Verification of synchrotron microbeam radiation therapy using a purpose-built optical CT microscope

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Abstract. This study presents an investigation of the use of 3-D dosimetry using optical computed tomography to provide verification of synchrotron microbeam radiation therapy (MRT). MRT is based on the remarkable tolerance of normal tissues to high doses of radiation when this dose is constrained to very narrow beams. At beamline ID17 of the European Synchrotron Radiation Facility, pre-clinical radiation therapy is delivered using an array of parallel microbeams of x-rays generated by a synchrotron-wiggler source. Measurement of the dose distribution around these microbeams requires a dosimeter with high spatial resolution, and the radiochromic plastic dosimeter PRESAGE™, used in conjunction with optical CT, is highly appropriate for this task. Two solid cylinders of 9.7 mm diameter PRESAGE™ were irradiated to create quality-assurance phantoms for the optical CT microscope using the dose-painting facilities at ID17. Images were analysed to ascertain the scanner linearity over the range 8 – 35 Gy and modulation-transfer function (MTF). With the initial scanner settings, MTF was found to be greater than 30% at 12 line pairs/mm and around 8% at 20.8 line pairs/mm, thus allowing individual lines of width 24 µm to be visualised. A further 9.7 mm PRESAGE™ sample was irradiated with a typical array of microbeams of FWHM 50 µm and centre-to-centre distance 400 µm. Results demonstrate how optical CT dosimetry may be capable (after further analysis) of making quantitative measurements of the peak-to-valley ratio of the microbeams. Finally, two samples of diameters 9.7 and 22 mm were irradiated from four directions using a typical MRT “cross-firing” pattern, and then imaged at two different image resolutions. The results show how optical CT dosimetry is able both to visualise the planned dose distribution and identify an incorrect treatment delivery.

1. Introduction
It is well established that normal tissues can tolerate high doses of radiation over small volumes. Despite the challenges involved in its implementation, microbeam radiation therapy (MRT) offers considerable promise in delivering lethal doses to a tumour while minimizing damage to the surrounding healthy tissue. The preclinical MRT research programme at the European Synchrotron Radiation Facility (ESRF) [1] involves very thin slice (“planar”) beams of x-rays, arranged in parallel arrays with spaces in between. Specifically, the individual microbeams are 20–50 µm wide, with 100–
400 µm centre-to-centre (c-t-c) spacing, delivering high peak dose values and relatively low valley dose values. Unlike the X-ray sources used in conventional clinical radiation therapy, a synchrotron facility can deliver extremely high dose-rates (hundreds of kGy min$^{-1}$). However, there is as yet no established physical dosimetric system for simultaneously providing accurate measurements of the doses in the microbeam peaks and valleys and at the same time providing 3-D spatial information on the volume as a whole. Monte Carlo simulations have been obtained [2] but these have yet to be validated by experimental measurements.

The main interest of this study is to investigate the potential of optical CT as a new candidate for dosimetry of the microbeams. Several studies have shown that the radiochromic plastic PRESAGETM is a promising 3-D dosimeter system for radiation therapy and a dedicated optical CT microscopy scanner has been constructed [3] to evaluate the dose deposited in MRT treatments. This abstract presents the first study showing that this scanner can indeed make quantitative dose measurements at high spatial resolution.

2. Materials and Methods
PRESAGETM was provided by Heuris Pharma (Skillman, NJ) in the form of cylinders with diameters 22, 18 and 9.7 mm. These were machined locally to give a uniform height of 60 mm, as shown in Figure 1. A Perspex phantom was constructed in-house to provide realistic scattering conditions during irradiation. The majority of investigations reported here used the 9.7 mm diameter samples.
Irradiations were carried out at the European Synchrotron Radiation Facility (ESRF) in Grenoble on the ID17 biomedical beamline. This beamline uses a wiggler source to produce an intense, highly collimated synchrotron x-ray beam from the 6 GeV electrons circulating at a beam current of approximately 200 mA. The beam has a filtered white beam spectrum, the lower energies being cut off through the use of 1.5 mm of aluminum and 1.0 mm of copper. This resulted in a maximum intensity at 83 keV, the energy spectrum covering the range 50 to 350 keV with a mean energy of 107 keV. The entrance dose on the samples was varied over several orders of magnitude, delivered at a dose rate of ~ 80 Gy per second per mA in the machine [1, 3]. The following irradiations were performed by moving the samples through the beam to provide various patterns mentioned:

- **Sample 1**: A linearity test pattern of seven $1.64 \times 1.64 \text{ mm}^2$ squares, spanning a dose range of 8 – 35 Gy, arranged on a 9.7 mm diameter cylinder;

