Post-processing techniques using 3D Slicer for T1-weighted MRI analysis of radiochromic gel dosimeters

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Abstract. Radiochromic FXG gel dosimeters were investigated for end-to-end validation of TG-119 plans delivered in the pre-clinical Elekta 1.5 T-7 MV FFF MR-Linac. Due to the noise levels in the T1-weighted MR images, this preliminary study investigated post-processing techniques available in 3D Slicer and their impact on gamma passing rates. Binomial blur and discrete Gaussian image filters were identified as the most impactful on increasing gamma passing rates for T1-weighted MR images; however, any application of image filters should be implemented with caution on the interpretation of the results.

1. Introduction
MR image-guided radiation therapy (MR-IGRT) systems require a modified clinical workflow to integrate MR images for daily adaptive re-planning. Various methods for confirmation of accurate treatment plan delivery have been performed using quasi-3D arrays, 2D arrays, and 3D dosimeters [1-12]. Ideally, a heterogeneous, anthropomorphic MR-visible and radiation-sensitive phantom would be used for a complete end-to-end clinical workflow assessment. Although commissioning phantoms using CT and MR-visible materials are in development, these depend on point and planar measurements using thermoluminescent dosimeters and films, which can miss dose information in three dimensions [13-15].

To meet this quality assurance (QA) need, end-to-end dosimetry with homogeneous and heterogeneous 3D dosimeters has been investigated using optical and MRI read-out techniques [5, 7-9, 12]. Prior to MR-IGRT systems, it was not possible to pre-scan, irradiate, and post-scan 3D dosimeters all in the same position. Several MR-IGRT systems are now in clinical use world-side and others are still in development, including the 1.5 MRI – 7 MV FFF linear accelerator (linac) (Unity MR-Linac, Elekta AB, Stockholm, Sweden), a prototype system combining a 1.0 T MRI with a 6 MV linac (Ingram Institute, Sydney, Australia), the Aurora RT 0.5 T magnet with 6 MV linac (MagnetTx, Alberta, Canada), and the MRIdian 0.35 T magnet with 6 MV linac (Viewray, Inc., Oakwood Village, Ohio, USA). With the MR-Linac and other MR-IGRT systems, we now have the capability for delivery of a treatment plan to a 3D dosimeter in the exact position that it was planned for with the possibility for real-time onboard MR imaging during irradiation and immediate MR imaging post-irradiation [8, 16]. Comparisons between treatment plan dose and measured 3D dosimeter dose with gamma passing rates greater than 90% for 3%/3mm distance to agreement (DTA) have been reported for non-MR visible...
plastic PRESAGE (optical read-out) and polymer gel (spin-spin relaxation rate $R_2 (=1/T_2)$ MRI read-out) dosimeters. In this study, we investigate post-processing techniques to modify the MR image quality for radiochromic gel (spin-lattice relaxation rate $R_1 (=1/T_1)$ MRI read-out) dosimeters that were irradiated in a pre-clinical Elekta 1.5 T-7 MV FFF MR-Linac and assess the impact on gamma pass rates.

2. Materials and Methods

2.1. FXG gel fabrication and MR imaging

Radiochromic gel dosimeters consist of a radiochromic reporter compound, a free radical source and solvent, an iron source, and a gelling agent. The Fricke xylene orange gel (FXG) formulation was as follows (all chemicals sourced from Sigma-Aldrich): 0.05 mM xylene orange disodium salt, ~96% wt% deionized water, 1 mM ferrous ammonium sulfate, 4 wt% 300 bloom gelatin, and 50 mM sulfuric acid. The mixture was poured into two liter-sized uniform phantoms then stored at 4°C and acclimated to room temperature prior to irradiation.

Pre-irradiation and post-irradiation images were acquired for each phantom using T1-weighted contrast enhanced (CE) MRI sequences (3D fast field echo (FFE), TR/TE = 11/4.6 ms, 400 x 400 x 300 mm$^3$ field of view, reconstructed voxels of 0.83 x 0.83 x 1.00 mm$^3$). T1-weighted CE and no CE are Philips-specific terminology for their 3D FFE sequences and do not indicate that an MR contrast agent was injected. The T1-weighted CE sequences spoiled the transverse magnetization using pulse phase cycling of the radiofrequency excitation pulses. Therefore, the no CE images included a mixed signal of the free induction decay (FID) and spin echo, and the T1-weighted CE images only contained the FID signal.

