INTERNATIONAL WORKSHOP ON

IMAGING

Villa Monastero, Varenna (Como Lake), Italy
September 26 – 29, 2023

IMAGING 2023

Villa Monastero, Varenna
September 26-29, 2023

INVITED SPEAKERS
ORALS
INDUSTRIAL CONTRIBUTIONS

DAY 1 - TUE 26 SEPT

Start	End			
09:00	10:00	*Registration and Coffee*		
10:00	10:30	*Welcome*	*Alberto BRAVIN, Daniela DI MARTINO*	

MORNING — **Title**

Data processing and Artificial intelligence

		Chair:	*Michele FUMAGALLI*	
10:30	11:00		Xavier PROCHASKA University of California Santa Cruz	From the Stars to the Sea: Accelerating Discoveries in Science with Artificial Intelligence
11:05	11:35		Francesca PALERMO CNR-Nanotec Roma	Identification of early imaging markers to predict dementia: the role of the gut
11:40	12:10		Gianfelice CINQUE Diamond Light Source	Synchrotron InfraRed for Molecular Imaging e.g. Cultural Heritage/Archaeology and BioMedicine at Diamond
12:10	12:30	*Group Photo*		
12:30	14:30	*Lunch*		

AFTERNOON

Combined methodologies (Hybrid technology) and New imaging applications

		Chairs:	*Marco PAGANONI / Marine COTTE*	
14:30	15:00		Paul LECOQ CERN	Time-of-Flight PET scanner: From Hope to Practice
15:05	15:25		Fiammetta PAGANO University of Milano-Bicocca and CERN	Heterostructured Scintillators: A Novel Approach to Achieving High Sensitivity and Fast Timing in TOF-PET
15:30	16:15	*Coffee*		
16:15	16:35		Carlo PEIFFER University College London	X-ray phase contrast strain imaging using edge illumination
16:40	17:00		Nicola MOSCO INFN - Torino	4D GRAPH-X: Grating-based phase contrast X-ray imaging
17:05	17:25		Sergei GASILOV Canadian Light Source	Tofu ez and tofu flow: interactive user-friendly tools for optimization of reconstruction parameters and batch processing of microCT data
17:30	17:50		Margaux BOUZIN University of Milano-Bicocca	Model-based image reconstruction for super-resolution photo-thermal imaging
17:55	18:10		Cristina MATTONE CAEN S.p.A.	Tools for Discovery meet Educational Labs!
18:10		*Free Time*		
19:30		*Welcome Party*		

DAY 2 - WED 27 SEPT

MORNING

Imaging for cultural heritage, homeland security and engineering

		Chairs:	*Anders KAESTNER / Giovanni ROMANELLI*	
09:00	09:30		Marine COTTE ESRF	Making advanced synchrotron radiation microscopes accessible and easy to use for heritage science
09:35	10:05		Alessandro TENGATTINI Institut Laue-Langevin	Simultaneous neutron and X-ray tomography at NeXT-Grenoble to explore coupled processes in porous media
10:10	10:30		Eberhardt LEHMANN Paul Scherrer Institut	How to present neutron imaging data from studies of cultural heritage objects best – the example of ancient Tibetan bronze sculptures
10:30	11:00	*Coffee*		
11:00	11:30		Antonella SCHERILLO ISIS Neutron and Muon Soucre, STFC	Neutron imaging application in Cultural heritage at ISIS – successful stories and new developments
11:35	11:55		Francesca TANSELLA University of Torino	Computed Tomography of ancient wood wind instruments and the possibility of rediscovering their sound.
12:00	12:20		Giulia MARCUCCI University of Milano-Bicocca	Micro-XRF and PIXE/PIGE Imaging of ancient Roman "glass-gems": insights
12:25	12:45		Matteo BUSI Paul Scherrer Institut	Advanced neutron imaging techniques at the Paul Scherrer Institute
12:45	14:30	*Lunch*		

AFTERNOON

		Chairs:	*Eberhardt LEHMANN / Raffaele AGOSTINO*	
14:30	15.00		Giovanni ROMANELLI University of Rome Tor Vergata	Incoherent inelastic neutron imaging applied to the catalytic conversion of molecular hydrogen
15:05	15:25		Davide MEREGALLI GILARDONI S.p.A.	X-Ray Image processing and Artificial Intelligence Algorithms applied to Homeland Security
15:30	16:00		Nikolay KARDJILOV Helmholtz-Zentrum-Berlin (HZB)	Recent Advancements in Neutron Imaging
16:05	16:25		Anders KAESTNER Paul Scherrer Institut	Quantitative analysis in neutron imaging
16:30	17:45		**Poster session-1 & Coffee** **(coffee till 17:00)**	
17:45	18:00		Luigi CIMMINO CAEN S.p.A.	Radiographic Imaging with muons for underground and safeguard applications
18:05	18:25		Elena LONGO Elettra - Sincrotrone Trieste S.C.p.A.	The SYRMEP X-ray imaging beamline of Elettra: recent advances for biomedical, environmental and cultural heritage studies
18:30	19:00		Diego DREOSSI Elettra - Sincrotrone Trieste S.C.p.A.	SYRMEP-LS: the new hard X-ray imaging beamline at Elettra 2.0
19:00		*Free Time*		

DAY 3 - THUR 28 SEPT

MORNING

Biomedical imaging for diagnosis and therapy: techniques and achievements

		Chairs:	*Gianfelice CINQUE / Alberto DEL GUERRA*	
09:00	09:30		Alberto DEL GUERRA University of Pisa	The Birth, The Growth and The Future of Physics in Medical Imaging
09:35	10:05		Silvia CIPICCIA University College London	Brain imaging: a great challenge from macro to nano
10:10	10:40		Viktor NIKITIN Argonne National Laboratory	Real-time X-ray tomographic imaging at the Advanced Photon Source
10:40	11:10	*Coffee*		
11:10	11:40		Paola COAN Ludwig Maximilian University	Synchrotron X-rays to elucidate anatomy, pathology and therapy
11:45	12:05		Sandro DONATO University of Calabria	Phase-contrast micro tomography for 3D virtual histology of paraffin-embedded human tissues
12:10	12:40		Julia HERZEN Technical University of Munich	Quantitative X-ray imaging – towards material-specific numbers from images
12:40	14:30	*Lunch*		

AFTERNOON

		Chairs:	*Giuseppe GORINI / Sam BAYAT*	
14:30	15:00		Raffaele AGOSTINO University of Calabria	Introducing µTomo2 and SoftX: STAR's beamlines for high-energy X-ray imaging
15:05	15:35		Marie JACQUET IJCLab/University of Paris-Saclay	The characteristics of the inverse Compton scattering source ThomX and the imaging plans
15:35	16:10	*Coffee*		
16:10	16:30		Maurizio SANTINI University of Bergamo	Image analysis for the determination of the diffusion coefficient in histological specimens by radiographs
16:35	16:55		Grammatiki LIOLIOU University College London	Flyscan compatible scanning schemes for x-ray µ-CT with a structured beam
17:00	17:20		Ian BUCHANAN University College London	Direct measurement of scattering signals with Edge Illumination and the difference from interferometric measurements of the same quantity
17:25	17:45		Morgane SOWINSKI CNRS/MNHN	Seeing inside the frog's body: from the larynx to the ear
17:50	19:30		**Poster session-2 & refreshment** **(refreshment at the bar till 18:45)**	
19:55		*Departure for Social Dinner*		
20:15		*Social Dinner*		

DAY 4 - FRI 29 SEPT

MORNING

Microtomography: present and future

		Chairs:	*Andrea ALIVERTI / Paola COAN*	
09:00	09:30		Mohsen SAMADI KHOSHKHOO CARL ZEISS S.p.A.	Extending Synchrotron X-ray Microscopy to the Laboratory – X-Ray Microscopy as a correlative imaging technique
09:35	09:55		Clara MAGNIN University of Grenoble Alpes	X-ray Phase Contrast and Dark-field imaging on laboratory equipment using random modulation
10:00	10:20		Joshua GOBÉ Lyon Neuroscience Research Center	High-resolution brain tractography from X-ray phase-contrast images
10:25	11:00	*Coffee*		
11:00	11:20		Sam BAYAT University of Grenoble Alpes	4D Synchrotron X-ray µCT Imaging of Lung Tissue Strain in Bleomycin-Induced Lung Injury in Rats
11:25	11:45		Andrea ALIVERTI Polytechnic of Milano	Micro-CT-derived ventilation biomarkers for precision preclinical response to therapy in a quantitative functional assessment of pathology and mouse model of lung fibrosis
11:50	12:10		Anna CAROLI Mario Negri IRCCS	Imaging in kidney disease
12:15	12:35		Eugenio VOCATURO CNR-Nanotec	Multiple instance Learning approaches for E-health and advanced diagnostics
12:40	12:50		**Conclusions**	
12:50	13:00		**Prize ceremony**	

INVITED

From the Stars to the Sea: accelerating discoveries in science with Artificial Intelligence

J. Xavier Prochaska

University of California Santa Cruz

I will briefly summarize the rise of big data in Astronomy & Astrophysics, two data-driven fields of science. I will then highlight advances in artificial intelligence which have accelerated research in Astronomy and Oceanography, especially in image processing and analysis.
With the next generation of major space and sea surveys upon us, machine learning will be essential to explore these massive datasets and, possibly, give rise to entirely unanticipated discoveries.

INVITED

Identification of early imaging markers to predict dementia: the role of the gut

F. Palermo[1,2], A. Sanna[1,2,3], L. Massimi[1], L. Maugeri[2], I. Bukreeva[1], M. Fratini[1,4], G. Gigli[2], N. Kerlero de Rosbo[1,5] C. Balducci[6] & A. Cedola[1]

[1] Institute of Nanotechnology—CNR, Rome, Italy. [2]Institute of Nanotechnology—CNR, Lecce, Italy. [3]Université Grenoble Alpes, Grenoble, France. [4]IRCCS Fondazione Santa Lucia, Laboratory of Neurophysics and Neuroimaging (NaN). [5]Department of Neurosciences, Rehabilitation, Ophthalmology and Maternal-Fetal Medicine (DINOGMI), University of Genoa, Genoa, Italy.[6] "Mario Negri" Institute for Pharmacological Research IRCCS

In elderly individuals, AD is often associated with frailty, a condition of increased susceptibility to internal and external stressors, reflecting a progressive accumulation of biological deficits across different organs and systems leading to negative outcomes. One of the main reasons explaining the multiple failures of clinical trials attempted so far for AD is the inability to timely predict its development.

We uncover, at pre-clinical level and within the asymptomatic time frame, early imaging predictors, which will distinguish frail subjects prone to develop AD from those that will not, using a multi-organ approach.

We have used multi-organ (brain, gut, eyes), multi-imaging techniques, including X-ray-phase contrast tomography and structural/functional magnetic resonance. We identified early morphological/structural/cellular changes in the gut that could be predictive of AD.

INVITED

Synchrotron InfraRed for Molecular Imaging

e.g. Cultural Heritage/Archaeology and BioMedicine at Diamond

Gianfelice Cinque

MIRIAM Beamline B22, Diamond Light Source, Harwell Campus, Didcot OX110DE UK
(honorary) MMC labs, University of Oxford, Engineering Sciences, Oxford OX13PJ UK

Gianfelice.Cinque@Diamond.ac.uk

The combination of optical microscopy with infrared (IR) absorption spectroscopy is a well-established analytical method, and since several decades employing Synchrotron Radiation for its enhanced source brightness and unique broadband spectrum.

Typical applications are in soft matter research, i.e. exploiting the molecular specificity and high sensitivity of IR photons to the building blocks of organic matter - in particular functional groups involving low-Z chemical elements like C, O, N and H - or absorption bands of low energy excitations in condensed/inorganic matter (e.g H-bond).

IR mapping (scanning microscopy) via Synchrotron microprobe is a landmark method to resolve the finest spatial details and achieve full bio/chemical information via point measurements on a range of microspecimens. Hyperspectral imaging via pixellated IR detector (full field microscopy via Focal Plane Array) is the new frontier to provide contrast images based on molecular difference across a wider field of view, or fast *IR snapshots* when time resolved experiments are the imaging goal. Viceversa, the game-changer method to access the nanoscale world is IR nanospectroscopy, which couples an Atomic Force Microscope for resolution with infrared spectroscopy for molecular excitation.

The complementarity of IR imaging to e.g. X-rays or neutrons is clear in its capacity to investigate the molecular scale versus the atomic one given by other harder photon/particle probes. In addition, infrared non-ionizing and truly non-destructive character makes it ideal for studying living matter - like imaging the metabolism of living mammalian cell in real time -, or fragile specimens – like probing the chemistry of paintings' degradation or the molecular distribution across artifacts surfaces.

Experimental examples carried on recently at the IR beamline MIRIAM of Diamond will be given in the field of Cultural Heritage/Archaeology and BioMedical applications.

10ps Time-of-Flight PET scanner: From Hope to Practice

P. Lecoq[1,2*], J.M. Benlloch[2], A. Gonzalez[2], G. Konstantinou[1,2], F. Loignon-Hulle[2], L. Zhang[3]

[1]Multiwave Metacrystal, Swtzerland
[2]Instuto de Instrumentación para Imagen Molecular (Centro Mixto CSIC-UPV), Spain
[3]Multiwave Technologies, France

*Corresponding author: paul.lecoq@metacrystal.ch

Abstract:

The future generation of radiation detectors is more and more demanding on timing performance for a wide range of applications, in particular for time-of-flight (TOF) techniques in PET cameras [1].

There is in particular a consensus for gathering Europe's multi-disciplinary academic and industrial excellence around the ambitious challenge to develop a 10 ps TOF PET scanner (TOFPET). The goal is to reduce the radiation dose (currently 5-25 mSv for whole body PET/CT), scan time (currently > 10 minutes), and costs per patient (currently > 1000 € per scan), all by an order of magnitude. To achieve this very ambitious goal it is essential to significantly improve the performance of each component of the detection chain: light production, light transport, photodetection, readout electronics.

The possibility to reach 10 ps time-of-flight resolution at small energies, as required in PET scanners, although extremely challenging, is not limited by physical barriers [2].

This talk will show how progress in nanotechnologies open new perspectives for the development of meta-scintillators, a new class of multifunctional multi-intelligent scintillators (Fig. 1).

Indeed, a number of disruptive technologies, such as multifunctional heterostructures, combining the high stopping power of well know scintillators with the ultrafast photon emission resulting from the 1D, 2D, or 3D quantum confinement of the excitons in nanocrystals, photonic crystals, photonic fibers, as well as new concepts of 3D digital SiPM structures, open the way to new radiation detector concepts with unprecedented performance.

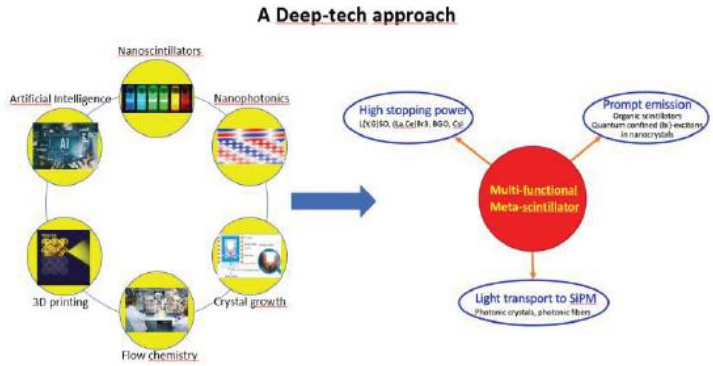

Fig. 1: Metascintillators, a deep-tech approach

References:

[1] Lecoq P ., "Pushing the Limits in Time-of-Flight PET Imaging" in IEEE Transactions on Radiation and Plasma Medical Sciences, vol. 1, no. 6, pp. 473-485, Nov. 2017.

[2] Lecoq, P., Morel, C., Prior, J. O., Visvikis, D., Gundacker, S., Auffray, E., ... & Benoit, M. (2020). Roadmap toward the 10 ps time-of-flight PET challenge. Physics in Medicine & Biology, 65(21), 21RM01

Heterostructured Scintillators: A Novel Approach to Achieving High Sensitivity and Fast Timing in TOF-PET

F. Pagano[1,2], N. Kratochwil[1], C. Lowis[1,4], G. Terragni[1,5], P. Mohr[1,4], M. Salomoni[1], L. Martinazzoli[1,2], W. Choong[3], Marco Paganoni[2,1], J. Cates[3], Marco Pizzichemi[1,2], Etiennette Auffray[1]

[1] *European Organization for Nuclear Research (CERN). Geneva, Switzerland*
[2] *University of Milano-Bicocca. Piazza dell'Ateneo Nuovo, 1, 20126 Milan, Italy*
[3] *Lawrence Berkeley National Laboratory, CA, United States of America*
[4] *Factuly of Chemistry and Biotechnology, FH Aachen University of Applied Sciences, Jülich, Germany*
[5] *Technical University of Vienna, Vienna, Austria*
Corresponding Author Email: fiammetta.pagano@cern.ch

Time-of-flight positron emission tomography (TOF-PET) is an advanced medical imaging technique providing high-resolution images of metabolic processes in the body. TOF-PET is a valuable tool for the early diagnosis, staging, and follow-up of various diseases e.g, cancer and neurological disorders. Its performance can be further enhanced by improving the coincidence time resolution (CTR) of the detector. The current challenge is to achieve a CTR below 100ps while maintaining high sensitivity. Heterostructured scintillators offer a potential solution to this tradeoff by combining materials with complementary properties and relying on the energy sharing mechanism of the recoil photoelectron.

In this study, we present recent advances in heterostructured scintillators, with a specific focus on BGO&EJ232 plastic scintillator heterostructures. Our investigation began with Monte Carlo simulations to investigate the energy sharing mechanism and optimize the geometry. We experimentally assessed the performance of heterostructures compared to bulk BGO for different lengths (3, 15, and 20mm) and investigated the degradation in timing performance due to depth-of-interaction (DOI). To mitigate this effect, we performed measurements in double-sided high-frequency readout, which yielded an 18% improvement in CTR (from 256 to 211ps) compared to single-sided readout, when considering all photopeak events. Our current focus is on scaling up our single-detector system. We performed Monte Carlo simulation studies with Geant4 and GATE to estimate the impact of heterostructures on the reconstructed image quality. We are also investigating machine learning clustering algorithms to optimize event classification and testing high-frequency multi-channel readout to measure the first TOF-PET module based on heterostructured scintillators.

[1] R. Turtos, et al. (2019) *Physics in Medicine & Biology* 64.18
[2] F. Pagano, et al. (2022) *Physics in Medicine & Biology* 67
[3] J.W. Cates, and W. Choong. (2022) *Physics in Medicine & Biology* 67.19 (2022)
[4] P. Mohr, et al. (2022) *IEEE Transactions on Radiation and Plasma Medical Sciences* 7.1

X-ray phase contrast strain imaging using edge illumination

C.Peiffer[1*], M. Endrizzi[1], C.H. Hagen[1], A. Olivo[1], P. R. T. Munro[1],
[1]*Department of Medical Physics and Biomedical Engineering, University College London*
*carlo.peiffer.20@ucl.ac.uk

Conventional X-ray strain imaging is based on taking two X-ray tomographic reconstructions of a sample in an unloaded and a loaded state, and then using digital volume correlation (DVC) in order to retrieve a 3D strain map [1]. There exist many other primary 3D imaging modalities that are exploited for strain imaging, like ultrasound imaging [2], optical coherence tomography [3] or magnetic resonance imaging [4], but compared to X-ray CT they have either a low penetration depth or a low resolution.

Conventional X-ray strain imaging has been used to investigate the mechanics of bones [5] and composites [6], and the degradation of Lithium battery electrodes [7]. It was also applied to a breast mimicking phantom with a hard inclusion mimicking a tumour [8]. Here, they used chalk particles in order to create a realistic 3D feature pattern, but the particles aggregated around the hard inclusion and also soft tissue feature contrast is expected to be much lower.

