Image-guided Radiation Therapy: Emergence of MR-Guided Radiation Treatment (MRgRT) Systems

D.A. Jaffray[1-3], M. Carlone[1,3], C. Menard[1,3], and S. Breen[1,3]

[1]Radiation Medicine Program, Princess Margaret Hospital/Ontario Cancer Institute, Toronto, Canada
[2]Department of Medical Biophysics and Institute of Biomaterials and Biomedical Engineering (IBBME), University of Toronto, Toronto, Canada
[3]Department of Radiation Oncology, University of Toronto, Toronto, Canada

ABSTRACT

Radiation therapy has been on the march toward highly conformal and precise placement of radiation dose within the human body. Development of image-guidance systems based upon x-ray and ultrasound have advanced our capabilities to the level of a few millimeters of uncertainty in many sites. However, there are a subset of existing applications, and potentially many new applications that could be improved upon or pursued if greater targeting accuracy could be achieved. This is motivating the creation of magnetic resonance image-guided radiation treatment units (MRgRT) that either operate simultaneously or provide pre-treatment MR-based targeting capabilities. In this review, the motivation for these pursuits, an overview of recent developments, and a commentary on the challenges they face is presented.

Keywords: Image-guidance, Radiation Therapy, Magnetic Resonance Imaging, Integrated

1. Trends in Image-guided Radiation Therapy

Advances in radiation therapy practice over the past 20 years have progressed in parallel with the introduction of new information into the process of target identification (CT and MR), planning (conformal and inverse planning), and execution of delivery (helical, intensity modulated, and volumetric arcs). The transition from technique-based approaches to prescribing and delivering the dose to a patient-specific image-derived treatment plan has been supported with the introduction of dose prescription standards that explicitly support the three-dimensional (3D) nature of the problem. The International Commission on Radiological Units (ICRU) reports #50 and #62 provide a comprehensive lexicon for the dosimetric and geometric prescription of treatment and it also provides an important mechanism for the accommodation of geometric uncertainties intrinsic to the treatment methods being employed. The planning target volume (PTV) is a geometric construct that expands (in 3D) upon the clinical target volume (CTV) itself to provide a volume to evaluate the coverage of the CTV target volume in the presence of geometric uncertainties. The sources of these geometric uncertainties have been very well characterized and arise from a number of sources, including, uncertainty in target delineation [1], intra-fraction motion [2,3], and inter-fraction motion. [4,5] It is also important to note that the determination of the appropriate PTV margin is dependent on the dose gradients that can be achieved and the number of fractions that are going to be delivered. Simply put, the steeper the dose gradient, the greater effect any displacement in the target position will have on the dose delivered. With respect to fractionation, the number of times the random uncertainties are sampled will influence the impact of geometric uncertainty on dosimetric errors. Low numbers of fractions will not assure the convergence to central-limit and as a result, greater margins are required. Reduction of intra and interfraction can be achieved through the use of image-guided treatments that employ imaging systems that are integrated with the treatment unit itself. There have been a large number of image-guidance equipped radiation therapy systems introduced to the market in the past 10 years. Of specific relevance to this review is the development of integrated imaging systems that provide direct visualization of soft-tissue.[6] The integration of CT scanners into the treatment room were one of the first methods of achieving soft-tissue targeting at the time of treatment.[7] The development of the rotational IMRT platform (Tomotherapy), provided the opportunity to apply megavoltage CT

Medical Imaging 2010: Physics of Medical Imaging, edited by Ehsan Samei, Norbert J. Pelc,
Proc. of SPIE Vol. 7622, 762202 · © 2010 SPIE · CCC code: 1605-7422/10/$18 · doi: 10.1117/12.848608

approaches and represents the first broad deployment of soft-tissue capable integrated IGRT systems.[8,9] The advances in flat-panel detectors[10] allowed substantial innovations in image-guidance using both megavoltage (MV) and kilovoltage (kV) x-rays. While the integration of kV x-ray systems with the radiation therapy treatment unit has been pursued since the 1950's [11], it is the availability of digital, real-time readout technology, such as, amorphous-silicon flat-panel detectors that have enabled the development of cone-beam CT for soft-tissue imaging of the patient in the treatment position.[12,13] These systems have now become the dominant method of positioning patients for both conformal and stereotactic radiation therapy. These systems have demonstrated that sub-mm targeting accuracy and precision can be achieved for unambiguous objects [14] and precision on the order of 2-4 mm can be achieved for the targeting of soft tissue structures such as the prostate and lung lesions.[15] However, the precision and accuracy that can be achieved by these systems in targeting other, low contrast soft-tissue lesions, or in the visualization of normal structures is less than acceptable for treating some targets with small (few mm) margins [16-18] or for applying adaptive strategies that allow very tight PTV margins (~0 mm or delineation uncertainty only).[19-21]

