Progetto: EuroBioimaging – ERIC: Technical-Scientific description
EuroBioimaging-ERIC Italia (EuBI-IT) è costituito da 16 diverse facility di imaging sparse in tutta Italia in 9 diverse città. Si sono organizzati in 4 nodi e coprono dall'imaging biologico a quello biomedico (Enti partecipanti: Università, Istituti CNR, IRCCS).

ITALY: Advanced Light Microscopy Italian Node: The Italian ALM Node is a large multi-modal and multi-sited Node that comprises five imaging facilities located in Naples, Genoa, Padua, Florence and Milan.The Italian ALM Node is a large multi-modal and multi-sited Node that comprises five imaging facilities located in:
Naples: Institute of Biochemistry and Cell Biology (http://www.ibbc.cnr.it/euro-bioimaging-facility/)
Genoa: Italian Institute of Technology (https://www.iit.it/research/lines/nanoscopy-nic-iit)
Padua: Laboratory of CA2+ and cAMP signaling in physiology and pathology (https://www.biomed.unipd.it/ricerca/aree-tematiche/cell-signaling/ca2-and-camp-signalling-physiology-and-pathology)
Florence: European Laboratory for Non-linear Spectroscopy, LENS (https://lens.unifi.it/)
Milan: Advanced Light and Electron Microscopy Bio-Imaging Centre (Alembic) (http://alembic.hsr.it)

These facilities have a long experience of mutual interaction and collaboration. The Node is coordinated by the Institute of Biochemistry and Cell Biology, Naples, an institute belonging to the National Research Council of Italy. The Node provides open-access imaging services to both academia and industry and serves about 1000 users annually. While each location provides access to a wide range of technologies, they also specialize in one or two specific technologies as listed below. The Node offers a complete service package starting from sample preparation and imaging to final image analysis, quantitation and visualization.

Specialties and expertise of the Node: The facilities of this Node offer a broad range of services but they specialize in particular in the following technologies and research areas:

Technologies

- Naples: Correlative light electron microscopy with 3D imaging, correlative microscopy with FRET imaging
- Genoa: Super-resolution, multiphoton and fast volumetric imaging
- Padua: Functional imaging, FRET-based imaging, FRAP, Two-photon microscopy in living cells, tissues and animals
- Florence: Non-linear microscopy, functional imaging in animals and structural imaging of cleared and expanded samples (human and animal), 2D - 3D single molecule localization and tracking
- Milan: Correlative microscopy with 3D tomography, large sample imaging, high-throughput microscopy and in-flow microscopy

Research applications

- Naples: Cell biology, membrane trafficking, signaling, cancer biology
- Genoa: Development of novel technologies and instruments for advanced diagnostics from the nano- to the macro-scale
- Padua: Signaling, neurobiology, intracellular signaling molecules real time imaging, two-color microscopy, biosensors generation and characterization

- o Florence: Human and mouse brain connectome reconstruction, Neurodegenerative diseases, Remapping of lost functions after stroke, Clearing specimens, Multimodal fiber-probe spectroscopy for tissue diagnostics, Bacterial biofilm
- o Milano: Cell biology, Neuroscience, Oncology, Immunology, Gene and Cell Therapy

The member groups also have experience with a wide spectrum of model systems including mammalian cell culture systems, insect cell culture systems, and model organisms like Drosophila, Zebrafish and mouse and also with handling human tissue samples.

Additional services offered by the Node

- o Support in experimental design
- o Technical assistance to use the microscopes
- o Practical training courses
- o Cell culture facilities
- o Wet lab space
- o Animal facilities
- o Data processing and analysis
- o Biosensors generation and characterization

Instrument highlights

The members of the Italian ALM Node are also involved in the development of novel imaging methods, instrumentation and reagents. These include:

- o Naples: FRET-based methods to detect large multi-molecular complexes, Raman microscopy, image analysis methods and microfluidics
- o Genoa: Super-resolution microscopy, fast volumetric light sheet, Expansion Microscopy, correlative light - atomic force microscopy (AFM-STED)
- o Padua: functional imaging, genetically encoded and chemical probes for functional imaging of intracellular signaling molecules and metabolites, whole brain and tissue two-photon microscopy
- o Florence: functional imaging, Raman imaging, whole brain and tissue expansion imaging
- o Milan: Correlative light Microscopy methods, High-throughput microscopy approaches and image analysis

