MEDAMI 2024 - Inflammation and Infection Imaging

Friday, 24 May 2024 - Sunday, 26 May 2024

Book of Abstracts

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The XEMIS2 camera installation progress at the Nantes University Hospital

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The XEMIS project aims to demonstrate the feasibility of a low-radioactivity medical imaging system. Its primary objective is to significantly reduce the amount of conventional injected activity, by a factor of 100, for imaging small animals. This breakthrough is envisioned within the realm of three gamma imaging and liquid xenon Compton telescope technologies. The presentation will provide an overview of the XEMIS project and the principles behind three gamma image reconstruction. Additionally, it will highlight progress on the installation of the XEMIS2 camera prototype at Nantes University Hospital in France, focusing on developments in detector mechanics, data acquisition electronics, and calibration
processes.

Can AI/ML/Deep Learning contribute to Molecular Imaging of Inflammation and Infection? / 4

Challenges in AI applied to medical image analysis in COVID-19 infection

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In recent years, the intersection of Artificial Intelligence (AI) and medical imaging has significantly advanced our capabilities in analyzing and understanding complex health issues. However, the lack of fully explainable and trustworthy AI systems still represents a big limitation in the effective deployment of AI tools in the clinical setting. The role of AI in enhancing image analysis for the detection and characterization of COVID-19 infection was explored, identifying three main challenges related to explainability and trustworthiness: the difficulty in explaining the deep model decision,

the difficulty in providing a clinically meaningful explanation, and the robustness issues that impede the full trustworthiness. Three different applications focused on the COVID-19 use case were developed and, in each application, a possible solution to each of these three main challenges was investigated. A fully automatic Deep Learning (DL) pipeline has been developed to predict the degree of severity of patients from chest X-rays and associated clinical data, exploring the possibility of explaining the prediction by using a visualization technique. A DL-based quantification software for the characterization of COVID-19 infection visible in Computed Tomography (CT) images was set up to produce quantitative indices representing qualitative characteristics immediately understandable to radiologists. It was validated in a multicenter study. Finally, a Machine Learning pipeline was developed for the prediction of the patient's severity grade from the radiomic features extracted from CT images. Particular attention was paid to the possibility of harmonizing data, also through a study based on CT acquisitions of a phantom. In each application, a trade-off between a good prediction/quantification performance and an improvement in the explainability (XAI) and reliability of the developed AI model was reached. In conclusion, AI-based methodologies were investigated involving other relevant phases beyond modeling, such as data preprocessing and post-processing of results using XAI approaches of medical relevance.

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Specific/upcoming tracers for fungal infection

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Invasive fungal infections such as aspergillosis are life-threatening diseases mainly affecting a growing number of immuno-compromised patients. Early diagnosis is crucial, but conventional imaging modalities such as CT or MRI lack specificity and sensitivity. Molecular imaging, especially using Positron Emission Tomography (PET) holds the potential to specifically target fungal infections thereby overcoming limitations of current diagnostic approaches. Whereas currently only indirect effects of infections can be detected e.g. by the increased glucose metabolism using 18F-FDG, only targeting the fungus itself would achieve the required specificity. Over the past decade a multitude of such directly targeting radiotracers have been developed and tested for their ability to serve as fungal specific imaging agents. These include antibody constructs and peptides targeting the fungal cell wall, radiolabelled sugars, antifungal drugs or siderophores targeting the specific iron metabolism of fungi. In this talk an overview of these developments will be given, their status towards clinical translation reviewed and potential pro and cons being discussed. Overall, these developments hold a great potential to change the diagnostic approach to allow early and specific detection of invasive fungal diseases.

