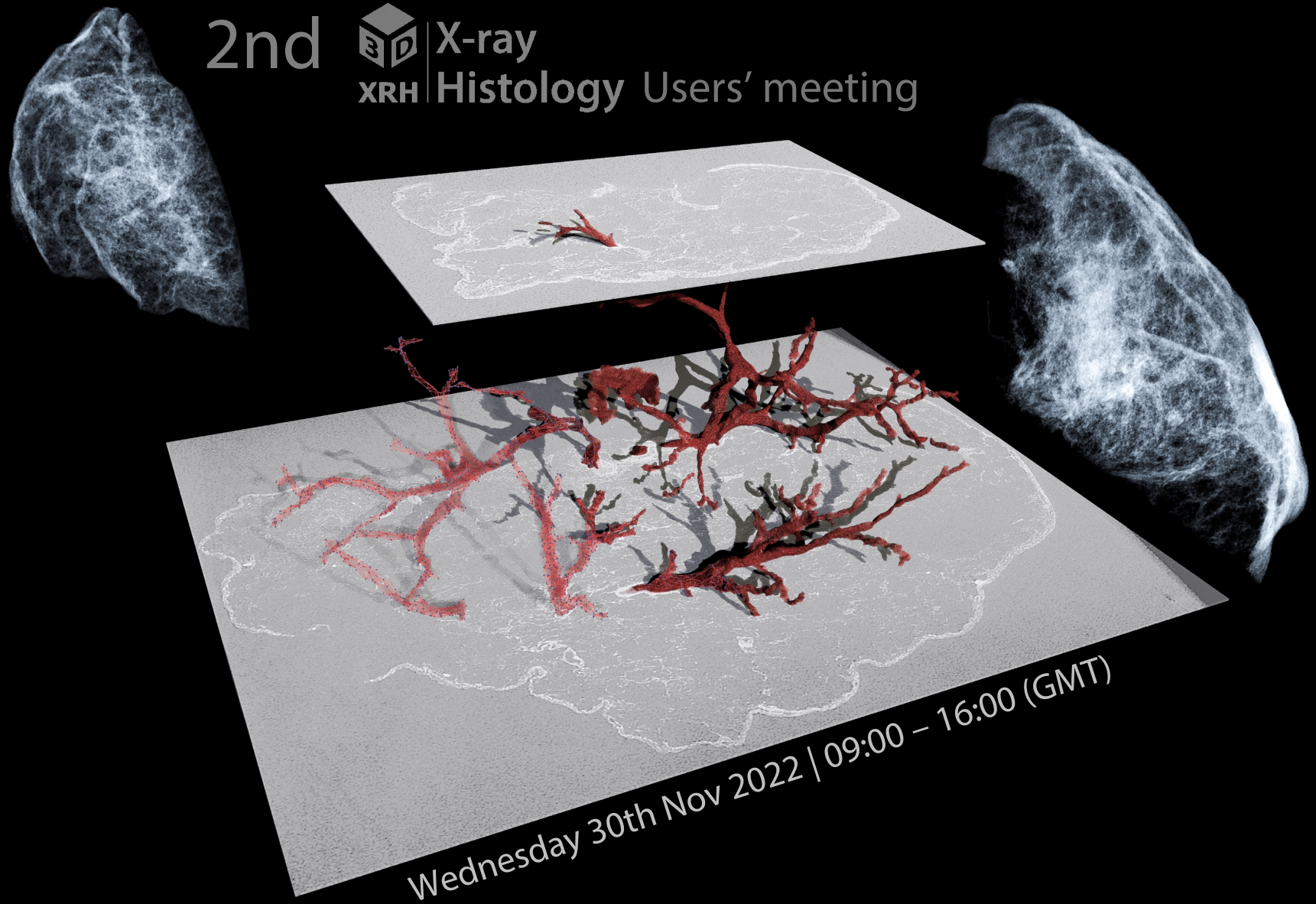
2nd X-ray Histology Users' meeting



Wednesday 30th Nov 2022 | 09:00 – 16:00 (GMT)

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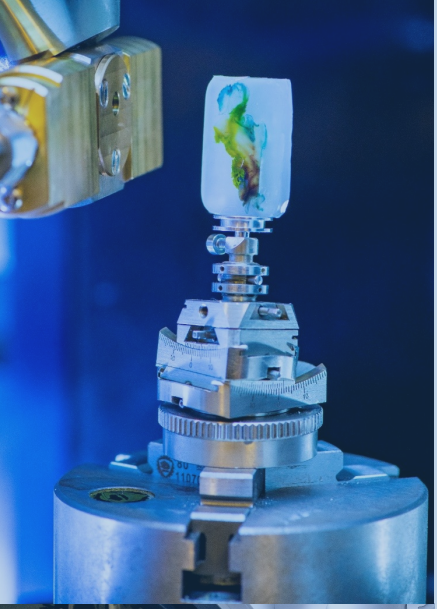

