

MRI-Linear Accelerator Radiotherapy Systems

G.P. Liney¹⁻⁴, B. Whelan⁵, B. Oborn^{4,6}, M. Barton¹⁻³, P. Keall⁵.

¹Ingham Institute for Applied Medical Research, Department of Medical Physics, Liverpool, Australia.

²Liverpool Cancer Therapy Centre, Radiation Physics, Liverpool, Australia.

³University of New South Wales, School of Medicine, Sydney, Australia.

⁴Centre for Medical Radiation Physics, University of Wollongong, Australia.

⁵University of Sydney, ACRF ImageX Institute, Sydney Medical School, Australia.

⁶Illawarra Cancer Care Centre, Wollongong, NSW 2500, Australia.

Abstract

The desire to utilise soft-tissue image guidance at the time of radiation treatment has led to the development of several hybrid MRI-linear accelerators. These systems have the potential to realise the benefits of MRI on the treatment table with the ability of real-time motion management and adaption on a patient specific basis. There are several MRI-Linacs currently being implemented covering both low and high magnetic field strength and two beam-field orientations. Clinical trials have only recently begun with this technology but their future use as standard radiotherapy practice seems assured. This review article summarises the challenges faced in developing such hybrid technology, the differences and advantages of each of the currently exploited solutions and their current status.

1. Introduction

State-of-the art radiotherapy has the ability to deliver highly conformal doses of radiation that can target tumours and avoid normal tissues with high precision. However, the limitations of conventional on-line imaging hinder this technology from achieving its true potential. Current imaging is often limited to a pre-treatment planning scan (usually CT) or set-up verification at the time of treatment with on-board x-ray. As a consequence, there is little or no adaption of the radiation dose to known changes in anatomy or physiological variations including that of the tumour target itself, that occur during the course of treatment [1-3]. Over the last two decades, the advantages of soft-tissue contrast with MRI have been increasingly exploited in radiotherapy planning to improve contouring, and many studies have also shown how functional MRI techniques can be used to monitor response to treatment. The inherent advantages of MRI has inevitably led to the pursuit of hybrid radiotherapy systems that incorporate this imaging capability in the treatment room to realise the benefits of real-time guidance and adaption. Pioneering work over the last few years on a low field MRI system combined with 3 cobalt radioisotope heads [4], has paved the way for the more recent developments of linear accelerator based systems or MRI-Linacs, which are the subject of this review.

This article reviews the difficulties associated with combining an MRI scanner and a linear accelerator into a single treatment device and summarises the major design differences and current status of the existing systems.

2. Integration Challenges

There are two main configurations of MRI-Linac being pursued with the radiotherapy beam described as being either ‘inline’ i.e. parallel to the main magnetic field, or ‘perpendicular’ to the field. A number of mutual interference effects can be expected to occur when operating a linear accelerator in the presence of a strong magnetic field. Both the magnitude and the orientation of the magnetic field play a part in this. These interactions can be best described from the perspective of each component part in the system and are summarised below.

2.1 The effects of a magnetic field on Linac operation

A standard clinical linear accelerator has a magnetic field tolerance of just 1 Gauss (0.0001 T) requiring careful consideration of the siting requirements of linacs and MRI scanners that may be closely located in radiotherapy departments. Little wonder then that the proximity of a field of up to 1.5 Tesla is a cause for concern! The first consideration, as the part of the linac closest to the magnet, is the operation of the multi-leaf collimator (MLC), which is used to shape the x-ray beam. More specifically the performance of each magnetic encoder used to control a motor driven leaf into the correct position can be degraded. Studies have shown that fields of 450 G (0.045 T) are sufficient to render these unusable [5]. Re-design or replacement with compatible components is an option but in most cases reducing the field is the pragmatic solution.