Conventional X-ray contrast is usually low for material combinations with similar absorption coefficients, including soft tissue. Therefore, X-ray phase contrast imaging (XPCI) using edge illumination [9] can improve the feature contrast to noise ratio in low Z composite materials and soft tissue and improve the DVC strain retrieval precision and resolution. In this study, we present a more realistic soft tissue phantom with a stiff inclusion of known shape and location. We use DVC in order to localise the stiff inclusion by its strain field and validate our findings with the help of a FE model.

[1] B. K. Bay et al. (1999) Digital volume correlation: Three-dimensional strain mapping using X-ray tomography. *Experimental Mechanics,* ***39***, 217–226.
[2] M. Tristam et al. (1986) Ultrasonic study of in vivo kinetic characteristics of human tissues. *Ultrasound in Medicine and Biology,* ***12***, 927–937.
[3] L. Chin et al. (2014) Analysis of image formation in optical coherence elastography using a multiphysics approach. *Biomedical optics express,* ***5***, 2913–2930.
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[7] D. P. Finegan et al. (2016) Quantifying bulk electrode strain and material displacement within Lithium batteries via high-speed operando tomography and digital volume correlation. *Advanced Science ,* ***3***, 1500332.
[8] J. G. Kim et al. (2012) Calculation of strain images of a breast-mimicking phantom from 3D CT image data. *Medical physics,* ***39***, 5469–5478.
[9] A. Olivo, R. Speller (2007) A coded-aperture technique allowing x-ray phase contrast imaging with conventional sources. *Applied Physics Letters,* ***91***, 074106.

4D GRAPH-X: Grating-based phase contrast X-ray imaging

N. Mosco[1*], D. Bersani[2], V. Ferrero[1], E. Fiorina[1], A. Lo Giudice[4], F. Pennazio[1], L. Ramello[1,3], S. Ranjbar[1,4], A. Re[4], A. Patera[5], P. Cerello[1]

[1]*Istituto Nazionale di Fisica Nucleare, Sezione di Torino, Via P. Giuria 1, 10125, Torino (TO)*
[2]*Istituto Nazionale di Fisica Nucleare, Sezione di Pisa, Largo B. Pontecorvo 3, 56127 Pisa (PI)*
[3]*Dip. Svil. Sost. e Transiz. Ecol., Univ. del Piemonte Orientale, P.zza S. Eusebio 5, 13100, Vercelli (VC)*
[4]*Dip. di Fisica, Università degli Studi di Torino, Via P. Giuria 1, 10125, Torino (TO)*
[5]*ALBA Synchrotron, Carrer de la Llum 2-26, 08290, Cerdanyola del Vallès, Barcelona, Spain*
*Corresponding author: nicola.mosco@to.infn.it

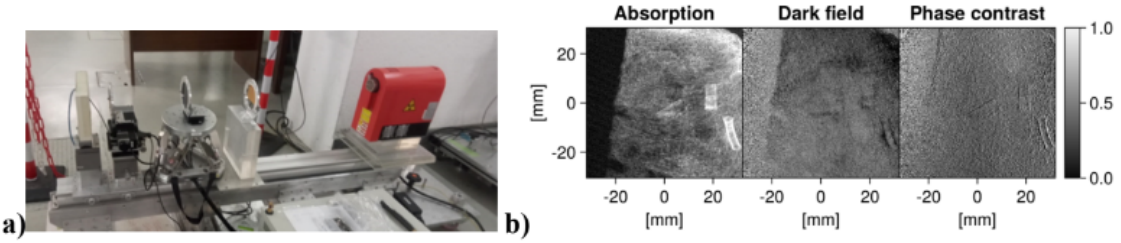

Figure 1: a) 4D GRAPH-X: left to right, the detector, the 3 gratings, and the microfocus X-ray source. **b)** Example signals for a baked product with plastic contaminants.

Phase-contrast X-ray imaging [1] is a promising technique for medical [2], material-sciences [3], food industry [4], and even cultural-heritage applications [5]. The interference pattern of a coherent X-ray beam is Fourier-analyzed to reconstruct, in addition to the absorption signal, also the dark-field (ultra-small angle scattering) and phase-contrast (a measure of the refraction angle) images [7].

4D GRAPH-X [6] is a Talbot-Lau interferometer employing a system of diffraction gratings, allowing for the simultaneous acquisition of the 3 different signals. It is depicted in Fig. 1 where one can identify, from right to left, the microfocus X-ray source; the 3 gratings, G0 (Au), G1 (Si), G2 (Au), of 5.25 µm pitch; and the CMOS flat panel detector (49.5 µm px size, 2304x2940 pxs). The whole setup length is about 120÷130 cm.

We discuss the setup optimisation and show how 4D GRAPH-X is able to provide relevant information for the detection of small contaminants in food products like bread and similar baked products. This could be further improved by supporting the analysis with automatic detection algorithms, from basic image analysis to machine learning techniques, in order to provide a system that can also be employed in the industry.

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[2] C. Gusenbauer, et al. (2016). *Case Studies in Nondestructive Testing and Evaluation,* **6**, 30–38.
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Tofu ez and tofu flow: interactive user-friendly tools for optimization of reconstruction parameters and batch processing of microCT data

S. Gasilov[1*], T. Farago[2]
[1] *Canadian Light Source*
[2] *Institute for Photon Science and Synchrotron Radiation, Karlsruhe Institute of Technology*
*Sergey.gasilov@lightsource.ca

X-ray microtomography (uCT) is a non-destructive imaging technique widely used in pre-clinical studies, biology, material science, environment research, and cultural heritage. In some cases, commonly available laboratory scanners fail to reveal objects' microstructure because of insufficient contrast, poor spatial and temporal resolution, or other factors. In such situations researchers turn to synchrotron imaging stations which often deliver desired information thanks to unique properties of synchrotron radiation as well as state-of-the-art imaging detectors and micropositioning systems. It is common that synchrotron users end their experiment with terabytes of data which have to be preprocessed, corrected, reconstructed, post-processed, and stitched. It can be challenging even for a specialist and oftentimes completely overwhelming for people with little experience in programming and image processing. In addition to complexity of data reconstruction pipelines handling of the uCT data requires pretty powerful hardware which is normally available at large-scale facilities but might be not be easily accessible back in the home laboratories.

Here we present *tofu* [1,2] – an open source Python software package for general image processing as well as tomographic reconstruction that supports parallel and cone beam, helical and laminographic geometries. While a number of other CT reconstruction engines, wrappers, and image processing toolkits are available, *tofu* has a number of distinctive properties which makes it very efficient:

1) *tofu* connects the image processing algorithms into a workflow on the *ufo* framework (OpenCL) layer [3]. Our benchmarks show that the overall throughput of systems with two or more GPUs can easily become limited by disk I/O performance and that reconstruction speed is comparable and even exceeds performance of PyHST and ASTRA engines;

2) *tofu* provides access to dozens of commonly used image processing filters as well as synchrotron-specific algorithms which can be incorporated into the reconstruction pipelines;

3) *tofu* offers graphical user interfaces for optimization of reconstruction parameters and batch processing of large amounts of data.

In the talk we are going to introduce the *tofu* software stack, show user interfaces, discuss the performance, and present a couple of application highlights.

[1] T. Faragó, S. Gasilov, et al (2022) *Journal of Synchrotron Radiation*, *29*(3).
[2] https://github.com/ufo-kit
[3] M. Vogelgesang, S. Chilingaryan, et al (2012) In 2012 IEEE 14th International conference on high performance computing and communication (pp. 824-829).

Model-based image reconstruction for super-resolution photo-thermal imaging

M. Bouzin[1*], M. Marini[1], L. Sironi[1], L. D'Alfonso[1], G. Chirico[1], M. Collini[1], L. Presotto[1]

[1]*Physics Department, Università degli Studi di Milano-Bicocca, Piazza della Scienza 3, 20126, Milano, Italy*
[*]margaux.bouzin@unimib.it

Super-resolution imaging has revolutionized the quantitative inspection of biological samples. The development of super-resolution far-field optical microscopy techniques, capable of pushing the resolution limit to length scales of only a fraction of the visible imaging wavelength, has indeed shed light onto details of the cellular architecture that were previously inaccessible by conventional diffraction-limited imaging.

Similarly, super-resolution methods can be exploited to broaden the applicability of imaging modalities operating beyond the visible range. In this work, we focus on label-free photo-activated thermal imaging and describe the conceptualization and experimental validation of a novel super-resolution imaging approach in the far-infrared. We take advantage of the photo-thermal effect primed by the absorption of raster-scanned focused visible laser light and of the detection of the resulting laser-induced temperature variations by a microbolometer thermal camera. Based on a full-wave forward model of heat diffusion according to the 3D heat equation, a super-resolved temperature-based image of light-absorbing entities in the sample is reconstructed by offline model-based image inversion. The total data acquisition time, which lies in the minutes range, significantly overcomes the hour-long imaging time of our previously described super-resolution strategies [1, 2].

We outline the theoretical foundations and provide initial validation of the proposed approach on synthetic reference samples. We demonstrate imaging capability at <5-µm resolution, thereby providing a ~200-time gain relatively to the effective mm-sized resolution of our thermal camera in conventional operation. We further investigate the theoretical limitations to the achievable resolution, and accordingly explore the possibility of performing far-infrared thermal imaging on ex-vivo biological samples down to the micro-scale. By providing temperature-based super-resolution maps of the distribution of photo-thermal endogenous entities at <5-µm resolution, our results expand the applicability of quantitative photo-activated thermal imaging to the characterization of both cultural heritage artifacts and biological samples on the tissue spatial scale.

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[2] M. Marini et al., 2021, *A novel method for spatially resolved thermal conductivity measurement by super-resolution photo-activated infrared imaging,* Mat. Today Phys., 18, 100375.

INVITED

Making advanced synchrotron microscopes accessible and easy to use for heritage science

M. Cotte[1,2*]

[1] *European Synchrotron Radiation Facility (ESRF), 71 Av. des Martyrs, 38000, Grenoble, France*
[2] *Laboratoire d'Archeologie Moleculaire et Structural (LAMS) CNRS UMR 8220, Sorbonne Université, Paris, France*
* cotte@esrf.fr

The application of analytical chemistry to study artworks has been intensely increasing over the last decades and tackle questions ranging from production to degradation processes of cultural heritage objects. Synchrotron techniques can offer detailed information to help answer these questions by deciphering the material composition and structure. In 2020, the ESRF was upgraded to become the ESRF-EBS (Extremely Brilliant Source), resulting in an increased brightness and coherence of the synchrotron beam, paving the way to cutting-edge analytical capacities. Besides, continuous developments of beamline instrumentations boosted their speed and efficiency. The micro-spectroscopy beamline ID21 has long been used for heritage science and will be even more with the refurbishment of the beamline and the installation of a new nano-scope. The heritage community is also exploiting and will further exploit other beamlines such as ID24/BM03 and LISA Italian beamline for spectroscopy, ID13, ID22 and ID11 for X-ray diffraction and the brand new beamline BM18 optimized for multi-scale phase contrast tomography [1].

The EBS upgrade has motivated the development of new access modalities for users, one of which is the Historical materials "BAG" (Block Allocation Group) [2]. Within the BAG, different projects are grouped together to exploit either high-angular resolution X-ray powder diffraction (HR-XRPD) at ID22 or high-lateral resolution (2D µXRPD mapping) at ID13. Regular access is given to these two beamlines twice a year, for 3 years. This presentation will provide detailed specifications on the analytical configurations accessible to the cultural heritage community at the ESRF, with a special highlight on the EBS and Heritage BAG opportunities.

[1] M. Cotte, K. Dollman, V. Fernandez, V. Gonzalez, F. Vanmeert, L. Monico, C. Dejoie, M. Burghammer, L. Huder, S. Fisher, W. de Nolf, I. Fazlic, H. Castillo-Michel, M. Salomé, M. Ghirardello, D. Comelli, O. Mathon and P. Tafforeau (2022) New Opportunities Offered by the ESRF to the Cultural and Natural Heritage Communities, *Synchrotron Radiation News*, 1-7.

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INVITED

Simultaneous neutron and X-ray tomography at NeXT-Grenoble to explore coupled processes in porous media

A. Tengattini [1,2*]

[1]*Institut Laue-Langevin (ILL), Grenoble, France,Grenoble, France*

[2]*Université Grenoble Alpes, CNRS, Grenoble INP, 3SR,*

*Corresponding author: tengattini@ill.fr

Porous media are a broad class of naturally occurring and engineered materials, ranging from concrete to food material and from rocks to bio-materials. In common they share a complex microstructure and a tendency to undergo coupled hydro-chemo-termo-mechanical processes.

Historically X-ray imaging has been the main approach to study their full-field response, but in a growing number of cases neutron imaging has proven equally essential to study processes, e.g., to explore the role played by hydrogen-rich substances, such as water, within them. Recent developments have significantly pushed the spatio-temporal resolution of neutron imaging as well as allowed for the acquisition of truly simultaneous neutron and x-ray tomographies. Their combined use is uniquely powerful, thanks to the high complementarity of their contrast. It allows not only to study different aspects of processes (*e.g.*, the interdependence between the opening of cracks and water penetration) but even aids in the identification of the different phases comprising a sample as highlighted in Fig. 1.

This contribution will propose an overview of recent developments in neutron imaging including the combined use of x-ray imaging, focusing on recent discoveries allowed by- and new venues opened in- the study of porous media. It will also detail the new venues opened thanks to the recently achieved major upgrade of the instrument NeXT-Grenoble.

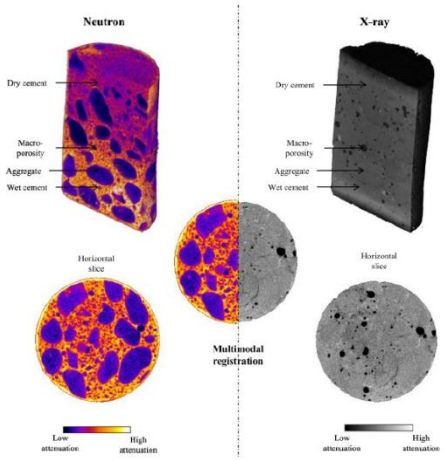

Fig. 1: Example of the unique complementarity of information provided by neutrons and X-rays in the study of concrete.

How to present neutron imaging data from studies of cultural heritage objects best – the example of ancient Tibetan bronze sculptures

E. Lehmann*, D. Mannes
Laboratory for Neutron Scattering & Imaging, Paul Scherrer Institut, Switzerland
*eberhard.lehmann@psi.ch

It has been shown by many important studies that neutrons can very efficiently be used to investigate cultural heritage object in a non-invasive way [1, 2]. Neutrons provide alternative and complementary contrast features compared to the more common X-rays. In particular, the higher penetration of metals and the high sensitivity for light elements make neutron imaging applications attractive for samples with a metallic cover and an organic content.
This is particularly valid for Buddhist bronze objects, which contain a sacred assembly of ritual materials like bones, flowers, wooden pillars or textiles. Although this kind of filling is practiced until today, the tradition goes back about a thousand years. Such old objects can be found in museums and collections and have historical and cultural, but also commercial values on the art market.
First tests of bronze Buddhist objects (Buddhas, Stupas) were done at the PSI´s neutron imaging facilities already in 2006 with success [3]. It was demonstrated, that only imaging with thermal neutrons can reveal the hidden organic content of sealed metal sculptures, a material combination where X-ray imaging methods are unsuited. Based on this experience, further investigation of about 100 important and historical samples from museums and private collections have been investigated successfully by neutron radiography and tomography (Fig.1).
But how to disseminate these important imaging data best? With our digital neutron image data, we are at the share point between neutron science and the museums scene, dealing with the history of Buddhism, particularly of Tibet. If the results are published in natural scientific journals, the audience is mostly interested in the used techniques and their performance. Providing the data as articles in cultural or historical magazines, requires tight interaction with art and cultural history experts for the interpretation of the new information. Such experts are unfortunately scarce and spread globally which make it hard to give the data the attention it deserves.

Therefore, we decided to make our results public as a platform in a data base format. Although this project is not finished yet, first approaches can be shown already. It is our intension to provide the data to the public but mainly to experts in the museum's scene for a further dialogue.
This contribution will give an overview about the data base, important findings, but also describes limits regarding transmission and data interpretation. Finally, we will comment in the importance of such information in the art market and the appearance of manipulated "fake images" to increase the value of items for sale.

Figure 1: Bodhisattva, Rietberg Museum Zurich (CH), BA 2007.65, picture of the item, neutron radiography,rendered segmentation of a tomography volume.

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INVITED

Neutron imaging application in Cultural heritage at ISIS – successful stories and new developments

Antonella Scherillo[1*], Giulia Marcucci[1,2], Anna Fedrigo[1,3]

[1] ISIS neutron and muon source, UK [2] Università degli Studi di Milano Bicocca, Italy [3] ILL, France

[*]antonella.scherillo@stfc.ac.uk

Scientific investigations and archaeometric studies have played a major role in the field of archaeology, especially with regard to materials that have been transformed through human activity, like metals. Neutron imaging techniques are used to shed light on the inner structure of composite materials, but also can be used for elemental investigations. In addition, the combined use of X-rays and neutrons provides additional element-dependent information which is fundamental in case of multi-phase objects inhomogeneous objects. In this talk, I will give some examples of how neutron imaging at the ISIS neutron and muon source, in conjunction with other techniques, can be pivotal to improve our knowledge of ancient manufacturing processes of metals, their technological evolution over the centuries, and how they degrade over time. I will also present novel advances in the implementation of Neutron Resonance Transmission Imaging (NRTI), a non-destructive 2D quantitative elemental analysis technique, performed at the INES Italian Neutron Experimental Station INES beamline operating at ISIS. Neutron spallation sources have high epithermal neutron fluxes, which is a profitable energy range for elemental and isotopic material characterisation thanks to the presence of intense resonance structures in the neutron-induced reaction cross-sections. The NRTI technique is based on the absorption in the sample of incident epithermal neutrons whose energy correspond to the one of absorption resonances, resulting in a transmitted neutron beam containing dips univocally related to the elemental composition. With a position sensitive neutron detector it is therefore possible to obtain 2D radiographies of the sample. However, in contrast with standard neutron radiography, through NRTI it is possible to obtain the distribution of elements and isotopes by selecting a resonance of interest, enhancing the contrast between elements with similar neutron attenuation coefficients. This striking features of NRTI make it suitable for the characterization of inhomogeneous samples, in particular but not limited to Cultural Heritage studies.

Computed Tomography of ancient wood wind instruments and the possibility of rediscovering their sound.

F. Tansella[1,2,*], L. Vigorelli[1,2,3], G. Ricchiardi [4], A. Re [1,2], L. Bonizzoni [5], S. Grassini [6], M. Staropoli[7] and A. Lo Giudice [1,2]

[1] *Dip. Fisica, Università di Torino, Via Pietro Giuria 1, 10125 Torino, Italy*
[2] *INFN, Sezione di Torino, Via Pietro Giuria 1, 10125 Torino, Italy*
[3] *Dip. Elettronica e Telecomunicazioni, Politecnico di Torino, C.so Duca degli Abruzzi 24, 10129 Torino, Italy*
[4] *Dip. Chimica, Università di Torino, Via Pietro Giuria 7, 10125 Torino, Italy*
[5] *Dip. Fisica "Aldo Pontremoli", Università di Milano, Via Celoria 16, 20133 Milano, Italy*
[6] *Dip. Scienza Applicata e Tecnologia, Politecnico di Torino, C.so Duca degli Abruzzi 24, 10129 Torino, Italy*
[7] *Conservatorio di Musica "Giuseppe Tartini", Via Ghega, 12, 34132 Trieste, Italy*
* Corresponding author: francesca.tansella@unito.it

X-ray imaging techniques are widely used in the field of Cultural Heritage, thanks their characteristic of providing, in a non-invasive way, information on the internal structure and on the state of conservation [1]. Particularly, thanks to 3D rendering software dedicated to Computed Tomography, it is possible to reconstruct 3D volumes that can be measured, virtually sectioned, rotated in any position to directly inspect the areas of greatest interest [2].

