Imaging and 3-D dosimetry: top tips for MRI and optical CT

Simon J Doran\textsuperscript{1,2}
\textsuperscript{1} Department of Physics, University of Surrey, Surrey, UK
\textsuperscript{2} CRUK and EPSRC Cancer Imaging Centre, Institute of Cancer Research, Sutton, Surrey, UK

Simon.Doran@icr.ac.uk

Abstract. The conference “refresher session” associated with this abstract reviews the main principles of the two most important imaging readout modalities for 3-D dosimetry: MRI and optical CT. Best practices for both these techniques are already described in several different places in the literature, but, for the uninitiated, there are a number of pitfalls. Here, I list some of the important considerations required to obtain good results from these methods and point to relevant prior work.

1. Introduction
Both MRI and optical CT are now well-established modalities for obtaining 3-D images of radiosensitive dosimetry phantoms. In the hands of an expert, both techniques can yield high quality results (e.g., [1, 2]). However, a number of pitfalls exist for the unwary researcher and, in order to obtain accurate results, a number of precautions (some obvious and some not-so-obvious) need to be taken. Commercial MR scanners and (to a lesser extent because the subject is some 20 years younger) optical CT scanners aim to make the acquisition of the 3-D data as simple as pushing a button. But although such developments are welcome, the data acquired can still lead to poor dose maps. The best way of avoiding this is to have a thorough understanding of the entire imaging process, and, to this end, previous “DOSGEL” conferences have included detailed articles on the background to both MRI and optical CT [3-7]. Familiarity with the dosimeter materials themselves is also important.

This article aims to distil the large body of knowledge into 10 easily digestible “top tips” for both MRI and optical CT. The suggestions are designed to encourage the reader to re-examine his or her protocol for acquisition and processing of 3-D dosimetry data, with the hope that this will lead to practical improvements in dose maps.

2. MRI
2.1 Decide whether MRI is the most appropriate technique.
As hinted at above, MRI has had much more time to mature as an imaging technology than has optical CT. For this reason, both the MRI equipment and the acquisition protocols tend to be more robust. Arguably, image artefacts have been better characterised and eliminated in MRI than optical CT. At the time of writing, MRI scanners are more widely available, although access is not always straightforward or cheap for the radiotherapy department. Quality control of the basic MR imaging process is embedded in the healthcare system in a way that is not true for optical CT. Furthermore, in
the specific area of gel dosimetry, there is a longer history of research into MRI methods, and the dosimeter materials themselves have been characterised more fully. Owing to the problems that occur at interfaces when using optical CT, MRI is probably also the preferred choice if one wishes to include inhomogeneities of varying densities in the sample to create a more anatomically representative phantom.

Set against this are a number of significant reasons for choosing optical CT. Optical CT is much cheaper and it is straightforward for a planning department to buy its own scanner, which will have very low running costs. Optical CT is a much faster technique than MRI if isotropic 3-D scans are required. (If what is needed is a small number of representative slices, arbitrarily oriented in 3-D, then MRI is more competitive.) The samples used in MRI tend to be water equivalent gels; this sets an upper limit to the temperature at which scanning can take place. PRESAGE™ as used in optical CT is a very robust material that allows it to be used in harsh environments [8]. The polymer gels used in MRI can suffer from oxygen-related inhibition (see below).

2.2 Use an optimised multi-echo sequence.
In order to create an image of radiation dose, one needs to measure an MR parameter that changes with absorbed dose. The most commonly chosen of these is \( R_2 \) (the reciprocal of the NMR relaxation time \( T_2 \)), and the standard method for obtaining the data required to compute an \( R_2 \) image is a multi-spin-echo pulse sequence. However, not all multi-echo sequences are created equal. In particular, the parameters chosen have a big influence on the signal-to-noise ratio and the acquisition time. De Deene and Baldock carried out an in depth study comparing different sequence designs [9].

2.3 Ensure that the 180° flip angles are properly adjusted.
The original method of multi-echo imaging was based on the Carr-Purcell-Meiboom-Gill (CPMG) pulse sequence, first proposed in the early days of NMR [10], which consists of a 90° excitation pulse followed by a string of 180° refocusing pulses. The imaging version of CPMG requires careful attention to the adjustment of RF pulse amplitudes. Modern scanners tend to use more sophisticated variants, often containing pulses with a much lower flip angle than 180°, in order to reduce RF power deposition. Furthermore, there is an increasing tendency for all the sequence adjustments to occur automatically during the “patient setup” and be hidden from the user. This “black box” approach can be dangerous. Additional complications involve the so-called “slice profile” of the RF pulses [11-13]. Since we require the final dose map to be accurate to within just a few percent, gel dosimetry is one of the most exacting quantitative tasks to use this type of multi-echo sequence. Quality assurance of the imaging results is a distinctly non-trivial exercise!

