Where does gel dosimetry fit in the clinic?

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Abstract. For over a decade our community has considered gel dosimetry a promising technique for the clinic, since it provides a unique methodology for three dimensionally dose measurement of the complex conformal dose distributions achieved by modern techniques such as Intensity Modulated Radiation Therapy. Even with improved gel dosimeters (such as normoxic polymer gel systems) and more accessible imaging for dose readout, this potential has not yet been fully realised. This may be because alternative tools have been able to more easily provide the technical and dosimetry quality assurance performed at specific steps in radiation treatment. The development of Adaptive Radiation Therapy is introducing complex processes for radiation treatment that depend on intricate links between various stages from imaging to treatment planning to radiation delivery, and back through loops depending to the level of adaptation. These links often involve human interpretation and intervention. Therefore, there is a greater need for comprehensive quality assurance of the whole radiation therapy process when adaptive techniques are first being developed, in regular quality assurance of the performance of these techniques within a radiation oncology program, and in independent outside credentialing of cancer centres by independent agents. I will attempt to make the case in this introductory paper to Dosgel08 that this is the role uniquely served by gel dosimetry.

1. Introduction

Radiation therapy is a dominant cancer therapy with an appropriate level use estimated in excess of 50% in developed countries [1,2]. Radiotherapy is a localized treatment intended to deliver a sufficient and uniform dose to the target, to achieve tumour control, while minimizing complications by limiting the dose to normal tissue. Over the years, external radiation therapy has progressed considerably towards this goal by the development of three dimensional (3D) conformal radiation therapy techniques [3,4] such as achieved by Intensity Modulated Radiation Therapy (IMRT). These are becoming standards of practice benefiting a significant proportion of patients [4-6]. Conformal therapy by brachytherapy has also advanced through improvements in delivery systems and in imaging for planning and for source localization.

The dose distributions resulting from 3D conformal therapy and IMRT are designed to fit tightly about the specific target volumes and, therefore, the possibility of missing the target increases, because of patient setup errors, organ motion, or even small fluctuations in treatment delivery. Therefore, the verification of the actual dose delivery is vital to the effective delivery of conformal radiation therapy [4,7-9]. The conformal dose delivery achieved in modern IMRT delivery techniques results in complex dose distributions characterized by non-uniform doses with large dose gradients in small spatial displacement. Furthermore, the doses are delivered dynamically, so that specific points in the
irradiated volumes may receive their final dose only over a total treatment time. Thus the dose measurement required for the verification of IMRT dose delivery becomes very labour intensive and often impractical with traditional dosimetry (e.g., using ion chamber, TLD, or film techniques) [10-12]. There is, therefore, great interest in developing new verification techniques that provide improved dosimetry techniques using flat panel devices, 2D and 3D arrays of detectors, scintillation devices and other means [9,13-15].

The limitations of conventional dosimeters spurred the development of gel dosimetry [7,16-18], the topic of this workshop. Gel dosimetry has shown considerable promise for high resolution, tissue equivalent 3D dosimetry for nearly two decades (see Figure 1). However, it has still not come into common clinical use. Initially this was the result of two problems: 1) the original polymer gel dosimeters (which had greater temporal stability) were difficult to prepare in the hospital setting as they contained toxic constituents and, until recently, required anoxic preparation and 2) ready access to imaging techniques for clinical reading of the gels was often very restricted. Recent developments suggest that these impediments are slowly being removed. The development of normoxic and less toxic polymer gel dosimeters, and the development of optical imaging techniques for readout in Fricke gel dosimetry, have made their use in the clinical setting more tenable. And, while MRI has historically been the standard imaging modality [17,19-21] for quantitative 3-D dose distributions, other physical properties of irradiated gel, such as opacity and density, also vary with dose as a result of the radiation-induced formation and precipitation of polymer. This provides the potential for dose imaging using optical techniques [22-25], or x-ray computed tomography (CT) [26-28]. These alternative imaging schemes are attractive since access to MRI, the gold standard imaging, is often very limited given the long waiting lists for patients requiring diagnostic scans [27,28]. Optical CT imaging (OptCT, to distinguish the technique from OCT, optical coherence tomography) is especially promising because of the ability to construct accurate low-cost benchtop scanners [22-25,29,30].