In addition to the trends toward soft-tissue image-guidance, there has been broad adoption of MR imaging in the RT planning context motivated by factors that include higher soft-tissue contrast (T1/T2) and its capacity to provide additional information (MRS, ADC, DWI) for the purposes of sub-target definition. Early adopters pursued the use of low-field imaging systems since they had larger imaging apertures and did not interfere with patient positioning needs for treatment.[22] Considering that these systems sacrificed imaging performance for access, the positioning motivation was not sufficient to see large uptake of these systems. In fact, there has been substantial interest in high field (1.5T) systems to provide higher performance applications such as chemical shift imaging (CSI), DCE-MR, and DWI. In this context, investigators have invested substantial effort into addressing the issues of distortion in MR images, which arise from a number of sources including field inhomogeneity, gradient non-linearity, and chemical shift effects.[23-25] The dominant of these is gradient non-linearity and this can be corrected through post-processing using calibration tables. In addition to distortions, there can also be signal non-uniformity, which may be interpreted as distortions when examining low-contrast structures. Overall, distortion issues have been addressed with methods reported in the literature and these are becoming integrated into clinical scanners. [23,24,26-29] The desire to replace CT scanning in the simulation process with MR imaging has also raised another important issue. CT images are used in the treatment planning process to estimate electron densities and allow accurate dose calculations within the human body. A number of investigators have developed methods to estimate electron density from MR images using look-up table and tissue classification schemes. [30] The growing value (image quality, SNR, delineation, motion assessment) and viability (geometric accuracy, cost, sequence maturation) has led the National RT Advisory Group (NRAG) in the UK to recognize the use of MR in radiation therapy planning as a valid pursuit stating in their recent guidelines report "Recommendation: all oncology departments should have access to a MRI scanner for planning. Ideally, all should have their own dedicated MRI scanner." These developments in the clinical setting are spurring manufacturers to develop dedicated systems for MR simulation in RT. These are taking the form of both complete systems, as well as, MR-compatible accessories for immobilization and the development of dedicated coil systems to support the immobilization and positioning requirements of radiation therapy. At the Princess Margaret Hospital, the Radiation Medicine Program has been studying the application of MR in RT planning and response assessment since 2003 with the use of a dedicated MR scanner (General Electric, Twinspeed, 1.5T, 8 Channel). Recently, a 3T MR scanner (Siemens, Verio, 3T, 70 cm bore) has been purchased and integrated into a mobile transfer system (IMRIS Inc, Winnipeg, Canada) in support of better workflow and to allow interventional procedures, such as, MR-guided brachytherapy applicator placement.[31]

2. Current Initiatives in MR-Guided External Beam Radiation Therapy

MR imaging developments have now gone beyond simulation to include the development of dedicated MR-guided treatment units. The motivation being that the target and normal structures can be readily visualized just prior to radiation delivery or during delivery to allow real-time tracking or monitoring of the treatment target and normal structures. Dempsey et al. of Viewray Inc. (USPTO Application #: 20090149735) have been pursing the development of a combination MR-scanner and ^{60}Co IMRT unit. Some of the issues and benefits of this approach are reviewed by Kron et al. [32] Fallone et al. have been developing a combination linear accelerator and resistive magnet for low-field MR imaging mounted on a rotating treatment gantry.[33,34] The group in Utrecht has been promoting the merits of high field (>1.5T) imaging in combination with a linear accelerator and have recently reported impressive results in terms of image quality achieved during irradiation.[35,36] In addition to direct integration, there are active projects to establish patient-transfer approaches that bring many of the benefits of MR imaging to the treatment room, but avoid the challenges of

direct integration.[21] Recently, the Radiation Medicine Program of the Princess Margaret Hospital has embarked on the creation of a multi-use facility that supports both MR-guided brachytherapy and external beam radiation therapy. An overview of the design and current status of these initiatives is provided below.

2.1 Utrecht Solution

Driven by in a interest in accurate targeting of MR-defined regions of disease[37], Lagendijk et al. have been pursuing the integration of a linear accelerator with a high-field (1.5T) magnetic resonance imaging system for several years. Briefly, the linear accelerator's radiation beam (6MV) originates outside the MR magnet, is orthogonal to the B field, and transits through a region on the magnet that has been re-designed to minimize attenuation and interference with the x-ray flux as it travels toward the patient. The major technological challenge that the group has been addressing is in the operation of a linear accelerator in a field larger than that of the Earth's. The key technical innovation (WO/2004/024235; filed 02.09.2003) is in the alteration of the magnet to create a low-field toroidal envelope in which the electron gun and accelerating components of the accelerator could operate (see Figure 1). Their solution is demonstrated to operate in their recent publication [38]. While the operation of the accelerator is exciting, the more surprising result is in their demonstration of very high image quality that can be achieved with the modified magnet and with the accelerator operating. In fact, they were able to demonstrate that there was no penalty in MR performance compared with a conventional Philips Achieva 1.5T scanner. It was not entirely clear that this level of performance would be possible in this first prototype without additional efforts in managing the influence of electronic/RF interference with the image formation process. The results presented in the 2009 PMB article provide conclusive evidence that a combined system with simultaneous operation of the MR unit and the linear accelerator is feasible. The innovative scheme used to provide the RF cage within the radiation-shielded room is also a valuable contribution in that it does represent a feasible approach to the problem. One of the problems the group came across was the impact of the MR on adjacent clinical

