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Editorial: Advances of synchrotron radiation-based X-ray imaging in biomedical research

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Editorial on the Research Topic
Advances of synchrotron radiation-based X-ray imaging in biomedical research

Synchrotron radiation-based X-ray imaging, particularly X-ray phase-contrast microtomography (PC-µCT), is of interest in biomedical research thanks to its non-destructive 3D hierarchical visualization power [1, 2]. Unlike laboratory microCT, PC-µCT enables high spatial resolution imaging with intense throughput [3]; thus, aiding the development of artificial intelligence (AI) algorithms for image analysis. Phase contrast enhances the discernment of soft tissue structures, making morphological characterization effective even without additional stainings [4–6].

These aspects allow PC-µCT to supplement traditional histology with 3D data, leading to the emergence of "virtual histology" as a complementary approach in the synchrotron imaging community [7–9]. However, sample preparation for multiscale and multi-techniques studies still remains a challenge.

The study by Young Lee et al. presents a step-by-step protocol for 3D virtual histology of unstained human brain tissue [10]. Initially designed for the SYRMEP beamline in Trieste, the protocol is also adaptable to other µCT imaging beamlines. It includes tissue preparation, µCT acquisition, reconstruction, post-processing, and validation against histology. The authors demonstrate how blood vessels and neurons appear in images acquired with isotropic voxel sizes of 5 μm^3 and 1 μm^3. Additionally, it facilitates the investigation of biological substrates such as neuromelanin and corpora amylacea, enabling the study of their spatial distribution using tailored segmentation tools validated by classical histology methods. This approach provides a means to explore the intricate architecture of brain tissue, offering valuable insights into its organization and potential pathological alterations.

The Research Topic also received contributions regarding the optimization of novel sample preparation methods: in one case for producing enhanced contrast in the visualization of specific sample features; in the other for boosting multi-modal investigations.

The paper by Fratini et al. focuses on optimizing sample preparation protocols to improve contrast-to-noise ratio (CNR) in PC-μCT imaging of white matter (WM) in the central nervous system (CNS) [11]. The study emphasizes the critical role of tissue fixation and dehydration in enhancing CNR for XPCT, which is essential for visualizing delicate WM structures like fibers. Key methodological optimizations include the selection of a fixative protocol involving ethanol perfusion followed by xylene dehydration. This approach preserves tissue architecture while effectively removing water, thereby enhancing phase contrast without the need for exogenous contrast agents. Additionally, structural alterations are minimized through the ethanol-xylene treatment, which helps prevent shrinkage or distortion commonly observed with other fixatives, thus preserving fine gray matter (GM) and WM details. The method improved the visibility of pathological features relevant to neurodegenerative diseases, such as demyelination or axonal damage. It enables high-resolution 3D imaging of WM microstructures, supporting preclinical research into conditions like multiple sclerosis or Alzheimer's disease. By improving CNR, the technique enhances the detection of subtle pathological changes while preserving tissue for downstream analyses (e.g., histology).

Sagar et al. demonstrate that optical clearing improves propagation-based PC-μCT imaging by reducing artifacts like air bubbles and cracks found in traditional formalin-fixed paraffin embedding (FFPE) methods [12]. Using Phytagel embedding, they achieved high-quality imaging of colon cancer specimens while preserving compatibility with standard histology. This method enhances PC-μCT by providing clearer, artifact-free imaging for better analysis.

Subsequently, to the optimal technical choices improving image acquisition, the processing of tomographic datasets always plays a crucial role. In the post-processing step, the application of AI tools for object detection and sample feature segmentation can be extremely advantageous in order to perform quantitative volumetric analysis on large datasets.

Lopes Marinho et al. evaluated various convolutional neural networks (CNNs) for segmenting PC-μCT images of magnesium-based biodegradable bone implants in sheep tibiae [13]. Accurate segmentation is crucial for assessing implant degradation and osseointegration. The study compared models like U-Net, HR-Net, U^2-Net, and both 2D and 3D versions of nnU-Net, using the intersection over union (IoU) metric to assess performance. Findings revealed that the 2D nnU-Net exhibited superior generalization capabilities, though all models faced challenges in accurately segmenting the degradation layer.

The study from Furlani et al. explores the biomechanical properties of collagenous tissues using PC-μCT combined with deep learning techniques to enhance the analysis of collagen bundles [14]. The paper demonstrates the ability to visualize collagen bundles in three dimensions across various body regions, applicable in both pre-clinical and clinical settings. The authors propose that deep learning-based semantic image segmentation can more effectively identify and classify collagen bundles compared to traditional thresholding methods. By employing neural networks, the study achieves quantification of structures in synchrotron phase-contrast images that were previously indistinguishable. Notably, this approach allows for the identification of collagen bundles based on their orientation, moving beyond the limitations of conventional techniques that rely solely on physical densities.

In conclusion, the Research Topic covers both the description of experimental approaches for image acquisition and computational post-processing segmentation pipelines. In addition, in the Research Topic an innovative approach is introduced that explores the feasibility of a dual-modal on-board imaging system combining spectral-CT and cone-beam CT (CBCT) using a cadmium zinc telluride (CZT) photon-counting detector (PCD) integrated into a linear accelerator (Linac) by Monte Carlo simulations. This approach, presented in the paper of Ye et al., aims to address limitations in conventional CBCT imaging, such as metal artifacts, insufficient soft-tissue contrast, and lack of functional or molecular imaging capabilities, which can hinder the precision and effectiveness of image-guided radiation therapy (IGRT) [15]. The study uses the Geant4 Application for Tomography Emission (GATE) software to design and validate the proposed system. The CZT detector's pixel size was optimized for a balance between photon detection efficiency and spatial resolution. Imaging performance was evaluated using a PMMA phantom containing calcium and contrast agents (iodine, gadolinium, gold), leveraging K-edge spectral imaging to differentiate materials. In conclusion, this novel approach could enhance IGRT by improving target delineation, treatment monitoring, and differentiation between tumor recurrence and treatment-related changes.

This Research Topic displays key advancements in PC-μCT imaging, from refined sample preparation to AI-powered analysis. Together, these studies reinforce PC-μCT as a powerful, non-destructive tool for virtual histology, offering deeper insights into tissue structure and disease.

Author contributions

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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