The MD Anderson experience with 3D dosimetry and an MR-linac

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Abstract. A recent extension of image guidance in radiation therapy has been brought about by the introduction of the MR-linac; a hybrid system comprising an MR imager and a medical linear accelerator. The University of Texas MD Anderson Cancer Center is one of seven institutes around the world that have collaborated with the manufacturer to develop this system and bring it into clinical use. In the process, a great deal has been learned about the influence of the magnetic field on radiation dose deposition and upon dosimetry systems. A number of dosimetry systems have been evaluated and issues affecting their performance have been investigated. The potential value of three-dimensional dosimetry systems has been explored.

1. Introduction

The benefits of visualizing a patient’s anatomy while in the treatment position led to the development of image-guided radiation therapy (IGRT) [1]. As an improvement over contemporary x-ray based IGRT, the feasibility of using magnetic resonance imaging (MRI) for radiation therapy position verification is being investigated, leading to the development of MR-image guided radiation therapy (MR-IGRT) [2]. Compared to x-ray imaging, MRI does not use ionizing radiation to generate images, and thus removes the concern for harmful effects from the imaging dose. MRI also offers superior soft tissue contrast, allowing the physician to delineate the target volume and surrounding structures with less uncertainty and potentially smaller margins. MR imaging protocols exist that acquire images rapidly, requiring less time than a CBCT image, and offering the potential to acquire 4D images in multiple planes. Because there appears to be no biological interaction between MR imaging and the treatment radiation, it is possible to image the patient during treatment and to monitor the location of the target volume in real-time. Functional imaging capabilities of MRI also allow the assessment of treatment response, during and post-treatment. Such assessment can allow treatment to be adapted according to the radiation response, providing a more personalized treatment for each patient.

Several MR-IGRT treatment machines have been designed; one system is currently commercially available while a second has received the CE Mark and is being marketed in Europe and elsewhere. The Unity MR-linac which combines a 7 MV linear accelerator with a diagnostic-quality MRI scanner was developed as a collaboration between The University Medical Center Utrecht (The Netherlands) and comprises a 7-MV linac (Elekta AB, Stockholm, Sweden), mounted on a ring around a 1.5 T MRI system (Philips, Best, The Netherlands) MRI system [3]. This system is presently installed at several sites and has received the CE Mark; at this writing it continues to undergo pre-clinical evaluation in the US. The MRIdian system based on a 0.3 T MRI and cobalt sources, which have subsequently replaced by a linear accelerator, also is commercially available (ViewRay, Oakwood, OH) [4]. Other systems are in development in Canada by the Cross Cancer Institute [5] and the Ingham Institute in Australia [6].
Despite the substantial benefits, MR-IGRT faces several challenges before it is likely to reach its full potential [2]. A major concern is the change in the delivered dose distribution when strong (≥ 1 T) magnetic fields are used for MR imaging. In photon beam radiation therapy, dose is delivered by secondary electrons that carry the energy transferred from the incoming photons. Secondary electrons are mostly forward peaked and deposit energy downstream, as they travel deeper into the patient, in segments of straight lines. In a magnetic field, however, the trajectories of secondary electrons are curved by the Lorentz force, shortening the path. When a secondary electron is generated in a dense medium and travels into a less dense medium, the electron may be able to follow a circular path and return into the original medium. Due to the lack of electron equilibrium, dose is increased in the upstream medium near the interface. This phenomenon is referred to as the electron return effect (ERE) and has been shown to pose clinical concerns [7]. Figure 1 shows the trajectory of an electron traveling from one medium to the next; the path changes in the presence of the magnetic field. The figure clearly demonstrates the ERE. [8] In measurements with a PRESAGE® dosimeter and radiochromic film (Figure 2) the ERE is observed to enhance dose at the interface by a factor of 1.3 ~ 1.4, over about 1 cm range [9].

The ERE can increase the dose at interfaces but the amount of increase depends on several factors. These include the media comprising the interface, the shape and orientation of the interface, the strength
and direction of the magnetic field, and the energy of the beam. Some measures such as using opposing beams or multiple beam angles have been shown to reduce the dose enhancement due to the ERE in simple geometries [7, 10]. However, it remains a concern for the treatment of heterogeneous treatment sites and regions containing airways and air-filled cavities.

2. Inadequacies of point and planar detectors
Conventional quality assurance (QA) procedures in radiation therapy generally rely on point and planar dosimeters to compare the measured dose to the planned dose at a few points of interest and in a few planes. For example, the Imaging and Radiation Oncology Core-Houston (IROC-Houston, formerly the Radiological Physics Center) QA Center uses thermoluminescence dosimeters (TLDs) and radiochromic film to evaluate the dosimetric performance of institutions wishing to participate in national cooperative group clinical trials [11]. In 2010, IROC-Houston reported that 20-30% of institutions participating in credentialing procedures had failed to deliver treatments that matched their own treatment plans within the IROC criteria. These data were measured using phantoms representing sites such as the head and neck, pelvis, spine, and lung [12]. A more recent report shows that even for irradiations performed since 2012, about 10% of irradiations did not meet the passing criteria [13]. It is of note that the IROC analysis evaluated the delivered dose in only two or three planes. Consequently, it is conceivable that a more comprehensive investigation would reveal either better or worse agreement between the plan and the delivered dose. Work in this area has demonstrated that, in some cases, a 3D evaluation identifies regions of disagreement that, because they appeared outside the plane of the 2D dosimeter, were not detected with film analysis [14, 15]. It is apparent that a more thorough means of measuring dose distributions is needed for MR-IGRT treatments, where the magnetic field changes the delivered dose distribution in a complicated fashion.

