High resolution 3D dosimetry for microbeam radiation therapy using optical CT

C McErlean¹, E Bräuer-Krisch², J Adamovics³, M O Leach⁴, and S J Doran¹,5
¹CRUK Cancer Imaging Centre, Institute of Cancer Research, London, UK
²European Synchrotron Radiation Facility, Grenoble, France
³Department of Chemistry and Biology, Rider University, Lawrenceville, NJ, USA
⁴Clinical Magnetic Resonance Research Group, The Royal Marsden NHS Trust, UK
⁵Department of Physics, University of Surrey, Guildford, UK
⁶Heuris Pharma, LLC, 412 Sunset Rd., Skillman, NJ, 08558 USA

E-mail: ciara.mcerlean@icr.ac.uk

Abstract. Optical Computed Tomography (CT) is a promising technique for dosimetry of Microbeam Radiation Therapy (MRT), providing high resolution 3D dose maps. Here different MRT irradiation geometries are visualised showing the potential of Optical CT as a tool for future MRT trials. The Peak-to-Valley dose ratio (PVDR) is calculated to be 7 at a depth of 3mm in the radiochromic dosimeter PRESAGE®. This is significantly lower than predicted values and possible reasons for this are discussed.

1. Introduction

Microbeam Radiation Therapy (MRT) is a new therapy that makes use of the fact that spatially fractionated dose is very well tolerated by normal tissue while being lethal to tumours [1]. Treatments involve delivering dose in narrow, well collimated x-ray beams the order of 50µm wide. Dosimetry of this therapy is challenging as there is no commercially available technique that can deliver the high resolution and high dynamic range measurements required [2]. Many developments have been made in the area of ‘multiple single point’ dosimeters, such as MOSFETs, and planar dosimetry including radiochromic film. However, with increasingly complex dose distributions there is a need for a truly 3D dosimetry technique for this therapy [3]. A 3D dataset provides advantages such as the ability to reconstruct in multiple planes, providing easier visualisation of any alignment problems. Furthermore, using a 3D dosimeter it is possible to provide ‘end-to-end’ quality assurance of the entire therapy process, including planning Computed Tomography (CT) scans and Treatment Planning calculations. Optical CT has been previously shown to be a potential candidate to fill this gap [4]. This type of dosimetry would be complementary to existing ultra-high resolution planar techniques.

The construction and characterisation of a version of our Optical CT microscope has been previously reported [4]. The Modulation Transfer Function (MTF) and dose response were measured through the use of specialised test objects [5]. It was observed that although quantitative measurements are possible at the millimetre scale, at high spatial frequencies the lower MTF results in an underestimation of the dose [6].

Here we present some initial results from a series of irradiations on the ID-17 Biomedical Beamline at the European Synchrotron Radiation Facility (ESRF) in Grenoble. The goals were to assess the visualisation of different MRT irradiation geometries with Optical CT and secondly, to test whether...
quantitative measurements could be made on the microbeams themselves. The Peak to Valley Dose Ratio (PVDR) is of significant interest in the MRT community as it is a metric which influences how safe and effective an MRT treatment will be. If the PVDR could be measured with our technique in 3D this would be a major advantage in bringing MRT closer to patient trials. However, given previous findings we expect to have to adapt our optical system in order to measure this value accurately.

2. Methods

Samples of PRESAGE® [7], a radiochromic dosimeter, were provided by Heuris Pharma (Skillman, NJ) in the form of 9.7mm and 22mm diameter cylinders and a series of cuvettes. The cuvettes were irradiated with a range of doses and their optical density was measured with a spectrophotometer. Several cylindrical samples were irradiated with a calibration test pattern of a range of doses allowing the Optical CT system dose response to be measured, as in [4].

The cylindrical samples were scanned using an improved version of the Optical CT system described in [4]. In previous work, the large datasets involved in CT images were a limiting factor during both acquisition and processing. In the new system the camera and computer used to acquire and process images have been upgraded. High quality images were acquired quickly using an Andor Zyla sCMOS camera, with a large pixel array (5.5 Megapixels) and a 100fps framerate. New CMOS technology means that high quality cameras are more affordable and the high pixel density and fast readout rate overcome previous limitations in projection matrix size. Images were saved and processed using a Dell computer with 256GB of RAM, allowing very large datasets to be held in memory at once. This means the time taken for acquisition and reconstruction is significantly improved over previous systems.

