Exploring Magnetic Resonance Imaging Guidance in Radiation Oncology

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Image guidance is a crucial advancement in radiation oncology treatment because it allows the tumor being treated to be viewed externally.[1] Without this capability, radiation oncologists would find it difficult to pinpoint the location of the tumor and structures affected by the treatment. Harold Johns, a Canadian medical physicist, said, "If you can't see it, you can't hit it, and if you can't hit it, you can't cure it."[2]

For decades, radiation oncologists have used kilovoltage and megavoltage radiographic port films and cone-beam computed tomography (CBCT) to visualize patients' anatomy and create treatment plans. Kilovoltage and megavoltage imaging result in superimposition of anatomical structures, while CBCT acquires cross-sectional slices without superimposition and allows for an almost 3D view of internal organs. Recently, magnetic resonance (MR) imaging linear accelerators have become available. MR imaging, like computed tomography (CT), displays cross-sectional images. Unlike kilovoltage, megavoltage, and CBCT imaging, which use ionizing radiation, MR imaging creates images with powerful magnets and electromagnetic currents and does not expose patients to ionizing radiation.[3] Radiation oncologists already employ MR imaging, when appropriate, for diagnostic evaluation. These images provide a clear picture of the tumor and surrounding healthy tissues.

The introduction of onboard MR imaging allows for soft-tissue discrimination and intratreatment monitoring that CBCT lacks.[3] Intertreatment motion can occur when the patient's anatomy changes between treatments. CBCT online adaptation exists; however, live imaging adjustments are not achievable with CBCT. MR imaging online adaptation recognizes changes in anatomy and permits the operator to adjust the plan before treatment delivery. MR imaging offers motion management that standard ionizing radiation linear accelerators cannot offer. Most non-MR imaging–based motion management systems, including optical surface monitoring, do not use medical imaging. These systems rely on infrared light to monitor the surface of the patient's skin and notify the treatment operator when substantial movement has occurred. Although these non-MR imaging–based systems can reduce the number of treatment errors due to motion, small changes in the position of the anatomy cannot be visualized. MR imaging–guided linear accelerators image internal structures during beam-on time and allow for adaptation of the plan if necessary.[4] The quality of images, motion management, and online adaptation create an appreciable difference when comparing CBCT with MR imaging–guided radiation therapy (MRIgRT).[4] However, concerns about implementing MR imaging guidance include cost, safety, necessary adaptations, and accuracy.[4-7] Because few MR imaging linear accelerators are in clinical use in the United States, understanding of MR imaging guidance is limited.[8,9]

Methods

The literature reviewed in this article was located through Primo by Ex Libris and PubMed. Key words used in the database search were *MRI-guided* and *radiation therapy*. These key words returned 870 results. The search was further refined by focusing on peer-reviewed articles published in the past 10 years, which returned 558 articles.

Initially, 75 articles were reviewed to assess current research on MRIgRT. Twenty-three articles discussing the implementation of MR imaging–guided linear accelerators, including advantages and challenges, were selected and further evaluated. These articles were organized by foundational knowledge of operations, accessibility, cost, and safety.

An online public access search engine was used to identify common MR imaging–guided linear accelerator manufacturers. Three manufacturer websites provided details on the function of MR imaging–guided machines, and 2 of those also had information regarding how many of their linear accelerators are currently in use.

Discussion

According to Hall et al, evidence shows that 50% of all cancer patients undergo radiation therapy treatment.[3] Therefore, the advancement of radiation therapy technology is integral to providing effective treatment. Linear accelerators are the primary treatment machines used to deliver external beam radiation therapy. When a linear accelerator includes onboard imaging systems to assist in treatment delivery, this is known as *image-guided radiation therapy*. Image-guided radiation therapy has improved the treatment delivery process by ensuring patient anatomy remains in the same position for each treatment. When image-guided radiation therapy was introduced, kilovoltage and megavoltage 2D images were used to visualize patient anatomy. The introduction of this imaging was groundbreaking, as the tumor and the surrounding organs at risk (OAR) could be visualized before delivering treatment, during beam-on time, and between treatment sessions.[3]

Later, the introduction of CBCT provided an opportunity to view anatomy as individual slices. CBCT was another pertinent milestone for image-guided radiation therapy, allowing radiation oncologists and dosimetrists to produce customized treatment plans for each patient. Although it does not construct images as comprehensively as a stand-alone CT machine, CBCT allows for increasingly detailed treatment plans and has resulted in superior outcomes for years.[3]

With the continual advancement of technology, MR imaging has shown promise for improved soft-tissue differentiation, tumor detection, and treatment plan personalization.[3] MR imaging is known for its superior contrast resolution and visualization of soft tissues. MR imaging produces higher-quality images for cancer treatment than does CT imaging because of the soft-tissue composition of common tumors; therefore, physicians often use MR imaging to help generate a diagnosis for cancer patients, and manufacturers have developed and released MR imaging–guided linear accelerators.