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[68Ga]Ga-deferoxamine for bacterial infection imaging –pharmaceutical development and first in human data

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Early and accurate diagnosis of infections could improve patient outcome and optimize treatement. Deferoxamine (DFO B), a drug used for iron detoxification, a siderophore, that can be utilized by bacterial and fungal species for iron acquisition, can be labelled with Ga-68 and has proven to enable imaging of bacterial and fungal infections in animal models. Here we report on the pharmaceutical preparation development of [68Ga]Ga-deferoxamine and first results of a clinical Phase I/IIa trial to establish safety, pharmacokinetics and imaging properties in bacterial infections (EudraCT: 2020-002868-31).
An automated synthesis for preparation of [68Ga]Ga-deferoxamine was established on two different synthesis modules (Modular-Lab PharmTracer and GRP 3V module). Radiolabelling of 100 µg deferoxamine in acetate buffer with cartridge purification and sterile filtration was included and quality control methods validated for clinical trial approval. So far 3 patients with infected joint prosthesis were enrolled in the clinical trial. PET imaging immediately 30min 1 and 3 h post injection was performed, measuring activity in blood and urine and HPLC-analysis of blood and urine metabolites.
Sufficient activity yield for patient studies was achieved with both modules using a single 68Ge/68Ga generator. Quality control met all pre-defined specifications with >95% radiochemical purity. In patients no sign of metabolic degradation was seen in blood, with a moderate rate of blood elimination, in urine 30-50% metabolites were detected. Serial PET imaging revealed rapid and stable accumulation in the infected area from 30-180min in 2 patients, corresponding with previous positivity in [18F]-FDG scan. Calculated effective radiation dose was <0.01mSv/MBq.
Pharmaceutical preparation of deferoxamine with Ga-68 can easily be performed using standard automated synthesis approaches, enabling cost-efficient and reproducible in-house production for patient use. Initial results in patients show slow pharmacokinetics, but still visualisation of infected areas More patient studies are needed to establish the clinical potential of [68Ga]Ga-deferoxamine.

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Opening New Possibilities for Inflammation and Infection Research using Dual-Tracer PET Imaging

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Background:
Dual-tracer PET imaging exhibits substantial potential for enhancing localization of infections and assessment of inflammation-related metabolic changes over mono-tracer PET. Recently, it has been demonstrated that in vivo imaging of inflammation using 89Zr labelled antibodies has a higher selectivity index compared with the commonly used tracer [18F]FDG, positioning it as a strategic tool for investigating inflammatory processes. Furthermore, the combination of 89Zr and [15O]H2O or [18F]FDG tracer pairs in one study can provide complementary information on perfusion or metabolism, enriching the information available for clinical application. Due to the complexity of conducting simultaneous dual tracer imaging in the clinic, we have developed a simulation framework tailored to create dynamic dual-tracer images from single-tracer data, thereby facilitating the evaluation of performing simultaneous dual-tracer PET imaging in a reasonable clinical context.
Methods:
Three representative ROIs—white matter, grey matter, and skull—were derived from [15O]H2O, [89Zr]atezolizumab, and [18F]FDG patient scans and integrated into the BrainWeb phantom, with a notable hot tumour identified on the skull from [89Zr]atezolizumab. An automatic simulation pipeline was set-up: modelling and extracting kinetic parameters from patient data, assigning the recovered time activity curve to the digital phantom and then performing the analytical simulation. The PET system was modelled based on a Siemens Biograph Vision 600 PET/CT scanner, and simulated projections were reconstructed (4 iterations, 5 subsets, with time-of-flight) using Software for Tomographic Image Reconstruction (STIR). Attenuation correction, normalisation calibration, randoms, scatter and Poisson noise were also included.

Results:
Figure displays a representative slice from each reconstructed dynamic images: A, B, C showcase combinations of dual-tracer pairs ([18F]FDG, [15O]H2O, and [89Zr]atezolizumab), while D, E, F correspond to mono-tracer images. The completion of this automated simulation pipeline enables the execution of simulation studies under clinically realistic conditions. Additionally, the inclusion of other tracers (e.g. [68Ga]Ga-FAPI) may be explored in future developments.

