

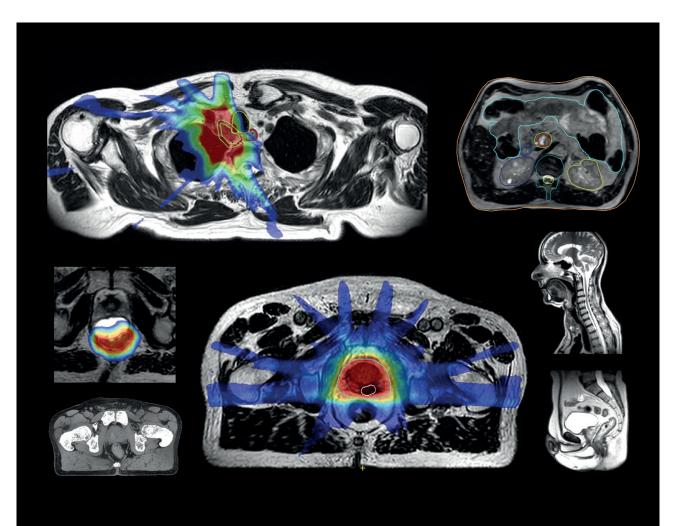
White Paper

Magnetic Resonance Imaging in Radiation Therapy

How MRI is propelling radiation therapy into a new era of clarity and insight

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The need for certainty

Radiation therapy (RT) improves the lives of millions of people annually. More than 50% of cancer patients receive RT at some point in their care, often at a fraction of the cost of other cancer treatments. Advancements in treatment delivery and imaging techniques have resulted in increasingly conformal treatments, improving patient prognoses and reducing adverse effects. Notably, the use of CT for treatment planning and image guided RT (IGRT) has significantly enhanced treatment precision. However, its inadequate soft tissue contrast and lack of real-time imaging limit the accuracy of contouring and planning and restrict adaptation to intrafraction changes.

In recent years, the need to further reduce uncertainties in RT (e.g. delineation, planning, and dosimetry) has resulted in significant growth of magnetic resonance imaging (MRI) in the RT workflow. MRI has become indispensable in treatment planning for many indications due to its unique ability to visualize soft tissues, allowing accurate identification of the target and organs-at-risk (OARs) (Figure 1 and 2). MRI has also been introduced into the treatment setting with the availability of integrated MR-Linac systems for MR-guided RT (MRgRT). MR-Linacs provide high quality soft tissue imaging ("see what you treat") at the time of treatment, enabling the management of both interfraction anatomical changes and intrafraction (real-time) motion.

However, there are still many misconceptions about MRI, hampering its mainstream adoption. This document aims to inform the RT community about the capabilities of MRI, address some of these misconceptions, and highlight the importance of using MR in both treatment planning and for online guidance to reduce uncertainties. Additional information on specific topics can be obtained in excellent, widely available review articles (van der Heide et al. 2019) (Keall et al. 2022) (Glide-Hurst et al. 2021).

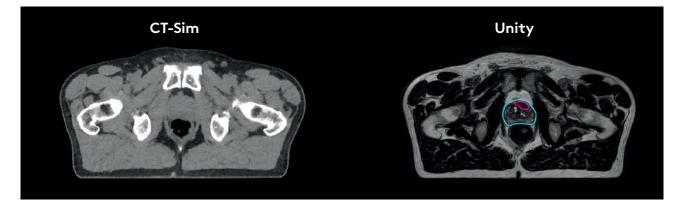


Figure 1. Example CT-simulation and Elekta Unity MR-Linac images of the prostate showing the possibility to visualize the dominant intraprostatic lesion on the MR image.

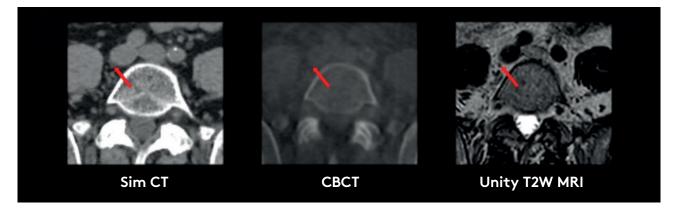


Figure 2. Lymph node oligometastases visualized on simulation CT, CBCT and T2W MRI on Unity. Images courtesy of The Townsville Cancer Centre, Australia.

The benefits of MRI in RT

MRI is the imaging modality of choice for diagnosing most cancer types. In RT, it's used in both offline and online settings. In the offline setting, the patient is not on the treatment table and the MR images are acquired for diagnosis, tumor staging, target and OAR delineation for treatment planning, and response assessment after treatments. In the online setting, the patient is on the treatment table and MRI is used to adapt contours, to assess and visualize motion, and to characterize biological processes (Figure 3).

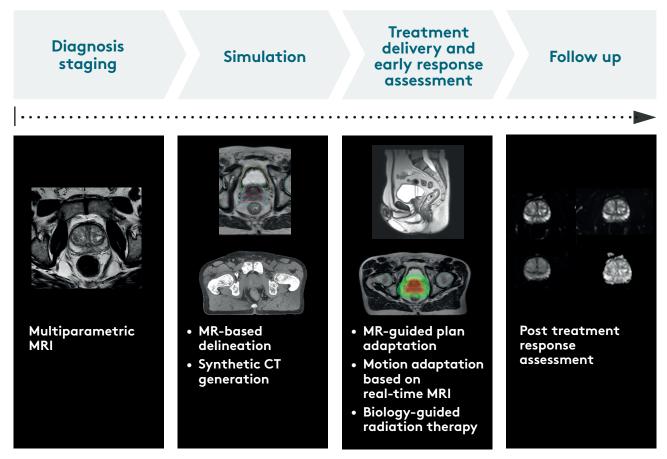


Figure 3. MRI as a key part of the RT care pathway from diagnosis through simulation, planning and adaptive treatment delivery, to response assessment.

The advantages of using MRI in the RT workflow

- Higher accuracy for personalized treatments Superior soft-tissue visualization and precise tumor localization allows more accurate contouring and online adaptation to the patient's daily anatomy
- Improved targeting for hard-to-treat cancers MRI allows improved targeting in the presence of motion (e.g. lung, prostate) and in challenging tumor locations previously not treated with RT (e.g. pancreas, kidney, oligometastases)
- Use of smaller margins Online adaptive MRI permits real-time adjustments during treatment giving clinicians certainty to reduce margins

- Fewer treatment sessions Highly accurate targeting enables hypo-fractionated regimens, such as SBRT, benefiting patients and reducing the burden on healthcare systems
- Improved understanding of tumor dynamics Daily real-time imaging reveals tumor response and changes, enabling highly personalized, biology-guided RT (BgRT) strategies.