Figure 1 - An illustration of the strength of gel dosimetry from an example with pencil beam irradiations on a bench top cobalt tomotherapy device[31]. The left hand image shows a maximum intensity projection (MIP) dose map of the 3-D dose plan generated by our in house treatment planning system. The middle figure is the MIP [32,33] image for the same dose delivery as determined by optical CT measurements on a VISTA cone beam CT system. The right hand image is a three dimensional 5% 5mm gamma evaluation of the Low gamma function [34,35]. In this particular case we have used the gel dosimeter to assess/commission our treatment planning system. From the location of the failures we have been able to identify limitations with the planning system algorithm.
Even with these improvements, gel dosimetry has not achieved the clinical prominence indicated by its promise in terms of resolution, tissue equivalence, etc. This may be because in many instances its practical use is more laborious than really required, especially in situations well handled by other techniques. For example, while gel dosimetry does provide a strong modality for the quality assurance of IMRT delivery, other techniques such as the use of film[36-38], dosimeter arrays[39-42] and portal imaging[43-45] provide sufficient assurance of dose delivery for the day to day clinical practice. Then perhaps the strength of gel dosimetry is not the evaluation of ‘familiar’ IMRT delivery (i.e., the delivery that has been well tested and established in a clinic).

2. Image Guided and Adaptive Radiation Therapy

The requirement for accurate targeting in conformal therapy was recently indicated by de Crevoisier et al. in a retrospective analysis of treatment plans for radically treated prostate cancer patients [46]. The authors revealed that the extent of rectal distension in their planning scans was a predictor for biochemical control. The observed result of target miss (since on treatment without rectal filling the prostate would have shifted) was that the biochemical control rates in the distended-rectum population were 60% (all stages) as opposed to 83% in the non-distended population.

This work serves to underscore the previous recognition of the importance to develop treatment setup and image guidance techniques [47,48]. On-line imaging (particularly cone beam CT) is prominent in this development of Image Guided Radiation Therapy (IGRT) [49-56]. IGRT is inherent in helical tomotherapy units [48,57] and has been augmented on conventional linacs by advances in x-ray detector technology and computing capacity [55,56,58-61]. IGRT is becoming a standard of care in radiation therapy [62] with over three quarters of the new radiation therapy units being installed with cone-beam CT systems for guidance. It should be noted that some do debate the value of IGRT with current technology[58].

