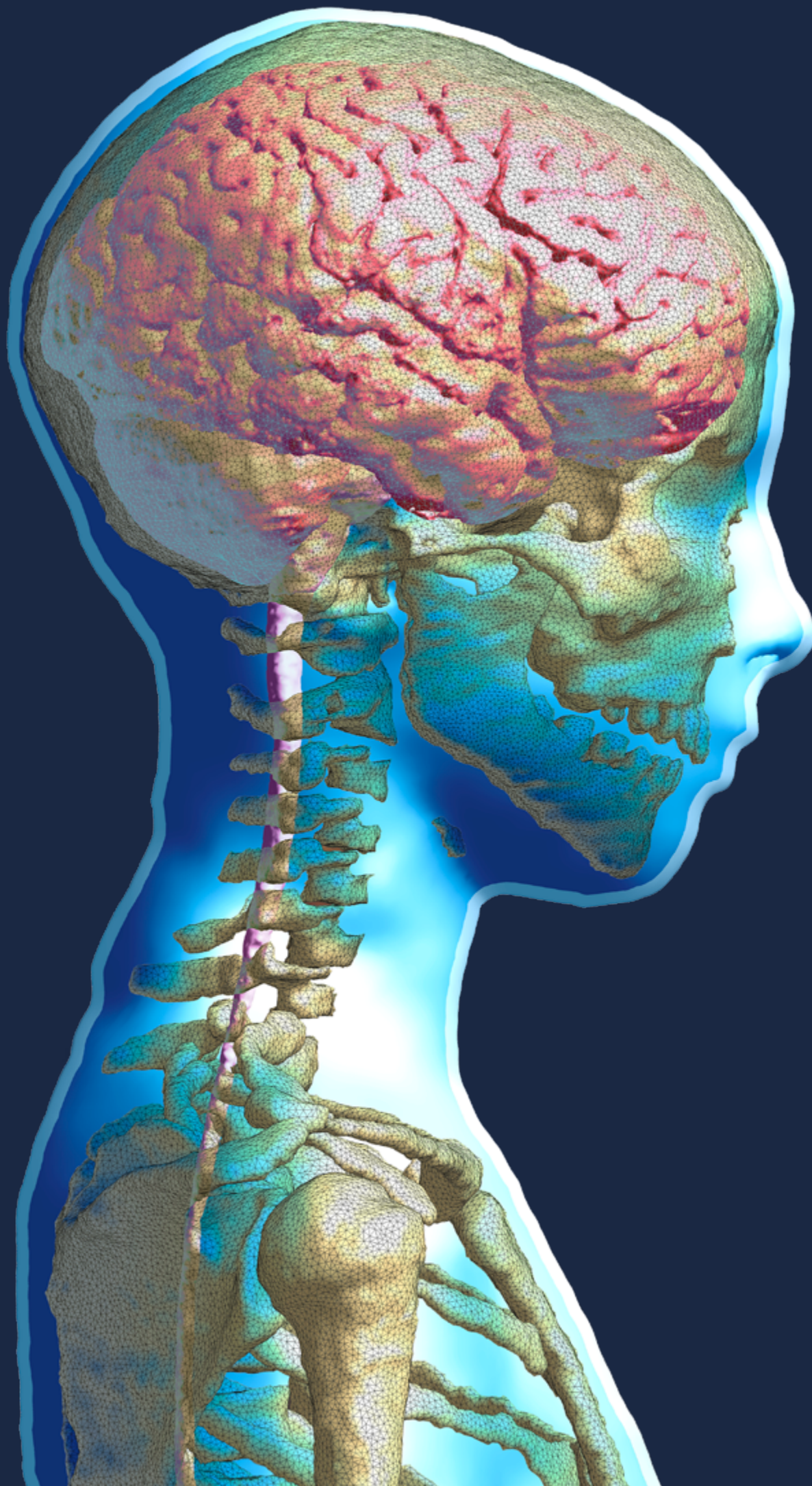




IT'S FOUNDATION 2014



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15 YEARS OF PROGRESS

Excellence in electromagnetics research and ambition made possible the establishment of the IT'IS Foundation in 1999. At the end of 2014, we celebrated 15 years of delivering on a commitment to make a tangible difference in people's lives by enhancing the safety and quality of emerging electromagnetic technologies and by contributing our knowledge to advanced medicine with a diversity of approaches and a continuity of purpose. As we are now in a better position to assess and explore the many opportunities made possible by scientific discovery, we have taken ambitious steps to position ourselves to achieve greater impact.

At the start of our second decade five years ago, the focus of our research activities shifted from EM and wireless safety to medical applications. The launch of our research initiative *IT'IS for Health* set an ambitious agenda for the following years, with a proactive focus on computational life sciences, in particular, the development of a computational framework with a series of verified and validated computable, functionalized anatomical models (Page 13) and the most powerful physical and tissue model solvers (Page 14). As we implemented and refined our strategic research initiatives, we sought new visionary partners and maintained a productive relationship with our existing collaborators to push the boundaries of medical technology (Page 10), and we embraced the growing interest in the applicability of our novel tools by those who are looking over the horizon (Page 6). Today, the projects related to *IT'IS for Health* garner well over 50% of our total funding.

We also pushed the boundaries of our mainstay electromagnetics research further: 1) our pioneering high-sensitivity, non-interfering, and traceable time-domain near-field scanner for the EMI analysis and optimization of densely integrated electronics was finalized (Page 12); 2) a novel hyperthermia system and treatment tool were developed (Page 16); and 3) novel algorithms for reconstructing 3D fields were developed. We expanded our broad spectrum of services supporting the wireless and medical industry in overcoming many EM limitations (Page 17). Joining new COST actions (e.g., BM1309, TD1402), research consortia (e.g., MDIC (US), V&V40 (US)), and standardization groups, further expanded our network in the global scientific community as well.

The rapid pace of our progress speaks to the remarkable commitment, intelligence, agility, and creativity of our staff, who are the true visionaries (Page 5). To maintain and expand our prolific portfolio of interconnected initiatives, we have consistently strengthened and expanded our diverse team of researchers and engineers with the greatest minds from 29 nations. Our success, however, would not be possible without our deep engagement in the research activities of ETH Zurich, EPFL, the University of Zurich, and all other partner universities in Switzerland and abroad (Page 10). In particular, we thank Professors Qiuting Huang, Klaas Prüssmann, Gábor Székely, and Juan Mosig for sharing infrastructure and advising our PhD students and PostDocs.

Highly committed and endowed with complementary scientific, medical, financial, and commercial expertise, the members of the board have overseen the implementation of our strategic initiatives with valuable insight, expert advice, and faithful guidance. The appointment of our newest board member, Prof. Stephan Bodis, brings new depth to the IT'IS Foundation Board, and will help further guide the execution and strategic prioritization of the many medically-related opportunities currently before us (Page 4).

We are grateful to our many sponsors and donors (Page 9) whose commitment and trust in our vision make it possible to pursue our goals year after year, especially the generosity of CTI, the Swiss Federal Office of Public Health, the Swiss National Research Foundation, and the EU Commission.

With the perspective of time, we have found that while strategies have changed, areas of support have shifted, technology has become more complex and competition has grown, the fundamental principles that guide our foundation endure. Our fifteenth anniversary allowed us to look back at our achievements, but more importantly, it compelled us to look ahead, to assess the research needs of the next decade and beyond, and to strategize for the future.

We remain committed to leading the way to the solutions of tomorrow.

Zurich, January 2015

Prof. Niels Kuster

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Antonino Cassarà, PhD, Postdoc
Bryn Lloyd, PhD, Project Leader
Lucas Portelli, PhD, Postdoc
Iris Szankowski, PhD, Scientific Coordinator
Dominik Szczerba, PhD, Project Leader

Sami Dzsaber, Intern
Yijian Gong, PhD Student
Marie-Christine Gosselin, PhD Student (EEO)
Adamos Kyriakou, PhD Student
Ioannis Vogiatzis Oikonomidis, MSc Student

Deepika Sharma, PhD Student
Lénárd Szolnoki, Intern
Frederico Teixeira, PhD Student
Andreas Wassmer, Intern
Philipp Wissmann, PhD Student

Christian Baumgartner, Scientific Assistant
Silvia Farcito, Scientific Assistant
Eveline Huber, Scientific Assistant
Dimce Iliev, RF Engineer
Roger Jacot, Scientific Assistant
Maria Jedensjö, Scientific Assistant
Heidi Moser, Scientific Assistant
Amie Rieseberg, Scientific Assistant

Patricia L. Bounds, PhD, Scientific Writer
Anja Burse, Photography, Art Director & Media Design
Eva Jakubcaninova, Administrative Assistant
Jacqueline C. Pieper, Finance & Administration (EEO)
Mayuko Sasaki, Graphic Design
Saskia Venema, Graphic Design
Daniel Walser, Movies

Tomasz Lisewski, Academic Visitor

External Advisors

Prof. Quirino Balzano, University of Maryland, US
Charlie Götschi/Markus Müller, Untersee Composites, CH
Albert Lenherr, Mechanical Engineering Consultant, CH

