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Role of magnetic resonance imaging in radiation therapy planning

Abstract

Computed tomography (CT) is essential in radiation treatment planning (RTP) since it provides information on electron density using tissue-specific attenuation coefficients, which are used to calculate the radiation dosage. It also provides lucid resolution of air-filled cavities, fat tissue and bony tissue.

Currently, MRI is frequently incorporated in RTP in conjunction with CT for contrast enhancement benefits for its superior anatomical soft tissue contrast that can visualize the extent of tumor soft tissue infiltration into normal tissues. The introduction of MRI has significantly reduced intra and inter-observer contour variability in a number of tumor sites.

MRI is a highly versatile modality with the availability of numerous sequences. Apart from anatomical information, MRI can provide functional information on tissue characteristics, and improves the accuracy of delivery which promotes dose escalation, as well as monitoring treatment and assess response.

Volume delineation is one of the earliest steps in RTP, meaning inaccuracies can induce error propagation throughout the treatment course. Adequate sequence selection is therefore a critical step. An ideal MR sequence would be accurate, resistant to artifacts, reproducible with high soft tissue resolution and low intra- and inter observer variability in order to optimize the consistency in imaging interpretation, dosimetry and ultimately better patient outcome.

This review will discuss important aspects of tumor delineation and sequence selection, followed by an introduction to major types of MRI sequences commonly used in RTP.

Keywords: radiotherapy planning, magnetic resonance imaging, MRI sequence selection

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Introduction

Radiation Oncology is undoubtedly an important pillar in cancer treatment. With an estimated 60% of all cancer patients should have RT as part of their management plan.[1] It is important to delineate tumor target and adjacent critical normal structures, also known as organs at risk (OAR) as accurately as possible. This will allow optimal dose coverage of the tumor and reduce dose to the surrounding healthy tissues.[2]

CT is essential in radiotherapy treatment planning (RTP) since it provides information on electron density using tissue specific attenuation values, which is essential in the radiation dose evaluation.[2,3] It also exhibits advantages such as wide availability, minimal geometrical distortion and clear resolution of air-filled cavities and greater visibility of fatty and bony tissues.[4] However, CT has poor soft tissue contrast, thus in certain circumstances MRI seems to be assistive in target delineation due to its superior anatomical soft tissue contrast.[3] Consequently, MRI images are often fused and registered with CT images in contour segmentation process. The introduction of MRI has significantly reduced intra and inter-observer variability in contouring.[5,6] In addition, MRI can provide functional information on tissue characteristics, which improves the accuracy of delivery and promotes dose escalation, as well as monitoring treatment and assess its response later.[7-10]

However, MRI is subjected to geometric distortions,[2,11] and does not provide information on electron density, unless a pseudo-CT is derived from MR images for dosage evaluation.[12] Another challenge for MRI is the long acquisition time making it susceptible to motion artifact, which may be reduced by ultrafast techniques.[13] The introduction of a MR-guided RT (MRgRT) system eliminates the aforementioned limitations by having a high-temporal cine MRI on-board to capture the positions of the tumor and OAR in real-time. These 4D-MRI are becoming more commercially available, which ensures there will be incremental utilization of MRI into the field of RT.[14] MRI is a highly versatile modality with numerous available sequences. Properties of tumors and their surrounding tissues differ; therefore, the ideal sequence for every site varies accordingly. Here, we present a narrative review on the utilization and selection of MR sequences for target delineation in RTP.

Target delineation and sequence selection

The primary goal of implementing MRI into RTP is to precisely delineate Gross Tumour Volume (GTV)/Clinical Target Volume (CTV)/Organs at Risk (OAR), this is especially essential in intensity modulated radiation therapy (IMRT)/stereotactic body radiotherapy (SBRT) delivery where steep dose gradients are present at the edge of targeted region. Target delineation is one of the earliest steps in RTP, thereby any inaccuracies can induce error propagation downstream. Adequate MR sequence selection is a critical step in achieving this goal. An ideal sequence should be accurate, reproducible with high soft tissue resolution and low intra- and interobserver variability in order to optimize the consistency in imaging interpretation.