Contact details: **Seetharaman Parashuraman:** Coordinator of the Italian ALM Node raman.sp@cnr.it; +39 081 6132 283

ITALY: Molecular Imaging Italian Node: The Multi Modal Molecular Imaging (MMMI) Italian Node is a multi-sited Node focused on biomedical imaging, and offering expertise and technical skills for the acquisition and analysis of "in vivo" images obtained by the most relevant state-of-the-art imaging technologies. The MMMI Italian Node comprises 8 research centers, each with its own specialties, located in 4 Italian cities (Turin, Milan, Naples, and Pisa). The Node provides the users with many services including a large repository of imaging agents/tracers for the available imaging technologies, and a number of cellular and animal models (mainly mice) reproducing the most relevant human pathologies. Support is available for advanced applications including quantitative assessment of biomarkers as well as "in vitro" assays for the validation of the imaging experiments.

Specialties and expertise of the Node: The Node is well equipped with chemical instrumentation and offers support in the design, characterization and testing of imaging probes (molecular, macro- and supra-molecular, nano- and micro-sized systems) for all the Imaging Modalities. The expertise at the Node's centers covers the design of targeting and responsive imaging procedures. Several MRI (from 1T to 9.4T), Optical Imaging, PET and SPECT scanners are offered in conjunction with the proper tracers at centers excelling in research on the investigated pathologies (Milan and Naples for neurological diseases, Pisa and Naples for cardiovascular diseases, Turin and Naples for oncological diseases, and Pisa for metabolic diseases). The Node has also strong expertise in imaging procedures within the integrated diagnostic MRI-PET and PET/CT with total body and district acquisition mode, as well as on quantitative morphology by standalone CT/microCT. High frequency ultrasound technology is also available providing high-quality morphological, and functional information.A biobank service is also available, providing analysis of biochemical components (DNA extraction, RNA, proteins, etc) of different types of biological materials.

Additional services offered by the Node

- o Relaxometry
- o Probe preparation
- o Animal preparation
- o Animal facilities
- o Cell culture, microscopy, histology
- o Wet lab space
- o Radiochemistry facility
- o Radionuclide production facility (cyclotron)
- o Laboratory for detector development and testing
- o Image processing and analysis
- o Biobanking
- o Methodological setup (e.g. design of study protocol and standard operation procedures)

Contact details: **Enzo Terreno**, Coordinator
Website: http://www.mmmi.unito.it/
Phone: +39 0116706451
e-mail: enzo.terreno@unito.it

ITALY: Digital Imaging Multimodal Platform Neuromed - DIMP NEUROMED: The Digital Imaging Multimodal Platform Neuromed - DIMP NEUROMED is a single- sited, multimodal Node aiming to provide access to an integrated digital analysis support for preclinical and clinical studies in the field of neuroscience, extending from the study and evaluation of animal models to their translation into clinical practice. It is composed of a preclinical (Multimodal Molecular Imaging) and clinical (Population Imaging) access to imaging technologies and molecular probes, producing digital images which are elaborated in a dedicated High Performance Computing System (Population Imaging). Data are collected with multimodal imaging instrumentation and analyzed to extrapolate imaging features to quantitative parameters of clinical interest. These parameters are exported to the classification of the clinical case. A similar approach is used for the study of cancer therapies response, which are first done with mice models and xenografted cancers.

Users can either perform their preclinical and population imaging studies using the measurement and analysis infrastructure, or profit of the large database of preclinical and clinical digital images in order to test their hypothesis with artificial intelligence tools developed by Neuromed (based on Convolutional Neural Networks and local TensorFlow applications).