Musical instruments are peculiar Cultural Heritage as, in addition to the object, it would be important to preserve the sound emitted by the instrument. When a wind instrument is played, the player's breath introduces significant amounts of water vapor into, causing rapid changes in humidity and temperature that lead to sudden stresses with consequent risk of fractures [3]. Due to conservation issues, it often happens that musical instruments preserved in museums cannot be played. This causes the loss of part of the reasons for which they were created: the ability to communicate something through their sound.

By performing computed tomography of a Transverse Flute from the late eighteenth century with reference elements, regarding the dimensions and the capacity to absorb X-rays, it is possible to obtain important data on the dimensions of the analyzed sample. This is a great help in the subsequently possibility to create accurate copies of wood wind instruments, giving chances to play these kinds of instruments, avoiding the risk to damage the originals and thus preserving their state of conservation.

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ORAL

Micro-XRF and PIXE/PIGE Imaging of ancient Roman "glass-gems": insights into the relationship between elemental distribution, colour, and ancient

G. Marcucci[1*], E. Gagetti[2], M.P. Riccardi[3,4], Q. Lemasson[5], Claudia Caliri[6], Giulia Maria Privitera[6], Francesco Paolo Romano[6], Francesca Rosi[7], Francesca Sabatini[7], David Buti[8], M. Musa[4], M. Novello[9], D. Di Martino[1]

[1] *Dipartimento di Fisica "G. Occhialini", Università degli Studi di Milano Bicocca and INFN, Sezione di Milano Bicocca, Milan, Italy*

[2] *Dipartimento di Beni Culturali e Ambientali, Università degli Studi di Milano "La Statale"(adjunct professor)*

[3] *Dipartimento di Scienze della Terra e dell'Ambiente and Arvedi Laboratorio – sede di Pavia, via Ferrata 9, Università degli Studi di Pavia, 27100 Pavia, Italy*

[4] *Università degli Studi di Pavia, via A. Ferrata 9, I-27100 Pavia, Italy*

[5] *FR3506 NewAGLAE, Ministère de la Culture/Chimie ParisTech, 14 quai François Mitterrand, 75001 Paris, France*

[6] *CNR-ISPC, Via Biblioteca 4, 95124 Catania, Italy*

[7] *CNR-SCITEC, via Elce di Sotto, 8 Perugia*

[8] *CNR-ISPC via Madonna del Piano 10, Firenze*

[9] *Ministero della Cultura, Direzione regionale musei del Friuli Venezia Giulia, Museo archeologico nazionale di Aquileia, via Roma 1, 33081 Aquileia (Udine), Italy*

*Corresponding author: giulia.marcucci@unimib.it

We present the results achieved through the application of micro- X-Ray Fluorescence (XRF) imaging on ancient Roman glass-based specimens to gather new hints on their dating, provenance, and glassmaking technology. Since Roman times, glassmakers achieved a rather advanced knowledge of glass production technology including a skilful control of the final colouring and transparency glass appearance. Proof of this expertise is the spread of numerous glassmaking workshops throughout the Roman Empire and related findings of archaeological glass artefacts still well preserved in numerous museums. In particular, there is a unique category of glass objects that were produced to mime natural gems and stones employed in jewellery. A rich and exceptional collection of more than 1300 gemstones mainly made of artificial glass ("glass-gems"), dating from the 2nd century BCE to the 3rd century CE and not yet fully investigated, is conserved at the National Archaeological Museum of Aquileia (Italy) [1, 2]. Aquileia was an important strategic Roman city from a military, economic, trading, and cultural point of view. Within the museum collection, a particular kind of glass-gems is characterised by a blueish matrix with inlays representing different figures (e.g., animals or leaves), some of which are made of a different colour from the matrix and are likely due to metal impressions, or with a golden wire. To determine the elemental composition of the different inlays and of the glass matrix, elemental imaging has been conducted via Particle-Induced X-Ray/Gamma Emission (PIXE/PIGE) mapping at the newAGLAE facility (C2RMF, France) [3] and via micro-XRF imaging [4] conducted in-situ at the National Archaeological Museum of Aquileia with portable XRF instrumentation provided by the MOLAB platform of ERIHS.it. The imaging campaigns allowed to detect the presence of gold in the wires of some inlaid glass-gems; other inlays without metallic ornaments and with a greenish colour have shown a concentration of lead and copper. The blueish matrixes are composed with a homogeneous concentration of cobalt and most gems, but not all, also show the presence of manganese. A discussion of the detected element distributions in association with the colours of the gems will be addressed, with a comparison between PIXE/PIGE and XRF imaging results. This characterisation is part of an extensive research project entitled "Glass-gems Exploration by Multidisciplinary Methods, Analyses and Experiments" (GEMMAE) [5,6,7], and a widely in-situ characterisation of glass-gems composition has been carried out with complementary non-destructive techniques like Raman spectroscopy and Mid-InfraRed (MIR) spectroscopy investigations to the imaging campaigns.

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Title: Advanced neutron imaging techniques at the Paul Scherrer Institute

M. Busi[1*], M. Strobl[1]

[1]*Laboratory for Neutron Scattering and Imaging, Paul Scherrer Institute, Villigen (Switzerland)*
*Corresponding author: matteo.busi@psi.ch

Neutron imaging is a powerful technique utilized by researchers to visualize the internal structure of materials with high spatial resolution, between a few micrometers and a few hundreds of micrometers. Recently, there have been groundbreaking advancements in neutron imaging technology that go beyond traditional attenuation contrast methods. This contribution will provide an overview of recent developments in advanced neutron imaging techniques, which can access length scales below the current state-of-the-art detector resolution, including Bragg edge imaging, grating interferometry, and dark-field imaging. Bragg edge imaging is a diffractive-based imaging technique that enables 2D mapping of crystallographic properties such as residual lattice strain, crystallographic phase transformation and evolution, texture and crystallite size. Recent method developments for efficient measurement at continuous sources [1] and application studies on additive manufacturing samples will be presented. Neutron grating interferometry is a technique that provides simultaneously attenuation, differential phase and dark-field contrast maps [2]. The latter relies on its sensitivity to underlying small-angle scattering interactions, which enables the investigation of structures in the range of a few tens of nanometers to a few micrometers through fitting of the measured real space correlation function [3]. Recent developments for the characterization of anisotropic scattering and applications in the field of soft matter physics will be shown. Lastly, polarized neutron imaging allows for the study of the interaction between a polarized neutron beam and magnetic fields present in the investigated specimens [4]. In particular, this method has been applied to quantitatively map magnetic crystallographic phases in iron-based materials [5].

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INVITED

Incoherent inelastic neutron imaging applied to the catalytic conversion of molecular hydrogen

G. Romanelli[1*]

[1]Dipartimento di Fisica and NAST Centre, *University of Rome Tor Vergata, Rome, Italy*
*Corresponding author: giovanni.romanelli@uniroma2.it

Incoherent inelastic neutron scattering from hydrogen can provide a range of spectroscopic and molecular-specific information over samples of interest for industrial chemistry, energy materials and catalysis. By combining such capabilities with the high-penetration power of neutrons and the possibilities available at state-of-the-art neutron instruments for imaging and tomography, one can tackle industrial applications under *in situ* and *operando* conditions.

Qualitatively, hydrogen (^{1}H) provides a simple element to be detected in neutron scattering and transmission experiments, also in a time-dependent approach over the time scales of seconds. However, quantitatively modelling the energy-dependent total scattering cross section of hydrogenous materials can be a challenging task, as it depends on the incident neutron energy, temperature, structural and dynamical properties of the system under investigation. In this framework, thermal neutron cross sections, within standard libraries and repositories, are available only for a handful of materials and at specific thermodynamic conditions [1,2].

Here, we discuss the challenges and opportunities in using incoherent inelastic neutron imaging in the framework of engineering and industrial applications. Specifically, we discuss the case of molecular hydrogen and its adsorption in porous materials for hydrogen storage and energy applications. Examples of the catalytic conversion of the molecule between its ortho and para modifications are provided to show the opportunities available in incoherent inelastic neutron imaging for kinetic investigations [3].

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INVITED

Recent advancements in neutron imaging

Nikolay Kardjilov[1*], André Hilger[1], Tobias Arlt[2], Ralf Ziesche[1], Robin Woracek[3], Alessandro Tengattini[4,5], Lukas Helfen[4], Markus Osenberg[1], Ingo Manke[1]

[1]Helmholtz Centre Berlin for Materials and Energy (HZB), Hahn-Meitner-Platz 1, 14109 Berlin, Germany [2]Technical University Berlin, Hardenbergstraße 36, 19623 Berlin, Germany [3]European Spallation Source ERIC, P. O. Box 176, SE-221 00 Lund, Sweden [4] Institut Laue-Langevin, 71 Avenue des Martyrs, 38000 Grenoble, France [5] University Grenoble Alpes, CNRS, Grenoble INP, 3SR, Grenoble, France
[*]Corresponding author: kardjilov@helmholtz-berlin.de

The material characterization by neutron imaging reached a new level after developing innovative techniques using different contrast mechanisms than the common beam attenuation. In this way properties of materials and complex systems can be resolved by position sensitive mapping of diffraction, small-angle scattering and refraction signals. In addition, the improved spatial and time resolution of the detector systems allows for micro tomography studies and 3D dynamic investigations.

Applications related to 2D and 3D visualization of material phase heterogeneities, texture, fluid dynamics, magnetic structures and phase transitions in applied materials will be presented [1].

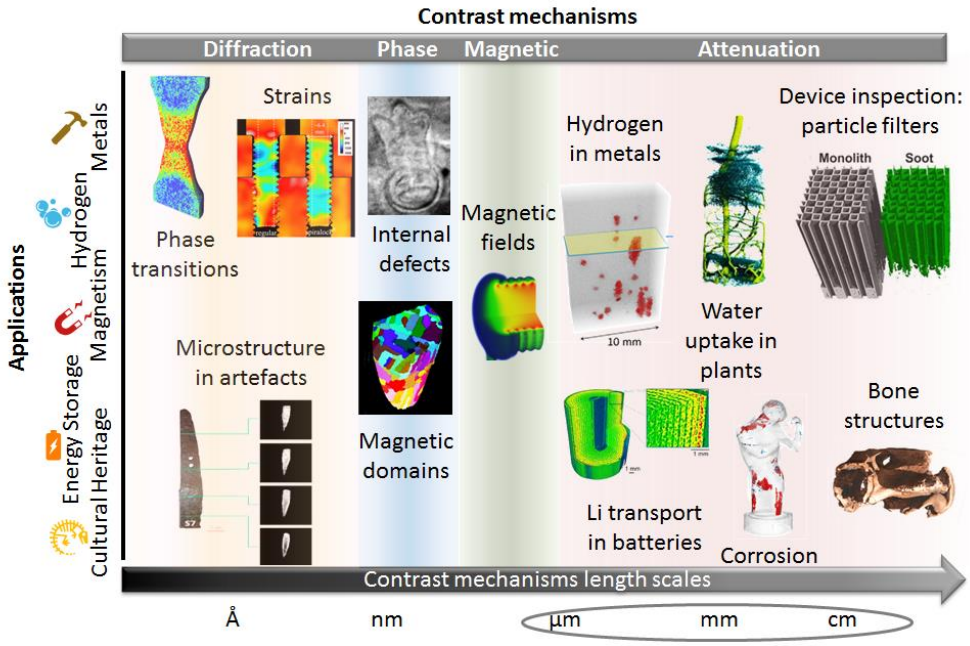

Figure 1 Different contrast mechanisms can be used to explore various length scales in materials and to study their properties and related processes. The relation between contrast mechanisms and different application fields is presented. The length scale presented on the lower axis relates to the corresponding contrast mechanism specified on the upper axis. For the attenuation-based image techniques the large length scale was emphasized by grouping the scales from µm to cm.

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Quantitative analysis in neutron imaging

Anders P. Kaestner

Laboratory for Neutron Scattering and Imaging, Paul Scherrer Institut, Villigen, Switzerland
*Corresponding author: anders.kaestner@psi.ch

Imaging is since many years used for the quantitative analysis of different samples. The nature of the quantified information depends on the purpose of the investigation. The quantitative analysis can be based on discrete regions or the distribution of the gray levels globally or in segmented image regions. A high signal-to-noise ratio (SNR) is crucial to reduce the uncertainties of any quantification task; therefore, a reliable denoising filter is needed. Dimensional measurements of, for example, volume and surface area require high precision and accuracy in the segmentation step. A frequently used analysis type in neutron imaging is quantifying the amount of water behind a region or even each pixel of a radiograph. Before calculating the water content, the first step is to remove biases introduced by scattering from the sample and the instrument background [1,2]. This bias correction is relevant to analyzing radiographs and tomography data as the bias propagates in the reconstruction process.

It is a misleading conception in early image processing classes that pixels of segmented images are discrete objects with defined sizes with no uncertainty. In fact, there are several sources of uncertainties [3]. E.g., how well the segmentation algorithm can cope with blurred edges, the uncertainties in determining the pixel size, and not to forget the impact of the SNR. Analysis using gray levels also includes the uncertainty of the pixel size, the SNR, and the uncertainty of the attenuation coefficients.

We will show examples of how the uncertainty from different quantities needed in the computation of the result propagates through the calculations and provide uncertainties beyond adding error bars based on the standard deviation of the measured region.

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ORAL

Radiographic Imaging with muons for underground and safeguard application

L. Cimmino[1,2*], F. Ambrosino[1,2], A. Anastasio[2], V. Masone[2], M. Mirra[2], L. Roscilli[2], G. Saracino[1,2]

[1] *University of Naples "Federico II"*
[2] *INFN, Division of Naples*

*cimmino@na.infn.it

Among the applications of fundamental Physics, that of muon radiography is one of the most recent and promising in the field of the imaging. By exploiting the great penetration power of cosmic muons into matter, it is possible to have direct images of the inside of a mountain or a blast furnace or the core of a nuclear reactor.

The muon radiography, also called Muography, is a technique based on the measurement of the absorption of the muon flux by a body. Muons are elementary particles, generated by the interaction of cosmic rays with the earth's atmosphere, with high penetrating power that can be detected with the use of highly segmented muon trackers.

Here we present an innovative muon tracker, cylindrically shaped and with a low power consumption, especially intended for applications with a limited power source. Its DAQ system is based on the EASIROC chip, designed for the readout of Silicon photomultipliers (SiPMs). The detector has been used in several underground measurement campaigns, during which we were able to test its detection performance and its resistance to mechanical stress.

The SYRMEP X-ray imaging beamline of Elettra: recent advances for biomedical, environmental and cultural heritage studies

E. Longo[1], A. Contillo[1], L. D'Amico[1,2], G. Saccomano[1,3], M. Kudrna-Prasek[1], N. Sodini[1], F. Zanini[1], D. Dreossi[1], G. Tromba[1]

[1]*Elettra-Sincrotrone Trieste S.C.p.A., 34149 Basovizza, Trieste, Italy.*
[2]*Department of Physics, University of Trieste, Trieste, Italy.*
[3]*Department of Engineering and Architecture, University of Trieste, Trieste, Italy.*

SYRMEP (SYnchrotron Radiation for MEdical Physics) is the hard X-ray imaging beamline of the Elettra synchrotron light source (Trieste, Italy) [1]. The experimental station, covering an energy range between 8.5 keV and 40 keV, suits several applications in the fields of life, earth and environmental sciences, materials engineering, and cultural heritage. The setup can be operated with either a monochromatic beam or a white/pink beam, spanning a pixel size ranging from 100µm down to 1 µm. The facility offers different imaging modalities including X-ray radiography, X-ray microtomography (microCT), multi-scale imaging, virtual histology and mosaic CT. The adjustable sample-to-detector distances, from 2 to 11 m, allow the implementation of propagation-based phase contrast techniques; especially advantageous for the visualization of soft matter. Thanks to the flexibility of the setup, other phase-sensitive imaging approaches can be executed and in-situ experiments performed. The beamline is equipped with specific sample environments, such as an induction furnace for in-situ heating up to 1450 ºC with precise temperature control; a mechanical testing device for pulling, compression or twisting of specimens; a human chest phantom for lung imaging. In addition, a heavy load stage has recently been installed for imaging of large and bulky samples. The beamline upgrade, foreseen within the Elettra 2.0 program, will cover a broader energy range up to 130 keV and will benefit of a much higher X-ray flux. This will enable new imaging approaches and extend the framework of possible applications at SYRMEP. Here presented is an overview of the beamline and the techniques currently available along with selected scientific examples related to biomedicine and cultural heritage.

[1] C. Dullin et al. "Multiscale biomedical imaging at the SYRMEP beamline of Elettra- Closing the gap between preclinical research and patient applications", Physics Open 6 (2021) 100050.

INVITED

SYRMEP-LS: the new hard X-ray imaging beamline at Elettra 2.0

D. Dreossi, A. Abrami, M. Altissimo, A. Bianco, E. Busetto, K. Casarin, L. Raimondi, G. Simonetti, G. Scian, G. Tromba

Società Sincrotrone Trieste ScpA

X-ray imaging with synchrotron radiation is a valuable tool in life science studies and is exploited in various fields like biology, zoology, botany, medicine, food science, paleontology. In general, researchers look for cutting edge technologies, capable to improve the performance of conventional systems in terms of spatial, contrast and temporal resolution. In order to cope with the emerging scientific challenges, a new hard x-ray imaging beamline is under construction at Elettra and will exploit the performances of a 6 T super bending magnet on the new storage ring Elettra 2.0. The large horizontal acceptance (up to 7 mrad) will guarantee more than 210 mm wide beam at the sample stage, with the possibility to select between monochromatic beam (in the range 12-120 keV) and pink beam. Thanks to a double strip multilayer monochromator and a combination of filters and a mirror, it will be possible to select the the energy bandwidth from a few to several percent up to to 50 keV or to use a "quasi" white beam (only filters) up to the maximum energy (around 10^{12} ph/s/0.1% BW at 145 keV in 7x0.8 mrad^2). A flexible setup (placed in a 12 m long experimental hutch) will be able to cope with a large variety of sample dimensions and weight with the possibility to do a multiscale tomographic scans. A medical facility in a satellite building it is also foreseen with the possibility to deliver 350 mm wide monochromatic beam to patients.

The Birth, The Growth and The Future of Physics in Medical Imaging

Alberto Del Guerra[1,*]

[(1)]University of Pisa, Department of Physics and INFN, Sezione di Pisa, Largo B.Pontecorvo 3, 56127 Pisa .
[(*)]Email: alberto.del.guerra@unipi.it

In this talk, the contribution of Physics in Medical Imaging to the exploration of a highly complex system such as the human body will be reviewed and the challenges for medical physicists as requested today by the rise of *personalized medicine* will be discussed.

The birth of the discipline of Physics in Medical Imaging could be dated more than 2500 years ago to Hippocrates (460-377 BC), a physician from Kos, known as the "Father of Medicine". He also developed the first technique ever of Medical Physics, and in particular of Medical Imaging, using wet clay put on the back of a sick patient for measuring the body temperature. After that early start, the medical imaging was represented by the *sight*, one of the five senses, that were the only diagnostic tools available. The discipline of Physics at that time was not known: there was "natural science" and "astronomy", later "chemistry" and "physiology", and finally "physics" in the 18th century. We had to wait until 1778 for the "*Société royale de medicine*" to introduce the term "*Physique Medicale*" (Medical Physics) that was used after since.