Prof. Theodoros Samaras, Aristotle University of Thessaloniki, GR
Dr. Asher Sheppard, US
Dr. Balint Szentkuti, EMC-RF Szentkuti, CH
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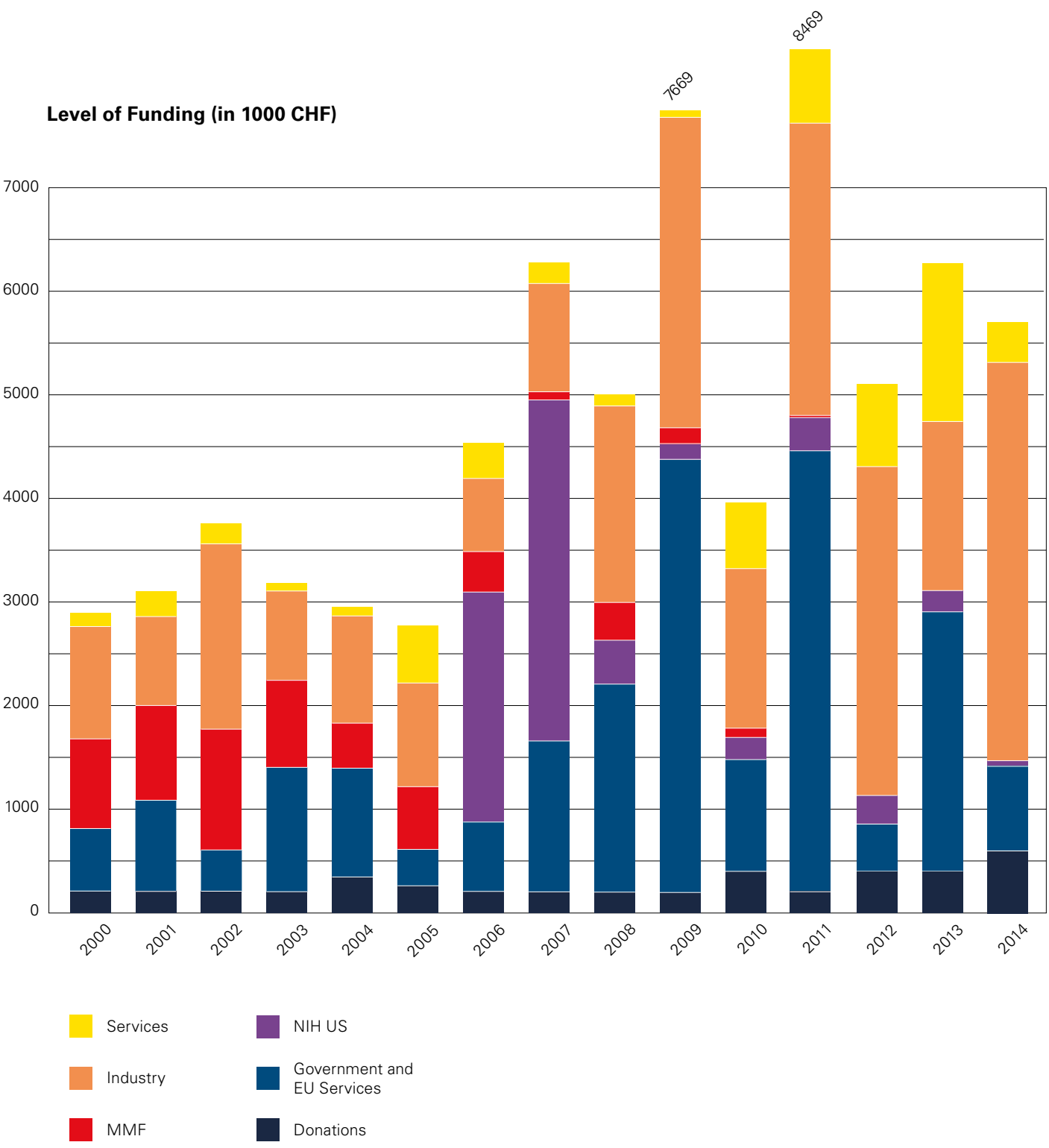
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Kevin Appareti, Philips Healthcare, US
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Dr. Noureddine Frid, Cardiatis, BE
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Krishna Kurpad, Biotronik, US
Dr. Brenda Kwak, University of Geneva, CH
Dr. Ignacio Larrabide, Pompeu Fabra University, ES
Oliver Leibach, Roche Diagnostics, DE
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Dr. Sung-Min Park, Medtronic, US
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Dr. Xavier Planes, Pompeu Fabra University, ES
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Dr. Emsad Puric, Cantonal Hospital Aarau, CH
Dr. Paolo Ravazzani, Polytechnic University of Milan, IT
Dr. Stefan Reimers, MED-EL, AT
Ronald Reitan, Boston Scientific, US
Dr. Carla Rohrer Bley, Vetsuisse, University of Zurich, CH
Prof. Martin Rössli, Swiss Tropical and
Public Health Institute, CH

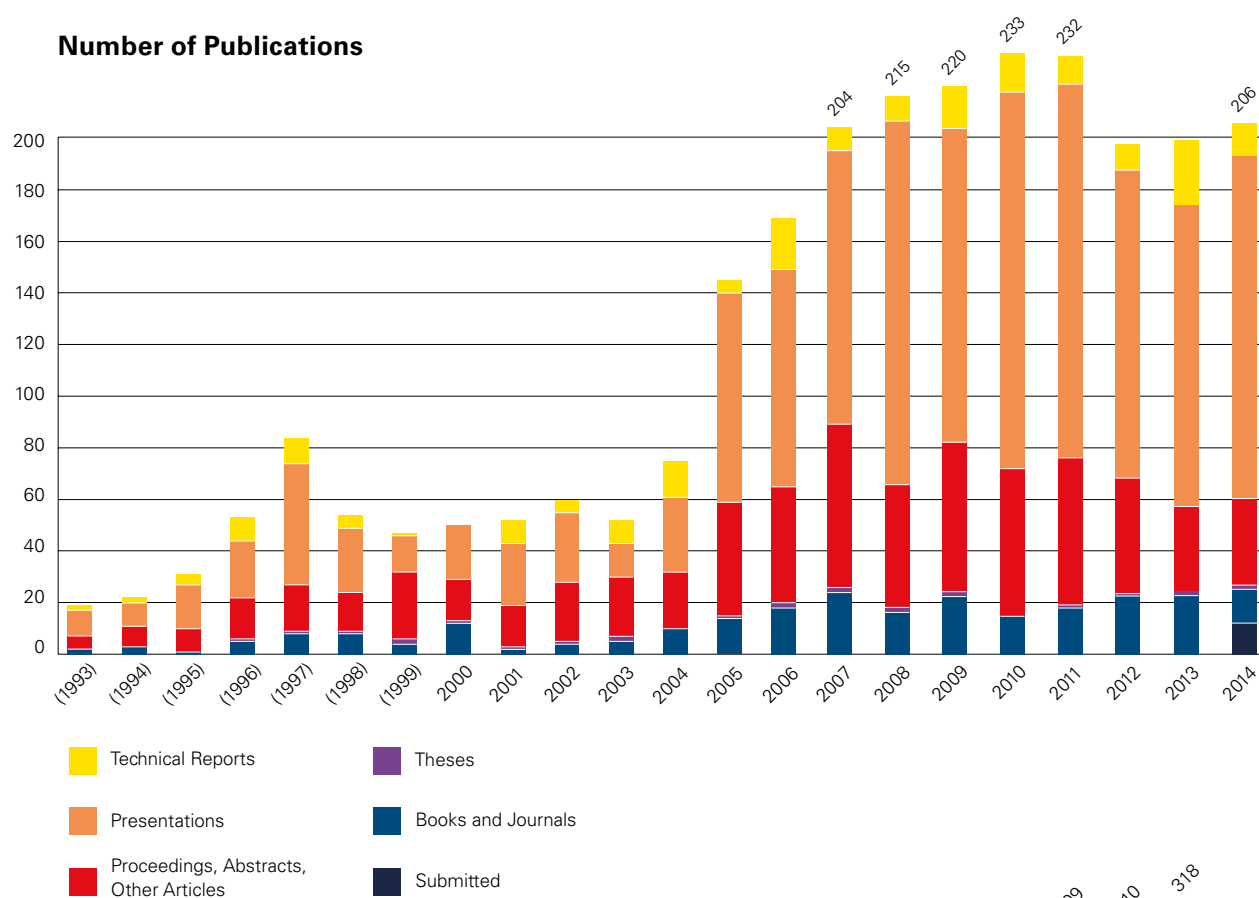
Dr. Rene Rossi, Empa, CH
Dr. Daniel Rüfenacht, Hirslanden Klinik, CH
Prof. Jorge Ruiz Cruz, Madrid University, ES
Brian Russell, Covidien, US
Marc Sallin, Montena, CH
Prof. Theodoros Samaras, Aristotle University
of Thessaloniki, GR
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Thierry Sarrebourg, Orange, FR
Gregor Schaeffers, MR:comp, DE
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KEY FIGURES

