of USI to conduct computer modeling studies in atrial fibrillation and heart failure.

Interventional Cardiology (Prof. Dr. M. Valgimigli, Dr. M. Moccetti)
The interventional cardiology research group participates in several national and international trials, which are coordinated by the research cardiovascular service (SRC), and runs multiple international interventional studies under the leadership of Prof. Valgimigli as global Principal Investigator (PI). This research group has published this year the primary and secondary results of the MASTER DAPT Trial, which involved 130 sites in Europe, Asia, South America and Australia and investigated the duration of dual and single antiplatelet therapy in patients at high risk of bleeding who underwent PCI. This group has also published this year the primary results of the SWISS APERO Trial, which compared in a randomised fashion two different devices for percutaneous closure of the left atrial appendage across eight sites in Switzerland, Belgium, France and Italy. This group is currently running the NATURE trial, which is investigating the role of a new thrombectomy device for the management of patients with ST segment elevation myocardial infarction with large thrombus burden and involves eight sites in Switzerland and Italy. This group has completed enrolment of the BIOFLOW DAPT, chaired by Prof. Valgimigli and is actively participating as recruitment sites in multiple randomised trials and registries, among which SWISS TAVI, MITRASWISS, SOS AMI, ABILITY, and AEGIS-2. This group is finally coordinating an international randomised controlled trial, named CONVINCE which is investigating the value of colchicine and/or edoxaban in COVID-19 positive patients who are managed outside the hospital. In 2021, Dr. Quagliana has completed his training as interventional fellow and Dr. Landi has replaced him. We will restructure in 2022 the fellowship program to be able to host 2 interventional fellows with each having 50% active role in the clinical and 50% in the research field, to further implement research projects while maintaining the clinical standards reached in the last years.

2) Cardiac surgery (Prof. Dr. S. Demertzis)

Laboratory Research (cardiovascular bio-engineering)
See also section 3: **Laboratories for Translational Research (LRT) of EOC**

Clinical Research (Prof. Dr. S. Demertzis, Prof. Dr. E. Ferrari)
Interprofessional electronic patient communication: The COVID-19 pandemic restrained in an unprecedented manner the face-to-face communication of families seeking information on their hospitalized loved ones and the interprofessional care teams (physicians, surgeons, nurses, physiotherapists). Those restrictions were generally perceived negatively. We developed a software-based communication solution to proactively and regularly convey all relevant information to the authorized family members. A prospective RCT, significantly supported by the USI (Prof. Schultz - Faculty of Communication) and SUPSI (Prof. Bianchi - Nursing Science) was conceived and completed. The positive results will be reported in 2022 (A. Pozzoli, C. Zurfluh, S. Demertzis).
Extracorporeal Circulation (Prof. Dr. S. Demertzis): 1) Intraoperative monitoring of the gaseous emboli (micro-air bubbles) that travel through the heart-lung machine and are filtered by the several machine components was introduced. Despite filtering, in some cases clouds of tiny bubbles (generally <200µm) still enter the patient and we are assessing their correlation with systemic inflammatory reactions or subtle neurological effects (S. Demertzis, S. Vandenberghe, M. Puthettu). Funded by the Swiss Heart Foundation. 2) Protecting the brain while treating the heart is a block of two projects focusing on quantification of air-bubbles captured in the heart chambers during open-heart surgery. One of the subprojects (AIRCATCH) is announced to be funded by the Fondo EOC-USI and the other is funded by the Foundation Fidinam (S. Demertzis, S. Vandenberghe, R. Krause – USI). 3) Analysis of venous drainage in extracorporeal circulation using different types of venous cannulas (E. Ferrari in collaboration with the University of Lausanne).
Coronary Artery Bypass Grafting (Prof. Dr. S. Demertzis): 1) The European Registry of Clinical Outcomes after external support of saphenous vein grafts (VEST) after coronary artery bypass grafting coordinated by S. Demertzis (PI) concluded patient enrollment and is registering the foreseen follow-up interviews. 2) Studies on the efficacy of different storage solutions for saphenous veins in coronary artery bypass grafting focusing on endothelial integrity were concluded in 2021 (F. Toto, E. Ferrari).
Cardiac Valves (Prof. Dr. E. Ferrari, Prof. Dr. S. Demertzis): 1) Two ongoing research projects focus on surgical techniques to reduce early complications of rapid-deployment sutureless aortic valves, paravalvular leakage and heart-blocks requiring implantation of a pacemaker (E. Ferrari). 2) Predictability of failure of surgical mitral valve repair analyzing preoperative imaging using machine learning. Initialization of a common project in collaboration with the USI (Prof. Krause, Euler Institute) (T. Torre, S. Demertzis). 3) Analysis of clinical data and outcome after implantation of transcatheter aortic valves (TAVI) in general for severe aortic stenosis (focusing on alternative access than the femoral artery) and in presence of concomitant significant tricuspid valve regurgitation (E. Ferrari). 4) Analysis of the predictability of clinical outcome after percutaneous implantation of Mitraclip for severe mitral regurgitation, depending of intraprocedural measurements of the pressure in the left atrium (E. Ferrari in collaboration with University of Tokyo and University Hospital San Raffaele of Milan). 5) Analysis of long-term outcomes under different anticoagulation / antiaggregation regimes after TAVI registered in the SWISS-TAVI registry is underway (E. Ferrari in collaboration with the University of Bern). 6) Analysis of the radiologically documented position of TAVI-in-TAVI implantations and the corresponding clinical outcomes (E. Ferrari in collaboration with the Washington University).
Thoracic Aorta (Prof. Dr. E. Ferrari, Prof. Dr. S. Demertzis): 1) Analysis of clinical outcomes after thoracic aorta endoprostheses (TEVAR) for different aortic pathologies (Th. Theologou, E. Ferrari, S. Demertzis). 2) Retrospective analysis of aortic size indices in patients with acute aortic dissection type A (S. Grego, S. Demertzis).
Rare Diseases (Prof. Dr. G. Conte, Dr. S. Grego): Research studies cover both inherited primary cardiac arrhythmia syndromes (IPCAS), and genetically imprinted aortic disease. The main research focus in IPCAS is the mechanistic understanding of atrial arrhythmias onset and maintenance in these patients. Several international registries including a large investigator-initiated European study on subcutaneous ICD in patients with Brugada syndrome, and a cantonal (Ticino) epidemiological survey on IPCAS patients are ongoing. Research on genetically imprinted aortic disease focuses on reverse tracing of family members after acute aortic dissection and the corresponding clinical and genetical analysis of risk profiles.

3) Cardio-anesthesiology and Cardiac Intensive Care (Prof. Dr. T. Cassina)
A prospective clinical study focusing on the kinetics of Neurofilament Light Chain after cardiac arrest as prognostic parameter of neurological damage is ongoing (collaboration with INSI – Dr. P. Agazzi).

4) Lugano Cell Factory (LCF) (Dr. L. Turchetto)
LCF is a Good Manufacturing Practice (GMP) facility authorized by Swissmedic for the production of Advanced Therapy Medicinal Products (ATMP)/transplant products. LCF has optimized and validated a manufacturing process for the GMP production of hyaline cartilage beads (Cartibeads) from human chondrocytes for the startup company Vanarix SA. LCF has also established a collaboration with the University of Manchester to act as a GMP manufacturing service for a gene therapy product related to the treatment of Duchenne Muscular Dystrophy (DMD). Moreover, the team developed a novel protocol for the production of clinical-grade human exosomes from cardiac progenitor cells patent [application N° 102017000035315_ (IT/CH/PCT) Device and method for exosomes production and purification]. LCF has cooperated with SUPSI for the development of a closed and integrated device to perform the whole exosomes manufacturing process (Exodevice project/Fidinam grant) and presently participates to a European consortium (MARVEL project/ H2020 grant) to improve the purity of the GMP grade exosomes. Ultimately, LCF operates also as Cardiovascular Tissue Bank (aortic and pulmonary valves, as well as pericardium for human use). Three cardiovascular tissues have been stored in 2021.

>> The list of publications of the Cardiocentro Ticino Institute is available on the EOC website at the following link.

1.4 Imaging Institute of Southern Switzerland

Prof. Luca Giovanella, MD
Medical and scientific director (until 2021)

Prof. Filippo Del Grande, MD
Medical and scientific director (from 2022)

The Imaging Institute of Southern Switzerland (IIMSI) includes the Clinic of Radiology (Head: Prof. Dr. F. Del Grande) [4 Radiology services in Bellinzona, Lugano, Mendrisio and Locarno EOC Regional Hospitals], the Clinic of Nuclear Medicine and Molecular Imaging (Head: Prof. Dr. L. Giovanella) [2 NM/PET-CT services, including, 2 thyroid outpatients clinics in EOC Bellinzona and Lugano Regional Hospitals and a 3-beds therapy unit in Bellinzona, respectively] and the Medical Physics Service (Head: Dr. S. Presilla). The Laboratory of Radiomics and Predictive Imaging (lead Prof. Dr. L. Ceriani) coordinates the main IIMSI research programme, focused on Radiomics, Artificial Intelligence and Imaging Biomarkers. A new Research Programme focused on Integrated Diagnostics (lead Prof Dr. L. Giovanella) was launched in 2020 focusing on convergences and integration of imaging, pathology and laboratory data. Finally, clinical validation studies of innovative imaging technologies and protocols are performed in Radiology and Nuclear Medicine (i.e. MRI protocols and sequences, new PET/CT detection systems).

1) Clinic of Nuclear Medicine and Molecular imaging

Integrated diagnostics (Lead Prof Dr. L. Giovanella)

- Artificial intelligence and machine learning to develop integrated diagnostic expert systems/neural networks. Collaborations: University of Padua, ICT EOC, Roche Diagnostics.
- Molecular imaging, molecular pathology and circulating biomarkers of thyroid cancer. Collaborations: Universities of Marburg, Essen, Paris Descartes, Zurich, Udine, Thyroid Committee-European Association of Nuclear Medicine - Vienna, EO Ospedali Galliera Genoa.

Thyroid diseases (Lead Prof Dr. L. Giovanella)

- Radioiodine-refractory thyroid cancer and re-differentiation strategies. Collaborations: Center of Excellence on Radioiodine Theranostics-Society of Nuclear Medicine and Molecular Imaging.
- Mitochondrial imaging in thyroid diseases. Collaborations: EO Ospedali Galliera Genoa, Thyroid Committee-European Association of Nuclear Medicine - Vienna, University of Turin, University of Messina, Universities of Augsburg, University of Giessen.

PET radiomics and predictive imaging of lymphomas (lead Prof. Dr. L. Ceriani)

- Development and validation of new PET-metrics, radiomic analysis and Artificial Intelligence tools. Collaborations: IELSG, SAKK, IOR, IOSI, Amsterdam University Medical Centre, Federazione Italiana Linfomi, United Kingdom Cancer Research Institute.
- Integration of PET/CT data, biological and genomic features (i.e. liquid biopsy) using Radiomics, Genomics and Artificial Intelligence tools to model new diagnostic/prognostic approaches. Collaborations: IELSG, SAKK, IOR, IOSI, Amsterdam University Medical Centre, Federazione Italiana Linfomi, United Kingdom Cancer Research Institute.

Theragnostics (Lead Dr. G. Paone)

- Clinical/research activities in theragnostic field for the therapy working group of Swiss Society of Nuclear Medicine (SGNM) particularly focused on PRRT and PSMA therapy (collaborations with Universitatsspital Bern, Novartis/AAA).
- Personalized dosimetry studies focused on selective internal radiotherapy with Y-90 (collaborations with Istituto Nazionale Tumori Milan, Boston Scientific and Mirada group).
- Production and updating therapeutic flow-charts in NETs and combined therapy protocols in mCRPC.

Evidence-based nuclear medicine (Lead Prof. Dr. G. Treglia)

- Production of evidence-based documents (systematic reviews and meta-analyses of diagnostic test accuracy) and guidelines on PET/CT. Collaborations: Cochrane and European Association of Nuclear Medicine, University of Lausanne, University of Groningen, University of Brescia, University of Mashhad, Fondazione Policlinico A. Gemelli Rome and EO Ospedali Galliera Genoa.

- Research-related activities for the PET working group of the Swiss Society of Nuclear Medicine focused on the achievement of reimbursement for new PET indications.

2) Clinic of Radiology

Musculoskeletal imaging (Lead Prof. Dr. F. Del Grande)

- Validation of work in progress MRI sequences for different musculoskeletal diseases. Collaboration: Johns Hopkins Hospital, Baltimore.

Onco-imaging and radiomics (Lead PD Dr. S. Rizzo)

- Radiomics of ovarian cancer: evaluation of imaging heterogeneity as predictor of outcome (multicentric study in collaboration with the University of Cambridge).
- Sarcopenia and chemo-related complications in ovarian cancer. Sarcopenia and chemo-related complications in pancreatic cancer (Prof. Dr. F. Del Grande)
- Structured report and radiomics in breast cancer lesions candidate to biopsies (multicentric study promoted by the Italian Society of Medical Radiology, SIRM) (Dr. H. Porpiglia)
- Quality assessment of CT reports performed by subspecialized radiologists compared to general radiologists.

Miscellaneous

- Machine learning in COVID-19 prognostication: retrospective collection of 280 patients from 10 different centers (total: 2800 patients) in a multicenter study (Lead University of Maastricht; local lead Dr. C. Puligheddu).
- COVID-19: pre-pandemic evaluation of lung GGO (Lead PD Dr. S. Rizzo and Prof. Dr. L. Ceriani).
- Role and feasibility of medical hypnosis for claustrophobic patients undergoing MRI examinations. Observational study on the role of medical hypnosis as an alternative to pharmacologic sedation for claustrophobic patients during MRI examinations (Lead Dr. N. Ferrera).
- Establishing ultrasound references for vascular structures in pediatric populations (Lead Dr. M. Cristallo).

>> The list of publications of the Imaging Institute of Southern Switzerland is available on the EOC website at the following link.

1.5 Institute of Pediatrics of Southern Switzerland

Prof. Giacomo Simonetti, MD
Medical and scientific director

Surgical and medical pediatrics focuses on the health of neonates, infants, children, and adolescents, their growth and development, and their opportunity to achieve full potential as adults. Pediatric care encompasses a wide spectrum of health services ranging from preventive health care to the diagnosis and management of acute and chronic (often congenital) diseases.

The Institute of Pediatrics of Southern Switzerland (IPSI) has a dedicated research unit, conducted by Prof. Dr. G.D. Simonetti, PD Dr. F. Vanoni, PD Dr. B. Goeggel Simonetti, Dr. A. Stefani-Glücksberg, Dr. C. Balice, RN, PhD, and scientific assistant A. Severi Conti. The pediatric research unit is included in the SwissPedNet, a Swiss based network that promotes pediatric clinical research in Switzerland. The research unit is mainly oriented on clinical research in different fields of pediatrics: Cardiology, Infectious disease, Neuropediatrics, Neonatology, Nephrology, Nursing sciences, Oncology, Rheumatology and Pediatric Surgery.

The principal areas of research for each subspecialty are:
Pediatric Cardiology-Nephrology (Dr. C. Leoni-Foglia, Dr. A. Stefani-Glücksberg, Prof. Dr. M.G. Bianchetti and Prof. Dr. G.D. Simonetti): childhood hypertension, cardiovascular risk factors in the young, Kawasaki disease. We participate in the Swiss Pediatric Heart Cohort and the International Pediatric Brugada Registry.
General Pediatrics (Prof. Dr. M.G. Bianchetti, Prof. Dr. G.D. Simonetti, PD Dr. F. Vanoni): Systematic reviews of rare diseases, or rare complications of frequent pediatric diseases. Moreover, fever phobia among parents in collaboration with the USI Institute of Public Health will be analyzed. A multicenter prospective RCT about fluid resuscitation in children with gastroenteritis is ongoing. We developed a general consent for pediatric patients that is under distribution at our polyclinic.
Pediatric Infectious Diseases (Dr. L. Kottanattu): we participate in a multicentric RCT on Pediatric Inflammatory Multisystem Syndrome Temporally associates with SARS-CoV-2 (RECOVERY study). We are involved in several registries (MoCHIV, CITRUS) that analyze the prevalence of rare infectious diseases in childhood. In 2020 we started a seroprevalence study of COVID-19 in pediatric population in collaboration with HuMabs, covering the different waves of pandemic.
Neuropediatrics (PD Dr. B. Goeggel Simonetti, Prof. Dr. G.P. Ramelli). In collaboration with SUPSI we promote a project on the early diagnosis of autism (Auto-Play-D). As members of national and international research consortiums we participate in studies on neurovascular diseases including stroke in childhood and young adults (IPSS, SNPSR, RCT PASTA Trial), intracranial dissection, pediatric FMD, epilepsy, autism spectrum disorders and cerebral palsy, inflammatory brain disease (Swiss-Ped-IBrainD), and long-term follow-up of high-risk neonates (Swiss Neo Net).
Neonatology-Nursing Science (Dr. C. Balice, RN, PhD, Dr. M. Ragazzi): Pain prevention in the newborn.
Onco-hematology (Dr. P. Brazzola): we are involved in 31 international studies (oncology protocols)/registries. We contribute to a non-interventional study for treatment of patient with hemophilia A with and without inhibitors (EMIIL, Roche).
Rheumatology (PD Dr. F. Vanoni): we participate in an international cohort rheumatology diseases registry. We strictly collaborate with the CHUV for the development of observational prospective and retrospective studies on treatment and outcome in inflammatory diseases. In particular, we contribute to develop a prospective study protocol on through serum level of anti-TNF alfa medication in non-infectious uveitis.
Pediatric Surgery (Dr. M. Mendoza, Dr. V. De Rosa and Dr. E. Montaruli): minimal invasive surgery, orthopedic and surgical trauma.