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Comparison between [18F]FDG-PET/CT and 99mTc-HMPAO-labeled leukocyte SPECT/CT imaging in a case series patients with suspicious of vascular prosthesis infection: to trust is good but to check it out is better

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Infection represents one of the most frequent causes of morbidity and mortality in patients with vascular prostheses. Prosthetic vascular graft infection (VPGI) can lead to severe and/or fatal outcomes if not early diagnosed. The Management of Aortic Graft infection Collaboration (MAGIC) criteria are used for the VPGI diagnosis. [18F]-FDG-PET/CT and radiolabeled white blood cells (WBC) scintigraphy can improve the radiologic diagnostic accuracy in PVGI. Nuclear medicine procedures are included in MAGIC criteria as minor criteria. The aim of this study is to compare [18F]-FDG-PET/CT and radiolabeled white blood cells scintigraphy in patients with PVGI. We retrospective evaluated 6 patients with suspected VPGI who underwent CT-angiography and both [18F]-FDG-PET/CT and WBC scintigraphy. According to MAGIC criteria 3 patients were classified as 'suspected infection' and 2 patients as 'confirmed infection'. Only in the patients with 'confirmed infection' both [18F]-FDG-PET/CT and WBC scintigraphy yield concordant results (both positive results) while in patients with 'suspected infection' [18F]-FDG-PET/CT was positive in 5 studies (false positive) and WBC scintigraphy was negative in all patients (true negative). We can state that, although [18F]FDG-PET/CT has a very high sensitivity, WBC scintigraphy, integrating planar with SPECT/CT images to allow better anatomical localization of findings, shows greater specificity, proving to be essential in the management of patients with vascular prosthesis infection, especially in the case of persistence of pathologic uptake of [18F]FDG despite the good clinical response to antibiotic therapy. Even if [18F]FDG-PET/CT is a valid nuclear medicine technique, especially due to its high negative predictive value, we always should pay attention to the possible false positive results due to non-specific causes of FDG uptake. The high diagnostic accuracy of WBC scintigraphy, to be confirmed in further studies with a large number of patients, should be considered as a possible major criterion for the diagnosis of VPGI.

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Specific/upcoming tracers for bacterial infection

Author: Milos Petrik[None]

Co-authors: Clemens Decristoforo ; Hubertus Haas

Despite the success of antibiotics, bacterial infections remain a serious global healthcare problem. The rise of highly virulent and multi-drug-resistant pathogens and continued life-threatening nosocomial infections in hospitals pose a major challenge to healthcare worldwide. Early and accurate diagnosis of infection is essential for effective treatment of patients and prevention of pathological complications. Currently, a number of diagnostic tests and methods are used in clinical practice. However, most of these methods lack specificity and/or sensitivity. The availability of a rapid and reliable tool for the diagnosis of bacterial infections represents a major unmet need, especially in the management of critically ill patients. As molecular imaging is already commonly used in clinical practice, it could become a valuable tool for clinical trials, patient care and precision medicine of infections. This talk will provide an overview of developments in tracers for imaging bacterial infections.

Contributed talks / 11

Comparison between three-phase bone scan and 99mTc-HMPAO-labelled white blood cell scintigraphy in patients with suspicious of hip or knee prosthetic infected loosening

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Prosthetic joint infection (PJI) is one of the worst complications after primary implant and revision. The differential diagnosis between septic or aseptic loosening is sometimes very difficult especially in a low-grade infection. Three-phase bone scan with 99mTc-hydroxymethylene diphosphonate (3phase-BS) and 99mTc-Hexamethylpropylene amine oxime (HMPAO) white blood cell scintigraphy (WBC) are frequently used to evaluate patients (pts) with painful prosthesis. We retrospectively assessed their respective role in 92 pts (53 women, 39 men) with suspected late (>24 months) PJI (25 hip; 67 knee). All patients performed 3phase-BS and WBC within 2 weeks. The final diagnosis was based on microbiological culture after arthrocentesis or sampling during single-stage prosthesis explantation or by clinical follow-up for at least 12 months. 3phase-BS was positive in all pts. WBC was negative for PJI in 66 pts: no accumulation of WBC over time was seen in periprosthetic regions in 17/66 pts, a stable or decreasing accumulation of labeled white blood cell over time was seen in 49/66 pts; WBC was positive for PJI in 26 pts, showing a WBC accumulation increasing over time in prosthetic and/or periprosthetic regions. Our results showed that a positive 3phase-BS does not allow to make a certain diagnosis. 66/92 pts without infection showed, in fact, inflammation/infection signs at 3phase-BS (false positive results) and negative findings at WBC (true negative results). In conclusion, positive 3phase-BS can often mislead for a correct diagnosis and needs always to further investigation to reach the differential diagnosis between septic and aseptic loosening of PJ. WBC showed very high diagnostic accuracy allowing to identify the presence or absence of infection. WBC confirmed its important role in the diagnostic algorithm of prosthetic joint infections.