The gold standard in evaluating the accuracy of tumor delineation is comparing image-derived GTV to the corresponding pathological

specimen, preferably "whole-mounted". This ensures the delineated GTV to represent the actual disease. However, tissue shrinkage and deformation during tissue processing and precise alignment of delineated tumour on MR with the pathological reference remains a challenge. Therefore, a robust and a standardized process of tissue preparation and registration methods are desirable, that remained a challenge till now. A surrogate way to address these uncertainties is to compare the volume delineated by multiple observers, with the presumption that the volume accepted by the majority represents the actual volume, or is comparable to the volume delineated on MRI with that of other imaging modalities. However, such studies investigate the inter-observer variability component, also demonstrate a lack of consistency in various aspects making sequence selection a real challenging decision.[15]

It is worth noting that while the sequence selection is crucial, several other factors need to be considered when implementing MRI into RTP, including patient positioning and immobilization, scan protocols, control for respiratory motion, peristaltic motion or OAR filling differences where relevant, geometric distortion correction and quality assurance program.[2]

MRI sequences

Fundamentally, the sequences can be either spin-echo- (SE) or gradient-echo-based (GE) with addition of other parameters. Basic SE sequence has a long acquisition time so it is susceptible to motion artifacts; however, it has high spatial resolution and provides the gold standard in intensity distortion. Turbo SE (TSE) is an SE-based sequence that can substantially accelerate scanning speed, and is therefore widely used in RTP. Other SE-based sequences include fluid-attenuation inversion recovery (FLAIR) and short tau inversion recovery (STIR) both are useful in brain imaging and capturing bone marrow changes, respectively. In comparison to SE, GE has a faster acquisition time, therefore has minimal motion artifact, but with a lower spatial resolution and is susceptible to field inhomogeneities-induced artifact. Such local field inhomogeneities can arise from metal implant-induced magnetic field change, thus should be avoided in patients with metallic prosthesis.[4]

Conventionally, the signal arising during the decay (relaxation) of proton magnetic moments after being excited by radio-waves within a strong magnetic field are exploited to generate images. The relative difference in tissue relaxation times defines T1 (longitudinal)- or T2 (transverse)-weighted images. However, if the properties that give rise to the parameters for T1w and T2w image generation do not differentiate tumor tissues from surrounding healthy tissue, these sequences will not be useful for tumor delineation such as T1w in prostate tumor.[4,16]

More sophisticated MRI techniques such as functional MRI focus on the biological status of the tumor. These sequences emphasize various intrinsic properties of the tissue, such as proton density, perfusion, diffusion and chemical composition. The highlighted properties, or "imaging biomarkers" can exist in tumor microstructure, differentiating them from surrounding healthy tissues, therefore can be used to complement anatomical information for target definition (including intra-tumor spatial heterogeneity), assess aggressiveness for dosage mapping, monitor treatment response and early prediction for treatment toxicity, re-occurrence and prognosis.[17]

As with bio-specimen biomarkers, the sensitivity and specificity of these sequences alters with the change in spatio-temporal profile of a tumor, most of the functional sequences are affected by multiple underlying biological processes. Therefore, sufficient biological and clinical validations are required before clinical implementation.

Diffusion weighted imaging (DWI)

DWI constructs image based on the mobility of water molecules in tissues, which can be quantitatively measured by applying a mono-exponential model, called apparent diffusion coefficient (ADC) value, or biexponentially as intravoxel incoherent motion (IVIM) to assess tissue perfusion and cell density concomitantly.[18] The mobility of water molecules is affected by several factors, including cellular space structure, membrane permeability, interstitial viscosity and cellular density.[19] These properties are valuable tools in identifying abnormal structures. For example, mobility of water is more restricted in hypercellular tissues such as malignant tumors and less restricted in glandular tissue, inflammation or tissues with significant necrosis.[16] These correlations have been validated with histological findings.[20]

The primary use of DWI in RTP is to assist target delineation, particularly the gross tumor in supplement to the conventional sequences. In addition, DWI can be used in monitoring treatment response, since tumor tissue undergoes regression and necrosis in response to daily radiation treatment, which leads to increased mobility of water molecules, reduced DWI signal and increased ADC.[2] DWI has also shown promising results in identifying the early radiation treatment response in patients with esophageal cancer, pancreatic cancer, locally advanced rectal cancer and cervical cancer.[9,21]