2.1. Visualisation

A number of samples were irradiated using the different geometries possible with MRT including crossfire, interlaced and pencil beams. Projection images were acquired in a fast, ‘low-resolution’ scan with $512 \times 512$ pixel images at 1000 angular positions. The goal of this exercise was to test whether these fast scans, under 3 minutes acquisition, could provide useful information which could be used to correct MRT alignment during treatment. The projections were reconstructed to $512^3$ matrix with isotropic voxels, size $51\mu m$ for the 22mm samples and $25\mu m$ for the 9.7mm samples. The reconstructions were carried out using in-house software written in IDL (Exelis Visual Information Solutions, Boulder, CO).

2.2. PVDR Measurement

A 22mm sample was irradiated end-on with a $10\times10$mm array of $50\mu m$ microplanar beams, with a centre-to-centre distance of $400\mu m$. This sample was scanned with 3200 projections, chosen to satisfy the Nyquist sampling limit, each of matrix size $1800 \times 1800$. Although the results presented here were reconstructed non-optimally to slices of $512 \times 512$ pixels, with non-isotropic $(45 \times 45 \times 12.8)(\mu m)^3$ voxels, we are currently working on improved acquisition and reconstruction techniques that will make full use of the large pixel density of the camera and lead to still higher spatial resolution.

3. Results and Discussion

The cuvette optical density measurements verified the linear response of PRESAGE® to dose and the Optical CT system’s dose response was found to be linear up to a dose of 100Gy. We are working on methods of extending the dynamic range of the system to avoid saturation at high doses.
Figure 1. (a) Maximum intensity projection image of 4 microplanar arrays of 7 × 7 pencil beams, peak dose 300Gy, reconstructed to a 512 × 512 array. This treatment was well aligned in the centre of the sample and the individual beams are easily visualised. (b) A reconstructed slice through an interlaced pattern, 200Gy peak dose. This slice clearly demonstrates that the MRT alignment was incorrect, producing overlapping beams on the right instead of the interlaced seen on the left. (c) An xy slice through a 3-port crossfire irradiation, 200Gy peak dose, and (d) the corresponding xz reconstruction that demonstrates the misalignment problem more clearly than the xy slice (marked by the dashed line). This emphasises the usefulness of having a 3D dataset to perform MRT QA.

3.1. Visualisation
Different MRT irradiation geometries were visualised with some results shown in figure 1. From the reconstructed 3D maps the dose was well visualised and it was relatively easy, compared with other dosimetry methods, to see where misalignments occurred. Overall, these quick ‘low resolution’ scans (512 × 512 pixels, 1000 projections) would be useful for MRT technicians.

3.2. PVDR Measurement
Profiles were measured from the median value of 5 reconstructed slices, giving an effective slice thickness of 65µm (see figure 2). The median value along each beam was calculated to give a PVDR of 7 at a depth of 3mm. This is an improvement over previous Optical CT measurements, however, it is significantly lower than the values predicted by Monte Carlo simulation, which are of order 70 [8]. Although our pixel size is smaller than the microbeams, it has been shown that in order to avoid under-sampling the peak dose, a resolution of better than 5 times the smallest feature is required meaning we need a resolution of 10µm. For Optical CT, the entire sample must reside within the Depth of Field (DoF) for all points to be in focus during rotation. However, there is a trade-off between magnification and DoF, limiting the resolution achievable for a given sample size. This DoF problem will be crucial in any efforts to extend the resolution of our system.
4. Conclusions
We have demonstrated here that Optical CT is a viable technique for QA of the geometrical aspects of MRT treatments. It is, arguably, the only method currently available to perform this task adequately in 3D, something that will increase in importance as MRT develops in a more conformal direction. With new technology, scans and reconstructions can be accomplished very quickly with a small, comparatively inexpensive scanner. Using this upgraded scanner, together with GPU-based reconstruction, it will be possible to acquire and reconstruct ultra-high resolution 3D datasets within 10 minutes, which is an acceptable time frame for use as a QA tool during treatment at the beamline.

It is clear that we need to extend the dynamic range and resolution of the system if quantitative measurements are to be made at microbeam level. Several approaches have been identified. These include: (i) accurate measurement of the point spread function and deconvolution of this known blur; (ii) sub-voxel reconstructions of linear features based on prior knowledge; (iii) CT zoom imaging; (iv) overcome the depth-of-field problem by extending a method introduced for Optical CT for tissue samples, in which the sample is scanned through the DoF such that each point in the sample is in focus at some time during the scan [9].

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6. References
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