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[18F]FDG-PET/CT and 99mTc-HMPAO-labeled leukocytes SPECT/CT imaging in a case series patients with possible infective endocarditis: which and when to use them

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Infective endocarditis (IE) is associated with high morbidity and mortality rates, often associated with local complications or distant embolization. The appropriate antibiotic therapy significantly reduces the risk of embolic complications. The prompt diagnosis is crucial to establish adequate therapy. The Duke criteria, based on clinical, biological/microbiological, and imaging parameters, are currently employed to diagnose IE, classifying the diagnosis of IE as definite, possible, or rejected. Nuclear medicine procedures, such as 2-deoxy-2-[fluorine-18]fluoro-D-glucose Positron Emission Tomography/Computed Tomography ([18F]FDG-PET/CT) and radiolabeled white blood cells (WBC) scintigraphy, are included in Duke major criteria. This study aims to compare [18F]FDG-PET/CT and WBC scintigraphy in patients with valve prostheses and possible IE to understand which and when to perform them. We retrospectively evaluated 7 patients with possible IE according to Duke's criteria. All patients underwent [18F]FDG-PET/CT and WBC scans within 10 days. [18F]FDG-PET/CT was positive in all patients showing high focal uptake of FDG (SUVmax > 4.5) on the prosthetic valve. WBC scintigraphy was negative in all patients showing no uptake or mild and decreasing accumulation of labeled leukocytes on heart prosthetic valve. Final diagnosis, based on 12 months of clinical follow-up, was negative for IE in all patients.
Our study showed 7 false positives [18F]FDG-PET/CT results and 7 true negative WBC scintigraphies results. WBC scintigraphy avoids unnecessary long antibiotic therapy. Our findings, even based on a small number of patients, suggest to perform [18F]FDG-PET/CT only in patients with a very low probability of IE, the high negative predictive value of [18F]FDG-PET/CT allows in fact to rule out the presence of IE. In patients with possible IE our data suggest to perform WBC scintigraphy. The high specificity of WBC scintigraphy allows to differentiate the non-specific [18F]FDG uptake due to aseptic condition from the specific FDG uptake due to infection.

Introduction to the Symposium

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Introduction: from an infectiologist's point of view

Introduction: from an internal medicine (inflammation) point of view

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SPECT imaging for infection/inflammation: State-of-Art, Challenges and Next Frontiers

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FDG-PET/CT in inflammatory disorders : State-of-Art, Challenges and Next Frontiers

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FDG PET/CT in infectious disorders : State-of-Art, Challenges and Next Frontiers

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Neuro inflammation - long Covid etc.

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Molecular imaging of Inflammation and Infection in Research and clinical practice – status and Next Frontiers / 20

Nuclear Imaging (eg. immune cell imaging)

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Advances in multimodality imaging to increase our understanding of the inflammation's role in healthy and diseased tissue / 21

MRI (eg magnetic nanoparticles)

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Fluorescence microscopy

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TSPO (18F-VC701) PET imaging in neuroinflammation for Parkinson disease

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The promise of PET/MRI in imaging the inflammatory contributions to heart-and-brain degeneration

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Applications of TB PET in infection/inflammation

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Advantages and applications of TB SPECT CZT in infection/inflammation

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What is parametric imaging and what are its advantages? alo include the role pf PET/CT

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Overview of AI/ML/Deep Learning: Physicist's view

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Overview of AI/ML/Deep Learning: Physician's view

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Today's available radiotracers

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Specific/upcoming tracers for viral infection

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FAPI

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ETSI

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Point of view of IAEA

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Round table

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Advances in multimodality imaging to increase our understanding of the inflammation's role in healthy and diseased tissue / **48**

Advances in Inflammation Imaging: Optical Techniques in Mesoscopic and Macroscopic Regimes