Another dominant effect is the influence on charged particles- in this case electrons- that are accelerated in the waveguide in order to produce the high energy x-ray beam. Magnetic fields can cause electrons to deviate and focus/defocus, in many cases causing a loss of beam current. The perpendicular systems suffer the worst with total beam loss at 14 G (0.0014 T) [6]. For the inline arrangement up to 79% beam reduction is observed at 600 G (0.06 T) [7], although this is dependent on electron gun design. These threshold fields can be managed in the majority of cases by reducing the field by passively shielding the equipment [8] and/or actively shielding the magnet itself to create a near zero Gauss region.

Secondary electrons, released as a consequence of the x-ray beam interacting with matter, are also influenced by magnetic fields. In the case of inline orientation there is an electron focussing effect (EFE) which concentrates electrons along the central axis of the magnetic field. This creates a substantive

increase in skin (entrance) dose from contaminating electrons prior to the beam entering the patient [9,10]. Results in our own lab show this can be easily mitigated with 2 cm of Perspex placed in the path of the beam and proximal to the patient, but electron purging methods may also be employed. In terms of electron transport within the patient, i.e. electrons released in the process of dose deposition, the same effect has been shown to be beneficial, facilitating dose enhancement in the targeting of certain structures [11]. For the perpendicular systems there is a bending of the electrons in a circular path away from the field and described as the ‘electron return effect’ (ERE) [12]. While there is no entrance dose issue, the ERE is characterised by a widening of the beam penumbra, asymmetric dose distributions particularly near tissue cavities, and a more moderate skin dose on exit. These effects can be remedied by using opposing beams or incorporating the magnetic field in the inverse planning solution. A diagram illustrating the concept of both EFE and ERE is shown in Figure 1.

2.2 MRI in the presence of a linear accelerator

The effect of the linear accelerator on the operation of the MRI scanner is perhaps less obvious but no less challenging. The most fundamental requirement of any MRI scanner is to ensure it is in an electromagnetically shielded room. This is typically achieved by situating the unit in a faraday cage (i.e. usually lining the room with copper). Any extraneous radiofrequency (RF) noise will cause severe interference in the image, and as such the linear accelerator must be either placed outside this room or made an integral part of the RF shield.

Another challenge is preserving the homogeneity of the main magnetic field (B_0). It has been demonstrated that the proximity of the accelerator and MLC cause increased heterogeneity within the extremely sensitive imaging volume of the scanner. This can be largely removed by the process of passive shimming as part of magnet installation. The impact of the MLC is minimal when placed at least 1 metre (standard SID) away from the isocentre of the magnet [13]. However when the equipment is moved, for example to change the treatment distance or change the gantry angle, the field needs to be re-adjusted. In this case, the process of dynamic shimming, i.e. changing the field with gradient or other electromagnetic coils within the scanner, over the volume of interest is sufficient to achieve this [10].

Another potential interaction is between the RF receiver coil, used to detect the image signal, and the incident beam. In diagnostic imaging the RF coil fits closely to the anatomy of interest in order to minimise noise and maximise image quality. On an MR guided (MRg) system this coil may be unavoidably placed in the path of the beam. This can not only attenuate the intended dose but also increase skin dose via secondary electrons. Furthermore, the beam can cause an electronic disequilibrium in the conductors or electronics (‘radiation induced current’) creating interference and image artefacts [14, 10]. Dedicated RF coils for MRg have been designed which are either radiotranslucent [15] or physically open and completely radiotransparent [16] to minimise these effects.

3. Existing Systems

At the time of writing there are four different MRI-Linac systems at various stages of implementation around the world. The trade-off between high field to improve image quality, and low field to minimise electromagnetic interactions and dosimetry effects has led to quite different designs, each with their own unique advantages.

3.1 MRI-Linac Specifications

Table 1 provides the details of the four current MRI-Linac systems being developed in order of the magnetic field strength. The two perpendicular beam-field systems (Elekta & Viewray) are now commercial products while the two remaining systems are working prototypes. Each of these four systems are shown in Figures 2 (a) to (c). Although a comprehensive overview of their technical

performance is beyond the intended scope of this article, each is briefly described below in order of field strength.