Then on November 8, 1895, Wilhelm Rontgen discovered the X-rays, and everything changed: Radiology, Radiotherapy and Radioprotection were born. However, a full understanding of many biological aspects in vivo was not yet achieved: everything was based on "seeing is believing". However, virtual anatomy was not enough: differences in tissue density were in some cases a good biomarker for a diagnosis, but not always enough for the therapy. The discovery of the radioisotopes by Marie and Pierre Curie and Henri Becquerel, the theory of the tracer by the chemist Gyorgy Hevesy and the invention of the cyclotron by Ernst Orlando Lawrence in 1929 for producing gamma-emitter radioisotopes such as $^{99}_{m}$Tc, and positron emitters such as ^{11}C and ^{18}F paved the way to the new specialty of Nuclear Medicine and to the novel Medical Imaging techniques, i.e, Single Photon Emission Tomography (SPECT) and Positron Emission Tomography (PET). Then by the end of the 20th century, the Physics in Medical imaging had completed its roster: the CT was joined by the Optical Imaging techniques (Bioluminescence and Fluorescence), PET and SPECT, US, MRI and fMRI, and very recently, Photoacustics.

I will shortly illustrate the state of the art of these techniques in the clinics, with a special emphasis to PET and the most recent applications of Hybrid Imaging (PET-MR; PET in Particle Therapy, MR driven Radiotherapy and Theranostic). The future of Physics in Medical Imaging will be more and more in the combined field of diagnosis and therapy, moving from Molecular Imaging to Biological Imaging within the "personalized medicine" scenario.

INVITED

Brain imaging: a great challenge from macro to nano

S. Cipiccia

University College London

Corresponding author: *s.cipiccia@ucl.ac.uk*

One of the greatest scientific challenges is study of the human brain. The complexity of this organ and how nanoscale structures are related to macroscale behaviours still needs to be understood. It is clear, to produce a unified model of the brain new imaging techniques and approaches are required.

Here we present the latest developments in x-ray ptychography, a nanoscale imaging technique, toward imaging of large brain volumes with nanoscale resolution.

Real-time X-ray tomographic imaging at the Advanced Photon Source

V. Nikitin[1*], F. De Carlo[1]
[1]*Advanced Photon Source, Argonne National Laboratory, Lemont, IL 60564, USA*
*Corresponding author: vnikitin@anl.gov

One of the requirements of tomographic imaging is to have reconstruction readily available soon after the data acquisition. Meeting this requirement is important for the optimization of scan parameters and sample alignment. More importantly, fast reconstruction will allow for AI data analysis and steering experiments, e.g., by automatic changing of environmental conditions according to the sample state or by triggering data-capturing processes for measuring devices.

At the Imaging group of the Advanced Photon Source, we developed and implemented in user operation two instruments to address the abovementioned requirement. First, we introduced a new real-time 3D tomographic imaging monitoring instrument TomoStream[1], which is able to : (1) perform real-time tomographic reconstruction of three arbitrary slices across the sample; (2) optimize alignment and data collection parameters on-the-fly; (3) trigger data save on-demand at any time while continuing the streaming monitoring; and (4) add to the saved data an arbitrary set of projections streamed before the data save trigger event. Additionally, we organized a three-lens 3D zoom-in/zoom-out to a region of interest centered on the intersection point of the three arbitrary slices, which significantly simplifies the whole data acquisition procedure.

Second, we developed a new package TomocuPy[2] for full 3D reconstruction, as a GPU alternative to the commonly-used TomoPy package. TomocuPy implements an asynchronous reconstruction pipeline involving parallel read/write operations with SSD disks, CPU–GPU data transfers, and GPU computations. All these operations are timely overlapped for different data chunks. Full reconstruction including read/write operations of a 2048x2048x2048 tomographic volume takes less than 7 s on a single Nvidia Tesla A100 and PCIe 4.0 NVMe SSD, and scales almost linearly increasing the data size. TomocuPy is also suitable for the multi-GPU and multi-SSD setup to work with large datasets (e.g., a 16384x16384x16384 volume of 16 TB size).

The developed software for tomographic reconstruction is publicly available and currently in use at micro- and nano-Computed Tomography beamlines (2-BM, 7-BM, and 32-ID).

[1] V. Nikitin, et. al (2022) Real-time streaming tomographic reconstruction with on-demand data capturing and 3D zooming to regions of interest. *J. Synchrotron Rad*, **29.3**, 816-822.
[2] V. Nikitin (2023) TomocuPy - efficient GPU-based tomographic reconstruction with asynchronous data processing. *J. Synchrotron Rad*, **30.1**, 179-191.

INVITED

SYNCHROTRON X-RAYS TO ELUCIDATE ANATOMY, PATHOLOGY AND THERAPY

P. Coan[1*]

[1]*Department of Radiology and Department of Physics, Ludwig-Maximilian University, Munich, Germany*

*Corresponding author: Paola.Coan@physik.uni-muenchen.de

Over the past decades, synchrotron X-rays have opened new avenues in biomedical research. The high degree of coherence and brilliance of synchrotron beams have made possible to reach unprecedented level of detail in the investigation of biological tissues through the application of advanced experimental techniques in *in-vitro* and *in-vivo* models. Sophisticated hard X-ray setups have been developed to examine the morphology and alterations due to pathology and treatments at smaller and smaller scales, from micro- down to nano-scale, on both human and animal specimens. These methodologies are the basis of what is now indicated in the literature as 3D 'virtual anatomical histology' by X-ray imaging. Results from selected scientific cases, ranging from pathology detection and analysis to the follow-up of the effects of novel treatments, will be presented. Special focus will be given to preclinical studies in the field of neuro-degeneration and neuro-oncology. The key requirements as well as main challenges of synchrotron biomedical imaging will be discussed.

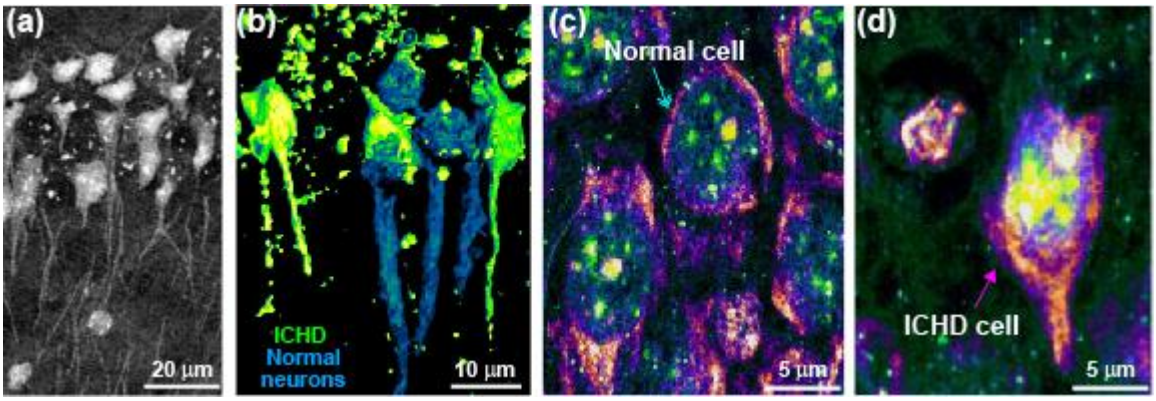

Figure 1 Multimodal imaging of neurons affected by amyloid and tau pathology (hyper-dense cells) in a mouse model of Alzheimer's disease [1].

[1] G. E. Barbone, A. Bravin, A. Mittone, A. Pacureanu, G. Mascio, P. Di Pietro, M. J. Kraiger, M. Eckermann, M. Romano, M. Hrabě de Angelis, P. Cloetens, V. Bruno, G. Battaglia, P. Coan (2022) X-ray multiscale 3D neuroimaging to quantify cellular aging and neurodegeneration postmortem in a model of Alzheimer's disease. *European Journal of Nuclear Medicine and Molecular Imaging*, **49**, pages 4338–4357, https://doi.org/10.1007/s00259-022-05896-5

Phase-contrast micro tomography for 3D virtual histology of paraffin-embedded human tissues

S. Donato[1,2,*], R.G. Agostino[1], L.M. Arana Peña[3,4], F. Arfelli[3], L. Brombal[3], R. Longo[3], F. Martellani[5], Romano A.[5], Rosano I.[5], G. Saccomano[4], G. Tromba[4], D. Bonazza[5]

[1] *University of Calabria and STAR-LAB, Rende, Italy;* raffaele.agostino@fis.unical.it
[2] *INFN, Division of Frascati, Frascati, Italy*
[3] *University of Trieste and INFN, Trieste, Italy;* lucia.arana@ts.infn.it, luca.brombal@ts.infn.it, fulvia.arfelli@ts.infn.it, renata.longo@ts.infn.it,
[4] *Elettra Sincrotrone, Trieste, Italy;* giulia.saccomano@elettra.eu, giuliana.tromba@elettra.eu
[5] *Surgical Pathology Unit, Cattinara Hospital, University of Trieste, Trieste, Italy;* fulvia.martellani@asugi.sanita.fvg.it, andrea.romano@asuits.sanita.fvg.it, ida.rosano@asugi.sanita.fvg.it, deborah.bonazza@asugi.sanita.fvg.it
* sandro.donato@fis.unical.it

A property fundamental to malignant diseases is invasiveness, i.e. the tendency of tumour cells to spread beyond the primary tissue layer to healthy surrounding tissues and distant organs. Currently, histopathological examination represents the gold standard in cancer diagnosis. Histopathology provides indications for diagnosis, classification, prognosis and consequent strategy for dedicated treatment. Histology, however, only provides 2D information in the selected cutting plane and while 3D histological volumes can be produced through serial sectioning or whole slide imaging [1], this process is labor intensive, may introduce processing artifacts and does not provide isotropic spatial resolution. On the other hand, the analysis of a virtual 3D volume would allow to evaluate, at micrometer scale, those features that cannot be fully analysed in 2D representative sections. X-ray based virtual histology [2,3] is an emerging technology that provides three-dimensional visualization of different features of soft-tissue specimens which can be virtually sliced at any point and in any direction. Virtual histology can enable guided sectioning of tissues in histological analysis for selecting the most suitable cutting plane when dissecting specimens and selecting histological sections, to optimally obtain the largest/most representative cross-section of the tumour. Micro-infiltrating carcinomas of the breast, cervix, and thyroid, were acquired by phase-contrast micro tomography (PhC-μCT) at the synchrotron facility Elettra (Trieste, Italy). By comparing histological and CT slices, pathologists agreed that PhC-μCT facilitates lesion classification, by distinguishing the morphology of different tissue components, and, most importantly, tissue invasion. By inspecting a volume image, pathologists can track the whole lesion, find evidence of invasions in locations of the tissue that may be missed in single or serial histological sections. Therefore, the proposed method could be a complementary tool for pathologists to potentially improve the diagnosis by avoiding the under-staging and reducing false negative rates.

[1] T.S. Haddad et al. (2021), *Nature protocols*, **16**(11), 4945-4962.
[2] P. Baran et al. (2018), *IEEE transactions on medical imaging*, **37**(12), 2642-2650.
[3] X. Bin et al. (2020), *Modern Pathology*, **33**(12), 2449-2457.

Quantitative x-ray imaging – towards material-specific numbers from images

Prof. Dr. Julia Herzen

Biomedical Imaging Physics, TUM School of Natural Sciences, Department of Physics &
Munich Institute of Biomedical Engineering, Technical University of Munich

Abstract

Phase-contrast X-ray imaging uses the refraction of X-rays to generate the contrast. It has been demonstrated to provide superior soft-tissue contrast in comparison to conventional attenuation-based X-ray imaging. However, quantitative imaging at high spatial resolution and high image quality still remains challenging. Some existing methods require assumptions on the composition of the specimen (e.g., single material and low attenuation) to retrieve the phase information and show less sensitivity in resolving small changes in electron density within the sample. Specimens violating these assumptions become impossible to image. Within a long-term proposal at the imaging beamline P05, we successfully designed and built an imaging setup based on 2D Talbot array illuminators (TAI) (Gustschin et al., 2021; Riedel et al., 2023; Schwarzenberg et al., 2022) and a speckle-tracking technique (Unified Modulated Pattern Analysis, UMPA) (Zdora et al., 2017), which overcomes these challenges. Our method accurately extracts the electron density distribution with higher sensitivity than comparable techniques and is compatible with a wide energy range. Here, we will review the potential of this quantitative imaging method by highlighting the recent results on biomedical applications.

Gustschin, A., Riedel, M., Riedel, M., Taphorn, K., Petrich, C., Gottwald, W., Noichl, W., Busse, M., Francis, S. E., Beckmann, F., Hammel, J. U., Moosmann, J., Thibault, P., & Herzen, J. (2021). High-resolution and sensitivity bi-directional x-ray phase contrast imaging using 2D Talbot array illuminators. *Optica, Vol. 8, Issue 12, Pp. 1588-1595*, *8*(12), 1588–1595. https://doi.org/10.1364/OPTICA.441004

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Zdora, M. C., Thibault, P., Zhou, T., Koch, F. J., Romell, J., Sala, S., Last, A., Rau, C., & Zanette, I. (2017). X-ray Phase-Contrast Imaging and Metrology through Unified Modulated Pattern Analysis. *Physical Review Letters*, *118*(20), 203903. https://doi.org/10.1103/PhysRevLett.118.203903

INVITED

Introducing µTomo2 and SoftX: STAR's beamlines for high-energy X-ray imaging

Raffaele G. Agostino

Department of Physics and STAR Infrastructure, University of Calabria, Rende (CS), Italy

The presentation will center around the progress made in developing the Imaging section of the STAR research infrastructure, which is currently finalizing two beamlines specifically designed for high-energy X-ray imaging.
µTomo2 will employ HE-LINAC branch-line beams (ranging from 65 to 350 keV) to perform microtomography on large, high-density samples. The experimental configuration will be tailored to each specific object by selecting from two detectors with different pixel sizes and adjusting the object-detector position within a wide range. A conventional micro-focus source, capable of accelerating voltage up to 190 kV and achieving a spot size as small as 0.5 µm, completes the setup.
In contrast, the SofX experimental station will be dedicated to imaging lightweight alloys, composite and polymeric materials, as well as biomedical samples. This is facilitated by utilizing the photon beams provided by the LE-LINAC branch-line (ranging from 17 to 80 keV). Similarly, the experimental station offers flexibility through the availability of two detectors, one of which utilizes "single-photon counting," along with a micro-focused source (120 kV - 5 µm).
In addition to these ongoing beamline projects, STAR also provides access to a cutting-edge SAXS apparatus (currently in the commissioning phase), which enables in-situ studies. Furthermore, the already operational µTomo1 microtomography station complements the range of available resources.
The entire Imaging section is an integral part of the STAR ecosystem, which includes six service laboratories catering to various fields within materials science, providing comprehensive support to users.

Characteristics of the inverse Compton scattering source ThomX and the imaging plans

M. Jacquet[1*], ThomX collaboration

[1]*Université Paris-Saclay, CNRS/IN2P3, IJCLab, 91405 ORSAY, France*
[*]marie.jacquet@ijclab.in2p3.fr

Currently, there are increasing demands for access to bright, tunable, monochromatic X-ray sources in the fields of medicine (imaging and therapy), cultural heritage studies and preservation, and industrial applications (materials science). Synchrotrons are the best light sources in terms of energy tuning and brightness but there are strong constraints on their use and diffusion, such as their size, construction and operating costs and the high demand for beam times. Currently, thanks to the increasing power of lasers, for a moderate cost and dimensions compatible with an experimental hall, compact Compton sources can provide a quasi-monochromatic X-ray beam of high flux and high brightness, compared to current laboratory sources (X-ray tubes).

The French project ThomX is a demonstrator of a high flux Compton source. The aim is to realize a compact, bright and energy tunable X-ray source in a constrained environment (museums, hospitals, laboratories). ThomX is being started at the Irène Joliot-Curie laboratory (IJCLab) on the Orsay campus of the University of Paris-Saclay and is designed to produce a total flux of 10^{12}-10^{13} ph/s and a brightness of 10^{10}-10^{11} ph/s/mm^2/mrad^2/0.1%bw with an energy tuning ranging from 45 keV to 90 keV. Thanks to the kinematics of the Compton scattering process, with this flux and the parameters of the machine, it is possible to obtain 10^{11} ph/s in 2-3% spectral width and a divergence of the order of 2 mrad with the simple use of a diaphragm [1]. To achieve these performances, both the electron bunch and the laser pulse must be stored in a storage ring and a high gain Fabry-Perot cavity, respectively [2].

Medical imaging (standard radiography or 3D tomography) is one of the application field of ThomX. Other techniques are possible such as phase contrast imaging, K-edge subtraction imaging or studies related to radiotherapy. Techniques based on X-rays diffraction or fluorescence can also be used with ThomX for material analysis or cultural heritage studies [3].

In this context, I will start by introducing the state of the art of the compact high-flux Compton sources, then I will present the ThomX project, its potential of applications, and I will finish with an overview of the current commissioning of the machine.

[1] M. Jacquet & C. Bruni (2017), *J. Synch. Rad., 24*, 1-11
[2] K. Dupraz et al. (2020), *Physics Open*, *Elsevier*, *5*, pp.100051
[3] M. Jacquet (2016), *Phys. Med., 32*, 1790-1794

Image analysis for the determination of the diffusion coefficient in histological specimens by radiographs

M. Santini[1,*], S. Fest-Santini[1], G.E. Cossali[1], N. Casatta[2] and C. Lupo[2]

[1] Dipartimento di Ingegneria e Scienze Applicate, Università degli studi di Bergamo, viale Marconi 5, 24044 Dalmine (BG), Italy
[2] Innovation Department, Diapath S.p.A. via Pietro Savoldini 71, 24057 Martinengo (BG), Italy

[*] e-mail: maurizio.santini@unibg.it

Abstract. The diagnosis of a cancer involves the study of a biopsy, suitably processed and treated and is essential for a correct diagnosis. Tissue processors performs the entire processing protocol automatically, often relying on empirical timing related to chemical diffusions in the samples. The determination of the diffusion coefficient in biological materials is still under study with, unfortunately, inaccurate results that may leads in tissue degradation. The authors present an experimental technique, based on image analysis of a multitude of X-ray high-resolution radiographs acquired over time, during a test in which a pork liver biopsy is immersed in one of the classic processing solvents (alcohol 70%). The attenuation of the intensity of the ionizing beam (emitted by a microfocus X-ray source) is proportional to the concentration of the solvent which diffuses in the histological preparation. The diffusion of the solvent in the sample can be approximated by a time-dependent diffusion equation:

$$\frac{\partial \rho}{\partial t} = \alpha \nabla^2 \rho \qquad (1)$$

An analytical solution of equation (1) in cylindrical coordinates is used to simplify the analysis and the solution of the related inverse problem allows to evaluate the diffusion parameter α.

Keywords: *diffusion coefficient, X-ray, biopsy*

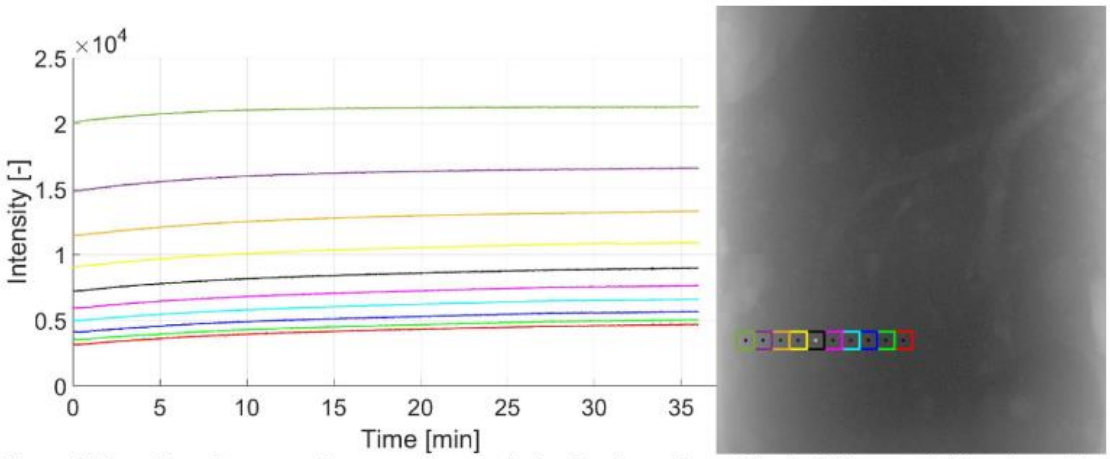

Figure 1. X-ray intensity attenuation *versus* time as obtained by the radiographies, in different radial locations, of a pork liver biopsy submerged in alcohol 70%.