The main goal of the research unit is to promote high-quality pediatric clinical research in the Italian speaking part of Switzerland and to help young fellows and medical students of Swiss Universities to participate in clinical research in pediatrics.
In the context of the Master of Medicine, we are also involved in 9 master thesis supervision and promotion of clinical research.

>> The list of publications of the Institute of Pediatrics of Southern Switzerland is available on the EOC website at the following link.

1.6 Institute of Pharmacological Sciences of Southern Switzerland

Prof. Alessandro Ceschi, MD, MSc
Medical and Scientific Director

The Institute of Pharmacological Sciences of Southern Switzerland (ISFSI), which was established in 2017, includes the Division of Clinical Pharmacology and Toxicology, with its clinical services including the Pharmacogenomics and Pharmacogenetics Unit, the Regional Pharmacovigilance Centre, a small Research Unit, and the Central Pharmacy Service, with the Hospital Pharmacy, Clinical Pharmacy, and Public Pharmacy. We advise other departments and healthcare professionals on safe drug use and promote the rational use of medicines. The final goal of our activities is to personalise drug therapy by optimising beneficial effects while minimising adverse effects and costs.

During 2021, the Regional Pharmacovigilance Centre has played a crucial role in the national landscape in strict collaboration with Swissmedic for the management and evaluation of adverse reactions reported in association with COVID-19 vaccines throughout the vaccination campaign in Switzerland. On this ground, aiming at collecting complementing information on COVID-19 vaccines' safety, the Research Unit has been exploiting VigiBase, the World Health Organization's global database of spontaneously reported suspected adverse drug reactions, and systematically and routinely querying the database by data mining techniques to promptly detect any safety signals. By using VigiBase as data source to gain further information on COVID-19 vaccines' safety, we also performed subgroup disproportionality analysis by age and sex to assess the reporting of acute inflammatory neuropathies with COVID-19 vaccines in comparison with other viral vaccines. Moreover, with the SARS-CoV-2 pandemic, the Regional Pharmacovigilance Centre contributed to set up an active pharmacovigilance activity to monitor COVID-19 vaccines' safety amongst the participants of the Corona Immunitas nationwide research program, which was implemented in 2020 by the Swiss School of Public Health to determine the SARS-CoV-2 immunity status of the Swiss population. Against this background, the Research Unit of ISFSI designed and is currently conducting a population-based prospective cohort study to evaluate the impact of socio-psychological factors on self-reported side effects with mRNA COVID-19 vaccines amongst the participants of the Swiss Corona Immunitas cohort.

Furthermore, ISFSI was actively contributing to a range of studies on different aspects of COVID-19 with a focus on immunological and vaccine-related aspects.

ISFSI is also an official sentinel centre of the European Drug Emergency Network Plus (Euro-DEN Plus) Project, which collects data on Emergency Department (ED) acute recreational drug presentations across Europe. Whilst not representative of the general population of drug users as a whole, by using a sentinel centre model covering, to date, twenty-four countries, the Euro-DEN Plus database provides a snapshot of the epidemiology of ED presentations related to acute recreational drug toxicity in Europe, and gathers systematic and structured toxicology surveillance data relative to such events. During 2021, we performed a matched case-control study in the Euro-DEN plus database on the characterization of risk factors for intensive care unit admission following acute recreational drug toxicity.

A further branch of the research activity conducted at ISFSI was in collaboration with the INSI within the Swiss Stroke Registry, a national web-based registry that includes all consecutive patients admitted to Stroke Units and Stroke Centres across Switzerland. During 2021, we performed an observational cohort population-based study aimed at assessing sex differences in the safety and efficacy outcomes of intravenous thrombolysis in acute ischemic stroke patients in relation to preadmission use of antiplatelet agents.

>> The list of publications of the Institute of Pharmacological Sciences of Southern Switzerland is available on the EOC web-site at the following link.

1.7 Institute of Laboratory Medicine

Dr. Franco Keller, PhD
Director

The Institute of Laboratory Medicine (EOLAB) was set up to meet the requirements of modern clinical laboratory medicine. EOLAB recognizes the importance of research into its activity to be continuously updated and to offer the best service and collaboration to all medical departments in EOC. The EOLAB specialists are actively involved in several scientific society boards as soon as national and international scientific society working groups.

The collaboration between the EOLAB and the EOC General Directorate (through AFRI and ICT divisions) allowed the creation of the EOC Biobank in 2019. The biobank plays an important role for researchers, as it allows them to obtain - in a short time - a sufficient number of samples to carry out their research by collecting and storing biological material indefinitely. Thanks to its quality system and the certification obtained from the Swiss Biobanking Platform (SBP), the EOC Biobank is a guarantee of sample integrity and therefore of high-quality research. The headquarters of the EOC Biobank is located inside the Microbiology Service EOLAB (SMIC). During 2021 EOLAB continuously collaborate with EOC Biobank providing infrastructure, logistic support and technical staff.

In the 2021 EOLAB activate 12 new collaboration studies.
The SMIC contributes with its known-how and data to several EOC internal projects as well as to external national and international projects. During 2020 microbiological examinations were pursued by HIV and HCV patients in the frame of national HIV and HCV cohort studies. Case reports on clinically significant cases with uncommon bacterial and fungal strains were published in collaboration with clinicians from EOC and colleagues of Swiss university hospitals. SMIC collaborates with ICCT into two projects: the former to explore the presence of viral antigen in circulating exosomes of SARS-CoV-2 positive patients, and a second to evaluate the possible correlation among circulating extracellular vesicles and enhanced procoagulant activity in SARS-CoV-2 Infection. SMIC is collaborating with INSI on a research project to establish a proven correlation between Hepatitis E viral infections and neurological manifestations and to evaluate Hepatitis E virus (HEV) involvement in Guillan-Barré Syndrome. After an acute hepatitis E outbreak in Southern Switzerland, in January 2017 the local public health authorities started an active program of food chain control and public education. In this retrospective study, all laboratory-confirmed acute cases of HEV infection diagnosed between 2014 and 2020 were analysed at SMIC to show that active public health measures can reduce the prevalence of HEV infection. The SMIC hosts the National Reference Laboratory for Legionella and contributes to national collaborations and international projects on the epidemiology and spread of Legionnaires' disease in Switzerland. The EOLAB laboratories of Hematology (LEM), Molecular Biology and Cytogenetic, actively participate in the SAKK project "34/17": Prospective, open-label, multicenter, phase-II trial of ibrutinib induction followed by ibrutinib plus venetoclax consolidation in patients with relapsed/refractory chronic lymphocytic leukemia.
The Clinical Biochemistry and Pharmacology Laboratory (BFC) is involved in a European network for the harmonization of steroid hormone quantitation in mass spectrometry and close collaboration with the pharmacology unit of the University of Turin and Amedeo di Savoia Hospital in Turin on pharmacology and pharmacogenomics fields.

>> The list of publications of the Institute of Laboratory Medicine is available on the EOC website at the following link.

1.8 Cantonal Institute of Pathology

Prof. Luca Mazzucchelli, MD
Medical and Scientific Director

The Cantonal Institute of Pathology (ICP) is actively involved in various research projects that aim to identify new methods to be introduced into routine diagnostics or to identify new markers that can be used both in prognosis and in predicting the efficacy of chemotherapeutic treatments: ICP research is essentially aimed at the molecular characterisation of diseases, mainly those in the field of oncology. IOSI is a privileged research partner of the ICP, with particular emphasis on cancers of the gastrointestinal tract and thoracic cavity, hematolymphoid neoplasms and urogenital cancers. Currently, ICP participates in almost 50 clinical trials and also collaborates with various Swiss and international pathology institutes. Main ICP research projects are detailed here below.

Role of BCL2 genetic heteroclonality in the pathogenesis of B-cell lymphomas with BCL2 rearrangement (L. Mazzucchelli). The current WHO classification of the lymphoid tumors classifies B-cell lymphomas with rearrangement of MYC and BCL2/or BCL6 (double/triple-hit lymphomas) in a new entity: high grade B-cell lymphomas with rearrangement of *MYC*, *BCL2* and/or *BCL6* (HGBL-DH). This entity is characterized by a heterogenic morphology including features of diffuse large B cell lymphoma (DLBCL) centroblastic or immunoblastic, unclassifiable DLBCL/Burkitt lymphoma, Burkitt lymphoma (BL), and composite lymphomas. It is accepted that the rearrangement of *MYC* and *BCL2* occurs at the same time in *de novo* high grade B-cell lymphoma whereas *MYC* translocation is a secondary event in HGBL-DH transformed from follicular lymphoma (FL). The synergistic effect of cellular proliferation and inhibition of apoptosis regulated by *MYC* and *BCL2*, respectively confers to HGBL-DH a particular aggressive behavior. However, until now it is not known whether BCL2 and MYC translocations occur in all neoplastic cells of HGBL-DH or they are restricted to a subpopulation of lymphoma cells. In addition, it is still unclear whether *BCL2* and *MYC* rearrangements are concomitant at the cellular level or they represent different clones in a lymphoma. To clarify these issues, we designed a new four colors break-apart probe for fluorescence in situ hybridization (FISH) studies that allows the evaluation of *MYC* and *BCL2* rearrangements together in the same cell. The study represents a unique opportunity to better elucidate crucial pathogenic mechanisms involved in double-hit lymphomas.

Genomics of diffuse large B cell lymphoma (L. Mazzucchelli, F. Molinari, A. Valera). Diffuse large B-cell lymphoma is a heterogeneous disease. Over the past few years, there have been several attempts for a better classification, particularly considering the cell of origin. The development of next generation sequencing (NGS) technology now offers new opportunities. There are already several published studies illustrating the potential of this approach in terms of lymphoma classification but also in terms of identification of predictive markers and personalized treatments. In collaboration with the Institute of Pathology of the University of Basel and the Hematology service of the EOC (Prof Dr. D. Rossi) we have developed a multigenic panel for the characterization of lymphomas based on the “Ion-torrent” technology, particularly suitable for the analysis of formalin-fixed and paraffin-embedded biopsy specimens. The panel includes 149 genes (covered by 4716 amplicons) and we are currently in the validation phase. Preliminary results are very promising and we are confident that we will soon be able to start clinical trials as well as move to its implementation in lymphoma diagnostics.

Digital Pathology and Artificial Intelligence (L. Mazzucchelli, V. Martin). Digitalization of pathology offers new opportunities to improve clinical service but also to develop research projects. ICP anticipates a gradual transition to digital pathology during 2022. In parallel, working groups have been formed in collaboration with Dalle Molle Institute for artificial intelligence to develop new diagnostic algorithms but also artificial intelligence applications to exploit the data that will be produced. The potential is enormous and the ICP remains open and available for any project in collaboration with other EOC institutes/departments. Specifically, the Institute is working on a project for the reconstruction of histological images concerning the evaluation of large samples. With this approach, it is hoped to facilitate the evaluation of very important parameters for the prognosis of the patients as the size of the neoplasm or the relationship of the tumor with the resection margins, or the correlation with preoperative radiological images.

The value of liquid biopsies to predict tumor response after neoadjuvant chemo-radiotherapy in advanced rectal cancer (M. Frattini). The standard treatment for locally advanced rectal cancer is multimodal therapy with neoadjuvant (pre-operative) chemo-radiotherapy (nCRT) followed by radical surgery. In 20-30% of cases, histopathologic analysis of the resected rectum will find a complete regression of the tumor as a consequence of nCRT. Rectal resection is associated with a significant risk of post-operative complications and long-term functional problems. Therefore, pre-operative identification of a complete pathological response to nCRT would spare many patients unnecessary morbidity. However, pathological response has only partial concordance with a clinical response. Therefore, even patients with a complete clinical response to nCRT, still undergo rectal resection as standard of care. We have proposed a proof-of-concept, prospective, observational study to investigate the value of liquid biopsies to predict and reflect tumor response after nCRT in patients with locally advanced rectal cancer. Our goal is to correlate quantitative (total amount) and qualitative (detection of specific gene alterations through NGS experiments) evaluation of circulating tumor DNA (ctDNA) in liquid biopsies to tumor response to nCRT at different timepoints throughout the multimodal therapy in patients with locally advanced rectal cancer.

Analysis of circulating tumour DNA in patients with non-small cell lung cancer (NSCLC) undergoing immunotherapy with checkpoint inhibitors (M. Frattini). For patients with metastatic lung cancer and a high expression of the immuno-oncological marker PD-L1, therapy with the immune checkpoint inhibitor pembrolizumab or atezolizumab is the standard therapy. Recent phase II clinical trials and interim analysis from phase III trials have demonstrated a great benefit from the addition of tiragolumab (another checkpoint inhibitor) to atezolizumab in patients charcaterized by PD-L1 expression >50%. Today, the response of these patients to therapy is checked every 9-12 weeks using computer tomography. This means that in a substantial proportion of patients, tumour progression is only detected when the general condition is worst and further tumour therapy is no longer possible. Recent data seem to indicate that a quantitative decrease in the ctDNA in the plasma correlates with the response to immunotherapy. The aim of the study is to use the quantitative progression of ctDNA to optimise the therapy. Patients with an early drop in ctDNA (>50%) compared to the initial level will continue with immunotherapy with the combination of atezolizumab and tiragolumab checkpoint inhibitors. Patients without a corresponding drop in ctDNA will be randomly assigned to one of two treatment groups: either they will also be further treated with atezolizumab+tiragolumab alone or they will receive platinum-based chemotherapy in addition to the combination of checkpoint inhibitors. With this study, we want to investigate whether early intensification of therapy in patients with insufficient drop in ctDNA after 2 cycles of immunotherapy may lead to a better prognosis and we want to investigate whether ctDNA measurement is a suitable biomarker for risk stratification and therapy adjustment. This is a study co-directed with IOSI (Dr P. Froesch), more than 10 Swiss centres (through SAKK involvement) and more than 10 European centres (from France, Spain, Germany, Italy). The trial will receive the financial support of Roche.

Sensitive screening in treatment of skin cancer (M. Frattini). Melanoma is a severe disease, relatively insensitive to standard chemotherapeutics, but recently vemurafenib, dabrafenib and trametinib have shown promising results. However, the efficiency of these therapies is strongly correlated with the presence of somatic mutations (SMs) in the BRAF oncogene in the cancer cells. Furthermore, recent data indicate that trametinib may benefit patients affected by SMs in the NRAS gene and moreover, SMs occurring in the KIT gene are correlated with susceptibility to other targeted drugs like imatinib. The aim of the project is to develop, in collaboration with a Danish company, three assays 20-200 fold more sensitive than available methods (Next Generation Sequencing and FDA-approved assays) also facilitating non-invasive monitoring.

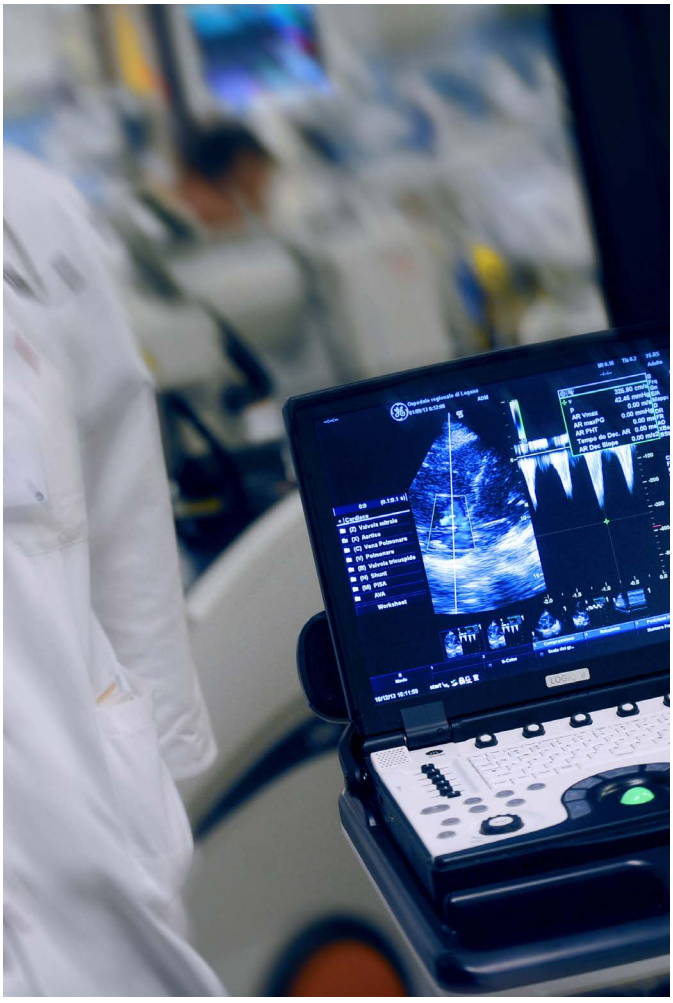
Sensitive diagnosis, prognosis and treatment planning on open platform of glioma brain tumours (M. Frattini). Brain tumors are one of the most aggressive and common cancers. About 28% of brain tumors are gliomas; glioblastoma (GBM) subtype is found in 17% out of this group. The classification and the treatment of gliomas is strictly correlated to the evaluation of several molecular markers (i.e. mutations in IDH1, IDH2, hTERT, H3F3A, HIST1H3B genes; MGMT (O6-methylguanine DNA methyltransferase) promoter methylation). The genetic status of IDH1, IDH2, H3F3A and HIST1H3B is fundamental for a proper classification of the tumor; MGMT promoter methylation status has clinical relevance because patients with hypermethylation benefit more from the combination of chemo (based on temozolomide) and radiotherapy; finally, TERT promoter genetic status is linked to adverse prognosis and to diagnosis of oligodendroglioma or glioblastoma. Nowadays, the available molecular assays are essentially made on tissue samples and suffer from method variation, low sensitivity and technical barriers. On these bases, the main purpose of our project is to improve these analyses providing a new, more sensitive and faster real-time PCR based methodology in collaboration with PentaBase ApS, a Danish company with which we have excellent collaborative relationships from years. In collaboration with Dr. F. Marchi (INSI), liquid biopsies will be collected from patients affected by gliomas and evaluated with the newly developed assays.