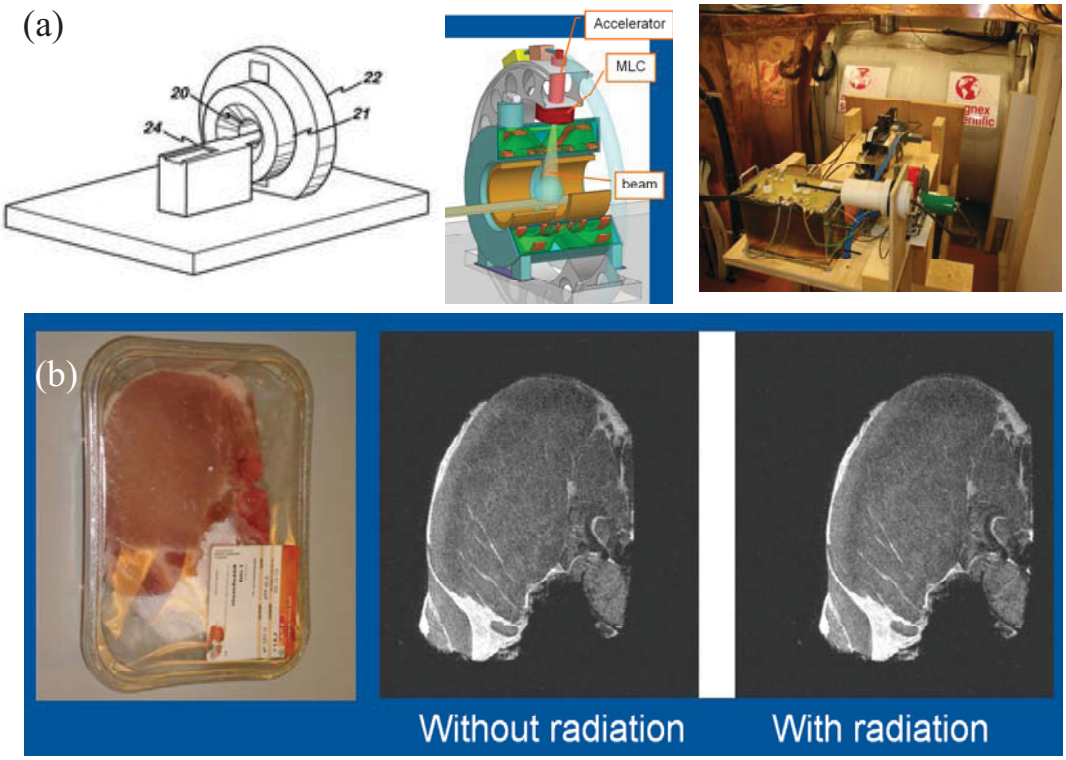

Figure 1. The Utrecht MR-linac design. (a) A key development is the modification of the magnet to create a low-field envelope around the magnet in which the electron gun and transport mechanism can operate, regardless of angle. (b) An image of butcher's meat acquired at 1.5T without and with irradiation by the 6MV photon beam. Figures provided courtesy of Jan Lagendijk.

accelerators. Even at distances of several meters, the performance of existing accelerators was influenced by the installation of the 1.5T magnet. [39] The increase in field detected at the other accelerators was on the order of 0.5-1.5 G over the earth's field. A re-calibration of the treatment unit returned them to the clinical specification. In addition to the inter-operability issues, the Utrecht group has been examining a variety of other issues that need to be addressed before such a system could be considered for clinical use. These include a detailed evaluation of the effect of the MR-field on the distribution of the radiation dose within and on the surface of the patient [35,40,41], evaluation of methods of correcting for image-distortion, and development of software methods for automatic segmentation of normal structures for on-line planning.[42]

2.2 Edmonton Solution

The approach used by the group at the University of Alberta is to employ an open, permanent magnet MR system. The linear accelerator is pointed between the magnet poles and thus has an unobstructed view of the patient [USPTO # 2009/0149735 A1]. In order to accommodate rotational therapy, the linear accelerator and magnet are coupled such that the MR magnet also rotates as the linear accelerator rotates around the patient. This is illustrated in Figure 2(a), which shows a miniature prototype of the combined bi-polar MR magnet and linear accelerator assembly. In this configuration, the linear accelerator is mounted perpendicular to the magnetic field produced by the bi-polar magnet and so the functionality of the linear accelerator will be compromised by the MR unless the two magnetic systems are decoupled. This is accomplished using magnetic shielding to reduce the magnetic field at the location of the linear accelerator to near zero. The magnetic shielding will also negatively affect the homogeneity of the magnetic field at the imaging zone of the MR unit. Imaging grade homogeneity of the magnetic field can be restored by introducing symmetric shielding components at the exit side of the MR magnet (in Figure 2(a), the shielding of the linear accelerator is shown in red, the balancing shielding is shown at the exit side in grey).
An advantage of this approach is that the magnetic decoupling of the bi-planar MR and the linear accelerator need only be solved once. By rigidly fixing the linear accelerator and the MR magnet and preserving this relationship at all gantry angles, the magnetic decoupling of the linear accelerator and the imaging properties of the bi-planar magnet are preserved during rotational therapy. A further advantage of this approach is the use of permanent magnets; these are stable and do not require cryogenics or water cooling (for resistive magnets) in a design which depends on rotation. As well, magnetic shielding of the linear accelerator can be accomplished without significant expansion of the magnet's fringe field. The permanent magnet, however, also poses challenges for a system suitable for imaging and treating humans. The prototype system shown in Figure 2(a) is small with a bore on the order of 20 cm. To increase this to a bore on the order of 70 cm, which is required for treating human patients, the scaling of the magnet is linear in all dimensions to first order. This produces a very large permanent magnet, which will be technically difficult to manufacture and install within a shielded radiotherapy treatment room.