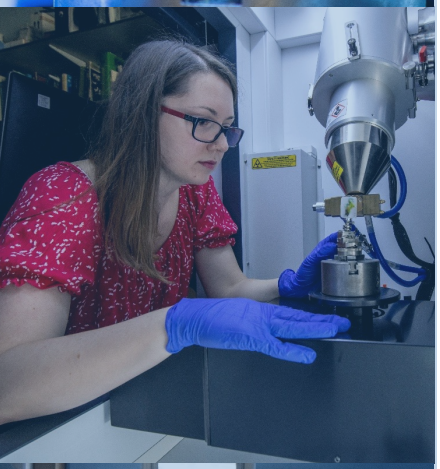

PROGRAMME SUMMARY

NOVEMBER 30TH, 2022
09:00-16:00 (GMT)

09:00 – 09:15

Welcome & Introduction

09:15 – 10:15

Session 1 – Facility background

10:15 – 10:30

Coffee Break

10:30 – 11:30

Session 2 – User talks (soft tissue)

11:30 – 12:00

Feedback session

12:00-13:00

Lunch break

13:00 – 14:20

Session 3 – User talks (Soft & hard tissue)

14:20 – 14:35

Coffee Break

14:35 – 15:20

Session 4 – User talks (Beyond)

15:20 – 15:50

Facility future

15:50 – 16:00

Wrap up

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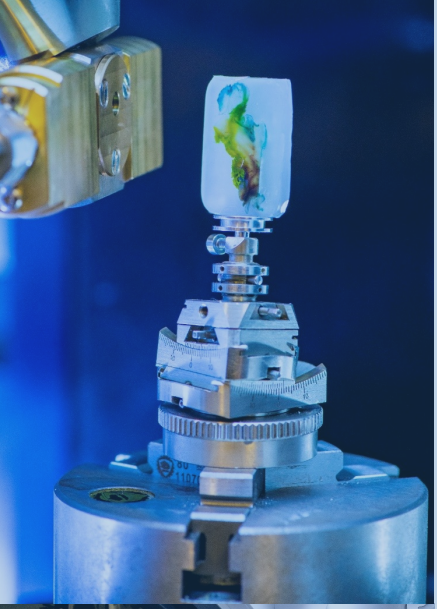

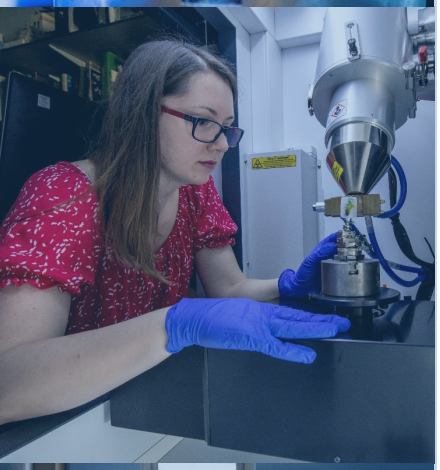

Welcome and Introduction

09:00-09:15

- 09:00-09:15 – Welcome and introduction

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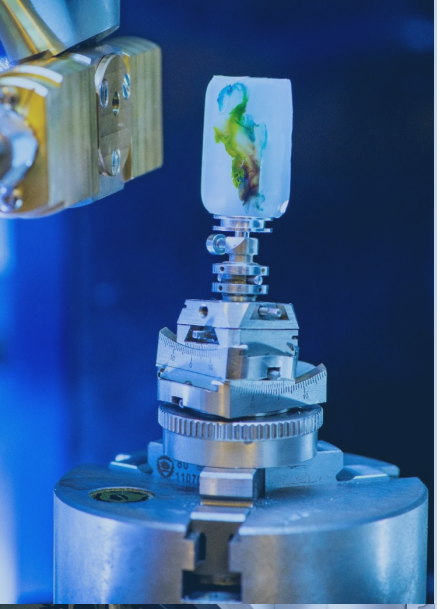

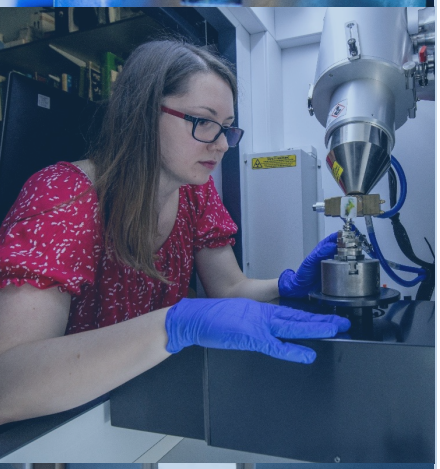

Session 1 – Facility background

09:15 - 10:15 (GMT)