One observation from the increased use of IGRT has been to note the potential for significant re-modeling of the tumour and surrounding tissue during the time course of the multiple fractions of radiotherapy[63,64]. This change of anatomy which might be seen over the weeks of IGRT has lead to the development of off-line approaches wherein the treatment plan is re-designed (daily or weekly) to accommodate volume changes ensuring consistent target coverage or avoidance of normal structures. Such Adaptive Radiation Therapy (ART) may incorporate kVCT (on an IGRT linac) or MVCT (on a tomotherapy unit) images and treatment monitoring and potentially for treatment planning (although the patient may be directed back to the CT simulator for replanning, see Figure 2). This process requires considerable data processing for image registration and analysis[62,65-67]. More sophisticated approaches envisage adaptation over each fraction [68]. The proposals for inter-fraction ART are not limited to corrections for tissue geometry. The potential for on-line dosimetry (perhaps via exit beam dosimetry with portal images or tomotherapy CT detectors) during each treatment raises the feasibility of dose delivery monitoring with subsequent correction as fractions continue through the treatment course.[69-73]. This implies that each fraction may delivery slightly different doses via slightly different MLC sequencing. Other researchers have proposed using biological and functional imaging to assess tumour response (perhaps looking at changes in hypoxic tissue as treatment progresses). These sophisticated plans require a change of subsequent dose delivery and the efficacy of the treatment will require that the dose is delivered correctly after all of these interventions. Therefore, the dosimetry problem initially introduced with the development of conformal therapy has become more complex still. Modern treatment is an increasingly complex process involving data transfer between sophisticated advanced equipment, often with human evaluation at critical steps to evaluate and choose between different courses of action at critical steps.
Figure 2 - A diagram showing some of the potential processes that are in current practice or have been envisaged for various strategies of adaptive radiation therapy. In general there is the common thread going from initial imaging for planning purposes (which may involve multiple modalities and image fusion), contouring by a physician or planning therapist, treatment planning by a planning therapist or dosimetrist with plan evaluation and review by physicists and radiation oncologists, data transfer to the treatment unit which has some kind of image guidance and perhaps exit dosimetry available and then treatment delivery. The adaptive process may be as simple as on-board imaging immediately prior to treatment with megavoltage portal imaging or kV imaging (perhaps cone beam CT) for setup validation with correction if required before treatment. As schemes get more sophisticated they may involve correction for patient motion perhaps by gating the radiation beam so that it is irradiating the patient when the target is in the beam port, or by dynamically collimating the radiation so that it follows the moving target of the beam to accommodate organ motion or even respiratory targeting in which the multi-leaf collimators are tracking the respiratory motion. This second approach may be more manageable in units in which the target is observed directly rather that the motion followed through surrogate measurements. This is one motivation for the proposed cobalt MRI units [70,71] which may enable imaging during the radiation delivery. In various schemes of inter-fraction adaptive therapy subsequent radiation delivery may be adjusted to ensure the dose delivery over a complete course is correct (based on comparison of daily doses determined by exit dose measurement to intended) of the account for biological response to treatment (either from changes in tissue/organ geometry in the treatment field to assessment of response by biological imaging). In each of these schemas, the processes are complicated and require sophisticated technology along with human interpretation and intervention. The quality assurance of these processes is not easily achieved by traditional QA tools and tests which usually focus at limited select points in the process.
3. Modern Radiation Therapy QA: From Dosimetry to Process validation

How well then is the radiation oncology community assuring that modern radiation therapy is well delivered? As noted above, there are a large number of techniques that have been established for dosimetric verification at specific stages of IMRT (for example, the assessment of individual port delivery through a given sequence of dynamic MLC at a given gantry angle). Similarly, various approaches have been proposed for the quality assurance of other technical components involved at different stages of IGRT [74-80]. Other workers have reviewed the particular experience of their QA programs perhaps to evaluate the impact of new technology, or to establish benchmark tolerances for deviations in particular tests [81-88].

An indication of the success of our efforts has been reported recently by Geoff Ibbott and colleagues at the Radiological Physics Centre. While credentialing institutions participating in IMRT clinical trials under the auspices of the National Cancer Institute, the RPC provided them with anthropomorphic phantoms (of the head and pelvis) containing various dosimeters and regions of interest for irradiation. The centres were given an IMRT objective and asked to irradiate the phantom using their usual IMRT planning and delivery. The results were sobering; about one third of the centres failed to achieve the goal of irradiating correctly within 7% dose or 4mm distance in the high dose region near the organ at risk.

The RPC experience, the results of analyses by various individuals in their clinics, and the deliberations of working groups are leading some to conclude that radiation therapy quality assurance programs need to be rethought. For example, people are suggesting that risk analysis be undertaken to identify critical points requiring greater vigilance. Also there is an appreciation that new approaches are required to look at the complete chain inherent to modern delivery accounting for the complex interactions and connections of the various components [89-92]. With this view it may be that clinical QA will become more of an integrated activity and I would advocate that gel dosimetry may have a unique role to play in this future.