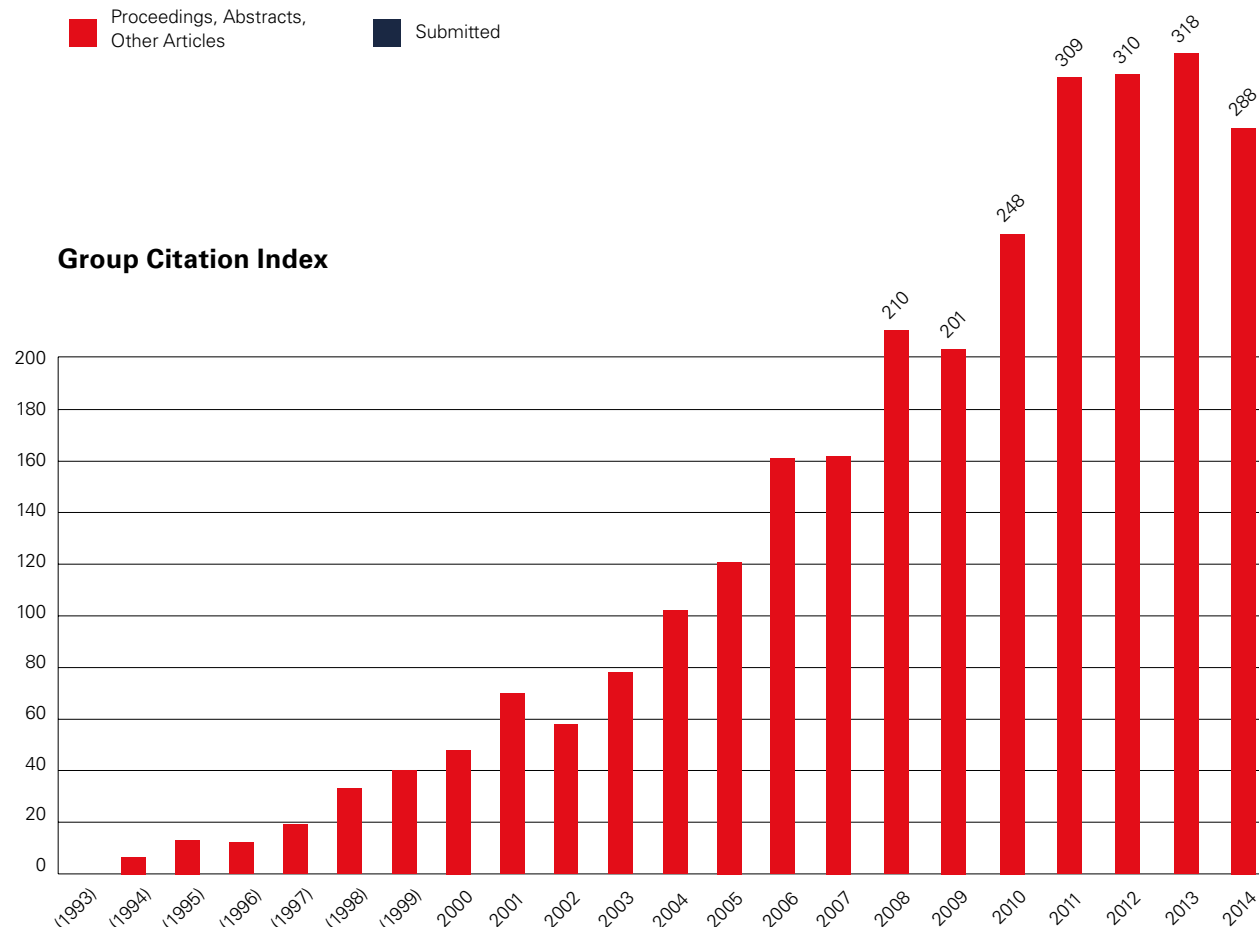


KEY FIGURES

Number of Publications



Group Citation Index



Years in parentheses (1993–1999) show citation development while at ETH, before IT'IS was established as an independent foundation.

The compiled index is based on data available from the Thomson Reuters Web of Science™ database; the number of citations reported are from peer-reviewed publications and excludes self-citations.

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6th Framework Programme of the EU (FP6), BE
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Commission for Technology and Innovation, CH
EUREKA, CH
Federal Office for the Environment, CH
Federal Office of Communications, CH
Federal Office of Energy, CH
Federal Office of Public Health, CH
Federal Institute for Occupational Safety & Health, DE
Federal Office for Radiation Protection, DE
National Institute of Environmental Health Sciences, US
National Institute of Standards and Technology, US
State Secretariat for Education, Research & Innovation, CH
Swiss National Science Foundation, CH
ZonMW, NL

Non-Profit Organizations

Foundation for Behaviour and Environment, DE
Health Canada, CA
KFG Contact Group for Research Matters, CH
Research Association for Radio Applications, DE
Research Foundation on Mobile Communication, CH
University of Zurich, CH

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AMI Semiconductor, CA
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Arizona Chemical, US
Biotronik, DE
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Clarins Laboratories, FR
CTIA, US
Disney Research, US
Ericsson, SE
GE Medical Systems, US
GSM Association, CH
Intel Corporation, US
International Business Machines Corp., US
Kaba, CH
LG Electronics, SK
Micro Systems Engineering, US
Mitsubishi Electric, JP

Mobile Manufacturer Forum, BE
Micro Systems Engineering, US
Motorola, US
Nokia, FI
Nokia Solutions and Networks, FI
NTT DoCoMo, JP
Panasonic, JP
Philips, NL
Phonak Communications AG, CH
Qualcomm Inc., US
Ruag, CH
Sagem, FR
Samsung, SK
Sensirion AG, CH
Siemens AG, DE
Sony Ericsson, JP
Sorin S.A.S., FR
St. Jude Medical Inc., US
Toshiba Medical Research Institute, US
Vodafone, GB

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Cardiatis S.A., BE
Felsenmeer AG, CH
maxwave AG, CH
MED-EL, AT
Schmid & Partner Engineering AG, CH
Sensimed AG, CH
VAT Vacuumvalves AG, CH
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Institute of Biomedical Engineering, ETHZ, CH
Institute of Robotics and Intelligent Systems, ETHZ, CH
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Laboratory of Thermodynamics in Emerging Technologies, ETHZ, CH
Neuroscience Center Zurich, ETHZ, CH
Center for Applied Biotechnology and Molecular Medicine, UZH, CH
Department of Neurology, UZH, CH
Institute of Pharmacology and Toxicology, UZH, CH
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University Children's Hospital Zurich, CH
University Hospital Zurich, CH
University of Zurich, CH
Cantonal Hospital Aarau, CH
Hirslanden Clinic, Zurich, CH
University of Applied Sciences, Zurich, CH
Center for Neuroprosthetics, EPFL, CH
Laboratory of Electromagnetics & Acoustics, EPFL, CH
Powder Technology Laboratory, EPFL, CH
Clinical Morphology & Biomedical Engineering, UNIBAS, CH
Computer Science Department, UNIBAS, CH
Department of Biomedicine, UNIBAS, CH
Laboratory of Biomechanics & Biocalorimetry, UNIBAS, CH
Medical Image Analysis Center, UNIBAS, CH
Orthopedic Section, Basel University Hospital, CH
Swiss Tropical and Public Health Institute, CH
University Children's Hospital Basel, CH
ARTORG Center for Biomedical Engineering Research, UNIBE, CH
Division Veterinary Pharmacology & Toxicology, Vetsuisse, UNIBE, CH
Institute for Social & Preventive Medicine, UNIBE, CH
Inselspital Academic Health Center, CH
University Hospital, Bern, CH
Laboratory of Pharmaceuticals & Biopharmaceutics, UNIGE, CH
Children's Hospital Geneva, CH
Geneva University Hospital, CH
Geneva University, CH
Hospital of La-Chaux-de-Fonds, CH
Institute of Computational Science, USI, CH
University of Applied Sciences of Southern CH, CH
Centre Hospitalier Universitaire Vaudois, CH
University of Wollongong, AU
Austrian Institute of Technology, AT
Medical University of Vienna, AT
Tissue Dynamics Laboratory, Paracelsus Private Medical University, AT
University of Vienna, AT
INTEC, University of Ghent, BE
Interdisciplinary Institute for BroadBand Technology, BE
McGill University, CA
University of Toronto, CA
Beijing University of Technology, CN
Third Military Medical University, CN
Zhejiang University, CN
Center of Radiation Medicine, Technical University of Berlin, DE
Charité – Universitätsmedizin Berlin, DE
Fraunhofer Institute of Toxicology and Experimental Medicine, DE
Friedrich Schiller University of Jena, DE
GSF – National Research Center for Environment and Health, DE
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Ludwig Maximilians University of Munich, DE
Max Planck Institute for Human Cognitive and Brain Sciences, DE
Max Planck Institute for Neurological Research, DE
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University Hospital Erlangen, Friedrich-Alexander-University, DE
University of Freiburg, DE
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Danish Cancer Society, DK
Department of Electronic Systems, Aalborg University, DK

University of Aarhus, DK
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Centro de Biología Molecular Severo Ochoa, Universidad Autónoma de Madrid, ES
Instituto de Biología Molecular y Celular del Cáncer (CSIC/USAL), ES
Institute of Applied Physics, ES
Finnish Institute of Occupational Health, FI
Helsinki University of Technology, FI
STUK – Finnish Center for Radiation and Nuclear Safety, FI
University of Eastern Finland, FI
University of Kuopio, FI
Association pour la Recherche Epidémiologique dans les Cancers de l'Enfant et de l'Adolescent, FR
Institut des Relations Publiques et de la Communication, France Supélec, Ecole Supérieure d'Electricité, FR
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University of Bordeaux 1, FR
Epidemiological Research and Surveillance Unit in Transport, Occupation and Environment, FR
Beatson Institute for Cancer Research, GB
Hammersmith Hospital, GB
Imperial College, GB
Keele University, GB
Oxford University, GB
University of Cambridge, GB
University of Leicester, GB
University of York, GB
Aristotle University of Thessaloniki, GR
National Technical University of Athens, GR
The Gertner Institute for Epidemiology and Health Policy Research, IL
Schneider Children's Medical Center, IL
Weizmann Institute of Science, IL
Indian Institute of Technology Kanpur, IN
Center for Information Technology IRST, IT
ENEA, IT
Institute of Biomedical Engineering, Politecnico di Milano, IT
University of Bologna, IT
University of Turin, IT
Fukushima Medical University Hospital, JP
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Tokyo Metropolitan University, JP
University of Tokyo, JP
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Utrecht University, NL
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University of Bergen, NO
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Karolinska Institute, SE
Stress Research Institute, University of Stockholm, SE
University of Uppsala, SE
Institute of Non-Ionizing Radiation, SI
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Illinois Institute of Technology Research Institute, US
Johns Hopkins Bayview Medical Center, US
Massachusetts Institute of Technology, US
University of Alabama at Birmingham, US
University of California Davis, US
University of California Riverside, US
University of Buffalo, US
University of Houston, US
University of Maryland, US
University of Miami, US
University of Wisconsin, US
Washington University, US