The limitation of DWI is its susceptibility to the geometric distortion, especially with single-shot spin-echo echo-planar imaging (SE-EPI), which is often used for DWI. Geometric distortion is more prominent when b-value is increased for a higher sensitivity.[22] A reduction in distortion is desired not only for the delineation purposes, but also to achieve better anatomical overlap with images obtained using other sequences for validation. To reduce distortion, selection of b-values are critical, and multi-shot sequences, segmented EPI, TSE-based readouts or non-EPI sequences must be adopted.[11]

In addition, DWI is not very specific and its alteration may be affected by many factors such as reduced cellular density as a result of necrosis or apoptosis, altered vasculature or cellular membrane permeability.[23] Nonetheless, DWI remains as one of the most studied functional sequence in MRI.

Dynamic contrast enhanced (DCE)

DCE MRI involves an intravenous injection of paramagnetic contrast agent, usually gadolinium-based. Sequential T1w images are captured as the contrast medium pass through vessels, changes could reflect overall and microvascular perfusion, permeability, and extracellular leakage space.[24] Similar to DWI, DCE can be quantitatively measured based on pharmacokinetic modeling, deriving the parameters such as transfer coefficient (K^{trans}) for permeability and perfusion and extravascular extracellular space volume (Ve) or rate constant (K^{ep}). (24)

DCE can measure tissue oxygenation and has been shown to correlate with tumor response to radiation in sites including brain, head and neck (HNC), liver, prostate, and non-small cell lung cancers (NSCLC).[7,8,25] This is based on the fact that hypoxia, a feature in cancer due to the imbalance between oxygen supply and consumption, is associated with tumor aggressiveness and radio-resistance.[26] DCE is also useful in distinguishing recurrent tumor, that are highly vascularized with increased permeability from radiation necrosis.[27]

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DCE has a high spatial resolution and is not susceptible to artifacts. However, T1 signal intensity and contrast agent concentration are not linearly correlated, which tends to cause inaccuracy in quantifying the hemodynamic parameters.[28] The image acquired on DCE is multifactorial including tissue relaxation time, permeability, vascularity and hypoxia, it is therefore not specific. In addition, scan parameters such as flip angle, repetition time and pre-contrast signal can all have impact on images. Although these limitations might be surmounted by combining with other sequences, they still impose obstacles for comparison across centers.[29]

MR spectroscopy (MRS)

MRS depicts the metabolic status of tissues by detecting the radiofrequency signals generated by endogenous nuclei such as ^{1}H, ^{31}P, ^{13}C, and ^{19}F, then the relative compositions of tissue metabolites can be measured.[24] In particular, diminished citrate level is observed in tumor tissue because of the change in metabolic pathway. Choline (Cho) is a metabolite produced during cell membrane biosynthesis, therefore a measure of cellular turnover. Elevated Cho may be observed in the presence of brain cancer. Similarly, creatine (Cr) that represents cellularity and metabolism may also be elevated.[30] Other common metabolites include N-acetylaspartate (NAA), a representation of neural density hence an indicator of neuronal injury, and lipid and lactate for hypoxia.[31]

The analysis and interpretation of MRS data may require extra expertise which limits its clinical use. The artefact from air-tissue interface in sites like HNC may also have impact on the data quality and affect interpretation. In body regions such as brain, prostate and breast, although MRS has shown promise in diagnosis and treatment response monitoring, its clinical application is still limited by the relatively low signal strength and sensitivity.[32]

Other sequences

Blood-Oxygen-Level-Dependent (BOLD) sequence is popular in examining neural function, where deoxyhemoglobin causes the signal change.[33] It might be useful in delineating critical neuronal structures, identifying tumor, or predicting response by detecting areas of hypoxia.[34] Tumour-oxygen-level dependent (TOLD) is sensitive to the alteration in the amount of oxygen molecules and may be integrated with DCE for hypoxia assessment.[35] MR elastography (MRE) can quantitatively measure the biomechanical properties such as elasticity and viscosity, and has been investigated in the context of breast cancer and liver fibrosis. Chemical exchange saturation transfer MRI (CEST) can quantify smaller macromolecules, such as glucose metabolism, which could be used to assess tumor aggressiveness and treatment response.[36]