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This presentation will highlight recent developments in imaging inflammation using advanced optical methods across macroscopic and microscopic scales. We will delve into hyperspectral imaging (HSI), which captures spatial and spectral data concurrently, and its application in various inflammatory conditions, including rheumatoid, psoriatic, and osteoarthritis, as well as graft-versus-host disease and multiple infections. Additionally, we will explore optical coherence tomography (OCT), akin to ultrasound in detecting backscattered light, utilized in imaging uveitis and inflammations in soft tissue, bladder, and coronary regions. The talk will also cover photoacoustic tomography (PAT), employing laser-induced acoustic signals for detecting inflammation in vascular systems, kidneys, joints, brain, and intestines. The synergy of combining techniques like HSI and OCT for enriched, complementary data will be emphasized, showcasing their potential to enhance diagnostic accuracy and treatment efficacy in medical physics.

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Inflammation Imaging with High Sensitivity Panel TOF PET Detectors

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Traditional PET scanners, with their full-ring design, have been invaluable in clinical diagnosis and research. However, it is evident that the ring geometry, with its relatively large radius, cannot always be the optimal choice for detector placement across all applications. Our interest lies in making PET systems flexible and modular, allowing their design to be tailored to both patient-specific needs and the specific objectives of the PET scan. Our previous work demonstrated that a simple 2-panel (30 x 30 cm) configuration can produce high-quality, distortion-free images suitable for practical applications, all while using significantly less detector material compared to conventional PET scanners. This work focuses on the modular aspect of panel detectors and the anticipated performance of 2 flat-panel detectors of size 120 x 60 cm based on 3 x 3 x 20 mm L(Y)SO crystals. A Monte Carlo study using GATE software and large HPC clusters evaluates the systems' performance, featuring Time of Flight (TOF) resolution down to 70 ps and Depth of Interaction (DOI) resolution down to 1.25 mm. Various phantoms (NEMA, XCAT, Derenzo) were used for performance evaluation, with the Siemens Biograph Vision PET/CT scanner serving as a reference. Transitioning to larger panels increases the Noise Equivalent Count Rate (NECR) by about a factor of 12. We demonstrate that panel detectors are modular, capable of producing images without distortion or artifacts, where excellent TOF is essential, and enhanced DOI contributes to image sharpness. Flexibility is an important feature of panel detectors, and sensitivity can increase by over threefold when panels are shifted from a panel-panel distance of 80 cm to 40 cm. The enhanced sensitivity and cost-effectiveness of panel detectors could significantly improve total-body inflammation imaging. This method could enable accurate localization and detailed characterization of inflammatory processes with substantially lower radiation exposure.

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Advantages of Total Body PET imaging

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The recent introduction of long axial field-of-view (LAFOV) positron emission tomography (PET) offers substantially larger axial coverage of the body and a substantially higher system sensitivity comparing with conventional short axial field-of-view systems. This provides new opportunities for applying PET in clinical practice. Some examples are reduction of scan duration for example in intensive care unit patients; reduction of the amount of tracer administered to the patient, which is very important when imaging younger patients or pregnant women; longitudinal or delayed imaging for using short- and long-lived tracers; and applications of total body dynamic or parametric imaging. In addition to this, new emerging techniques, such as artificial intelligence and imaging

with multiple radiotracers could aid in a more general clinical application of LAFOV PET. The objective of this presentation is to highlight these opportunities especially for imaging infection and inflammation and to indicate future directions with LAFOV PET.

Technical challenges for imaging inflammation and infection / 51

Progress on the Development of the Emission Tomography Standardization Initiative (ETSI) Standard Format for List-Mode PET Raw Data (PETSIRD)

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The recent advancement of data science methods in emission tomography (ET) has highlighted the need for standardization in the access, use, and sharing of the unprocessed raw list-mode acquisition data to exploit their high fidelity spatio-temporal information before the production of the respective DICOM images. The Emission Tomography Standardization Initiative (ETSI) was founded in 2022 from an international consortium of academic and industry experts to define open, extendable, and vendor-agnostic ET data formats to facilitate: (i) inter-scanner data harmonization; (ii) building of large-scale raw data sharing repositories for the effective deployment of Artificial Intelligence models; and (iii) development of advanced data analysis and emission tomography imaging application methods.

