MASTER THESIS PROJECT in the Prof. COAN's LMU GROUP

'Brilliant X-Rays for Medical Diagnostics'

Our group at the LMU Chair of Medical Physics in Garching (LS Parodi) is working on biomedical applications of X-ray phase contrast CT and of novel imaging methods, and is looking for a highly motivated **MASTER STUDENT** to work with us. The group is affiliated to both the Department of Radiology/Medicine Faculty and the Department of Physics, of the LMU.

Project Title: "X-ray 3D imaging-based evaluation of therapeutic strategies to slow down glaucoma-related neurodegeneration in animal models"

Scientific Case: Glaucoma is the second cause of blindness worldwide due to progressive and multifactorial degeneration of retinal ganglion cells (RGC) in the inner retina and loss of their axons in the optic nerve. The disease progresses without symptoms leading to irreversible visual field loss and optic nerve damage. Currently, intraocular pressure (IOP) reduction is the only treatment. Mitochondria regulate cellular processes and are involved in cell death. They are in high number in the visual system and supply cells with ATP. Patients with mitochondrial disorders show visual impairment, loss of RGC and blindness. Time between cellular dysfunction and cell loss can give an opportunity for therapeutic intervention by normalizing mitochondrial function. Targeting mitochondria could be a potential disease modifying treatment for optic neuropathies where no treatment is currently available. Coenzyme Q10 is a ubiquinone present in the inner membrane of the mitochondrial electron transport chain. Idebenone, a synthetic analogue of coenzyme Q10, with potent antioxidant activity, alleviates glaucoma, based on its electron carrier function to normalize mitochondrial respiratory chain and on its ability to stimulate several metabolic pathways. Excitotoxicity is a common mechanism leading to neuron death and contributes to RGC death. It has been reported that pharmacological blockade of mGlu1 receptors attenuates monosodium glutamate-induced RGC death in mice. In this scenario, the possibility of monitoring the effect of treatments with a non-destructive and full-organ approach is key for the comprehension and the assessment of new therapeutic strategies. X-ray phase-contrast micro-CT (X-PCI-CT) is a powerful technique for tissue-conserving virtual histology, which is density-based, label-free and multiscale and can serve as the basis for quantitative analyses of neuroinflammation markers such as activated microglia, of degenerating shrunk neurons and of vascular features within the retina. X-PCI-CT has the great advantage upon standard histology of visualizing structures in 3D and allowing virtual sectioning in the 3 main axes without cutting, staining and processing every single slice. Furthermore, synchrotron X-PCI-CT can visualize soft tissues with contrast and spatial resolution that cannot be reached with post-mortem MRI imaging or standard micro-CT.

Experiments: To examine the potential neuroprotective effects of the specific treatment protocols (idebenone and mGlu1 receptor antagonists), two different glaucoma mice models will be used. Different animal groups will be treated with different drugs administered either in the pre-symptomatic phase or in the symptomatic phase after the increase of IOP (weekly measured by a tonometer). The eyes will be dissected out at the end of the treatments, formalin fixed and paraffin embedded for imaging (at the European Synchrotron Radiation Facility, ESRF) and immunohistochemistry. The propagation-based X-PCI-CT technique will be used with a multi-scale setup affording detector voxel sizes of 3x3x3 μm^3 and 0.7x0.7x0.7 μm^3.

Overall Project Objectives: To study the potential therapeutic effects of idebenone and mGlu1 receptor antagonists in experimental models of glaucoma by using a high-sensitivity microscopic approach based on X-PCI-CT for multiscale, *post-mortem* 3D virtual-histology.

Specific Thesis Work Objectives: You will participate in the multiscale imaging session and learn how to set and carry on an X-PCI-CT experiment. You will reconstruct X-PCI-CT datasets to derive 3D visualizations of the entire globe and of the retina regions, which will first be evaluated qualitatively and compared to histological findings. The CT image reconstruction will require the optimization of several parameters and the correction of possible artifacts related to the experimental setup and data acquisition procedure. The quantitative analysis of reconstructed phase-contrast CT datasets will be guided by the specific questions set by the medical partners. You will quantify morphological tissue alterations derived from glaucoma and from the treatment via appropriate (semi-)automatic algorithms. You will learn to extract meaningful structural parameters by segmentation and 3D visualization. Your work will play a crucial role within this project, and will be instrumental to the successful publication of our results.

Candidate: Previous knowledge in Phython and/or Matlab is an asset (but it is not mandatory). The candidate should be interested in developing new analysis tools for image quantification.

Scientific and academic context: This Master project will be realized within an international and interdisciplinary framework involving physicists and neuroscientists from the Ludwig Maximilians University (Germany), the ESRF (France), the Sapienza University and Neuromed Institute (Italy). The student will work in a highly motivated network with a long tradition of collaboration and excellence in biomedical research.

Start date: flexible

Please get in contact with us if you are interested in knowing more - we would be happy to hear from you!

Contacts:

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