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Communications Research Center, Industry Canada, CA
Danish Council for Strategic Research, DK
Electronics and Telecommunication Research Institute, SK
Federal Communications Commission, US
Federal Office for Radiation Protection, DE
Federal Office for the Environment, CH
Federal Office of Communications, CH
Federal Office of Energy, CH
Federal Office of Public Health, CH
Food and Drug Administration, US
Health Council of The Netherlands, NL
Health Protection Agency, GB
International Agency for Research on Cancer, FR

National Institute of Information & Communications Technologies, JP
National Institute of Environmental Health Sciences, US
National Institute of Standards and Technology, US
National Research Council, IT
Norwegian Institute of Public Health, NO
Public Health England, GB
Radio Research Agency, SK
Russian Academy of Medical Science, RU
SITT, Industry Canada, CA
South African Bureau of Standards, ZA
Spanish National Research Council, ES
State Radio Monitoring Center, Ministry of Information Industry, CN
State Secretariat for Economic Affairs, CH
Telecommunication Metrology Center, CN
World Health Organization, CH

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Alnair, JP
Antia Therapeutics, CH
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FRONIUS International GmbH, AT
GE Healthcare, US
Healtis, FR
Hirslanden Private Hospital Zurich, CH
Huber + Suhner AG, CH
IBM, CH
Image Guided Therapy, FR
Imricor Medical Systems, US
Incos Boté Cosmetic GmbH, DE
Istituto di Ricerche Biomediche Antoine Marxer, S.p.A., IT
Kaba AG, CH
maxwave AG, CH
MCL Technology Limited, GB
MED-EL, AT
Mitsubishi, JP
Motorola, US
Micro Systems Engineering, Inc., US
Nokia Research Center, FI
NTT Communications, JP
NTT DoCoMo, JP
Pfisterer International AG, DE
Philips Medical Systems, NL
Phonak Communications AG, CH
Qualcomm, US
Research and Consulting Co. Ltd., CH
Roche Diagnostics, DE
Schmid & Partner Engineering AG, CH
Siemens AG, DE
Sorin Groupe, FR
St. Jude Medical Inc., US
Swiss Federal Railways, CH
Swisscom, CH
Synoste, FI
Synopsis Inc., US
Torptronics Engineering AG, SE
T-Mobil, DE
THESS, GR
TILAB S.p.A., IT
Toshiba, JP
Vodafone, UK
Volvo Car Corporation, SE
Vratis, PL
York EMC Services, GB
ZMT Zurich MedTech AG, CH

PROJECTS

EM Technology

TD SENSOR	Development of time-domain near-field field sensor technology
DAK-TL	Development of a dielectric measurement system (DAK) for thin layers
WEMS	Development of procedures and instrumentation for demonstration of worker's EM safety
ELF Shielding	Development of a reference frame for assessing the effectiveness of shielding structures for power lines

EM Exposure & Risk Assessment

sXc, sXv, sXh	Development of optimized exposure systems for bio-experiments from static to GHz
sXv – NTP/NIEHS	Development, manufacturing, installation, and detailed dosimetry of the reverberation chamber-based exposure system for the NIEHS <i>in vivo</i> studies
NRP-Sleep	Effect of RF electromagnetic radiation on human sleep EEG and cognitive tasks
FP7 ARIMMORA	Identification of a possible causal relationship between EMF exposure and cancer, with a special focus on childhood leukemia
FP7 GERONIMO	Generalized EMF Research using Novel Methods
ANIMEX	Development, manufacturing, installation, and detailed dosimetry of a reverberation chamber-based exposure system for INERIS
CREST	Characterization of the RF exposure due to novel usage scenarios or new technologies for mobile communications devices

IT'IS for Health

CTI S4L-CAPITALIS	Extension of the <i>Sim4Life</i> platform (S4L) for the analysis and optimization of neurovascular and neurological devices and treatments in the head
ViP 2.0 / 3.0	Development of the next generation of high-resolution anatomical models
ViP-P/VM/M	Development of novel posers, a methodology for enhanced volume meshes of anatomical structures, and a physically-based morphing tool
MIDA-FDA	Development of a functionalized high-resolution head and neck model for EM-neuron interaction modeling
CLS-FUS	Transcranial Focused Ultrasound; Sonoknife; Liver motion during FUS interventions
CLS-V&V40	Development of novel concepts for the verification and validation of computational life sciences software platforms and their applications
MRI#	Development of 3T-MRI exposure risk probability based on local temperature safety considerations
MRIneo	Development of MRI exposure risk probability of fetuses and newborns based on local temperature safety considerations
PiX	Experimental solution for MR-safety evaluation of medical implants
HT-KSA/UsZ	Development of novel hyperthermia hardware and treatment planning software for superficial soft tissue sarcoma in animals
MagnetoTheranostics	Early detection and treatment of prostate cancer lymph node metastases using nanomagnetic particles (Swiss-NanoTera project)
EMF- PDT	Identification of optimal <i>in vitro</i> photodynamic therapy (PDT) and RF-EMF-mediated hyperthermia conditions for cancer treatment
REPLICATIONS	Validation and mechanistic investigation of modulation-specific cellular EM effects published by Zimmermann et al.
STANDARDIZATION	Participation in regulatory activities (standards committees & governments)

INTERFERENCE AND COMPATIBILITY EVALUATION SYSTEM (ICE_y)

Absolute and traceable emission measurements of electric and magnetic near-fields are essential for analyzing compatibility and potential interference sources in highly integrated systems and devices. Existing measurement systems, however, are incapable of providing such detailed and exact measurements. The limitations of traditionally used non-isolated probes are mainly to blame, as they modify the local field distribution at the device under test (DUT), have undefined receiving characteristics when used in arbitrary field distributions, and cannot be calibrated with reasonable measurement uncertainty to traceable standards. As a result, the measurement technology does not comply with the QA requirements and specification processes of device manufacturers and integrators due to the lack of interlaboratory and intersystem comparability of near-field EMC/EMI measurements. Further disadvantages of current EMC/EMI scanners include the lack of well-defined EM boundary conditions; the lack of effective shielding against environmental signals for small signal tests (e.g., GPS interference); the lack of measurement automation, including scanning conformal to the DUT surface for absolute measurements; the generally low acquisition speeds of the measurement receivers; and the lack of phasor measurements.

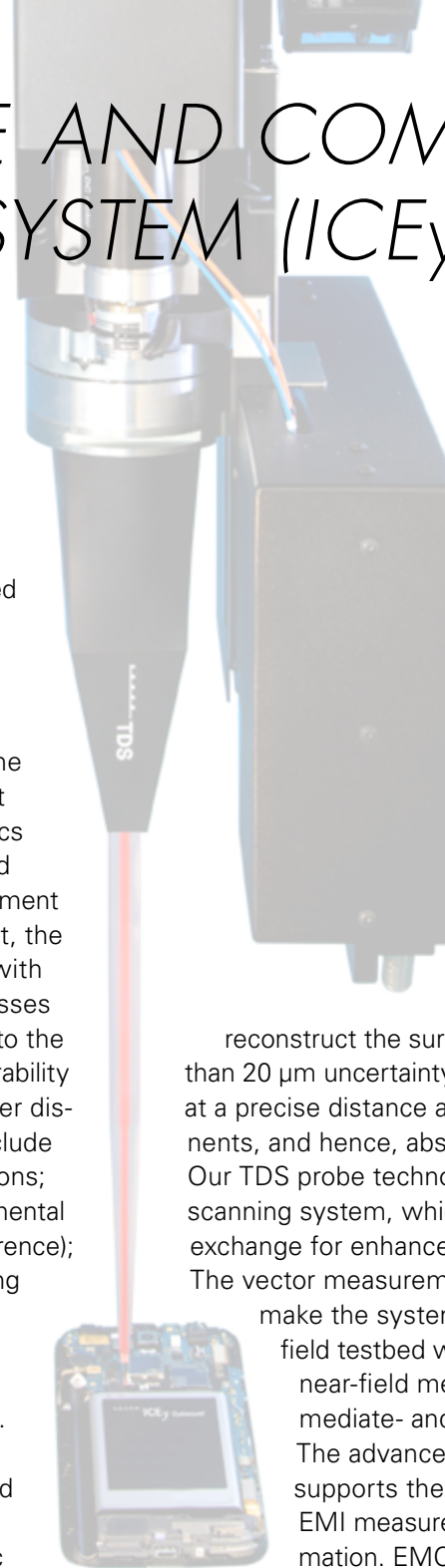
In our 2011 Annual Report, we first introduced our Time-Domain Sensor (TDS) active optical near-field field probe technology for magnetic and electric field measurements in the RF domain. Although the TDS probe technology overcame the limitations of existing EMC/EMI near-field scanning probes, there was no suitable integrated EMC/EMI scanning solution to fully implement the novel features of our TDS technology and overcome the remaining issues of current EMC/EMI near-field scanners, specifically absolute field measurements. In cooperation with a leading mobile communication chip manufacturer and SPEAG, IT'IS initiated the development of a phasor EM near-field interference and compatibility evaluation system, ICE_y, with the objective that SPEAG would commercialize the system after completion of the project.

