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Clinical Applications for Diffusion MRI in Radiotherapy

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Abstract

In this article, we review the clinical applications of diffusion MR imaging in the radiotherapy treatment of several key clinical sites, including those of the CNS, the head and neck, the prostate and cervix. Diffusion-weighted MRI (DWI) is an imaging technique that is rapidly gaining widespread acceptance due to its ease and wide availability. DWI measures the mobility of water within tissue at the cellular level without the need of any exogenous contrast agent. For radiotherapy treatment planning, DWI improves upon conventional imaging techniques, by better characterization of tumor tissue properties required for tumor grading, diagnosis and target volume delineation. Because diffusion weighted MRI is also a sensitive marker for alterations in tumor cellularity, it has potential clinical applications in the early assessment of treatment response following radiation therapy.

Introduction

Diffusion MRI is a technique that measures the mobility of water within tissue at the cellular level[1,2] without the need of any exogenous contrast agent and is sensitive to cellular changes in the microenvironment that alter molecular mobility. The thermally-driven random movement of water molecules, or Brownian motion, along a magnetic field gradient induces signal attenuation and can be quantified by a diffusion coefficient (mm^2/s). These principles can also be applied to tissues in biologic systems where the movement of water molecules occurs in both the intra and extracellular domains and is impeded by cell membranes, extracellular tortuosity and macromolecules.[3–5] In most tissues, the intracellular compartment contributes most of the MRI signal by volume, but the relatively high mobility in the extracellular space has a strong influence on the net measured mobility. Diffusion MRI is sensitive to complex biophysical processes mediated by the volume fraction of water in the intra-/extra-cellular domains, water interaction with intracellular constituents, and the degree to which extracellular water is “free” versus hindered by tortuosity. In addition, non-thermal, semi-random motions are manifest as diffusion-like signal attenuation. A clear example of this is cardiovascular-driven blood perfusion through the (semi)random capillary

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network. Given these complexities, the term “apparent” diffusion coefficient (ADC) is used to reflect the fact that a singular pure diffusion coefficient in tissues is not measurable by MRI, and that ADC values are influenced by acquisition conditions.

Despite these caveats, diffusion weighted (DW) imaging is a fast, simple, and readily available MR imaging technique. In comparison to other functional MR imaging techniques, it is practical for clinical use in a variety of applications. Diffusion weighted MRI can be used for lesion detection, diagnosis, grading and further characterization of tumor tissue properties. Disruption of the normal tissue structure, e.g., the disruption of the prostate capsule and fluid flow by the presence of tumor cells can lead to alterations in the diffusion coefficient. A simplistic, though conveniently useful concept is that ADC values are inversely related to tumor cellularity. That is, tissues having relatively high cell density tend to exhibit lower ADC values due to the impeded water movement amongst the cell-packed milieu. Diffusion weighted MRI is also a sensitive marker for alterations in tumor cellularity and the early assessment of treatment response. Successful treatment leads to necrosis, alters cell membrane permeability and water homeostasis, leading to changes in tumor cell density. Increased ADC values following effective cytotoxic therapy reflects a decrease in tumor cellularity. These cellular changes can be detected early, prior to changes in tumor size and therefore is a potential, early non-invasive imaging biomarker of response and overall survival.[6,7]

Acquisition and Technical Issues

Diffusion MRI is obtained by inserting additional strong magnetic field gradient pulses within an MR imaging sequence to create diffusion sensitive (weighted) images. Typically a pair of additional pulses is used where the first pulse “encodes” locations of the ensemble of water molecules and the second “decodes” location. Any molecular movement between encode-decode events creates signal loss that is analyzed as a function of diffusion encoding gradient strength. More specifically, the diffusion gradient has “direction” (eg. along right/left axis), so random molecular movement along the given direction is being probed. The extent of diffusion weighting (or MR signal loss) depends upon the duration, time and amplitude of applied diffusion gradients, which is often composited into a scalar factor, called the b-value (s/mm^2). If no additional diffusion gradient pulses are applied, the b-value equals zero. The signal intensities in diffusion weighting images decrease with increasing b-value and the diffusion coefficient. While signal decreases with b-value in diffusion-weighted MRI (DWI), tissue contrast attributable to differences in water mobility increases with b-value, therefore heavily diffusion-weighted images are widely used to accentuate (detect) cellular dense tissues/lesions by reading qualitative DWI. Quantitative ADC maps derived from DWI acquired with two (or more) b-values reflects the local mobility of water molecules calculated on a pixel-by-pixel basis.[8]