ETSI is now focusing on the development of PETSIRD: an open standard format for Positron Emission Tomography (PET) list-mode raw data. The components of PETSIRD are (i) its data elements (coincidence events, geometry, correction factors, physiological signal etc.); (ii) a container of the data elements architecture and its access protocols built with Microsoft Research's YARDL metalanguage; and (iii) a use-cases software toolkit facilitating the basic utility of the standard. ETSI successfully conducted its first hackathon in November 2023 where a group of about 30 international participants from industry and academia worked together to produce a basic use-cases toolkit of an initial PETSIRD version to support: (i) gating and sub-sampling of PETSIRD data; (ii) conversion of simulated raw data from ROOT to the PETSIRD format and building of a PETSIRD demo dataset; (iii) implementation in existing open-source PET reconstruction tools of a basic PETSIRD interface; and (iv) independent open-source reconstruction of PET images from PETSIRD demo data.

PETSIRD format can introduce a paradigm shift in PET imaging by enabling the standardized open access to the wealth of unprocessed information inherently encapsulated in list-mode PET data to spark innovation and wider AI technology deployment.

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Role of multi-phase scintigraphy

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Euro-BioImaging ERIC: Open access imaging services enable cutting-edge research - an ISIDORe project evaluating COVID-19 effects with mouse brain imaging

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Euro-BioImaging ERIC is a European Research Infrastructure Consortium and an ESFRI Landmark that provides open access to imaging technologies, training, and data services in biological and biomedical imaging. Euro-BioImaging contributes to crucial societal challenges by actively participating in EU-funded projects, such as ISIDORe, to provide the scientific community with access to cutting-edge imaging services and expertise. ISIDORe, Integrated Services for Infectious Disease Outbreak Research, is a Horizon Europe project bringing together 154 service providers to advance research on epidemic-prone diseases.

Within ISIDORe, Euro-BioImaging contributed to an innovative project to create an automated mouse brain alignment tool. The tool was developed at the Euro-BioImaging Nodes in Finland (FiAM and Turku PET Centre) to understand better brain-related disorders that COVID-19 patients can experience - such as headaches, confusion, loss of smell and taste, seizures, and stroke. The study hypothesised that the virus may be able to reach the brain and cause a severe and abrupt infection. It was crucial to investigate the localised effects of COVID-19 using positron emission tomography (PET) imaging, which allows non-invasive whole-body imaging of metabolic processes, to comprehend better how the coronavirus functions, potentially prevent its actions and possibly treat the infection.

The COVID-19-related inflammatory processes were studied using PET imaging in a mouse model of COVID-19-induced brain damage. In addition to in vivo PET imaging, autoradiography studies were performed to study brain regions that are below the resolution limits of the PET. Usually, these analyses are performed manually, entailing long analysis times, inaccuracies, and high variability. In this case, a customised pipeline for analysis of autoradiographic images was developed to quantify the autoradiography images, greatly enhancing data analysis. This novel approach was made possible through a combination of the Euro-BioImaging user access services and funds from the ISIDORe project.

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Exploring Inflammatory Pathways: Optical Nanoscopy Reveals Cytokine-Induced β-Cell Stress Signatures

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β-cell failure in both Type-1 and Type-2 Diabetes is intricately linked to the inflammatory cascade mediated by pro-inflammatory cytokines. To analyze the molecular intricacies underlying cytokine-induced β-cell dysfunction, we employed advanced super-resolution optical microscopy techniques. Specifically, we utilized Expansion Microscopy (ExM), a groundbreaking method enabling nanoscale imaging of biological specimens without the need for expensive optical instruments. In this study,

we investigated the inflammatory impact of interleukin-1β (IL-1β) and interferon-γ (IFN-γ) on Insulinoma 1E (INS-1E) β-cells using ExM-based fluorescence super-resolution imaging. Our findings revealed profound alterations in β-cell morphology and subcellular organization following 24-hour exposure to IL-1β and IFN-γ. Notably, we observed an ˜80% increase in mitochondrial circularity, a ˜40% reduction in insulin granule density accompanied by mis-localization of the remaining granules, and the emergence of F-actin-positive membrane blebs. Additionally, we identified a previously unrecognized fragmentation of the microtubule network, with a ˜37% reduction in branch density. These observations provide unprecedented insights into the subcellular effects of pro-inflammatory cytokines on β-cell function, complementing existing molecular data. Our study establishes a novel optical microscopy framework for interpreting β-cell dysfunction and paves the way for future ex-vivo and in-vivo investigations aimed at unraveling the pathophysiology of Diabetes mellitus.