2.4 Look at the raw and fitted data, and check that they appear sensible.
Given a piece of software that claims to calculate \( R_2 \), it is very tempting simply to believe the results, particularly if the software comes from a reputable scanner manufacturer. However, even if the algorithm has been correctly coded, the non-linear fitting methods used (e.g., Levenberg-Marquardt [14]) tend to be quite sensitive to the initial guesses for the model parameters. This can lead to convergence of the algorithm at a local rather than a global minimum in parameter space, with the result that the final, fitted values are incorrect. Furthermore, as a result of the RF flip angle issues described in 2.2 above, the data may not match the assumed form of the model and this would not be obvious merely from looking at the output \( R_2 \) map.

Thus, it is very important to pick a representative sample of the voxels in the final dose map and, for each voxel, look at a graph plotting echo time vs. image intensity. Check that the fitted curve passes correctly through the points and that there are no obvious outliers. Assess visually the signal-to-noise and try to form an impression of the reliability of the data, which may be different in different regions of the phantom.
2.5 Check that there is no spatial distortion in the MR images.
Unlike in optical CT, the image formation process in MRI is susceptible to a number of different effects that can give rise to geometric distortion (e.g., gradient non-linearity, eddy currents, chemical shift and sample susceptibility) [15, 16]. This may not be obvious, but, particularly at the edges of the field-of-view, it can be significant, certainly exceeding the “2%-2 mm gamma criteria” used in [2]. Specialised distortion assessment phantoms are available, and the types of test that need to be performed have been described by de Deene [3, 5].

2.6 Check whether the pulse sequence is heating up the sample during scanning.
NMR relaxation times are notoriously sensitive to temperature and this can have a significant effect on the results of a gel dosimetry experiment [17]. In order to be able to perform an accurate calibration, one has to ensure that the sample temperature at the time of imaging is the same for both the test sample and the calibration sample. At a basic level, this requires a constancy of the ambient temperature in the scanner room and an appropriate equilibration of the sample temperature with that of the ambient air (particularly important if the sample has been stored in a refrigerator). However, a more tricky problem is that running an MRI pulse sequence deposits energy in the sample and so heats it up. The larger the number of pulses and the higher the flip angle, the more heat is deposited. This is especially problematic for multi-echo sequences designed for the quantitative measurement of $R_2$ and de Deene has made measurements of this effect [3]. The simplest solution to the problem is to increase the repetition time of the MRI pulse sequence, but this may lead to extremely long imaging times.

2.7 Use a consistent and appropriate delay between irradiation and scanning.
Unfortunately, the polymerisation that is used to detect the deposition of dose in polymer gel phantoms does not happen instantly: it is an ongoing process that cannot be “frozen” at an arbitrary time. Hence, the $R_2$ value of the gel samples continues to evolve long after the actual irradiation. This issue was recognised very early on in the development of gel dosimetry [18], but no general solution exists to the problem. Each researcher needs to evaluate his or her own particular dosimeter and determine an appropriate time after irradiation at which to perform the imaging readout.

2.8 Ensure that the gel sample is not contaminated by oxygen.
The radiation-induced polymerisation proceeds via the creation and propagation of reactive free radicals, which become attached to the end of a growing chain. This process is very sensitive to even small quantities of oxygen [19], because, in the presence of oxygen, peroxide radicals are created and these react very readily with the growing polymer chains, thus terminating the polymerisation reaction at an early stage. Two approaches are available for avoiding these problems: (a) manufacture the gels in completely anoxic conditions (e.g., in a nitrogen-filled glove box) and pour the mixture into oxygen-impermeable containers, or (b) use a normoxic gel formulation. Much has been written on this subject previously [20, 21].

2.9 Use the same size containers for both calibration and measurement.
There is evidence that the response of polymer gel samples to radiation dose varies slightly depending on the size of the container used to hold the gel. The polymerisation reaction is exothermic and so the explanation proposed [22, 23] is that the different gel volumes lead to different internal temperature rises during polymerisation. These, in turn, change the reaction rates of the various steps, the lengths of polymer chains produced and hence the $R_2$ value and calculated dose.

2.10 Beware of potential fractionation effects.
One of the supposed benefits of polymer gels is that they are integrating dosimeters, i.e., they record the total dose to which they have been exposed, leading to the ability to verify complex multi-exposure treatments such as IMRT. However, Karlsson et al. discovered significant differences for
some gel formulations depending on whether the dose was given to the gel in a single fraction or in multiple exposures [24].