2.2. Treatment planning and plan delivery

Reference step-and-shoot IMRT plans based on the TG-119 IMRT commissioning tests were created in a Monaco treatment planning system (TPS) (research version 5.19.02) using CT images acquired of the homogeneous cylindrical phantoms [5, 17, 18]. Monaco TPS for the Elekta MR-Linac used Monte Carlo dose calculations in a graphical processing unit environment that incorporated a 1.5 T $B_0$ field. Monaco plan doses were calculated with 1-3% statistical uncertainty per control point and 0.2-0.3 cm grid spacing. At the time of plan delivery, complete cross-validation of the Monaco TPS had not yet been done, and greater uncertainties in dose were expected (conventional TPS calculations include up to 3% dose uncertainties in clinical use due to different factors). The Elekta MR-Linac was also in its pre-clinical phase at the time of plan delivery (prior to final system upgrades to the CE marked and 510(k) cleared Unity system currently in clinical use). Most notably, rigorous MLC calibration and MR to MV isocenter registration had not yet been completed at the time of plan delivery, affecting the accuracy and delivery of adapted plans based on daily MR images. A workflow comparable to the current clinical adapt-to-position (ATP) was used for treatment delivery. Daily T1-weighted no CE MR images (same MRI sequence parameters as for T1-weighted CE described above) were acquired for fusion with the CT to create the daily adapted plan based on the phantom position in the pre-clinical MR-Linac. MR images acquired with T1-weighted no CE were found to have superior visibility of edges and reduced noise compared to T2-weighted and T1-weighted CE images; however T1-weighted no CE could not be used for post-processing of dose for the FXG formulation [5]. These daily adapted plans were then delivered in the pre-clinical MR-Linac and post irradiation MR images were acquired of the gels in the same position as described above.

2.3. Gamma analysis and post-processing with 3D Slicer

After acquisition of the pre-irradiation and post-irradiation MR images, the relative volumetric dose distributions quantified in the gels were compared to calculated doses from the Monaco TPS using 3D Slicer (version 4.6.2) [19, 20]. 3D Slicer was an open source software platform that could be used for a wide variety of applications and has been validated for TPS plan comparisons using gamma analysis.
The 3D Slicer workflow has been described previously and is summarized below: using the SlicerRT extension, import and load DICOM files of the TPS dose, structures, pre-irradiation MRI, and post-irradiation MRI; subtract the MRI prescan from the MRI postscan; transform the subtracted MRI volume to match TPS plan volume using the adapted plan fusion coordinates; post-process as needed and scale to relative dose; assess 3D gamma analysis using the Dose Comparison module [5].

A gamma criterion of 7%/4mm DTA was used by IROC for IMRT head and neck plans for 2D gamma analysis of film [24]. While 3D dosimetry studies have used other gamma criteria for 3D gamma analysis along with other metrics for plan delivery assessment, this initial study utilized 7%/4mm along with stricter gamma constraints (5%/3mm and 3%/3mm) as a comparison with passing cut-offs of 80% [24–27]. Up to approximately 5% differences in gamma passing rates were found depending on small changes to scaling for relative doses. A 10% maximum dose threshold (TH) was applied for all gamma analysis, regardless of the gamma criteria. Due to the standard deviation as a result of noise in MR images (up to ~10% of the mean MR signal intensity), it should be noted that there is a risk of voxels passing with 3D gamma analysis using loose criteria such as 7%/4mm.

Image filters that could potentially improve the MR image quality were assessed. The 3D slicer post-processing tools used for this study were the following image filters: median, mean, binomial blur, box mean, curvature flow, discrete Gaussian, grayscale grind peak, Laplacian sharpening, min max curvature flow, rank, and smoothing recursive Gaussian. These image filters included a variety of techniques, including direct (such as median) and recursive (rank), linear (mean) and nonlinear (median), and retention (median) and sharpening (Laplacian sharpening) of boundaries. After the optimal image filters were identified, a combination using the histogram matching image filter was also investigated. The use of any image filter should be implemented with caution to modify the raw data set, which could also perturb the data in an unexpected manner and may result in hiding issues with the plan delivery.