Within this project, an automated near-field testbed for system- to chip-level EMC/EMI evaluations in the RF domain was successfully developed. The system can emulate free-space or metallic boundary conditions in the scanning volume contained inside a fully EM shielded chamber, and combines a large scanning volume of $500 \times 500 \times 120 \text{ mm}^3$ with micrometer resolution. A novel computer vision, contactless surface detection system can

reconstruct the surface profile of the DUT with better than $20 \text{ }\mu\text{m}$ uncertainty, allowing for conformal scanning at a precise distance above arbitrary electronic components, and hence, absolute field measurements. Our TDS probe technology has been integrated into the scanning system, which also supports automatic probe exchange for enhanced measurement automation.

The vector measurement receiver and our TDS probes make the system the first true phasor EM near-field testbed with the option to propagate close near-field measurement results into the intermediate- and far-field regions in the future. The advanced measurement control software supports the planning and execution of EMC/EMI measurements with a high level of automation. EMC/EMI near-field measurement results can be overlaid conformally on top of the surface structure and image of the DUT with the various viewers of the postprocessing software.

The first ICE_y interference and compatibility evaluation systems have been used for chip-level near-field EMC/EMI analysis and screening applications since early 2014. The results of this latest project in the area of sensor technologies were presented at EDAPS 2013, ATMS 2014, EMC Tokyo 2014, and URSI conferences. The next step is to implement a reliable near- to far-field transformation for EMC emission testing, which traditionally requires large (semi-)anechoic EMC test facilities.



VIRTUAL POPULATION 2.0 & 3.0 – HIGH-RESOLUTION ANATOMICAL MODELS FOR MEDICAL DEVICE EVALUATION

The IT'IS Foundation has been at the forefront of developing high-resolution, accurate, whole-body anatomical models for nearly a decade. The first version of the Virtual Population, ViP 1.0, has become the gold standard in biophysical modeling, as evidenced by the over 500 citations of our reference paper (Christ et al., 2010) and the usage of our ViP models by >400 groups worldwide for research purposes, including dosimetric assessments of ionizing and non-ionizing radiation, tissue mechanics, acoustics, particularly ultrasound, and implant development.

the torso and the limbs to $0.5 \times 0.5 \times 0.5 \text{ mm}^3$ throughout the entire body; 3) more consistent tissue property assignment based on our open access database (www.itis.ethz.ch/database/) of various dielectric and thermal tissue parameters as well as perfusion, density, and viscosity information collected in the literature was achieved; 4) surface processing was enhanced by applying a novel in-house method to resolve complex, thin, and narrow tissues in a tetrahedral mesh, followed by surface extraction and further processing, including curvature- and



As the applications of the models became more extensive and the solvers more powerful, enhanced models were needed to handle the growing complexity of the endpoints studied while maximizing the reliability of the results. The optimization of cardiovascular implants for effective treatment, for example, requires multiscale simulations involving computational fluid dynamics, structural and tissue mechanics, and tissue adaptation models. To meet these challenges, Versions 2.0 & 3.0 feature improved anatomical accuracy and detail and high-quality unstructured meshes with topologically conforming surfaces (non-manifold geometries) for effective use with finite element (FE) solvers.

For the development of the latest ViP 3.0 models, new procedures tailored to meet their expanding functionality and complexity were implemented: 1) internal quality control guidelines ensured that all structures requiring segmentation were listed and a description of the method to define individual tissues was provided; cross-validation routines were performed by various members of the development team; and a log file describing the changes to each model of every newly released version was generated; 2) all models were resegmented at higher resolution by up-sampling the ViP 1.0 models from $0.5 \times 0.5 \times 1.0 \text{ mm}^3$ in the head and $0.9 \times 0.5 \times 2.0 \text{ mm}^3$ in

feature-adaptive smoothing; and 5) numerous anatomical refinements were included. Further details are available in our second ViP reference paper (Gosselin et al., 2014) published in a special edition of *Physics in Medicine and Biology*, and based on our presentation at the 4th International Workshop on Computational Phantoms organized by IT'IS in 2013.

The resulting next generation of Virtual Population models consists of smooth, yet feature-rich and topologically conforming surfaces, making them ideal for simulations performed with various numerical methods for a broad range of medtech applications. ViP 2.0 models can be used with general FE solvers, while ZMT Zurich MedTech has helped to transform the high-fidelity models into the computable ViP 3.0 (see Pages 14–15).

As a diverse set of models is essential to better represent the general population, we will continue to segment new anatomies, especially for non-Caucasian phantoms. Furthermore, innovative methods are being developed to circumvent whole-body segmentation and generate models based on existing anatomies by manipulating BMI to alter fat or muscle content, adding refinements such as enhanced vascular details, and adding pathological deformations.

SIM4LIFE:

A COMPUTABLE, FUNCTIONALIZED ANATOMICAL MODEL-CENTERED APPROACH TO COMPUTATIONAL LIFE SCIENCES

Numerical modeling is rapidly becoming the preferred approach for developing new therapies/treatments and diagnostic methods and for designing novel and next-generation medical devices. Simulations can provide a wealth of information that is not accessible through measurements. Until now, however, the modeling of technical devices and diagnostic and therapeutic tools has been possible only under simplified environmental conditions, greatly limiting the transferability of results to systems that involve complex living tissues and organs. This limitation has prevented the application of simulations for safety and efficacy evaluations to support regulatory submissions and to replace or supplement experimental investigations and clinical studies.

The ongoing *IT'IS for Health* research initiative on computational life sciences aims to propel numerical modeling in life sciences forward by integrating the intricacies of the physiological and physical mechanisms of the human body into reliable, complex, and realistic anatomical models. At the core of this initiative is *Sim4Life*, a project to create a computational framework with a series of verified and validated computable, functionalized anatomical models and the most powerful physical and tissue model solvers. As it entails ambitious innovation and detail at all levels of development, the generated knowledge is synthesized by a systematic approach that bridges physics, biology, engineering, and mathematics.

Functional Information

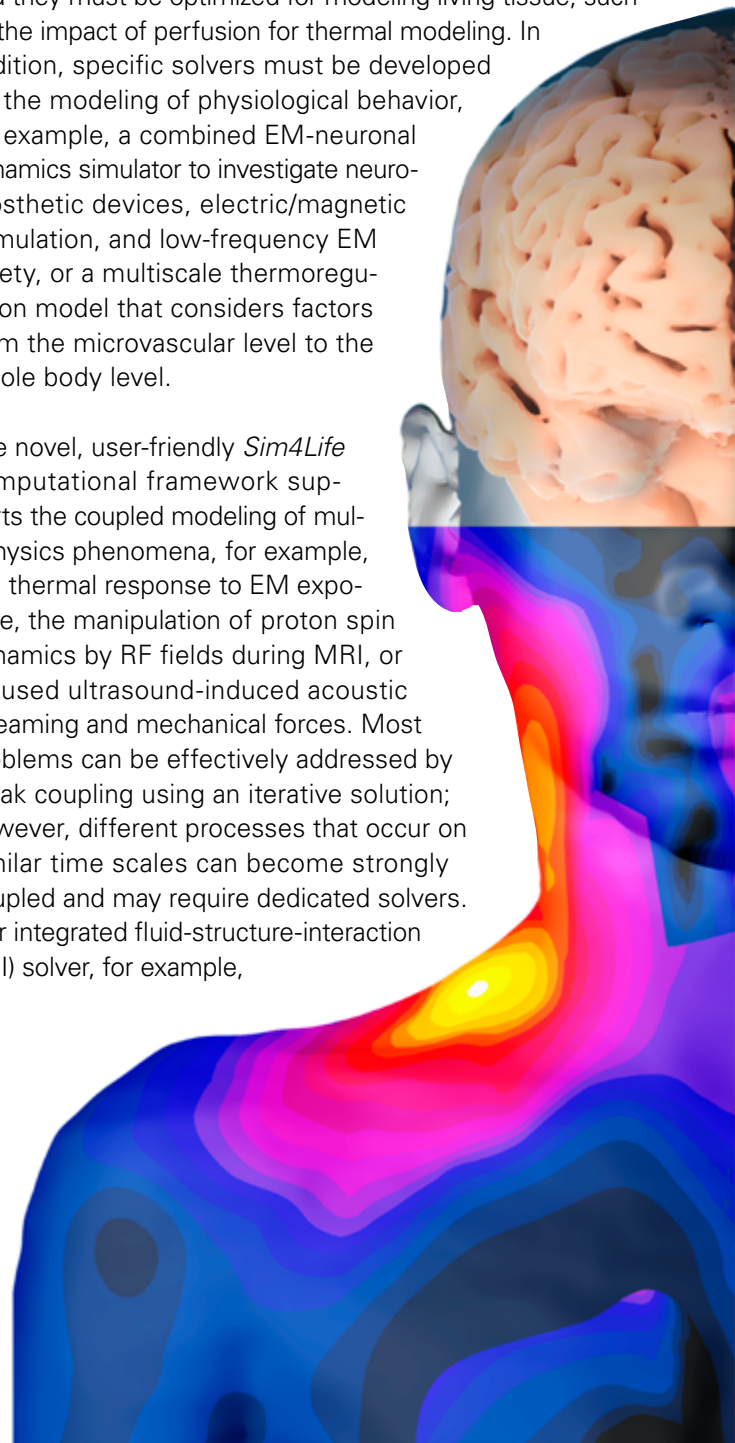
An important objective of the *Sim4Life* project was to develop and continually improve an integrative computational framework that covers a broad spectrum of spatial and temporal scales within a single modeling framework for understanding and visualizing the dynamic mechanisms underlying the human body. Functional information, such as tissue properties, tissue behavior, physiology and disease models, and novel physics solvers must be integrated into our highly detailed Virtual Population anatomical models. For example, anatomically and physiologically realistic computational models of neuronal dynamics and blood perfusion can determine how physical forces (electromagnetic fields, thermal exposure) generate physiological responses (neural activity, thermoregulation). Furthermore, the framework must be linked to an extensive and accurate database covering a wide range of physical