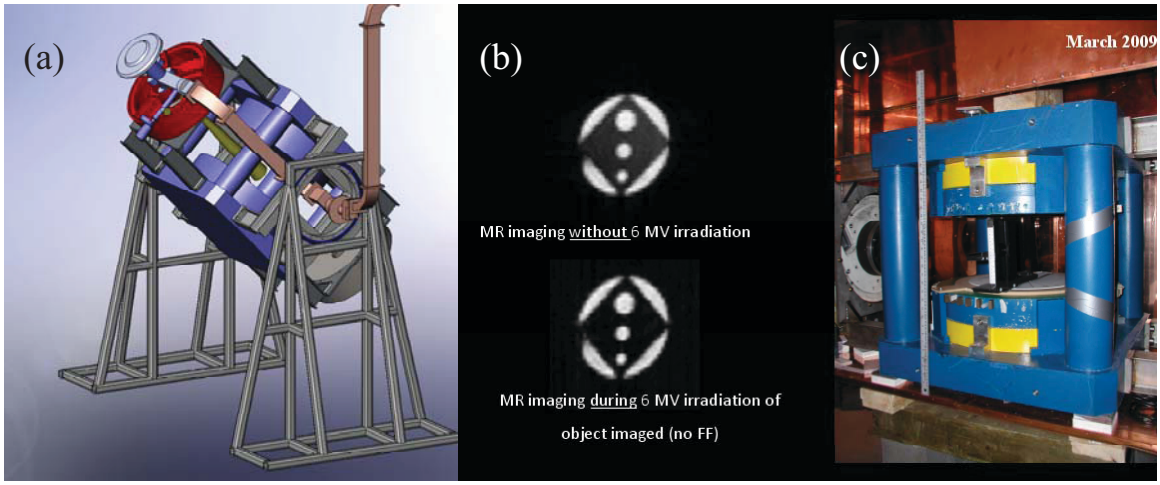

Figure 2. The Edmonton MR-linac design. (a) A rotational assembly carries a permanent magnet (blue) that rotates with respect to the patient. The accelerator is mounted orthogonal to the rotational axis and also rotates about the patient. (b) An MR image of a test phantom acquired with and without the radiation beam operating. (c) A photo of the current, non-rotating assembly. Figures provided courtesy of Gino Fallone.

The group at the University of Alberta has reported first images in the prototype system.[33] These images were obtained on a system that was stationary (see Figure 2(c)). The permanent magnet operates at a 0.2 T magnetic field and the assembly provided sufficient magnetic shielding of the linear accelerator to reduce the magnetic field to a value close to that of the earth's magnetic field (0.05 mT). The imaging magnetic field strength, 0.2 T, is lower than most diagnostic MR units, which currently operate at 1.5 and 3 T, but is sufficiently large to provide images for image guidance purposes.[22] Images of a white acrylic phantom immersed in a $CuSO_4$ solution were obtained with the linear accelerator not producing and when the linear accelerator is producing x-rays at the same time as MR image acquisition. No image distortions were observed, however the SNR was observed to decrease from 80 to 16 for the different imaging conditions.

2.3 MR-^{60}Cobalt Solution

The challenges associated with the integration of an electron linear accelerator and MR scanner have raised interest in the use of radioactive sources for this application. Dempsey et al. of Viewray Inc. (USPTO Application #: 20090149735) have been pursing the development of a combination MR-scanner and ^{60}Co IMRT unit and have raised funds for this activity. In their design, they propose to use up to 3 sources and corresponding MLCs to deliver IMRT distributions. Briefly, the proposed embodiment uses a double-donut design for the MR system similar to that used in GE's interventional MR unit [43,44] and will operate at moderate field strengths (< 1T). A rotating gantry carrying the sources and collimation assemblies is to be installed between the double donuts of the MR unit. In their recent article, Fox et al.[45] review the advantages and disadvantages of ^{60}Co-based external beam systems and argue that the combination with an MR scanner will work to address other issues associated with the use of Cobalt. Specifically, they argue that (i) the penumbra achieved is competitive with that of an accelerator (4-7 mm) even for a 2 cm diameter source, (ii) the magnetic field of the MR eliminates contamination electrons, (iii) the use of three radiotherapy heads provides a competitive dose rate, and (iv) the penetration of a ^{60}Co photon beam is not important with IMRT. It is the last point that is the primary topic of the paper in which they present a detailed comparison of dose distributions achieved with conventional linear accelerator generated (6 & 18 MV) photon beams to those generated using a model of MLC-modulated ^{60}Co treatments. These studies were performed across a number of treatment sites and conclude that competitive dose distributions can be achieved using existing double-focused MLC technology and existing ^{60}Co source designs. There are a number challenges that remain for this approach. Kron et al. provide a detailed description of the ^{60}Co approach in their 2006 article.[32] The approach presented is very similar in design to that of Dempsey, but suggests a helical tomotherapy approach to delivery. This would allow pneumatic collimation for minimal interference and rapid source shuttering in gating applications. They also raise the interesting fact that ^{60}Co is ferromagnetic. It is not clear that this will be significant given the profile of the large mass of rotating components which must also be taken into consideration when considering field uniformity and eddy current induction. Regardless of the challenges, it is rumored that such a system will be available in the market within the next 36 months.