The versatility of MR imaging explained

The versatility of MRI for visualizing anatomy and tissue function is one of its most useful features, but where does this versatility come from? How are MR images made and optimized, and what information can we glean from them?

Obtaining an MR image

The MRI signal originates from hydrogen atoms, which are abundant in the human body (particularly in water, fat, and soft tissue in general), and behave like tiny magnets. In a strong magnetic field (typically 1.5T or 3.0T), the hydrogen atoms tend to align with the magnetic field. This is called the equilibrium state. A radiofrequency (RF) pulse is used to tip the hydrogen atoms away from the equilibrium state. This process is called excitation. Once the RF pulse stops, the excited hydrogen atoms decay back towards their equilibrium state and realign with the magnetic field. This decay process emits a signal, which is detected by sensitive receive coils placed very close to the body and is used to produce the MR image. The decay is characterized by two relaxation times referred to as longitudinal (T1W) and transversal (T2W).

Distinguishing different tissue types

A key principle of MRI is that different tissues and tumor types have different T1W and T2W relaxation values. By tuning MR sequence parameters, the appearance of the image can be manipulated to be more T1-weighted or T2-weighted, allowing the contrast between tumor and OARs to be optimized. Table 1 provides an overview of different signal intensities. If the signal intensity is high, the tissue appears white (hyperintense) in the image, while a low signal intensity is characterized by dark (hypointense) pixels.

Signal	T1-weighted	T2-weighted
		ALL AND
High (white)	FatBloodWhite matter (intermediate to bright)	 Fat (generally) Water content including CSF, bladder, and gallbladder Edema
Intermediate (grey)	• Grey matter • Muscle • Liver • Kidney	White matterLiverKidney
Low (black)	 Bone/teeth Air Edema Cerebrospinal fluid (CSF) 	 Bone/teeth Air Blood vessels (depending on flow characteristics)

Table 1. Overview of signal intensities for T1- and T2-weighted MR sequences

Going beyond anatomical imaging

The signal intensity of hydrogen atoms is affected by their surroundings, which further increases the versatility of MRI. It allows certain biological processes to be visualized using MRI, such as diffusion, perfusion, blood velocity, or hypoxia. This information can be used to detect biological changes in tumors or OARs, and to guide dose (de-)escalation to certain parts of the tumor.

Balancing SNR, scan time and spatial resolution

Field strength and signal-to-noise ratio (SNR) are proportional to each other—higher magnetic field results in a higher signal and, therefore, a higher SNR. When acquiring MR images choices must be made in respect of SNR, scan time and spatial resolution (Figure 4). Having a higher SNR can directly result in lower scan times, higher spatial resolution, or a combination of the two. Spatial resolution refers to the ability to differentiate fine details in an image. Higher spatial resolution is essential for capturing small and intricate structures. These choices are reflected in Unity protocols (See Figure 5 for an example of a prostate case).

MRgRT requires rapid high-quality imaging and so a high field MRI system is preferrable to produce adequate spatial resolution in a reasonable time frame.

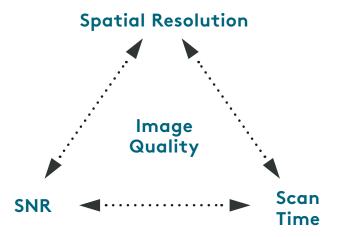


Figure 4. MR image quality is a balance between spatial resolution, SNR and scan time.

Powered by
PHILIPS

MR imaging

Diagnostic quality MRI-powered by Philips MR imaging

Elekta Unity was developed to have MR capabilities as close as possible to mainstream MR systems. Its MRI component is based on the 1.5T Philips Ingenia platform, providing diagnostic quality imaging and full diagnostic and therapy simulation capabilities. Elekta's partnership with Philips enables easy use of diagnostic techniques and innovations on Unity.

This imaging performance is further strengthened by the electromagnetic decoupling of the linac and MRI components, so that neither influences the other. This allows MR images to be acquired as the gantry rotates and while the patient is being irradiated.

How MRI is used to drive adaptation for every patient

MRI is unique in the fact that it not only provides excellent soft-tissue contrast to account for daily changes in patient position and anatomy, but that it also provides the possibility to obtain real-time images during treatment delivery. As a result, MR-guided adaptive radiation therapy can account for interfraction motion and volumetric changes, while it also allows for intra-fraction motion correction, thereby enabling margin reduction and the implementation of new treatment paradigms. Another very promising field of interest is the use of MR biomarkers to monitor changes in biological characteristics and use this information to adapt a treatment plan or even a treatment regimen.

In this chapter we will describe current practices and real-life examples on how MRI capabilities are used to adapt for anatomical changes, motion and patient's biology:

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Adapting to anatomical changes

MRI is used to visualize anatomy in the offline setting and is routinely used for treatment planning alongside CT. Now, with the introduction of commercial synthetic CT solutions, MR-only planning workflows are becoming more attractive and common for various anatomical locations.

Unity uses online MRI to capture daily anatomical changes, allowing additional contouring or

adaptation of previously defined contours at the time of treatment. Since time constraints are stricter in the online setting, only a single or small number of MR images are acquired.

The following sections describe how MRI is applied in RT workflows for different body sites to adapt for anatomical changes.

Pelvis

Multi-parametric MRI (involving the acquisition of at least T2-weighted and diffusion-weighted images) is standard for characterizing and grading prostate tumors. Grading is often performed using an objective scoring system, such as PI-RADS (Prostate Imaging Reporting and Data System). The images required to identify and grade a prostate tumor can be acquired on Unity, with no significant difference to diagnostic 3T MRI (Almansour et al. 2021).

Elekta Unity pelvic MRI protocols are based on consensus from leading international institutes (Figure 5). These include T2-weighted protocols with different resolutions that can be used to quickly update the prostate and OARs contours, and even to visualize the dominant intraprostatic lesion (DIL). A simultaneous integrated boost to the DIL is shown to be clinically beneficial (Kerkmeijer et al. 2021). Moreover, these online MR images provide visual clarity for sparing of sensitive structures, such as the neurovascular bundles (Figure 6), the internal pudendal artery, and the urethra. Such clear visualization of both target and OARs gives clinicians confidence to decrease margins to 2 mm or even 0 mm, and "I can now see the prostate as clearly as I can see it on a diagnostic MRI scanner."

Alison Tree, MD Prostate Tumor Site Group Lead of the MR-Linac Consortium

to investigate ultra-hypofractionation. Favorable clinical results have been achieved using just two treatment fractions (Westley et al. 2024).

Similarly, these protocols can be used to define a GTV boost for organ preservation in the treatment of rectal cancer (Figure 7). The boost volume is clearly visible using MRI, whereas it can't be seen by CT. Moreover, MR images can reveal the need to adapt the boost, since the target can change significantly between fractions. Treating rectal cancer patients on Unity has demonstrated high response rates, excellent organ function, limited side effects, and improved disease-related symptom management (Boeke et al. 2022) (Daamen et al. 2024).