Use of MR sequences in specific tumour sites

Brain: MRI is a part of routine target volume delineation and treatment response assessment in brain cancers,[37] and is described as the "gold standard" in stereotactic radiosurgery (SRS) treatment for brain tumor by American Association of Physicists in Medicine (AAPM) Task Group (TG-101).[38]

The introduction of MRI allowed better tumor and OAR delineation, and significantly reduced intra- and interobserver variability.[39] Currently, both European Organization for Research and Treatment of Cancer (EORTC) and US/Canadian Radiotherapy and Oncology Group (RTOG) recommend native and contrast enhanced T1w (T1CE) and thin sliced T2/FLAIR to be used in delineation of glioma in RT.[40,41] The choice of particular sequences depends on the grade of glioma and whether there is an intact blood brain barrier (BBB). For example, T2/FLAIR is recommended for detection of low-grade glioma with an intact BBB for delineation, whereas T1CE is indicated for high grade glioma or to exclude possible high-grade transformation.[42] The downside of conventional MRI techniques is that the use of single sequence may underestimate the distribution of malignant cells. Thus, T2/FLAIR abnormalities are taken into consideration especially in non-resected gliomas.[37]

Functional MRI is perhaps most extensively used in characterizing intracranial lesions. While T1CE alone only has 50% specificity in differentiating tumor progression from radio-necrosis.[43] 100% sensitivity and 83% specificity has been demonstrated by Bisdas et al in using K^{trans} derived from DCE for glioma recurrence detection.[8] DCE has also been shown to predict glioma with high potential of aggressiveness.[44] In addition, a sub-form of DWI, diffusion tensor (DTI) has been shown to improve the delineation of HGG than T1w alone.[45] Its quantification fractional anisotropy is helpful in delineating and sparing neural tracts.[46,47] DTI also has the potential to predict the invasiveness of high-grade tumor and pattern of recurrence.[48,49]

Radio-labelled amino acid PET scan has been shown to be useful for the identification of tumor extent as there is a higher uptake in biologically active tumor tissue and low in normal brain,[50,51] and has been recommended by the Response Assessment in Neuro-oncology (RANO), European Association for Neuro-Oncology (EANO) and ESTRO.[52] MRI has a sensitivity of 96% in detecting tumor tissue, but only 53% specificity, when MRI and PET are combined, the sensitivity becomes 93%, and specificity raises to 94%.[53] There is also less interobserver variability, especially at the skull base.[54] Therefore, an approach with multiparametric MRI in combination with CT and amino acid PET appears to be the ideal way of target volume delineation. These modalities are still being experimented, but surely will be contributing heftily to RTP in the future.[42]

Head and neck: Radiation dose delivery is intrinsically challenging in the head and neck region due to the close proximity of critical normal structures to the tumor. Late treatment-related toxicities such as xerostomia and dysphagia are common and can significantly impact quality of life of the patients.[55]

Currently, the mainstream strategy is complementing CT with the soft tissue information from MRI.[56] T2w fast spin echo (FSE) with fat suppression and post contrast T1w FSE with or without suppression are most commonly used sequences in both diagnostic and RTP.[57] In nasopharyngeal cancer, T1CE can uncover up to 40% of patients with intracranial infiltration that is missed on CT alone and MRI is helpful in identifying subtle bony invasion and has less interobserver variability. In Sinonasal cancer, conventional sequences are helpful in identifying tumor spread identified as hyperintensity on T2w and less enhancement on T1CE.[58] In oropharyngeal tumors, T1CE allowed better base of tongue tumor delineation, and T2w/FLAIR are thought to be ideal for parotid imaging.[59] However, for laryngeal and hypopharyngeal tumors, MRI does not show superiority over CT when compared with pathological specimen.[60,61]

Functional sequences, in particular DWI, has been extensively examined in HNC. The studies mainly focus on identifying regions within the tumor for dosage escalation and personalize oncological therapy based on their response prediction.[62,63] Several studies have highlighted the high specificity and sensitivity of DWI in detecting metastatic lymph nodes, where significantly lower ADC is observed. DWI is exceptionally useful in sub-centrimetric cervical lymph nodes, where the sensitivity is increased to 76% in comparison to 7%

