Preliminary investigations of a dynamically deforming target-in-gel dosimeter

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Abstract. To increase the clinical utility of deformable gel dosimeters an X-ray CT visible target region is introduced into the DEFGEL dosimeter, with the goal to enable the determination of the change in marginal doses around planned boundaries. The production of the dosimeter components is detailed and the requirements in making, deforming, irradiating and analysing the dosimeter are explored with several areas of required improvement identified. A single degree of motion is used to deform the dosimeter with the intent of identifying the volumetric dose changes caused by the deformation. The planned target volume dose structure was registered to the physical target region present in an optical CT data array and the dose volume histograms of the target volume while static and undergoing deformation are investigated and reported. The total dose to the target volume was shown to decrease by 9.4% due to a 1cm compression of the entire dosimeter volume. Further ways to improve the use of the target region are suggested with a view to improving the dose map information that can be obtained from target-in-gel dosimeters.

1. Introduction

Polymer gel dosimeters [1] are uniquely suited for the validation of the effects of motion and deformation [2] in radiotherapy treatment planning systems and treatment delivery [3]. The registration of points is usually achieved by tracking the movement of fiducial markers which provide details of motion within the entire volume of the dosimeter [4]. The lack of internal features makes it difficult to assess the accuracy of a volumetrically targeted treatment plan, as the only structure observable is the outside of the dosimeter volume, which would presumably contain all treatment volume margins.

It may be that the addition of an internal feature to define a target region can improve the assessment of dose coverage in a planning target volume (PTV) [5], or indeed any volume that changes as a result of motion and deformation. There is also the complicated issue of quantifying the dosimetric impacts of motion, positioning and deformation, which may be approached with more rigour by 3D dosimeters that can measure whilst undergoing dynamic changes. This internal feature is implemented as gel dosimeter material nPAG with the addition of an X-ray contrast agent in the form of Isovue. The resulting dosimeter configuration is termed the IDEFGEL (Isovue + DEFGEL [6]). The ability to discriminate between in and out of volume dose is performed through the investigation of the resulting dose volume histograms in each region. By comparing a static and deforming case it is expected that the amount of dose that is deposited in material that moves into or out of target region can be volumetrically assessed.
and provide a measurement of the degree to which a margin should be extended to deal with a given range of motion or deformation.

The following study was conducted using a concentration of 0.7% w/w Isovue that provided a contourable target region within the dosimeter volume. A simple breathing motion is used to provide the deformation of the dosimeter that is to be examined, with the intent being that a direct correlation between the volumetric deformations can be drawn to the change in the total dose delivered to the two volumes. The impact of several external factors as well as those directly involved in the delivery and measurement of the dose distributions in the target volume are discussed with several proposed causative relationships detailed, with the intent that addressing these factors will produce a clinically viable gel dosimeter containing a dose sensitive target region that is visible on X-ray CT.

2. Method
The feasibility of the gel dosimeter containing an Iodine doped nPAG (InPAG) target region were investigated through analysis of the change in dose response localized within and around the target volume as it underwent a repeatable deformation. The impact of Isovue on the nPAG dosimetric properties is outlined in a previous article and the production process follows closely that of Yeo et al [6], with details of inserting the target region outlined below.

2.1. Gel formulation, production and target region insertion
The nPAG used in this study is the same formulation used by Yeo et al [5] and is composed of 6 % w/w gelatine (Type A from porcine skin, Sigma Aldrich Ltd., Oakville, Canada) for the hydrogel matrix. Dissolved in this matrix are 3 % w/w N,N’-methylene-bis-acrylamide (Bis) and 3 % w/w acrylamide (Aam)(both from Sigma Aldrich Ltd.). The remaining mass is DI water, with 0.01 mM hydroquinone and 5 mM of Bis[tetrakis(hydroxymethyl-phosphonium)]sulphate (THPS) added to combat autopolymerisation and atmospheric oxygen diffusion respectively with the target region containing 0.7% w/w Isovue as detailed by Watson et al [7]. The standard nPAG formulation is first poured into a plastic PET sample container lined with a latex membrane and a hollow plastic cavity is inserted into the center of the gel with a foil lining used to seal the top of the vessel. A portion of the same batch of nPAG mixed with 0.7% w/w Isovue and set inside the cavity. This concentration was used as it was the smallest amount that still provided enough contrast in X-ray CT. Using 0.7% w/w of Isovue provides more definition for the edge of the target region but to minimize the impact on the dosimetric properties a lower concentration was used. With further experimentation and better knowledge of the dosimetry and chemistry changes stemming from the addition of Isovue 0.7% w/w will be used. A silicone mold the same shape and dimension of the plastic pipette bulb used to create the cavity in the dosimeter was manufactured and the target gel is set in this material. The silicone is well sealed to prevent oxygen diffusion during setting and has the added advantage of not adhering to the gel surface, allowing the gel to be easily removed. For this study 3 samples of this configuration were fabricated with one sample containing several internal fiducial markers at the target boundary to track the magnitude of motion.