Current Implementation of MRIgRT

Between 10 000 and 15 000 medical linear accelerators are in use worldwide, and approximately 96 of those machines use onboard MR imaging guidance.[8-11] The reviewed literature indicated 3 common manufacturers of MRIgRT systems. The number of manufacturers and the production of linear accelerators with onboard MR imaging will likely increase as more clinical trials and data are published.

Hehakaya et al surveyed the staff from 7 hospitals to assess current knowledge about and perception of MRIgRT.[5] According to the survey's findings, staff thought MR imaging–guided linear accelerators were advanced technology with technical benefits that could allow for diagnostic and treatment opportunities.[5] Those skeptical about implementing MRIgRT felt that way because of the limited amount of clinical effectiveness data and number of machines currently in clinical use.[5]

Although the interviewees from the Hehakaya et al study believed in the need for more clinical information on the implementation of MRIgRT,[5] several studies exist that document the effectiveness of using the technology. For example, a 2022 study of stereotactic MRIgRT for localized prostate cancer conducted by Ristau et al evaluated 68 patients who received ultrahypofractionated MR imaging–guided stereotactic prostate irradiation.[12] The study followed the patients

through the treatment process and will continue to monitor them for 5 years. Based on the data collected from the treatment, MRIgRT has the potential to benefit prostate patients. As a result of the capability for online adaptation in MRIgRT, the patients received a higher dose to the tumor and lower doses to the surrounding organs. With a total dose of 37.5 Gy over 5 fractions, the use of MRIgRT allowed for 95% planning target volume coverage at 95% of the target dose and simultaneous focal boosting of macroscopic tumors with no acute toxicities and acceptable lower grade toxicities to surrounding healthy tissues.[12]

Ristau et al compared previous studies' results to support the predicted outcome in their study. These studies showcased positive results of using MRIgRT systems. When reviewing the treatment plans for the patients undergoing prostate irradiation, MR imaging allowed customized treatment plans for each patient. The customization permitted online adaptive planning for the tumor volume and OAR. Due to the lower OAR dose, patients exhibited less injury to those structures. Based on these data and the positive results of previous case studies, Ristau et al suspect the final 5-year results will affirm the effectiveness of this treatment.[12]

Feasibility and Challenges

After new technology is introduced, accomplishments and challenges coexist. The first challenge with incorporating an MR imaging–based linear accelerator is the cost. Parikh et al performed a cost analysis comparing CT imaging with MR imaging for image guidance in radiation therapy.[7] The costs included clinical, personnel, and equipment costs for original installation and yearly maintenance. The total sales price of TrueBeam STx linear accelerator (Varian) equipped with CBCT onboard imaging and ExactTrac (Brainlab) was estimated to be $4.75 million, with estimated annual maintenance costs of $417 500.[7] The list price for a MRIdian Linac (ViewRay Systems) was approximately $7.8 million, with an estimated annual maintenance cost of $550 000.[7] During installation, the radiation therapy vault needed additional shielding for the magnet. The magnet cost $363 per a square foot more compared with the CT vault.[7] In addition, an MR imaging–guided linear accelerator requires additional shielding to prevent the magnet from interfering with the electron stream required to produce the treatment beam. Finally, MR imaging–guided radiation treatment is a longer examination and costs $1625 more than a CT treatment based on personnel and clinic costs. Parikh et al concluded that the overall cost of MRIgRT is 18% higher than that for CT-guided radiation therapy.[7]

In addition to higher costs compared with CT guidance, there are other factors to consider with MRIgRT. Choudhury et al focused on the physics and technology required to operate the new equipment.[1] For example, research indicates that the MR imaging magnet could interfere with the electron stream of the treatment beam. The Lorentz force causes electrons in the treatment beam and the secondary electrons exiting the patient from photon interaction to circle back toward the original location, known as the *electron return effect.* The electron return effect poses the potential danger of increased patient dose in anatomical areas of adjacent air and tissue structures.[13] However, additional shielding built into the linear accelerator and quality control procedures decrease the likelihood of the electron return effect increasing the total treatment dose.

