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Diffusion Weighted Imaging with ADC Mapping and Spectroscopy in Prostate Cancer

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Abstract

Prostate cancer is a major health problem and the exploration of noninvasive imaging methods that have the potential to improve specificity, while maintaining high sensitivity is still critically needed. Tissue changes induced by tumor growth can be visualized by magnetic resonance imaging (MRI) methods. Current MRI methods include conventional T₂-weighted imaging, diffusion weighted imaging (DWI) with Apparent Diffusion Coefficient (ADC) mapping and magnetic resonance spectroscopy (MRS). Techniques such as DWI/ADC provide functional information about the behavior of water molecules in tissue; MRS can provide biochemical information about the presence or absence of certain metabolites, such as, choline, creatine, and citrate. Finally, vascular parameters can be investigated using dynamic contrast enhanced MRI. Moreover, with whole body MR and DWI, metastatic disease can be evaluated in one session and may provide a way to monitor treatment. Therefore, when combining these various methods, a multiparametric data set can be built to assist in detection, localization, assessment of prostate cancer aggressiveness and tumor staging. Such a comprehensive approach offers more power to evaluate prostate disease than any single measure alone. In this article, we focus on the role of DWI/ADC and MRS in the detection and characterization of prostate pathology.

Keywords

Prostate; Magnetic Resonance Imaging; Proton; Diffusion Weighted Imaging; ADC map; metastatic; MRS; Spectroscopy; Whole body; MRSI; contrast imaging; Cancer

1. Introduction

Prostate cancer is a potentially curable disease and the combined effects of early detection and therapeutic intervention are likely the key elements that explain the observed reduction in cancer mortality over the last 20 years¹. Prostate cancer is associated with a significant mortality rate¹. Although our current paradigms and treatments for prostate cancer have resulted in substantial progress, the disease frequently evades long term control and cure. It is imperative that we continue to search for new possibilities for the detection, assessment of progression and monitoring of treatment of prostate cancer¹. In general, prostatic lesions

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usually present with clinical symptoms, for example, nocturia, increased frequency of urination, and/or abnormal serum results levels of prostate specific antigen(PSA)². However, other prostate conditions, such as benign prostatic hyperplasia (BPH) or inflammation also present with similar clinical symptoms.

Current methods for detection of prostate cancer include the digital rectal exam (DRE), PSA testing, and if needed, trans-rectal ultrasound (TRUS) biopsy. Because DRE is anatomical limited to the posterior and lateral aspects only of the prostate gland during DRE decreases sensitivity of the exam^{3,4}. Thus, stratification of PSA levels is currently the most often used index for prediction of malignancy in the prostate⁵. PSA levels between 4.0–10 ng/mL are suggestive of malignancy and PSA levels greater than 10.0 ng/mL are considered highly suggestive of malignancy⁵. To verify the presence of cancer in patients further evidence is needed. Thus, TRUS biopsy is utilized to sample regions of the prostate to obtain prostatic tissue for histopathologic examination and Gleason scoring⁶. There are several drawbacks to TRUS biopsy; prostate lesions maybe invisible on ultrasound and the sampling error rate that occurs with TRUS lowers its sensitivity and specificity⁴. Therefore, newer radiological imaging methods are currently under investigation for detecting, localizing and characterizing prostate cancer^{7–9}.

The radiological challenge is to provide an assessment of the anatomical, physiological, functional, and metabolic activity of prostate and surrounding tissue for increased accuracy of diagnosis before and after treatment. Such radiological biomarkers are under investigation, for example magnetic resonance (MR) imaging with T₂-weighted imaging (T2WI), diffusion-weighted imaging (DWI), magnetic resonance spectroscopy (MRS), and dynamic contrast enhanced MR imaging (DCE-MRI). These various MR parameters are increasingly being utilized in a multiparametric paradigm for imaging of the prostate. In this article, we focus on the role of DWI/ADC and MRS in the detection and characterization of the prostate pathology. DCE-MRI is reviewed in an accompanying manuscript and not fully discussed here.¹⁰

2. Magnetic Resonance imaging with T2-weighted Imaging

Protocols for MR of the prostate are still changing as technical advances allow and arguably even necessitate regular adjustments to obtain the best possible diagnostic information. Traditionally, prostate MRI was obtained using surface coils and later an endorectal coil was developed that improved visualization of the prostate and has become the “gold standard” at 1.5T¹¹. With the introduction of higher field strengths (e.g., 3T), surface coils can be used either alone or in conjunction with endorectal coils¹².