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in conventional MRI. These findings hold true when compared with histopathological studies.[64-66]

DWI can also be used to predict treatment response after RT or chemoradiation therapy (CRT). Patients with low pre-treatment baseline ADC corresponds to better response.[63,67] The early prediction of tumor response could potentially allow timely adaptation of RTP or further personalization of treatment dose, potentially dose de-escalation for the early responders. Several studies have demonstrated a significantly elevated ADC compare to pre-treatment baseline in the complete responders.[63] This may be explained by a loss of tumor integrity from RT.[57] In addition, DWI is insensitive to the acute inflammation and studies have shown that DWI demonstrates a higher positive predictive value than anatomical imaging in detecting early reoccurrence.[68]

Majority of the studies on the application of DCE in HNC focuses on prediction and early assessment of treatment response. A correlation of an increased or high overall K^{trans} with good treatment outcome was suggested.[69,70] The data on the use of functional MRI in HNC remained preliminary, especially for DCE and MRS. Hence; further detailed research is desired before their integration and incorporation into routine clinical practices.

Lungs: RT plays a significant role in lung cancer treatment, especially in inoperable non-small cell lung cancer (NSCLC) patients that constitutes the majority in this cohort.[71] The introduction of SBRT escalated tumor control to 98% in early-stage NSCLC, with a 17% risk of grade 3–4 toxicity.[72,73] The high dose per fraction can potentially cause significant toxicities hence particular attention on OARs is required to ensure safe treatment delivery. Patients with more centrally located tumor (< 2cm from main proximal bronchial tree) are traditionally excluded from SBRT treatment due to proximity of tumor to the central normal structures such as oesophagus, heart, spinal cord, brachial plexus, central airway, major vessels and chest wall.[72,74]

The current workflow utilizes 4DCT and F-18-FDG PET for tumor delineation.[75] Inter-fractional shifts from primary tumor and vertebrae ranges from 5-7 mm but can be as high as 3 cm on CT.[76] CT produces larger uncertainties of up to a few centimeters for spinal cord and oesophagus owing to its low tissue contrast.[75] For PET scan, the low spatial resolution of 5-7mm means tumors of less than 4 mm may not be detected.[77]

MRI can differentiate lung tumor from other pathologies such as lung collapse, consolidation or effusion better than CT or PET.[16] There are two major challenges encountered when choosing sequences, to reduce the poor signal-to-noise ratio (SNR) due to low tissue density of lung parenchyma and respiration and cardiac motion induced artefacts.[78] Sequences have been investigated to quantify lung motion include fast low-angle shot (FLASH) and true fast imaging with steady-state precession (TrueFISP). The former acquires 3 images per second, and the later acquires 10 with a sub-optimal signal-to-noise ratio. Both of them generated the images of diagnostic quality.[79] Kumar et al.[80] reviewed 30 articles concerning anatomical detection, MRI-based motion analysis and functional imaging for lung tumors and pulmonary nodules. Various sequences had been explored deeply, including volumetric interpolated breath-hold (VIBE), a T1w 3D spoiled GRE sequence, T1w and T2w TSE, half-Fourier acquisition single-shot TSE and inverse-recovery (IR) sequences. However, it still remains a challenge to optimally balance acquisition time, signal-to noise ratio and susceptibility to motion artifacts. They suggested that although anatomical tumor infiltration and mediastinal lymph nodes could be demonstrated by conventional sequences, their use in radiation oncology for GTV delineation warrants further investigation for possible tumor deformation during respiration.

