High resolution X-ray Phase Contrast Imaging for studying the effects of novel radiotherapies

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X-ray Phase Contrast Computed Tomography (PCI-CT) can be used to non-invasively study soft tissues and to investigate in 3D the morphology of bio-pathologies with high detail and sensitivity. This imaging method allows to study target organs with a multiscale approach. In previous work, our team has imaged rat brains bearing 9L glioblastoma, and has shown that PCI is suitable to discriminate between healthy and cancerous tissue [1]. Moreover, we obtained a proof of concept in our studies, that the technique can be used to analyse the different effects of applied X-ray radiotherapies on a rat animal model. We irradiated in-vivo healthy and brain tumour bearing rats with standard broad X-ray beam (BB), Microbeam and Minibeam Radiation Therapies (i.e. arrays of beamlets with tens or hundreds micrometre width, respectively - MRT [2] and MBRT [3]) by using different levels of delivered dose. We compared the three treatments in terms of radiation-related effects by investigating the treated tissue by means of 3D PCI-CT. Following the first promising results on rat brains, the study was extended to rat lungs, which were irradiated with radiotherapy protocols similar to those used for brains. The choice of focusing also on lung cancer is determined by the high oncological relevance of the case: it remains the most common tumour in men worldwide [4] with an incidence that has been increasing during the last decades. We analysed treated healthy rat lungs in 3D and with spatial resolutions down to sub-micron scale to understand the optimal geometrical configuration and doses to be delivered to spare healthy tissues.

For the first part of the study, 49 rats implanted with 9L glioblastoma, as well as 23 non-implanted rats, were alternatively treated with MRT, MBRT and BB with different beam sizes and peak doses at the European Synchrotron Radiation Facility (France). The selected peak doses were: 200, 400 and 600 Gy for MRT; 180 and 350 Gy for MBRT and 5, 10 and 15 Gy of BB irradiation. Two days after irradiation, rats were imaged using Magnetic Resonance Imaging (MRI) at the IRMaGe MRI facility of Grenoble, in order to compare tumor sizes at the moment of treatment (or just after) with the sizes measured at the time of the PCI-CT experiment. The sequences used were a T\textsubscript{2}-weighted spin-echo sequence and two T\textsubscript{1}-weighted spin-echo sequences before and 30s after the injection of Gd contrast agent. As for lungs irradiations, 96 rats were divided into 11 groups depending on the delivered beam and dose: 1) controls; 2-3) BB of 30 and 50 Gy; 4-7) MRT of 50, 100, 300 and 600 Gy as peak doses; 8-11) MBRT 50, 100, 300 and 600 Gy as peak. After the organ extraction and fixation, all the samples were then imaged by X-ray PCI-CT by using a sCMOS CO.Edge 5,5 camera with different pixel size combination depending on the sample to be imaged. Rat brains were analysed with either a monochromatic beam of 35 keV and a pixel size of 3 μm or a pink beam and 0.7 μm as pixel size while rat lungs were imaged with a 22 keV energy X-ray monochromatic beam and pixel sizes of 1.63 and 0.65 μm.

X-ray PCI-CT allows the recognition and differentiation of brain and lungs anatomical details down to the cellular level and identification of microscopic cancerous cell-clusters far from the main lesion, tissue necrosis, tumour oedema, high-density calcifications as well as micrometric MRT-transsections for brains, while for lungs, radiation induced fibrosis is visible. The latter can be visualized as thickening of alveolar walls, expansion of alveolar spaces and destruction of their normal structures, which are replaced by irregular, abnormal air spaces and large areas of scarring.

X-ray PCI-CT provides a very detailed visualization of anatomical structures. It can reproduce the accuracy of histology in discriminating tissues [1] but extended to the full organ volume and not limited to a 2D slice. The method appears to be well suited for investigating cancer development and radiotherapy effects on both the studied biological targets. In the future, other types of tumours and target organs will be considered and the method will be also tested for image-guidance during radiotherapy.

References