Personalized cancer monitoring (M. Frattini). Monitoring of cancer progression is mainly done by bi-monthly imaging of the tumor. Cancer patients can be better treated if their cancers are monitored closely. PCR-based genetic analysis of cancer specific mutations is a fast, inexpensive alternative. However, this method is only available for patients carrying typical (hotspot) mutations in a few cancers. Using simple blood samples, we will enable sensitive and inexpensive monitoring of all cancers for true personalized treatments. Based on NGS data from the clinics from the solid, diagnostic biopsy, in collaboration with a Danish company we will design, manufacture and validate tumor- and patient specific, real-time PCR-based monitoring and ctDNA purification assays for blood samples. We will sell at least twenty assays per patient to the clinic, allowing for bi-weekly monitoring and early response to resistance acquisition of tumors.

>> The list of publications of the Cantonal Institute of Pathology is available on the EOC website at the following link.

1.9 EOC Department of Medicine

PD Pietro Cippà, MD
Head of Department



The EOC Department of Medicine supports and promotes translational and clinical research in several areas related to internal medicine. The need for conveying common research interests and fostering interdisciplinary collaborations guided the development of a Local Research Unit (LRU) of the EOC Department of Medicine, starting from the previously established research unit of the Division of infectious diseases. The new LRU was recognized by the CTU-EOC in June 2021, promoted the first research project on code discussions amongst junior physicians in Summer (Dr. M. Bedulli) and is currently expanding the research portfolio with the support of a first study nurse. We report here the most relevant clinical research projects of the year. The work on translational research performed by the Hepatology (Prof. Dr. A. De Gottardi) and the Nephrology (PD Dr. P. Cippà) groups is included in the section dedicated to the Laboratories for Translational Research
See also section 3: **Laboratories for Translational Research (LRT) of EOC**

1) General internal medicine (Dr. B. Balestra, Prof. Dr. L. Gabutti, Prof. Dr. A. Ogna, Prof. Dr. M. Pons)
Quality and appropriateness of care, inspired by the "Choosing Wisely" campaign, are among the most important research lines. The group of Prof. Gabutti is part of a consortium, supported by the Swiss Personalized Health Network, which aims to improve the quality of healthcare by collecting data from individual hospitals available in an interoperable data exchange network. Other topics of interest are arteriosclerosis (CATCH study, Prof. Dr. A. Gallino) and cardiovascular risk factors, including studies on discontinuing statins in multimorbid older adults without cardiovascular disease, on natriuria in stress hypertension and on arterial stiffness in association with alcohol intake, kidney function and blood magnesium levels (PD Dr. R. Del Giorno, Dr. V. Gagliano).

2) Infectious diseases (Prof. Dr. E. Bernasconi)
The ongoing pandemic of SARS-CoV-2 has stimulated several research projects and successful collaborations. We highlight relevant studies on (1) the response to mRNA vaccines in health care workers (PD. Dr. O. Giannini), and in patients with multiple sclerosis (in collaboration with the INSI); (2) SARS-CoV-2 seropositivity among residents and staff of long-term care homes (in collaboration with SUPSI); (3) SARS-CoV-2 post-exposure prophylaxis (in collaboration with the University Hospital of Geneva); (4) microbiome changes in persons infected with SARS-CoV-2 and in persons who received a mRNA vaccine (in collaboration with the EOC Department of Surgery). We are also pursuing an international collaboration on inflammatory cytokines in the pathogenesis of COVID-19, and a study with the University Hospital of Lausanne on Long COVID. Moreover, a phase 1-2 study for the prophylaxis of COVID-19 with a new monoclonal antibody against the receptor binding domain of the SARS-CoV-2 spike protein is in preparation and will involve IRB, IOSI, the CTU-EOC, and our division. In addition, we developed an antibiotic stewardship program (COMPASS study), and we started a study to optimize the diagnostic strategy in elderly patients with suspected pneumonia (OCTOPLUS study) in collaboration with the University Hospital of Geneva. We continue to actively contribute to the Swiss HIV Cohort Study (SHCS) (**www.shcs.ch**), one of the world's largest epidemiological and clinical studies in the field of HIV. The successful scientific activity in 2021 is reflected in the relevant number of published studies.

3) Nephrology (PD Dr. P. Cippà)
The kidneYimmune study provides a prospective in-depth characterization of the immune response to viruses (including SARS-CoV-2), bacteria and vaccines in a cohort of dialysis patients from all EOC hospitals (PD Dr. O. Giannini). We contribute to international studies focused on quality and accessibility to dialysis (Dr. S. Pianca), on the monitoring of the vascular access for hemodialysis (Dr. D. Giunzioni) and we are evaluating the role of volume management in hemodialysis patients with obstructive sleep disorder (PD Dr. V. Forni Ogna). We recently launched a research project aimed at identifying predictors of successful peritoneal dialysis treatment, one of the cornerstones of home renal replacement therapy (Dr. A. Bellasi). Moreover, we work on experimental and translational models of kidney disease, and we are developing artificial intelligence-based algorithms to take advantage of the knowledge obtained by single cell technology in the interpretation of kidney biopsies (Dr. A. Rinaldi).

4) Gastroenterology and Hepatology (Prof. Dr. A De Gottardi)
We developed novel applications of artificial intelligence to improve the accuracy of colonoscopy for the detection of benign polyps and colorectal cancer lesions (Dr. G. Lollo). The data obtained in two international clinical trials will contribute to set novel standards of care in colorectal cancer screening. Predictive models in patients with advanced chronic liver disease are being developed to identify trajectories of movement, temperature, voice and cognitive functions, as assessed by using wearable devices, to detect behavioral changes that predict and prevent the occurrence of complications (Dr. A. Galante, Dr. D. Pizzagalli).

5) Pneumology (Dr. M. Bernasconi)
Several studies on the diagnostic approach in patients with suspected SARS-CoV2 pneumonia and on the long-term consequences of COVID-19 were performed in the last year (Dr. P. Gianella). Night-time sleep disordered breathing linked to chronic kidney disease, and non-invasive high-frequency ventilation applied to radiotherapy and radiological diagnostics are among the main research interests of Prof. Dr. A. Ogna. The research of Prof. Dr. M. Pons is focused on obstructive and central sleep apnea in patients with ischemic stroke. Research on dyspnea management and palliative care for patients with advanced chronic obstructive pulmonary disease is ongoing in collaboration with the Palliative and Supportive Care Clinic IOSI-EOC (Dr. T. Fusi-Schmidhauser). Moreover, EOC contributes to the Swiss Severe Asthma Registry (Dr. P. Gianella).

6) Endocrinology (Prof. Dr. P. Trimboli)
Clinical research in Endocrinology is mainly focused on thyroid disorders. We published relevant studies on thyroid cancer diagnosis, on the potential relationship between COVID-19 and thyroid diseases and we are involved in the preparation of the new international guidelines on thyroid ultrasound and the therapy for hypothyroidism. A new study about the performance of different formulations of levo-thyroxine in patient undergone bariatric surgery was launched in collaboration with the EOC Department of Surgery and we started a collaboration with the Dalle Molle Institute for Artificial Intelligence on hypothyroidism. More recently, Dr. C. Camponovo has implemented a study to evaluate the effects of anti-CGRP on bone metabolism in collaboration with the INSI.

7) Cardiology (PD Dr. M. Di Valentino, Dr. G. Moschovitis)
We participate to the Swiss Atrial Fibrillation Cohort (Swiss-AF), a national study coordinated by the University of Basel and focused on the relationship between atrial fibrillation and the structure and the performance of the brain. More recently we started a research project on the association between electrocardiographic findings and outcome in COVID-19 patients (PD Dr. F. Regoli).

8) Dermatology (PD Dr. H. Beltraminelli)
Clinical research projects in different fields of dermatology are currently ongoing (Dr. C. Mainetti). PD Dr. C. Mangas is active in the field of melanoma with the recent participation to a Swiss-International retrospective study about markers in patients treated with ipilimumab and a multi-national prospective phase 4 study about target therapy in melanoma (BERING Melanoma). PD Dr. H. Beltraminelli participated to several different national and international multicentric studies (skin lymphoma, Martorell-ulceration, artificial intelligence) and coordinates a project aiming at the development of dermatopathology in Subsaharan Africa. Dr. I. Terrani is following a master's thesis on isotretinoin therapy.

9) Clinical Nutrition (Dr. N. Ossola)
We are involved in clinical research projects on long-term parenteral nutrition (in collaboration with the University of Bern) and on prehabilitation for patients undergoing major abdominal surgery in collaboration with the EOC Department of Surgery (Dr. M. Quarenghi).

>> The list of publications of the EOC Department of Medicine is available on the EOC website at the following link.

1.10 EOC Department of Surgery

Prof. Pietro Majno-Hurst, MD
Head of Department

In 2021, as described below, clinical research activity has further increased in most surgical specialties, giving a clear sign of a successful academic transition of our Department.

1) Visceral Surgery
In 2021, we pursued our clinical research activity through our own clinical trials, through participation in international trials (COVID Surg Cancer, COVID Surg Week), and international registries, and through projects of translational research in collaboration with our lab lead by Prof. Dr. G. Iezzi (See also section 3: **Laboratories for Translational Research (LRT) of EOC**). We also produced a fair number of high quality video-publications on surgical techniques.

In **colorectal surgery** (Prof. Dr. D. Christoforidis, Dr. S. Popeskou, Dr. F. Mongelli et al.), along the lines of the past years, our research projects focused mainly on rectal cancer, and outcomes in minimal invasive surgery. Following findings of the LIBRECA study, the MIBRECA study was launched, aiming at finding correlations between rectal cancer associated microbiome and response to pre-operative chemoradiotherapy. We concluded the RCT on the effect of Ondansetron for the treatment of defecatory dysfunction after rectal resection for cancer (HODOLAR). A new study (MICROBAL), aiming at identifying correlations between the microbiome and this time anastomotic leakage after left colorectal resection was also started. A study comparing fully laparoscopic right colectomy to the conventional laparoscopic technique was concluded. The RCT comparing percutaneous vs. laparoscopic transversus abdominis plane (TAP) block to improve post-operative pain control after colectomy has also been recently concluded. Finally, a study on outcomes after laparoscopic colorectal surgery in octogenarians is under way. In proctology, a prospective study on outcomes with a new technique to treat anal fistulae (VA-LIFT) has been started.

In **bariatric surgery** (Dr. F. Garofalo, Dr. M. Marengo, Dr. F. Volonté, Dr. F. Mongelli et al.) research topics focused on revisional and conversional bariatric surgery, post-operative pathway optimization, the role of microbiota, and new surgical and anesthesia techniques with several ongoing RCTs and prospective studies. The double-blind RCT assessing the efficacy of TAP block for post-operative pain control was successfully concluded. We enroll patients for the SLIM Trial, a Swiss RCT investigating the effectiveness of long and short alimentary limb in Roux-en-Y gastric bypass. Other prospective studies investigating the role of indocyanine-green fluorescence, the long-term effect of gastric pouch resizing, and gut microbiome shift in revisional bariatric surgery are ongoing.

In **robotic visceral surgery** (PD D. La Regina, Dr. R. Pini, Dr. S. Spampatti, Dr. F. Mongelli et al.) several studies are running, such as the RCT comparing erector spine vs. TAP block in patients undergoing robotic-assisted inguinal hernia repair. Other ongoing studies regard surgical techniques, postoperative surgical pathways, and long-term incisional hernia incidence in robotic visceral surgery.

In **hepato-pancreatico-biliary surgery** (Prof. Dr. P. Majno, Dr. A. Cristaudi, Dr. R. Roesel, Dr. L. Bernardi et al.) we focused our research on surgical techniques and innovation. We have developed and described the “Lugano” technique for pancreatico-jejunal reconstruction after pancreas resection obtaining promising results with our first 30 cases. In a clinical trial conducted together with the University of Pisa, we are comparing laparoscopic to robotic liver resections according to a score of procedure complexity. We are participating in the ongoing Bi-Le trial, a multricentric Swiss trial that examines the impact of cholangiography using a white lipid solution to control biliostasis after liver resection, on the rate of post-operative biliary fistula. Finally, we have started a trial that examines the impact of sharing a patient’s biography on final post-surgical perceived satisfaction.

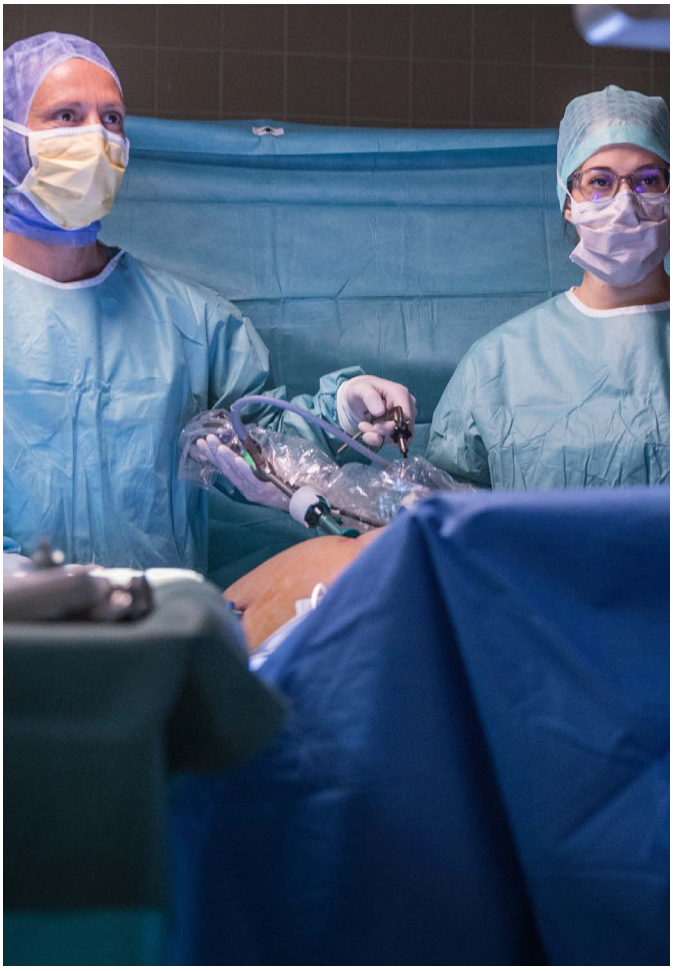
2) Vascular Surgery (Dr. L. Giovannacci, PD Dr. J. Van den Berg, Dr. G. Prouse, Dr. A. Robaldo, Dr. L. Ettorre, PD Dr. H. Stricker et al.)
The COVID-19 pandemic occupied a significant part of our research activity. The extensive daily ultrasound screening that was carried out in all critical stage COVID-19 patients offered relevant results. We published 2 studies covering risk factors and stratification methods for deep vein thrombosis in critical stage SARS-CoV-2 patients. Furthermore, we published one paper reporting the impact that the pandemic had on the treatment of patients with critical limb ischemia and participated in a multicentre study on the impact of the pandemic on the care of patients with chronic and acute aortic disease. We also participated in an update of the European Society for Vascular Surgery guidelines on the Management of Acute Limb Ischaemia in light of the COVID-19. In the field of aortic surgery, one of the research projects aimed at analyzing the 5-year outcome after aortic surgery in relation to the analysis of body composition with dedicated software on pre-operative CT scans. The results of this study may direct future conditioning and better selection before aortic surgery. We also designed a multicenter RCT to test safety and efficacy of Metformin, used in non-diabetic patients, to reduce the growth of abdominal aortic aneurysms (patient recruitment is planned to begin in 2022 with a study duration of 5 years). We participated in a multicentre trial that analyzed the outpatient treatment of the femoropoplitеal district with 4 F or 6 F introducers, to evaluate the outcome of treatment with smaller size introducer sheaths, which will likely set the future trend. Finally, a study analyzing the value of multidisciplinary work by quantifying the relevance of weekly multidisciplinary vascular meetings has been concluded in 2021, showing impacting results.