There are several technical issues to consider in obtaining DWI imaging. As previously indicated, diffusion weighted MRI is not only sensitive to diffusion of water molecules, but can also reflect capillary perfusion.[1,2,9] Biologic processes including edema and inflammation can also affect the measured apparent diffusion coefficient (ADC) values. An accurate estimation of the measured ADC therefore depends upon the proper choice of b

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values and analysis method. To reduce the effect of perfusion–related signals from the measured diffusion coefficients, the ADC should be calculated from at least two diffusion weighted images with one at a modest low b-value (~50–200 s/mm^2) other than 0 and another at a high b value (~800 – 1000 s/mm^2).[8] There is a potential advantage to even higher b-value (>1000) diffusion weighted images that may improve the delineation of tumors with highly restricted diffusion from benign tissue but at the price of poor signal to noise which can be compensated by longer scan times. Further studies to determine its value compared to conventional diffusion weighted imaging or apparent diffusion coefficient (b < 1000) are still needed.[10–12]

Diffusion weighted MR images are not only sensitive to random motion of water molecules, but also to bulk movement of the organ, e.g., due to cardiac and respiratory motion.[4,13] These motions will degrade the quality of diffusion weighted images and can create artifacts and quantitative errors. All of these acquisition issues can create additional challenges for obtaining body diffusion imaging.

As indicated, diffusion gradients are directional and diffusion of water molecules in tissue is a three-dimensional process not necessarily equal in all directions. Directional mobility of tissue (i.e. anisotropy) is typically mathematically modeled as a tensor, and diffusion tensor imaging (DTI) measures the diffusion along multiple gradient directions (at least 6, and typically >16) to detail tissue microstructure patterns, particularly for highly anisotropic tissue such as white matter. To greatly mitigate influence of tissue anisotropy on mean diffusivity measures, DWI from three orthogonal gradient directions are combined for ADC calculation.

Clinical Applications for Diffusion MRI

In the following section, we review the potential role for diffusion MRI in radiotherapy treatment planning specifically in regards to target volume delineation, tumor response assessment, and prediction of normal tissue toxicity in several key clinical sites including brain tumors, head and neck cancer, prostate cancer, and cervical cancer.

Brain Tumors

Diffusion weighted MRI is helpful for the grading of malignant gliomas. Low ADC values are used as indicators for high-grade gliomas and correlate with poor survival in malignant astrocytomas independent of tumor grade. [14,15] Several studies have also demonstrated that diffusion MRI is a sensitive and early indicator of both treatment response and overall survival in brain tumors. [6,16–19]

Malignant gliomas are heterogeneous tumors. Due to the complexity of tissue changes following therapy, tumor heterogeneity hinders the use of change in whole-ROI/VOI mean apparent diffusion coeffiecent (ADC) as an indicator of tumor response. Alterations in the tumor following therapy may involve cell swelling (secondary to loss of cellular water homeostasis) followed by subsequent necrotic or apoptotic cell death. In addition, there may be changes in the free extra-cellular water, e.g. increase in edema. The interplay of all of these factors may produce transient decreases and increases in regional diffusion values,

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which may be underestimated using the ROI/VOI mean ADC. An alternative voxel-wise analysis was devised to help mitigate the heterogeneity issue[20–22]. In this voxel-wise approach for image analysis, parametric response maps (PRM) retain regional changes in apparent diffusion coefficients (both increasing and decreasing) that can be further quantified. When this PRM approach was applied to a population of patients with high-grade gliomas, the percentage of the tumor volume undergoing a significant increase in ADC 3 weeks after the initiation of treatment was predictive of both response and survival. Patients stratified based upon PRM (ADC) analysis at 3 weeks were found to have significantly different time to progression and overall survival. [16]