Flyscan compatible scanning schemes for x-ray μ-CT with a structured beam

G. Lioliou[1], A. Charman[2], A. Astolfo[1], O Roche i Morgó[1], S. Cipiccia[1], P. Munro[1], M. Endrizzi[1], D. Bate[2,1], A. Olivo[1], and C. K. Hagen[1]

[1]*Department of Medical Physics and Biomedical Engineering, UCL, Malet Place, London WC1E 6BT, UK*
[2]*Nikon X-Tek Systems Ltd, Tring, Herts HP23 4JX, UK*
*Corresponding author: g.lioliou@ucl.ac.uk

X-ray phase contrast CT (XPC-CT) gives access to increased contrast for weakly attenuating samples. Our group has dedicated the best part of the last decade to developing an XPC-CT technique based on beam structuring (amplitude modulation of the beam); this is achieved by using a mask with alternating absorbing and transmitting septa placed immediately upstream of the sample [1]. There are two distinct sensing mechanisms: beam tracking and edge illumination; both are compatible with "single-frame" retrieval approaches, which – at least in principle - allows for fast flyscans to be implemented, where the sample is continuously rotated. However, the beam structuring also creates an under-sampling problem; to obtain complete datasets and achieve the best possible spatial resolution, extensive sample stepping, called dithering, had so far been applied at each rotation angle. As a result, full sampling scans tended to be long, as dithering can only be implemented in a step-and-shoot manner. We have recently proposed two alternative sampling schemes, cycloidal [2] and cycloidal-spiral [3], which are flyscan compatible, while largely preserving the achievable spatial resolution.

In this talk, we present results for the different sampling schemes. We also discuss how optimal conditions (in the sense of the Nyquist-Shannon theorem) can be derived for these schemes. All results are compared to a dithered (full sampling) acquisition, which had, so far, been the gold-standard for acquiring μ-CT data with a structured beam. Preliminary findings, based on simulations, are shown in Fig. 1; these suggest that cycloidal flyscans can indeed yield high-quality μ-CT images, whilst being much quicker than their full sampling step-and-shoot counterpart.

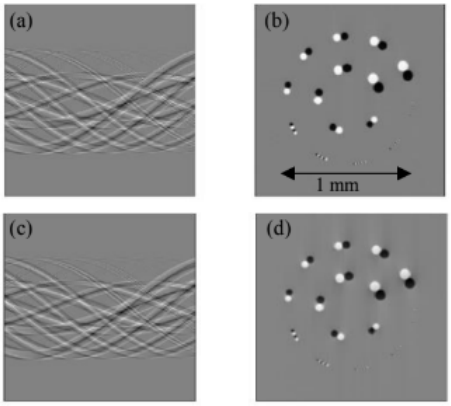

Fig. 1. Simulated phase sinogram ((a) and (c)) and reconstructed axial slice ((b) and (d)) for a full sampling (step-and-shoot) (top row) and cycloidal flyscan (bottom row) of a numerical resolution phantom with features ranging from 8 μm to 83 μm. A total of 268 angular steps over 180° were simulated for each case.

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[2] C K Hagen *et al.,* (2020) *Phys. Rev. Applied* **14**, 014069.
[3] G Lioliou *et al.,* (2022) *Sci. Rep.* **12**, 21336.

Direct measurement of scattering signals with Edge Illumination and the difference from interferometric measurements of the same quantity

I. Buchanan[1*], S. Cipiccia[1], C. Navarrete[1], C. Peiffer[1], L. Fardin[2], A. Astolfo[1], T. Partridge[1], M. Esposito[1], M. Endrizzi[1], C.K. Hagen[1], P.R.T. Munro[1], A. Bravin[2], D. Bate[3], A. Olivo[1]

[1]*Department of Medical Physics and Biomedical Engineering, UCL, WC1E 6BT, UK*

[2]*European Synchrotron Radiation Facility, 38043 Grenoble, France*

[2]*Nikon X-Tek Systems Ltd., Tring Business Centre, Tring, Herefordshire, UK*

*Corresponding author: ian.buchanan.15@ucl.ac.uk

Scattering theory predicts that when X-rays encounter a layer of spherical particles, their spatial intensity follows a Gaussian distribution (the Guinier approximation), followed by a fourth-order decrease in intensity with scattering angle (Porod approximation). The former region, which shrinks with increasing particle size, can be probed outside synchrotron with phase-based imaging methods. These measurements are commonly referred to as dark field (DF) measurements, but different X-ray Phase Contrast imaging (XPCi) researchers mean different things when using this term. In interferometric XPCi methods such as Grating Interferometry (GI), DF refers to the destruction of an interference pattern and depends on the system-defined auto-correlation length (itself a function of photon energy, interference pattern period, and propagation distance from sample to detector). By varying the auto-correlation length, it is possible to deduce local particle sizes from their varying DF signals [1].

Edge Illumination (EI, [2]) is a non-interferometric XPCi method that directly measures the distribution of scattering angles in the Guinier region. We demonstrate that, when measuring a sample's average DF signal in an EI system, the result is independent of system parameters, and further explain how the signal varies with particle size and distribution, and photon

ORAL

Seeing inside the frog's body: from the larynx to the ear

M. Sowinski[1*], R. Kieber[2], S. Letourneur[2], N. Joly[2], P. Picart[2], E. Brun[3], T. Scotti[4], L. Sabatier[4], M. Muller[5], J-M. Chassot[6], N. Pollet[7], N. Chai[8], P. Tafforeau[9], C. Berruyer[10], R. Boistel[1]

[1]*Laboratory CNRS - MNHN UMR 7179 MECADEV 55 rue Buffon FR - 75005 Paris, France, morgane.sowinski1@mnhn.fr, rboistel@gmail.com*
[2]*LAUM, CNRS 6613, Institut d'Acoustique - Graduate School (IA-GS), Le Mans Université, Avenue Olivier Messiaen, 72085 Le Mans, France, nicolas.joly@univ-lemans.fr,[3] pascal.picart@univ-lemans.fr, remi.kieber13@gmail.com, stephane.letourneur@univ-lemans.fr*
[3]*Inserm UA7 Strobe, Université Grenoble Alpes, 2280 Rue de la piscine 38000 Grenoble, FRANCE, emmanuel.brun@inserm.fr*
[4]*LMA, UMR 7031 AMU - CNRS - Centrale Marseille, 4 impasse Nikola Tesla CS 40006 13453 Marseille, FRANCE, scotti@lma.cnrs-mrs.fr, sabatier@lma.cnrs-mrs.fr*
[5]*Mechanical and Aerospace Engineering Department, NC State University, 911 oval drive, Raleigh, NC 27695, USA, mmuller2@ncsu.edu*
[6]*Institut Langevin, ESPCI Paris, CNRS, PSL University, 1 Rue Jussieu 75005 Paris, FRANCE, jeanmarie.chassot@espci.fr*
[7]*Laboratoire Evolution, Génomes, Comportement et Ecologie (EGCE)- UMR9191 IDEEV, Université Paris-Saclay, CNRS, IRD, 12 route 128 91190 Gif sur Yvette, nicolas.pollet@universite-paris-saclay.fr*
[8]*Ménagerie du jardin des plantes, MNHN, 57 Rue Cuvier 75005 Paris, FRANCE, norin.chai@gmail.com*
[9]*ESRF 71 Avenue des Martyrs CS-40220 38043 Grenoble, FRANCE, paul.tafforeau@esrf.fr*
[10]*UCL Engineering Science 141 Christian Street London E1 1RS, United Kingdom, c.berruyer@ucl.ac.uk*
[*]Corresponding author: morgane.sowinski1@mnhn.fr

Acoustic communication involves two processes in Anurans: sending signals and receiving them [1]. The signal sent changes due to environmental parameters and differs from the signal received. Yet, calling frogs hear in a wide range of habitats, in open or closed, absorbent or noisy environments [2]. In these conditions, frogs have adapted to their environment during evolution [3]. To understand this evolution of their communication system, we have to examine structures dedicated to the emission (vocal apparatus) and reception (auditory apparatus) of signals. It requires non-destructive imaging methods to see inside the body at tiny scales. We have explored their anatomy and functional morphology using an integrative, and multimodal approach.

State-of-the-art non-invasive imaging modalities provide images rich in quantitative anatomical and functional information on specimens from heritage collections and in vivo [4]. We will present different methods: MRI, X-ray microtomography, and X-ray phase contrast imaging (synchrotron), ultrasonic elastography, full-field OCT, and full-field Heterodyne holography laser Doppler vibrometry. We will start with observation and discuss imaging techniques to study frogs' vocal and auditory apparatus. Then we will describe the methods and protocols used for segmentation, morphometry, and numerical simulation that we have used in our research.

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X-ray Phase Contrast and Dark-field imaging on laboratory equipment using random modulation

C. Magnin[1,2 *], L. Quénot[2], D. Cenda[1], B Faure[1], B. Lantz[1], E. Brun[2]

[1] *Xenocs SAS, 1-3 All. du Nanomètre, 38000 Grenoble, France*
[2] *Univ. Grenoble Alpes, INSERM UA7, STROBE, 3800 Grenoble, France*
* Corresponding author: clara.magnin@inserm.fr

Phase contrast and dark-field imaging provide different and complementary information compared to conventional absorption-based X-ray imaging [1] allowing to probe more finely the structure and composition of a sample. The transfer of phase and dark-field imaging from synchrotron to laboratory equipment is a challenging task [2].

Here we extended the "Modulation Based Imaging" (MoBI) method to phase, dark-field and directional dark-field retrieval on laboratory X-ray equipment using a Xeuss instrument (Xenocs SAS, Grenoble, France). Experimentally a random pattern membrane is imaged with and without the sample. This operation is repeated several times while moving the membrane. All the images are then processed using the LCS algorithm [3] extended to dark-field to recover the different images modalities. Result on a phantom is shown in Figure 1.

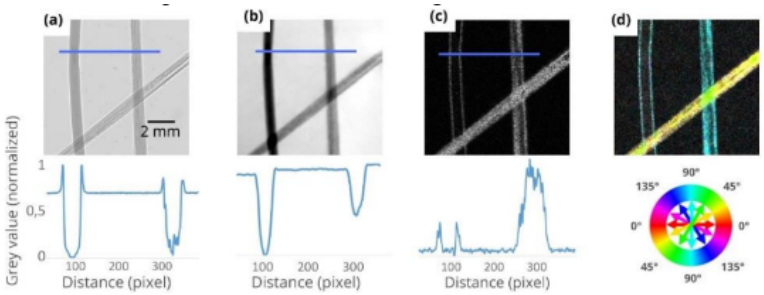

Figure 1 Attenuation (a), phase (b), dark-field (c) and directional dark-field (d) images of a nylon wire (left) and two bundles of carbon fibers with different orientations. Profiles along the blue lines are given bellow.

In the attenuation image we cannot distinguish the nylon and the carbon bundles because their absorption is close. However, in the phase contrast image, there is greater contrast between the two. Similarly, the fibers create a stronger dark-field signal than the nylon. The directional dark-field image highlights two different directions of the carbon fibers while showing the lack of preferential orientation in the nylon.

Promising phase, dark-field and directional dark-field images have been obtained on low-coherence equipment using the MoBI method. Future work will involve the optimization of the setup and 3D tomographic reconstruction of phase and dark-field.

[1] Alberto Bravin *et al* 2013 *Phys. Med. Biol.* **58** R1.
[2] Quenot, L., Bohic, S., & Brun, E. (2022). X-ray Phase Contrast Imaging from Synchrotron to Conventional Sources : A Review of the Existing Techniques for Biological Applications. *Applied Sciences*, *12*(19), 9539.
[3] Quénot, L., Rougé-Labriet, H., Bohic, S., Berujon, S., & Brun, E. (2021). Implicit tracking approach for X-ray phase-contrast imaging with a random mask and a conventional system. *Optica*, *8*(11), 1412-1415.

High-resolution brain tractography from X-ray phase-contrast images

J. Gobé[1], M. Chourrout[1], A. Vacavant[2], H. Rositi[2], F. Chauveau[1*]

[1]*Univ. Lyon 1, Lyon Neuroscience Research Center, CNRS, INSERM, Lyon, France*
[2]*Univ. Clermont Auvergne, Institut Pascal, CNRS, SIGMA Clermont, Clermont-Ferrand, France*
*Corresponding author: chauveau@cermep.fr

X-ray phase contrast tomography (XPCT) is an emerging imaging technique enabling the acquisition of images with an isotropic resolution down to the micrometer scale. Its unequalled contrast within soft tissues such as the brain proves particularly relevant in neuroscience for label-free ex vivo imaging of animal models [1]. The ability to non-destructively image structures that are purely 3D such as the white matter tracts calls for the development of dedicated tools. We here present a pipeline to perform an XPCT-derived tractography of the rodent brain.

Imaging was performed at a voxel size of 6.5µm^3 at ESRF (beamlines ID-17/19) and SOLEIL (beamline ANATOMIX), using propagation-based technique. Mouse or rat brain samples (with a focal demyelination obtained through a stereotaxic injection of lysophosphatidylcholine, LPC) were fixed in formaldehyde 4% and then dehydrated in successive ethanol baths to maximize white-to grey matter contrast. The script (written in Python 3.9, with numpy, scipy, nibabel modules) is based on the computing of the first order derivatives tensor of the image and the determination of fiber direction by analysis of its eigenvalues and eigenvectors, as already reported for light-sheet images [2]. Diffusion Toolkit was then used to perform tractography (http://trackvis.org/dtk/). The script takes as an input the pre-processed (deringing, brain extraction) volumes and returns the fractional anisotropy and fiber orientation maps as well as the white matter tractography (Fig. 1).

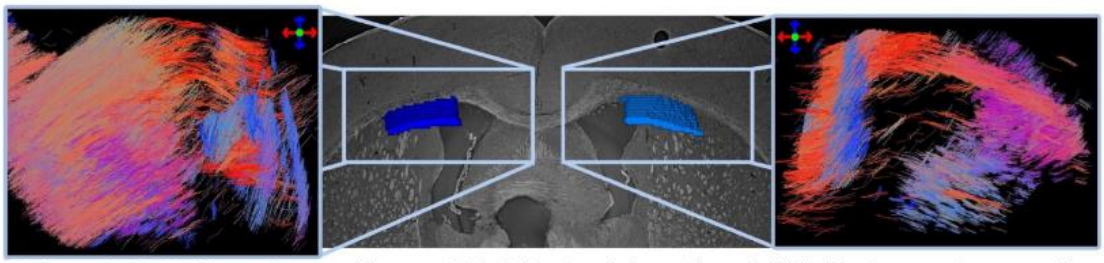

Figure 1: XPCT image (gray) with control (dark blue) and demyelinated (light blue) areas. Corresponding local tractographies showing interrupted fibers on the demyelinated side.

We provide the first example of tractography obtained from XPCT data, which could fill the gap between diffusion-based MRI (100µm resolution) and light-sheet microscopy (1µm resolution).

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4D Synchrotron X-ray µCT Imaging of Lung Tissue Strain in Bleomycin-Induced Lung Injury in Rats

Richard T. Deyhle Jr.[1,2], Luca Fardin[3], Irma Mahmutovic Persson[1,4], Jose Luis Cercos-Pita[5], Gaetano Perchiazzi[5], Lars E. Olsson[1,2], Sam Bayat[3*]

[1] *Lund University, Medical Radiation Physics, Department of Translational Medicine, Lund, Sweden*
[2] *Skåne University Hospital, Malmö, Sweden*
[3] *Université Grenoble Alpes, Inserm UA07 STROBE Laboratory, Grenoble, France*
[4] *Lund University BioImaging Center, Faculty of Medicine, Lund University, 221 42 Lund, Sweden*
[5] *Uppsala University, Hedenstierna Laboratory, Uppsala, Sweden*
*Corresponding author: sbayat@chu-grenoble.fr

Pulmonary fibrosis is characterized by excessive and heterogeneous deposition of extracellular matrix (ECM) components, particularly collagen, altering the local lung tissue stiffness [1]. However, there are no techniques to assess the local ECM micromechanics in lungs, *in vivo*. We applied a time-resolved synchrotron radiation phase contrast µCT technique (4D-µCT) to investigate local ECM deformation under controlled ventilation in bleomycin-induced lung injury [2]. Here, we computed and qualitatively compared images of local lung strain distribution within the lung tissue in normal and bleomycin-injured rat lungs using a previously described image-registration based processing pipeline [3]. X-rays from a synchrotron source were monochromatized at 38 keV. A free propagation phase-contrast setup was used with a sample to detector distance of 3.5 m. Images were reconstructed using the Paganin phase retrieval algorithm. Projection images were acquired at a constant frame rate using a fast camera (PCO Edge), coupled with optics determining a pixel size of 6 µm and 10 ms time resolution.

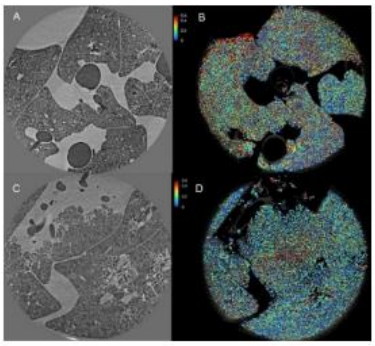

Figure 1 Sample phase-contrast (A, C) and local strain maps (B, D) in a representative control (A, B) and bleomycin-injured lung (C, D), under positive-pressure ventilation. Note the reduced tissue deformation particularly in fibrotic regions, and strain magnitudes comparable to control in normal appearing regions in bleomycin-induced lung injury. Color scale range (B, D) is 0 to 0.5.

Figure 1 shows sample phase-contrast CT and composite strain maps in a representative control and bleomycin rat. Further quantitative analysis of the local strain data is underway. In conclusion, we show the first quantitative images of local strain acquired in normal and bleomycin-injured *in vivo* rat lungs, at 6 µm voxel resolution. This approach will allow to investigate how the ECM micromechanical alterations influence fibrogenesis and vice-versa. Assessing the involved mechanisms will provide insight for developing new therapies.

[1] Deng, Z., et al. *Int J Biochem Cell Biol*, 2020. **126**: p. 105802.
[2] Mahmutovic Persson, I., et al. *Front Physiol,* 2020. **11:** p. 584.
[3] Cercos-Pita, J.-L., et al. *Sci Rep,* 2022. **12(1):** p. 1-11.

INVITED

Imaging in kidney disease

Anna Caroli

Medical Imaging Laboratory, Bioengineering Department, Istituto di Ricerche Farmacologiche Mario Negri IRCCS

Over the past few years, kidney imaging has seen great advances, allowing assessment of kidney structure and morphology, perfusion, function and metabolism, and oxygenation, as well as microstructure. Medical imaging is becoming increasingly important in the evaluation of kidney physiology and pathophysiology, showing promise to overcome the limitations of current markers and improve kidney disease management. A variety of imaging modalities are currently available to probe the kidney, particularly ultrasonography, CT, PET, renal scintigraphy, and multiparametric MRI. Given that the range is broad and varied, kidney imaging techniques should be chosen based on the clinical question and the specific underlying pathologic mechanism, taking into account contraindications and possible adverse effects. Integration of various modalities providing complementary information will likely provide the greatest insight into renal pathophysiology. This presentation will highlight major recent advances in kidney imaging, with a focus on kidney MRI. Current challenges, recent achievements, and gaps to be filled will be also discussed.