3. Opportunities offered by 3D dosimetry
In an effort to improve upon the sparse sampling offered by 0D and 2D dosimetry, three dimensional (3D) dosimeters were developed to provide volumetric dose information with high spatial resolution [16, 17]. Materials that have been investigated recently include polymerizing gels, radiochromic gels, and radiochromic plastic materials such as PRESAGE® (Heuris Pharma, Skillman, NJ, USA) [18]. Gel dosimeters can be analyzed with one of several read-out methods including MRI, x-ray CT, and optical-CT [19, 20]. Radiochromic plastics do not generate a signal that is visible with MR or x-ray CT, and therefore are customarily analyzed with optical CT methods [21]. The capacity of 3D dosimetry to measure and compare volumetric dose distributions offers this modality the potential to perform as a complement to, or a substitute for 0D and 2D dosimetry.

4. Dosimeters in magnetic fields

4.1. General concerns
Before 3D dosimeter systems could be employed as viable QA tools in magnetic field environments, it was essential to first determine whether a magnetic field could affect the response of the dosimeters. There have been few investigations on how a strong magnetic field affects conventional dosimeters. A 2009 report described the magnetic field effects on a Farmer NE2571 ion chamber [22]. Two experiments were described: a GEANT4 Monte Carlo simulation and measurements with the Farmer NE2571 chamber in the magnetic field produced by an electromagnet. Depending on the orientation of the chamber and the strength of the magnetic field, the response of the ion chamber varied 10-15%. More recent data have been reported that characterize a number of cylindrical ion chamber models in a 1.5 T magnetic field [23]. These authors showed that chamber design and construction played important roles in the magnitude of the effect. For some of the instruments evaluated, the orientation of the ion chamber axis to the magnetic field contributed a significant effect; the influence of the magnetic field was considerably greater when the chamber was perpendicular to the magnetic field. O’Brien and colleagues also have shown that even small air gaps around an ionization chamber altered the reading
of the instrument, suggesting that the use of water-equivalent plastic phantoms could lead to measurement errors [23, 24].

The complications experienced with ion chambers largely can be minimized through selection of an appropriate chamber design, by avoiding air gaps and by taking care to align the chamber parallel to the magnetic field. Perhaps the best solution, at least for reference dosimetry, involves the use of a suitable ion chamber in a water phantom. However, the design of most MR-guided treatment units makes this inconvenient and potentially dangerous due to the high voltages in use.

For making relative measurements, motor-driven water phantoms are desirable, but most are unsuitable for use in a magnetic field. Consequently, a 3D volumetric dosimeter is attractive to avoid some of these complications. In addition, some 3D dosimeters such as Fricke gels exhibit a response that is measurable with MR imaging. This offers the very unusual opportunity to analyze the dosimeter with the MR component of the MR-IGRT system, immediately following irradiation with the treatment component of the system. A further benefit is the avoidance of moving the dosimeter from the treatment device to an imaging system. In fact, with the MR-linac, imaging is possible during irradiation, allowing for a real-time display of accumulated dose.

4.2. Influence of magnetic fields on dosimeter sensitivity

The effect of a magnetic field on the sensitivity of a polyurethane-based radiochromic dosimeter similar to PRESAGE® was investigated using cuvettes that fit into a PMMA phantom that was designed to fit between the pole pieces of an electromagnet [25]. Doses of approximately 1, 4, 7 and 10 Gy were delivered, with either \( B = 0 \) or \( B = 1.5 \) T. The net OD change due to irradiation was calculated by taking the difference between the average OD of the irradiated cuvettes and that of unirradiated cuvettes that were handled identically. OD was determined using a GENESYS\textsuperscript{TM} 10S UV-VIS spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA). ANOVA was performed in R-statistical software to test whether the magnetic field had a significant influence on the dose response curve. The measurements suggested an under-response of approximately 2% in the presence of the magnetic field. However, it was subsequently recognized that the dose delivered in a 1.5 T magnetic field per photon (and consequently, per monitor unit) is approximately 0.5% lower than in the absence of a magnetic field [23]. It is likely that what appeared to be an under-response of the dosimeter was actually a reflection of the lower delivered dose in the magnetic field. Despite the small decrease in response compared to measurements at \( B = 0 \) T, the response of the polyurethane radiochromic dosimeter at \( B = 1.5 \) T was strictly linear, with \( R^2 > 0.99 \).