3) Plastic, Reconstructive & Aesthetic surgery (Prof. Dr. Y. Harder, Prof. Dr. D. Schmauss et al.)
Projects in clinical research: our department is focusing on research that studies the efficacy and quality of different reconstructive procedures after breast cancer surgery. Accordingly, we study the quality of life in oncoplastic breast reconstruction after

extensive tumorectomy (collaboration with Dr. F. Meani; CSSI, EOC) and advantages and disadvantages of pre- and subpectoral implant-based breast reconstruction in a RCT funded by SNSF/ SAKK (collaboration with Prof. Dr. W. Weber, University Hospital Basel). We also participate in a multicentric observational cohort study on immediate breast reconstruction following mastectomy (IRMA: collaboration with Dr. B. Lipp-von Wattenwyl; CSSI, EOC). Furthermore, we evaluate the rate of ischemia-associated delayed wound healing or skin necrosis after repetitive local heat preconditioning of the skin in reduction mammaplasty (collaboration with Prof. Dr. H.G. Machens, Munich). Finally, we study the user friendliness of a newly launched tissue expander for reconstructive breast surgery after mastectomy that is MR-compatible and allows for prepectoral placement despite the need for adjuvant radiotherapy of the thoracic wall and reimbursement policies of Swiss insurance companies for reduction mammaplasty and abdominoplasty in the treatment of symptomatic breast hypertrophy and abdominal skin excess, respectively (2 master-thesis projects USI).
Projects in basic research (MD-PhD project; Dr. A. Weinzierl): ee collaborate with the Institute for Clinical & Experimental Surgery of the Saarland University, Homburg/Saar in Germany (Prof. Dr. M.W. Laschke) to evaluate in small animal models different strategies to improve the microcirculation and ischemic tolerance of critically perfused musculocutaneous tissue of flap tissues, including dietary restriction patterns, phytochemical treatment options and the injection of microvascular fragments. Further, we analyse survival and engraftment patterns of autologous fat transplants and their underlying cellular and molecular mechanisms, as well as influencing factors such as the organism's metabolism.

4) Orthopedics and Traumatology (Prof. Dr. C. Candrian, Prof. Dr. G. Filardo, PhD, PD Dr. M. Delcogliano et al.)
The Orto-Trauma Clinical Research Team, founded in 2017, is now a well-established reality in the EOC research panorama. The aim of the clinical research team of the Orthopaedic and Traumatology Service is to improve the current knowledge as well as the treatment strategies in the field of Orthopaedics and Traumatology. In this light, systematic reviews and meta-analyses are performed to synthesise the existing literature, and innovative clinical trials are planned to increase the strength of the current knowledge and explore new interesting fields. Moreover, the team takes part in national and international multi-centre studies that involve some of the most important research centres in Europe. The research group is also conceived as an opportunity offered to all residents of the Orthopaedics and Traumatology Service of all the EOC Hospitals, to move their first steps or deepen their knowledge in the field of Orthopaedic research.

5) Urology (Prof. Dr. A. Gallina, Dr. N. Fossati, PD Dr. J. Renard et al.)
The Urology service is actively involved in the field of uro-oncology clinical research. In particular, it contributes to several ongoing clinical trials including patients affected by prostate cancer. Recently, a prospective trial evaluating a novel tracer for pre-operative staging with PET/CT scan has been approved for patients affected by high-risk prostate cancer and candidate for radical prostatectomy plus pelvic lymph node dissection. Furthermore, the Urology service significantly contributes to ambitious translational projects, aimed at identifying novel biomarkers for therapy response in newly diagnosed



prostate cancer patients. During 2021, the Urology service has been asked by the Schweizer Krebsbulletin – periodical newspaper of the SAKK – to provide an expert review on the current application of PSA screening for prostate cancer prevention. Finally, the Urology service has become part of two important multi-institutional collaborations investigating the optimal management of patients with prostate cancer recurrence. In 2021, several abstracts from these collaborations have been accepted at the two most important urological international meetings (EAU and AUA), as well as the national Swiss urological congress.

6) Thoracic surgery (PD Dr. S. Cafarotti, PD Dr. M. Patella, Dr. A. Tessitore, Dr. E.M. Minerva et al.)
From the scientific point of view, 2021 was the natural evolution of the previous year. We finalized several projects on thoracic malignancies like lung cancer, mesothelioma and thymic epithelial tumors. Most collaborative works were done with our Swiss partner USZ, but we also embraced more international projects. One of the most important study of 2021 included 7 centers all over the world, it was presented at the American Thoracic Society Meeting and published in one of the most relevant journal of our specialty. We did not forget our local reality, investigating infective pleural disease during the pandemic and in a longer period. We are also interested to provide a critical view on the quality of care offered in our region and we are working on collecting different indicators. In 2021 we definitively reinforced our concept of modern and holistic view of thoracic surgery and we started several projects in collaboration with other specialties and with external cultural and technical partners.

>> The list of publications of the EOC Department of Surgery is available on the EOC website at the following link.

1.11 EOC Department of Gynecology and Obstetrics

Prof. Andrea Papadia, MD, PhD
Head of Department

The EOC Department of Gynecology and Obstetrics is a functional department which includes the Services of Gynecology and Obstetrics of the four hospitals of EOC. Aim of the Department is to coordinate the activities of the services (to concentrate specific pathologies, such as oncologic patients and preterm deliveries, in order to improve clinical outcome) and aligning them to the vision and mission of the hospital trust, with a particular focus on safety and quality of care.

The EOC Department of Gynecology and Obstetrics, which was founded in 2019, is rapidly acquiring a solid scientific profile. From its foundation in 2019 the scientific output of the Department is significant increased over time in terms of scientific publications. Similarly, the number of open clinical trials has increased sharply in the past two years. In 2021 the module Women for the Master of Medicine at USI was completed with success and several master thesis were started.

The Department is part of an international scientific network involving other Swiss and European Universities and Hospitals (these include but are not limited to University of Bern, Sapienza University of Rome, Università dell'Insubria in Varese, Università Milano Bicocca, Università Cattolica del Sacro Cuore Rome, Universidad La Pay in Madrid, Istituto Nazionale Tumori in Milan, Ospedale Sacro Cuore Negrar, Ospedale degli Infermi Biella).

Current areas of ongoing research include:

- Sentinel Lymph node mapping in gynecological malignancies
- Gynecologic oncology surgery and complication rates
- Surgical management of endometriosis
- Gynecologic surgery and SARS-CoV2 infection
- Pregnancy and SARS-CoV2 infection
- Use of a compression device to improve surgical outcome of cesarean section
- Pregnancy and Iodine deficiency
- Breast reconstruction following mastectomy
- Immune landscape and breast cancer
- Axillary management in breast cancer
- Clinical post market application of a Breast Cancer Locator Guidance System
- Use of different devices for the management of urinary stress incontinence

>> The list of publications of the EOC Department of Gynecology and Obstetrics is available on the EOC website at the following link.

1.12 EOC Department of Anesthesiology, Emergency and Intensive Care Medicine

Prof. Paolo Merlani, MD
Head of Department

The EOC Department of Anesthesiology, Emergency and Intensive Care Medicine (DAEICM) is a functional Department. Each of the four hospitals of the EOC has its own DAEICM with a local Director, coordinating the three services (anesthesiology, emergency medicine; intensive care medicine) of his hospital. The DAEICM-EOC headed by Prof. Dr. P. Merlani coordinates and support the local DAEICM for patients' care, medical education (both pre- and postgraduate) and for research purposes. Aim of the Department is to align the twelve services of the DAEICM-EOC to the vision and mission of the EOC, focusing particularly on patient's safety and quality of care. The DAEICM is responsible for the didactic module "Critical Care Medicine" for students at the Master of Medicine of USI. Moreover, the Department encourages and supports students in the compilation of a master's thesis and/or a doctoral thesis. During the first part of 2022 it is expected to finalize the constitution of a dedicated LRU for the DAEICM-EOC. The main aim of the LRU is to support researchers/investigators of the DAEICM-EOC in their research activities from study conception to manuscript submission in a peer review international journal. Each service of the Department has his own research projects, conducted as single center or in conjunction with other Swiss or foreign research centers. The LRU of the Department wants to encourage research projects among the different services, especially at the transition of care. Quality improvements trials and process-variables studies are scarce in medicine and particularly in the acute care setting.

From the different currently research projects of the DAEICM-EOC here we indicate a selection of the most relevant ones:

- Diagnostic accuracy and applicability of POCUS (Point Of Care UltraSound) by specific indications in the three different specialties
- Peri-operative pain management with different modalities: systemic versus local anesthesia
- Chronic pain management of different etiologies
- Application of different regimens of muscle relaxation
- Complications occurring during the COVID-19 pandemic in the critical care population (bleeding and thrombo-embolic events; herpes simplex reactivation; etc.)
- Peri-operative blood transfusion practices
- Cost-effectiveness analysis of different procedures in Anesthesiology
- Approach to the patient with mild traumatic brain injury in the emergency service
- Communication's skills of doctors for outpatients in the emergency service

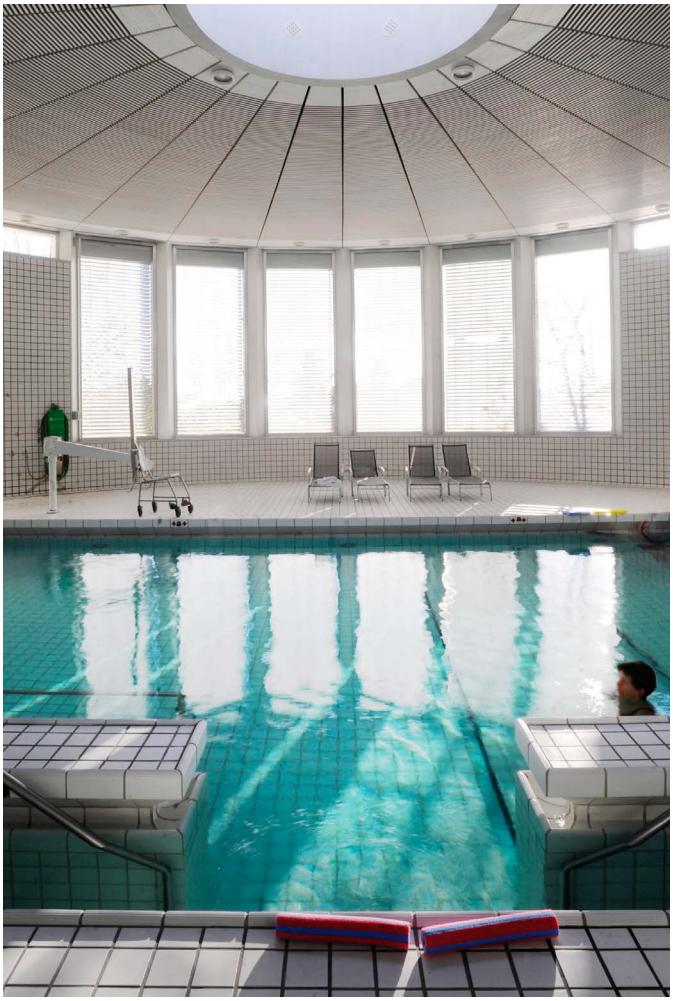
>> The list of publications of the EOC Department of Anesthesiology, Emergency and Intensive Care Medicine is available on the EOC website at the following link.

As mentioned above the newly formed LRU of the DAEICM-EOC is expected to further improve the quantity and the quality of research. Different projects are already on track, like: application of artificial intelligence and machine learning technique for early identification of nosocomial infection in the intensive care setting; impact of delayed transfer of patients from the ward to the ICU; predictors of different transfer-times form the emergency to the ICU; improving communication's skills in the emergency service. Furthermore, the LRU wants to support nurse-leaded research.

2. Other EOC Services

2.1 EOC Rehabilitation Clinic (CREOC)

Nicola Schiavone, MD
Medical director



CREOC, the Rehabilitation Clinic belonging to EOC, takes care of patients with the aim of improving their quality of life. CREOC work is based on a biopsychosocial model: this means that we try to improve together biologic, psychologic and social field. The goals of our job are: to reduce the pain, to improve the range of motion and the strenght of legs and arms, to improve breathing capacity and to make the patient more physically performant.

Together with Hildebrand Clinic, we belong to REHA TICINO, that is the main cantonal organization dealing with rehabilitation. CREOC inpatient are admitted in Faido and Novaggio, where they can follow differents predefined rehabilitation programs, depending on their main illness.

During Coronavirus pandemic, CREOC in Faido was dedicated to COVID-19 affected patients, while CREOC in Novaggio was dealing with COVID-19 affected patients after critical care hospitalization.

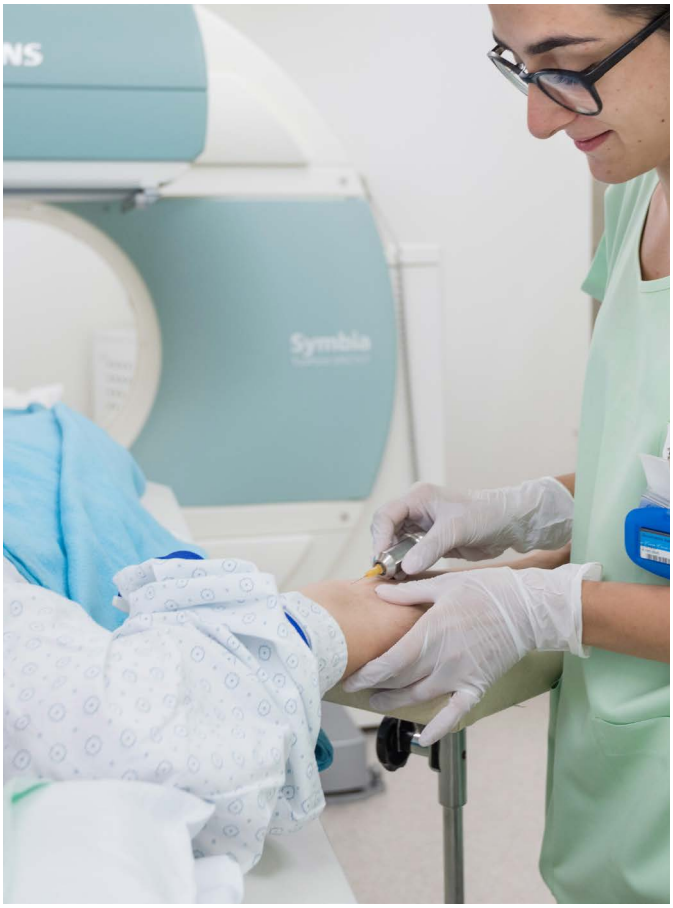
CREOC manages also outpatient in different EOC hospitals and provides musculoskeletal rehabilitation in several hospital wards.

Inside CREOC there are interest groups dealing with posturology, pelvic floor rehabilitation, pulmonary rehabilitation and recently COVID-19 affected patients in rehabilitation. These interest groups were also involved in research activities in 2021 publishing book chapters and scientific articles and presenting the results of their research in several national and international congresses.

>> The list of publications of the EOC Rehabilitation Clinic is available on the EOC website at the following link.

2.2 EOC Nursing Research Centre

Annette Biegger, MSc
Head of EOC Nursing Division



In recent years, the EOC Nursing Division has promoted organisational and cultural improvements in order to advance the quality of care. This has led to changes concerning the organisation and philosophy of care, as well as the electronic documentation of nursing activities. In addition, great attention has been given to the advancement of nurses' knowledge and skills, which resulted in the implementation of the Nurse Specialist and Clinical Expert roles. These professional figures are crucial for the development of advanced nursing skills and for the clinical governance of professional activities. Furthermore, given the increasing complexity of patients and health systems, new nursing roles are emerging at the EOC, such as the advance practice nurse. To support this process, investment has also been made in people with specific research training (PhD) and dedicated offices.
In the medical field, knowledge rapidly evolves: something that was effective yesterday may no longer be effective today. Hence the importance of developing research studies focused on the nursing field, to provide nurses with new evidence and develop new expertise. Polit & Beck (2006) define nursing research as a "systematic inquiry designed to develop knowledge about issues of importance to nurses, including nursing practice, nursing education, and nursing administration".
Nursing research activities, with dedicated resources, were first registered at IOSI in 2010 and are annually documented in the EOC Annual Scientific Report and EOC Nursing Activity Annual Report. In September 2016, the Centre of Competence for Nursing Research was established within the EOC Nursing Division with the following mission: to promote the development and quality of nursing care in response to the health needs of the population, promoting innovation and nursing research in all clinical realities of the EOC and maintaining a close link between research (theory) and nursing care (practice).

In the coming years, the plan is to expand the network of colleagues and/or nursing research offices within the EOC sites. Today, a research office and/or nurse are active across different sites, including IOSI, IPSI, ICCT, Bellinzona and Lugano regional hospitals (ORBV and ORL). At the moment, in each of these hospitals/institutes there is at least a nurse dedicated to nursing research: Angela Tolotti at IOSI, Sarah Liptrott at ORBV, Elena Corina Luca at ORL, Colette Balice-Bourgois at IPSI and Michele Villa at ICCT. Laura Moser works as data manager for the IOSI research team. From September 2021 Loris Bonetti is the new head of the EOC Centre of Competence for Nursing Research, in which Laura Steiner works as research nurse: he has substituted Dario Valcarenghi, who retired. Nurses active in research are now part of the "CooRI" team, which coordinates EOC research activities and research development plans in the nursing field.

The following are the main activities the research network is responsible for:

- To develop training courses on research topics to be offered to all EOC nurses, but especially to nurse specialists. This is critical to create essential synergies with clinical realities and the network of clinical experts and clinical specialists within EOC.
- To promote and support the cultural and scientific production by colleagues (preparation of abstracts, posters, journal articles, research projects. etc.).
- To collaborate with colleagues with managerial roles and colleagues from clinical governance for the collection and/or critical analysis of data, the dissemination of evidence and the development of internal guidelines.
- To develop and implement nursing research projects, using either quantitative, qualitative or mixed methods.
- To develop and maintain collaborations with national and international nursing research associations and networks.

Research questions usually arise from needs identified by nurses working in clinical practice or holding managerial roles and are answered through studies, which can be carried out with internal or external resources and funding. Internal resources are mainly used to conduct 'action-research' studies-planned and developed together with nurses involved in clinical practice and in the context of interest, aimed to explore a specific clinical or professional phenomenon in order to change and improve nursing practice. Such studies are 'context-related' and therefore results can be transferred to similar realities, but usually cannot be generalized. Despite this, such action-research studies are deemed important as they require a proactive role from professional teams and stimulate reflective thinking and critical review of their professional practice. Other studies conducted, especially those externally funded, tend to focus on phenomena of clinical or professional interest of a more general nature.