(Aside: A fundamental disadvantage of chemical dosimetry is that the dosimeter property from which absorbed dose can be calculated (in this case $R_2$) is dependent not only on dose, but on a number of other factors including some relatively complicated reaction kinetics that are sensitive to the thermal history of the sample. All of problems 2.6−2.10 are linked with such chemical effects. There are also concerns relating to the ability of monomer units to diffuse within the gel, which can lead to anomalous readings in regions of very high dose deposition (ref), and finally, there can be frustrating inter- and even intra-batch variations of calibration constants (ref) between samples that are all prepared using nominally the same procedure. Medical physicists generally prefer to rely on physical radiation detectors like ionisation chambers, which also have the advantage of giving an instantaneous result, without having to wait for a chemical reaction to occur. These issues may perhaps be a contributing factor to the relatively slow clinical uptake of gel dosimetry compared with, say, arrays of diodes.)

3. Optical CT

3.1 Clean the apparatus well and keep sample surfaces pristine.

MRI is an imaging technique that is limited by signal-to-noise ratio (SNR). This is caused by the relatively small difference between nuclear energy levels, which leads to a low “signal” term, and the inability to cool the sample below the freezing point of gel water, which leads to a relatively high level of thermal noise from the probe. Standard clinical x-ray CT is also SNR-limited, this time because of restrictions on the amount of dose that patients can receive. By contrast, optical CT can use an effectively unlimited number of photons to improve its “counting statistics”, simply by increasing the exposure time of the camera or by averaging multiple exposures. The ideal optical CT scan is thus not truly SNR-limited. However, in practice we do see noise and much of this is caused by “dirt”.

On its path from the source to the camera, light has to pass through a number of media and interfaces. Each surface in the optical path has the potential to become scratched or dusty. The outside of the matching tank can also be contaminated with oily liquids that are difficult to clean and that leave smeary marks. In principle, effects like this that are time-invariant can be “calibrated out” using the “correction scan” procedure described below. However, it is always better to start with high-quality data that need little correction. Keeping equipment and samples clean and the surfaces well polished should improve image quality.

More troublesome, perhaps, are the effects of contaminants in the matching liquid and sample. Dust particles enter the matching tank from the surrounding air or are introduced when the samples are loaded, and these build up over time. The particles appear as dark specks and are particularly noticeable in high-resolution scans. They often move about, carried by convection currents or the slow turning of the sample. The reconstruction algorithm is unable correctly to take account of these unwanted time-varying features in the projections and this results in artefacts in the reconstructed images. If the impurities are embedded in the sample, then the black specks move around coherently with the sample and are reconstructed as high intensity features in the image. This may or may not be troublesome, but one should always be aware that if any feature is completely opaque, then this removes from the dataset all information from ray-paths that pass through the contaminant.

3.2 Devote time to optimising the composition of the matching liquid.

In contrast to x-rays, whose direction of travel is not affected by the orientation of boundaries between materials, light is refracted when it crosses an interface. The refractive index of the dosimeter (around 1.33 for water-based gels and 1.5 for PRESAGE™) is very different from that of air, and the light ray-
paths deviate substantially from the parallel lines required by the standard “back-projection” CT reconstruction algorithm. Cylindrical samples act like 1-D lenses and it is difficult to generate artefact-free images from this type of data. The current generation of scanners solve this problem by placing the sample inside a tank of “index-matching” liquid. Taking the simplest example, that of PRESAGE™, which does not need a container, we require that the matching liquid has an index that is as close as possible to that of the dosimeter. The liquid is generally made from a mixture of two components (one with a higher and one a lower index than the dosimeter). These are combined in a proportion tailored to the given batch of dosimeter.

Getting the right proportions can be time-consuming, particularly if the quantity of matching liquid to be produced is large. However, the time spent pays dividends in a large reduction of the “sample edge” artefact in the final image and a corresponding increase in the volume of the dosimeter that yields accurate data. It is not always appreciated that the region of the final dose image that is affected by the edge artefact extends well beyond the bright ring seen on images.

3.3 Choose the right sample containers.

To date, PRESAGE™ is the only solid optical CT dosimeter. Others are gel-based and thus need a container. Doran et al. [25] showed how to model the general situation in which the gel, the container and the matching liquid all have slightly different refractive indices. Many of the clear plastics commonly used to make bottles (e.g., polyethylene terephthalate, PET) have an index that it significantly higher than that of gel, but it is possible to obtain specialist plastics (e.g., Teflon FEP®), which match well. The latter are strongly recommended, as the difference in the projection profiles near the sample edge is considerable.