2.4 University Hospital of Umeä - Patient Transfer Solution

The desire to employ MR imaging for targeting in radiation therapy motivated the University Hospital of Umeä to install a 1.5T Siemens Espree scanner in an adjacent room at 90^o to the rotational axis of a Siemens linear accelerator. A trolley-based transfer system taken from the Siemens intra-operative X-ray and MR system (Myabi System) was adapted for the application and permits transfer of the patient from the treatment unit to the MR and vice-versa. The total transfer distance is approximately 20 meters and it is indicated that this transfer can be performed in < 2 minutes. The authors have targeted a total treatment time, post-localization of less than 20 minutes for their treatment of prostate cancer. The advanced state of this development have allowed these investigators to focus on a number of the logistic issues. Specifically, they have developed methods for electron density over-ride in the context of sites requiring heterogeneity correction, the use of alternative 're-registration' fiducial systems (lasers, optical, MV, kV) to link the MR images to the treatment reference frame, and the pursuit of an ultra-short (0.07 and 4.76 ms) echo time sequence (UTE) to test the potential for enhancement of bone in MR images.

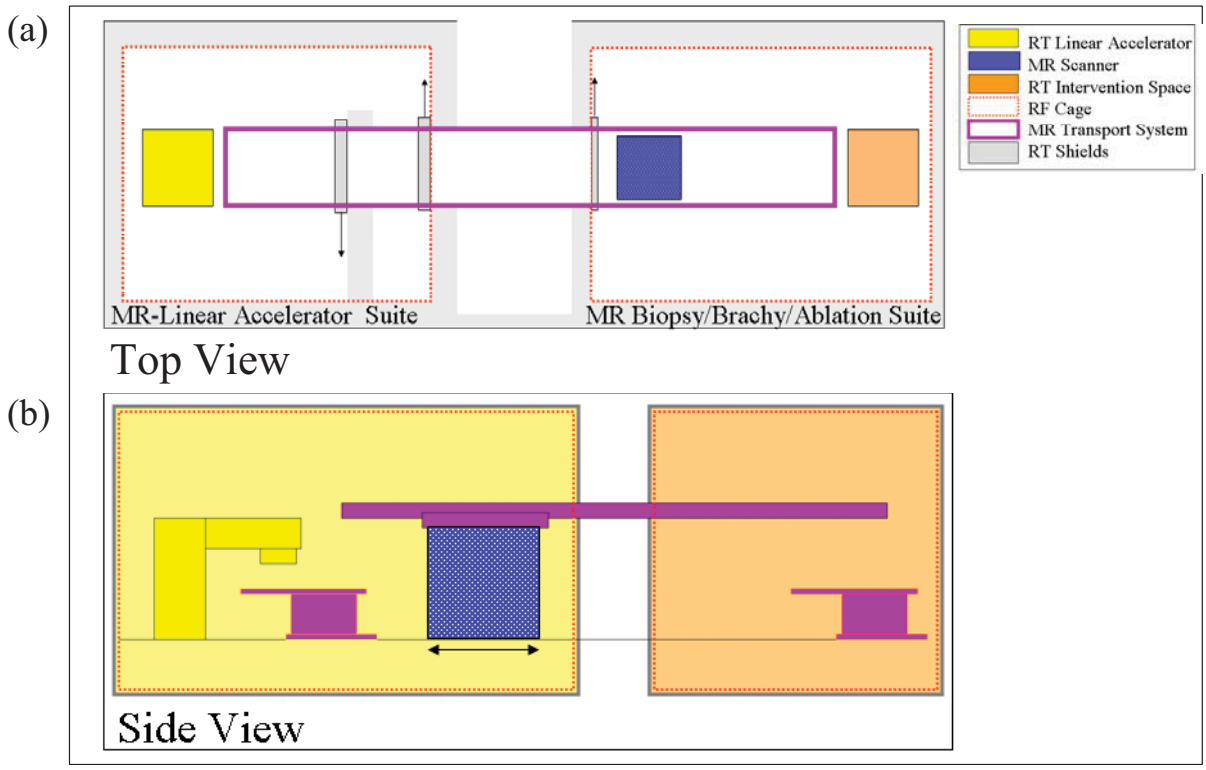

Figure 3. Mobile magnet solution in development at the Princess Margaret Hospital, Toronto, Canada. The system employs a rail system to move the magnet between a brachytherapy interventional suite and the external beam treatment room. (a) The overhead view shows the need for radiation and RF shielding doors systems. (b) Robotic positioning systems will be required to transfer the patient from the accelerator isocentre to the MR imaging bore. The removal of the magnet from the accelerator environment will assure operation of the accelerator and conventional dosimetric performance.

