Ultra-high resolution optical CT dosimetry for the visualisation of synchrotron microbeam therapy doses

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Abstract. Optical CT is a method that can potentially provide both accurate dosimetry at high spatial resolution and 3-D visualisation over a large field-of-view in a single dataset. The major factors limiting spatial resolution in previous studies are analysed here and it is shown that improvements in equipment specification can overcome many of these. The need for ultra-high spatial resolution in the verification of microbeam radiation therapy verification is demonstrated and example images of a PRESAGE® sample are presented.

1. Introduction

It is well established that normal tissues can tolerate high doses of radiation over small volumes. Therefore, radiation effects in tissue are dependent not only on dose but also on the volume exposed [1]. X-ray microbeam radiation therapy (MRT) [2] is an advanced form of treatment that exploits these effects to deliver lethal doses to a tumour, while minimizing damage to the surrounding healthy tissues, by precisely controlling the size of irradiated regions. MRT using x-ray microbeams generated by a synchrotron is being pioneered at the European Synchrotron Radiation Facility (e.g., [3, 4]) and Brookhaven National Laboratory (e.g., [5]).

Many different techniques have been investigated to obtain accurate dosimetry of this challenging situation [6]. Optical CT is particularly exciting, because of the possibility of obtaining data with microscopic resolution, over the entire field-of-view of a macroscopic object. This would allow the entire microbeam treatment to be visualised with accurate dosimetry at each 3-D location. We have previously described the construction of an optical CT microscope [7]; we have developed a protocol for measuring the modulation transfer function of an optical CT scanner [8]; and we have presented preliminary results of the application of this protocol to our optical CT microscopy system, together with examples of the measurement of a synchrotron microbeam treatment applied to a PRESAGE® dosimeter [9].

The spatial resolution in our previous work was limited not by the imaging method per se, but rather by the camera and computing hardware available at the time that work was performed. Here, we show how advances in equipment performance — driven to a great extent by the explosive recent
growth of digital imaging and image sharing in the consumer sector — have the potential to make a significant difference to the capability of high-resolution 3-D dosimetry.

The key bottlenecks in the optical CT imaging process can be summarised as follows:

- Unlike the case of MRI, in which a small sub-volume can easily be excited and imaged within a larger object, it is not straightforward (although some techniques do exist) to obtain zoomed images of small regions using CT. This means that to obtain high spatial resolution images of extended objects, one needs to acquire projection images with large matrix sizes. Until relatively recently, scientific cameras capable of recording such projection images were prohibitively expensive.

- Transferring the data from the camera to the acquisition computer has, to date, been time-consuming for large frame sizes. When combined with the Nyquist requirement on the number of projections that must be acquired for correct image reconstruction, this led to prohibitively long acquisition times with our previous equipment.

- Ultra-high resolution datasets are very large (typically, tens of GB). The first stage of CT reconstruction is to create sinograms for the projection data. From a resource perspective, the most significant step here is a transposition of the data and this step is hugely inefficient if the data cannot all fit in memory at the same time.

- Large datasets require a significantly increased computational power for performing the back-projection, compared with the datasets acquired for standard clinical verification tasks.

- Visualisation and display of the results of imaging with such large 3-D matrix sizes has been, and to a certain extent still is, difficult.

2. Methods

As in our previous study [9], PRESAGE® was provided by Heuris Pharma (Skillman, NJ) in the form of cylinders of diameters 22 mm and 9.7 mm. These were machined locally to give a uniform height of 60 mm. Experiment 1 was designed to demonstrate the need for high spatial resolution. A 22 mm sample was irradiated end-on with a set of dose patterns consisting of six slits for each of a number of different doses in the range 20 – 80 Gy. This pattern was repeated with four different slit widths from 52 µm to 416 µm. Experiment 2 aimed to verify the so called “cross-firing” configuration of MRT [3], in which the irradiation was delivered from four directions by orienting the sample at 0°, 45°, 90° and 135° with respect to the beam. The dose delivered was 140 Gy and the irradiation arranged to create a uniform cubic region (1 mm x 1 mm x 1 mm) of dose deposited by the overlap of all four microbeam parallel arrays, each of which contained beams with a nominal FWHM 50 µm and separated by 400 µm.

Data were read out using the University of Surrey optical CT microscopy system, previously described in [7, 9]. For Experiment 1, the original Orca II BT 1024-G (Hamamatsu, Japan) was used with acquisition matrix size 512 x 512 pixels. However, for Experiment 2, a new camera, the pco.Edge (PCO AG, Kelheim, Germany) was tested. This has the capability of exceptionally rapid acquisition and output of images (up to 100 fps). For the initial trial, the system was operated in asynchronous mode, with the rotation stage in continuous motion and frames acquired every 100 ms. Two 3-D images were acquired: one with a large field-of-view to capture the full MRT treatment, and the second with a higher spatial resolution over a limited axial range. The first raw dataset consisted of 4000 projection images, each of size 960 x 1440, with isotropic pixels of size (24 x 24) µm² over a field of view of (23 x 34) mm², while for the second we acquired 5000 projections of size 2560 x 586 with non-isotropic pixels of size (4.4 x 22) µm² over a field of view of (11.3 x 10.3) mm², limited by the installed memory on the acquisition computer. Processing was performed using IDL on a 2010 Mac Pro with 24 GB of RAM and movies created using the medical imaging application OsiriX.
3. Results and discussion

Figure 1 displays a summary of the results obtained from Experiment 1. Notice how, for the two wider slit patterns (416 and 208 µm), the gradients of figure 1(d) are very similar, whereas for the 108 µm slit pattern, the gradient (and hence the apparent dose-response of the PRESAGE®) is around 40% lower. This is a straightforward manifestation of the effect of the modulation transfer function, but illustrates the fact that significant changes in pixel value occur even for structures that are several times the nominal spatial resolution (in this case around 20 µm). Whilst this type of effect is commonly tolerated in qualitative diagnostic imaging, resulting as it does merely in a reduction in image contrast, it leads to problems in the quantitative imaging of radiation dose and suggests that ultra-high resolution methods will be needed if MRT verification is to be successful.

Figure 2 provides a graphic illustration of the quality of data that can be obtained by imaging this type of sample at higher spatial resolution. The individual microbeams are clearly resolved and it is easy to see how this type of image, together with the full 3-D reconstruction - see accompanying multimedia files - could be used for diagnosing problems with the complex equipment required to implement MRT.

At the time of writing, our ability to handle the very large image datasets generated is still limited by the computing platform attached to our imaging camera. However, it is now possible to purchase desktop workstations with installed RAM of up to 256 GB and parallel-compute (GPU) cards that will speed up processing significantly. At the same time, the introduction of true-3D displays is on the horizon and we expect to be able to perform advanced visualisations in the near future.
4. Conclusion
Optical CT shows significant potential for ultra-high resolution dosimetry. It can already be used to visualise the results of sophisticated microbeam radiation therapy treatments in 3D and future work will focus on the degree to which we can achieve truly quantitative dosimetry measurements.

**Figure 2:** (a) Single projection from large field-of-view dataset from Experiment 2, showing mainly successful MRT treatment, but with a prominent horizontal band requiring further investigation; (b–d) example projections from the smaller field-of-view ultra-high resolution dataset, showing very clear resolution of the microbeams. Note the particular utility of view (b), which demonstrates that the dark horizontal band seen in (a), (c) and (d) is due to a plane of extra-wide microbeams.

5. References
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