The following are the research studies currently active, funded by EOC or other funding bodies:

- A phase III randomised controlled clinical trial to verify the efficacy of a patch (Mepitel Film) in reducing the incidence of skin lesions for patients with breast cancer under radiotherapy treatment. This is a multicentre trial, under our responsibility, conducted in collaboration with Hirslanden Klinik in Zurich.
- An observational cohort study to detect the incidence of complications related to the use of three central vascular catheters (AVI-PICC-CVC) in cancer patients.
- A mixed-methods study (NuBE Project), in collaboration with Università Cattolica of Milan, which aims to identify which relational and communicative behaviours of nurses in oncology promote patients engagement, in order to develop a reliable psychometric tool to identify such behaviours.
- A pilot project to test a complex intervention delivered by oncology nurses aimed at promoting a healthy lifestyle among cancer patients. The intervention is based on patient engagement theory. The study will be conducted in partnership with Università Cattolica of Milan.
- A mixed-methods study which aims to investigate nursing care provided to patients affected by COVID-19; the study, in particular, focuses on the perspective of patients, family members and nurses.
- Another study currently ongoing in collaboration with SUPSI is exploring the effectiveness of continuing nursing education (DAS) on the quality of nursing care.
- An observational study on the introduction of sonography in nursing practice in the urology department of the San Giovanni Hospital, with the aim of developing professional skills and improving nursing care (appropriateness of bladder catheterisation).
- An investigation of a Mindfulness Based Stress Reduction program was held in ORBV, which was open to participants from all professional categories. The study explore the effect of the program on mindfulness practices, stress and psychological well-being.

Other studies are being planned in collaboration with colleagues working in the various clinical settings.
In 2021 the first EOC nursing research congress took place in Lugano, in which 58 abstracts from EOC nurses were presented, meaning that nursing research is fervent at the EOC. The event was very successful and appreciated by the EOC nurses. In 2022 the second edition will take place on the 12th of October.

It is also important to underline the great participation of many EOC nurses at 10th Research Day in Human Medicine of Southern Switzerland, in which a specific parallel section was dedicated to nursing research projects. Three nursing projects were also presented during the plenary part of the conference.

Moreover, in 2021, the collaboration between the EOC Competence Centre for Nursing Research and the SUPSI Competence Centre for Health Practices and Policies was officially consolidated. This collaboration between clinical and academic fields will be strategic for the development of nursing research and the nursing profession at the EOC and in the Ticino context.

>> The list of publications of the EOC Nursing Research Centre is available on the EOC website at the following link.

2.3 EOC Information and Communications Technology Division

Marco Bosetti
Head of EOC Information and Communications Technology Division (ICT)

The “Information and Communications Technology Division” (ICT) is the IT department of EOC. With more than 90 employees, it covers the traditional IT services like infrastructure, operations and support. Moreover, it implemented in-house and maintains the Geco that is the clinical information system of EOC since 2007. For this reason, ICT has extensive experience in integration and analysis of clinical records.

The ICT is actively involved in research activities mainly through his new dedicated team named Datascience and Research that provides both technical and consultant expertise. Besides internal resources, the ICT strategic development foresees the establishment of collaborations with external organizations. The collaboration with the Swiss AI Lab (IDSIA) aiming at applying cutting edge artificial intelligence techniques on EOC data was established in 2019. Since 2019 the ICT is part of the Swiss Personalized Health Network (SPHN) to develop IT tools in the field of personalized medicine.

ICT is the central point for extraction and analysis of clinical data supporting EOC researcher and Master of Medicine students in teaching activities, scientific publications and writing of funding proposals. The pipeline of running research projects includes a multicentre radiomics project (project SPHN-Imagine in collaboration with USZ), dialysis treatment optimization (project Interreg-InterACTIVE-HD 2.0 in collaboration with POLIMI), various artificial intelligence projects in collaboration with IDSIA (bioinformatics to evaluate the kidney senescence, analysis of perinatal depression clinical study data), multicentre benchmarking of overprescription (Choosing Wisely campaign), analysis of patient blood management, telemedicine applications, chronobiological work shift planning in collaboration with Polypoint AG.
The suite of research software/infrastructure solutions developed and maintained by ICT includes an electronic case report forms (e-CRFs) to manage clinical trials, an event driven direct data entry database to manage both biobanks and surveys, a Clinical data warehouse, tools to anonimize clinical narratives and a high throughput cluster for -Omics/RNA seq data analysis.

>> The list of publications of the EOC Information and Communications Technology Division is available on the EOC website at the following link.

3. Laboratories for Translational Research (LRT) of EOC

3. Laboratories for Translational Research (LRT) of EOC

Prof. Andrea De Gottardi, MD PhD
Director

The Laboratories for Translational Research (LRT) of EOC are dedicated to applied biomedical research by a multidisciplinary approach and aim to improve health and to understand human diseases. Our research teams are interdisciplinary and include biologists, biochemists, physicians, pharmacologists, technicians and students. We use cutting edge technologies ranging from biomolecules to cellular cultures and organoids, to organs on a chip from animal and human origin. We are committed to work with animal models only when strictly unavoidable. The administrative team supports all research groups in the management of all administrative and financial tasks. In addition to our focus on translational research, we are dedicated to teaching and training young scientists to foster their career in basic and clinical research. Open positions for master and doctoral thesis are available.

The Laboratories for Translational Research were born in 2019 from the initiative and support of EOC and are funded by private donations, by charitable organizations, by biotech companies and by foundations for scientific research. In October 2021 the laboratories moved to the new research building located in via Francesco Chiesa 5 in Bellinzona. More information is available at the following link: **https://lrteoc.ch/.**

Laboratory for cardiovascular theranostics (Prof. L. Barile)

Role of senescence in cardiovascular diseases

- In vitro model of senescence in human cardiomyocytes: our lab is active in studying the role of senescence in cardiovascular diseases. In particular, an in vitro model of premature senescence in human cardiomyocytes (functional cardiac cells) was developed using the Induced Pluripotent Stem Cells (iPS) technology. This model is a unique platform for the study of cellular mechanisms lying behind senescence-associated cardiac diseases in human. The platform will be the basis of an important study aiming to evaluate the susceptibility of senescent cardiomyocytes to SARS-CoV-2.
- In-vivo stress-induced senescence: the role of senescence is also studied in-vivo in animal model of myocardial infarction. The acute ischemic event induces the formation of fibrotic tissue and the accumulation of senescent cells that release factors that can alter the functionality of heart cells. This may contribute to exacerbate the necrosis process resulting from the acute ischemic event. We aim to studying possible “senolytic” and/or “senostatic” approaches to ameliorate senescence-associated damage in the heart.

Exosomes and extracellular vesicles as liquid biopsy

- Extracellular vesicles (EV) as biomarkers: recently, our lab has completed a series of studies performing molecular analysis of the biofluid-derived extracellular vesicles. We profiled surface protein and membrane lipids of plasma and serum-derived EV. The EV-based diagnostic test standardized at our lab has been evaluated as diagnostic tool in acute cardiac rejection following heart transplantation to discriminate different types of rejection as well as for prognosis of severity of rejection. We recently evaluated the lipid composition of circulating EVs and their diagnostic potential after myocardial ischemia. Very recently we used the profiling of EV as prognostic tool for predicting severity in COVID-19 patients.
- Role of EV as mediators of inflammation: our lab has made important advances in research studying the role of circulating EVs resulting from the inflammatory process following an acute ischemic event of the myocardium. We proved that inflammatory EV secreted by polarized macrophages carrying inflammatory cytokine such as IL-1α, IL-1β e have direct cytotoxic effects on heart cells.

Regenerative medicine technologies research group (Prof. M. Moretti)

Our lab adopts an interdisciplinary approach, at the intersection of engineering, biology and medicine, aiming at regenerating biological tissue substitutes in vitro. Our major competences are represented by advanced technologies such as biofabrication and microfluidics, enabling tools for the generation of innovative constructs replicating the complexity of in vivo biology. In more detail, in our lab we generate 3D

tissues based on cell co-cultures mainly of human origin, embedded in suitable biomaterials and cultured in engineered environments providing biophysical and mechanical stimuli. Our lab mainly focuses on musculoskeletal tissues, producing biological replicates with a scale ranging from microfluidic devices to macro-scale constructs of clinically relevant dimensions. The microarchitecture of physiological tissues can be hierarchically replicated, spanning from mimicking the interface between different tissues (e.g. tissues composing the joints or the tendon bony insertion) down to the reproduction of microscale tissue features (e.g. bone trabeculae or microvascular networks). From a translational point of view, smaller scale devices are currently being improved towards high throughput platforms usable for drug screening purposes and testing of personalized therapies, whilst bigger scale constructs could be translated to biological substitutes usable in clinics for the regeneration of diseased tissues. In particular, we are working on reproducing bone, cartilage and skeletal muscle constructs, to improve drug discovery and to personalize available therapies in fields such as bone tumors, osteoarthritis and muscle fibrosis. In the field of bone tumors, we demonstrated that our models were able to reproduce the effects of known anti-tumor drugs on cancer cells better than simple 3D cancer cell models. We are also working on improving the mechanical properties of the support matrix through bioprinting techniques, and on increasing the throughput of our system to enable drug screening with a higher throughput. About skeletal muscle, we are studying models able to replicate the main features of fibrotic muscle tissue, to provide advanced tools to researchers searching for new therapies. The currently generated models have shown that they can replicate the organization of muscle fibers, the presence of a vascular network similar to that present in vivo, and better reproduce the altered production of extracellular proteins in pathological conditions as compared to the corresponding 2D models. In our lab we also develop patient-specific multi-tissue 3D models, such as microfluidic models of an osteoarthritic joint, that allow to compare different possible therapeutic approaches for the single patient and can represent an innovative instrument for the development of personalized therapeutic regimens for osteoarthritis and other orthopedic pathologies.

Gastroenterology and Hepatology research group (Prof. A. De Gottardi)

One of the main research interests of the gastroenterology and hepatology group is the gut-liver axis. We investigate the fundamental principles of host-microbe interactions in the gut and the way how they can affect liver diseases and the development of portal hypertension. The gut and the liver communicate in a bidirectional way and influence each other in physiological and/or pathological conditions. This communication occurs through the portal circulation (that carries gut-derived products to the liver) and through the biliary system (that transports the bile from the liver to the intestine). In chronic liver disease, disturbances in the gut-liver axis may lead to bacterial translocation from the intestinal lumen to lymph nodes and to extra-intestinal organs. This may over activate the immune system, promoting the progression of liver disease. The main aim of our research is to understand how the disruption of the gut mucosal and vascular barrier occurs and how this may affect the course of liver diseases and the progression of portal hypertension. We are moreover interested in discovering the mechanisms that are responsible for the development of fatty liver disease. Since no efficient treatment is currently available, we aim to understand the role of Paneth cells, a particular family of intestinal immune cells, in the regulation of lipid metabolism and lymphatic circulation. Intestinal and mesenteric lymphatic networks are the largest and major routes for dietary fat uptake and transport, re-circulation of interstitial fluids and immune cells along the gut-liver axis. We use experimental models of acute or chronic liver disease and portal hypertension, intestinal organoids and cell cultures together with cutting edge molecular biology technologies.

Cellular and molecular cardiology research group (Prof. G. Vassalli)

The research group of Prof. Vassalli has investigated the biological role and the therapeutic potential of secreted extracellular vesicles (EV), particularly of nanosized vesicles of endosomal origin called exosomes, in cardiovascular diseases, with a focus on acute myocardial infarction. Studies from the lab showed that EV secreted by human cardiac mesenchymal-derived progenitor cells were endowed with beneficial biological activities, as demonstrated in both in vitro and in vivo myocardial infarction models and chemotherapy-induced cardiotoxicity models. These properties included cytoprotective, pro-angiogenic, anti-fibrotic, and pro-proliferative effects in cardiomyocytes. In collaboration with the Department of Heart Surgery at Zurich University Hospital, we also demonstrated that such EV significantly reduced infarct scar in a preclinical model of acute myocardial infarction in pigs. Furthermore, our research group is actively studying the role of miRNA carried by cardiomyocyte derived-extracellular vesicles in heart development. Particularly, we aim to understand the physiological signaling that unlock cardiomyocyte proliferation to the development of new therapeutic strategy in myocardial regeneration. Our lab has a major expertise in EV isolation and characterization. In vitro and in vivo model for EV functional evaluation has been developed and optimized in the past years. In vitro EV are tested on cardiomyocyte (from neonatal mouse or human iPS-derived), cardiac fibroblast (mouse and human) and on a human heart organoid (iPS-derived cardiomyocyte and cardiac fibroblast). The use of 3D culture is a cutting edge technique that allow to perform experiments taking into account the synergistic effect of cardiac cells under different stimuli. In vivo acute myocardial infarct models were used for studying the effects of human cardiac mesenchymal-derived progenitor cells on ischemic cardiac injury. An in vivo model of chemotherapy-induced cardiotoxicity was also developed.

Surgical research group (Prof. G. Iezzi)

The research activity of our group focuses on the interaction between gut microbiota and immune system in gastrointestinal diseases, primarily colorectal cancer (CRC), or in systemic diseases of surgical relevance, such as obesity. Starting from the analysis of the gut microbiota and the immune contexture in human samples, our research group aims at:

- identifying novel biomarkers predictive of long-term response to surgical or medical treatment;
- identifying patients at high risk of recurrence who may benefit of additional therapies;
- developing novel therapeutic concepts based on gut microbiota conditioning through administration of selected probiotics or targeted antibiotics.

The gut microbiota consists of trillions of microorganisms critically shaping immune system development and immune responsiveness, through their effects on host metabolism. In pathological conditions associated with increased gut permeability, such as cancer or

inflammatory diseases, defined species of the gut microbiota translocate from the lumen into the lamina propria of the intestinal mucosa and therefore directly interact with epithelial cells and infiltrating immune cells. Recent studies of our research group in CRC have demonstrated the capacity of bacterial components of the gut microbiota to induce, upon direct contact with tumor cells, expression of chemokines recruiting into the tumor bed immune cells predictive of favorable clinical outcome. Analysis of tumor-associated microbiota in human CRC samples has led to the identification of a group of bacteria positively associated with high immune cell infiltration and prolonged patients' survival. Immunomodulatory properties of identified bacteria and their capacity to promote antitumor effects are currently being investigated in in vitro and in vivo models. On the other hand, defined bacterial species enriched in CRC tissues have been found to mediate pro-tumorigenic effects. In particular, Fusobacterium nucleatum, is associated with a poor response to chemotherapy and unfavorable prognosis. In collaboration with IOSI, a clinical study has recently been initiated, to evaluate the effectiveness of pre-operative antibiotic therapy with metronidazole to reduce tumor colonization by Fusobacterium nucleatum in patients with CRC undergoing surgery. A more recent project related to obesity, aims at characterizing microbial species present in the visceral fat of obese patients and their potential association with long-lasting effectiveness of bariatric surgery. In collaboration with the Service of Infectious diseases and ISFSI, our research group has also evaluated the impact of the gut microbiota composition on immune responses to SARS-CoV-2 in COVID-19 patients and in healthy subjects undergoing vaccination.

Neurodegenerative disease research group (Prof. P. Paganetti)
Protein conformation disorders: abnormal protein conformation, deposition and proteotoxicity are common traits of progressive degenerative disorders of the brain causing relatively frequent diseases but also rare inherited syndroms. The protein Tau is involved in the development of several brain disorders, most prominently Alzheimer's disease, and less frequent progressive tauopathies, including frontotemporal dementia and parkinsonism linked to chromosome 17 caused by mutations in the gene encoding for Tau. The disorders are associated with the brain deposition of tau in fibrillary tangles. When deposited Tau presents several characteristics modifications such as hyperphosphorylation and a pathological conformation. How this occurs and causes neuronal dysfunction is poorly understood, but the presence and distribution of tangles correlate well with the cognitive loss observed in patients afflicted by the disorder.

Nephrology research group (PD P. Cippà)
The function of the kidney depends on the precise organization and coordination of more than 30 cell types, forming the functional units called nephrons. A variety of clinical conditions, such as diabetes, drug toxicity, and autoimmune diseases, can damage kidney cells and alter the balance necessary for the organ to properly function. Since the kidney loses the ability to generate new nephrons after birth, the maintenance of renal function after kidney injury depends on the compensatory adaptation of the remaining nephrons, and the ability of the kidney to repair damaged nephrons. Unfortunately, this process is often incomplete and can result in the persistence of altered cells and a dysfunctional tissue architecture, which contribute to the progression of renal disease towards renal failure. In this stage the kidney damage is irreversible, and the patient rely on dialysis or kidney transplant to survive. Our research aims to characterize and better understand the biological processes of kidney repair. The goal is to support functional tissue regeneration processes and prevent the progression to chronic kidney disease.