INVITED

Multiple Instance Learning approaches for E-health and advanced diagnostics

E. Vocaturo

CNR-NANOTEC Rende (CS), Italy

A Multiple Instance Learning (MIL) problem consists of classifying sets of points, called bags. The points inside the bags are called instances. Different from the classical supervised classification, in an MIL problem, during the learning phase, only the labels of the bags are known, whereas the labels of the instances inside the bags are unknown. Various MIL applications are found in different fields, such as text categorization, image classification, bankruptcy prediction, speaker identification, and video analysis. For example, in text categorization, the aim is to associate a text (bag) to a particular topic of interest on the basis of some keywords (instances), while, in image classification, the objective is to categorize an image (bag) on the basis of some its sub-regions (instances).

An interesting application of the MIL is also in diagnostics by means of medical images. In this case, the objective is to discriminate between non-healthy and healthy patients on the basis of their medical scan (bag): a patient is "positive" if he/she presents at least an abnormal sub-region (instance) in his/her medical scan; vice versa, a patient is "negative" if all the sub-regions (instances) in his/her medical scan are healthy. This example fits very well with the so-called standard MIL assumption, which is often adopted in the presence of two classes of bags and two classes of instances: based on this assumption, a bag is positive if it contains at least a positive instance (non-healthy sub-region), and it is negative if all its instances are negative (the healthy sub-regions).

We present some MIL applications aimed at discriminating, by means of medical images, between non-healthy and healthy patients in three different medical fields: melanoma detection, pneumonia detection and diabetic retinopathy detection. Extensive numerical results are also discussed.

POSTER SESSION 1

September 27th, 16:30-17:45

P1.1	Matteo BUSI Paul Scherrer Institut	Advanced neutron imaging techniques at the Paul Scherrer Institute
P1.2	Margherita SIMONI University of Roma Tor Vergata	Neutron imaging for the catalysed hydrogen conversion in metal organic frameworks
P1.3	Federico CARUGGI University of Milano-Bicocca	Development of a Triple-GEM detector with strip readout and GEMINI chip for X rays and neutron imaging
P1.4	Agostino CELORA University of Milano-Bicocca	A multipurpose software for imaging studies and tomographic inversion applied to X-ray detection
P1.5	Maria Caterina CROCCO University of Calabria and STAR IR	A non-destructive numismatic and archaeometric study of Roman coins
P1.6	Alessandro RE University of Torino	Development of a setup for imaging, elemental and structural non-invasive characterization of materials based on a liquid anode X-ray source
P1.7	Martina FRANCHI University of Roma La Sapienza	Assessing readability of the text in ancient paper fragments by a photometric statistical analysis
P1.8	Giulia MARCUCCI University of Milano-Bicocca	A neutron imaging investigation on Roman brass samples coming from ancient Mediolanum town
P1.9	Maya MUSA University of Pavia	Unravelling the morphology of bulk meteorite samples by neutron imaging and diffraction

P1.1

Title: Advanced neutron imaging techniques at the Paul Scherrer Institute

M. Busi[1*], M. Strobl[1]

[1]*Laboratory for Neutron Scattering and Imaging, Paul Scherrer Institute, Villigen (Switzerland)*
*Corresponding author: matteo.busi@psi.ch

Neutron imaging is a powerful technique utilized by researchers to visualize the internal structure of materials with high spatial resolution, between a few micrometers and a few hundreds of micrometers. Recently, there have been groundbreaking advancements in neutron imaging technology that go beyond traditional attenuation contrast methods. This contribution will provide an overview of recent developments in advanced neutron imaging techniques, which can access length scales below the current state-of-the-art detector resolution, including Bragg edge imaging, grating interferometry, and dark-field imaging. Bragg edge imaging is a diffractive-based imaging technique that enables 2D mapping of crystallographic properties such as residual lattice strain, crystallographic phase transformation and evolution, texture and crystallite size. Recent method developments for efficient measurement at continuous sources [1] and application studies on additive manufacturing samples will be presented. Neutron grating interferometry is a technique that provides simultaneously attenuation, differential phase and dark-field contrast maps [2]. The latter relies on its sensitivity to underlying small-angle scattering interactions, which enables the investigation of structures in the range of a few tens of nanometers to a few micrometers through fitting of the measured real space correlation function [3]. Recent developments for the characterization of anisotropic scattering and applications in the field of soft matter physics will be shown. Lastly, polarized neutron imaging allows for the study of the interaction between a polarized neutron beam and magnetic fields present in the investigated specimens [4]. In particular, this method has been applied to quantitatively map magnetic crystallographic phases in iron-based materials [5].

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[2] Strobl, M., et al. "Neutron dark-field tomography." *Physical review letters* 101.12 (2008): 123902.
[3] Strobl, Markus. "General solution for quantitative dark-field contrast imaging with grating interferometers." *Scientific reports* 4.1 (2014): 7243.
[4] Strobl, M., et al. "Polarization measurements in neutron imaging." *Journal of Physics D: Applied Physics* 52.12 (2019): 123001.
[5] Busi, M., et al. "Polarization contrast neutron imaging of magnetic crystallographic phases." *Materials Today Advances* 16 (2022): 100302.

P1.2

M. Simoni[1]*, C. Andreani[1,2], R. Senesi[1,3], and G. Romanelli[1]

[1]*Dipartimento di Fisica and NAST Centre, University of Rome Tor Vergata, Via della Ricerca Scientifica, 1, 00173, Rome, Italy*
[2]*Istituto IPCB-CNR, Viale J.F. Kennedy 54, 80125 Naples, Italy*
[2]*Istituto ISM-CNR, Via Fosso del Cavaliere, 100, 00133 Roma, Italy*
*Corresponding author: margherita.simoni@alumni.uniroma2.eu

Time-resolved neutron imaging was used to investigate the ortho-para hydrogen conversion (opC) in the HKUST-1 metal organic framework (MOF) at the IMAT beamline of the ISIS Neutron and Muon Source. Currently MOFs are attracting interest as potential hydrogen storage materials [1], rendering necessary to investigate the framework-dihydrogen interactions. MOFs are known to act as catalysts for the opC [2]. Energy-selective neutron imaging allowed us to characterize the conversion rate as a function of time, for different areas of the sample. Results reported for hydrogen at 17 K show that the ortho-hydrogen conversion rate depends linearly on the ortho concentration and has an average characteristic conversion time of 58 minutes, significantly lower than that of the free hydrogen (ca. 79 hours [3]). Moreover we show that this technique provides a unique insight into the adsorption and conversion kinetics, and that the possibility to explore the spatial distribution of the sample renders it particularly appealing for industrial and engineering applications.

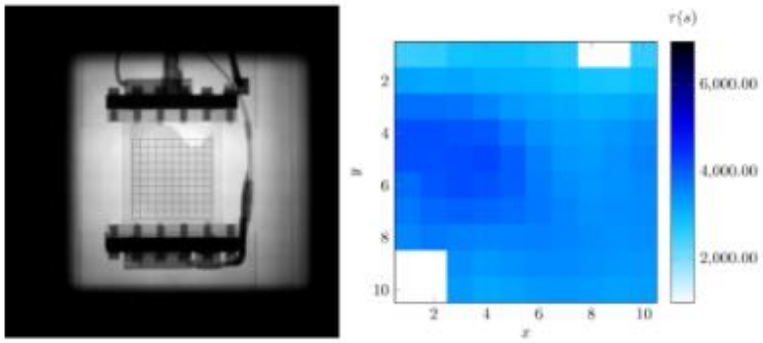

Figure 1 The first image shows a radiograph of the sample container loaded with HKUST-1 and liquid H_2, a grid is overlaid to represent the different areas for which the conversion time (τ) is calculated. The second image shows the spatial distribution of τ, the outliers in the top right corner are due to the absence of the powder, those in the bottom left portray an area where hydrogen failed to reach.

[1] M. P. Suh, H. J. Park, T.K. Prasad, D. Lim (2012) Hydrogen Storage in Metal–Organic Frameworks. Chem. Rev., 112, 782–835.
[2] D. M. Polyukhov, N. A. Kudriavykh, S. A. Gromilov, A. S. Kiryutin, A. S. Poryvaev, and M. V. Fedin (2022) Efficient MOF-Catalyzed Ortho–Para Hydrogen Conversion for Practical Liquefaction and Energy Storage. ACS Energy Lett., 7, 4336–4341.
[3] C. A. Swenson (1950) The Catalysis of the Ortho Para Conversion in Liquid Hydrogen. J. Chem. Phys. 1950, 18, 520−52

P1.3

Development of a Triple-GEM detector with strip readout and GEMINI chip for X rays and neutron imaging

F. Caruggi[1,2]*, S. Cancelli[1,2], A. Celora[1], G. Gorini[1,2,3], G. Grosso[3], F. Guiotto[4], A. Muraro[3], E. Perelli Cippo[3], M. Petruzzo[1], O. Putignano[3], M. Tardocchi[2,3], G. Croci[1,2,3]

[1]*Dipartimento di Fisica "G. Occhialini", Università di Milano-Bicocca, piazza della Scienza 3, Milan, Italy*
[2]*INFN, Sezione Milano-Bicocca, piazza della Scienza 3, Milan, Italy*
[3]*Istituto per la Scienza e Tecnologia dei Plasmi, CNR, via Cozzi 53, Milan, Italy*
[4]*Dipartimento di Fisica, Università di Padova, via F. Marzolo 8, Padova, Italy*
*Corresponding author: f.caruggi@campus.unimib.it

Thermal neutron imaging can be a useful tool in the study of the internal structure of an object. The different attenuation properties of the materials with respect to X rays give rise to different interactions and the result is a complementary non-destructive analysis, which can provide important additional information. This technique has been successfully employed in different areas of work [1], especially in material science [2] and cultural heritage studies [3] [4]. This paper describes the development of a new detection system for the detection and 2D imaging of thermal neutrons, and its characterization performed with X ray emissions. The system features the use of a gaseous detector, based on the Gas Electron Multiplier technology, and a fully digital electronic readout, with a combination of custom-made ASICs (called GEMINI) and FPGA boards, enabling fast single photon counting. The detector can be thus used directly for X ray imaging, while the addition of a suitable converter in its active volume allows for detection of neutrons and for reconstruction of their tracks. One way of achieving this is to have additional GEM foils layered with a neutron-sensitive material, as for example B_4C. [5] The readout system is based on a x-y strip structure and features the reconstruction of single events through the center of mass methodology, allowing for accurate tomography of both X rays and neutrons, with sub-mm spatial resolution, in combination with sub-ms time resolution and high rate capabilities (up to MHz/mm^2). The paper focuses firstly on the description of the system and its working principle, to then describe the characterization, as well as preliminary results of X ray imaging on different samples.

[1] I. S. Anderson, R. L. McGreevy, H. Z. Bilheux (2009) *Neutron Imaging and Applications*. Spinger.
[2] N. Kardjilov, I. Manke, A. Hilger, M. Strobl, J. Banhart (2011) Neutron Imaging in Material Science. *Materials Today, 14(6),* pp. 248-256.
[3] M. Dinca, D. Mandescu (2015) Thermal Neutron Tomography for Cultural Heritage at INR, *Physics Procedia, 69*, pp. 646-652.
[4] D. Di Martino, M. Bellanova, E. Perelli Cippo, R. Felicetti, A. Scherillo, J. Kelleher, Z. Kis, G. Gorini (2018) A neutron diffraction and imaging study of ancient iron tie rods. *Journal of Instrumentation, 13(5)*, C05009.
[5] A. Muraro et al (2021) MBGEM: a stack of borated GEM detector for high efficiency thermal neutron detection. *The European Physical Journal Plus, 136,* 742.

P1.4

A multipurpose software for imaging studies and tomographic inversion applied to X-ray detection

A. Celora

University of Milano-Bicocca

A multipurpose software, called REVOLT, has been developed to fully exploit the imaging capabilities of Triple-GEM 2D cameras for X-rays and neutrons detection. Tomographic inversion techniques and synthetic data production methods are based on the relation between the 2D spatially resolved signal on a detector and the 3D signal emission in the experimental space. The core task of the REVOLT software is to provide the needed relation matrix between the two quantities via a numerical-geometrical approach. REVOLT development and validation are here described, followed by an example of application on a pixelated triple-GEM detector experiment. The software is a Monte Carlo routine based on Line Of Sights (LOSs) evaluation of a virtual voxel grid of the experiment volume. The underlying idea is to evaluate how much the emission from a point in space would contribute to the counts on each detector pixel on the base of geometrical properties, to relate each detector pad to a set of weighted emitting voxels. The results of the routine had been evaluated via analytical comparison and numerical models, by confrontation with MCNP simulations, obtaining positive results. The first application of the software is to simulate the data produced by a pixelated GEM detector at the HVPTF (High Voltage Padova Test Facility) experiment in order to optimize the camera optical set-up. Furthermore the routine is paired with a Tikhonov regularization method for tomographic inversion to reconstruct X-ray emission images from the actual data obtained in the 2023 HVPTF experimental campaign. The image reconstruction based on the REVOLT software and the GEM detector data allowed, for the first time, to identify the X-ray emission region between the electrodes of the HVPTF machine, therefore providing a key element for the study of the physics behind the micro-discharges in the experiment. The results show the potential of the tool, both for synthetic data production and for tomographic reconstruction purposes.

P1.5

A non-destructive numismatic and archaeometric study of Roman coins

M. C. Crocco[1,†,*], R. Filosa[1,†], A. Smeriglio[1,†], V. Formoso[1], R. C. Barberi[1], A. Solano[2], M. Cerzoso[3], A. Polosa[4], V. Cerrone[4], R. G. Agostino[1]

[1] *Physics Department & STAR Research Infrastructure, Università della Calabria, 87036 Rende (CS), Italy - mariacaterina.crocco@unical.it, andrea.smeriglio@unical.it, raffaele.filosa@unical.it, vincenzo.formoso@fis.unical.it, riccardo.barberi@fis.unical.it, raffaele.agostino@fis.unical.it*
[2]*Department of Informatics & STAR Research Infrastructure, Università della Calabria, 87036 Rende (CS), Italy - andrea.solano@unical.it*
[3]*Brettii and Enotri Museum, Salita S. Agostino, 87100 Cosenza, Italy - m.cerzoso@comune.cosenza.it*
[4] *Department of Scienze dell'Antichità, Sapienza University, Piazzale Aldo Moro 5, 00185 Roma, Italy - annalisa.polosa@uniroma1.it, cerrone.1792031@studenti.uniroma1.it*
†*These authors contributed equally to this work*
*Corresponding author: mariacaterina.crocco@unical.it

Thirteen Roman coins have been the subject of a non-destructive numismatic and archaeometric analysis. In particular, we studied thirty Roman coins that were discovered in the so-called "Grotta delle Ninfe" near Cerchiara di Calabria in Calabria, Italy, and are currently preserved at the Brettii and Enotri Museum in Cosenza, Calabria, Italy [1,2]. This coins, due to the nearby sulphurous water source, have followed a degradation process. The inscriptions cannot be read at all because of a heavy layer of corrosion products (Figure 1a). In this work, we characterized by X-ray fluorescence and X-ray microtomography (µCT) to id entify the constituent material, coinage stamp, and inscriptions present on the coins [3].We were able to decipher some inscriptions using the µCT, and we discovered the provenance and manufacturing era of the coins by numismatic research (Figure 1b). With our study, we have found that some coins are in orichalcum, while others are in copper. Furthermore, we have identified the historical period to which they belong and we can conclude that the coins were minted during the reign of Augustus, Vespasian, Domitian and Trajan, the imperial era coinage.

(a) (b)

Figure 1 (a) M4 coin and (b) microtomography slice

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P1.6

Development of a setup for imaging, elemental and structural non-invasive characterization of materials based on a liquid anode X-ray source

A. Re[1,2,3*], F. Tansella[1,3], L. Vigorelli[4,1,3], A. Alessio[1,2,3], L. Guidorzi[1,3], C. Donazzolo[1], A. Lo Giudice[1,2,3], F. Picollo[1,2,3], M. Truccato[1,2,3]

[1] *Department of Physics, University of Turin, 10125 Torino (Italy)*
[2] *NIS Inter-departmental Centre, Torino (Italy)*
[3] *National Institute of Nuclear Physics (INFN), Turin Division, 10125 Torino (Italy)*
[4] *Department of Electronics and Telecommunications, Polytechnic of Turin, 10129 Torino (Italy)*
*Corresponding author: alessandro.re@unito.it

In the last decades, a novel technology for X-ray sources based on the use of a liquid anode has been developed, in order to increase the maximum achievable brilliance by at least one order of magnitude compared to conventional microfocus sources [1]. With this innovative equipment, a High-Brilliance X-ray laboratory (HiBriX Lab) is presently under development at the University of Torino, hosted at the NIS inter-departmental Centre. It was designed by integrating different detectors and focusing optics to represent a unique laboratory in Italy and with a handful of comparable examples in the world. The aim is to cover several applications such as: material characterization via μXRD and μXRF maps; investigation of detector performances in terms of charge collection efficiency or as a function of damage effects; single cell level radiobiology; X-ray imaging (2D radiography and 3D computed tomography - CT) of objects having a wide size range.

Procurement of the different components has been almost completed and their integration is underway, developing specifically dedicated software for system control. To date, concerning the microfocused branch of the lab, a minimum spot size of about 25 microns has been achieved by means of a set of twin paraboloidal mirrors, and a maximum flux density of 2.7×10^{10} ph s^{-1} mm^{-2} has been obtained with a polycapillary optics system specifically delivered by INFN X-lab in Frascati. On the other side, where a 30° cone beam is available, a versatile X-ray imaging setup is installed, which allows the acquisition of radiographs and tomographic scans of very different kinds of samples: objects of dimensions in the sub-mm to few tenths of cm range, with wide variability in atomic number and density values, such as the samples of interest in the field of cultural heritage.

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P1.7

Assessing readability of the text in ancient paper fragments by a photometric statistical analysis

Martina Franchi

University of Roma La Sapienza

Ancient documents are important historical sources. They have often been found in a fragmented condition due to their conservation status. In this work, we studied fragments of paper found in 1996 during excavation of the Quattro Santi Coronati complex, in Rome, and dated between the second half of the 1400s and the first half of the 1500s. The fragments present discoloration of the text, therefore they are only partially readable. To bring to light the faded text we enhanced the images of the fragments and we have investigated photometric features by statistic estimators to compare the initial fragment image with the enhanced image produced. For the enhancement, different methods present in the literature were chosen. The statistical analysis of the photometric features made it possible to understand the change that took place after the enhancement. The aim was to identify the enhancement which improves readability both as a subjective assessment and for optical character recognition (OCR) systems.

P1.8

A neutron imaging investigation on Roman brass samples coming from ancient Mediolanum town

Giulia Marcucci[1,2], Antonella Scherillo[2], Daniela Di Martino[1]
[1] Dipartimento di Fisica "G. Occhialini", Università degli Studi di Milano Bicocca and INFN, Sezione di Milano Bicocca
[2] ISIS Neutron and Muon Source, Didcot, UK

We present the application in the Heritage Science field of a recently advanced neutron imaging technique, called Neutron Resonance Transmission Imaging (NRTI), performed at the INES (Italian Neutron Experimental Station) [1] beamline of the ISIS spallation neutron source [2].
The NRTI technique relies on the measurement of the beam attenuation due to the resonant absorption of epithermal neutrons (0.3 eV< E_n < 100 eV) by the nuclei of a material. Since resonance structures appear at specific energy for each nuclide in their neutron-induced reaction cross-sections [3], they can be used to identify and quantify isotopes in materials and objects.
NRTI allows the localization of isotopes and elements distribution within 2D (and potentially 3D) maps of the bulk of the analysed object, with the peculiar enhancement in terms of contrast between isotopes with similar attenuation coefficients due to intrinsic characteristics of this method.
The peculiarities of NRTI make it suitable for the characterization of inhomogeneous samples [4,5] and it can be applied to archaeological objects as it is a non-destructive technique.
Within this context, a set of crucible fragments related to bronze and brass objects production in Roman Italy (I-II AD) [6] has been investigated through a combination of NRTI and other well-consolidated non-destructive nuclear techniques. These crucibles consist of mass-produced terracotta pots, coated with a thick layer of refractory clay. Inside, metallic inclusion related to copper and zinc alloy production can be present. Some fragments show metallic depositions on their surfaces, while others could contain traces inside their volume. Therefore, standard investigations with X-rays or ion beams could not be adequately sufficient to disclose brass traces and composition.
At present, NRTI analysis returned the qualitative elemental composition of the fragments, revealing the presence of brass and bronze. In addition, arsenic, antimony, silver and lead were detected in their bulk.
These kinds of archaeological samples are an example of inhomogeneous objects that can be interesting to be investigated with the NRTI technique, exploiting its possibility of visualising the elements (and isotopes) distribution within the bulk.