Another image analysis approach applied to brain metastases has been developed. Evaluating the entire ADC histogram may be important in assessing tumor response in brain metastases to therapy by reflecting changes in both low ADC (high cellularity) and high ADC (possible edema and necrosis). Therefore, a diffusion abnormal probability accounting for both of these changes was generated for each tumor voxel and then summed altogether in a new index, termed the diffusion abnormality index (DAI). In a preliminary study of 24 patients, early changes in the DAI were analyzed to predict response of brain metastases in patients receiving whole brain radiotherapy (WBRT). (Fig 1) The results demonstrated that early changes in the DAI measured from pre-RT to the end of RT was a significantly better predictor of post-treatment response than changes in gross tumor volume observed during the same time interval.[23] There is a potential role for DWI in improving early response assessment in brain metastases.

Multi-parametric imaging biomarkers may provide further improvement in the early assessment of treatment response. PRM approach was used to quantify hemodynamic alterations in relative cerebral blood volume (rCBV) in high-grade gliomas at 1 and 3 weeks during chemo-radiation and was found to be a strong predictor of early cancer treatment outcome.[24] Further analyses demonstrate that the combination of both PRM (ADC) as well as PRM (rCBV) obtained at 3 weeks during treatment had a stronger correlation in prediction of overall survival than any baseline clinical or single treatment response imaging metric. [21] PRM is an imaging biomarker that provides an opportunity for radiation oncologists to identify early patients with regional responses that may be resistant to therapy and may benefit from alternative treatment strategies such as an adaptive conformal radiation boost plan.

Conclusions

Clinical data demonstrates the potential for diffusion-weighted MRI to provide a non-invasive method of monitoring early therapeutic response to treatment in malignant brain tumors.[37–38] Accurate response assessment in malignant gliomas has significant implications for patient management, particularly in treatment decision-making and determination of treatment efficacy in clinical trials. Early response assessment may allow the future development of adaptive radiation treatment plans to identify patients who may require further treatment intensification prior to completion of treatment. However, further prospective multi-institutional trials validating these analyses are warranted prior to its incorporation into routine clinical practice.

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Diffusion MRI Applications in Identifying Radiation-induced Brain Injury

While radiation is an effective treatment for many cerebral tumors, late neurocognitive dysfunction is a devastating clinical problem.[26] Late delayed CNS associated radiation effects are characterized by demyelination, vascular abnormalities and ultimately radiation necrosis. Cognitive dysfunction is typically observed more than 6 months post-irradiation[25] and can occur in the absence of any apparent structural lesions. Diffusion tensor MRI provides a non-invasive method of analyzing changes to the normal tissue prior to the development of irreversible late CNS toxicity. Imaging biomarkers, such as DTI indices potentially provide a mechanism to identify a window of opportunity for therapeutic intervention.

A prospective diffusion tensor imaging (DTI) study was performed in high-grade gliomas (n=19), low-grade gliomas (n=3), and benign tumors (n=3) in patients receiving partial brain irradiation with DTI obtained before, during, and after radiation.[27] During the initial three months post-RT, dose-dependent demyelination was noted predominantly in regions receiving high RT doses. However, diffuse demyelination was noted at 6 months following completion of radiation even in areas receiving lower RT doses. This study confirms that DTI indices can detect early changes in the normal appearing white matter of CNS patients receiving partial brain irradiation. The potential latency suggests that imaging may play a role in identifying high-risk patients in whom early drug intervention may help to avoid permanent late radiation-induced white matter deficits.[28]