Can AI/ML/Deep Learning contribute to Molecular Imaging of Inflammation and Infection? / 55

Advancements in Parametric Imaging: Applications, Challenges, and Opportunities

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Parametric imaging is emerging as a powerful tool in medical imaging, offering a deeper understanding of physiological processes by quantifying parameters such as blood flow, metabolic rate, and perfusion. Despite its potential, its clinical application has been limited so far, primarily due to the extensive scan durations required. This presentation seeks to underscore the principles of parametric imaging, its applications specifically in the domain of infection and inflammation, while exploring its challenges, and opportunities that could redefine its clinical use in the future. In the last years, significant innovations have already begun, facilitating the clinical integration of parametric imaging. These include the availability of the long-axial field of view (LAFOV) systems, the recent approval of CE Marked tool for direct parametric imaging reconstruction, and advanced techniques for deriving both population-based and image-derived input functions (PBIF & IDIF)1. These advancements hold the promise of overcoming the primary obstacles of traditional parametric imaging by significantly cutting down scan times and enhancing quantification accuracy, although the issue of motion artifacts in short dynamic acquisition still remains a concern 2,3. Among its various applications, parametric imaging has demonstrated its efficacy in primarily facilitating the differentiation of inflammation from malignancies, traditionally using radiotracers like 18F-fluorodeoxyglucose (FDG), and now expanding with the exploration of additional tracers, including oxygen-15 labelled water ([15O]H2O)4–6. This specific capability to discern metabolic patterns characteristic of infection and inflammation has the potential to enhance the diagnostic precision and enable more informed treatment planning. In conclusion, with the expanding use of new tracers and the advent of new technologies, parametric imaging can stand poised to revolutionize clinical practice, enabling more accurate and personalized patient care.

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TO BE REMOVED: Progress on the Development of the Emission Tomography Standardization Initiative (ETSI) Standard Format for List-Mode PET Raw Data (PETSIRD)

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The recent advancement of data science methods in emission tomography (ET) has highlighted the need for standardization in the access, use, and sharing of the unprocessed raw list-mode acquisition data to exploit their high fidelity spatio-temporal information before the production of the respective DICOM images. The Emission Tomography Standardization Initiative (ETSI) was founded in 2022 from an international consortium of academic and industry experts to define open, extendable, and vendor-agnostic ET data formats to facilitate: (i) inter-scanner data harmonization; (ii) building of large-scale raw data sharing repositories for the effective deployment of Artificial Intelligence models; and (iii) development of advanced data analysis and emission tomography imaging application methods.

ETSI is now focusing on the development of PETSIRD: an open standard format for Positron Emission Tomography (PET) list-mode raw data. The components of PETSIRD are (i) its data elements (coincidence events, geometry, correction factors, physiological signal etc.); (ii) a container of the data elements architecture and its access protocols built with Microsoft Research's YARDL metalanguage; and (iii) a use-cases software toolkit facilitating the basic utility of the standard. ETSI successfully conducted its first hackathon in November 2023 where a group of about 30 international participants from industry and academia worked together to produce a basic use-cases toolkit of an initial PETSIRD version to support: (i) gating and sub-sampling of PETSIRD data; (ii) conversion of simulated raw data from ROOT to the PETSIRD format and building of a PETSIRD demo dataset; (iii) implementation in existing open-source PET reconstruction tools of a basic PETSIRD interface; and (iv) independent open-source reconstruction of PET images from PETSIRD demo data.

PETSIRD format can introduce a paradigm shift in PET imaging by enabling the standardized open access to the wealth of unprocessed information inherently encapsulated in list-mode PET data to spark innovation and wider AI technology deployment.