09:15 - 09:30

“Purpose of XRH facility” (Philipp Schneider)

09:30 - 09:45

“Where we stand and what we have achieved” (Orestis Katsamenis)

09:45 - 10:15

“Unique technologies at XRH facility” (Philipp Basford)

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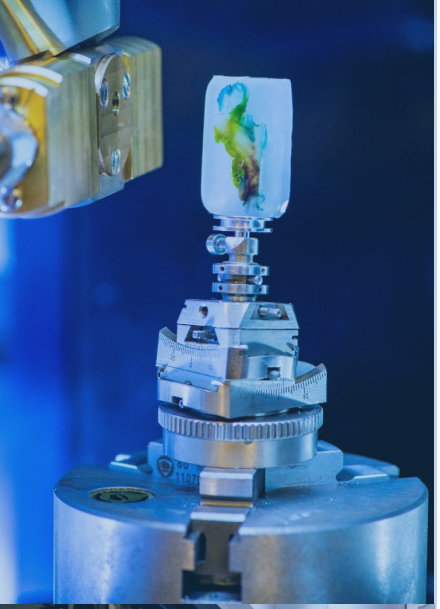

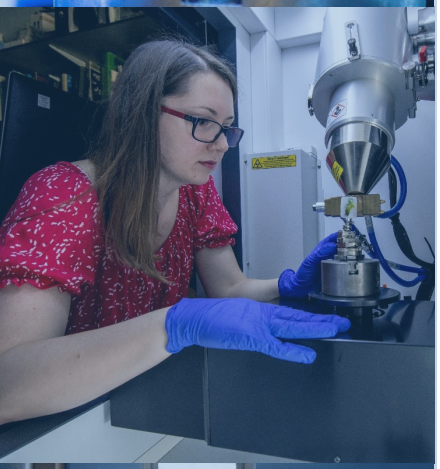

Coffee break

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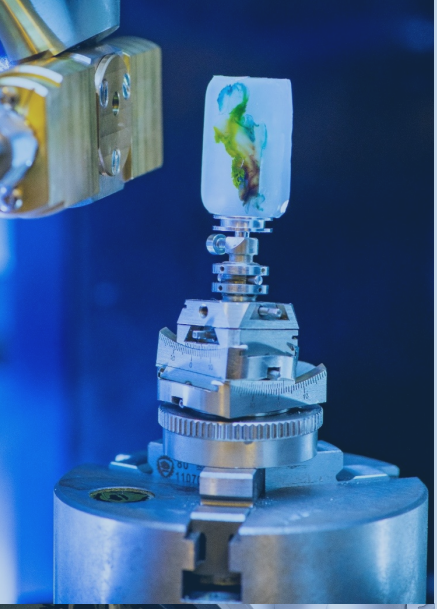

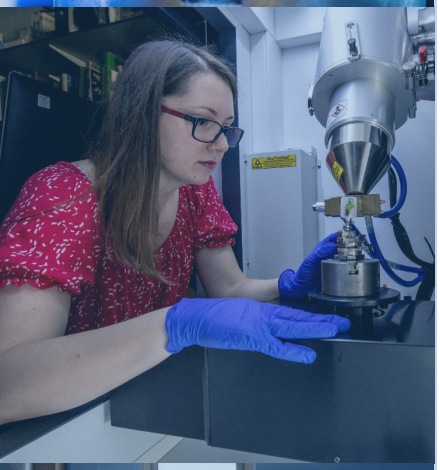

Session 2 – User talks (soft tissue)

10:30 - 11:30 (GMT)

10:30 - 10:50

Jan H. von der Thüsen – *Pathology and Clinical Bioinformatics, Erasmus Medical Centre, Rotterdam, NL*
"Deep learning and co-registration for semi-automated correlation of digital pathology and micro-CT images in lung pathology" [in person]

10:50 - 11:10

Davis Laundon - *Human Development and Health (Medicine), University of Southampton, UK*
"Correlative multiscale microCT-SBF-SEM imaging of resin-embedded placental tissue" [in person]

11:10 - 11:30

Patricia Goggin - *Clinical and Experimental Sciences (Medicine), University of Southampton, UK*
"An investigation of granulomatous lung disease using light microscopy, transmission electron microscopy and X-ray CT" [in person]