Radiation-associated changes in the hippocampus region due to demyelination or axonal injury may lead to long-term deficits in learning, memory, and executive function. Fractional anisotropy (FA) is a diffusion tensor index that reflects overall white matter fiber integrity. In patients receiving whole brain radiation, there was a significant decrease in FA noted in the para-hippocampal cingulum (Fig 2), along with an increase in radial diffusivity (i.e. perpendicular to fiber axis) suggesting radiation induced early demyelination. In this preliminary study, there was a correlation between early diffusivity changes in the para-hippocampal cingulum and associated late declines in verbal recall.[29] These results suggest that longitudinal studies using DTI indices may be a useful non-invasive biomarker to monitor patients receiving therapeutic interventions, such as hippocampal sparing WBI during RT and may predict for long-term cognitive outcomes.[30]

Conclusions

Diffusion tensor imaging provides a potential opportunity for early drug interventions including novel therapies such as pioglitazone, a peroxisome proliferator-activated receptor agonist and angiotensin-converting enzyme inhibitors such as ramipril that may limit the effects of radiation damage to normal brain tissue and potentially reverse the initial radiation injury without diminishing RT tumor control. [25] The rate and degree of radiation damage to cognition likely varies depending on which pathways are affected and may not be limited to the sparing of one specific region, such as the hippocampus.

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Head and Neck Tumors

Diffusion weighted imaging may be helpful in the detection and diagnosis of nodal metastases in the radiotherapy treatment planning of head and neck cancer. Accurate lymph node staging with CT and MRI scans can be difficult in distinguishing benign reactive adenopathy with metastatic adenopathy and identifying nodal metastases in clinically undetectable lymph nodes. FDG-PET scans can detect regional lymph nodes with an overall sensitivity of 80% and specificity of 86%; however, the sensitivity is lowered to 50% in clinically undetectable lymph nodes. Therefore, additional physiologic parameters obtained from MR imaging may provide additional information.

Several studies have investigated DW-MRI obtained prior to surgical resection and pathologic tumor tissue specimens. [31–33] These results reported improved accuracy in the detection of metastatic lymph nodes using DWI compared to conventional turbo-spin echo imaging. There was also added value with DWI in the detection of subcentimeter nodal metastases with a higher sensitivity at 76% but further comparisons with other imaging techniques are required. The common observation is that malignant lymph nodes have lower ADC than in benign adenopathy. However, the presence of necrotic lymph nodes can falsely reflect increasing ADC values while benign nodal infiltration can cause decreases in ADC similar to metastatic tumor level. Standardization of the appropriate sequence and ADC threshold values as well as validation in prospective, large multi-center trials are needed.

There are several technical considerations in obtaining DWI in head and neck tumors such as the increased susceptibility to motion artifact relative to brain due to swallowing, breathing, jaw movement, and coughing. There is also the proximity of the sinuses with the air-tissue boundaries as well as metallic dental amalgams and irregular shape of the head and neck anatomy that can increase magnetic field inhomogeneity thereby hindering effective fat signal suppression that is essential for DWI. Both bulk motion, poor magnetic field homogeneity and presence of unsuppressed fat signal can lead to spatial distortion, spurious signal artifact and quantitative ADC errors.

DW-MRI in Response Assessment

Volumetric analysis using CT scans yield variable results in predicting outcome. FDG-PET scans have been extensively investigated and correlate with late tumor response. However, post-treatment induced inflammatory changes can lead to difficulties in data interpretation.

DW-MRI has the ability to detect tissue microstructural changes prior to macroscopic tumor changes. A preclinical study using a head and neck squamous cell carcinoma mouse model demonstrated DW-MRI as an early imaging biomarker of response.[34] Longitudinal DWI studies obtained during chemo-radiation show that early changes in ADC noted at 1–2 weeks following treatment were predictive of increased tumor control. Multivariate analysis demonstrated that increases in ADC noted at both 2 and 4 weeks during chemo-radiation were independent predictors of 2-year locoregional disease control. Galban et al demonstrated that regions of increasing PRM (ADC) in locally advanced head and neck squamous cell carcinomas were more likely to be found in complete responders compared to partial responders.[35] DWI MRI may also have a role in evaluating response post chemo-

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radiation by identifying residual and recurrent tumor from post therapeutic treatment changes. Using an ADC threshold of $1.3x10^{-3}$ mm^2/s, there was a 95% specificity and 96% sensitivity in identifying tumor recurrence.