Figure 5. Different pre-set prostate protocols available on Elekta Unity, chosen according to clinical indication or departmental needs. The fast protocol (resolution 1.4 x 1.4 x 3.0 mm) minimizes session time, scanning the whole anatomy in 1:27 minutes. The balanced protocol (resolution 1.2 x 1.2 x 2.0 mm) takes 2:44 minutes. The high-resolution protocol (1.2 mm³ isotropic voxels, acquired in 4:38 mins) is preferred for boost strategies because it helps to visualize the DIL.

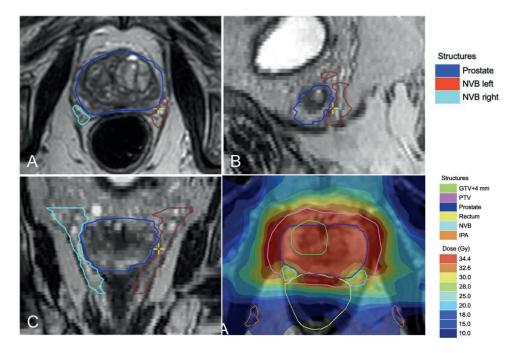


Figure 6. Neurovascular bundle (NVB) contouring for OAR sparing. Transversal, sagittal and coronal plane of contours and 5 x 7.25 Gy MRgRT plan dose distribution. Images adapted from Teunissen et al, Adaptive MR-guided neurovascular-sparing RT for preservation of erectile function in prostate cancer patients. https://doi.org/10.1016%2Fj.phro.2021.09.002. Licensed under CC BY 4.0.

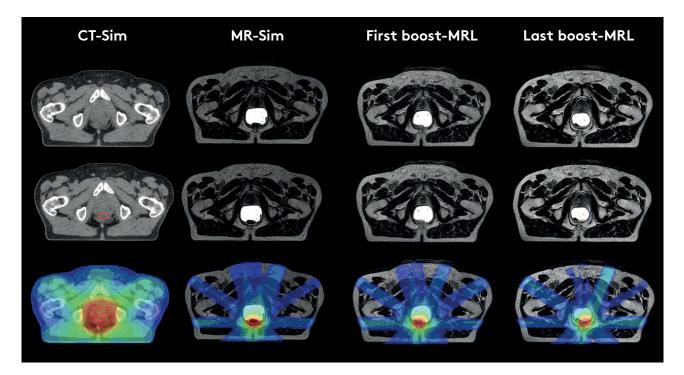


Figure 7. Example of CT-Sim, MR-Sim and Elekta Unity images for treating a rectum patient with an adaptive boost to the target. While on CT imaging no boost volume can be defined, this is clearly visible on MR images. Moreover, the different location of the target between the first and last boost shows the importance of adapting the boost volume.

Brain

Stereotactic radiosurgery (SRS) and fractionated stereotactic RT (SRT) are increasingly used in the treatment of brain metastases and intracranial tumors to minimize neurocognitive effects. High resolution, geometrically accurate imaging and precisely focused high-dose radiation are of paramount importance in these cases. It has been shown that brain metastases and primary brain tumors can change significantly during treatment with migrations in the order of centimeters (Figure 8), so daily MR imaging is vital for plan adaptation (Stewart et al. 2021).

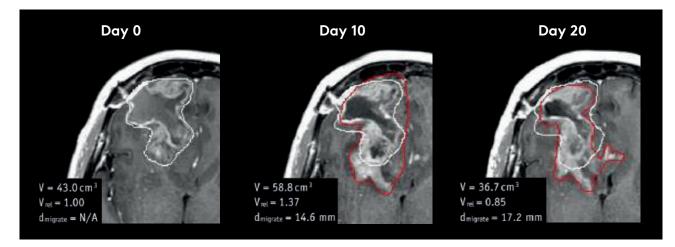


Figure 8. Brain tumor migration, not visible on CT, is apparent at day 10 and day 20 using MR imaging on Elekta Unity. MR images adapted from Stewart et al. 2021 and courtesy of Chia-Lin Tseng.

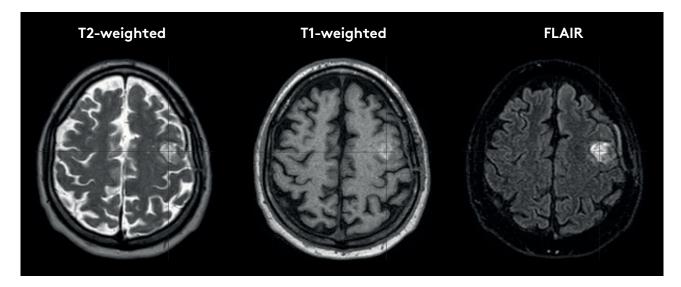


Figure 9. Example of a T2-weighted, T1-weighted and FLAIR MRI of the same patient acquired on Elekta Unity, which can all be acquired within 4 minutes with sub-millimeter resolution.

Due to the need for small PTV margins, MRI requirements are particularly demanding for intracranial stereotactic RT. T1-weighted and inversion-recovery sequences have been used most to visualize primary brain tumors and edema (Maziero et al. 2021). Unity includes both a T1-weighted sequence and a fluid-attenuated inversion recovery (FLAIR) sequence, which are also used in the diagnostic setting. The FLAIR sequence eliminates signal from fluids, like CSF, to highlight peritumoral edema. The T2-weighted sequence shows structures with high water content, which is used for tumor and OAR visualization. These sequences can be acquired within 4 minutes, with sub-millimeter resolution (Figure 9).

Head-and-neck

Head-and-neck cancer (HNC) remains a challenging tumor site, at risk of significant radiation-induced side effects. OAR sparing is therefore critical to reduce treatment toxicity. MRI allows better definition of the tumor and OARs, less inter-observer variability, and higher sensitivity to detect lymph nodes compared to CT (Jager et al. 2016). It can detect a decrease in tumor size as early as the first two weeks of treatment and allows more confident assessment of tumor and OAR changes during treatment (Bahig et al. 2018). This can be achieved with submillimeter resolution using the T1- and T2-weighted sequences available on Unity. T1-weighted images are generally considered best for gross structural information, while T2-weighted images can distinguish pathology from surrounding tissues.

Another important feature of MRI for HNC is the use of fat-suppression to attenuate the fat signal, while keeping the water signal intact (Figure 10). This is especially useful for fat-adjacent structures, which are common in this body site. A recent study compared fat-suppressed sequences with non-fatsuppressed sequences on Unity. Fat-suppression showed favorable quantitative and qualitative outcomes, leading to better GTV segmentation, and improved parotid gland, lymph node and pterygoid muscle structure visualization (Salzilo et al. 2022).