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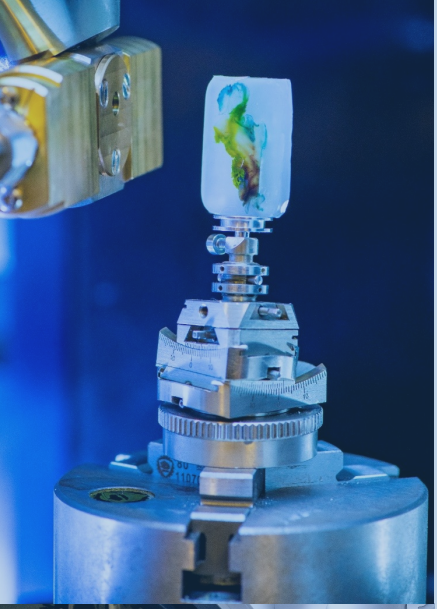

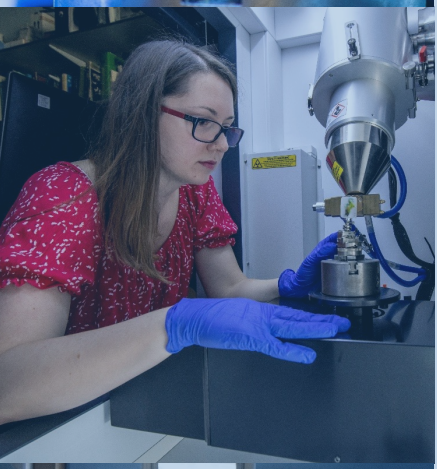

Feedback session

11:30 - 12:00

- 11:30-12:00 Feedback and discussion of new survey

Please let us know of any publications produced that have come from this work. Email us…

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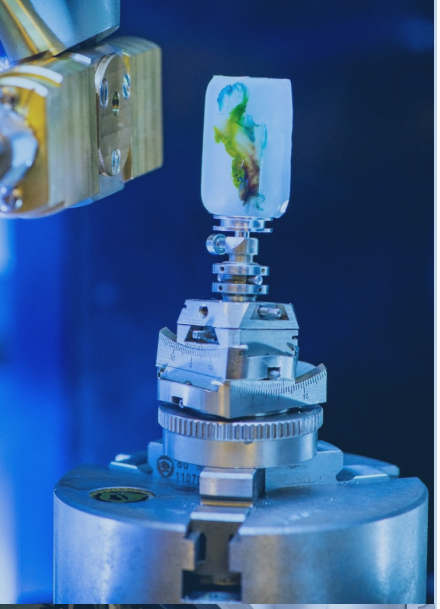

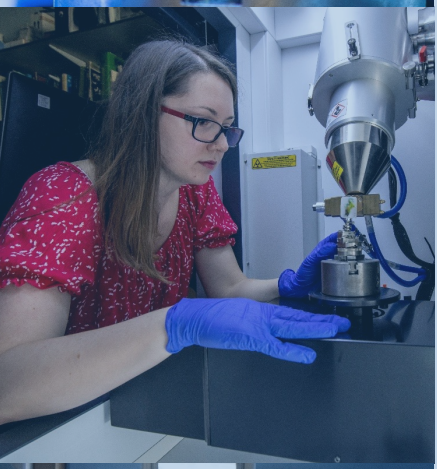

Lunch break

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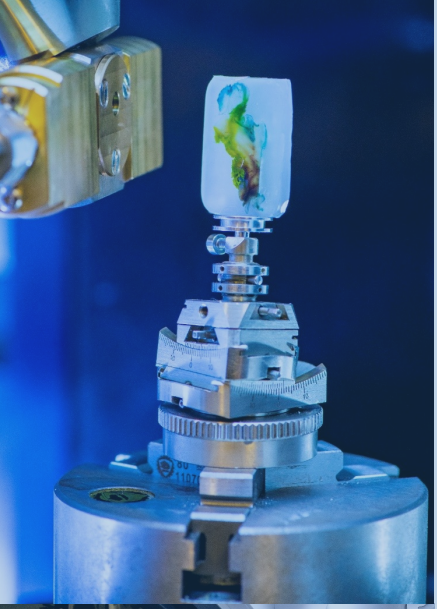

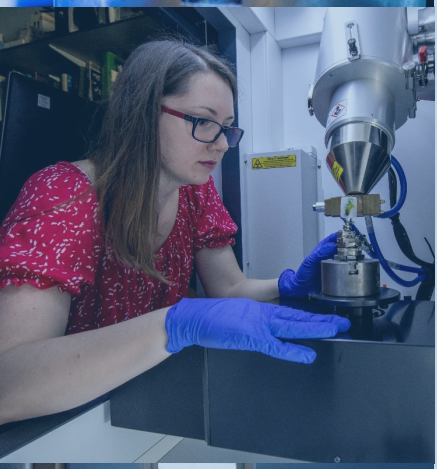

Session 3 – User talks (soft & hard)