2.5 Princess Margaret Hospital - Mobile Magnet Solution

The research and clinical activities of the Princess Margaret Hospital have identified three clinical treatment sites that can motivate the direct integration of MR imaging into the treatment room. These are (i) adaptive radiation therapy for treating cervical cancer, (ii) targeting liver lesions in stereotactic body radiation therapy (SBRT), and (iii) high accuracy treatment of spinal lesions. The research program in adaptive interventions has motivated the development of a process for on-line adaptation for patients receiving radiation therapy for cervical cancer. In a recent study of alternative adaptive strategies, the volume of normal tissue irradiated can be significantly reduced only through on-line re-planning approaches.[19,46] The encouraging development in this research has been in the use of completely unsupervised re-planning in the inverse planning studies (Orbit Workstation, Raysearch Laboratories, Stockholm). These unsupervised methods would allow an on-line approach to be pursued provided segmentation of structures was automated and robust. Given our previous experience in on-line scan-plan-treat methods in the palliative population,[47] we are confident a clinical process can be established that would operate in a viable clinical time interval (<30 minutes). The treatment of liver lesions would be best performed with an integrated unit to allow target visualization and tracking, however, the technology is not currently available. The current use of active breathing control (ABC) methods and abdominal compensation methods minimize motion and will provide an excellent bridging approach for an adjacent MR unit to improve the accuracy of targeting. While these methods would also apply to lung SBRT, the motivation is not as clear, as these are easily localized on cone-beam CT images due to the high contrast in a lung background. Finally, SBRT for paraspinal lesions is a growing practice and the ability to visualize the cord itself at the time of treatment, not just the spinal canal, would provide a systematic adjustment of several mm to be capitalized upon during integrated planning and delivery. In addition to the applications of MR in the external beam setting, we have an active program in MR-guided brachytherapy. The proposed design will provide dual-use of the MR unit for both these applications and could be extended to operate as an MR simulator for the radiation therapy department. A schematic of the design is shown in

Figure 3 and, in this case, is restricted to uses in external beam and brachytherapy. The proposed system employs a 1.5T MR unit that is translated on rails between the shielded brachytherapy suite and the shielded linear accelerator vault. Both environments contain a patient support and transfer systems. Specific to the external beam operations, a robotic table will transfer the patient between the accelerator and the MR unit. The MR unit will be moved to within a safe operating distance of the accelerator for imaging and withdrawn to assure normal operation of the accelerator and imaging subsystems. In addition to applications in image-guidance the approach has a number of important merits: (i) convenient, high-quality MR-based response assessment capabilities for longitudinal studies with the patient in the treatment position (advantage of high performance MR), (ii) equivalent imaging in the treatment room, as would be found in the simulation setting, (iii) nearly standard maintenance and repair of the treatment unit, (iv) no modification to dosimetry due to complete absence of MR field during delivery, (v) high throughput when the MR unit is not engaged, (iv) access to the MR unit in the brachytherapy suite (or simulation suite for a tri-purpose configuration), and (v) cost-savings in terms of MR system and on-going service contracts. Penalties include the cost and maintenance of the rail system and shielding complexities. These will be examined as the project moves forward over the next 18 months.

3. Challenges to MR-RT Treatment Unit Integration

3.1 Dosimetry in the Magnetic Field

Megavoltage x-rays deposit dose by interacting with the target tissues and producing photoelectric, Compton, or pair electrons. These scattered electrons initially have energies that can be in the MeV range, and this energy is transferred to the target tissues during subsequent electron interactions. Since electrons are charged particles, these electrons will be subject to the Lorentz force, $\mathbf{F} = q(\mathbf{v} \times \mathbf{B})$, where $\mathbf{v} \times \mathbf{B}$ is the cross product between the electron velocity $\mathbf{v}$, and the magnetic flux density $\mathbf{B}$. In the situation where the x-ray beam is perpendicular to the magnetic field direction, the net result is that a circular motion will be imposed on the scattered electrons. At megavoltage energies, electrons are