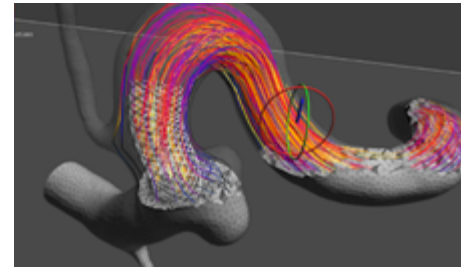
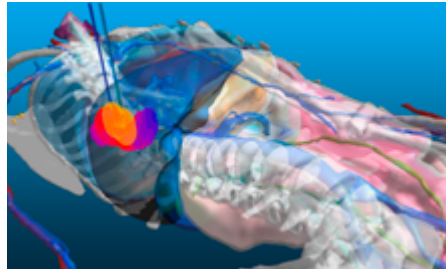
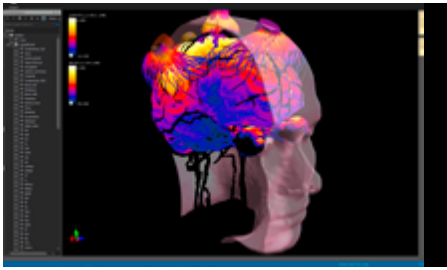
and physiological properties. To this end, IT'IS has taken on a pioneering role in providing a publicly available and continually updated tissue parameter database based on literature review and an online discussion forum.

Physics Solvers for Computable Phantoms

To handle the full complexity of human anatomy, powerful physics solvers must be able to handle complex, noisy geometries and large numbers of degrees of freedom, and they must be optimized for modeling living tissue, such as the impact of perfusion for thermal modeling. In addition, specific solvers must be developed for the modeling of physiological behavior, for example, a combined EM-neuronal dynamics simulator to investigate neuro-prosthetic devices, electric/magnetic stimulation, and low-frequency EM safety, or a multiscale thermoregulation model that considers factors from the microvascular level to the whole body level.

The novel, user-friendly *Sim4Life* computational framework supports the coupled modeling of multiphysics phenomena, for example, the thermal response to EM exposure, the manipulation of proton spin dynamics by RF fields during MRI, or focused ultrasound-induced acoustic streaming and mechanical forces. Most problems can be effectively addressed by weak coupling using an iterative solution; however, different processes that occur on similar time scales can become strongly coupled and may require dedicated solvers. Our integrated fluid-structure-interaction (FSI) solver, for example,





simultaneously solves the computational fluid dynamics, biomechanics, mesh adaptation, and deformation problems. This is essential for the accurate modeling of blood flow and vessel wall interactions to analyze the initiation and progression of vascular diseases, such as aneurysms and atherosclerosis.

A special set of solvers and tools in *Sim4Life* is being developed to better represent the anatomical variability of the general population, as our family of Virtual

Population models is currently limited to 10 base models. Four novel approaches have been devised to facilitate this expansion:

- 1) conducting biomechanical simulations to adjust postures or control changes in fat and muscle content;
- 2) applying novel interactive morphing tools to manipulate organ and body shapes;
- 3) applying multistage image registration methods to adapt existing models to patient specific data;
- and 4) incorporating breathing movements by applying 4D imaging-derived deformation fields.

Verification and Validation

Verification and validation as well as the determination of the related confidence intervals are essential for establishing the credibility and reliability of any simulation and analysis tool for numerical modeling. At IT'IS, verification is achieved by meticulously confirming and documenting that the models can correctly reproduce analytical or numerical benchmark solutions within a determined uncertainty for all relevant physical phenomena. Validation is always an

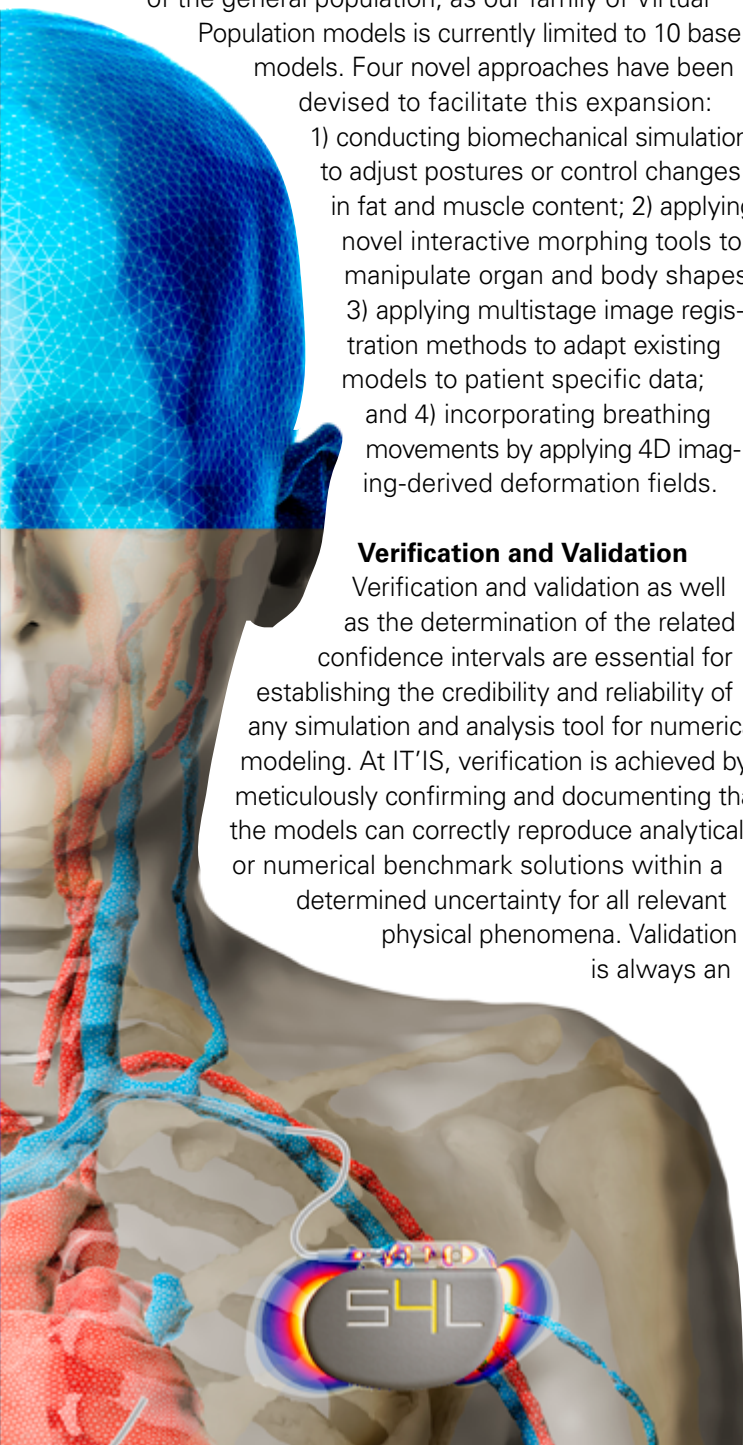
application-specific task, typically requiring experimental validation in combination with a detailed uncertainty analysis. We generally follow the standardized approach of the National Institute of Standards and Technology (NIST) and the ISO *Guidelines for Evaluating and Expressing the Uncertainty* (GUM). The determination of MRI patient exposure and safety in the presence or absence of medical implants is an example of a validated application.

Collaboration with ZMT Zurich MedTech

As the *Sim4Life* computational framework supports the simulation of complex dynamic processes within vast three-dimensional models, a robust and sustainable modular platform and graphical user interface are required to grant an extensive group of in-house and partner researchers reliable and instant access to our current and future research developments. In collaboration with ZMT Zurich MedTech, a unique platform was developed to offer: 1) context-aware interactions and maximum ease-of-use; 2) an integrated Python scripting environment allowing for a high degree of customization, and advanced analysis; 3) powerful, simultaneous visualization of artificial and anatomical geometries, medical image data, and measurement and simulation results and the seamless integration of medical image-based information; and 4) dataflow-oriented processing pipelines for combining analyses and/or simulation modules into flexible networks.

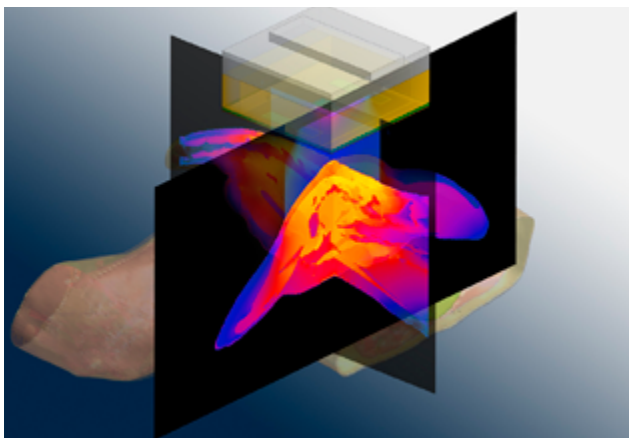
Next Development Objectives

The continued development of our *Sim4Life* simulation platform will remain the core activity of the IT'IS computational life sciences group and the *IT'IS for Health* initiative. We are currently 1) investigating techniques to individualize our computable, functionalized anatomical models for personalized medicine applications using the wide range of data accessible through modern diagnostic tools; 2) developing novel simulators of dynamic physical and physiological phenomena in the human body (e.g., a model of cortical activity); and 3) developing extended code and application validation methodologies. Continuing and accelerating these advancements will also require new collaborations with institutions to expand and add new features to the Virtual Population models for studying physical and physiological processes from the cellular to whole body level and interactions with external physical stimuli as well as for advancing personalized medicine.