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P1.9

Unravelling the morphology of bulk meteorite samples by neutron imaging and diffraction

G. Marcucci[1,2], F. Salvemini[3], V. Luzin[3], M. Musa[4], M.P. Riccardi[4], R. Rossini[1,2,5], M. Clemenza[6], C. Cattaneo[7], D. Di Martino[1,6]

[1]Physics Dept. "G. Occhialini", University of Milano-Bicocca, Milano, Italy, [2]STFC, Rutherford Appleton Laboratory, ISIS Facility, Harwell, UK, [3]ACNS, ANSTO, Sydney, Australia, [4]Earth Science Dept., University of Pavia, Pavia, Italy, [5]Physics Dept, University of Pavia and INFN, Pavia Section, Italy, [6]INFN, Milano Bicocca, Milano, Italy [7]Osservatorio Astronomico Cà del Monte, Cecima (PV), Italy

Meteorites are rare and fascinating materials that also play a fundamental role in the study of planetary and cosmological research [1]. We can define three main categories: stony, iron and stony-iron meteorites. Stony meteorites consist mostly of silicate minerals and may contain small spheroidal grains (known as chondrule and containing mafic minerals), while iron meteorites consist mainly of an iron-nickel alloy, being a source of metallic iron in ancient times. Most common stony meteorites (ordinary chondrites) usually have an uneven distribution of phases and elements throughout their volume. To derive the original provenance or date of a meteorite, investigations are typically based on compositional analyses by destructive methods (such as mass spectrometry or metallographic techniques). Despite some cross sections can be sourced for analytical studies, meteorite samples are considered rare and further sampling should be avoided. Therefore, a non-destructive technique to obtain the "bulk" composition would be desirable, although challenging for conventional laboratory-based instrumentations. To obtain in-depth information on the bulk composition of meteorites, neutron imaging and diffraction are very powerful complementary techniques. While neutron-based techniques were considered in the 1960s and 1970s - especially neutron activation analysis [2]- mass spectrometry, microscopies, and metallographic studies were later preferred [1]. However, recently, the application of techniques based on X-rays or neutrons has been revived, with the scope of applying a non-invasive approach [3-5]. In the framework of a collaboration between the Dept. of Physics of Milano-Bicocca and the Earth Science Dept. of the University of Pavia, we have recently developed a protocol for in-depth non-destructive characterization of stony meteorites [6-7]. In order to extend the breath of our research, the protocol has been applied to a set of samples of carbonaceous and iron meteorites provided by the Planetario e Osservatorio Astronomico G.Giacomotti -Cà del Monte- Cecima (PV), Italy. Preliminarily, bulk density measurements and XRF analysis were performed to detect major elements (Si, Fe, Mg, Al, Ca), minor elements (like Na, Ni, Mn) and trace elements (like Ba, Cl, Sr, Ti). Raman spectroscopy on some slices (already available) complements the results. In addition, a neutron tomography experiment was carried out at DINGO beamline (ANSTO facility, Sydney) to derive three-dimensional distribution, size and shape of the composing minerals. Neutron diffraction texture measurement was carried out as well (at KOWARI, ANSTO facility) to determine crystallographic relationship between major phase and other minor minerals in the meteorite body. In this paper results of our investigation campaign demonstrate some new insights into structural classification of meteorites based on the information gathered on the structural features of the major and minor phases, and the evidences collected about possibly different states of metamorphism the meteorites went through over the eons of time after its formation (such as impacts and reheating).

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POSTER SESSION 2

September 28th, 18:00-19:30

P2.1	Sergey GASILOV Canadian Light Source	Biomedical imaging and microtomography at Canadian Light Source
P2.2	Simone CAPUTO University of Calabria	Semantic segmentation of X-ray phase-contrast microtomographic images of adult insect specimens using a convolutional neural network
P2.3	Carlo PEIFFER University College London	Quantitative comparison between beam tracking with analyser based imaging for measuring ultra small angle X-ray scattering using synchrotron radiation
P2.4	Clara MAGNIN University of Grenoble Alpes	X-ray Phase Contrast and Dark-field imaging on laboratory equipment using random modulation
P2.5	Vincenzo FORMOSO University of Calabria and STAR IR	Monitoring the effects of combined calcimimetics and tolvaptan treatment on renal cysts growth in animal models of human Polycystic Kidney Disease by 3D enhanced X-ray microtomography
P2.6	Paola PERION University of Trieste and INFN Trieste	Spectral micro-CT for simultaneous gold and iodine detection, and multi-material identification
P2.7	Ju Young LEE University of Calabria	Virtual Histology of Human Brain tissue using Phase-Contrast X-ray Microtomography
P2.8	Sandro DONATO University of Calabria	Comparison of novel reconstruction algorithms for low-dose breast computed tomography with synchrotron radiation
P2.9	Angelo TAIBI University of Ferrara	Spectral micro-CT of osteochondral samples with iodine cationic contrast agent
P2.10	Fabien CHAUVEAU University of Ferrara	Virtual histology of human cerebral amyloid angiopathy
P2.11	Hafiz Muhammad FAHAD Ludwig Maximilian University	DAPHNE4NFDI: DAta from PHoton and Neutron Experiments - the synchrotron imaging use case
P2.12	Davide BUSEGHIN Polytecnich of Milano	A fully automated deep learning algorithm to derive micro-CT imaging biomarkers describing lung fibrosis progression and response to therapy in mice
P2.13	Alberto ARRIGONI Mario Negri IRCCS	Brain connectivity and microstructure in COVID-19 patients with olfactory or cognitive disorder

P2.1

Biomedical imaging and microtomography at Canadian Light Source

S. Gasilov[1*]
[1] *Canadian Light Source*
*Sergey.gasilov@lightsource.ca

X-ray microtomography (uCT) is a non-destructive imaging technique widely used in pre-clinical studies, biology, material science, environment research, and cultural heritage. In some cases, commonly available laboratory scanners fail to reveal objects' microstructure because of insufficient contrast, poor spatial and temporal resolution, or other factors. In such situations researchers turn to synchrotron imaging stations which often deliver desired information thanks to unique properties of synchrotron radiation. At Canadian Light Source two imaging beamlines (BMIT) were constructed for the purpose of pre-clinical and biomedical research. The maximum beam energy is 140 keV and the beam cross-section exceeds 110x7 mm^2 at 100 keV photon energy. Thanks to availability of satellite laboratories and proximity to the veterinary college of University of Saskatchewan, BMIT belongs to a handful of synchrotron beamlines where imaging of small and medium-size animals can be performed *in-vivo*. This opportunity was utilized to study lung, heart, and bone pathologies as well as for tissue engineering. Due to radiation dose constraints such projects mostly involve imaging with voxels of ~10 microns. In addition to function live imaging capability each beamline is equipped with a microscope to enable tomography with spatial resolutions down to one micron. High throughput, and ultra-fast imaging are also possible. These capabilities are used by a very wide community of material scientists, battery and fuel cell researchers, plant biologists, and other academics as well as industrial clients. Lastly, recently commissioned large field of view detector can be used to image tens of centimeters large fossils with 25-70 micron voxels.

We will give more details about BMIT instruments, capabilities, and limitations, show some research highlights, and explain modes of access to the CLS facility.

P2.2

Semantic segmentation of X-ray phase-contrast microtomographic images of adult insect specimens using a convolutional neural network.

S. Caputo[1*], P. Bruno [1], F. Calimeri [1], E. De Rose [1], S. Donato[1], A. Giglio[1], R.G. Agostino [1]

[1] *University of Calabria:* pierangela.bruno@unical.it, francesco.calimeri@unical.it , edoardo.derose@unical.it, sandro.donato@fis.unical.it , anita.giglio@unical.it, raffaele.agostino@fis.unical.it

* Simone Caputo: simone.caputo@outlook.it

Image segmentation, which is a pixel classification technique to achieve separation and labeling of specific structures of interest from the rest of the image, is a key task in image processing [1]. Current technologies make it possible to acquire tomographic images quickly, obtaining an enormous amount of data from which quantitative information can be obtained through segmentation. In recent years, to make image analysis faster, a rapidly growing segmentation technique exploits the use of neural networks. In particular a convolutional neural network (CNN), called SegNet, was used in this work [2]. The samples studied are insects named *Tenebrio molitor* [3] and we focused on the analysis and segmentation of their reproductive system. Samples have been subjected to exposure to a particular herbicide, and the goal is to look for morphological differences that may be created in the development of the animal due to the exposure. The images were acquired at the Elettra synchrotron facility in Trieste (Italy) [4], using the propagation-based phase-contrast techinque. The main parameters used are a polychromatic beam with average energy of 20 keV and pixel size of 4 µm. The dataset consists of 30 samples of different ages, half of which underwent treatment while the remaining half are used as controls. An initial segmentation was done manually, providing the network the accurate labels on which to learn. To improve the efficiency of the network, the training process was repeated several times by increasing the number of samples used for learning each time. The best performance result is an accuracy of (90 ± 2)% and was achieved using 12 samples in the training phase. In addition to the good results obtained by the network, this allowed us to greatly reduce the time for analysis of the entire dataset.

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P2.3

Quantitative comparison between beam tracking with analyser based imaging for measuring ultra small angle X-ray scattering using synchrotron radiation

C.Peiffer[1*], L.Brombal[2,3], C. J. Maughan Jones[1], F. Arfelli[2, 3], A. Astolfo[1], D. Dreossi[4], M. Endrizzi[1], C. K.Hagen[1], A. Mazzolani[1], R. H. Menk[3, 4, 5], L. Rigon[2, 3], A. Olivo[1], P. R. T. Munro[1]
[1]*Department of Medical Physics and Biomedical Engineering, University College London*
[2]*Department of Physics, University of Trieste, Via Valerio 2, 34127 Trieste*
[3]*Istituto Nazionale di Fisica Nucleare, Sezione di Trieste, Via Valerio 2, 34127 Trieste*
[4]*Elettra Sincrotrone Trieste SCpA, S. S. 14km 163.5, 34012 Basovizza (TS)*
[5]*Department of Computer and Electrical Engineering, Midsweden University, Sundsvall, Sweden*
*carlo.peiffer.20@ucl.ac.uk

X-ray phase contrast imaging (XPCI) methods give access to contrast mechanisms that are based on the refractive properties of matter in addition to attenuation contrast. One of these mechanisms is known as dark field, or ultra small angle X-ray scattering (USAXS) contrast. It arises due to refraction events caused by sample features with length scales below the physical resolution of the employed imaging system [1], that usually result in the broadening of the angular distribution of the X-ray beam. USAXS contrast can therefore give insight into sub-resolution structural information, which is an ongoing research topic in the vast field of the different XPCI techniques.

Analyser based imaging (ABI) [2] is a well-established monochromatic XPCI technique that uses a perfect crystal in Bragg reflection mode to analyse the angular intensity distribution of the X-rays transmitted through a sample. Beam tracking (BT) [3], on the other hand, is an emerging XPCI technique that, instead of a crystal, uses a mask with apertures that pre-shape the broad source X-ray beam into small beamlets that interact with the sample. The resulting beam shape is then analysed via detector pixels that are small compared to the beamlet cross section. BT is an interesting new XPCI because of its simple setup, robustness to vibrations and because it has already been applied to compact, incoherent and polychromatic laboratory X-ray sources [4].

In this study, we quantitatively compared the USAXS signal retrieved by BT with the gold standard of ABI using a synchrotron X-ray source. For this, we conducted a Kolmogorov Smirnov test tailored to our problem. We found that, provided certain conditions are met, the two methods measure the same quantity. This unifies historical research results from ABI and BT/EI into one body of research and allows researchers an alternative to using crystals for USAXS measurements.

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P2.4

X-ray Phase Contrast and Dark-field imaging on laboratory equipment using random modulation

C. Magnin[1,2 *], L. Quénot[2], D. Cenda[1], B Faure[1], B. Lantz[1], E. Brun[2]

[1] *Xenocs SAS, 1-3 All. du Nanomètre, 38000 Grenoble, France*
[2] *Univ. Grenoble Alpes, INSERM UA7, STROBE, 3800 Grenoble, France*
* Corresponding author: clara.magnin@inserm.fr

Phase contrast and dark-field imaging provide different and complementary information compared to conventional absorption-based X-ray imaging [1] allowing to probe more finely the structure and composition of a sample. The transfer of phase and dark-field imaging from synchrotron to laboratory equipment is a challenging task [2].

Here we extended the "Modulation Based Imaging" (MoBI) method to phase, dark-field and directional dark-field retrieval on laboratory X-ray equipment using a Xeuss instrument (Xenocs SAS, Grenoble, France). Experimentally a random pattern membrane is imaged with and without the sample. This operation is repeated several times while moving the membrane. All the images are then processed using the LCS algorithm [3] extended to dark-field to recover the different images modalities. Result on a phantom is shown in Figure 1.

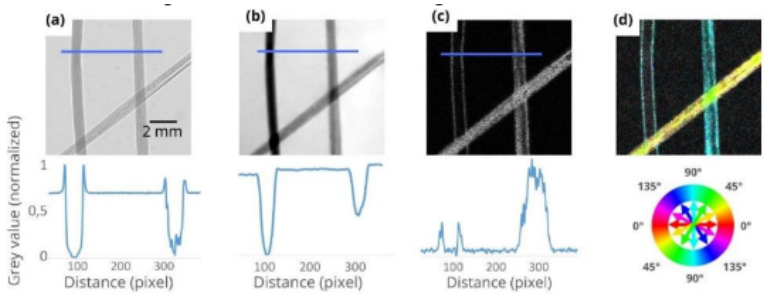

Figure 1 Attenuation (a), phase (b), dark-field (c) and directional dark-field (d) images of a nylon wire (left) and two bundles of carbon fibers with different orientations. Profiles along the blue lines are given bellow.

In the attenuation image we cannot distinguish the nylon and the carbon bundles because their absorption is close. However, in the phase contrast image, there is greater contrast between the two. Similarly, the fibers create a stronger dark-field signal than the nylon. The directional dark-field image highlights two different directions of the carbon fibers while showing the lack of preferential orientation in the nylon.

Promising phase, dark-field and directional dark-field images have been obtained on low-coherence equipment using the MoBI method. Future work will involve the optimization of the setup and 3D tomographic reconstruction of phase and dark-field.

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P2.5

Monitoring the effects of combined calcimimetics and tolvaptan treatment on renal cysts growth in animal models of human Polycystic Kidney Disease by 3D enhanced X-ray microtomography.

Annarita Di Mise[1], Vicente Torres VE[2] Alberto Bravin[3], Alberto Mittone[4], Raffaele Giuseppe Agostino[5], Riccardo Barberi[5], Maria Caterina Crocco[5], Giovanna Valenti[1], Vincenzo Formoso[5*]

1 Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari, Bari, Italy
2 Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA.
3 University Milano Bicocca, Department of Physics, Milano, Italy
4 Argonne National Laboratory | ANL · Division of X-ray Science
5 Physics Department, University of Calabria, Arcavacata Di Rende (CS), Italy
**Corresponding author: vincenzo.formoso@unical.it*

Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disease characterized by the progressive growth of renal cysts disrupting renal architectures[1]. Tolvaptan, a selective antagonist of the vasopressin V2 receptor (V2R), is the only approved drug able to slow cyst progression in patients[2,4]. We analyzed the effects of tolvaptan treatment on renal cysts growth in animal models of human ADPKD. We used high-resolution X-ray microtomography for early evaluation of the ultrastructure of renal cysts .

We have analysed 12 kidneys deriving from control rats or rat models of ADPKD (PCK rat).

X-ray microtomography revealed that the increase in PCK kidney volume was mainly due to the expansion of the medulla for large cysts. The cysts affecting PCK kidneys are primarily restricted to the medullary region but are equally significant and numerous in a more distal scan. Interestingly, PCK rats treated with tolvaptan display an intermediate phenotype, with smaller cysts primarily located in the medulla, which appear fewer in the distal section, where the percentage of apparently normal parenchyma is much more evident, resulting in a significant reduction of the total kidney volume compared to PCK non-treated rats.

Fig. 1 shows a mid-sagittal reconstruction of a PCK kidney (treated with tolvaptan) affected by cysts in the entire length.

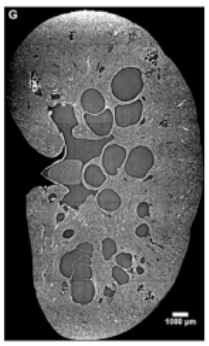

Image analysis suggests that large cysts originate from the fusion of neighboring smaller cysts.

The main aim of this study is to evaluate by X-ray microtomography the therapeutic effect on renal cyst growth of tolvaptan combined with calcimimetics, allosteric CaSR activators, which have been proposed as possible therapeutic targets[5,7].

Our results indicate that X-ray microtomography could provide novel information regarding the structure and distribution of the cyst in PKD and the effects of a therapeutic intervention.

This aim is to perform an ultrastructural analysis of the therapeutic effects of the proposed treatment using high-resolution X-ray microtomography, determining three-dimensional (3D) structures of renal cysts at micrometer to submicrometer resolution, along with conventional histochemistry.

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P2.6

Spectral micro-CT for simultaneous gold and iodine detection, and multi-material identification

P. Perion[1,2*], L. Brombal[1,2], R.H. Menk[2,3,4], F. Arfelli[1,2]

[1]*University of Trieste, Department of Physics, Via A. Valerio 2, Trieste, Italy*
[2]*Istituto Nazionale di Fisica Nucleare, Division of Trieste, Via A. Valerio 2, Trieste, Italy*
[3]*Elettra-Sincrotrone Trieste, S.C.p.A., S.S. 14-km 163.5 in AREA Science Park, Basovizza, Trieste, Italy*
[4]*Department of Computer and Electrical Engineering, Mid Sweden University, Holmgatan 10, Sundsvall, Sweden.*
*Corresponding author: paola.perion@phd.units.it

Multiple energy bin spectral micro-CT (μCT) is an advanced imaging technique that allows multi-material decomposition according to their specific absorption patterns at a sub-100 μm scale. Typically, iodine is the preferred CT contrast agent for cardiovascular imaging, while gold nanoparticles (GNPs) have gained attention in recent years owing to their high absorption properties, biocompatibility and ability to target tumors [1].

In this presentation, we demonstrate the potential for multi-material decomposition through spectral μCT imaging of a test sample at the PEPI lab of INFN Trieste [2]. The sample, consisting of gold, iodine, calcium, and water, was imaged using a Pixirad1/PixieIII chromatic detector [3] with multiple energy thresholds and a wide spectrum (100 kV) produced by a micro-focus X-ray tube. The results demonstrate the simultaneous detection and separation of the four materials at a spatial scale of 35 μm, suggesting the potential of this technique in improving material detectability and quantification in a range of pre-clinical applications, including cardiovascular and oncologic imaging.