Parkinson research group (PD G. Melli)
Parkinson's disease (PD) is a chronic progressive neurodegenerative disease associated with intra-neuronal accumulation of aggregated alpha-synuclein (α-Syn) protein, but unfortunately current knowledge still does not address the underlying pathogenic mechanisms. Consequently, PD lacks both an effective causal treatment and definitive early diagnostic criteria. In the recent years a large amount of evidence has shown that peripheral tissues like skin autonomic nerves, gastro-intestinal mucosa, salivary glands show immunoreactivity to pathogenic forms of α-Syn. Thus, peripheral tissues, that can be easily biopsied, contain nervous tissue prone to the pathology, and bear potentially important information on disease mechanisms. Our laboratory has a strong translational attitude and aims to set-up novel pathway biomarkers of disease by analyzing skin biopsy and peripheral fluids via advanced new biotechnology. Our group has published several papers on the detection/characterization of α-Syn and its pathogenic species in the skin of PD and other neurodegenerative diseases like atypical parkinsonisms plus we demonstrated that PD patients present a somatosensory small fiber neuropathy that correlates with disease duration and progression. More recently we published several papers on the specific profile of surface proteins of blood- and CSF-derived extracellular vesicles (EVs), which stratifies patients with PD and atypical parkinsonisms. These EV markers are related to circulating inflammatory and immune cells. We are now profiling prodromal and early phases of disease to identify specific signature and we are investigating how peripheral inflammation and immune dysregulation can contribute to brain neuronal cell death in PD. These projects take advantage of a biobank and clinical database for PD and atypical parkinsonisms that the PI Giorgia Melli established at INSI in Lugano since 2015.

Pathology research group
The Pathology Research Group is actively involved in various research projects that aim to identify new methods to be introduced into routine diagnostics or to identify new markers that can be used both in prognosis and in predicting the efficacy of chemotherapeutic treatments: research is essentially aimed at the molecular characterisation of diseases, mainly those in the field of oncology.
For more information see also chapter 1.8 **Cantonal Institute of Pathology**

>> The list of publications is available on the EOC website at the following link. LRT-EOC publications are included in the EOC Institute/Department with which the concerned laboratory is affiliated.

4. Research Services

4.1 Clinical Trial Unit EOC

Prof. Alessandro Ceschi, MD, MSc
CTU-EOC Director

The mission of CTU-EOC is to promote and increase clinical research within EOC by offering high quality services for the implementation and conduction of clinical trials in all fields of medicine ensuring the application of national and international regulatory requirements.
The activity of the CTU-EOC has increased since its inception in 2012, thanks to the consolidation of internal collaborations with the EOC Institutes and Departments and the network with the Local Research Units (LRUs), as well as external collaborations, and thanks to the strengthening of some services such as biostatistics, data management, data science, and proof reading.

Since 2020, the CTU-EOC is a full member of the Swiss Clinical Trial Organization (SCTO), which is a not-for-profit Organization acting as the central cooperation platform for patient-oriented clinical research in Switzerland, and includes the CTUs of the University hospitals and cantonal hospital St. Gallen.

During 2021, the CTU-EOC took in charge 51 projects performing different activities including the coordination of multicenter trials. The most requested service was the development of databases, electronic case report forms (eCRFs), followed by the monitoring and the submission to Regulatory Authorities. In 2021, an increase in projects dealing with health-related data and biological samples occurred (21 out of 51), while projects on drugs and medical devices decreased slightly.

The introduction in 2021 of the general consent coupled with the creation in 2019 of the EOC Biobank promoted the initiation of research projects on biological data and samples (non clinical studies).

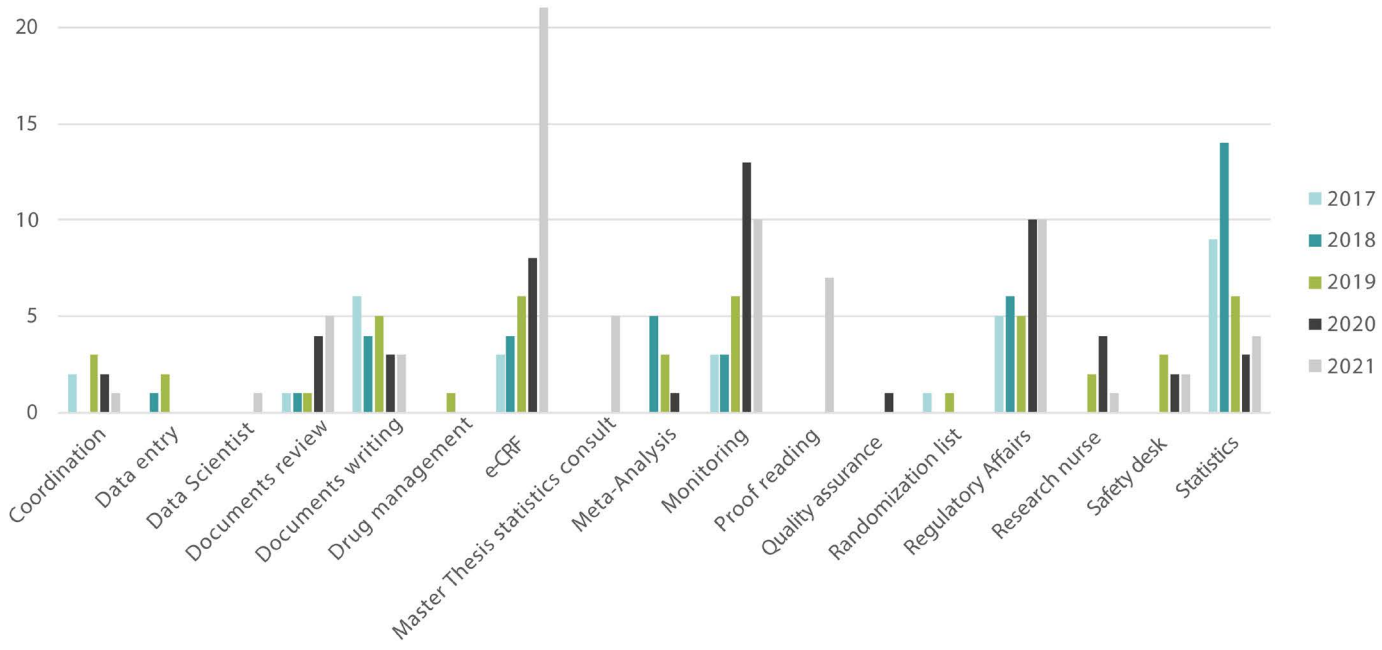


Figure 1: *Services provided by the CTU-EOC in the last 5 years*

Further to provide the whole range of competences required to support a clinical study, CTU-EOC also provides individual support to students, particularly of the USI Faculty of Biomedical Sciences, who have to perform their master or doctorate thesis.

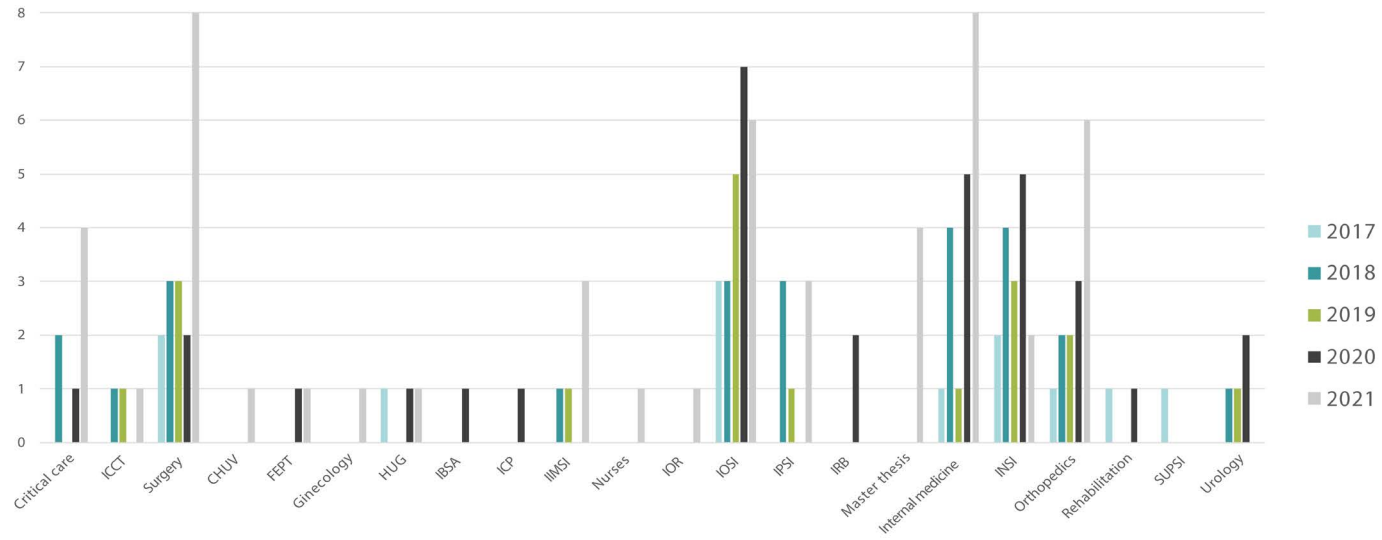


Figure 2: *Collaborations of the CTU-EOC in the last 5 years*

Abbreviations not mentioned in the text: CHUV: Centre hospitalier universitaire Vaudois; IBSA: Institut Biochimique SA; ICCT: Istituto Cardiocentro Ticino; ICP: Istituto Cantonale di Patologia; IIMSI: Istituto Imaging della Svizzera Italiana; IOSI: Istituto Oncologico della Svizzera Italiana; IPSI: Istituto Pediatrico della Svizzera Italiana; INSI: Istituto di Neuroscienze Cliniche della Svizzera Italiana

In 2021, some collaborations with researchers outside EOC also started, e.g. with Hôpitaux Universitaires de Genève (HUG), Fondazione Epatocentro Ticino (FEPT), Istituto di ricerca in Biomedicina (IRB), Institute of Oncology Research (IOR), and Scuola Universitaria Professionale della Svizzera italiana (SUPSI).

Education

Despite the limitations due to COVID-19, CTU-EOC was able to maintain the educational program in clinical research with the second highest number of participants ever recorded. CTU lectures consisting in online training sessions on current specific research topics were introduced. The courses given within the PhD programs of the Faculty of Biomedical Sciences at USI are also fully integrated into the CTU-EOC educational program and are offered in English in the spring session and in Italian in the fall session. CTU-EOC actively contributes to the SCTO educational platform, ensuring a constant exchange and update in the field at the national level.

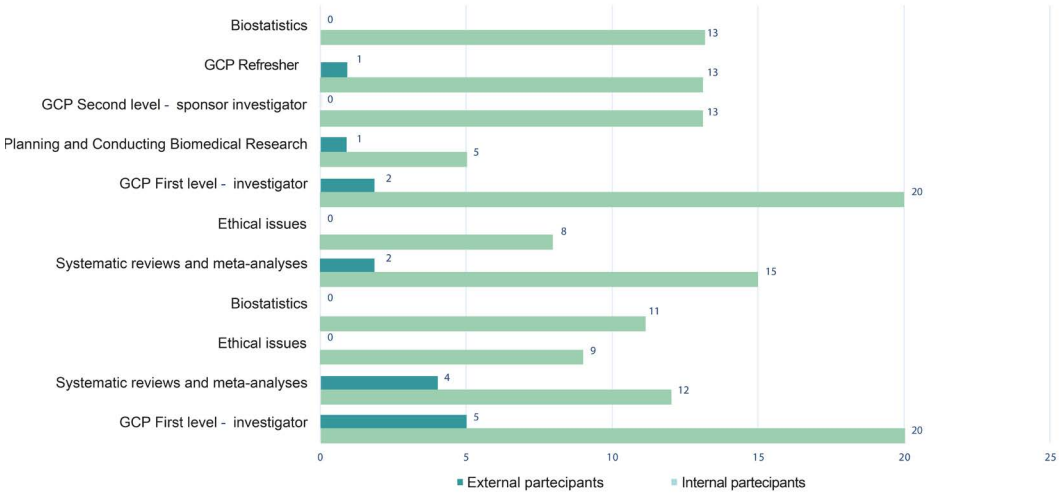


Figure 3: *Courses organized by the CTU-EOC in 2021*

Events

CTU-EOC, in collaboration with the AFRI EOC and the USI Faculty of Biomedical Sciences, organized the 10th Research Day in Human Medicine of Southern Switzerland, with special anniversary keynote lectures and a press conference on the launch of the EOC-USI Research Fund. The event was also part of the 25 years celebration of the University. The participation has constantly increased over the years, both in numbers of abstracts submitted and in number of attendees (321 in 2021).

More information are available at the following link:
www.ctueoc.ch/giornata-della-ricerca/

>> The list of publications of CTU-EOC is available on the EOC website at the following link.

4.2 Grants and Fundraising Unit

The Grants and Fundraising Unit is part of the AFRI EOC. The office was established in 2021 in order to optimize the process of acquisition of third-party funding for EOC researchers. The office offers personal guidance and administrative support on acquiring and managing selected national and international research funds.
Private third-party funding in the form of grants or donations for research projects encourages talented researchers working on innovative projects aimed at ensuring effective, appropriate, and efficient health treatments.
EOC and USI have joined forces to create the EOC-USI Research Fund, whose mission is to promote biomedical research and enhance the results of research conducted by researchers active at the two institutions.
Supporting the progress of scientific research means being aware that research and the investments allocated to it affect all of us.

Thanks to your precious contributions, we can:

- improve the quality of health care in the territory
- meet the needs and requirements of patients and their families
- train the medical and health personnel of tomorrow

Whether you are a private individual, foundation, business or researcher – we are at your service, advising and providing support on any matter related to philanthropic commitment and private third-party funding at EOC.

For more information:
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4.3 EOC Biobank

In recent years there has been an evolution in performing research. If before it was mainly oriented on data analysis, and less on translational studies, now a research acquires more value if clinical data are also associated with genetic and molecular data.

A Biobank is a non-profit service unit, regulated by international guidelines, that collects and distributes biological material in an organized manner. Biological material can be tissue or human biological fluids such as blood, saliva, urine, and cells, including all molecular fractions (proteins, RNA, DNA, etc.) derivable from them, from healthy subjects or those affected by disease. The biological material stored in biobanks is valuable material because it allows having available in a short time a significant number of samples. In order to perform more easily research projects in particular areas, such as rare diseases, it is important to promote a network of biobanks accessible to researchers and whose samples have a quality standard according to pre-established and shared criteria. In fact, the biobank, as opposed to a basic repository, collects and stores samples by applying quality standards that ensure the integrity of the sample throughout its lifecycle and allow the association of clinical data to support its context.

The EOC Biobank is an operational management entity that collects, stores and distributes biological material ensuring the highest quality standards required by international guidelines for biobanks and thus ensures:

- Quality and integrity of the sample throughout its life cycle
- Operator safety
- Donor confidentiality
- Application of current regulations
- Traceability of biological samples and health data

The close collaboration between the Institute of Laboratory Medicine (EOLAB), the CTU-EOC and the ICT Division of the EOC has allowed to obtain in 2020 the NORMA label issued by the Swiss Biobank Platform.

Since its opening in September 2019, the EOC Biobank has received 6 collections, 5 related to specific projects and 1 related to the COVID-19 seroteca.

In order to achieve greater benefit of the biobank, the use of the general consent for research purposes is strongly supported by stakeholders. The EOC General Directorate engaged its introduction in all its infrastructures at the beginning of 2021.

The EOC biobank is accessible not only to EOC researchers but to all research groups interested in benefiting from a dedicated infrastructure for the collection and storage of biological material, as well as for their use.

For more information:
Marco Cantù
EOC Biobank Coordinator
Via Mirasole 22A
6500 Bellinzona, Switzerland
Tel. +41 (0)91 811 17 77
biobanca@eoc.ch

4.4 Intellectual property

Intellectual property (IP), and related rights, indicates a system of legal protection to protect creative and inventive activities from commercial abuse and illicit reproduction. The significance of intellectual property is primarily of commercial nature.
EOC promotes the development of scientific knowledge and the enhancement of the results of research activities, also through the transfer of technology related to the intellectual creations of EOC researchers. All inventions and any other innovation likely to be the subject of an industrial patent (or similar title related to intellectual property) that has a patrimonial value and is susceptible of exclusive rights are governed by the EOC regulation on intellectual property (last revision: December 2021).
The EOC Intellectual Property Commission (IP Commission) is in charge of the implementation of this regulation. This commission is composed by collaborators of the EOC General Directorate. The USI Technology Transfer Manager is also a member of this commission and supports its activities. The IP Commission has the competence on the protection and enhancement of inventions or potentially patentable and / or otherwise protectable inventions. The IP Commission is required to meet every time there is a request for the patentability of an invention or any subject of intellectual property.

4.5 General consent for research purposes

In 2021, the AFRI EOC started the introduction of the General Consent for for research purposes in the EOC Institutes and Departments.
A large part of research is based on patients' personal health data contained in their medical records, such as laboratory test results, treatments administered and genetic predispositions. All the biological material collected in the hospitals and no longer required for treatment is also very important for research purposes.
Patients can make a contribution to the research by agreeing for their clinical data and/or biological samples to be stored, sent to third parties and reused for research purposes, subject to approval by the competent Ethics Committee. Through the introduction of the General Consent for Research in the EOC hospitals, the patients may now give or not their consent on the use of their personal health data and biological samples for research purposes.