3.4 Use a correction scan.

The Beer-Lambert law \( I = I_0 \exp(-\alpha x) \) describes optical absorption in a dosimeter, with the term \( I_0 \) representing the incident light intensity. In an imaging context, \( I_0 \) is a spatially varying parameter (i.e., its value is different for each pixel of the projection images) that takes into account a range of intensity modulating effects that are not caused by radiation-induced changes in the dosimeter. These include: (a) directional variations in the light source intensity; (b) background absorption in the dosimeter; (c) spatial variations in the detector sensitivity — these must be time-invariant; and (d) static imperfections in the light transmission properties of the system components.

The easiest way to account for these properties is to scan the sample prior to irradiation and then again afterwards, keeping all the scanner settings constant. As described in [25], as simple division of the two datasets will result in a dataset with the unwanted variations removed. However, it should be noted that any intensity variations that are additive (e.g., a constant ambient light contribution) are not removed correctly by this procedure. These should be eliminated at source if possible, or alternatively an estimate subtracted from both the correction scan and data scan raw data before they are combined. This is the normal method for eliminating the “dark current” contribution [26].

3.5 Make sample changing easy and reproducible.

If designing one’s own optical scanner, it is highly desirable to include the ability to re-load samples accurately and reproducibly with a minimum of adjustment, both in terms of the vertical and lateral position and also the rotation angle. This is particularly relevant for the correction scan described above. If the sample repositioning can be achieved to a pixel level of accuracy, then it becomes possible to correct for sample imperfections (scratches, inclusions, etc.) as well as broad variations in the light field.
3.6 Add a dye to the matching liquid.

As described above, the correction scan method is capable of taking into account background absorption in the dosimeter. However, if the unirradiated dosimeter is absorbing to any great extent, then there will be a large intensity variation across the projections images in the correction scan, with the region outside the dosimeter being very bright. This reduces significantly the dynamic range that is available to record radiation-induced changes. The problem can be circumvented by adding a dye to the matching liquid whose absorption coefficient matches that of the unirradiated sample. Note that one should not allow the detector in the camera to saturate, as “blooming” can occur — see [27] for further details.

3.7 Beware of scattering.

It is well known that the Beer-Lambert law is only an approximation for scattering systems. At high scatterer concentrations, the exponential relationship breaks down, so that the whole basis of the optical readout (via spectrophotometry using cuvettes as well as via optical CT) is not valid. However, even at much lower concentrations, optical CT imaging can be badly affected. Although very few comparative studies have been performed to date, it seems reasonable that CCD-based techniques will suffer more than scanned laser techniques. De Jean et al.[28] and Bosi et al. [29] have presented initial data showing how scans using the Modus commercial device are affected by scatter.

3.8 Check for unwanted reflections in the apparatus.

In [30], Jordan warns of the dangers of multiple reflections at optical interfaces. In some cases, these may lead to interference fringes. In optical apparatus where there are shiny metal components, there is the potential for light to enter the detector via complex reflection paths and contaminate the desired signal.

3.9 Compare calibrations with a spectrophotometer.

There is a tendency in optical CT dosimetry to “normalise” data, on the basis that the relationship between dose and change in absorption coefficient is linear. This procedure hides changes in dose-response characteristics between batches and may obscure important effects [31]. Babic et al. [32] have shown that, at least for the Fricke dosimeter, careful methodology allows an absolute relation between dose and change in optical absorption coefficient to be obtained. It is recommended that the results of the CT imaging reconstruction be compared with spectrophotometer measurements on cuvettes irradiated to the same dose (but see Sec. 2.9 for a caveat if polymer gel dosimeters are being used.)

3.10 Understand the chemical and radiation physics properties of the samples.

As hinted at earlier, the number of publications characterising the radiochromic materials used in optical CT is much smaller than the equivalent body of literature for polymer gel MRI dosimetry. Two examples illustrate the need for users of optical CT to be vigilant: (i) Babic et al. [31] showed that when using Fricke gels, the source of xylenol orange (Aldrich, Sigma or Sigma-Aldrich) made a significant difference to the dosimeter properties. After some detailed detective work, a very interesting story emerged and led to recommendations for the procedure to be followed when using xylenol orange Fricke gels. (ii) PRESAGE™ is known to be radiologically non-equivalent to water (and hence soft tissue). The first comprehensive analysis of the difference in radiation physics properties has recently been completed by Gorjaara et al. [33]. Looking at the results of their Monte Carlo simulations, it appears that the density-corrected depth-dose curve for PRESAGE™ is different to that of water. Further work is necessary to establish whether this has implications for the calibration procedure for this dosimeter — can Oldham’s depth-dose method [34] be used? — and whether simply providing a CT scan of a PRESAGE™ phantom to a treatment planning system leads to an accurate calculation of the absorbed dose.
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