Some users even use high-quality MRI to define individual elective lymph nodes for irradiation, instead of elective neck irradiation. This allows large dose reductions in several OARs, such as the submandibular glands, carotid arteries and thyroid (Reinders et al. 2024).

Online MR workflows help clinicians to account for deformation caused by tumor response, weight loss, or inflammation. This can potentially improve local tumor control, reduce radiation-induced side-effects, and improve quality-of-life for HNC patients (de Mol van Otterloo et al. 2021) (Chen et al. 2017).

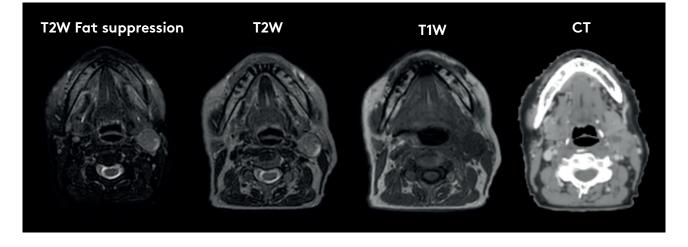


Figure 10. Fat suppression on MR images can visualize targets better on MR compared to non-fat suppressed images or CT images.

Abdomen

Abdominal cancers, such as pancreatic and liver tumors, remain among the most challenging malignancies to contour. Target motion, predominantly caused by breathing, is one of the biggest challenges. Traditionally, moving targets are imaged using 4D-CT, potentially with the addition of intravenous contrast. However, the poor soft tissue contrast of CBCT does not allow direct visualization of both the target and OARs, so the use of fiducials is often needed to localize abdominal targets during treatment.

"On CBCT you can't distinguish the pancreas from the duodenum and bowel tissue, and you can't visualize the tumor in the pancreas. On Elekta Unity, you can see the pancreas, the tumor and the duodenum. This is important because all these structures change position from day to day. With this information, you can change the patient's treatment plan daily to compensate for these variations."

Prof. Dr. Martijn Intven

Radiation Oncologist at UMC Utrecht, The Netherlands

By contrast, MRI allows both the target and OARs to be clearly visualized without the need for invasive fiducial placement (Gani et al. 2021). Moreover, several strategies can be applied to eliminate artifacts caused by motion of the target, OAR or other high contrast anatomy. They can be used to characterize the motion and consider it for treatment planning. Various clinical studies describe the clinical advantages of MR-Linac treatments enabled by imaging in the presence of motion, highlighting the importance of daily plan adaptation for improved clinical outcomes (Eijkelenkamp et al. 2023) (Chuong et al. 2023) (Tringale et al. 2022).

MRI strategies for image acquisition in the presence of motion include:

1. 3D VANE XD—reducing motion artifacts during free-breathing

3D VANE XD is a free-breathing imaging strategy that suppresses motion artifacts using specific acquisition and reconstruction techniques. The acquisition is continuous over the complete respiratory cycle, resulting in an average image of moving targets and OARs. 3D VANE XD is also useful when the target is not moving significantly but is obscured by artifacts caused by the motion of other features. 3D Vane XD is available on Unity with both T1W and balanced T2W/T1W contrast. These can be acquired with or without fat suppression to highlight specific structures (Figure 11). 3D VANE XD can be used to treat the average position with margins to accommodate the individual's motion range.

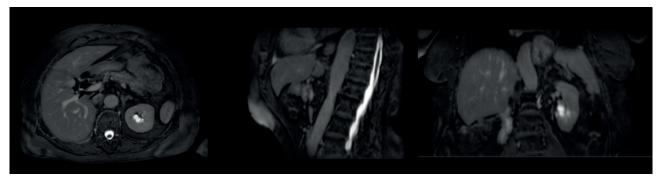


Figure 11. Balanced 3D VANE XD with fat suppression, showing no motion artifacts and a clear depiction of anatomy.

2. Navigated—eliminating motion artifacts during free-breathing

The Navigated technique is also a free-breathing imaging strategy, but the system only acquires MRI data in the exhale phase (expiration). No patient action or placement of external markers is required. Unity automatically determines the exhale phase using a T2-weighted navigated scan, which visualizes the internal anatomy. Both the target and OARs can be clearly defined since there are no motion artifacts (Figure 12). Combined with exhale gated treatments (when treatment is only delivered in the exhale phase during free-breathing), this is an effective motion management option.

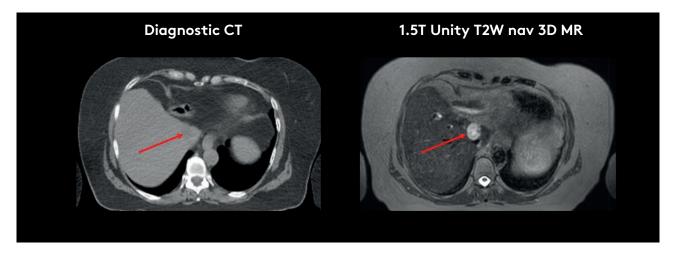


Figure 12. Comparison of diagnostic CT and 3D T2-weighted navigated MRI of a liver tumor. Clear visualization of the target and OARs enables fiducial-free liver SBRT. Images courtesy of Genesis Care St. Vincent's Clinic, Sydney

3. Breath hold—eliminating target motion

Another method available to suppress respiratory motion is for the patient to perform a voluntary breath-hold, in either (deep) inspiration or expiration. Unity can acquire sub-millimeter resolution images within a single 18-second breath-hold for three different contrasts (Figure 13).

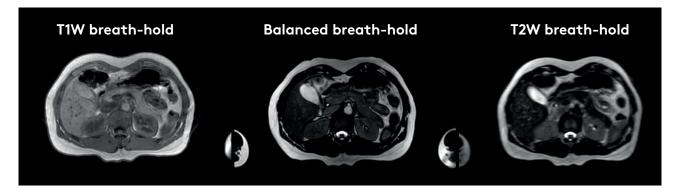


Figure 13. Different breath-hold sequences, acquired by Unity in 18 seconds. Resolution: 0.98 mm² for T1W/balanced BH (slice thickness 4 mm), 0.85 mm² for T2W (Slice thickness 5 mm).

Thorax

Thoracic targets, such as non-small cell lung cancer or oligometastases, benefit from SBRT and high biological effective doses. However, the use of large PTVs to account for uncertainties can cause severe toxicity (Merckel et al. 2024). MRI better distinguishes tumor and OARs (especially (ultra-)centrally located tumors) and helps to reduce inter-observer variability (Bainbridge et al. 2017). The same motion management strategies described for abdomen (above) can be used for moving thoracic targets. Studies already show that daily imaging allows significant margin reduction as the tumor shrinks (Figure 14 top). Moreover, the ability to track the tumor in realtime during treatment helps to further reduce margins and decrease toxicity (Figure 14 bottom).