Specialties and expertise of the Node: Beyond the conventional functional imaging equipment (including among others a micro PET/CT and a 7T MRI system), the available instrumentation includes a Digital microPET/CT (RAYCAN E180) scanner, which, unique in Europe, allows to obtain high resolution functional images in dynamic mode, with time slices as short as 30 seconds thanks to its extremely high sensitivity.NEUROMED develops its own dedicated image reconstruction algorithms, image visualization and analysis techniques. Brain segmentation, textural characterization and statistical analysis algorithms developed by the center are available for precise quantitative analysis. The equipment has been recently completed by one of the most modern high performance computing systems based on the Memory Driven Computing architecture by Hewlett Packard Enterprise (HPE), which has been developed specifically for "-omics" studies and population imaging studies. Access to the digital imaging platform iPLAT, with customized artificial intelligence and convolutional neural network-based image analysis software developed by the Neuromed scientists for the classification of neurological and oncological diseases based on medical images, is provided.

Additional services offered by the Node

- o Project planning and methodological setup
- o Wet labs
- o Cell culture facilities
- o Animal housing
- o Chemistry and radiochemistry labs
- o Biobanking
- o Data processing and analysis
- o Data storage

Contact details

Administrative coordinator:
Dr. Emilia Belfiore
dimp@neuromed.it

Scientific coordinator (representation in the Panel of the Euro-BioImaging Nodes)
Prof. Dr. Nicola D'Ascenzo
nicola.dascenzo@neuromed.it

ITALY:Phase Contrast Imaging Flagship Node Trieste: The Italian Phase Contrast Imaging Flagship Node is based on the SYRMEP beamline of the Elettra Synchrotron light source (Trieste). The main characteristics of Synchrotron Radiation, namely monochromaticity, high intensity and spatial coherence, allow the effective application of phase contrast techniques. Differently from conventional radiology, where the image formation relies on the absorption properties of the sample, these approaches are sensitive to the phase shifts produced by the sample on the incoming X-rays. Phase contrast is particularly effective for imaging of soft biological tissues, where the conventional technique has strong limitations due to the poor intrinsic X-ray absorption. The beamline provides two stations working with monochromatic or white/pink X-ray beam for planar and Computed micro-Tomography (microCT) imaging. A CT system based on a micro-focus X-ray source, named TomoLab, is available, if required in the proposal, as auxiliary facility. The Node offers full packages including image acquisition, reconstruction and data reduction tools.

Specialties and expertise of the Node: Being part of the Elettra facility, the SYRMEP beamline is open to external users since 2000. The beamline control system has a user friendly interface, to facilitate the access by researchers without specific knowledge of Synchrotron Radiation. The beamline staff has several years of expertise in X-ray techniques, image processing and analysis, matured collaborating with users and imaging groups of other laboratories. Competences in application of new modalities like the low dose phase contrast CT, suited for in-vivo studies, and in dosimetry, have also been developed. A software package for CT reconstruction, SYRMEP Tomo Project (STP), has been specifically designed for the beamline users and offers flexible solutions to satisfy the various experimental needs. The research team has also developed Pore3D, a software library for quantitative analysis of 3D images. The library includes several functions and procedures for performing filtering, segmentation, skeletonization as well as the extraction of quantitative values.

Instrument highlights: Special features of instruments at the Italian Node are:

- o The possibility to perform multi-scale Synchrotron Radiation imaging in propagation-based phase contrast modality at different resolution levels (imaging pixel sizes from 1 μm to 50 μm, according to the sample sizes and characteristics).
- o The use of a dedicated Analyzer Based Imaging setup working with a monochromatic beam in the X-ray range between 15 keV and 35 keV.
- o The possibility to optimize the imaging protocol and reconstruction workflow according to the specific application (using the different pre-processing/reconstruction algorithms available in the STP).
- o The high flexibility of the experimental station that allows to fulfill different user requirements (in-situ, implementation of new instrumentation, etc.).

Contact details

Dr. Giuliana Tromba
SYRMEP Beamline Coordinator
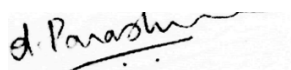giuliana.tromba@elettra.eu
+390403758587
SYRMEP Beamline:
https://www.elettra.trieste.it/elettra-beamlines/syrmep.html
TomoLab:
https://www.elettra.trieste.it/lightsources/labs-and-services/tomolab/tomolab.html
Pore3d Library:
http://www.elettra.eu/pore3d

Seetharaman Parashuraman   Dr. ssa. Claudia Miele
Co-ordinator, Italian ALM node of EUBI-IT   Direttore f.f.
                                                      IEOS-CNR