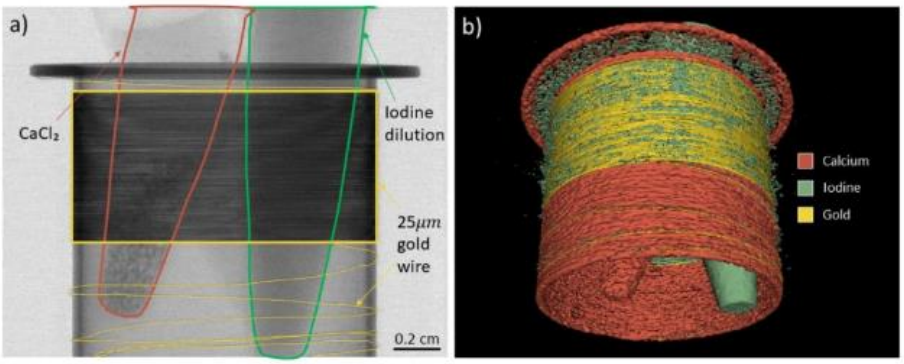

Figure 1 a) Projection image of the sample with its main components. b) 3D rendering of the decomposition of calcium, iodine and gold (water is not shown for the sake of clarity).

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P2.7

Virtual Histology of Human Brain tissue using Phase-Contrast X-ray Microtomography

JY. Lee[1,2*], A. Mack[3], U. Mattheus[3], S. Donato[4,5], R. Longo[5,6], G. Tromba[7], E. Longo[7], L. D'Amico[6,7], S. Mueller[2], J. Bause[2], T. Shiozawa[3], K. Scheffler[2,8], GE. Hagberg[2,8]

[1]*Graduate Training Centre of Neuroscience, University of Tübingen, Germany*
[2]*Max Planck Institute for Biological Cybernetics, Tübingen, Germany*
[3]*Institute of Clinical Anatomy and Cell Analysis, University of Tübingen, Germany*
[4]*Department of Physics and STAR-LAB, University of Calabria, Italy*
[5] *Istituto Nazionale di Fisica Nucleare (INFN), Italy*
[6] *Department of Physics, University of Trieste, Italy*
[7]*Elettra Sincrotrone Trieste, Italy,*
[8]*Department of Biomedical Magnetic Resonance, University Hospital Tübingen, Germany*
*Corresponding author: ju.young.lee@tuebingen.mpg.de

Imaging unstained soft tissue with X-rays is challenging due to its low X-ray absorption rate. However, phase contrast microtomography (PC-CT) using coherent synchrotron light yields unique contrast for microstructures within the tissue. Here, we present an overview of the biological features that can be identified from PC-CT of post mortem human brain tissue. We acquired PC-CT images with 1 - 5 micron voxel size from formalin-fixed paraffin-embedded samples from the human brain stem, motor cortex and somatosensory cortex.

Our results show that blood vessels [1], fiber tracts and large neurons could be identified. Additionally, we could detect microstructures such as neuromelanin and corpora amylacea. Feature extraction algorithms such as edge detection or thresholding are useful for segmentation and allow quantification of density and size of the structures. Since PC-CT measurements are non-destructive, complementary analysis with histological methods can be followed up, allowing for validation and further investigation of molecular properties. We see great potential for PC-CT in investigating the microstructure of label-free human brain tissue.

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P2.8

Comparison of novel reconstruction algorithms for low-dose breast computed tomography with synchrotron radiation

S. Donato[1,*], B. Arhatari[2], P.C. Brennan[3], L. Brombal[4], B. Golosio[5], S. Lewis[3], D. Lockie[6], H.M. Quiney[7], S.T. Taba[3], T.E. Gureyev[7]

[1]*University of Calabria, STAR-LAB and INFN, Rende, Italy;*
[2]*Australian Synchrotron, ANSTO, Melbourne, Australia;* arhatarb@ansto.gov.au
[3]*University of Sydney, Sydney, Australia;* amir.tavakoli@sydney.edu.au, patrick.brennan@sydney.edu.au, sarah.lewis@sydney.edu.au
[4]*University of Trieste and INFN, Trieste, Italy;* luca.brombal@ts.infn.it
[5]*University of Cagliari and INFN, Trieste, Italy;* golosio@unica.it
[6]*Maroondah BreastScreen, Eastern Health, Melbourne, Australia;* lockie.darren@gmail.com
7 University of Melbourne, Melbourne, Australia; quiney@unimelb.edu.au, timur.gureyev@unimelb.edu.au
* sandro.donato@fis.unical.it

Breast cancer is the leading cause of cancer deaths for women worldwide. 2D mammography is the screening technique in most countries, however, it still generates high rates of both false positives and false negatives. Recently, breast computed tomography (bCT), a fully 3D technique, is emerging as a new technique for improving early detection of breast cancer. One of the challenges for this technique is to combine the need for high spatial resolution and soft tissue contrast with a low-dose CT data acquisition. While clinical bCT systems rely only on the absorption properties of the sample, phase contrast (PhC) imaging improves the visibility of low-contrast features by utilising X-ray refraction. Synchrotron-based monochromatic PhC bCT has been shown to outperform currently clinically available bCTs, providing higher spatial resolution and signal-to-noise ratio, at the same radiation dose [1]. At Elettra Synchrotron (Trieste, Italy) and the ANSTO Australian Synchrotron (Melbourne, Australia), research towards clinical application of PhC bCT is ongoing [2]. In this context of PhC bCT, the present study aims at comparing two novel CT reconstruction algorithms, namely the unified fast reconstruction (UTR) [3] and a customized simultaneous algebraic reconstruction algorithm (cSART) [4], by using objective metrics such as contrast-to-noise ratio (CNR) and spatial resolution. Ten fresh breast mastectomy samples and two QRM phantoms were scanned at the Imaging and Medical beamline of ANSTO in propagation-based PhC configuration at a mean glandular dose (MGD) of 2 mGy (4 mGy for the phantoms) and 32 keV energy, using two flat panel detectors (Hamamatsu C10900D and Xineos-3030HR) with 100 µm pixels. Our results demonstrate that, compared to conventional filtered-back-projection reconstruction, UTR and cSART can yield up to 1.5 times higher CNR while preserving spatial resolution. Moreover, given their inherent flexibility, UTR and cSART can be tuned to privilege either CNR or spatial resolution.

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P2.9

Spectral micro-CT of osteochondral samples with iodine cationic contrast agent

Simone Fantoni[1,2], Paolo Cardarelli[3]*, Angelo Taibi[3,4], Francesco Brun[5,6], Renata Longo[6,7], Fulvia Arfelli[6,7], Fabio Baruffaldi[2], Virginia Cristofori[8], Claudio Trapella[8], Luca Brombal[6,7]

1. Department of Industrial Engineering, Alma Mater Studiorum, University of Bologna, 40136, Italy
2. Medical Technology Laboratory, IRCCS Istituto Ortopedico Rizzoli, 40136 Bologna, Italy
3. Istituto Nazionale di Fisica Nucleare (INFN), Division of Ferrara, 44122 Ferrara, Italy
4. Department of Physics and Earth Sciences, University of Ferrara, 44121 Ferrara, Italy
5. Department of Engineering and Architecture, University of Trieste, 34127 Trieste, Italy
6. Istituto Nazionale di Fisica Nucleare (INFN), Division of Trieste, 34127 Trieste, Italy
7. Department of Physics, University of Trieste, 34127 Trieste
8. Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy
** Corresponding author, cardarelli@fe.infn.it*

Micro computed tomography (µCT) is the gold standard for non-destructive 3D imaging of samples in the centimetre scale. Despite its ability to achieve micrometer-level spatial resolution, conventional µCT has limited effectiveness in revealing intricate details of biological samples due to the subtle attenuation differences present in soft tissues. To overcome this limitation contrast-enhanced µCT (CEµCT) has been introduced [1]. This technique relies on the use of highly absorbing contrast media which selectively fill structures or bond to compounds of interest, thus enhancing their visibility. However, tissue discrimination is often not optimal since a contrast-medium-filled region might not be distinguishable from a contiguous naturally highly absorbing detail (*e.g.*, bone). The availability of small-pixel spectral detectors equipped with multiple energy thresholds has made it possible the development of spectral µCT (SµCT) systems. These detectors enable the acquisition of two (or more) images simultaneously, each corresponding to a specific X-ray energy interval. Such images, obtained at different X-ray energies, can be employed as input for a spectral-decomposition algorithm, allowing the generation of 3D density maps for selected basis materials (such as water/iodine). If the contrast medium possesses a suitable K-edge energy, the detector energy threshold can be adjusted to be the same of the K-edge, thereby improving discrimination capabilities through material-decomposition. This approach overcomes the inherent lack of specificity in CEµCT and enables both quantitative assessment of contrast media concentration and the creation of virtual non-contrast images. In this contribution we present SµCT results obtained by using osteochondral bovine samples perfused with a cationic iodine-based contrast medium (CA4+), having a selective affinity with negatively-charged glycosaminoglycans (GAGs) in cartilage due to electrostatic attraction [2,3]. Images are acquired with a novel multimodal X-ray imaging system [4], integrating a CdTe spectral detector (Pixirad-PixieIII) with a pixel size of 62 × 62 µm^2 over a matrix of 512 × 402 pixels (32 × 25 mm^2). Pixirad features two energy thresholds and a charge-sharing compensation mode [5,6]. The reconstructed images demonstrate a well-defined separation between the iodine-perfused cartilage and the underlying trabecular bone structure without requiring any manual segmentation. In addition, they allow to quantify the contrast medium concentration, reflecting the GAGs gradient naturally found across the cartilage, which can be considered as indicator of the health state of the tissue. Reconstructed images were compared with CEµCT data recorded with a commercial scanner based on conventional integration detector (SkyScan 1072, SkyScan, Aartselaar, Belgium), by using similar X-ray tube parameters and exposure. The SµCT images demonstrate quantitative material discrimination capabilities and comparable spatial resolution.

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P2.10

Virtual histology of human cerebral amyloid angiopathy

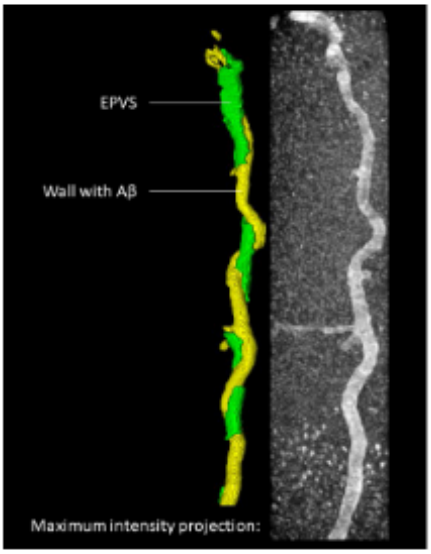
M. Chourrout[1], D. Meyronet[2], E. Brun[2], F. Chauveau[1]*

[1]*Univ. Lyon 1, Lyon Neuroscience Research Center, CNRS, INSERM, Lyon, France*
[2]*Hospices Civils de Lyon, Lyon, France*
[3]*Synchrotron radiation for Biomedicine (STROBE), Saint Martin d'Hères, France*

*Corresponding author: chauveau@cermep.fr

Cerebral amyloid angiopathy (CAA) is characterized by amyloid-β (Aβ) deposits in and around the walls of blood vessels. CAA diagnosis requires postmortem confirmation by immuno-histochemistry. Topology is one of the main diagnosis criteria [1,2], but its assessment in 2D is limited. Thus, phase-contrast tomography (XPCT) could improve diagnosis with morphometric data.

The tissue bank of Hospices Civils de Lyon (Cardiobiotec, CRB-HCL) provided a cohort of 8 deceased patients presenting different stages of CAA. Fresh-frozen 1-cm^3 brain samples from frontal cortex and cerebellum were fixed, dehydrated and imaged at high resolution (3.09 µm) using XPCT (SOLEIL, ANATOMIX, proposal 20220319). For image processing, a watershed-based segmentation was performed within Amira-Avizo (Thermo Scientific). 3D measures — such as tortuosity or wall thickness — can be obtained from the segmentation with ImageJ.



From the segmentation of the deposits in a few large vessels (mean inner diameter >10 µm), we could determine the spread of the disease on a vessel-basis and on a sample/patient basis. Figure 1 shows the final segmentation from a patient diagnosed with severe CAA; enlarged perivascular spaces (EPVS), shown in green, are a commonly associated hallmark.

For the first time, XPCT has been tested for its ability to yield diagnostic classification of CAA. Aβ deposits in the vessels can be characterized by additional morphometric parameters.

Figure 1: Multi-class segmentation of the vessel (colored).
Maximum intensity projection of the image (gray).

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P2.11

DAPHNE4NFDI: DAta from PHoton and Neutron Experiments - the synchrotron imaging use case

Hafiz Muhammad Fahad[1], Martin Rädler[1], Anton Barty[2], Bridget Murphy[3], Astrid Schneidewind[4], Sebastian Busch[5], Jan-Dierk Grunwaldt[6], Christian Gutt[7], Wiebke Lohstroh[8], Frank Schreiber[9], Tobias Unruh[10], Paola Coan[1].

[1] Ludwig Maximilians University, Munich, [2] DESY, Hamburg; [3] Christian-Albrechts-Universität zu Kiel, Kiel; [4] Forschungszentrum Jülich, Jülich; [5] Helmholtz-Zentrum Hereon, Geesthacht; [6] Karlsruhe Institute of Technology, Karlsruhe; [7] Universität Siegen, Siegen; [8] Technische Universität München, Munich; [9] Eberhard Karls Universität Tübingen, Tübingen; [10] Friedrich-Alexander-Universität Erlangen-Nürnberg, Nuremberg

DAPHNE4NFDI is one of the twenty-six consortia of the National Research Data Infrastructure (NFDI), which are funded by the German Research Foundation (DFG). DAPHNE4NFDI focuses on research with photons and neutrons at large-scale research facilities and it aims at providing open access to research experimental data, to integrate user-oriented solutions and to leverage a comprehensive scientific infrastructure. The project is a partnership between 7 research institutions and 11 universities from different scientific disciplines and other international partners - including DESY, LMU and ESRF. The management of research data and the electronic recording of all relevant parameters during scientific experiments are key challenges for the sustainability of research data at synchrotron facilities, where numerous scientific experiments in the field of condensed matter research are performed every year in collaboration with external research groups.

Over the past decades, the application of synchrotron X-rays has revolutionized biomedical research. Technological advances in phase-contrast X-ray computed tomography, both with and without the use of contrast agents, have ushered in an era of non-invasive, three-dimensional visualization and navigation through tissue structures. This ground-breaking capability allows researchers to study tissue changes resulting from pathology and various treatments at the micro- to nano-scale. This applies to a wide range of specimens, from whole organs to subcellular structures, in both human and animal subjects. This innovative approach, often referred to as 3D 'virtual X-ray histology', has attracted considerable interest and acceptance. As a result, it generates a significant amount of data up to several petabytes per year. Effective management of such a substantial data influx requires tailored solutions for electronic data capture, coupled with robust data management and storage capabilities, as well as for the repository of processed (reduced) data and analysis code to go with each publication in order to maximise data reuse and transparency.

Within DAPHNE4NFDI, our LMU team represents the Bio-imaging & computed tomography synchrotron user community and is actively involved as a discussion partner, tester and early user.

P2.12

A fully automated deep learning algorithm to derive micro-CT imaging biomarkers describing lung fibrosis progression and response to therapy in mice.

Davide Buseghin[1,2], Erica Ferrini[3], Martina Buccardi[4] Elena Vincenzi[5], Andrea Grandi[6], Francesca Pennati[1], Andrea Aliverti[1], Franco Fabio Stellari[6]

[1] Department of Elettronica, Informazione e Bioingegneria, Politecnico di Milano, Milano, Italy, [2] ANTEHM, Spoke 3, Italy; [3] Department of Veterinary Science, University of Parma, Italy; [4] Department of Mathematical, Physical and Computer Sciences, University of Parma, Italy; [5] Department of Computer Science, Bioengineering, Robotics and Systems Engineering, University of Genoa, Genoa, Italy;[6] Chiesi Farmaceutici, S.p.A., Corporate Pre-Clinical Research and Development, Parma, Italy.

Micro-CT (μCT) imaging enables longitudinal studies in lung fibrosis mouse models highlighting parenchymal changes[1]. In this study a DL-model based on U-Net architecture[2] was used to automatically segment the whole lung, right and left lobes to segment severe fibrotic areas that results as dense as surrounding tissue and normally required manual segmentation.

C57bl/6 mice were treated twice with BLM or saline (Sal) at day 0 and 4, then Nint group was treated daily with Nintedanib. All mice underwent μCT imaging longitudinally at 7, 14 and 21 days and end-inspiration (P01) and end-expiration (P02) datasets were generated from each scan. The aeration compartments [3] and functional parameters were derived and normalized on Sal mean values, except for the %non-aerated tissue. Histological endpoints were measured on whole lung, LL and RL and correlated to μCT results.

BLM administration provoked an acute pulmonary inflammation which resulted in a marked increase of both total volume and %hypo-aerated tissue at day 7. The non-aerated tissue progressed from 7 to 21 days mostly in the apical of the lung. Several parameters showed that the LL was more fibrotic than the RL one. Interestingly, the FRC tended to increase at day 21 both in the LL and RL but not in the whole lung, revealing compensatory effects in the caudal portion of lung.

Nint group exhibited a significant anti-fibrotic effect by reducing the non-aerated tissue and preventing the lung function decline. μCT biomarkers showed an overall tendency to slow down fibrosis progression up to 21 days and histological analysis fully corroborated μCT results.

We successfully applied a fully automated DL-based algorithm to μCT imaging for the assessment of lung fibrosis progression and response to therapy. μCT data derived from the whole lung, LL and RL accurately showed regional changes in lung morphology during fibrosis evolution associated with lung function decline which could reveal diverse mechanisms of action for putative drugs, supporting their translation to clinic.

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P2.13

Brain connectivity and microstructure in COVID-19 patients with olfactory or cognitive disorder

Alberto Arrigoni[1,2*], Mattia Previtali[1], Sara Bosticardo[3], Giulio Pezzetti[4], Sofia Poloni[1], Serena Capelli[1], Angela Napolitano[4], Andrea Remuzzi[5], Ferdinando Luca Lorini[4], Maria Sessa[4], Alessandro Daducci[4], Anna Caroli[1], Simonetta Gerevini[4]

[1]*Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo, Italy*
[2]*Politecnico di Milano, Milano, Italy*
[3]*University of Verona, Verona, Italy*
[4]*ASST Papa Giovanni XXIII, Bergamo, Italy*
[5]*University of Bergamo, Bergamo, Italy*
*Corresponding author: alberto.arrigoni@marionegri.it

The COVID-19 pandemic has affected millions worldwide, causing mortality and multi-organ morbidity. Neurological complications have been recognized [1]. This study aimed to assess brain structural, microstructural, and connectivity alterations in COVID-19 patients with olfactory or cognitive impairment using multi-directional diffusion-weighted MRI (DW-MRI).

The study included 16 COVID-19 patients with cognitive and memory deficits (COVID-CM), 35 COVID-19 patients with olfaction disorder (COVID-OD), and 14 controls. A state-of-the-art processing pipeline for DW-MRI pre-processing, mean diffusivity and fractional anisotropy computation, and white-matter fibers' tractography was developed for the study. Brain parcellation required for assessing network connectivity and region-specific microstructure was based on a T1-weighted scan and pertinent anatomical atlases.

Compared to controls, COVID-CM patients showed overall gray matter atrophy, and both COVID-19 patient groups showed regional atrophy and cortical thinning. Both groups showed a significant increase in gray matter mean diffusivity, and COVID-CM patients also showed an overall increase in white matter diffusivity and a decrease in white matter anisotropy. Graph-based analysis revealed reduced network modularity, with an extensive pattern of connectivity increase, in conjunction with a localized reduction in a few connections, mainly located in the left hemisphere. The left cingulate, anterior cingulate, and insula were primarily involved in both patient groups.

In line with previous findings [2], this study showed significant alterations in brain morphology, microstructure, and connectivity in COVID-19 patients with olfactory dysfunction or cognitive and memory deficits. These findings suggest the presence of underlying neurodegeneration and neuroinflammation, as well as compensatory mechanisms at play.

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