The system with the highest magnetic field strength is the Unity system from Elekta (shown in Figure 2 (a)). This system is being investigated by a founding consortium of seven centres in the UK, Europe and USA. Their original design built in Utrecht is based on a 1.5 Tesla clinical magnet (Philips, Achieva) with a small gap in the gradient coil and magnet windings [17]. The beam is on a rotating gantry and passes through the superconducting cryostat avoiding a small range of angles where the superconductor is connected. The electron gun resides in a zero field zone and angle specific shim settings are further used to remove the influence of the gantry on the image. Out of all the systems this magnet comes closest to the performance and imaging capability of a standard diagnostic scanner.

The only other system that can be described as ‘high field’ in MRI-Linac terms, is the 1.0 Tesla Australian phase II prototype [18] located in south west Sydney. The basis for this system is the open magnet design shown in Figure 2 (b). This includes dedicated gradient and RF coils which maintain the patient opening and permits orientation of the patient and beam in either direction, making it a versatile imaging and treatment unit. This system is also different to the others in that it has a fixed gantry, providing flexibility in design and also greater efficacy for proton therapy. However, this also means that to recreate multiple beam angles the patient has to be re-positioned or, for full arc therapy, a patient rotation system has to be used [19].

The Aurora-RT system (from MagnetTx Oncology Solutions) was developed from the University of Alberta group who provided some of the earliest experiments and technological developments in the MRI-Linac field. Their research began in 2008 with a head-only prototype [20] which has since translated into the current whole-body patient version operating with a 0.5 T magnet (Figure 2 (c)). This system is an inline configuration, but in contrast to the Australian version has a combined rotating biplanar magnet and beam gantry. The magnet has a number of unique features; it is a high temperature superconductor meaning it can be turned on and off relatively easily. An iron yoke is used within the bore that contains the fringe field within the isocentre so there is minimal effect from electron contamination. Both the Alberta and Australian systems can be dismantled into component parts and sited in conventional radiotherapy bunkers.

The last on the list in terms of field strength is the MRIdian system [4] shown in Figure 2 (d). At 0.35 Tesla, it provides sufficient image quality for the purpose of guidance, whilst minimising the interactions experienced by higher field systems. The original version of this system utilised radioactive cobalt as a radiation source, and was the basis for the MRg clinical trials to date. A newer version of this system has since been commercially released which replaces the cobalt source with a linear accelerator; existing systems can be upgraded. A particular strength of this system is the integration of on-line registration and planning capabilities.

3.2 Current status of MRI-Linacs

In 2017 the two commercial systems began patient trials; The honour of the first ever MRI-Linac in human treatment went to the Unity system at Utrecht in May, embarking on a small cohort of spine metastases patients using 3 or 5 field approach [21]. It was quickly followed in July by ViewRay with the first patients treated at Henry Ford Hospital, USA. This marked the successful transition of their system into a linear accelerator having already demonstrated a track-record in adaptive radiotherapy on the cobalt units since 2014 [22].

The Unity system is currently in situ or scheduled for imminent installation at a total of 21 clinical and research centres across the world. As of early 2018, Viewray had surpassed the 50th system milestone and was installing four new linac systems plus an additional cobalt system upgrade.

The MagneTx Aurora-RT system was installed in 2013 and provided the first ever images from an inline system in 2014. The Australian phase II magnet was installed in 2016 with first images in 2017. More recently the first ever vertical images for treatment guidance were demonstrated [16]. Both of these prototype systems have successfully implemented the use of an integrated MRg treatment beam and first patient trials are eagerly anticipated.

4. Future Developments

The commercialisation of two of the four current systems secures the future of MRI-Linac in the clinic, with business cases reliant on many system installations over the coming years. The early clinical findings for pancreatic cancer [23] have raised tremendous interest in the community, and experts in the field predict that MRI-Linac will become the standard clinical system in radiotherapy over the next decades.