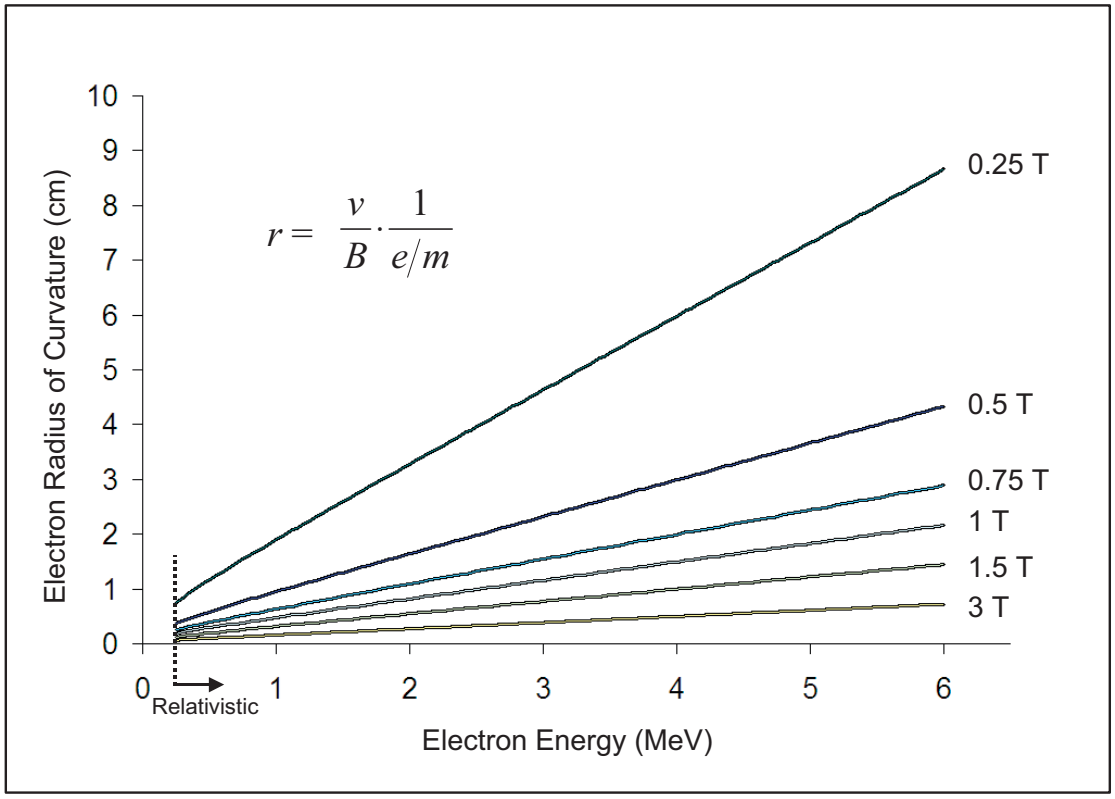

Figure 4. Relationship between the radius of curvature and the kinetic energy of an electron travelling orthogonal to the magnetic field. For relativistic energies, the dependence on electron energy appears linear. This has been plotted for a range of magnetic field strengths being considered for MRgRT systems. The range of electron energies is large corresponding to the continuum of electron energies produced in Compton scattering events and the polyenergetic spectrum of a 6MV photon beam.

predominantly scattered in the same direction as that of the incident photons. Thus, the predominant effect of a perpendicular magnetic field will be a shifting of the dose deposition pattern laterally, in a direction that is perpendicular to both the incident photon direction and the magnetic field direction. Figure 4 shows the dependence radius of curvature on the applied magnetic field for a range of electron kinetic energies. The wide range of electron energies (<6 MeV) that will be present in the body and surrounding air will result in a wide range of radial motions (on the order of several cm to < 1 mm). It is important to note, that for dense materials, the short distance between collisions will diminish interfere with the appearance of a radial path. However, in air, the effect of the field will be more noticeable due to the range and distances between collisions.

A peculiar effect occurs in heterogeneous tissue geometries where a lower density tissue is distal to a higher density tissue. This situation is not uncommon in radiotherapy; for instance in lung radiotherapy a lower density tissue (lung) is distal to the superficial higher density tissues. The situation also occurs at the beam exit, where the air surrounding the patient clearly has a lower density than the body tissues. In these cases, scattered electrons in the lower density medium have a sufficiently large range such that their circular path can return them to the originating high density tissue. This effect has been called the "dose or electron return effect"[35,41,48,49] and it can significantly increase the dose at the high to low density interface. It will have to be considered carefully when designing radiotherapy plans in the presence of a transverse magnetic field.

To understand the general effect of dose deposition in a magnetic field, it is useful to study the two geometries that dominate the integrated MR-RT solutions.

In the first geometry, a fixed magnetic field orientation is employed with a radiation source (^{60}Co or linear accelerator) rotating around the magnetic field axis. This is the geometry employed in the Utrecht and Viewray designs. In this geometry, the cross-product of the magnetic field and the direction of scattered electrons rotates in the patient reference frame, and so the direction of the lateral shift of the dose distribution in the patient reference frame will be gantry angle dependant.[34] This is advantageous since for an opposed pair of beams, the lateral shift can largely be cancelled, and the dose return effects can be reduced, but not eliminated. For the fixed magnetic field geometry at low field strengths (0.2 T), the dose disturbance for a parallel-opposed-pair (POP) in a phantom with low and high density materials is very small, on the order of 5% or less at the tissue interfaces. At higher field strengths (1.5 T) the dose disturbance is more significant and displays a more complicated pattern at both the lateral edges of the beam and at the tissue interfaces.[34] It is important to remember, when discussing these effects, that the dominant direction of electron travel is not, by any means, the only direction of electron travel.

The second geometry is one in which the cross product of the magnetic field and dominant electron flux direction is aligned with the rotation axis of the gantry, regardless of the orientation of the gantry. This geometry is employed by the group at the University of Alberta.[33] In this case, the lateral shift of the dose deposition pattern will be constant at all gantry angles, and so there will be an additive affect in the case of a POP beam arrangement. Thus, for this geometry, the principle effect will be shift the dose distribution laterally. The dose return effect will still be present and will not be cancelled by a simple opposed pair beam arrangement. At lower field strengths (0.2 T) this effect is significant and would need to be accounted for in the planning. Raaijmakers and colleagues have suggested that IMRT can be effectively used to compensate for the dose distribution perturbations caused by a transverse magnetic field.[50] While it may be feasible to produce dose distributions that are more consistent with usual clinical objectives using an optimization strategy in a research setting, the practicality of producing dose distributions consistent with clinical experience in a clinical process is an open question whose solution remains to be determined.