Conclusions

Due to the heterogeneous response of tumors to head and neck cancer treatment, the ability to identify early regions of poor response to chemo-radiation that may benefit from an adaptive radiation treatment plan with focal dose escalation may further improve local control. The ability of DW imaging to improve target volume delineation, early tumor response assessment and differentiate between normal post-treatment changes suggests an important clinical role in radiotherapy. However, further validation is required prior to its routine clinical use.

Prostate Cancer

Target volume definition based upon CT scans is proving to be a limiting factor in advancing the precision of radiation treatment of prostate cancer. Superior soft tissue contrast provided by MRI has resulted in the investigation of the roles of multi-parametric MRI for the detection, localization and delineation of prostatic cancer. To this end, T2-weighted, diffusion-weighted (or ADC), DCE, and H1 spectroscopy images all have been investigated. T2-weighted MRI is the primary modality used in prostate MR imaging and can delineate tumors in the peripheral zone. However, the transition zone is more variable with increasing age and many benign lesions including post-radiation, hormonal treatment, post-hemorrhage, chronic prostatitis, hyperplasia can all resemble tumor.

There is emerging evidence suggesting that multi-parametric MRI is superior to CT scans, and C^{11}-choline PET may not provide any additional value for the detection and delineation of prostate cancer.[36] The current, key question is whether diffusion imaging (or ADC) plays a critical or a supplementary role for the detection and delineation of prostate cancer. Further the sensitivity and specificity of using MR diffusion imaging to delineate the target volumes for external beam radiation therapy and brachytherapy needs to be determined.

In the last several years, clinical investigations have been performed to evaluate the capability of diffusion weighted imaging to detect and to delineate prostate cancer. Systematic random prostate biopsy is prone to sampling errors which can often lead to inaccurate Gleason score grading and prostate cancer detection. DW imaging is a reflection of tumor cellularity and tumor aggressiveness and therefore can be used to determine suspicious regions for MR-guided prostate biopsy. Overall, the results based on the evaluation of pathological tumor specimens demonstrate that diffusion imaging can detect prostate cancer with a sensitivity and specificity of 80% or greater, which is superior to results usingT2-weighted images alone. (Figure 3)[37–39] Similar findings are also reported in identifying recurrent prostate cancers after radiation therapy.[40,41]

A recent study investigated the appropriate ADC cut-off threshold required to delineate prostate cancer in the peripheral zone (PZ) with the use of an endorectal receiver coil at 1.5 T.[38] The radiologist was able to detect 43 out of 60 lesions (size > 0.1 cm) in the PZ of 52

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patients. Among the 43 cancers, an ADC threshold of $1.4x10^{-3}$ mm^2/s missed 4 lesions, while a cutoff threshold of $1.6x10^{-3}$ mm^2/s missed one. At the voxel-level, the low cutoff threshold had a sensitivity of 82% and a specificity of 85%, while the higher threshold resulted in 95% of sensitivity but a specificity of only 65%. (Figure 4) The addition of DW imaging to T2 weighted imaging significantly improved the accuracy of tumor volume delineation of PZ prostate cancers. [42] Overall, MR diffusion imaging has been recognized as providing additional complementary information compared to T2-weighted images alone.

Dynamic contrast-enhanced MR imaging consists of a series of fast T1-weighted sequences covering the entire prostate before and after rapid injection (2–4 mL/sec) with a bolus of a low-molecular-weight gadopentetate dimeglumine (concentration, 0.1–0.2 mmol/kg) that measures tumor vascularity. Several studies have investigated the incremental benefit of T2-weighted, ADC, and DCE images, by adding them sequentially to increase specificity for prostate cancer localization.[43–45] Results regarding the additional information provided by DCE imaging toT2-weighted and ADC images have remained inconsistent.[43,46] Standardized techniques and analytic tools for DCE MRI need to be further developed.