In the medium term, the systems described thus far will apply already proven image gating and tracking techniques and go on to treat more difficult cancers. In the longer term, the increased accuracy facilitated by MRI guidance will also change how radiation is delivered, enabling higher dose, shorter course treatments, benefitting both patients and the health system through increased efficiency. Furthermore, the functional imaging capabilities of MRI will enable adaptive physiological targeting, further boosting treatment efficacy and personalisation. MRI offers a broad range of functional imaging capabilities, for example R_2^* imaging is correlated with hypoxia [24], diffusion weighted imaging with cellularity [25], blood-oxygen-level dependent (BOLD) contrast imaging with neural activity [26] and dynamic contrast-enhanced (DCE) imaging with vascular permeability [27]. Acquiring such information at every fraction offers the opportunity to target tumour heterogeneity, monitor treatment efficacy and enable rapid changes of treatment plans to improve therapy. Ultimately an MRI-Linac system that can offer adaptation based on both anatomy and physiology would seem the logical goal of this technology.

With the clear growth in MRI-guided x-ray therapy, it would seem natural for scientists and clinicians to consider real-time MRI guidance in proton or more generally particle therapy (MRgPT) as the next step (Figure 3). Particle therapy offers superior dose distributions over x-ray therapy due to the ability to accurately deliver pencil beams that stop within the volumes of interest. The same benefits of improved anatomical accuracy and requirements for MR-based solutions to electron density calculations apply, and advances made with MRI-Linacs and particularly inline systems will facilitate the move to MRgPT. A ‘Future of Medical Physics’ review paper has recently been published on this topic [28]. This article provides a broad overview of this exciting work, which includes at least four patents describing real-time MRI-guided proton/particle therapy systems, and the various groups that have investigated modelling and experiments related to MRgPT.

Finally we note the research program based in Germany which is developing a ‘proof of concept’ system where MR images of a phantom have been acquired with a clinical scanner whilst proton beam delivery was occurring [29]. With the compelling rationale for MRgPT, and with the advances seen in MRI-Linacs, the possibility of a clinical prototype MRgPT system within the next 5 years should be not be considered beyond the realms of possibility.