Bainbridge et al. reviewed the inter-observer variability and commented that the addition of PET to CT reduced inter-observer variation from 1.0 mm to 0.4 mm.[74,75] Adding MR sequences to CT and PET did not result in further improvement in interobserver variability, although this might be related to the lack of experiences in interpreting MRI contouring.[78]

As in other locations, studies have been investigating the use of functional MRI in lung cancer. In animal models DCE was able to differentiate radiation induced pneumonitis and fibrosis.[81] DWI can identify critical OAR sub-structures such as brachial plexus in Pancoast tumor allowing careful design of RT plans to reduce dose to the plexus.[82] DWI also shows comparable capability to PET in demonstrating malignant lymph nodes with higher specificity whenever there is inflammation.[83] Similar to FDG-PET, DWI was able to differentiate tumor from consolidation.[84] Unfortunately, DCE was not shown to be useful in predicting tumor response with consistency in lung cancer. Other imaging such as hyper-polarised ^{3}He and ^{129}Xe have been studied for delineating OAR by identifying healthy well-ventilated regions of the lung in advanced NSCLC with a promising result.[85,86]

Pancreas: Less than 20% of patients with pancreatic cancer present with resectable disease.[87] In patients with inoperable disease, definitive conventional CRT serves as consolidation therapy following chemotherapy.[88,89] Although CRT leads to the improved local control, GI toxicity was observed with no additional benefits in overall survival compared to chemotherapy alone.[90,91] The introduction of SBRT has since substantially reduced OAR toxicity and may improve overall survival.[88,92,93]

Despite of the controversial role of RT in pancreatic cancer, current imaging strategies utilize contrast enhanced CT complemented with PET/CT for tumor delineation.[88] Studies comparing GTV delineated with different imaging modalities with surgical specimen have shown mixed results and no optimal imaging modalities were identified.[94-99] One study recommended T1w for pancreatic GTV visualization and T2w to assess the extent of pancreatic tumor when it compressed pancreatic or common bile duct.[94] Previous study showed DWI was able to achieve a sensitivity of 0.86 and a specificity of 0.91 in detecting pancreatic tumor,[100] however, as it was difficult to differentiate pancreatic cancer from pancreatitis or normal tissue using DWI, it is not recommended for tumor contouring.[94] A small study demonstrated ADC increases in post-treatment and correlates with the degree of response.[99]

Cervical: The recommended definitive treatment for locally advanced cervical cancer involves concomitant EBRT and chemotherapy, followed by brachytherapy.[101,102] MRI has been shown to be able to discriminate GTV from adjacent normal uterine tissue and surrounding OARs, namely the bladder, rectum, bowel and vagina.[103] MRI is recognized by RTOG and GEC ESTRO as the most precise and reliable modality in gynecological tumor delineation.[104-106] MRI also allowed dose escalation with 10-20% survival gains with reduced RT related GI and urinary morbidity.[106]

In particular, T2w sequences gives a better contrast at the boundary of the tumor than T1w, whereas ADC gives a smaller GTV than T2w.[107] Conflicting results were achieved when comparing GTV delineated with T2w to that of surgical specimens.[108,109] The addition of ADC increased the contrast and lead to less inter-observer variability, despite its lower anatomical resolution.[110] ADC

also uncovers up to 16% of suspicious regions that is absent on T2w. Therefore, rather than mapping individually, a combination of T2w and ADC may be a better solution.[107] Nevertheless, the latest GEC ESTRO guidelines recommend a contouring strategy using T2w sequence as the gold standard for tumor delineation in image guided adaptive brachytherapy (IGABT), whereas T1CE and DWI are complementary and optional.[105] One study has demonstrated that the three different targets (GTV, high-risk clinical tumor volume and intermediate-risk clinical target volume) as defined by GEC ESTRO exhibit significantly different ADC, their ADC remained stable during the course of brachytherapy, therefore it has the potential to be beneficial for better delineation in the grey zone on T2w.[111] However, DWI is susceptible to geometric distortions and artifact induced by titanium applicator, therefore its use in brachytherapy may be limited in certain scenario.[112]

In patients treated with neoadjuvant CRT, post-treatment skewness of the ADC histogram and percentage change in ADC predicts and favorable response.[21,113]

Prostate: It is well established that EBRT is the standard and effective treatment for localized prostate cancer.[114,115] Both ASTRO and National Comprehensive Cancer Network (NCCN) guidelines suggest that the introduction of IGRT is beneficial in improving treatment outcome and reducing OAR toxicity.[116]

MRI is superior to CT in depicting the prostate capsule and the intra-prostatic heterogeneity.[117] It generates less inter-observer variability and less toxicity to OAR while maintaining comparable tumor control rates.[118-120] These benefits have also been suggested by ACR Appropriateness Criteria.[121] In addition, hip prosthesis in patient would produce less image distortion in MRI compared to CT.[122]