Different signal intensities from a T2WI sequence (TE>80ms) were found to potentially characterize regions of prostate cancer; normal prostatic tissue in the region of peripheral zone has high T2WI signal, whereas, a low T2WI signal was found to correlate with pathological prostatic tissue^{13–19}. Typical recommended T2WI parameters for axial, coronal, and sagittal MR imaging are repetition time/echo time (TR/TE) 5000/80–149ms, field of view (FOV) between 14–20 cm, imaging matrix at least 256×256, slice thickness (ST) at least 3–4mm. There are some prostate tumors in the peripheral zone that are isointense. Some tumors arise in the transition zone of the prostate and may have similar signal characteristics to benign prostate hypertrophy (BPH), thus reducing sensitivity (60%–75%) of T2WI alone^{13–22}. However, at 3T, reports have shown an increase in sensitivity and specificity using T2WI, presumably due to increased SNR and contrast to noise (CNR) ratios (Figure 1). In addition, there have been reports that using a surface coil at 3T is equivalent to an MR exam with endorectal coil at 1.5T, but larger studies are needed to fully evaluate those findings²³. Despite of improvement in visualization of the prostate

morphology on T2WI, there still exists a need for increased specificity and obtaining “functional” cellular and metabolic information about prostate tissue; this is being pursued through adjunctive imaging as DWI and MRS

2.1 Diffusion-Weighted Imaging and Apparent Diffusion Coefficient Mapping

Diffusion weighted imaging (DWI) can provide valuable cellular information about tissue in addition to the conventional T₁- and T₂-weighted imaging^{9,24–32}. DWI provides important information about the movement and functional environment of water in tissue and reflects cellular status of normal and pathological tissue^{33–35}. Furthermore, DWI is sensitive to changes in the micro-diffusion of water within the intra-(ICS) and extracellular spaces (ECS) and cytotoxic edema due to alterations in the dependent sodium-potassium pumps.^{33–36} If there are changes in the ICS, ECS or sodium-potassium pumps, the apparent diffusion coefficient (ADC) will reflect these changes and potentially serve as a biomarker of tissue response^{28,32,37,38}. For example, after a disruption or restriction of the flow of water within a tissue, cytotoxic edema occurs, such as: changes within the tissue due to growth of tumors^{27,39}; metastatic lesions^{31,40}; or ischemic events (e.g., stroke)^{24,33,35,41,42}. These alterations in different tissue types alter the diffusion of water which results in changes in signal intensity on the DWI (either hyperintensity or hypointensity) generally before they are seen on a T₂-weighted image^{24,41}. The reason for these signal intensity changes on DWI are not exactly known; however, there is evidence that these changes may be attributable to many factors, such as shifts of water from the extracellular space to the intracellular space, increased tortuosity of the diffusion pathways, restriction of the cellular membrane permeability, increased cellular density, and/or disruption of cellular membrane depolarization^{25,35,36,41,43,44}. Reduced diffusion of water in prostate cancer has been attributed to increased cellularity of malignant lesions that restricts water motion in a reduced extracellular space⁴⁵. Moreover, DWI also provides an important quantitative biophysical parameter, called the apparent diffusion coefficient of water (ADC).