Using multi-parametric MRI is also challenging to differentiate prostate cancer from stromal hyperplasia (SH) and glandular hyperplasia (GH). A recent study showed that the average ADCs and associated confidence intervals in central gland carcinoma, SH foci, and GH foci had little overlap, as $1.05x10^{-3}$ mm^2/s (95% CI:0.97, 1.11), 1.27 (95% CI: 1.20, 1.33), and 1.73 (95% CI:1.64, 1.83), respectively.[47] The areas under the ROC curve were 0.99 and 0.78 for differentiation of carcinoma from GH and SH, respectively.

There are several technical issues that are important to note with different image technologies, lesion size, tumor cell density, and the location of the lesion all which can significantly alter the DWI imaging results. Diffusion-weighted images using 1.5 T without the use of an endo-rectal coil was limited by the signal-to-noise ratio and produced noisy ADC images. However, the use of an external phase-coil array at 3T seems to yield image quality that is equivalent to that obtained with an endo-rectal coil at 1.5 T.[48]

There is limited data on the early assessment of treatment response to radiation therapy using DWI. An initial study has detected significant changes in ADC at week 6 during a fractionated RT course.[49] However, the value of DWI imaging obtained during RT for early assessment of response to prostate cancer by radiation needs to be further evaluated.

Conclusions

In summary, considering the available imaging modalities for prostate cancer radiation therapy, emerging evidence supports that multi-parametric MRI, including diffusion imaging, is superior for prostatic cancer detection and localization. Whether using multi-parametric MRI to define a boost target for intensified radiation therapy can lead to better outcomes, or reduce toxicity has to yet be demonstrated in prospective clinical trials.

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Gynecological Cancer

The prognostic and predictive value of dynamic contrast enhanced (DCE) MRI for radiation therapy outcomes of cervical cancers has already been demonstrated by several studies.[50,51] These studies suggested that well oxygenated and better perfused tumors were more sensitive to radiation while tumors with increased non-enhancing volumes attributable to necrotic or hypoxic tumor at baseline and persisting during the early course of RT were associated with worse overall and progression free survival. The key question is whether diffusion weighted imaging can provide any additional complimentary information for guiding radiation therapy in cervical cancers.

Several studies have shown the potential of ADC measurements in the diagnosis and treatment response assessment of cervical cancers to radiotherapy.[52–57] An initial study of 49 patients with cervical cancer has shown that the median ADC value ($1.1x10^{-3}$ mm^2/s) in cervical cancer is significantly lower than in normal cervical tissue ($2.1x10^{-3}$ mm^2/s),[56] indicating a robust discrimination of cervical cancer from normal tissue using ADC. In another study, the ADC defined tumor volume of cervical cancer was compared to tumor volumes defined by 40% of max SUV of FDG PET, the latter is the standard functional imaging for pre and post RT evaluation.[52] There was good spatial overlap noted between the two tumor volumes, and the mean SUV on the contours of the ADC defined tumor volumes was approximately 34% of the max SUV, suggesting that tumor sub-volumes with an increase in metabolic activity on FDG PET also had a greater cell density (or low ADC). Another study investigated the ADC values in the GEC ESTRO target volumes for image guided adaptive brachytherapy of locally advanced cervical cancer.[55] Using an ADC of $1.2x10^{-3}$ mm^2/s as the threshold to define low diffusion, they found that 37%, 20% and 11% of respective brachytherapy gross tumor volume, high-risk clinical target volume, and intermediate-risk target volume had low diffusion. These studies suggest that it is worthwhile to further investigate using ADC imaging as a means to define a boost target volume for advanced cervical cancers by either a highly conformal external beam radiation therapy boost plan or with brachytherapy. Early ADC changes during a course of chemoradiation therapy for cervical cancers have been evaluated in two studies.[54,57] In both studies, diffusion MRI was obtained prior to chemo-radiation therapy, and at 2 weeks during concurrent cisplatin and radiation delivered for 5 weeks. The response was determined by the tumor volume change at the end of the treatment. All patients except one had a partial response. The ADC values in the cervical cancers increased robustly after receiving 2 weeks of chemo-RT. The early ADC changes were significantly correlated with tumor volume response at the end of RT. However, whether this early ADC response noted during in chemo-radiation treatment in cervical cancer predicts for improved overall survival requires further investigation.