5. References

- [1] Erridge SC, Seppenwoolde Y, Muller SH, van Herk M, De Jaeger K, Belderbos JS, et al. Portal imaging to assess set-up errors, tumor motion and tumor shrinkage during conformal radiotherapy of non-small cell lung cancer. *Radiotherapy and Oncology* 2003;66:75-85.
- [2] Seppenwoolde Y, Shirato H, Kitamura K, Shimizu S, van Herk M, Lebesque JV, et al. Precise and real-time measurement of 3d tumor motion in lung due to breathing and heartbeat, measured during radiotherapy. *Int J Radiat Oncol Biol Phys* 2002;53:822-834.
- [3] Keall PJ, Mageras GS, Balter JM, Emery RS, Forster KM, Jian SB, et al. The management of respiratory motion in radiation oncology report of aapm task group 76. *Med Phys* 2006;33:3874-3900.
- [4] Mutic S, Dempsey JF. The Viewray system: Magnetic resonance-guided and controlled radiotherapy. *Seminars in radiation oncology*. 2014;24:196-199.
- [5] Yun J, St Aubin J, Rathee S, Fallone BG. Brushed permanent magnet dc mlc motor operation in an external magnetic field. *Medical physics* 2010;37:2131-2134.
- [6] St Aubin J, Steciw S Fallone B. Effect of transverse magnetic fields on a simulated in-line 6 mv linac. *Physics in medicine and biology* 2010;55:4861.
- [7] St. Aubin J, Steciw S Fallone B. Effect of longitudinal magnetic fields on a simulated in-line 6 mv linac. *Medical physics* 2010;37:4916-4923.
- [8] Whelan B, Kolling S, Oborn BM, Keall P. Passive magnetic shielding in mri-linac systems. *Physics in Medicine & Biology* 2018;63:075008.
- [9] Bielajew AF. The effect of strong longitudinal magnetic fields on dose deposition from electron and photon beams *Med. Phys.* 1993; 20, 1171–1179.
- [10] Liney GP, Dong B, Begg J, Vial P, Zhang K, Lee F et al, Experimental results from a prototype high-field inline MRI-Linac. *Med. Phys.* 2016; 43: 5188-5194.
- [11] Oborn BM, Ge Y, Hardcastle N, Metcalfe PE, Keall PJ, Dose enhancement in radiotherapy of small lung tumors using inline magnetic fields: A Monte Carlo based planning study, *Med. Phys.* 2016; 43, 368–377.
- [12] Raaijmakers AJE, Raaymakers BW, Lagendijk JJW. Integrating a MRI scanner with a 6 MV radiotherapy linear accelerator: Dose increase at tissue-air interfaces in a lateral magnetic field due to returning electrons. *Phys. Med. Biol.* 50, 1363–1376 (2005).
- [13] Kolling S, Oborn B Keall P. Impact of the MLC on the MRI field distortion of a prototype MRI-linac. *Medical physics* 2013;40:121705.
- [14] Burke B, Wachowicz K, Fallone BG, Rathee S. Effect of radiation induced current on the quality of MR images in an integrated linac-MR system. *Med Phys* 2012; 39(10): 6139- 6147.
- [15] Hoogcarspel SJ, Zijlema SE, Tijssen RHN, Kerkmeijer LGW, Jurgenliemk-Schulz IM, Lagendijk JJW, Raaymakers BW. Characterization of the first RF coil dedicated to 1.5 T MR guided radiotherapy. *Phys Med Biol* 2018; 63 (2); doi: 10.1088/1361-6560/aaa303.
- [16] Liney GP, Dong B, Weber E, Rai R, Destruel A, Garcia-Alvarez R, Manton DJ, Jelen U, Zhang K, Barton M, Keall P, Crozier S. Imaging performance of a dedicated radiation transparent RF coil on a 1.0 Tesla inline MRI-linac. *Phys Med Biol.* <https://doi.org/10.1088/1361-6560/aac813>.
- [17] Lagendijk JJ, Raaymakers BW, Van Vulpen M. The magnetic resonance imaging–linac system. *Seminars in radiation oncology*. Elsevier. 2014;24:207-209.
- [18] Keall PJ, Barton M Crozier S. The Australian magnetic resonance imaging–linac program. *Seminars in radiation oncology*. 2014;24:203-206.
- [19] Whelan BM, Liney GP, Dowling J, Rai R, McGarvie L, Holloway L, Fein I, Wilkins R, Barton M, Keall P. An MRI-Compatible patient rotation system - Design, construction, and first organ deformation results. *Med Phys*. 2016, doi: 10.1002/mp.12065.
- [20] Fallone B, Murray B, Rathee S, Stanescu T, Steciw S, Vidakovic S, et al. First mr images obtained during megavoltage photon irradiation from a prototype integrated linac-mr system. *Medical physics* 2009;36:2084-2088.
- [21] Raaymakers BW, Juregenliemk-Schulz IM, Bol GH, Glitzner M, Kotte ANTJ, van Asselen B et al. First patients treated with a 1.5 T MRI-linac: Clinical proof of concept of a high-precision, high-field mri guided radiotherapy treatment. *Physics in Medicine & Biology* 2017;62:41-50.
- [22] Acharya S, Fischer-Valuck BW, Kashani R, Parikh P, Yang D, Zhao T et al. Online magnetic resonance image guided adaptive radiation therapy: First clinical applications. *International Journal of Radiation Oncology• Biology• Physics* 2016;94:394-403.

