Verification of stereotactic cranial radiotherapy treatments with MR-based gel dosimeters: practical aspects

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Abstract: Image Guided Radiotherapy (IGRT) systems allow delivering high doses of radiation to a tumour with great precision and accuracy. In this work, we use patient-specific head MR-based gel dosimeters as an end-to-end test to commission IGRT delivery systems, for stereotactic cranial radiotherapy, and investigate possible sources of errors associated with practical aspects of the measurements. A CT scan of a patient is used to 3D print the shape of the cranial bones to create head phantoms with MR-based gel inside. Each phantom was used as a patient, following the radiotherapy workflow which includes: taking a CT scan of the phantom, calculating the dose distribution using a treatment planning system (TPS) and delivering the radiation calculated by the TPS to target three different lesions: Big, Medium and Small. Each phantom was then scanned on an MR scanner to obtain a T2 map (linear with dose), which was then rigidly registered with the CT scan of the phantom based on the phantom structures. Good agreement was obtained between the normalized R2 (=1/T2) values and TPS simulations. The relationship between R2 values and dose was investigated based on 3D regions including each lesion. Good linearity was found, but different R2-dose values relationship was obtained depending on the selected regions. The impact of applying a registration based on each lesion (and not the phantom structures) was also tested. Results show that the registration has an impact on the relationship between R2 values and dose, and although absolute dose measurements are still not possible with these MR-based gel dosimeters, they provide very detailed geometrical 3D information to validate IGRT radiotherapy treatments with high level of accuracy.

1. Introduction

Magnetic resonance (MR)-based gel dosimetry is of great interest to Stereotactic Ablative Radiotherapy (SABR) and Stereotactic Radiosurgery (SRS) [1-4]. CyberKnife and BrainLab delivery systems use image guided radiotherapy (IGRT) to deliver high doses of radiation to the tumour in very few fractions. IGRT requires complex interactions between different systems which need to be verified to ensure that the correct dose distribution is being delivered. A great level of geometrical and dosimetric accuracy is required for these treatments to be effective in improving tumour control and reducing toxicity [5]. This work was part of a commissioning program for image guided stereotactic cranial radiotherapy of
multiple metastases. Patient-specific MR-based 3D gel phantoms were used as an end-to-end test to validate the accuracy of IGRT systems. An identical phantom with inserts for ionization chambers was used for absolute dose measurements. Procedures associated with MR-based gel dosimetry and possible sources of errors associated with practical aspects of the measurements were investigated.

2. Material and Methods

2.1. IGRT treatment planning systems
Two different treatment planning systems (TPS) software were used to calculate a plan to treat multiple metastases in the brain using different IGRT delivery systems. BrainLab Elements (v1.5) and Accuray Multiplan (v5.2.1) were used to calculate the doses delivered. Relevant differences between the two platforms include that Elements automatically performs the majority of user subtasks in optimizing the beamlet placement and weighting, while Multiplan has a comparable automated approach once the collimator apertures are defined by user choices. A CT scan of a patient with three approximately spheroid-shaped metastatic lesions (termed “Big” (5.4 cm³), “Medium” (0.57 cm³) and “Small” (0.15 cm³)), separated by at least 50mm, was used to create a treatment plan using the two TPS.

2.2 3D printed patient-specific phantoms and plan irradiation
Three identical patient-specific hollow head phantoms (with sub-millimetre spatial accuracy) were 3D-printed based on the selected patient planning CT scan (RTsafe, Athens, Greece). RTsafe uses 3D printing techniques to replicate the shape of the cranial bones with a material of bone-like density, with a 2 mm thick skin-mimicking layer to seal and to provide rigidity. Two phantoms (gel phantoms) were filled with VIPAR radiosensitive polymer MR-based gel [6], that polymerizes with radiation and the changes in spin-spin (T2) relaxation times can be measured with a MR scanner. One phantom (ionization chamber phantom) contains three ionisation chamber inserts to perform absolute dose measurements by placing a chamber in the middle of each planning target volume (PTV). A semiflex ionization chamber (type 31010, PTW, Germany), with sensitive volume of 0.125cm³, was placed in the middle of the Big lesion, while two pinpoint ionization chambers with sensitive volumes of 0.015cm³ (type 31006 & 31014, PTW, Germany) were placed in the middle of the Medium lesion and Small lesion. This phantom is reusable and needs to be filled with water before being irradiated.

The treatment plans created on the patient CT were calculated so that the delivered doses would always be below 12 Gy (for doses > 12 Gy T2 values no longer vary linearly with dose [3]). The plans were re-calculated on the CT of the phantom (gel phantom or ionization chamber phantom depending on the availability). Each gel phantom and ionization chamber phantom pair were irradiated as per the patient plan, using stereoscopic planar x-ray on a Cyberknife or ExacTrac on a Varian LE Clinac.