Conclusions

Diffusion MR imaging is a promising imaging biomarker for cervical cancer. Further investigation in its clinical application to radiotherapy treatment planning is warranted. Robust changes in ADC are noted early during the course of RT in cervical cancer

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indicating its potential as a predictive marker. DW imaging may provide complementary information to DCE MRI for the early assessment and prediction of clinical outcome.

Summary

Diffusion weighted MR imaging is a functional imaging technique that requires no contrast agent and is also rapidly and easily obtained as part of routine MR imaging evaluations. Diffusion weighted and diffusion tensor imaging has extensive clinical applications in radiation oncology. DWI provides important information regarding early assessment of treatment response. Other emerging applications include improvement in diagnosis and staging by defining areas of tumor aggressiveness based on tumor cellularity, determination of target volumes for biopsy, quantitative assessment of changes to normal appearing white matter following radiation and in defining potential non-responding tumor regions that may benefit from an additional radiotherapy boost. However, standardization of the imaging protocols and validation in large multi-center trials is still required prior to its routine clinical use.

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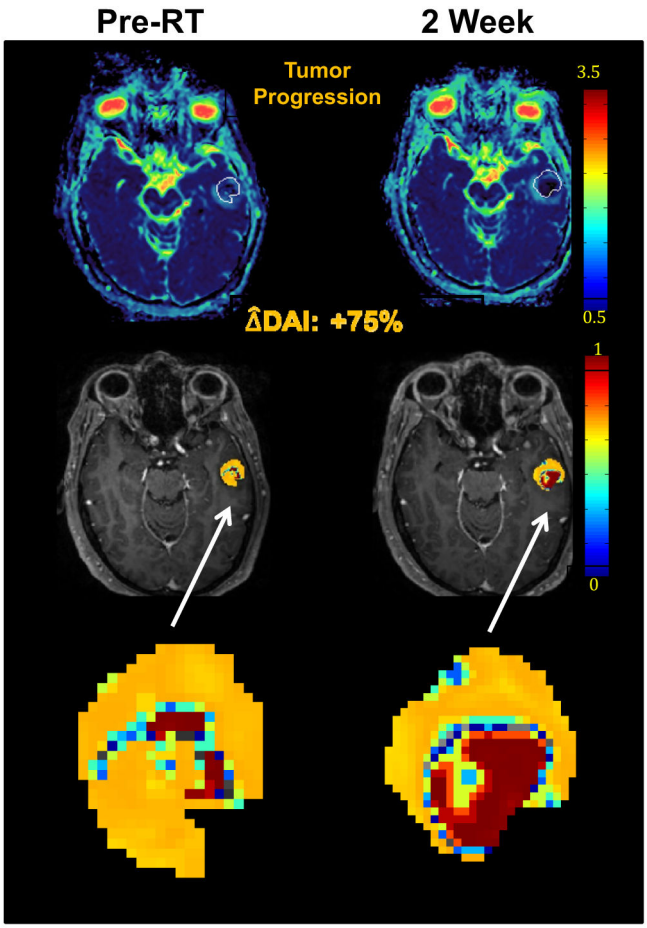

Fig 1.

Diffusion abnormality index (DAI) of a patient with a brain metastasis treated with whole brain radiation therapy. DW MRI was obtained both pre RT (left column) and at the end of RT (right column). Top row: color-coded ADC maps; middle row: DAI maps; bottom row: zoomed DAI maps of the tumor. The tumor volume showed no significant change from pre RT to the end of RT. However, the DAI increased by 75% from pre RT to end of RT, suggesting tumor progression which was confirmed by post-Gd T1-weighted MRI one month post RT.