- [23] Rudra S, Jiang N, Rosenberg SA, Olsen JR, Parikh PJ, Bassetti MF, Lee P. High dose adaptive MRI guided radiation therapy improves overall survival of inoperable pancreatic cancer. *International Journal of Radiation Oncology•Biology•Physics* 2017;99:E184.
- [24] Chopra S, Foltz WD, Milosevic MF, Toi A, Bristow RG, Menard C, Haider MA. Comparing oxygen-sensitive mri (bold r2*) with oxygen electrode measurements: A pilot study in men with prostate cancer. *International journal of radiation biology* 2009;85:805-813.
- [25] Gibbs P, Liney GP, Pickles MD, Zelhof B, Rodrigues G, Turnbull LW. Correlation of adc and t2 measurements with cell density in prostate cancer at 3.0 tesla. *Investigative radiology* 2009;44:572-576.
- [26] Ogawa S, Lee TM, Kay AR, Tank DW. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proceedings of the National Academy of Sciences* 1990;87:9868-9872.
- [27] Turnbull LW, Buckley DL, Turnbull LS, Liney GP, Knowles AJ. Differentiation of prostatic carcinoma and benign prostatic hyperplasia: Correlation between dynamic gd-dtpa-enhanced mr imaging and histopathology. *Journal of Magnetic Resonance Imaging* 1999;9:311-316.
- [28] Oborn BM, Dowdell S, Metcalfe PE, Crozier S, Mohan R, Keall PJ. Future of medical physics: Real-time mri-guided proton therapy. *Medical Physics*, 44(8):e77–e90, 2017.
- [29] Schellhammer S, Karsch L, Smeets J, L'Abbate C, Henrotin S, van der Kraaij E, Lühr A, Quets S, Pawelke J, Hoffmann A. First in-beam MR scanner for image-guided proton therapy: beam alignment and magnetic field effects. *Radiotherapy and Oncology*, Volume 127, Supplement 1, S315-6, 2018.

Table 1: Configuration details of each of the current MRI-Linac systems in order of magnetic field strength.

System (company)	Radiation	Field Strength	Magnet Type	Orientation
Unity (Elekta)	6 MV	1.5 T	Closed superconductor	Perpendicular
Australian	4 & 6 MV	1.0 T	Open superconductor	Both
Aurora-RT (MagnetTx)	6 MV	0.5 T	Biplanar, high temp superconductor with steel yoke	Inline
MRIdian (Viewray)	Co or 6 MV	0.35 T	Split superconductor	Perpendicular

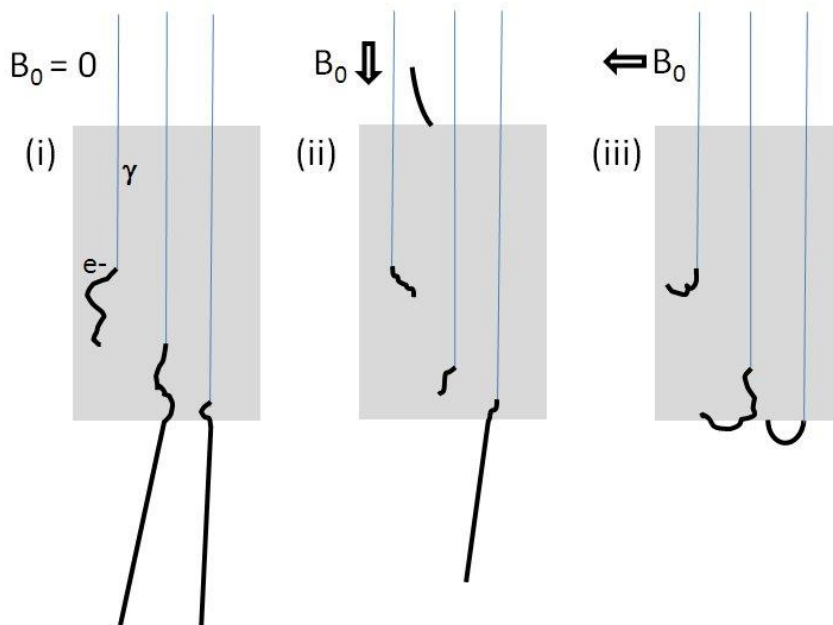


Figure 1: Illustration of the effect of a magnetic field on photon dosimetry: (i) the normal situation with no magnetic field; (ii) an inline magnetic field creates a focussing of electrons (EFE) within the patient and of any external contaminating electrons towards the surface; (iii) a perpendicular magnetic field causes electrons to move in an arc causing a lateral shift of the intended delivery and a return effect upon beam exit (ERE).



Figure 2: (a) Elekta's 1.5 Tesla Unity system at University Medical Centre in Utrecht, The Netherlands; This was the MRI-Linac used for the first in man treatments in May 2017 (courtesy of Bas Raaymakers, UMC).