2.3 MRI data acquisition and dose readout
Each gel phantom was scanned in the standardized radiotherapy treatment position for head and neck using a thermoplastic mask as per the treatment. This was the same set-up used to irradiate the gel phantoms and the ionization chamber phantom for each treatment. The MR scanner was performed at 1.5T with a Siemens Aera, 18-channel surface coil (Siemens, Erlangen, Germany) 24 hours after irradiation. A 2D fast spin echo sequence with multiple echo times was employed (TR/TE=2000ms / 36, 436, 835, 1230ms, voxel size = 1.4 x 1.4 x 2 mm³, bandwidth = 780 Hz / px) and a T2 relaxation time was calculated on a pixel-by-pixel basis. A 3D map of gel R2 values can be obtained, by applying the inverse of the T2 relaxation times (R2 = 1 / T2 map).

2.4 Dosimetric analysis
The T2 map and the CT scan of the gel phantom (or the ionization chamber phantom) together with the calculated treatment plan and TPS dose distribution was sent to the manufacturers. RTsafe provides a data analysis service which reports the agreement between the measured doses and the TPS simulated doses, after registering the T2 map with the CT scan provided.
An independent analysis was performed in this work using the same T2 map and the CT scan of the gel phantom that were provided to the manufacturers. Matlab® was used to analyse the data and to compare the gel R2 values with TPS dose values. Normalization can be performed interactively based on a region of interest (ROI) within one of the lesions and a background area selected on a low dose region within the phantom. A square region within the Big lesion was used to normalize both gel R2 and TPS dose values, and 1D gamma criteria of 5%, 2mm was applied to assess the agreement. A comparison was also performed based on normalized local differences.

The relationship between gel R2 values and TPS doses was investigated by applying four different registrations for each of the two phantom gels used. The T2 map was rigidly registered with the phantom CT on 3D slicer based on the phantom structures of the gel and using the RTsafe registration as a starting point. A local rigid registration between the T2 map and TPS dose map was also performed to obtain three registered T2 map images, one for each lesion (registration by lesion).

2.5 MRI analysis
In addition to the MR scan recommended by the gel manufacturer (Post1: within 48h of irradiation), we also performed scans prior to irradiation (Pre scans) and at later time points (Post2: one week after irradiation and Post3: one month after irradiation). With this additional data, the uniformity of the gel pre-irradiation was investigated, as R2 values drifts can in principle be associated with gravity or imperfections of the preparation. The stability of the R2 values over time was also investigated.

3. Results and discussion

3.1 Dosimetric analysis
For the phantom gels irradiated, good agreement was reported by RTsafe according to their analysis. Similarly, our independent analysis showed a good agreement overall. Normalized R2 values from two different gel phantoms irradiated and planned with Accuray Multiplan (delivered with a Cyberknife with stereoscopic planar x-ray) and Brainlab Elements (delivered with a Varian LE Clinac with ExacTrac) are shown in Figure 1a (phantom Gel 1) and b (phantom Gel 2), respectively. Good agreement is obtained by taking a randomly selected profile (±1mm) in the central region of each lesion, as shown in Figure 1. 1D Gamma of 5%, 2mm is also shown for quantification of the agreement. Lower normalized R2 values were observed for the Medium and the Small lesions for phantom Gel 1 in comparison with the simulated profiles (Figure 1a). In Figure 1b, a small shift of about 1mm is visible in the Medium lesion but normalized values agree well with simulations in all lesions for profiles taken in different directions. Sagittal and coronal slices are not shown but the same results were observed.

Subtracting the normalized TPS dose to the measured dose gives important visual information. In Figure 2, one can see the extension of the shift observed in Figure 1b by looking at both axial and coronal slices. A small shift on the small lesion was also observed. Differences found here can reach 20%, but will not necessarily have a clinical impact if the defined gamma criteria would only fail in a small percentage of points, or if a good agreement can still be found within the defined distance to agreement. However, local differences help to visualize and identify regions where a discrepancy might exist, and draw the attention of the users to regions which must be carefully assessed.

In Figure 1b, depending on the slice and directions where the profile is taken the shift in the anterior-posterior direction can reach 2mm. These differences might change with the applied rigid registration. However, assessing the quality of the registration might be difficult as different modalities are being registered (CT and MRI) [7].
Figure 1. (a) Graphical display of Gel 1 phantom normalized R2 map values showing a middle axial slice crossing the Big, Medium and Small lesions. Respective normalized 1D gel phantom profiles taken in each lesion are shown in comparison with the 1D TPS. Registration based on the phantom head structures was applied here and both R2 map and TPS dose distribution were normalized to the same ROI within the Big lesion. Red to blue directions represent left to right direction of the plotted profiles. One standard deviation is shown. The 1D gamma (5%, 2 mm) is also shown. (b) The same is shown for Gel 2.

Figure 2. Difference between the Gel 2 phantom R2 values and TPS dose values after both being normalized to the Big lesion. Axial and sagittal slices are shown in regions were the central Medium lesion and Small lesion are visible.