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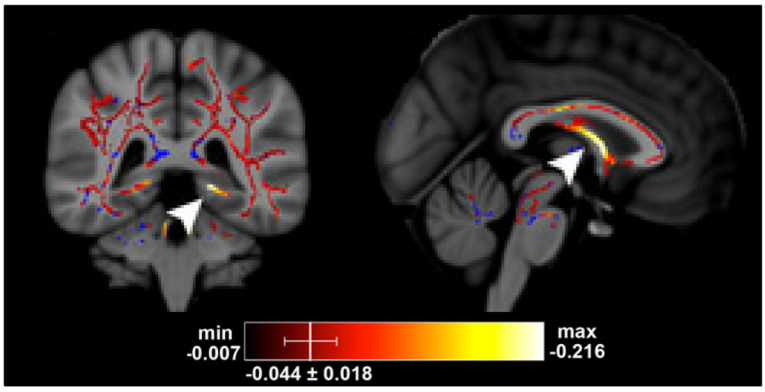

Fig 2.

Tract-based statistical analysis (TBSS) of diffusion tensor images in patients receiving whole brain radiation therapy. There was a significant decrease in FA in the left inferior cingulum (left) and fornix columns (right) from pre RT to end of RT. Hot colors indicate a significant decrease in FA on the TBSS skeleton, and blue represents the TBSS skeleton without significant changes.

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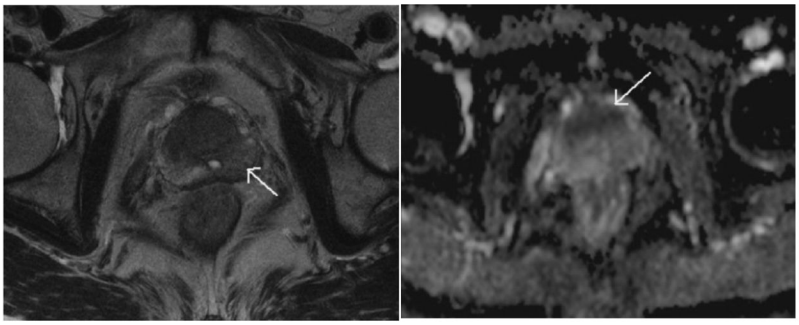

Fig 3.

A 72-year-old patient with a serum PSA level of 4.1 ng/mL, the T2W imaging (left panel) showed a hypointense area in the left peripheral zone (arrow); discrimination of cancer from BPH in the transition zone was difficult. The ADC map (right panel) depicted a cancer focus in the anterior prostate as a hypointense area (arrow). Pathologic results revealed a cancer focus well correlated with the finding of the ADC map, but no malignancy was found in the left peripheral zone. Reprinted with permission from Miao et al in Eur J Radiol 2007;61:297–302.

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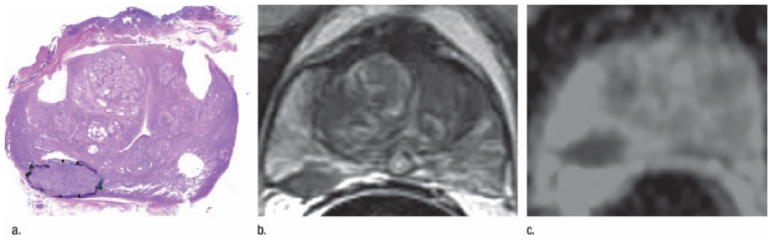

Fig 4.

A 66-year-old patient with prostate cancer: presurgical PSA, 5.52 ng/mL, clinical stage, T1C; surgical Gleason score, 3+4; and pathologic tumor volume, 4.77cm^3. Whole-mount step-section histopathologic map shows prostate gland (a) Only one (of 12) slices shown; tumor was present on seven slices. (b) Closest transverse T2-weighted image corresponding to matching pathologic slice. (c) ADC map of slice in b. Reprinted with permission from Mazaheri et al in Radiology 2009;252:449–57.