

PhD Thesis title: 'Monte Carlo and experimental small-field dosimetry applied to spatially fractionated synchrotron radiotherapy techniques'.

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ABSTRACT:

Two innovative radiotherapy techniques are under development at the ID17 Biomedical Beamline of the European Synchrotron Radiation Facility (ESRF): the microbeam radiation therapy (MRT) and, more recently, the minibeam radiation therapy (MBRT). Their main features are the use of submillimetric field sizes (which explore the limits of the dose-volume effect) as well as the spatial fractionation of the dose.

The resulting biological response appears to challenge many of the current paradigms in radiotherapy. In particular, a remarkable healthy tissue tolerance to very high doses in one fraction was observed in several MRT studies. Additionally, MRT rendered significant growth delay or, in some cases, complete eradication of animal tumour models. The success of the preclinical studies has paved the way to the preparation of forthcoming MRT clinical trials, which are currently in preparation at the ESRF.

MBRT was based on the idea of overcoming the inherent limitations of widespread clinical implementation of MRT which, nowadays, is confined to synchrotrons. Since the different irradiation parameters can lead to dissimilar biological effects with respect to MRT, in vivo experiments are also planned at the ESRF in order to assess the therapeutic index of this promising modality.

This PhD work deals with different features related to small (micrometre-sized) field dosimetry involved in these techniques. Monte Carlo (MC) simulations and experimental methods were used with this aim in mind.

The core of this work consisted of the development and benchmarking of a MC-based computation engine for a treatment planning system (TPS) devoted to MRT within the framework of the preparation of forthcoming MRT clinical trials. The MC calculation engine included complete characterisation and modelling of the synchrotron source, as well as beam transport through 42 m of optical elements up to the patient position. Computed dose distributions from photons sampled according to the probability

distributions derived from the beam model were experimentally verified by using several detector systems in homogeneous and heterogeneous media. Good agreement between simulations and measurements validated the photon beam model for its use in MRT dose calculations.

The next step towards a full computation engine for a TPS included the dose calculation in a patient model, reconstructed from Computed Tomography (CT) images. To this direction, the decoupling of the CT image voxel grid (lateral size in the order of mm) to the dose bin grid, which has micron dimensions in a transversal direction to the microbeams, was performed. Optimisation of the simulation parameters, the use of variance-reduction techniques and parallelisation methods were applied in order to speed up the planning process.

Additional achievements were the definition of safe MRT irradiation protocols, the assessment of scatter factors in MRT and the further improvement of the MRT therapeutic index by injecting a contrast agent into the tumour.

Finally, a dosimetry protocol for future preclinical studies in MBRT was established. The objectives achieved in this thesis have provided the dosimetric tools for forthcoming MRT clinical trials in pets and the MBRT preclinical trials in small animals.

References to author publications that relate specifically to the dissertation:

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6. **I. Martínez-Rovira**, J. Sempau and Y. Prezado, "Monte Carlo-based treatment planning system calculation engine for microbeam radiation therapy" (*Med. Phys.*, *in press*).