For more information:
Direzione Generale EOC
Ufficio del Consenso Generale, AFRI EOC
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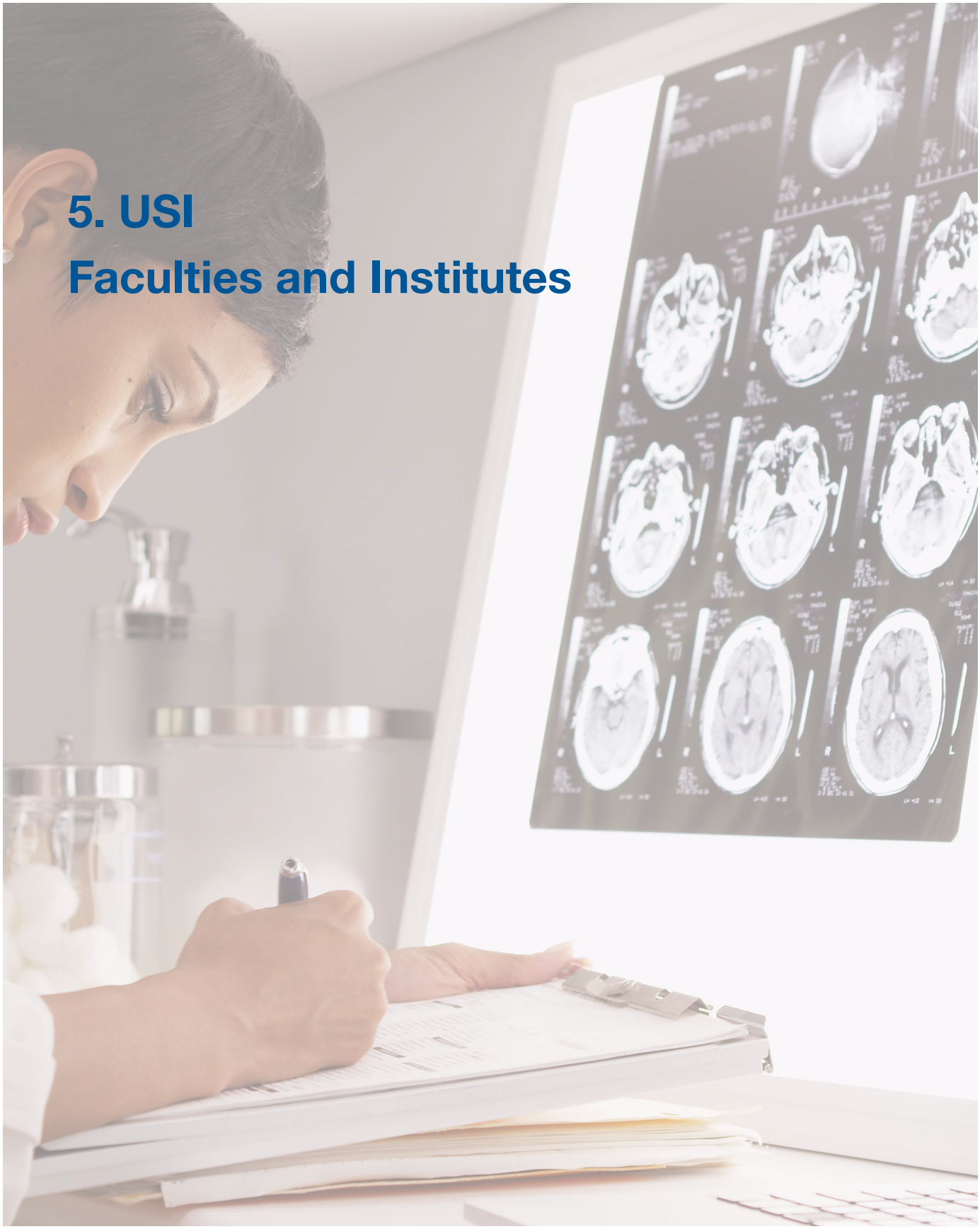
Tel.: +41 (0)91 811 12 12
E-mail: info.cg@eoc.ch



5. USI
Faculties and Institutes

Research activities in biomedical sciences at USI are mostly organized within the Institutes of the Faculty of Biomedical Sciences, but also comprise more interdisciplinary activities in domains of computational sciences, health economics, and health communication in cooperation with the Faculties of Informatics, Economics, and Communication, Culture and Society.

5.1 USI Faculty of Biomedical Sciences

USI Faculty of Biomedical Sciences was established in 2014 with the aim of addressing an important national problem: the dearth of physicians trained in Switzerland. To reach its goal, the Faculty offers from 2020 a Master of Medicine (three years of clinical training), in cooperation with ETH Zurich and University of Basel regarding academics, and with EOC, clinics, and general practitioners regarding clinical training. The Master addresses the new challenges of medical practice by combining clinical and scientific training with communication skills. The Faculty is also offering a joint Master'programme in Cognitive Psychology in Health Communication with Vita-Salute San Raffaele University, Milan.

The Faculty is offering a PhD program in Biomedical Sciences with majors corresponding to its main research areas, i.e. immunology and cell biology, cancer biology and oncology, (human) neurosciences, (human) cardiovascular sciences, drug sciences, public health and computational biomedicine, as well as a Medical Doctor Programme. Moreover, the Faculty organizes an Executive Programme in Sleep Medicine (with the University of Bern), in Gastrointestinal, Gynecological and Prostate Cancer (with the European Schoool of Oncology) and in Patient's Communication (with Fondazione Sasso Corbaro). Finally, the Center of Advanced Studies on Entrepreneurship in Biomedicine (CASE BioMed) adds to the medical and scientific education at the Faculty by offering advanced programmes in innovation and entrepreneurship.

The Faculty currently comprises more than 20 full, associate and assistant professors, as well as a large number of adjunct, titular professors, and of private lecturers; these mostly include directors and senior scientific staff of the EOC presented in sections 1-3 of this report.

Research in the Faculty is developed in immunology and basic cancer research at the two affiliated institutes IRB and IOR and in the Laboratories for Translational Research of EOC. Epidemiological and clinical research is performed within the Institute of Public Health at USI and in the institutes and centers at EOC; finally, research in computational biomedicine is developed at the Euler Institute:

- the Institute for Research in Biomedicine (IRB; **www.irb.usi.ch**), affiliated and based in the Bellinzona campus. IRB was founded in 2000 with the goal of advancing the study of human immunology, with particular emphasis on the disease-relevant mechanisms of host defense. Since 2010, it is affiliated to USI as part of its Faculty of Biomedical Sciences. It currently comprises 13 research groups about 120 international collaborators.
- The Institute of Oncology Research (IOR; **www.ior.usi.ch**), affiliated and based in the Bellinzona campus, hosts researchers from all over the world performing basic and translational research in oncology with special focus on cancer biology, genomics, molecular oncology, experimental therapeutics. Since 2017, IOR is affiliated to USI as part of its Faculty of Biomedical Sciences. The Institute currently comprises 8 research groups and about 70 researchers and PhD students.
- the Institute of Public Health (IPH), see below section 5.2.
- the Euler Institute (**www.euler.usi.ch**), common to the Faculties of Informatics and Economics. Euler is USI's central node for interdisciplinary research and the connection between exact sciences and life sciences. Euler applies advanced computational methods to fields such as Life Sciences, Medicine, Physics, Mathematics, and Quantitative Methods. It currently comprises four professors, as well as several adjunct professors and groups leaders and about 45 researchers and PhD students.

5.2 Institute of Public Health (IPH)

Prof. Emilano Albanese, MD
Institute Director

The Institute of Public Health (IPH) is an inter-faculty Institute and one of the five training and research entities supported by the Faculty of Biomedical Sciences of the Università della Svizzera italiana. Members of the IPH perform research, training and practice, and provide services across a broad range of activities related to public health. The IPH is the 'antenna' in Ticino of the Swiss School of Public Health (SSPH+) and is home to research programs articulated across several research projects. In addition, IPH members provide support and scientific advice on the methodology of epidemiological, biomedical, behavioral, and other areas of research, from the conception, to the conduction, through the implementation of studies with various designs and spanning qualitative and quantitative methodological approaches. IPH is an USI inter-faculty Institute with members from the Faculty of Communication, Culture and Society, the Faculty of Economics, and of Biomedical sciences.

The IPH staff currently includes the Director, 4 tenured Professors, 2 Senior Researchers, and several Postdoctoral Fellows, PhD students, and research Assistants. Their backgrounds range from the medical field, to epidemiology, health economics, health communication, health promotion and behavior, communication, public management and policy, psychology, and marketing, through the social and health sciences.

Members of the IPH conduct a variety of studies in the fields of aging, mental health, ethics, public health, socio-emotional well-being, cognitive development and decline, social media addiction, cognitive and social neuroscience, clinical psychology, psychophysiology, social psychology, human behavior, nutrition and physical activity, vaccine acceptance, social integration, and health psychology. Study designs include epidemiological, population-based studies, experimental studies, qualitative studies (interviews and focus groups), fMRI studies, media content analyses, psychophysiological studies, scoping reviews, systematic reviews, meta-analyses, and RCTs. Target populations include older adults (+65), younger adults (18-35), adolescents (<18), and healthcare providers.

Researchers at the IPH have strong collaborations at the local (e.g., Canton of Ticino, ProSenectute Ticino e Moesano, Alzheimer Ticino, SUPSI), national (all Swiss universities, ETHZ, and EPFL) and international level (University of Vienna, University of Parma, University of Milan, University of Turin, and Loughborough University, University of Pittsburgh Graduate School of Public Health, Imperial College London, University of Valencia, University of Nottingham, University of York, University of Kent, National University of Ireland Galway, and many more), as well as with the World Health Organization, UNICEF, SDC, and many NGOs based in Switzerland and abroad.

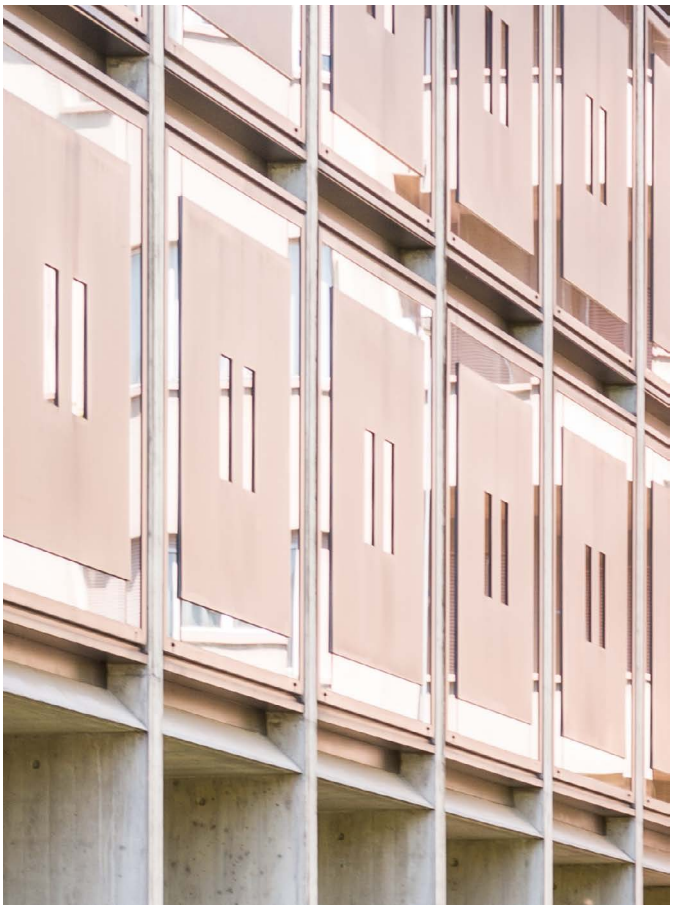
Members of the IPH give courses in various USI Bachelor's degrees, and within the USI Master in Medicine, the Master in Communication, Management and Health, and the Master in Cognitive Psychology in Health Communication, Masters of Marketing, Master in Public Management and Policy, Master in Corporate Communication, Master in Digital Fashion. Other graduate trainings include the SSPH+ Summer School in Public Health Policy, Economics, and Management, the Net Megs and more.

The IPH is committed to promote the highest ethical and methodological standards in population sciences and embraces a strong participatory action research approach and community engagement of the public and of all relevant stakeholders. Both research and training at the IPH ultimately aim to improve public health, to inform policy decisions and practices, and to contribute to positively influence individual behaviors and societal practices that promote and protect health, prevent diseases, and favor optimal and equitable care based on needs.

5.3 Other USI Faculties and Institutes

The institute of Economics (IdEP; **www.idep.eco.usi.ch**) supports research and teaching activities in the broad field of economics and public management. The research interests of IdEP members also include health economics and public health. Their research focuses on issues of public interest such as ageing and cognitive decline, mental health, sleep deprivation, and the determinants of the increasing health care costs. IdEP also organizes a Master of advanced studies in health economics and management (NETMEGS). Since 2012 IdEP coordinates the activity of the Center for Economic and Political Research on Aging (CEPRA). The center aims at stimulating empirical research on population aging, pension and health care design and spending, at promoting academic training on this topic, and at disseminating research output to a specialized and a general audience, through workshops, conferences, and public debates. Finally, since 2012 IdEP is part of the national research project Swiss learning health.

Within the Faculty of Communication, Culture and Society, there are specific competences related to health communication and literacy (prof. Schulz, prof. Hannawa); the Faculty also offers a master program in Communication, Management and Health. The Institute of Public Communication also closely cooperates with the Institute of Public Health to conducts research to understand determinants of health-related behaviors and to develop strategies to change behavior, focusing on communication (BeCHANGE research group). This includes topics such as making healthy behaviors‘easy’options for people, communicating complex health messages and increasing vaccine acceptance and uptake.



6. Peer-reviewed publications

7. Research projects activated in 2021

8. Research funding

9. 2021 Research Highlights

6. Peer-reviewed publications

A comprehensive computer literature search of PubMed/MEDLINE database was carried out independently by two different collaborators of the EOC Academic education, Research and Innovation Division. The last database search was performed in March 2022. The string search was built using keywords based on the different EOC sites.
The following inclusion criteria were used in the selection process: a) peer-reviewed articles listed in PubMed/MEDLINE with at least one co-author affiliated with EOC; b) final publication of the article in a scientific journal issue in 2021. Articles listed in PubMed in 2021 as "Online ahead of print" before their publication in final or print format were therefore excluded from the current analysis.

Journal Impact Factor (IF) and Journal IF Quartile of the scientific journals in which EOC researchers published their peer-reviewed articles were also evaluated using data from the Journal Citations Reports (JCR) 2020.

The scientific activity carried out by the EOC researchers, based on the inclusion and exclusion criteria mentioned above, resulted in 815 peer-reviewed articles. The year 2021 showed a significant increase of the EOC scientific production - as illustrated in Figure 4 – confirming the uptrend reported the previous year.

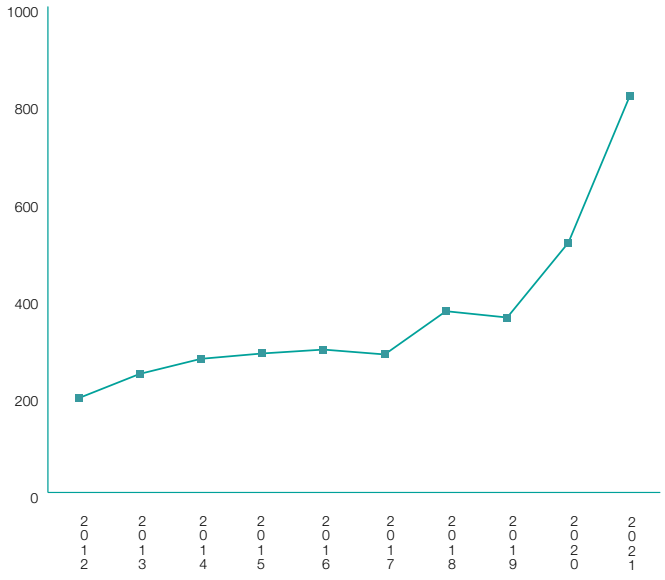


Figure 4. *Number of EOC peer-reviewed articles published by the EOC researchers in the last 10 years.*

Most of the EOC peer-reviewed publications in 2021 were original articles or reviews (709, 87%). Notably, 14% (N=98) of them were published on high impact factor journals (Journal IF ≥ 10). Key data are summarized in the figures below.

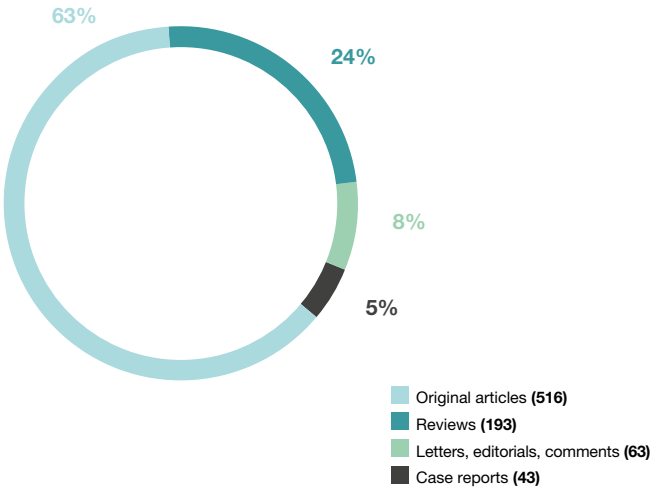


Figure 5. *Number and type of the peer-reviewed articles published in 2021 (N = 815). Meta-analyses, surveys and research letters are classified as original articles. Systematic reviews without meta-analyses, case reports with review of the literature, protocols and consensus papers are classified as reviews.*

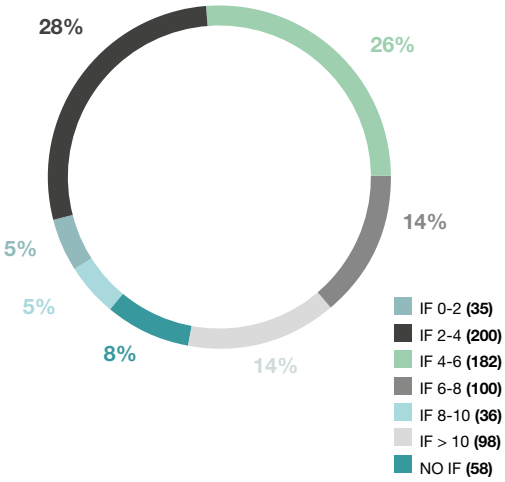


Figure 6. *Journal IF of the scientific journals in which peer-reviewed original and review articles were published in 2021 (N = 709).*

[1]Journal IF is defined as citations to the journal in the Journal Citations Reports (JCR) year to items published in the previous two years, divided by the total number of scholarly items (also known as citable items - these comprise articles and reviews) published in the journal in the previous two years. A Journal IF of 1.0 means that, on average, the articles published one or two years ago have been cited one time (Source: Clarivate Analytics).