4. Clinical role(s) for gel dosimetry

It is clear from the discussion above and from the illustration in Figure 2, that IGRT is a complex process and that the treatment of a particular patient with adaptive approaches requires considerable effort. I would suggest that one way to assess if the process is working well is to use gel dosimetry to mimic a patient throughout all the process including the various adaptive steps. Similar schemas that have been proposed over the years illustrating the strength of gel dosimetry for quality assurance of IMRT [12,93-96] and of precision stereotactic delivery [97]. Recently a couple of groups [98-100] have shown that gel and radiochromic solid polymer dosimeters operate well in the RPC phantom. Preliminary investigation has also shown that gel dosimeters can be used in conjunction with dynamic phantoms [101]. In all these examples, the gel dosimeter mimics the target and surrounding volume sufficiently well that contouring and imaging are possible and the complete planning and delivery validated.

The same approach is readily adapted to the evaluation of ART in a given clinic (see Figure 3). With suitably stable dosimeters, the tests could be run over multiple fractions to validate inter-fraction adaptation. While the dosimeter and phantom preparation should be done by the physics group (or perhaps a credentialing service), the rest of treatment planning and delivery should be performed by the individuals taking on their various roles as in patient treatment (e.g., CT imaging by planning therapists, contouring by oncologists, computerised treatment planning by the planning RTs and dosimetrists, plan evaluation by physicists and oncologists, treatment setup, onboard imaging and delivery by the treatment therapists, etc). Then the tool would be handed over to the physicists at the end of the process for the final confirmation that the intended dose delivery was achieved. The intent is to perform the quality assurance of the complete adaptive flow for the treatment of the patient in the clinic. There will be further tests required if the gel dosimetry fails. However, good performance at regular intervals would provide a measure of confidence in the operation of the comprehensive program. While this application of gel dosimetry is not much different than that envisaged since the
Figure 3 – An example of the implementation of a gel dosimetry quality assurance assessment of an Adaptive Radiotherapy Procedure. In this particular case the work is to QA the simple case of cone beam kVCT verification and correction of patient setup prior to treatment. In the process QA advocated in this paper various steps could include: 1) preparation of the sample and insertion of sample into an appropriate phantom (preferably anthropomorphic) by the physics team, 2) imaging and contouring of images by the CT therapists and radiation oncologist, 3) treatment planning by the dosimetrist/planning therapist then transfer of the beam data and phantom images to the treatment unit, 4) set up verification in this case with the cone beam CT available on the linear accelerator, 5) adjustment of patient setup (in this case through a automated table shift determined by the Varian registration software as per clinical practice, 6) dose delivery as per the treatment plan, (steps 4-6 would be performed by treatment therapists) 7) subsequent removal of the dosimeter and dose imaging by the physics team and 8) data registration and 9) test evaluation by the physicists. In this image the image on the left at 8) is the treatment plan and the image on the right is the measurement. The colour was above is the gamma evaluation, our software enable comparison of the dose volume histograms for any contour specified.

In the early days of gel dosimetry, the change is that the verification is not limited to testing individual steps in the treatment process, but rather in the validation of the whole process.

5. Conclusions

The last few years have continued to push gel dosimetry into the clinic. New dosimeter formulations and more readily available imaging have made its use more attractive. Along with the internal ART and IGRT quality assurance that I am advocating, many of the uses suggested in the past are still valid. Gel dosimetry is well suited for the commissioning of treatment delivery and treatment planning in
difficult situations that may require high resolution data, and the commissioning of new treatment techniques using an approach similar to Figure 3 but executed by an implementation team. We will hear about these uses over the next four days of this workshop, and I am looking forward to learning how we can better use the gels that we have been so passionate about for these many years. The take home message I want leave you with at the onset is that we have too often advocated the use of gel dosimeters when other tools were much more suitable. This may have hurt the adoption of the technique. I believe gel dosimetry will finally come to fruition when we advocate its use where other tools cannot serve.

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7. References

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