13:00 - 14:20 (GMT)

13:00 - 13:20

Roxana Carare - *Clinical and Experimental Sciences (Medicine), University of Southampton, UK*
"Micro-CT in the journey of discovery of new biomarkers for Alzheimer's disease" [online]

13:20 - 13:40

Sherif Elsharkawy - *Centre for Oral, Clinical and Translational Sciences, King's College London, UK*
"Unveiling the Role of Disordered Proteins in Pathological Calcifications"

13:40 - 14:00

Jacob Trend – *Biological Sciences, University of Southampton, UK*
"Organisation of cortical porosity - a key contributor to bone development?" [in person]

14:00-14:20

Charles Burson-Thomas – *Mechanical Engineering, University of Southampton, UK*
"Characterising Joint Geometry by Making Useful Reductions of Medical Imaging Data" [in person]

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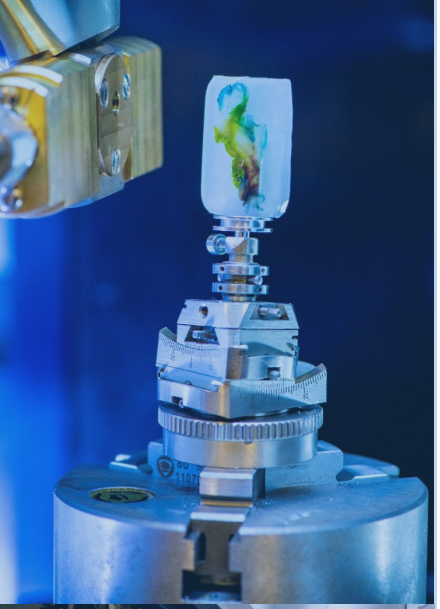

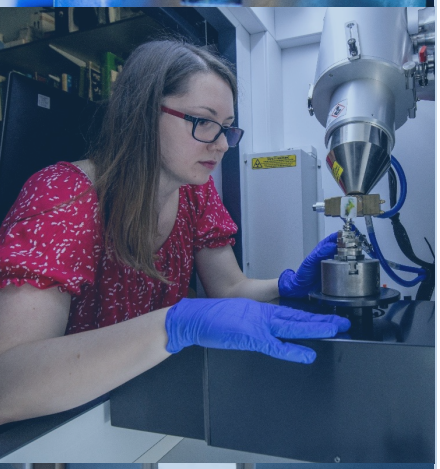

Coffee break

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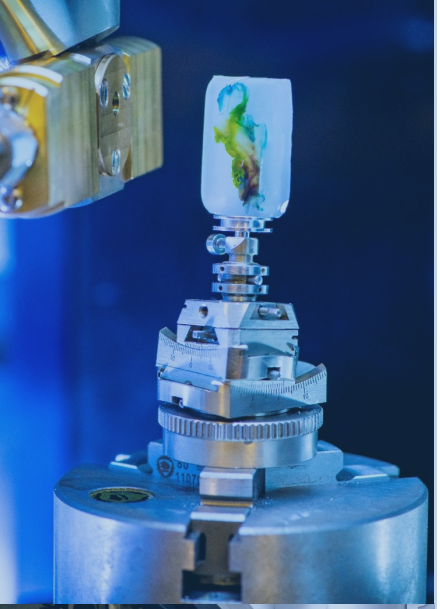

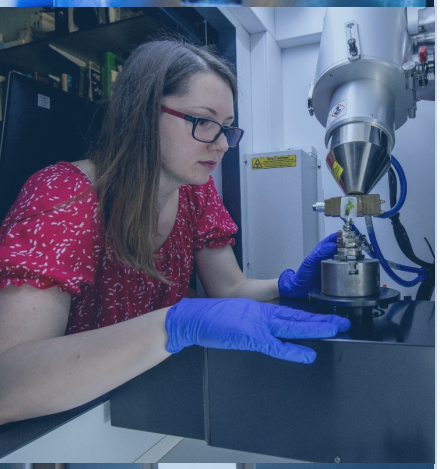

Session 4 – User talks (beyond)

14:35 - 15:20 (GMT)

14:35-14:50

Gavin Foster - *Ocean and Earth Science, University of Southampton, UK*
"TBA"

14:50-15:05

Dimitris Fatouros – *Pharmaceutical Technology, Health Sciences, Aristotle University of Thessaloniki, GR*
"X-ray Micro Computer Tomography: a powerful tool for structural and functional characterisation of novel drug delivery systems" [online]