- **Sample 2**: An MTF test pattern, consisting of a set of near-ideal line-pairs, with a range of spacings from 0.68 – 35.7 lp/mm (732 – 14 \text{ \mu m}), arranged on a 9.7 mm diameter cylinder;

![Image](image.png)

**Figure 3**: Reconstructed images from the 3-D datasets of (a) Sample 1, and (b) Sample 2; the numbers overlaying the square patterns in Sample 1 are the doses in Gy; the letters overlaying Sample 2 denote the line spacings in lp/mm as follows: (A) 1.37, (B) 2.04, (C) 2.73, (D) 3.43, (E) 0.68, (F) 4.10, (G) 5.43, (H) 27.8, (I) 35.7, (J) 10.2, (K) 13.5, (L) 5.43, (M) 20.8, (N) 6.85; (c) plot of deposited dose vs. measured optical density, demonstrating linearity of optical CT scanner; (d) calculated MTF for the scanner in this configuration based on the measurable results from the bar pattern.
Sample 3: A typical $3 \times 3$ mm$^2$ array of parallel microbeams of nominal FWHM 50 μm and c.t.c. 400 μm projected onto a centred 9.7 mm diameter PRESAGE$^\text{TM}$ cylinder, with entry dose 600 Gy;

Sample 4: A typical “cross-firing” [1] MRT treatment, with beams entering the sample from four directions (0, 45, 90 and 135$^\circ$), applied to a 22 mm-diameter sample, with entry dose 300 Gy;

Sample 5: The same dose distribution as for Sample 4, but delivered to a 9.7 mm sample and with entry dose 140 Gy. This delivery failed for technical reasons and, although a further sample was irradiated and imaged successfully, we present these results to show the important role of 3-D dosimetry in providing quality assurance of this complex process.

Imaging was performed using the optical CT microscopy scanner described in [3]. As illustrated in Figure 2(b), the illumination arrangement is made more compact by replacing the collimated light source with a flat panel illuminator (Phlox PHLOX-LEDR-BL-100x100-S-Q-1R-24V). Spectrophotometer analysis using PRESAGE$^\text{TM}$ samples from the same batch, in standard optical cuvettes, was used as an independent measure to validate the optical CT measurements. The image field-of-view (FOV) is approximately 12 mm, and the 2-D slices were reconstructed onto matrices of $1024 \times 1024$ from a set of 800 projections, each of $512 \times 512$ pixels. Note that this enhanced pixel resolution is justified by the Nyquist Theorem at the centre of the FOV though not at the edge.

3. Results and Discussions

Figures 3(a,b) show a typical slice from the reconstructed images of Samples 1 and 2 respectively. Since we know from many previous studies that the optical response of PRESAGE$^\text{TM}$ is linear with dose, the straight line evident in Figure 3(c) provides good evidence that the new scanner has a linear response in its measurement of optical density. A similar measurement (results not shown) with squares irradiated between 20 and 80 Gy gives results that are equally linear ($r^2 > 0.994$ for both measurements). Obtaining profiles across each of the line patterns in Figure 3(b) shows that lines are resolved for all patterns up to and including (M) at 20.8 lp/mm (24 μm line width), and that the MTF at (K) 13.5 lp/mm (37 μm line width) is well over 30%.

The results of imaging Sample 3 are shown in Figure 4. One of the interests of microbeam radiation therapy (MRT) system on ID17 microbeam line in ESRF is to deliver the lethal doses to a tumour while minimizing damage to the surrounding healthy tissue. For the normal tissue sparing to be effective, the “valley” dose in the gaps between adjacent microbeams must be kept below a certain threshold. An important goal of the current research is to measure this peak/valley ratio and to compare the empirical results with Monte Carlo measurements. To do this successfully, it will be
necessary to deconvolve the known MTF from the profile in Figure 4(b), which should be achievable. However, even before accurate dosimetry at the microbeam lengthscale is demonstrated, the mere ability to image the microbeams at such high resolution is already proving important. Figure 5 shows the results of imaging the full MRT treatment applied to Samples 4 and 5. In particular, Figure 5(b) illustrates a failed treatment, showing graphically just why a full 3-D verification is important for such a new treatment modality.

4. Conclusions
We have demonstrated how the University of Surrey optical CT microscopy scanner can make accurate relative dose measurements at moderately high spatial resolution (1.64 mm)\(^2\). Images can be formed of structures at spatial resolutions of 25 microns and possibly lower, and MTF curves generated. We anticipate that it will be possible to use this information to deconvolve the lineshape of the microbeam profile and make measurements of the doses deposited by individual microbeams. These encouraging results suggest that the methods will be applicable to the synchrotron microbeam radiation therapy application. A brief initial study has shown that the technique is well able to detect errors in delivery.

Acknowledgement
The authors gratefully acknowledge the allocation of beam time at ESRF and the associated funding for experiment MD-439.

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