The ESTRO guidelines conclude that T2w MRI is the best modality in differentiating the prostate and the peri-prostatic structures.[117] Studies show that the utilization of MRI resulted in a smaller CTV of about 10-35% than CT alone.[6,123] MRI is useful in delineating the apex and the base, where a higher incidence of tumor occurs.[5,124] CT-MRI delineation leads to significantly lower urinary frequency and urinary retention toxicity scores than CT-only delineation, although no significant difference in overall urinary or rectal toxicity were observed.[125]

Apart from evaluating extra-capsular and seminal vesicle invasion, a key advantage of MRI in RTP is the ability to visualize intra-prostatic lesions.[126] Prostate cancer is known to be heterogeneous and multifocal. This property renders the healthy tissue to be susceptible to toxicity if the whole gland is targeted. In addition, local recurrences often occur at the original site of dominant intra-prostatic lesion.[127-129] Therefore, a focal boost to regions of high tumor burden is logically beneficial, and may be visualized with the help of DCE.[25] Several studies demonstrated that focal dose escalation can be achieved by delineating prostate with MRI without causing more toxicity to rectal walls, and has good clinical feasibility.[10,130-132]

Sequences including T2w, DWI, DCE and MRS have been investigated extensively for prostate cancer.[9,125,133] A multi-parametric (mpMRI) approach combining T2w, DWI and DCE yields the highest sensitivity in intra-prostatic tumor nodule detection than each modality alone when compared to whole mount histology.[134] However, PI-RADS2.1v and several other studies suggest that mpMRI underestimate tumor volume and extent compared to histology.[135-138]

In addition, ADC can be used to identify the aggressiveness of the lesions that are most likely to benefit from dosage escalation. Studies have also shown that there is marked increase in ADC after treatment, which positively correlates with good outcomes.[9]

Rectum: Patients with locally advanced rectal tumor are recommended to have neoadjuvant RT prior to surgical resection.[139] There are currently no guidelines available on the choice of MR sequences for tumor delineation. As T2w images is known to be the gold standard for staging because it captures the three layers of rectal wall as well as the mesorectal fascia relatively well, it is therefore adapted to tumor delineation, though it is recommended that it be performed in RT treatment position.[4]

There are few studies investigated the use of MRI in GTV delineation. To date most of them are investigating inter and intra-observer variation in target delineation. There is little data on the correlation of MRI contouring with pathology specimen. This is mainly because in neoadjuvant therapy the planning process followed by CRT will cause tumor regression and deformation.[140] In contouring studies, T2w yields better inter-observer consistency with a larger tumor volume than DWI, and the addition of DWI to T2w can increase sensitivity from 82-84% to 93-95%.[140,141]

DWI has also been studied for assessing the response to neoadjuvant CRT. Similar to HNC, a lower pre-treatment ADC in rectal tumor corresponded to improved treatment response.[142,143] This may be explained by less necrosis in tissues with low ADC, which is correlated to better tissue perfusion, higher oxygen concentration and a non-acidic microenvironment, therefore more susceptibility to treatment. Some studies suggest that responding lesions exhibit an increase in ADC during and after CRT, in contrast to the non-responding lesions, which remain stable to pre-treatment value,[143-146] while others proposed that DWI volumetry, rather than ADC value is more response-predictive.[147,148]

Conclusion

In summary, over the past decades, there has been a huge advance in imaging technologies in radiation treatment for cancer. The advantage of better soft tissue contrast and lack of ionizing radiation made MR an attractive imaging modality for RTP and frequent treatment response assessment during treatment Conventional sequences, such as T1w and T2w images allow good anatomical delineation in the majority of tumor sites. However, various functional sequences focusing on water diffusion, perfusion, and chemical properties may contribute extra layers of value. They may be used complementary to anatomical information, providing biological information of the tumor and therefore allow assessment of tumor aggressiveness, early response and recurrence prediction and post-treatment monitoring. Although the use of MRI is still in infancy in some tumor sites, it is a promising tool that is worth exploring in the era of MRgRT, with the aim of further treatment and dose personalization for patients.

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Conflicts of interest

Author declares there are no conflicts of interest.

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