15:05-15:20

Neil J Gostling – *Biological Sciences, University of Southampton, UK*
"Dinosaurs, Dodos, Eggs and Beyond…"" [in person]

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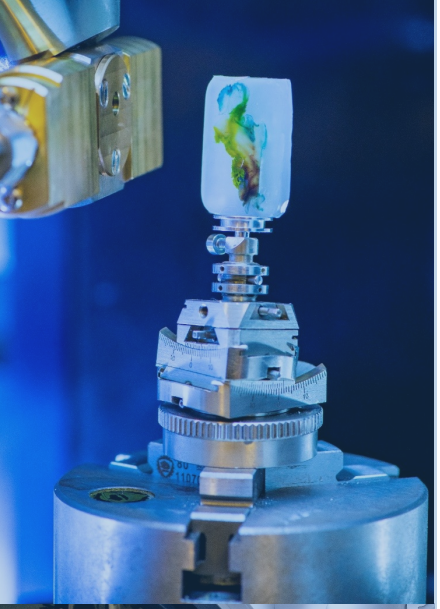

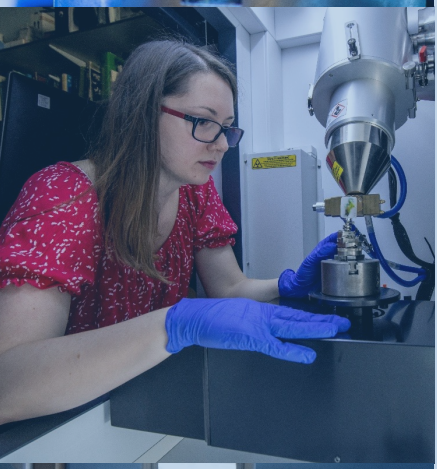

Feedback survey

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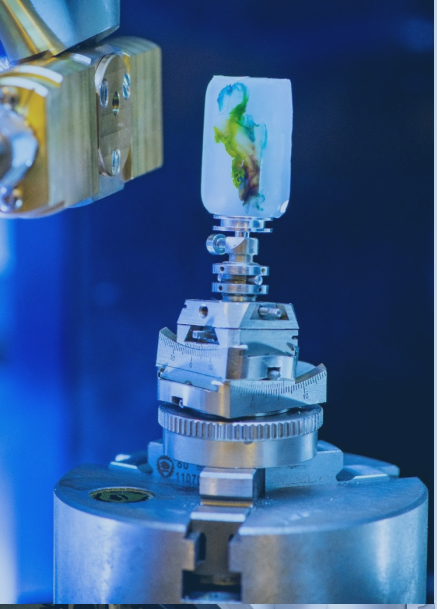

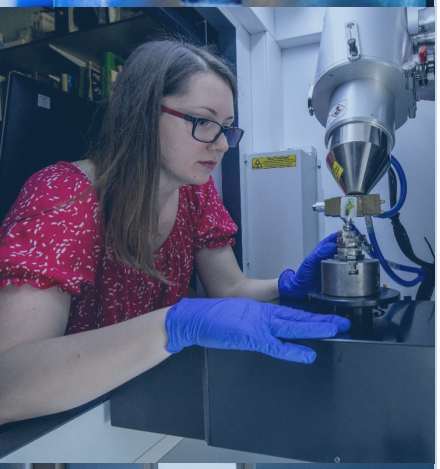

Facility future

15:20-15:50

- 15:20-15:50 Where next?

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Abstracts – Session 2

Jan H. von der Thüsen – *Pathology and Clinical Bioinformatics, Erasmus Medical Centre, Rotterdam, NL*
Title: "Deep learning and co-registration for semi-automated correlation of digital pathology and micro-CT images in lung pathology"
Summary: "Several areas of pulmonary pathology could benefit from three-dimensional reconstruction. This may aid our understanding of the biology of the diseases in question. but may also generate new insights for the classification of specific histopathological patterns, thereby providing an important conceptual feed-back loop. Annotation of multi-level digital pathology images is laborious and repetitive, and automated segmentation and classification may constitute a solution. This would also enable the automated generation of masks which can then be used for registration with micro-CT images of the blocks from which the slides were originally derived. In 2 proof-of-concept studies, we annotated images of pulmonary adenocarcinoma and COVID-19 pneumonia specimens, classifying patterns of adenocarcinoma architecture and thrombotic phenomena, respectively. The annotations were used to generate masks which were then registered with micro-CT images, which were subsequently analysed for various morphometric characteristics"