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Challenges and solutions for imaging inflammation and infections with whole body and brain-dedicated PET

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We highlight challenges and possible solutions to use PET for imaging inflammation and infection. We also report on the current design of the 4D-PET brain dedicated scanner, financed by the EU through an ERC-AdG, and report on the performance results measured with respect to sensitivity and spatial resolution. We also show some images obtained with phantoms. We describe the process followed to calibrate the detectors and determine
the scanner performance. Innovative detector and scanner designs will also be mentioned in order to improve the scanner performance in the near future. The 4D-PET scanner could be optimal to diagnose and monitor inflammation in the brain.

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Advances in preclinical MR molecular imaging of inflammation

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Inflammation is a critical factor in a spectrum of diseases, spanning from primary immune-mediated inflammatory conditions to prevalent disorders such as cardiovascular diseases, metabolic disorders, and neurodegenerative processes. Yet, our understanding of the complex mechanisms driving immune responses remains limited, primarily due to a scarcity of cellular and molecular insights obtained in their natural context. In this context, in vivo molecular imaging emerges as an invaluable tool for elucidating information about inflammatory biomarkers, pathways, and cells. This approach not only enhances diagnostic capabilities but also facilitates the guidance and monitoring of therapeutic interventions while pinpointing novel targets for further research.
Among the array of clinically available imaging modalities, MRI stands out as the preferred choice when coupling molecular/cellular information with high spatial resolution.
This contribution seeks to offer an overview of advancements in preclinical research within this domain. Various MRI contrast modes will be explored, encompassing traditional T1 and T2 relaxation agents, cutting-edge CEST and hyperpolarized probes, and methodologies based on 19F-MRI detection. Furthermore, the potential for clinical translation of these techniques will be discussed.

Molecular imaging of Inflammation and Infection in Research and clinical practice – status and Next Frontiers / 60

FDG-PET/CT in inflammatory disorders : State-of-the-Art, Challenges and Next Frontiers

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Over the last twenty years, [18 F]FDG-PET/CT emerged as a day-to-day useful tool for assessing inflammatory and infectious disorders due to the expression of glucose transporters on various cells involved in the process, mainly neutrophils, the monocyte-macrophage family and fibroblasts.
Despite a lack of specificity, [18 F]FDG-PET/CT has the advantage of allowing whole-body functional imaging together with anatomical localization and details. In inflammatory diseases, [18 F]FDG-PET/CT was best validated by meta-analyses (MA) in polymyalgia rheumatica (PMR), large-vessel vasculitis
(LVV), sarcoidosis and inflammatory bowel disease (IBD).
In LVV, the pooled sensitivity ranged between 82 and 84% in two MA (range 61-93%) with a pooled specificity of 79 and 87% (range 60-96%). The negative likelihood ratio was remarkably low (0.20-0.23) allowing to rule out the diagnosis with a high degree of confidence. Several grading systems were described for both LVV and cranial giant cell arteritis. In the latter, the pooled sensitivity was lower (58%), probably due to limited spatial resolution. However, specificity was very high (97%). Limited data are available on the potential of [18 F]FDG-PET/CT for treatment monitoring. Diagnostic performances in PMR are encouraging considering that LVV and PMR represent a disease continuum. In sarcoidosis, [18 F]FDG-PET/CT showed efficient in the diagnosis, disease extent, assessment of pulmonary disease activity, and to a lesser extent, monitoring of therapeutic response. No meta-analysis is available up to now, except in cardiac sarcoidosis in which pooled sensitivity and specificity are both 84% with a very low negative likelihood ratio (0.20). [18 F]FDG-PET/CT has an established role in several guidelines for the assessment of suspected cardiac sarcoidosis, provided appropriate acquisition protocols are used.
The use of [18 F]FDG-PET/CT in IBD showed highly sensitive (85%) and specific (87%) to assess disease extent and early response to therapy in limited numbers of patients but requires specific bowel preparation.
Other indications include the recent use of [18 F]FDG-PET/CT in IgG4 related disorders (IgG4-RD)

and retroperitoneal fibrosis (RPF), and rheumatic diseases. [18 F]FDG-PET/CT showed promising results in limited numbers of patients with IgG4-RD and RP by aiding to diagnosis and evaluation of disease extent but also by providing prognostic information and treatment response assessment. Experience in rheumatology has more focused on the evaluation of research questions.

Technical challenges for imaging inflammation and infection / 61

Next generation PET/CT