3. Results and Discussions

3.1. Post-processing filters

The post-processing image filters listed above were first assessed for the TG-119 AP PA plan. A variety of parameters and number of iterations were applied for each image filter. Across all applied image filters, the gamma passing rates were 98.55 ± 0.32% for 7%/4mm criteria; 90.83 ± 2.72% for 5%/3mm; and 79.39 ± 5.24% for 3%/3mm. The image filters resulting in the highest 3%/3mm gamma passing rates were binomial blur image filter (Repetitions 2), discrete Gaussian image filter (Variance 1), and smoothing recursive Gaussian image filter (Sigma 1). The image filters resulting in the highest 7%/4mm gamma passing rates were curvature flow image filter (# Iterations 3), min max curvature flow image filter (# Iterations 5), and binomial blur image filter (Repetitions 1). Due to potentially misleading higher passing rates for 7%/4mm, the binomial blur (used nearest neighbor averaging) and discrete Gaussian (used separable convolution with discrete Gaussian kernels) image filters were further assessed using a combination.

Applications of the binomial blur image filter and discrete Gaussian image filter resulted in comparable gamma passing rates with lower NSA (number of signal averages, also known as number of excitations NEX) to the application of simpler image filters, such as the median image filter, with higher NSA. Increasing NSA increased the acquisition time linearly (1:54 minutes, 5:42 minutes, and 9:29 minutes for NSA = 1, 3, and 5, respectively). The use of greater NSA may still be required for analysis of MR images acquired at very low field strengths to improve SNR [12]. The combination of binomial blur and discrete Gaussian image filters did not guarantee higher gamma passing rates for higher NSA.

3.2. TG-119 Plan Analysis
Using the binomial blur, discrete Gaussian, and a combination using the histogram matching image filter, the gamma passing rates for all TG-119 plans are listed in Table 1 with all images acquired using T1-weighted CE and NSA = 1 sequences.

| TG-119 Plan | Post-processing | 7%/4mm | 5%/3mm | 3%/3mm |
|-------------|-----------------|--------|--------|--------|
| AP PA       | Binomial Blur Image Filter | 98.25% | 92.34% | 83.71% |
|             | Discrete Gaussian Image Filter | 98.03% | 92.00% | 83.69% |
|             | Histogram Matching Image Filter | 98.15% | 92.27% | 84.02% |
|             | Median Image Filter | 98.68% | 92.24% | 82.01% |
| MultiTarget | Binomial Blur Image Filter | 95.96% | 53.85% | 34.43% |
|             | Discrete Gaussian Image Filter | 95.78% | 55.52% | 35.54% |
|             | Histogram Matching Image Filter | 95.73% | 54.20% | 34.80% |
|             | Median Image Filter | 96.07% | 48.50% | 30.62% |
| Prostate    | Binomial Blur Image Filter | 95.69% | 46.93% | 28.49% |
|             | Discrete Gaussian Image Filter | 95.77% | 47.94% | 28.79% |
|             | Histogram Matching Image Filter | 95.97% | 48.48% | 29.53% |
|             | Median Image Filter | 96.12% | 47.16% | 29.12% |
| Head/Neck   | Binomial Blur Image Filter | 94.05% | 48.53% | 30.07% |
|             | Discrete Gaussian Image Filter | 93.88% | 49.90% | 30.85% |
|             | Histogram Matching Image Filter | 94.33% | 50.04% | 31.07% |
|             | Median Image Filter | 94.28% | 44.82% | 27.56% |
| C-Shape     | Binomial Blur Image Filter | 94.64% | 51.04% | 31.86% |
|             | Discrete Gaussian Image Filter | 94.43% | 51.90% | 32.49% |
|             | Histogram Matching Image Filter | 95.01% | 52.60% | 32.94% |
|             | Median Image Filter | 94.79% | 47.94% | 29.99% |

The homogeneous large FXG dosimeters used for TG-119 IMRT plan evaluation passed all 7%/4mm gamma criteria. However, the other more complex plans had gamma passing rates that dropped more steeply for 5%/3mm and 3%/3mm gamma criteria, which could be attributed to the longer plan delivery times for the complex step-and-shoot IMRT plans as well as the limitations to this pre-clinical system.

4. Conclusions
As shown in this study and in the literature, the post processing of measured signal can significantly affect the gamma passing rate, and thus needs to be specified in the QA protocol. The results of this study demonstrated that optimizing post-processing techniques can improve gamma passing rates with the binomial blur and discrete Gaussian image filters identified as the most impactful for T1-weighted CE MR images. This study demonstrated using an MR-visible 3D dosimeter to eliminate registration errors between pre-irradiation imaging, plan delivery, and post-irradiation imaging of the dosimeter.

Future work in a fully clinically commissioned MR-Linac system should investigate further improving the combination of MR image acquisition sequence parameters with considerations for diffusion and post-processing to improve gamma passing rates for tighter gamma criteria as well as investigating additional metrics to gamma passing rate for analysis of the plan delivery quality.

5. References
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