4.3. The benefits of Fricke gel dosimeters in a magnetic field

Preliminary work has been conducted by Lee et al to investigate the feasibility of using 3D Fricke-type gel dosimeters both for analysis of dose distributions and for real-time dose observations [26]. The Elekta Unity MR-Linac with a 1.5 T magnetic field was used for these studies. Fricke-type dosimeters were prepared in 97% w/w Milli-Q water with 3% w/w gelatin (300 Bloom), 1 mM ferrous ion, 0.05 mM xylene orange, 50 mM sulfuric acid, and 1 mM sodium chloride. The dosimeters were prepared in a plastic flask approximately 8.5 cm in diameter and 6 cm in height. The dosimeters were stored at 4° C prior to irradiation and imaging.

To demonstrate the response post-irradiation as well as in real time, the dosimeters were irradiated in air, with a part of each dosimeter outside the treatment field to act as a reference. A pair of perpendicular fields was used, an “anterior” field delivered 10 Gy to the center of the dosimeter through the top of the dosimeter and a “lateral” field delivered 20 Gy through the side of the dosimeter. This arrangement constructed an overlapping region of high dose with regions of lower dose on either side. MR imaging was performed with the MR-Linac to observe the change in paramagnetic properties pre- and post-irradiation using a T1-weighted sequence of TR = 500 ms and TE = 20 ms. MRI during irradiation was done in the MRL using a balanced fast field echo sequence with TR = 5 ms and TE = 1.7 ms.

Lee et al. observed a significant increase in pixel value between un-irradiated and irradiated regions. The increase in pixel value and corresponding dose was also visible during irradiation. Figure 3
demonstrates this increase in pixel value with dose, indicating that the signal increases in a linear fashion. Visibly, the dosimeter underwent a color change from yellow to purple with the formation of the xylenol orange – ferric complex. Following irradiation, the dosimeter demonstrated the 3D dose distribution as indicated in Figure 4.

**Figure 3.** An example of the increase in MR signal of a gel dosimeter during irradiation [26].

**Figure 4.** A gel dosimeter irradiated with two perpendicular beams. The MR images on the right demonstrate the 3D nature of the measurement [26].

Perhaps the most comprehensive investigation of 3D dosimetry for measurement of dose distributions from an MR-guided treatment unit was published by Rankine et al [27]. This study involved the use of a PRESAGE® dosimeter to evaluate the dose distributions from a ViewRay MR-cobalt system. The
authors evaluated several simple dose distributions, and also several IMRT distributions selected from those recommended by the AAPM [28]. As has been shown above, the 3D dosimetry system demonstrated excellent agreement with other methods including treatment planning system calculations and ionization chamber measurements. This test was admittedly less challenging, given the low field strength of the magnetic field, but is still a good demonstration of the value of 3D dosimetry.

5. Array dosimeters in magnetic fields
Several 2D and quasi 3D array detectors have been evaluated in magnetic fields. Such detector arrays have benefits for routine QA procedures due to their large dimensions and the ability to provide information about the radiation output and beam profile in real time. However, such devices exhibit differences in their behavior in magnetic fields.

The Starcheck maxi® MR (PTW, Freiburg, Germany) was evaluated for its ability to display machine output and beam profiles. This device contains ion chambers arranged in orthogonal and diagonal linear rows, with 3 mm spacing. Measurements of output were generally consistent with measurements using conventional ion chambers in a water phantom. Measurements of beam profile demonstrated the influence of the magnetic field due to the detector geometry. Most of the chambers along the array’s Y axis are surrounded by phantom material, except for the chambers close to the central axis which are surrounded by other chambers. When adjacent to another chamber, a chamber’s response appears to be increased approximately 2% over that of chambers surrounded by phantom material.

Similarly, the IC Profiler-MR (Sun Nuclear, Melbourne, Florida, USA) likewise has been evaluated. It shows a similar response depending on the orientation of the ionization chambers. The response of the IC Profiler-MR is improved by executing the manufacturer’s calibration procedure in the MR-linac beam, with the magnetic field energized.

Finally, the ArcCheck-MR (Sun Nuclear, Melbourne, Florida, USA) has been evaluated in a magnetic field. Unlike the two devices described above, the ArcCheck uses semiconductor detectors. No direct influence of the magnetic field on the detectors was observed, but issues arose with the calibration procedure. Sun Nuclear recommends irradiating the ArcCheck from a number of different orientations, several of which are either not achievable with the Elekta MR-linac or cause the beam to pass through high-atomic number structures, interfering with the measurement. A solution for this issue is presently being investigated.

6. Summary
The complex dose distributions produced by today’s treatment equipment and delivery techniques require more advanced dosimetry systems to provide confidence that the delivered distribution is consistent with the planned distribution. 3D dosimetry techniques are valuable to enable acquisition of volumetric information with a single irradiation. The emerging field of MR image-guided radiotherapy requires the presence of strong magnetic fields that can affect the performance of most conventional dosimetry systems. However, several novel 3D dosimeters have been shown to perform well in the presence of magnetic fields and are shown to provide quantitative dose distributions in volumetric fashion. While the available data are preliminary, these results indicate the potential for 3D dosimeters, including both gels and radiographic polyurethane, to provide reliable measurements in clinically relevant circumstances.

7. References
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