HARNESSING TECHNOLOGY TO CREATE ADVANCED RF HYPER- THERMIA DELIVERY CONCEPTS

Hyperthermia is a non-invasive treatment modality to heat malignant tumors. During treatment, tumors are heated to 42–44 °C to increase cell sensitivity to the effects of ionizing radiation and chemotherapy. Heating is achieved by applying electromagnetic fields (EMFs) in the radiofrequency (RF) range generated by antennas placed outside the body.



Despite its long history of use and its proven effectiveness as an adjuvant therapy to radiotherapy, hyperthermia has not yet gained wide clinical acceptance. One of the limiting factors is the variability in outcome; mainly attributed to poorly controlled hyperthermia application due to the lack of or inadequate treatment planning, poor control of applied fields due to incorrect excitation or relative positioning with respect to the patient, or the use of inappropriate frequencies and technologies. Improvement in the quality of hyperthermia treatment remains a multifaceted technical challenge. To deposit energy at the desired location within a structure as complex as the human body, requires:

- accurate anatomical models of the patient's body in the region of the tumor and applicator(s), based on CT or MRI images, with the correct electrical/thermal properties allocated to each tissue
- a validated model of the RF applicator
- treatment optimization by electromagnetic (EM), thermal, and tissue damage modeling
- exact replication of the optimized configuration modeled by exact placement of the applicator(s) in the same position with respect to the patient anatomy and generation of the excitation, and preferably, appropriate feedback.

We have developed an applicator and treatment-planning system using new paradigms for enhanced QA to improve

outcomes. Patient-specific models are semi-automatically segmented based on the MRI or CT images for accurate EM/thermal/tissue damage modeling. Validated applicator models are automatically positioned and varied to optimize the treatment. Currently, thermal modeling includes non-linear changes in perfusion of the tissues with temperature and discrete blood vessels. Tissue damage modeling is based on CEM43.

Correct positioning of the applicator with respect to the patient and the application of the correct excitation field from each applicator to achieve maximum positive and negative interference are essential to effective treatment. To overcome the shortcomings of many existing systems, a novel approach – derived from technologies more commonly employed in defense systems – that measures the total radiated field irrespective of reflection, mismatch, cross coupling, and changes in any of these has been developed. The sensors are an integral part of the applicator and do not directly couple with other applicators. A cavity-backed slot antenna allows for the placement of a current sensor inside the cavity to measure element excitation, while preventing direct coupling to fields from other elements; thus, the desired measurand is isolated.

Data acquisition electronics are integrated into each element for the measurement of the current's amplitude and phase. The coupling matrix for the entire array can be rapidly and accurately determined by exciting each element separately. Excitation amplitudes and phases can be directly measured and confirmed to be as planned. Applicator supports are generated by the treatment optimization tool using rapid 3D printing technologies. This ensures exact relative positioning defined for a specific patient and aids placement with respect to the patient surface, such that the registration differences between treatment planning and the treatment are minimized.

In summary, the system overcomes several existing shortcomings, namely, the optimization of specific endpoints (e.g., tissue damage, temperature), the accurate positioning of the applicators, and the effective correction of the coupling and mismatch.

Predictive treatment planning has become a reality.

SERVICES

The IT'IS Foundation offers a wide range of R&D services to both academic and commercial partners to develop solutions and applications, from multiscale and multiphysics simulations to near-field measurements in the fields of physics, engineering, and medical technology. These service platforms are implemented in our state-of-the-art laboratories and engage the broad expertise and skills of our researchers and employees. Services include, but are not limited to:

RF Safety and Compliance Evaluation of Transmitters

The IT'IS Foundation is regarded as the pre-eminent, truly independent institute for dosimetric evaluation. We are committed to developing the most accurate, flexible, and suitable testing procedures in conjunction with regulators, national standards laboratories, and industry (see page 10). Our close cooperation with leading system manufacturers (e.g., SPEAG, ZMT Zurich MedTech) allows us to provide the best possible services based on the most recent and cutting-edge testing technologies.

MRI Safety & Compliance Evaluation of Implants

The IT'IS Foundation offers reliable and efficient solutions to address the safety of MRI and compliance of active and passive implants in MRI environments according to the latest ISO/IEC recommendations. Our involvement in standardization committees and close collaborations with regulatory bodies enables us to extend our network of partners and remain competitive in the field. Our comprehensive solutions include device RF characterization and numerical modeling at MRI frequencies, model validation test planning, and document preparation for FDA submissions. We also perform investigations on fundamental aspects of RF-implant interactions and provide customized solutions for mitigation of patient risk.

Communication Link System Design

We provide expert consultations on standards and homologation rules, including the revision of technical requirements, the assessment of regulation procedures, and the evaluation of impending standards. We also offer full development and design services for custom-specific antennas with optimized link budgets for operation in complex environments (e.g., on or inside the body).

Computational Life Science Evaluations and Analyses

The IT'IS Foundation provides expert, customized analyses and evaluations of specific medical diagnostic and therapeutic applications using our cutting-edge multiscale and multiphysics platform *Sim4Life*. We couple our expertise in bioelectromagnetics, computational engineering, and regulatory processes to maintain our excellence in computational life sciences. In addition, new models and features are continually developed for the Virtual Population (ViP), our suite of advanced computational phantoms. Our comprehensive database of the physical parameters of biological tissues is also updated and refined continually. The database is publicly available to the scientific community at www.itis.ethz.ch/database/.

Exposure Systems

The IT'IS Foundation designs and develops various exposure systems for *in vitro*, *in vivo*, and human studies on EM interactions. These systems can be customized to meet specific needs and are optimized for efficiency and flexibility while providing maximum homogeneity, a wide dynamic range, and a variety of amplitude modulation schemes. The exposure systems are suitable for a wide range of applications, including assessments of health risks, efficacy of therapies, or mechanisms associated with exposure to electromagnetic fields. The *Sim4Life* simulation platform is used to carefully evaluate the customization and optimization of each system. Additional features include compatibility with the close monitoring of environmental parameters and double-blinded experiments.

Safety White Papers

The IT'IS Foundation provides a full range of safety white papers that emerge from extensive research activities in health risk assessment and safety evaluations. Numerous international organizations, industries, and government agencies have entrusted the IT'IS Foundation to draft white papers for existing and future technologies as well as for specific devices.

Workshops

The IT'IS Foundation organizes customized workshops in collaboration with our national and international partners.

INFRASTRUCTURE

Dosimetric, Near-Field, and EMC/EMI Facilities

Semi-Anechoic Chamber

This shielded, rectangular chamber has the dimensions 7 x 5 x 2.9 m (L x W x H). It is equipped with a reflecting ground plane floor, and half of its walls are covered with electromagnetic absorbers. The chamber contains an integrated DASY52NEO system and can be utilized for all research activities involving dosimetric, near-field, and far-field evaluations, the optimization and synthesis of handheld devices, body-mounted transmitters, implants, desktop applications, micro-base and pico-base station antennas, exposure setups, calibration procedures, EMI tests, MRI safety tests, and compliance testing of implants.

Two Reverberation Chambers

The Blue and NIEHS reverberation chambers have the dimensions 4 x 3 x 2.9 m and 3.7 x 2.2 x 2.7 m (L x W x H), respectively. Both chambers are equipped with two mechanical stirrers and provide controlled and consistent environments for EM emissions and immunity testing, as well as shielding effectiveness and susceptibility testing of electromagnetic equipment.

Facility for Dosimetric Compliance Testing

IT'IS Foundation shares a facility with Schmid&Partner Engineering AG, which meets the requirements for dosimetric evaluations. The documentation of Class C accreditation has been completed.

Technical Equipment and Instrumentation

Spectrum and Network Analyzers

- 1 HP 8753E Network Analyzer, 30 kHz–6 GHz
- 1 HP APC 85033B Calibration Kit
- 1 Rohde & Schwarz FSP Spectrum Analyzer, 9 kHz–30 GHz
- 1 Rohde & Schwarz ZVA24 Vector Network Analyzer, 10 MHz–24 GHz
- 1 Rohde & Schwarz ZVA50 Vector Network Analyzer, 10 MHz–50 GHz
- 1 Rohde & Schwarz ZV-Z52 Calibration Kit

Signal Generators and Testers

- 3 Agilent 33120A, Waveform Generators
- 1 Agilent 33250A, Waveform Generator
- 1 Agilent E8251A Signal Generator, 250 KHz–20 GHz
- 3 Anritsu 3700A
- 2 Anritsu MG3700A
- 1 HP 8647A, Signal Generator 250 KHz–1000 MHz
- 1 Rohde & Schwarz CMU200
- 1 Rohde & Schwarz CMW500
- 1 Rohde & Schwarz CTS55, Digital Radio Tester
- 1 Rohde & Schwarz SMIQ02B, Signal Generator
- 2 Rohde & Schwarz SML02, Signal Generators
- 1 Rohde & Schwarz SML03, Signal Generator
- 1 Rohde & Schwarz SMT06, Signal Generator
- 1 Rohde & Schwarz SMU200A, Signal Generator
- 1 Rohde & Schwarz SMY02, Signal Generator