Another benefit of treating lung patients on Unity is the large imaging field-of-view, providing excellent accuracy and fidelity, and the large lateral treatment field, allowing treatment of lateral targets with the patient comfortably positioned centrally in the bore (Ferris et al. 2024).

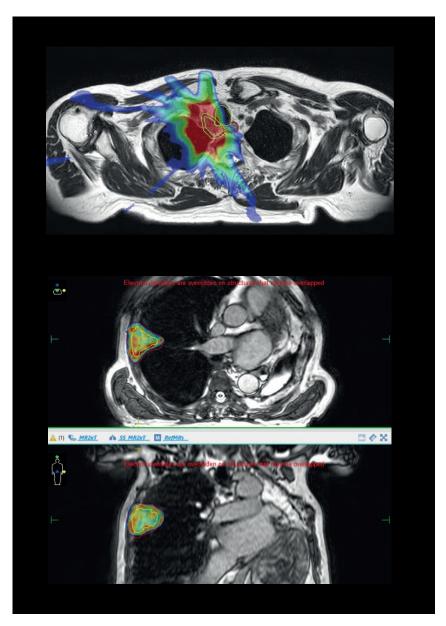


Figure 14. Top: A mediastinal lymph node metastasis treated on Unity. The dose distribution of the original plan is projected on the reduced target size at the 12th fraction. Images taken from (Merckel et al. 2024), licensed under CC BY 4.0.

Below: A lateral lung squamous carcinoma treated on Unity with comprehensive motion management, imaged using the 3D Vane XD technology. Courtesy of Advanced Radiation Oncology (ARO) department, IRCSS Ospedale, Negrar.

Adapting to intrafraction motion

Respiratory motion is a key challenge for treating abdominothoracic tumors and hampers the application of highly conformal radiation doses to such targets due to blurring of the dose distribution. As described above, MR can image in the presence of motion for contouring and planning purposes. In addition, MR allows motion to be viewed in realtime, during treatment on the MR-Linac, using cine MRI. Combining multiple, orthogonally positioned 2D MR slices allows the full 3D motion of the target or OARs to be seen. On Unity, alternating sagittal and coronal slices can be acquired every 175 ms (5.7 Hz). This ensures that the dominant superiorinferior motion is captured in every slice, and secondary motion is captured in alternate slices. Together with automatic gating, cine imaging can be used to pause the radiation beam when the target is outside a pre-defined gating window (Brown, 2023). This allows margin reduction to just a few millimeters. For this technique, the total latency of the system, which includes the frequency of imaging, can be adapted to reflect the underlying anatomical processes. For example, prostate motion occurs within a much longer time scale, so real-time imaging can have a lower frequency in the order of <1 Hz. For fast moving respiratory targets, realtime imaging is performed using a mixed (balanced) T2W/T1W contrast. For slower moving targets, like prostate or head-and-neck tumors, T2-weighted cine imaging provides improved visualization of the target and OARs (Figure 15).

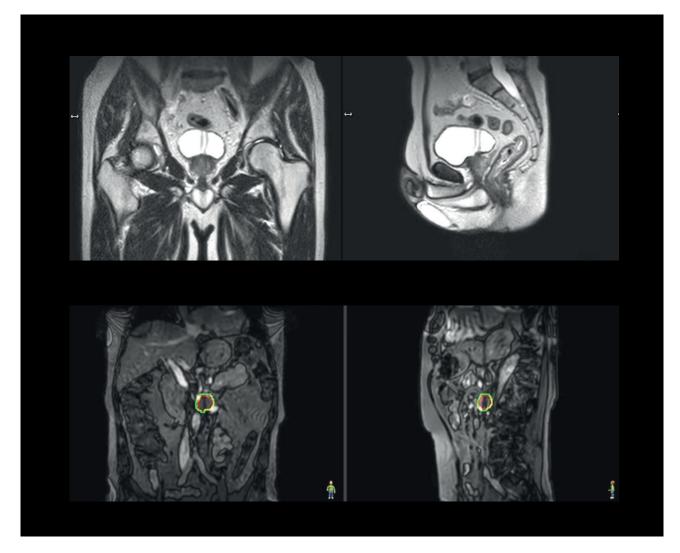


Figure 15. Top: Balanded cine sequence for real time monitoring of fast moving respiratory targets. Bottom: T2-weighted cine sequence for real time monitoring of the prostate. Images courtesy of UMC Utrecht.

Adapting to biological information: Biology-guided RT (BgRT)

As well as providing excellent visualization of anatomical features, MRI can also characterize biological information, such as diffusion, perfusion, metabolism, or hypoxia, through the use of MR imaging biomarkers. Modification of an individual's treatment based on their biological information (biology-guided RT or BgRT) using these MR imaging biomarkers is shown to be effective (Kerkmeijer et al., 2021). Additionally, Unity enables detection of biological changes during the course of treatment (often before detection of anatomical changes), allowing prompt clinical decisions based on that information. For example, dose could be escalated when tumor response is lacking or de-escalated when tumor response is evident. BgRT can also be used to define a boost volume or even to change the treatment approach.

Unity provides a unique platform to develop, validate and implement these approaches by routinely acquiring sequential high-quality biomarker images during an individual's course of treatment. Also, Unity BgRT will be integrated within the routine treatment process, requiring no separate session for the patient. BgRT is being actively pursued by many Unity users and is facilitated by the Biomarker Working Group in the MR-Linac consortium.

Diffusion-weighted imaging (DWI) is one of the most promising MRI biomarkers. DWI detects and characterizes the movement of water molecules in tissues, which is different in tumors compared to healthy tissues due to their cellular density. DWI changes in tumors, specifically the apparent diffusion coefficient (ADC), are shown to correlate with clinical outcomes (Xie, et al., 2015). Robust, standardized DWI sequences are available on Elekta Unity (Figure 16), powered by high-field MRI, high SNR, and fast scan times (DWI brain: 4:26 min, DWI prostate: 3:31 min).

Studies have demonstrated the excellent accuracy, repeatability and reproducibility of DWI on Unity, in both phantoms (Kooreman et al. 2019) (Kooreman et al. 2020) (Subashi et al. 2022) and throughout the body in patients (Boeke et al. 2020) (Ingle et al. 2022) (Lawrence et al. 2021) (Thorwarth et al. 2020) even when the gantry is rotating and dose is being delivered.

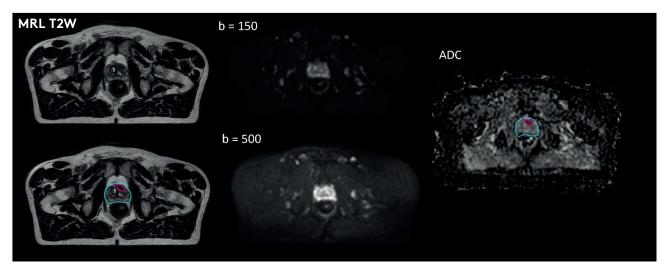


Figure 16. Example of diffusion-weighted images and the calculated ADC map, showing restricted diffusion in the dominant prostatic lesion.