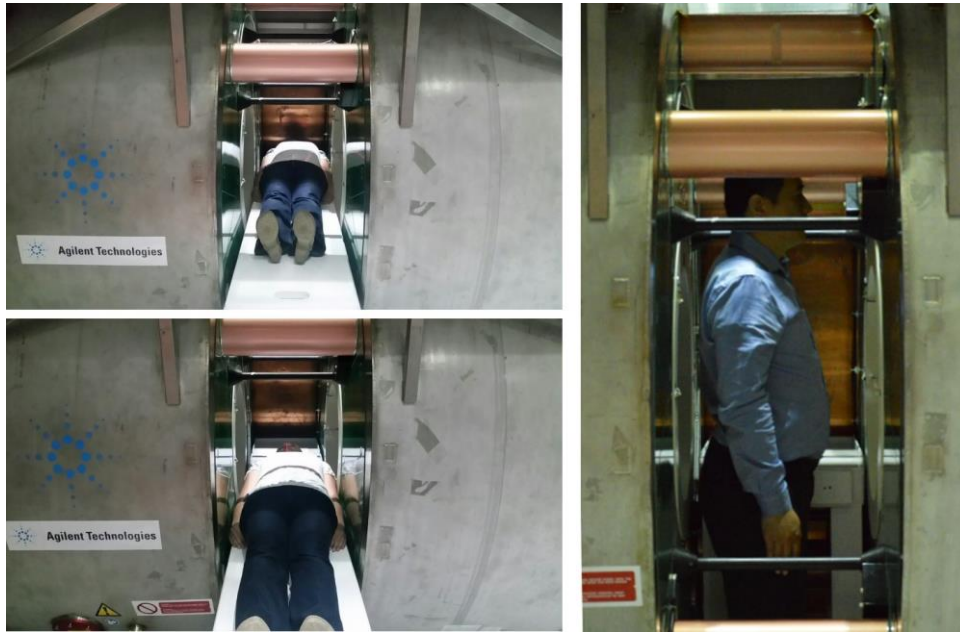


Figure 2: (b) The Australian MRI-Linac: Photographs of the magnet gap illustrating (left) supine positioning and (right) standing positioning that is possible with this open system. The treatment beam can be orientated either inline or perpendicular to the magnet bore.



Figure 2: (c) Illustration of the Aurora-RT system courtesy of B. Gino Fallone (MagnetTx Oncology Solutions, Edmonton, Alberta, Canada). The patient opening has a clearance of 110 cm x 60 cm and the table can move laterally to position off-centre treatments at the magnet isocentre.



Figure 2: (d) A new linear accelerator version of the MRIdian system at Washington University in St. Louis, USA (photograph courtesy of Olga Green, PhD).

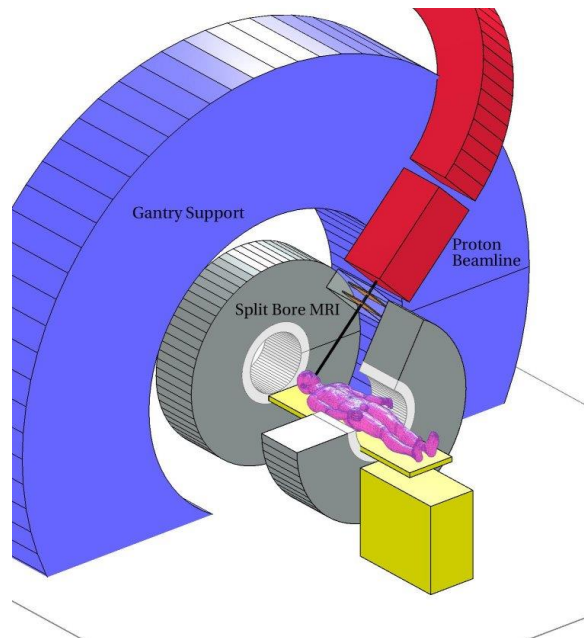


Figure 3: Artist's impression of a future MR-guided proton therapy facility.