In Figure 3a and c TPS dose values were plotted against the R2 values by selecting an independent 3D region around each lesion (Big, Medium and Small), for Gel 1 and Gel 2, respectively. When 3D slicer rigid registration is applied based on the phantom structures, some data spread is visible. In Figure 3b and d, the TPS dose values were also plotted against the R2 values, using the same 3D regions, but for each region a different registration was applied (registration by lesion). The spread of the data is reduced (Figure 3b and d) when compared to the spread obtained with the phantom structures based registration (Figure 3a and c) and a clear linear relationship between R2 values and dose is visible. This suggests that the registration has an effect on the relationship between dose and R2 values.

A calibration curve was fitted for each of the four plots in Figure 3. Distinct calibrations curves were obtained from the three regions using the registration by the phantom structures (Figure 3a and c). The average difference between the overall (identified as “All” in Figure 3) calibration curve gradient, which includes all data from the three regions, and the individual calibrations is 5.6% for Gel 1 and 1.3% for Gel 2. By applying a registration by lesion, the spread of the values is reduced as explained, but the
difference between the calibrations curves did not improve much (4.7% difference for Gel 1 and 1.2% for Gel 2).

For Gel 1, the difference in the calibration curve could be due to a non-uniform response of the gel to radiation or MR-scanner based non-uniformities. This difference might explain why in Figure 1a, the normalized results for Gel 1 were lower for the Medium and the Small lesions when compared with the TPS simulations. For Gel 2, the spread is quite visible for the Medium lesion, but it is likely due to the shift found. An improvement is clear after registration by lesion. Despite the spread, good uniformity was found within the entire Gel 2 phantom, giving confidence for the use of only one normalization value to analyse the entire phantom.

For an additional assessment of the radiotherapy treatments, absolute dose measurements were obtained for each lesion with the ionization chamber phantom. Differences between measured dose and the mean dose within the PTV calculated with each TPS are shown in Table 1.

| Diff. (%) Meas - TPS | Multiplan (n=2) | Elements (n=2) | Mean ± sd (n=4) |
|----------------------|----------------|---------------|----------------|
| Small                | -5.8           | -4.6          | -5.2±2.3       |
| Medium               | -1.0           | -1.1          | -1.0±1.0       |
| Big                  | 0.9            | -0.9          | 0.0±1.4        |

Table 1. The difference between ionization chamber measurements and TPS mean dose in the PTV is shown for each lesion. TPS dose was calculated from two different TPS software, Accuray Multiplan and Brainlab Elements.

Small differences were found between measured and simulated doses, with the exception of the Small lesion, which could be explained by the ionization chamber volume averaging. Uncertainties on the estimate at the center of the PTV could be due to positional error and charge to dose conversion.
3.2 MRI analysis

Pre irradiation measurements showed a good uniformity of the gel phantom with an average R2 value prior to irradiation of 0.00100 ± 0.00002 ms⁻¹. No drifts were observed and all variations in R2 were attributed to noise. Comparison between the phantom MR scanned R2 values in different times are shown in Figure 4. On areas receiving high doses, Post2 and Post3 R2 exhibited an increase (13% and 19%, respectively for all lesions) when compared to Post1 R2 (a day after irradiation). This suggests gradual changes occur to the phantom gel post-irradiation. In addition, one month after irradiation (Post3 time point), it was possible to detect gel deformation, as the lesions appeared to be mismatched with the initial dataset (Post1). Further investigations with localised co-registration of each lesion suggest that shifts of up to 2mm may have occurred. This is in agreement with the manufacturers recommendations of scanning the phantom within 48h in order to avoid changes.

![Figure 4](image)

*Figure 4.* Post1 (within 48h after irradiation) R2 against Post2 (one week after irradiation) and Post3 (one month after irradiation) R2 values for all three lesions. Resulting pattern suggests misregistration at the Post3 time point, confirmed by further processing (not shown).

4. Conclusion

In this work we irradiate commercial patient-specific MR-based gel phantoms with high doses of radiation using complex IGRT treatment plan delivery systems. An overall good agreement was found between the TPS doses and the gel R2 values after normalization. An approximately linear relationship between dose and R2 values was found, but the gradient of the linear relationship was dependent on the selected region within the phantom. This behaviour is well-suited to relative localized dosimetric measurements and gives valuable geometrical information to assess complex radiotherapy plans. Additional independent irradiations using an ionization chamber phantom were essential to have confidence on the absolute dose values delivered. The spatial precision and dosimetric accuracy were both found adequate for stereotactic radiotherapy. Discrepancies recorded illustrate the achievable practical limits in our clinic. Further refinement is necessary before absolute dose values can be derived from the gel phantoms alone.

5. Acknowledgments

The Radiotherapy work was co-funded as a collaborative project by SEPnet Royal Marsden Hospital and RTsafe. The MRI work was partially funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, and by CR-UK (grant number C33589/A19727). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. We acknowledge RTsafe for all the support given throughout this work.

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