[2] Scientific journals are assigned to a subject category by JCR and ranked by Journal IF. The Journal IF rank is then transformed in a percentile value. The Journal IF percentile is used to calculate the Journal IF Quartile. Q1: Journal IF percentile ≥ 75; Q2: 75 < Journal IF percentile ≤ 50; Q3: 50 < Journal IF percentile ≤ 25; Q4: 25 < Journal IF percentile (Source: Clarivate Analytics).

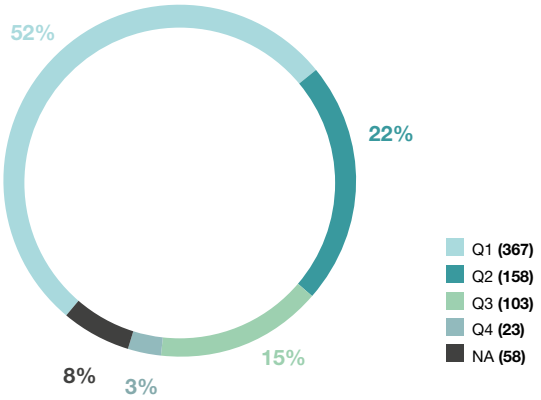


Figure 7. *Journal IF Quartile of the scientific journals in which peer-reviewed original and review articles were published in 2021 (N = 709). Journals can appear in multiple subject categories; in this case, the highest Journal IF Quartile was selected. Scientific journals without Journal IF are classified as NA.*

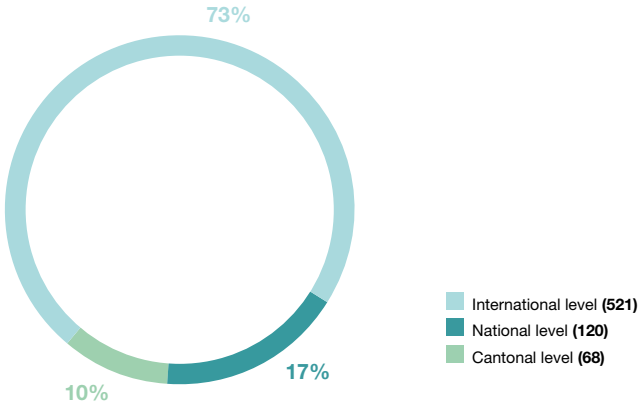


Figure 8. T*ype of scientific collaboration (local, national of international) based on the peer-reviewed original and review articles published in 2021 (N = 709).*

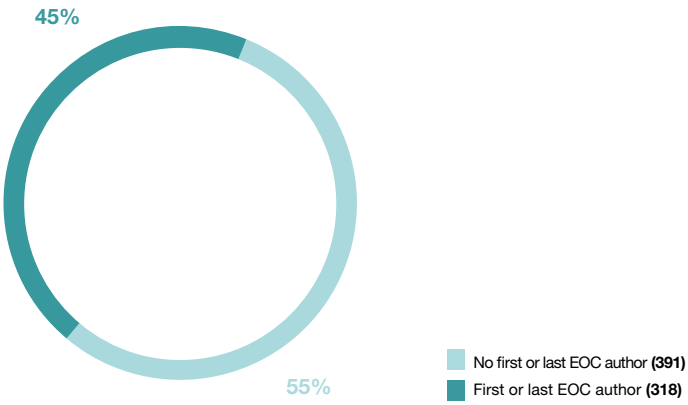


Figure 9. *Number of peer-reviewed original and review articles published by EOC researchers as first or last author in 2021 (N = 709).*

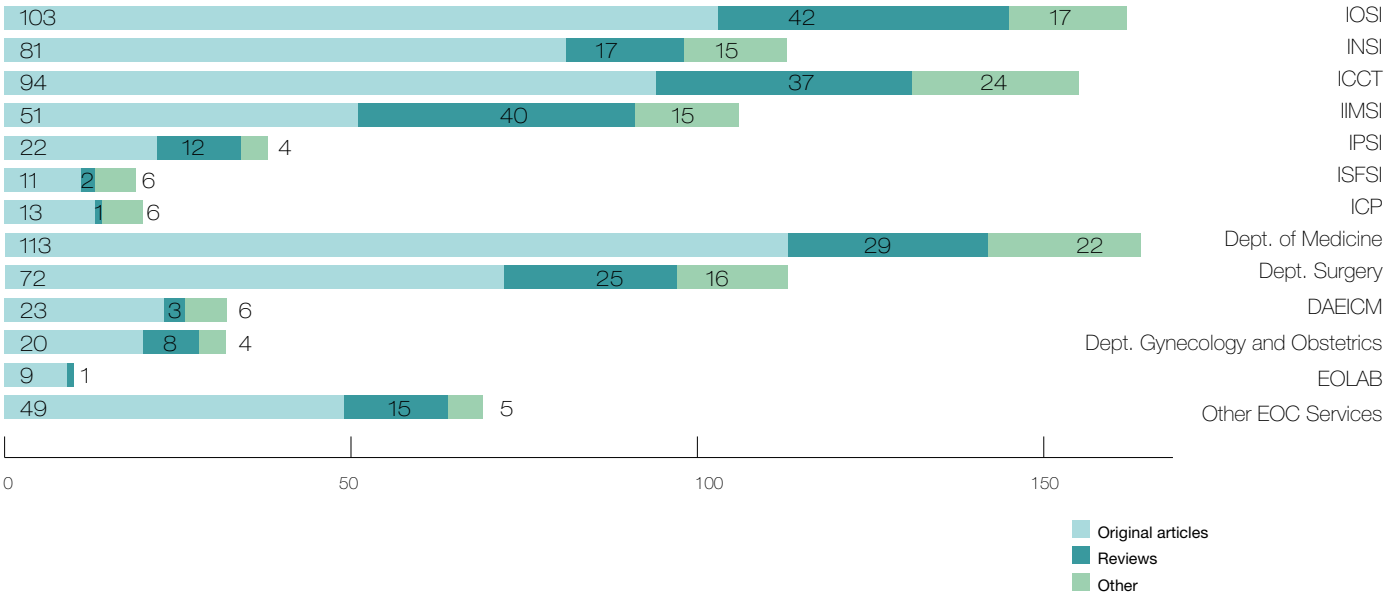


Figure 10. *Number of peer-reviewed articles published by each EOC Institute and Department in 2021. Publications shared among different EOC Institutes/Departments were counted for each Institute/Department involved. LRT-EOC publications are included in the EOC Institute/Department with which the concerned laboratory is affiliated. Less than 10% of the EOC scientific publications were from LRT-EOC.*

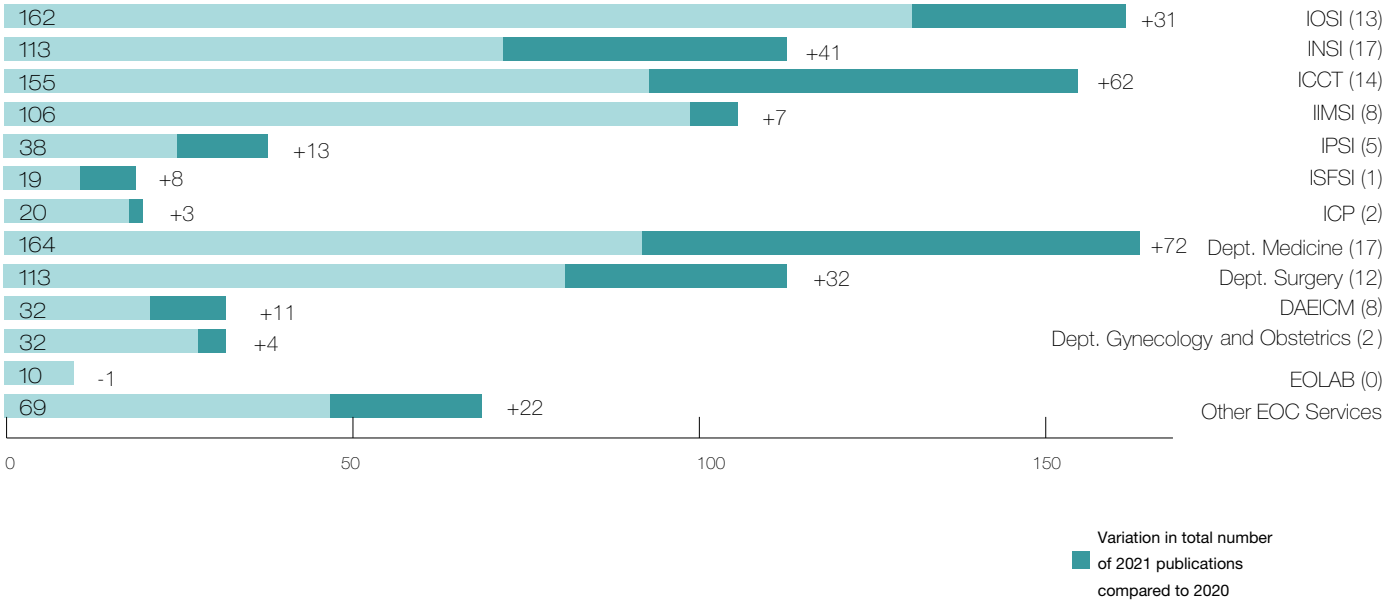


Figure 11. *Comparison of the total number of peer-reviewed publications in 2021 (shown on the bar) versus 2020 by the EOC Institutes and Departments. Publications shared among different EOC Institutes/Departments were counted for each Institute/Department involved. The name of the Institute/Department with the related number of Professors and PD are indicated on the vertical axis.*

Overall, EOC research activities saw a noticeable increase in productivity in 2021 compared to 2020. Beyond the quantitative metrics, a significant increase of original articles and reviews published in Q1 journals was reported in 2021, as a surrogate marker of the improved quality of the scientific outputs at the EOC hospitals and labs.

>> The list of publications is available on the EOC website at the following link.

7. Research projects activated in 2021

Research projects conducted at the EOC hospitals are recorded into a dedicated database. A total of 129 research projects involving persons that require authorization by the Ethics Committee and/or Swissmedic were activated in 2021. As of 31.12.2021, 345 research projects are ongoing at the EOC hospitals.

Figure 12 shows the number of EOC research projects by the category to which are assigned on the basis of the type of effect they have on participants. Almost 55% (N=70) were non-clinical trials, of which 30 (43%) belonging to the sub-category of research projects with further use of pre-existing health-related data and/or biological material. The remaining were clinical trials (N=59) of which over 70% investigating medicinal products. Notably, 75% (N=44) of the clinical trials were randomized. According to available data, in 2021 EOC researchers conceived and promoted 56 reseach projects, which were mostly non-clinical trials (N=46). Just over half of the research projects were funded, primarly clinical trials (85% of them funded).

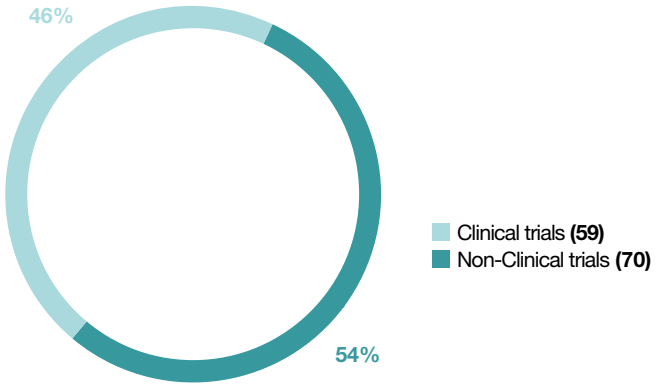


Figure 12. *Number of EOC research projects activated in 2021 (N = 129).*

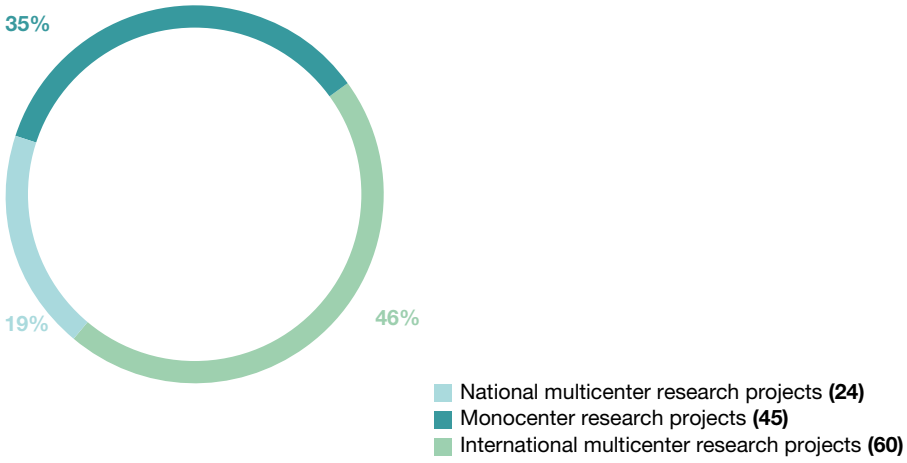


Figure 13. *Number of EOC research projects with single or multiple participating sites activated in 2021 (N = 129).*

[3] Data only available from 2018. Research projects activated prior to 2018 and still ongoing are not included in the metrics.

[4] Non-clinical trials are research projects that do not actively induce an effect among research participants but they just collect health-related personal and/or take biological samples (Source: kofam.ch).

[5] Clinical trials are research projects that actively induce an effect among research participants – using medicinal products, medical devices or other health-related interventions – to investigate their impact on participants' health or the structure and functioning of the human body (Source: kofam.ch).

Figure 14 summarizes the number of EOC research projects, divided into clinical and non-clinical trials, opened in 2021 by Institute/Department. The research project was assigned based on the EOC affiliation of the Sponsor-Investigator/Project Leader/Principal investigator, whichever apply.

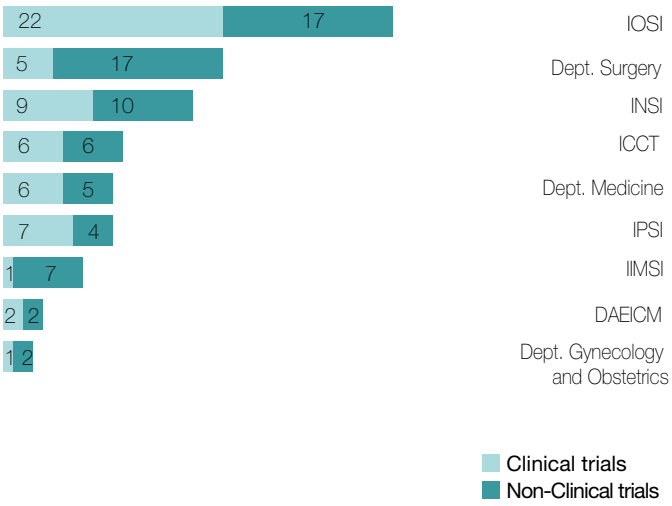


Figure 14. *Number of EOC research projects activated in 2021 by Institute/Department (N = 129). Clinical and non-clinical trials are also shown.*

Overall, statistics for 2021 on new activated research projects at the EOC hospitals are consistent with the data reported in 2020.

8. Research funding

Overall, more than CHF 8 Mio of external funding for research activities were obtained by EOC researchers in 2021 (including grants and donations). The external funding increased compared to the previous year.
Among the different EOC Institutes and Departments, ICCT, IOSI, INSI and LRT-EOC achieved the highest external funding for current ongoing research projects.

9. 2021 Research Highlights

- A significant number of peer-reviewed scientific articles was published by EOC researchers in 2021 (N = 815), most of them as original or review articles (N = 709, 87%). Overall, the number of publications increased by 301 (+37%) compared to publications in 2020. EOC research was mainly clinical with less than 10% of EOC scientific publications related to LRT-EOC.
- Peer-reviewed original and review articles were published in scientific journals showing very heterogeneous Journal Impact Factors (IFs) with a median value of 4.467. Notably, a total of 98 original articles and reviews (14%) were published on high impact factor journals (Journal IF ≥ 10).
- Just over half of peer-reviewed original and review articles was published in scientific journals ranked in the Journal IF quartile Q1, demonstrating the high quality of the EOC scientific production in 2021.
- Most of peer-reviewed original and review articles (90%) published in 2021 was the result of national or international collaborations.
- The EOC researcher was the first or last author in about half of the peer-reviewed original and review articles; this finding demonstrates that many of the research projects have been conceived and conducted at EOC.
- 129 new research projects involving persons – 70 non-clinical and 59 clinical trials - activated in 2021 and 345 ongoing research projects at the EOC hospitals and labs.
- More than CHF 8 mio of external funding in 2021 with ICCT, INSI, IOSI, and LRT-EOC achieving the highest funding for current ongoing research projects.
- Overall, EOC research activities saw a significant increase in productivity and quality outputs in 2021 compared to the previous year.

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