Additional quantitative biomarkers have been implemented on Unity in the research setting, including IntraVoxel Incoherent Motion (IVIM) to characterize both perfusion and diffusion from a single scan; T1W, T2W, and T1P mapping to quantitatively map relaxometry parameters; oxygen-enhanced imaging to determine hypoxic areas; and Chemical Exchange Saturation Transfer (CEST) to detect cellular proteins that directly correlate with cell proliferation (<u>Elekta BgRT bibliography</u>).

Debunking MRI myths

MRI may seem complex and difficult if you're unfamiliar with the technology and terminology. Such unfamiliarity has led to myths, incorrect information, and poor understanding of its benefits. So, let's get some facts straight and answer some frequent questions about MRI and the MR-Linac.

Is geometrical accuracy and field homogeneity as good as CT?

The ability of MRI to accurately depict tumor and OAR location is often debated. While it's true that CT suffers less from geometrical inaccuracies, modern MRI systems compensate for any inaccuracies to a large extent. Unity always compensates in all three dimensions, which results in maximum distortions of 0.8 mm for a large spherical volume of 350 mm (Snyder et al. 2020) and much smaller distortions for smaller volumes. Moreover, the pre-defined Unity protocols ensure all parameters are tuned to achieve high geometrical accuracy (Hasler et al. 2023).

Another important aspect is the homogeneity of the magnetic field. This is extremely good on Unity, with typical errors in the order of 0.1-0.2 mm (Tijssen et al. 2019). In addition, studies looking at the longitudinal stability of multiple Unity systems all concluded that there was high temporal stability and good agreement between systems (Wetscherek et al. 2022) for various quantitative measurements with and without radiation and gantry rotation.

Do implants interfere with MRI?

A common misunderstanding is that patients with implants cannot be treated with MRgRT. On the contrary, in many cases patients can be safely imaged and MRI even has a clear advantage over CBCT. While implants often cause large streaking artifacts in CT and CBCT images, which hamper target visualization, any artifacts with MRI are generally much more localized (Figure 17 and Figure 18). Using pre-set sequences, the target and nearby OARs can be visualized without geometric distortions in patients who have hip implants (van Lier et al. 2021) (McDaid et al. 2024). For this reason Unity customers prefer MRgRT over CBCT guidance for prostate patients with hip implants. Teeth implants can also cause large streaking artifacts on CT and CBCT images, whereas they simply appear as a localized void on high resolution MRI images (Figure 17). Additionally, a study on the safety of MRI in 1509 patients with implanted cardiac devices reported no long-term clinically significant adverse events (Nazarian et al. 2017).

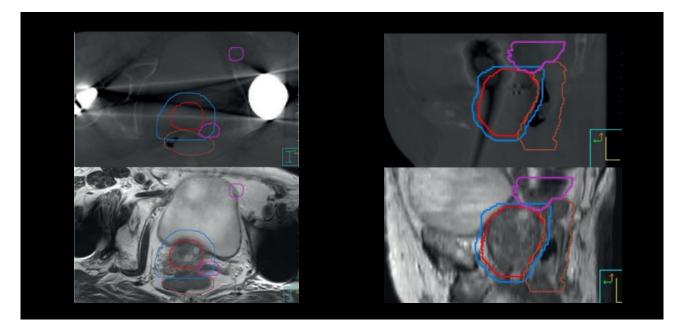


Figure 17. CBCT (top) and MR-Linac (bottom) images of a patient with bilateral hip implants. On the CBCT streaking artefacts are observed obscuring the target area. Images courtesy of The Royal Marsden Hospital.

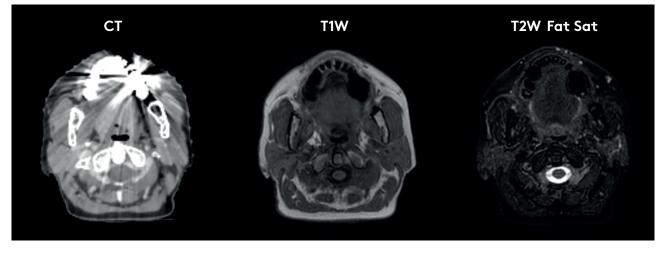


Figure 18. Example of the influence of teeth implant on image quality. On the CT the target area is obscured by metal streak artefacts, where on the MR image a localized signal void is observed.

What about susceptibility and chemical shift phenomenas?

Susceptibility artifacts arise from the differences in magnetic susceptibility of different tissues or materials, such as metal implants or air-tissue interfaces, which can lead to geometric inaccuracies. This only generally becomes problematic at MR field strengths ≥3T. On Unity, the pre-set protocol parameters (e.g. bandwidth) ensure that magnetic susceptibility is very low. A study of clinical cases showed a maximum susceptibility effect of 0.24 mm (Hasler et al. 2020).

Another factor that could lead to geometrical accuracies is the chemical shift, which results from differences between the resonance frequencies of fat and water. Again, Unity protocol settings ensure that this is very low and not noticeable.

Does SAR cause an increase in body temperature?

The Specific Absorption Rate (SAR) is a measure of the energy deposited in a certain tissue. Very high SAR values could lead to an increase in tissue temperature. Since Unity's MR component is based on a diagnostic MRI system, the SAR in all sequences is well within international guidelines and is not an issue for clinical treatments. Acceleration techniques, like Compressed SENSE, can even decrease SAR further.

How easy is it to introduce MRI into RT workflows?

While the underlying technology of MRI is impressive, the use of MRI for RT can be straightforward. Just as MR simulators have predefined sequences, Elekta Unity has a large library of pre-defined, anatomy-specific protocols. These pre-set protocols are designed specifically for Unity and support a large range of anatomies and motion management strategies. They optimize contrast, resolution, SNR, and acquisition time (like standardized CBCT or CT settings) and are acquired with a single mouse click, without the need to tweak any parameters.



The Elekta MR-Linac Consortium has been of paramount importance in developing and testing some of these sequences clinically. This makes MR imaging on Unity easy, inspiring confidence and giving the best results based on expert consensus.

An MRI sequence, or a RF pulse sequence, is a particular setting of MRI parameters that determines the appearance of the MR image. MRI protocols define a set of MRI sequences for a specific anatomy. On Elekta Unity and Philips scanners this is also called an ExamCard.

Will MRI slow the treatment down?