DASY, iSAR, EASY4MRI, MITS, PiX

- 1 INDY (3 year old child head) Phantom
- 1 ISABELLA (6 year old child head) Phantom
- 1 METROLAB, THM 1176, Magnetic Field Sensor
- 1 SPEAG AMIDV2, Audio Magnetic Field Probe
- 1 SPEAG AMIDV3, Audio Magnetic Field Probe
- 3 SPEAG ASTM Phantoms
- 2 SPEAG DAE4, Data Acquisition Electronics
- 4 SPEAG DAEasy4MRI, Data Acquisition Electronics
- 1 SPEAG DAK 12/3.5/1.2E
- 2 SPEAG DASY52NEOs
- 4 SPEAG EASY4MRI
- 1 SPEAG EE3DV1, E-Field Probes
- 1 SPEAG EE3DV3, E-Field Probes
- 1 SPEAG EF3DV6, E-Field Probe
- 2 SPEAG ELI4 Phantoms
- 2 SPEAG ER3DV6, E-Field Probes
- 1 SPEAG ET1DV4, Dosimetric Probe
- 2 SPEAG ET3DV6, Dosimetric Probes

- 1 SPEAG EU2DV2, Probe
- 1 SPEAG EX3DV3, Dosimetric Probe
- 3 SPEAG EX3DV4, Dosimetric Probes
- 1 SPEAG H1TDS7zV1, H-field Time Domain Sensor
- 1 SPEAG, H1TDSxV1, H-field Time Domain Sensor
- 4 SPEAG H3DV6, H-Field Probes
- 3 SPEAG H3DV7, H-Field Probes
- 1 SPEAG HAC RF Extension
- 1 SPEAG HAC T-Coil Extension
- 1 SPEAG HU2DV1, Probe
- 4 SPEAG iSAR2 (2 Flat, 1 Head & 1 Quad)
- 1 SPEAG SAM V6.0 Phantom
- 3 SPEAG T1V3LA, Temperature Probes
- 2 SPEAG T1V3, Temperature Probes
- 1 SPEAG T1V3LAB, Temperature Probe
- 1 SPEAG ES3DV2, Temperature Probe
- 1 SPEAG TSIL, Temperature Probe
- 1 ZMT MITS 1.5 w/Phantoms
- 1 ZMT MITS 3.0 w/Phantoms
- 1 ZMT MITS Gradient
- 1 ZMT PiXE64
- 1 SPEAG D900, Validation Dipole
- 1 SPEAG D835, Validation Dipole
- 1 SPEAG D1640, Validation Dipole
- 1 SPEAG D1800, Validation Dipole
- 1 SPEAG D1900, Validation Dipole
- 1 SPEAG D5GHz, Validation Dipole
- 1 SPEAG CD835V3, Validation Dipole
- 1 SPEAG CD1880V3, Validation Dipole
- 1 SPEAG CD2450V3, Validation Dipole
- 2 SPEAG PiXitor 64 MHz
- 1 Log-Periodic Antenna (650–4000 MHz)
- 2 Generic Phones (835/1900 MHz)

Meters

- 3 Agilent 34970A Data Acquisition Units
- 2 Agilent E4419B, 4 HP 8482A, Power Meters
- 1 Handyscope HS3 Data Acquisition Unit
- 1 Handyscope HS4 Data Acquisition Unit
- 3 HP 436A, 3 HP 8481A, Power Meters
- 1 Magnet Physik FH49–7030, Gauss/Teslameter
- 2 Rohde & Schwarz NRP2 Power Meters

Amplifiers

- 1 Amplifier Research 10S1G4A, Amplifier, 800 MHz–4.2 GHz
- 1 Kalmus 717FC RF Power Controller, 200–1000 MHz
- 1 LS Elektronik 2450 Amplifier, 400 W / 900 MHz
- 3 LS Elektronik 2449 Amplifiers, 200 W / 900 MHz
- 2 LS Elektronik 2448 Amplifiers, 60 W / 900 MHz
- 3 LS Elektronik 2452 Amplifiers, 200 W / 1800 MHz
- 1 LS Elektronik 2451 Amplifier, 60 W / 1800 MHz
- 1 LS Elektronik 2447 Amplifier, 5 W / 1800 MHz
- 2 LS Elektronik 2780 Amplifiers, 40 W / 2140 MHz
- 8 Mini-Circuits Amplifiers, ZHL42, 700–4200 MHz
- 2 Mini Circuits Amplifiers, ZVE-8G, 2–8 GHz
- 1 NucleTudes ALP336 Amplifier, 1.5–2.5 GHz
- 2 Ophir 5141, 700 MHz–3 GHz

Other Equipment

- 8 Maury 1878B, 3-Step Tuners
- 1 Narda EHP-50 EM Field Probe Analyzer, 5 Hz–100 KHz
- 1 Narda ELT-400 Magnetic Field Probe, 1 Hz–400 KHz
- 1 Siemens, Universale Messleitung, (0.5) 1–13 GHz
- 2 SPEAG Dipoles SCC34 Benchmark
- 3 SPEAG, SHO V2 RB, RC&RP, OTA Hand Phantoms
- 6 Validation Dipoles D835, D900, D1640, D1800, D2450, D5GHz

Computers

- 52 Laptop Computers (from Apple, Asus, Lenovo)
- 12 Intel Core i7 based, 16–31GB RAM
- 14 Intel Core i7 based, 4–15GB RAM
- 8 Intel Core i5 based, 4–15GB RAM
- 6 Intel Core2Duo based, 1–3GB RAM
- 12 Intel Core2Duo based, 4–15GB RAM
- 49 Workstation Computers (custom built, and from Dalco, HP)
 - 1 Intel Xeon based, dual socket, 16-31GB RAM
 - 5 Intel Xeon based, 16–31GB RAM
 - 2 Intel Core i7 based, 64GB RAM
 - 14 Intel Core i7 based, 32–63GB RAM
 - 11 Intel Core i7 based, 16–31GB RAM
 - 10 Intel Core i7 based, 4–15GB RAM
 - 1 Intel Core i5 based, 4–15GB RAM
 - 1 Intel Core2Duo based, 4–15GB RAM
 - 2 AMD Opteron based, Dual socket, 16–31GB RAM
 - 1 AMD Opteron based, Dual socket, 4–15GB RAM
 - 1 Intel Pentium 4 based; Dell, 1–3GB RAM
- 10 Clusters and Specialized Computational Systems (from Dalco, Nvidia)
 - 1 Nvidia S1040 based computational cluster, 4 nodes (each with 4xNvidia T10 GPUs, 16GB VRAM, QuadCore CPUs, 32GB RAM)
 - 2 Intel Xeon based, Dual socket, 64–255GB RAM, Quad Tesla GPU
 - 1 Intel Xeon based, Dual Socket, 8–63GB RAM
 - 3 Intel Xeon based, Dual Socket, 64–255GB RAM
 - 2 Intel Xeon based, Dual Socket, 256–1023GB RAM
 - 1 Intel Xeon based, Quad Socket, 512GB RAM
- 5 Servers (from Dalco, Synology, QNAP, Apple)
 - 1 Intel Xeon based, Dual socket, 4–15GB RAM
 - 1 Intel Core2Duo based, 8GB RAM
 - 2 Intel Atom based NAS, >30TB network file storage
 - 1 Marvell ARM based NAS, 8TB network file storage
- 18 Miscellaneous Computer Hardware
 - 5 Nvidia Tesla GPU PCIe Cards (attached to workstations)
- 10 Apple AirPort Extreme WiFi base stations
- 1 Xerox Monochrome Laser Printer
- 1 Xerox Color Laser Printer
- 1 Personal Tablet, Intel Atom based

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IT^{IS} FOUNDATION

History

The IT^{IS} Foundation was established in 1999 through the initiative and support of the Swiss Federal Institute of Technology in Zurich (ETHZ), the global wireless communications industry, and several government agencies. IT^{IS} stands for Information Technologies in Society.

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Funding

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Sensor Technology

Dr. Sven Kühn
+41 44 245 9694
kuehn@itis.ethz.ch

EMC, Transmitters Health Support Systems

Dr. Myles H. Capstick
+41 44 245 9743
capstick@itis.ethz.ch

Comp. Electrodynamics

Dr. Nicolas Chavannes
+41 44 245 9740
chavannes@itis.ethz.ch

Comp. Life Sciences EM Cancer Treatment

Dr. Esra Neufeld
+41 44 245 9698
neufeld@itis.ethz.ch

President

Prof. Peter Niederer
+41 44 245 9696
niederer@itis.ethz.ch

Director

Prof. Niels Kuster
+41 44 245 9690
kuster@itis.ethz.ch

Associate Director

Dr. Myles H. Capstick
+41 44 245 9743
capstick@itis.ethz.ch

Main Office Address

IT^{IS} Foundation
ETH Zentrum ETZ
CH-8092 Zurich
Switzerland

Phone +41 44 245 9696
Fax +41 44 245 9699

Mailing Address and Labs

IT^{IS} Foundation
Zeughausstrasse 43
CH-8004 Zurich
Switzerland

info@itis.ethz.ch

Certification Research

Dr. Mark G. Douglas
+41 44 245 9680
douglas@itis.ethz.ch

Dosimetry

Dr. Eugenia Cabot
+41 44 245 9681
cabot@itis.ethz.ch

Health Risk Assessment

Prof. Niels Kuster
+41 44 245 9690
kuster@itis.ethz.ch

Exposure Systems

Dr. Manuel Murbach
+41 44 245 9694
murbach@itis.ethz.ch

Virtual Population

Dr. Davnah Payne
+41 44 245 9686
payne@itis.ethz.ch

www.itis.ethz.ch