Davis Laundon - *Human Development and Health (Medicine), University of Southampton, UK*
Title: "Correlative multiscale microCT-SBF-SEM imaging of resin-embedded placental tissue"
*Summary: "*Three-dimensional biological microscopy presents a trade-off between spatial resolution and field of view. Correlative approaches applying multiple imaging techniques to the same sample can therefore mitigate against these trade-offs. Here, we present a workflow for correlative microscopic X-ray microfocus computed tomography (microCT) and serial block face scanning electron microscopy (SBF-SEM) imaging of resin-embedded tissue, using mammalian placental tissue samples as an example. This correlative X-ray and electron microscopy (CXEM) workflow allows users to image the same sample at multiple resolutions, and target the region of interest (ROI) for SBF-SEM based on microCT. We detail the protocols associated with this workflow, and demonstrate its application in multiscale imaging of horse placental villi and ROI selection in the labyrinthine zone of a mouse placenta. These examples demonstrate how the protocol may need to be adapted for tissues with different densities."

Abstracts – Session 2

Patricia Goggin - *Biomedical Imaging Unit, University Hospital Southampton, Southampton, UK*

Title: "An investigation of granulomatous lung disease using light microscopy, transmission electron microscopy and X-ray CT"

Summary: "I will present an interesting case of granulomatous lung disease and describe some of the innovative imaging approaches used to investigate it. This case involves a 44-year-old glass factory worker, who contracted? a viral infection in Florida. The patient underwent wedge resection of the right upper lobe and right medial lobe by VATS for biopsy.

Slicing revealed at least two relatively well-circumscribed white/grey lesions measuring up to 5 mm. The lung parenchyma was found to contain numerous non-necrotising epithelioid granulomata. These granulomata are located subpleurally, peribronchially and within the septa. On polarisation, there were possibly some scattered small fragments of refractile material present within some of the giant cells. The background lung parenchyma also displayed thickening of the terminal arterioles, features suggestive of pulmonary hypertension. these features present raise the possibility of sarcoidosis but the occupational history also raises the suspicion that this may also be contributing to the granuloma formation.

Tissue was processed for transmission electron microscopy (TEM) avoiding osmium tetroxide and left unstained (no UA Pb) and analysed using TEM, energy dispersive X-ray microanalysis (EDX) and X-ray micro computed tomography.

A sample of Lucite (a polymethylmethacrylate glass interleaving powder used in the patient's workplace) was also characterised using scanning electron microscopy, EDX and X-ray micro computed tomography.

This case illustrates how multiple techniques can be employed in a correlative diagnostic workflow to investigate foreign bodies."

Abstracts – Session 3

Roxana Carare - *Clinical and Experimental Sciences (Medicine), University of Southampton, UK*
Title: "Micro-CT in the journey of discovery of new biomarkers for Alzheimer's disease"
Summary: "Experimental evidence in different species demonstrates the drainage of cerebrospinal fluid (CSF) into the nasal mucosa. In humans, most of the CSF drains across arachnoid villi into the blood. There is evidence from radiological studies in humans that PET tracers reach the nasal mucosa from the CSF, and their expression in the nasal mucosa decreases in Alzheimer's disease. This project aims to demonstrate firstly the anatomical connections between the cerebral subarachnoid space and the nasal mucosa and, secondly, the changes in the levels of CSF biomarkers within the nasal mucosa. We will test the following hypotheses: 1) there are leptomeningeal sheets around the olfactory nerves that penetrate the cribriform plate, thus providing a communication between the SAS and nasal mucosa; 2) neurofilament light and beta-transferrin, CSF biomarkers for Alzheimer's disease, are found in the nasal mucosa and their expression decreases with age and in Alzheimer's disease. The methodology consists of 1) micro-CT imaging of human cribriform plate and nasal turbinates; 2) serial sectioning of formalin-fixed paraffin-embedded post-mortem cribriform plates with olfactory nerves in situ, followed by histological analyses; 3) biochemical analyses of phospho-tau, total tau, neurofilament light, beta-transferrin, Abeta40, Abeta42. This project will delineate the anatomical pathways for transfer of proteins from the CSF into the nasal mucosa and will pave the way for the development of non-invasive specific and sensitive biomarkers enabling the early diagnosis and monitoring of Alzheimer's disease. It will also unlock the potential of developing novel drug delivery routes into the brain via the nose."

Jacob Trend – *Biological Sciences, Environment and Life Sciences, University of Southampton, UK*
Title: "Organisation of cortical porosity - a key contributor to bone development?"
Summary: "The heterogeneous organisation of cortical porosity within murine bone is poorly defined and the molecular rationale for its existence is unknown. To investigate this, we have utilised both desktop and synchrotron radiation computed tomography to assess whole bone and microstructural phenotypes during post-natal development. The development of novel image analysis techniques has permitted the assessment of cortical porosity in development and in diseased states."