In addition to the effect of the magnetic field on the distribution of dose, the field will also affect the measurement of dose. Absolute radiation dosimetry calibrations are typically performed using ionization chambers that rely on charge collection in an air cavity. While it is likely these methods can still be applied, greater care must be taken in the methodology.[51] Alternatively, other dosimetry methods may need to be developed for the measurement of surface doses or the performance of patient-specific geometry. Given the challenges of placing conducting wire leads in the MR environment, optical methods may be required to assure robust, simple dosimetry in the clinical setting. [52] In general, the dosimetry issues associated with delivering radiation dose in the presence of magnetic fields are not resolved. While the groups in Utrecht and Edmonton have done a great deal to frame the magnitude of the problem and to dispel theoretical problems, much work remains before these systems have the well-characterized dosimetric characteristics that we are used to in current clinical practice. The field will likely have to strike a compromise between the dosimetric uncertainties and geometric certainties that such systems may offer.

3.2 Function and Performance Issues

Dosimetric issues aside, there remain a large number of function and performance issues that will need to be addressed for the integrated solutions to be viable. In addition to the conventional needs of radiation shielding for a radiation therapy unit, the additional requirement of RF shielding needs to be addressed. Fortunately, there is substantial flexibility in both the radiation shielding doors and in the RF shielding door design. Sliding and swing door designs for both of these currently exist and should be easily adapted. It is more than likely that the RF cage will sit within the radiation shield allowing 'noisy' components to sit between the shields. The traditional practice of introducing dosimetry systems and cabling into the room as needed will no longer be possible without substantial forethought. Watertank scanning, for example will need to be re-examined as a beam commissioning methodology. Given the ready adoption of Tomotherapy's alternative commissioning methods, it is likely that the field will be open to alternative approaches as required in this setting. While success in the isolation of the accelerating system components has been achieved by the Utrecht and Edmonton groups, other noise sources including MLC motor noise must also be considered.[53,54] In general, the approach taken by the Utrecht group (in their prototype) to isolate the bore and effectively cap the ends with the patient in-place should be robust against these noise sources.

In addition to achieving acceptable MR imaging performance and understanding the dose delivered by such systems, it is also necessary to geometrically calibrate the spatial targeting system. It is unclear how this will best be achieved with the systems. It is not common to calibrate the absolute reference frame of the images arising from an MR scanner in the world coordinate system. Given that it is not straightforward to localize the radiation beam directly within the MR image (as is the case in HIFU), it is necessary to cross-calibrate the two systems. This can be achieved through the use of an EPID-like device using methods akin to that used in recently developed XMR systems.[55] The stability of these calibrations for various imaging sequences and objects will also require investigation. Ideally, a method to constantly assure geometric calibration between the systems should be developed. In general, it is not clear what level of precision and accuracy these systems will have given the various factors at play. However, failure to achieve better than 2 mm accuracy in the cross-calibration will seriously undermine all the motivation for building such systems.

3.3 Logistic, Safety and Cost Issues

In addition to the functional and performance issues, there are also a large number of operational issues that need to be considered before these systems go into clinical use, or before they are sufficiently motivating for broad uptake across the community. While the radiation therapy community has a very good track record with respect to radiation safety, the introduction of MR safety issues into the same setting will compound the complexity of the various safety systems and processes. During the implementation of our MR simulation units that Princess Margaret Hospital, a department-wide safety course was implemented to familiarize the staff with the 'different thinking' that needs to be present in the setting of an MR scanner. Conventional RT practice of routinely introducing different immobilization devices into the treatment setting needs to be re-thought in the MR context. The establishment of an MR safety committee is a necessary step. In fact the ACR offers comprehensive guidelines to be considered in the design of MR units to allow safe staging of emergency response staff for patient emergencies. These must also be considered in the MR-RT setting. Practical issues such as the process of pre-screening patients for daily, fractionated radiation therapy in an MR setting and the impact on patient throughput should also be considered. Existing radiation therapy service activities for such a system would tend toward a Tomotherapy model, since MR service is beyond the skill set of most internal service staff. Furthermore, the compound units will also have heightened safety oversight to assure tools and devices are managed appropriately.

4. Summary

MR-guided RT units are being developed to increase the accuracy with which radiation therapy can be placed within the body. These approaches offer methods to either track mobile targets or allow on-line adaptation to changing disease and normal anatomy. Despite the substantial technical challenges raised, there has been significant progress in both integrated and adjacent approaches. It is likely that a variety of research platforms capable of MR-guided RT will be available in the next few years. It will be interesting to see what 'killer applications' arise from these studies, such that the substantial investment and operating costs of the units will be justified.

Acknowledgements

The authors would like to acknowledge the contribution from a number of individuals and programs. We thank Dr. J. Lagendijk of the Utrecht Medical Centre, Utrecht, Netherlands for provision of the images and valuable discussions. Dr. G. Fallone of the Cross Cancer Institute, Edmonton, Alberta, Canada for the images and photographs. We are grateful to Mr. K. Brown of Elekta Oncology Systems for his on-going dialog on the role of MR for image-guidance in radiation oncology. The contributions of T. Shay, S. Hushek and L. Petropoulos of IMRIS, Inc. are also appreciated. The support of Raysearch Laboratories in our investigations of adaptive radiation therapy has helped build motivation for these developments and is greatly appreciated. In addition, the Radiation Medicine Program's experience in MR for radiation therapy has been supported through funding from Varian and General Electric. The senior author would like to thank the Canadian Foundation for Innovation (CFI) and Ontario Research Fund–Research Excellence (ORF-RE) Program of the Ontario Ministry of Research and Innovation (MRI) for their support.

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