While MRI is generally slower than CT, most 3D sequences are acquired in just a few minutes, or even within a minute. For example, high-resolution 3D brain images are acquired within 4 minutes, a T2-weighted prostate image can be acquired within 1 minute, and a breath-hold thorax or abdomen acquisition takes only 18 seconds on Unity. This is enabled by optimized protocols, a high-performance MR system, and acceleration techniques, such as Compressed SENSE). It has also been shown that contouring and contour adaptation is faster on MR images compared to CT (Pathmanathan et al. 2019), making MRI more beneficial overall for adaptive radiotherapy. As additional MRI data can be gathered during the adaptive process, multi-parametric imaging is possible without additional time penalty.

Compressed SENSE

Compressed SENSE is an acceleration technique that speeds up image acquisition without compromising image quality. This allows different MRI contrasts to be acquired with high resolution and in short scan times (i.e. a few minutes, or even seconds for breath-hold acquisitions) (Geerts-Ossevoort, et al., 2018). This innovative technology has been transferred from the diagnostic setting to radiation therapy in collaboration with Philips as our MR imaging partner.

How comfortable are MR-Linac treatments?

MR-Linac treatments have demonstrated a high patient tolerability (de Mol van Otterloo et al. 2021). In a MOMENTUM study on patterns of care, tolerability, and safety of Elekta Unity, none of the 943 patients discontinued treatment, disproving initial concerns that patients might not tolerate MRgRT due to claustrophobia or discomfort (de Mol van Otterloo et al. 2021). Moreover, while MRI can be noisy, techniques are available to reduce acoustic noise, such as Philips SoftTone. This is especially useful for head-and-neck patients, for whom sufficient hearing protection can be challenging.

Conclusion

MRI is a versatile and extremely powerful imaging modality for oncology and is especially valuable for RT. Elekta Unity's high-performance MRI system and robust, anatomy-specific protocols make it easy for users to harness the power of MRI to visualize both tumors and OARs. As discussed, this is enormously useful for adapting treatments daily, automatically gating the beam in real time or shifting the beam to a new position, and visualizing changes at a biological level. MRI is therefore key for oncology and precision RT and ready for clinical primetime for radiotherapy departments.

References

- Almansour, H. et al. 2021. Prospective Image Quality and Lesion Assessment in the Setting of MR-Guided Radiation Therapy of Prostate Cancer on an MR-Linac at 1.5 T: A Comparison to a Standard 3 T MRI. Cancers, Volume 13, p. 1533.
- 2. Atun, R. et al. 2015. Expanding global access to radiotherapy. The Lancet Oncology, 16(10), pp. 1153-1186.
- Bahig, H. et al. 2018. Magnetic Resonance-based Response Assessment and Dose Adaptation in Human Papilloma Virus Positive Tumors of the Oropharynx treated with Radiotherapy (MR-ADAPTOR): An R-IDEAL stage 2a-2b/ Bayesian phase II trial. Clinical and Translational Radiation Oncology, Volume 13, pp. 19-23.
- 4. Bainbridge, H. et al. 2017. Magnetic resonance imaging in precision radiation therapy for lung cancer. Translational lung cancer research, 6(6), pp. 689-707.
- 5. Boeke, S. et al. 2022. Online MR guided dose escalated radiotherapy for organ preservation in distal rectal cancer. Clinical and Translational Radiation Oncology, Volume 37, pp. 153-156.
- 6. Boeke, S. et al. 2020. Serial DWI in HNC treated on a 1.5T MR-Linac and benchmark to a reference 3 T diagnostic MR-scanner. Physics Track. Volume 152, pp 927-928.
- Brown, K., 2023. Elekta Unity Comprehensive Motion Management—Explained. Available at: <u>https://www.elekta.com/products/radiation-therapy/unity/assets/Elekta%20Unity%20Comprehensive%20Motion%20</u> <u>Management%20Explained.pdf</u>
- 8. Carr, M. et al. 2023. Towards simulatin-free MR-linac treatment: utilizing male pelvis PSMA-PET/CT and populatoin-based electron density assignments. Physics in Medicine & Biology, Volume 68, p. 195012.
- 9. Chang, E. et al. 2009. Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial. Lancet Oncology, 10(11), pp. 1037-1044.
- Chen, A. et al. 2017. MRI-guided radiotherapy for head and neck cancer: initial clinical experience. Clinical and Translational Oncology, Volume 20, pp. 160-168.
- 11. Chuong, M. et al. 2023. Stereotactic MR-guided on-table adaptive radiation therapy (SMART) for borderline resectable and locally advanced pancreatic cancer: A multi-center, open-label phase 2 study. Radiotherapy & Oncology, Volume 191, p. 110064.
- 12. Daamen, L. et al. 2024. Quality of life and clinical outcomes in rectal cancer patients treated on a 1.5T MR-Linac within the MOMENTUM study. Clinical and Translational Radiation Oncology, Volume 45, p. 100721.
- 13. de Mol van Otterloo, S. et al. 2020. The MOMENTUM Study: An International Registry for the Evidence-Based Introduction of MR-Guided Adaptive Therapy. Frontiers in Oncology, Volume 10, pp. 1-9.
- de Mol van Otterloo, S. et al. 2021. Patterns of Care, Tolerability, and Safety of the First Cohort of Patients Treated on a Novel High-Field MR-Linac Within the MOMENTUM Study: Initial Results From a Prospective Multi-Institutional Registry. International Journal of radiation oncology biology physics, 111(4), pp. 867-875.
- 15. Eijkelenkamp, H. et al. 2023. Clinical outcomes after online adaptive MR-guided stereotactic body radiotherapy for pancreatic tumors on a 1.5 T MR-linac. Frontiers in Oncology, Volume 13, p. 1040673.
- 16. Elekta, 2024. Elekta Unity biology-guided radiation therapy. Available at: <u>https://www.elekta.com/medical-affairs/bibliographies/elekta-unity-biology-guided-radiation-therapy/</u>
- 17. Ferris, W. et al. 2024 Technical note: A simple method for patient-specific. Journal of applied clinical medical physics, Volume pre-print, p. e14353.
- Gani, C. et al. 2021. Marker-less online MR-guided stereotactic body radiotherapy of liver metastases at a 1.5 T MR-Linac – Feasibility, workflow data and patient acceptance. Clinical and Translational Radiation Oncology, Volume 26, pp. 55-61.
- Geerts-Ossevoort, L. et al. 2018. Compressed SENSE. Speed Done right. Every time. Available at: <u>https://www.philips.com/c-dam/b2bhc/de/resourcecatalog/landingpages/ingeniaelition/White_Paper_Compressed_SENSE-opt.pdf</u>
- 20. Glide-Hurst, C. et al. 2021. Task group 284 report: magnetic resonance imaging simulation in radiotherpay: consierations for clinical implementation, optimization, and quality assurance. Medical Physics, 48(7), pp. e636-e670.
- 21. Hasler, S. et al. 2023. Geometric distortions in clinical MRI sequences for radiotherapy: insights gained from a multicenter investigation. Acta Oncologica, 62(11), pp. 1551-1560.
- 22. Hasler, S. W. et al. 2020. Tumor site specific geometric distortions in high field integrated magnetic resonance linear accelerator radiotherapy.. Physics and imaging in radiation oncology, Volume Jul 15, pp. 100-104.
- Ingle, M. et al. 2022. Quantitative analysis of diffusion weighted imaging in rectal cancer during radiotherapy using a magnetic resonance imaging integrated linear accelerator. Physics and Imaging in Radiation Oncology, Volume 23, pp. 32-37.
- 24. Jager, E. et al. 2016. Validated guidelines for tumor delineation on magnetic resonance imaging for laryngeal and hypopharyngeal cancer. Acta Oncologica, Volume 55, pp. 1305-1312.
- 25. Keall, P. et al. 2022. Integrated MRI-guided radiotherapy opportunities and challenges. Nature Reviews Clinical Oncology, Volume 19, pp. 458-470.