Both gel containers were placed in a refrigerator at 4°C and set for 12 hours before the target region was inserted into the larger gel volume and standard nPAG poured into the remaining gap at the top of the dosimeter. The latex membrane was sealed and remained in the form fitting sample holder and set for 10 more hours before imaging and irradiation.

2.2. Motion phantom setup
The IDEFGEL samples were housed in an acrylic cylinder holder lined with soft foam to centre the dosimeter in the holder without impeding deformation and ensuring the “relaxed” position was repeatable for all 3 samples. The cylinder holder was placed in a Modus Medical Devices Quasar™ respiratory motion phantom and fixed in place using a phantom setup board built at RMIT University (Melbourne, Victoria). The phantom setup board prevented the compressed gel from shifting the position of moving components when relaxing and made repeating setups on multiple devices with several samples an easier process. The imaging and irradiation setup is pictured in Figure 1.
Figure 1. (Left) Motion phantom setup on a linac couch with the gel housed in the thorax phantom where the wood motion insert is located. The motion setup is held in place by a phantom setup board. (Right) the IDEFGEL housed inside the acrylic holder surrounded by a layer of foam.

The Quasar phantom was used to simulate a breathing motion of 1 cm in magnitude at a rate of 20 breaths per minute. It was noted that there seemed to be some damping of the oscillation due to over compression of the gel and some possible slippage of components in the motor.

2.3. Imaging and treatment planning
A Phillips Brilliance Big Bore X-ray CT was used for imaging the dosimeters housed in the motion phantom as pictured in Figure 1. A 4D CT of the dosimeter containing multiple fiducials was captured with a set of bellows attached to the motion phantom to track the breathing pattern. Standard CT of the other two samples were imaged to investigate the uniformity the target regions between samples and for planning treatments on.

A static CT plan was created in Eclipse and the visible Iodinated nPAG (InPAG) target region was denoted as the PTV. A dose of 1.5 Gy was prescribed to the target volume to ensure irradiation corresponded with the full dynamic range of the IDEFGEL [7].

2.3.1. Irradiation of IDEFGEL. The treatment plan was delivered using a Varian TrueBeam medical linear accelerator (Varian Medical Systems, Palo Alto). The plan was delivered to one sample that remained static and one sample that underwent the same motion during delivery as imaged on the 4D CT. The treatment plan was a VMAT protocol that delivered 208 MU through two 180° arcs.

The samples were all then read out using a Modus Medical Devices (London, Ontario) VistaCT Optical CT scanner.

3. Results
Dose coverage within the target volume is a metric that can be used for an assessment of how large the variation introduced by motion is, with several tools available for analyzing the extent of dose coverage and agreement between planned and delivered dose. The plan DVH for the target region was reported using the CERR MATLAB extension and a binary mask of the structure volume was overlaid on the gel volume array using the target region boundaries as co-location points. The comparison of DVH’s for the PTV is plotted in Figure 2.
Figure 2. Cumulative DVH for the planned treatment volume compared to the doses measured in the target volume of the static and deforming IDEFGEL samples. The doses have been calibrated using the calibration factors in Watson et al [7].

A second structure was delineated in eclipse that encapsulated the gel dosimeter volume with the exclusion of the target region. This region includes the peripheral doses at the boundaries of the PTV and dose wash due to the VMAT protocol. The boundaries of this dose structure in eclipse extend beyond that of the ITV and include some volume that was expected to receive no dose which could artificially inflate the perceived effect of excess dose deposited due to dose wash. However, including the entire gel volume was considered a more sensible option rather than defining an arbitrary boundary within the dosimeter that had no correlation to a physical feature, such as the boundary created by the Isovue in the target volume. The DVH of the remaining IDEFGEL volume in the static and deforming samples is displayed in Figure 3.

Figure 3. Cumulative DVH of the dosimeter volume excluding the target volume for the static and deforming IDEFGEL compared to the plan DVH. A scaled calibration factor is used to account for a small amount of Isovue diffusion prior to irradiation, this factor is explained in more detail by Watson et al [7].