Incorporating MRIgRT creates the opportunity for online adaptive treatment plans. Online planning allows the radiation oncologist to adjust the size of the treatment volume during each treatment to conform to daily changes in the tumor and surrounding OAR. Choudhury et al reviewed the process for performing adaptive planning and the technology that would be necessary.[1] Specific software allows the linear accelerator to perform online adaptive planning. A quality control system accompanies the software for automated processes.[1] With current treatment machines and software, a physicist and radiation therapist must evaluate the treatment plan to determine its safety and accuracy. MR imaging–guided online adaptive treatment requires quality control testing each time the plan is modified. Therefore, automated quality control will be imperative to replace the physically completed quality control procedure by the physicist.

Lastly, Choudhury et al discussed the anatomy that is visualized efficiently with MR imaging–guided linear accelerators.[1] MR imaging requires longer periods to obtain images than does CT imaging, making it

more challenging to image anatomical locations with more likelihood of motion such as the lungs and heart. Hardware and software systems create fast sequences for the MR imaging linear accelerators.[1] A primary disadvantage of using these fast sequences is degradation of image quality. Although these images do not meet standard MR imaging quality, the visualization of anatomy is preferrable to CBCT imaging.

Safety Concerns

MR imaging–guided linear accelerators offer a reduction in radiation dose compared with CBCT guidance but with additional safety concerns. Because MR imaging machines employ strong magnets, new protocols and guidelines are necessary. The American College of Radiology developed industry standards for MR imaging machines.[14] All MR imaging–guided linear accelerators follow these standards.

MR imaging suites have 4 zones categorized according to differing magnetic strengths.[6] Zone I allows for safe public access. Zone II is a slightly more controlled area in the treatment facility. Only those who have completed a screening can enter zone III, a restricted area. Zone IV contains the MR imaging linear accelerator. Patient screening concepts have been introduced previously for radiation therapists; however, they will be much more in-depth with the MR imaging standards. The advanced screening questions include body piercings, medical devices and equipment, and medical implants. Most recent medical devices, equipment, and implants include an information card or label stating whether the object is MR imaging safe. When information is missing, the radiation therapist and oncology nurse must contact the physician and determine the device's manufacturer to investigate. Unsafe devices, equipment, and implants can cause excessive heating or pulling of the apparatus.[6] This phenomenon can damage the device and the equipment as well as injure the patient. Therefore, proper protocols and guidelines are crucial to ensuring the safety of everyone involved in the treatment.

Specialized Applications of MRIgRT

Patient motion, anatomical changes, and target volume discernment are critical components of image guidance in radiation oncology.[4] Currently, CT-guided imaging cannot create images during radiation treatment. Attempting CT-guided images during treatment would substantially increase the radiation dose to the patient. Images obtained by 2 separate radiation devices will not produce high-quality and accurate results. MR imaging–guided linear accelerators can reduce the total radiation dose and allow intratreatment imaging.[4] This capability permits the radiation oncologist to visualize the treatment area and evaluate daily changes in the patient's internal organs. MR imaging linear accelerators include software that permits 3D and 4D imaging. The goal of 3D and 4D imaging is to allow radiation oncologists to see the physical movement of internal organs during beam-on time. This allows for more customizable plans with a higher tumor dose and decreased dose to the surrounding OAR.

According to Otazo et al, the current drawback to MR imaging–guided linear accelerators is the increased time to acquire images.[15] However, rapid MR imaging techniques allow for fewer samples and automatic reconstruction to reduce the total time required. Thus far, this software has had a positive effect on the machine's efficiency. Otazo stated that rapid MR imaging techniques could reduce the original MR imaging method's time by 50%.[15]

A noteworthy application of MRIgRT is functional imaging. Functional MR imaging depicts biological functioning of the imaged tissue. For example, functional MR imaging can identify areas of hypoxic cells based on blood perfusion. Hypoxic cells respond substantially less to radiation treatment than do cells with typical oxygen levels. This application empowers the radiation oncologist to identify areas of hypoxic cells to ensure that these areas receive an appropriately intensified dose.[4] Current radiation treatment identifies the tumor, and the tissue volume receives a standard uniform amount of radiation. According to Keall et al, this approach contributes to local tumor recurrence in more than 95% of patients with glioblastoma because of inadequate irradiation of regions with radioresistant tumor cells.[4] Therefore, employing functional imaging in MRIgRT could be vital to reducing recurrence.

Procedural Modifications With MRIgRT

Incorporating MR imaging–based linear accelerators does not substantially alter the treatment planning

timeline. According to Raaymakers et al, the sequence requires only 2 modifications.[16] There are 2 imaging options before treatment planning. For the first option, the patient undergoes CT and MR imaging. The resulting images are sent directly to the dosimetrist to begin the construction of a treatment plan. For the second option, the patient undergoes MR imaging only. The MR image is transmitted to the dosimetrist for planning. However, because linear accelerators need a CT image to formulate the electron density for dose calculations, the dosimetrist must upload the MR image to a system that will use it to create a pseudo-CT image.[17] Using computer software to create a pseudo-CT eliminates the required pretreatment CT, reducing the amount of radiation dose to the patient.