- 26. Keall, P. et al. 2022. ICRU Report 97: MRI-guided radiation therapy using MRI-linear accelerators. Journal of the ICRU, 22(1), pp. 1-100.
- Kerkmeijer, L. et al. 2021. Focal Boost to the Intraprostatic Tumor in External Beam Radiotherapy for Patients With Localized Prostate Cancer: Results From the FLAME Randomized Phase III Trial. Journal of Clinical Oncology, 39(7), pp. 787-796.
- 28. Kooreman, E. S. et al. 2019. Feasibility and accuracy of quantitative imaging on a 1.5T MR-linear accelerator. Radiotherapy and Oncology, Volume 133, pp. 156-162.
- 29. Kooreman, E. et al. 2020. ADC measurements on the Unity MR-Linac A recommendation on behalf of the Elekta Unity MR-Linac consortium. Radiotherapy and Oncology, Volume 153, pp. 106-113.
- 30. Lawrence, L. S. et al. 2021. Accuracy and precision of apparent diffusion coefficient measurements on a 1.5T MR-Linac in central nervous system tumour patients. Radiotherapy and Oncology, Volume 164, pp. 155-162.
- 31. Maziero, D. et al. 2021. MR-Guided Radiotherapy for Brain and Spine Tumors. Frontiers in Oncology, Volume 11, p. 626100.
- McDaid, L. et al. 2024. Geometric distortion caused by metallic femoral head prosthesis in prostate cancer imaging on an MR Linac: in-vivo measurements of spatial deformation. British Journal of Radiology, Volume Pre-print, pp. 1-6.
- Merckel, L. et al. 2024. Stereotactic body radiotherapy of central lung tumours using a 1.5 T MR-linac: First clinical experiences. Clinical and Translation Radiation Oncology, Volume 45, p. 100744.
- 34. Nazarian, S. et al. 2017. Safety of Magnetic Resonance Imaging in Patients with Cardiac Devices. The New England journal of medicine, 377(26), pp. 2555-2564.
- 35. Nyholm, T., 2009. Systematisation of spatical uncertainties for comparison between MR and a CT-based radiotherapy workflow for prostate treatments. Radiation Oncology, 4(54), pp. 1-9.
- 36. Pathmanathan, A. et al. 2019. Comparison of prostate delineation on multimodality imaging for MR-guided radiotherapy. British Journal of Radiology, Volume 92, p. 20180948.
- 37. Reinders, F. et al. 2024. Detectability and intra-fraction motion of individual elective lymph nodes in head and neck cancer patients on the Magnetic Resonance Image guided linear accelerator. Physics and imaging in radiation oncology, Volume 29, p. 100532.
- S.R. de Mol van Otterloo 2024. Patient expectation and experience of MR-guided radiotherapy using a 1.5T MR-Linac. Tech Innov Patient Support Radiat Oncol., Volume 29, p. 100224.
- 39. Salzilo, T. et al. 2022. Development and implementation of optimized endogenous contrast sequences for delineation in adaptive radiotherapy on a 1.5T MR-Linear-accelerator (MR-Linac): A prospective R-IDEAL Stage 0-2a quantitative/qualitative evaluation of in vivo site-specific qu. MedRXiv, p. 1.
- 40. Snyder, J. et al. 2020. Commissioning of a 1.5T Elekta Unity MR-Linac: a single institution experience. Journal of Applied Clinical Medical Physics, 21(7), pp. 160-172.
- Stewart, J. et al. 2021. Quantitating interfraction target dynamics during concurrent chemoradiation for glioblastoma: a prospective serial imaging study. International Journal of Radiation Oncology Biology Physics, 109(3), pp. 736-746.
- 42. Subashi, E., 2022. Longitudinal assessment of quality assurance measurements in a 1.5T MR-Linac: Part II -Magnetic resonance imaging. Journal of Applied Clinical Medical Physics, 23(6), p. e13586.
- 43. Thorwarth, D. et al. 2020. Quantitative magnetic resonance imaging on hybrid magnetic resonance linear accelerators: Perspective on technical and clinical validation. Physics and Imaging in Radiation Oncology, Volume 16, pp. 69-73.
- 44. Tijssen, R. et al. 2019. MRI commissioning of 1.5T MR-Linac systems a multi-institutional study. Radiotherapy and Oncology, Volume 132, pp. 114-120.
- 45. Tringale, K. et al. 2022. Stereotactic ablative radiation for pancreatic cancer on a 1.5 Telsa magnetic resonancelinac system. Physics and Imaging in Radiation Oncology, Volume 24, pp. 88-94.
- 46. van der Heide, U. A. et al. 2019. MRI basics for radiation oncologists. Clinical and Translational radiation oncology, September.pp. 74-79.
- 47. van Lier, A. et al. 2021. Geometrical imaging accuracy, image quality and plan quality for prostate cancer treatments on a 1.5 T MRLinac in patients with a unilateral hip implant. Physics in Medicine & Biology, 66(20), p. 205013.
- Westley, R. et al. 2024. Interim Toxicity Analysis From the Randomized HERMES Trial of 2- and 5-Fraction Magnetic Resonance Imaging–Guided Adaptive Prostate Radiation Therapy. International Journal of Radiation Oncology Biology Physics, 118(3), pp. 682-687.
- 49. Wetscherek, A. et al. 2022. Longitudinal stability of MRI QA up to two years on eight clinical 1.5T MR-Linacs. Frontiers in Physics, Volume 10, pp. 1-14.
- 50. Xie, H. et al. 2015. Effectiveness of the apparent diffusion coefficient for predicting the response to chemoradiation therapy in locally advanced rectal cancer: a systematic review and meta-analysis. Medicine, 94(6), p. e517.



Hope for everyone dealing with cancer.

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