Some key dose metrics from the DVHs above are collated in Table 1.
Table 1. The significant dose values of the two regions present in the IDEFGEL for both the static and DEF samples compared to those in the delivered treatment plan. The mean values are weighted to represent the volume average of the dose structure. The minimum dose values in the greater dosimeter volume are subject to more uncertainty than the other gel results due to RI mismatch artefacts.

| PTV            | Dosimeter Volume |
|----------------|------------------|
|                | Max(Gy) | Mean(Gy) | Min(Gy) | Max(Gy) | Mean(Gy) | Min(Gy) |
| Plan           | 1.52    | 1.32     | 0.68    | 1.29    | 0.21     | 0.01    |
| Static         | 1.78    | 1.16     | 0.18    | 1.36    | 0.51     | 0.03    |
| DEF            | 1.89    | 1.05     | 0.14    | 1.14    | 0.55     | 0.03    |

By being able to isolate the regions of the dosimeter and analyse the dose metrics of the PTV and the greater dosimeter volume independently the impact of the DVH analysis should be greater and inform more rigorous absolute dose measurements in conjunction with other dose metrics that are more suitable to conformation analysis of the 3D dosimeter volume.

4. Discussion
The analysis of the target region in this study was focused upon the dosimetric features of the plan comparison, which led to a focus upon the dose volume histogram of the target region rather than a gamma test. Given the simple object shapes that were present in this study, both in the dosimeter and planned dose delivery, the comparison of DVHs for the static and deforming cases provides a more meaningful study of a single feature. This feature is of course the deformation of the target region as the applied breathing motion forces it to depart from the conformation expected by the plan, quantifying the impact of this motion directly in relative dose terms.

In the comparison of the dose coverage of the target region displayed in Figure 1 it is evident that the deformation of the target region has reduced the dose delivered to the target region, decreasing the mean dose delivered to the volume as documented in Table 1. The decrease in mean dose to the volume is likely to stem from the plan assuming a static volume as expected. The change in dosimeter volume introduces peripheral gel material into the target volume receiving a higher dose, while some mass from the target region is forced outside the primary beam decreasing the dose readout when the gel is once again in the static state. This effect can also be seen in Figure 3 where the DEF sample DVH receives on average a much higher dose compared to the static sample and has a higher mean dose. A large portion of the dosimeter volume also exceeds the dose expected according to the plan DVH indicating that these parts of the dosimeter volume spent significant portions of time in the target region during treatment delivery.

The static gel irradiation does not appear to correlate well with the planned dose distribution, to a significant degree when inspecting the absolute dose values present in Table 1. This discrepancy points to an error in the calibration function used to convert the transmission values from OCT to dose, which may be an effect of several factors. As has been stated previously the diffusion of Isovue out of the target region presents an issue as there is a spatial and temporal dependence on dose response due to the change in the consumption rates of the monomers proposed to be caused by Iodine. The oxygen permeability of the latex membrane is also higher than would be considered ideal and while housing it in a less oxygen permeable container was done, it seems to have had a limited buffering effect. Combating these issues is an ongoing process and subject to immediate investigation.

The relative comparison of the static dosimeter to the IDEFGEL provides a quantification of the degree to which the deformation has blurred the expected dose distribution. The amount of outer dosimeter gel pushed into the target region appears to have collected 9.4% of the dose delivered to the target region, derived from the total dose deposited in both regions for both samples, a reasonably significant amount for a 1 cm compression of the material. The spreading of the maximum and minimum dose values is also interesting given the expected dose blurring, but with the suspected dose calibration inconsistencies it is difficult to derive a solid conclusion from these values.
5. Conclusion
A target region containing 0.7% w/w Isovue X-ray contrast agent was successfully fabricated from the same gel batch as the outer dosimeter and used to measure a planned dose distribution to the contoured target region in both a static and deforming configuration. By performing comparisons of the DVHs of the two samples to one another, it can be seen that the degree of motion was enough to significantly impact the dose coverage of the target region. The IDEFGEL measurements are precise enough indicate that the addition of the target region as a physical feature that is dose sensitive can provide meaningful results in terms of assessing the dosimetric impact of the margins included in treatment planning, most pertinently in this study margins for motion and deformation. The IDEFGEL dosimeter is currently restricted to simple shape configurations and equally simple dose structures in planning. These restrictions do provide a focus on single phenomena for the conducted test and can be probed further for dose 3D distribution shape analysis. The calibration of the dose response function appears to have been severely impacted by external environmental factors and the change in chemistry caused by diffusion of the Isovue throughout the dosimeter volume, necessitating extremely strict controls on the time scale at which the experiments are conducted for not only the deformation study but also the calibration studies. With further optimization of the contrast agent concentration and the dosimeter configuration a IDEFGEL that can reliably assess the impact of motion and deformation on 3D dose distributions is achievable and can inform treatment planning that involves margins to account for motion and deformation.

6. References
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