Abstracts – Session 3

Sherif Elsharkawy - *Centre for Oral, Clinical and Translational Sciences, King's College London, UK*

Title: "Unveiling the Role of Disordered Proteins in Pathological Calcifications"

Summary: Pathological calcification is an abnormal accumulation of calcium minerals on soft tissues, which leads to many extra-skeletal diseases. The mechanism of mineralization in functional tissues such as bone and teeth are resulted from a regulated cellular process including promoting mineralization in desired areas and inhibiting it in other areas that is controlled by soluble and insoluble biomacromolecules including proteins, lipids and polysaccharides, which are directing nucleation of minerals on substrates. One example of pathological calcification occurs in brain tissue, which is more common among patients with Parkinson's and Alzheimer's diseases. In these cases, the presence of osteogenesis markers was depicted in calcified vasculature regions with α-Synuclein-positive structures. There is growing evidence that intrinsically disordered proteins contribute to intermolecular interactions at the protein–mineral interface. Here, we aimed to determine the critical role of disordered proteins in driving pathological calcifications, which is currently unknown. In this study we have investigated mechanisms of pathological calcifications within brain pineal glands that occur in neurodegenerative patients. Formalin fixed paraffin embedded (FFPE) pineal gland tissues were studied with micro-CT and then sectioned for immunohistochemistry studies. The microstructure of tissues was analyzed by scanning electron microscopy (SEM). In order to analyze the secondary structure of proteins surrounding the minerals, Fourier Transform Infrared imaging (FTIR imaging) was performed on all cases and healthy tissues as a control. The whole pineal gland tissues were scanned with micro-CT to visualize the distribution of the calcium phosphate minerals. The size and numbers of minerals were extensively higher in Alzheimer's disease samples compared to control. The immunohistochemistry analyses were performed for alpha-synuclein and beta-amyloid proteins as well as calcium minerals. The amyloid aggregates were evident in diseased tissues and both diseased tissues showed higher levels of calcium deposits compared to control. The FTIR imaging confirmed the conformation of proteins surrounding the minerals. This promising information gathered from this work is a starting point to get closer to find a universal mechanism based on disordered protein assemblies into amyloids and spherulites that triggers the formation of calcified structures in soft tissues."

Abstracts – Session 3

Charles Burson-Thomas – *Mechanical Engineering, University of Southampton, UK*

Title: "Characterising Joint Geometry by Making Useful Reductions of Medical Imaging Data"

Summary: "It is surprisingly easy to amass a great deal of digital data from medical imaging. Often, the challenge is to turn this large number of measurements into a smaller amount of useful information, which helps shed light on a research question. Characterising the geometry of synovial joints, from medical imaging data, is necessary in the design of minimally invasive implants and to investigate the relationship between joint geometry and risk of osteoarthritis. Two methods to perform this geometric characterisation will be discussed: statistical shape modelling and quantifying congruence with an elastic foundation. In this talk, the focus will be on the nature of each methodology, where certain data is discarded, where information/assumptions are added, and ultimately how each method takes a large dataset and extracts some helpful information from it. In a time when there is much excitement about the potential of AI for medical imaging analysis, it is also interesting to reflect on how useful reductions, and adding appropriate information, can be an effective approach to medical image data analysis."

Abstracts – Session 4

Gavin Foster - *Ocean and Earth Science, University of Southampton, UK*
Title: ""
Summary: ""

Dimitrios G. Fatouros – *Pharmaceutical Technology, Aristotle University of Thessaloniki, GR*
Title: "X-ray Micro Computer Tomography: a powerful tool for structural and functional characterisation of novel drug delivery systems"
Summary: "This presentation will briefly describe the application of X-ray Micro Computer Tomography as a process analytical technology for the structural and functional characterisation of 3D printed dosage forms and devices (microneedles) and the ability of Micro-CT imaging to provide insight in the 3D morphological characteristics of excised tumors, allowing the quantification of volume and spatial distribution of three main anatomical features of interest."

Neil J Gostling – *Biological Sciences and IfLS, Environment and Life Sciences, University of Southampton, UK*
Title: "Dinosaurs, Dodos, Eggs and Beyond…"
Summary: "Neil Gostling is an evolutionary biologist and palaeobiologist, along with his collaborators, takes a multidisciplinary approach to answer a broad range of evolutionary questions. He has been lucky enough to work on unique material from the Isle of Wight to uncover the neuroanatomy of dinosaurs, and has used bones from living birds to begin to address questions about the sex of fossils from the Cretaceous of China. Additionally, the group's work looks and the origin of flight and other biomechanical questions."