The dosimetrist then creates a treatment plan based on the images. The most popular treatment plan for MR imaging–based machines is intensity-modulated radiation therapy. This treatment conforms the radiation beam to the tumor's shape, and the beam remains stationary when delivering the radiation. For CT-based and MR imaging–based systems, physicists and radiation therapists perform quality assurance testing to ensure the treatment is safe and efficient before the first treatment.[16]

CT-based and MR imaging–based systems have the same workflow for the first day of treatment. However, during treatment delivery using MRIgRT, the radiation therapist performs MR imaging for guidance.[16] The imaging process often involves an extended timeframe as MR imaging sequences take longer to perform. Then, the radiation oncologist evaluates the MR imaging and determines whether online adaptations are necessary. The occurrence of online adaptation is likely and depends on multiple factors. These might include treatment type, daily organ location, tissue response to treatment, and radiation oncologist's preferences. Recontouring and plan alterations can increase the duration of treatment delivery by up to 20 times.[3] The automated quality control is run before treatment delivery for the adaptations.

Case Study: MRIgRT's Role in Treating Prostate Cancer

Li et al reported treatment data for a 65-year-old patient with prostate cancer.[18] The patient underwent CT and MR imaging simulation for treatment planning (see **Figure**). The CT data provided the electron density for dose calculations, and MR imaging allowed for drawing treatment volumes and identifying OAR. The patient's treatment plan involved intensity-modulated radiation therapy. The radiation prescription was 36 Gy during 6 weeks of treatment on an Elekta Unity MR imaging linear accelerator. Throughout the 6-week treatment, the volume that encompassed the tumor decreased in size by 49%. During each treatment, the radiation oncologist performed online adaptations to the treatment plan to accommodate changes in the treatment volume's size. Due to the patient's treatment plan alterations, the bladder dose decreased by 16%, and the rectum dose decreased by 12%. The patient tolerated the treatment well and did not appear to have any acute toxicities to

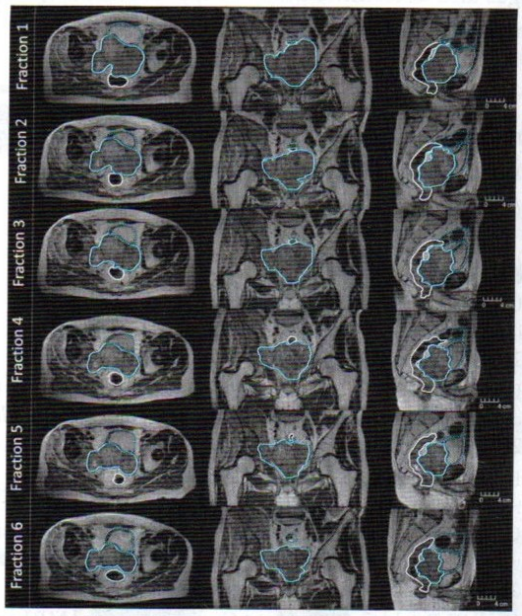


Figure. *Magnetic resonance (MR) images collected during beam delivery for each fraction on a MR imaging linear accelerator during radiation therapy treatment. The clinical target volume (solid medium blue line), rectum (solid white line), bladder (blue and white line), and large bowel (dotted dark blue line) are displayed. Li W, Winter J, Padayachee J, Dang J, Kong V and Chung P (2022) Case report: MR-guided adaptive radiotherapy, some room to maneuver.* Front Oncol. *12:877452. doi:10.3389/fonc.2022.877452. Reprinted with permission under the Creative Commons Attribution 4.0 International License. https://creativecommons.org/licenses/by/4.0/*

the OAR. Without the online adaptations facilitated by MR imaging guidance, the patient would have received a higher dose to the surrounding structures and an increased risk of toxicity to those structures.

Conclusion

Research suggests that MRIgRT will have a promising role in the future of image-guided radiation therapy. The ability of MRIgRT to image-plan volumes during beam-on time, reduce patient dose, and maximize target dose implies a greater ability to customize treatment plans. However, health care facilities must evaluate the challenges, particularly the costs associated with purchasing and operating the machine, training personnel, and modifying the current building structure. Radiation therapy treatment will continue to evolve; therefore, facilities must be knowledgeable about the changes and determine the best approach to improving treatment for patients.

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