The ADC is an indicator of the movement of water within the tissue and provides a measure of the flow and distance a water molecule has moved. The ADC quantifies the combined effects of both diffusion and capillary perfusion. A “decreased” ADC is interpreted as “reduced” flow of water or diffusion, whereas in tissue with an “increased” ADC there is no restricted water flow. The ADC has been related to the state of tissue during the growth of tumors or progression of cancer. With proliferating cells, there is an increase in cellular density and a decrease in the amount of ICS or ECS available, this leading to a reduction in the ADC^{27,32,46}. If there is cellular degradation or necrosis, the flow of water is increased with concurrent increases in the ADC. Thus, DWI and ADC have become powerful indicators for characterization of prostate tissue, particularly in differentiating between benign and malignant lesions^{12,39,45,47–68}.

Several studies have demonstrated that DWI/ADC mapping increased sensitivity and specificity at both 1.5T or 3T when used in conjunction with conventional MR imaging and MRS (Figures 2 and 3). In general, regional ADC map values differ depending on location and tissue composition; malignant lesions have a lower ADC values (about 20–40%) than benign or normal prostatic tissue as shown in Table 1. Also, there are regional variations in the “normal” tissue values for different zones of the prostate, for example, in the peripheral zone ADC values are greater (1.5 to $2 \times 10^{-3} \text{mm}^2/\text{s}$) than the ADC values in the central zone (1.4 – $1.7 \times 10^{-3} \text{mm}^2/\text{s}$). There has been only one conflicting report that listed ADC values of non-treated malignant prostate lesions to be higher than that of normal prostatic tissue; the result may have been confounded by the acquisition techniques⁴⁷.

Some authors have stratified the ADC values into benign and malignant and demonstrated that DWI/ADC mapping can increase the sensitivity (54%–98%) and specificity (58%–

100%) of prostate MRI in the detection of cancer when DWI is used in conjunction with T2WI, as shown in Table 1.

Diffusion weighted imaging can be obtained using different MR pulse sequences, for example, fast spin echo(FSE)^{56,69}, line scan diffusion(LSDI)^{70,71}, but most prostate MR exams are carried out with echo planar imaging(EPI)^{11,39,72}. The DWI-EPI sequences are acquired in the axial plane to match the T2WI and MRS with at least three different b values, a minimum repetition time(TR), and fat suppression. Typical DWI parameters at 1.5T are TR/TE=3900/78ms, NEX=3, ST=4mm, 1–2mm gap, imaging matrix=128×128, sense reduction factor=2, and b = 0, 100–1000 s/mm². These parameters should be optimized depending on the scanner and magnetic field strength used. The acquisition of different b-values allows for the creation of trace apparent ADC maps on a pixel-by-pixel basis for quantitative analysis according to the equation.

$$ADC = \sum_{i=1}^n \frac{\ln(S_i/S_0)}{b_i} \quad (1)$$

where b_i = the diffusion gradient values; $(b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3))$, γ = gyromagnetic ratio, G = gradient strength, δ = diffusion gradient duration, Δ = time between diffusion gradient pulses, S_0 = 1st image ($b=0$), and S_i = i th image.

Single shot FSE diffusion sequences have some advantages such as decreased sensitivity to eddy currents, susceptibility and chemical shift artifacts, FSE have some disadvantages, such as, decreased spatial resolution, reduced coverage, magnetization transfer, and lower SNR. Recent reports have demonstrated as much as 20% difference in the ADC map values between different prostate tissues when using these sequences. It is not clear as to why the ADC map values are different, but there are several potential explanations. For example, the FSE sequences have lower SNR, “contrast averaging” the averaging all the echoes in a single k-space could be underestimating the diffusion anisotropy of prostate tissue^{56,69,73}. Other novel DWI sequences involve LSDI. Briefly, LSDI uses multiple diffusion-weighted SE column excitations to create a two-dimensional image and this acquisition scheme reduces the sensitivity to motion. In addition, there is a reduction in susceptibility artifacts and geometric distortions⁷⁴. Line scan diffusion has been used for prostate imaging in conjunction with T2WI and the ADC maps values were $1.61 \pm 0.37 \times 10^{-3} \text{ mm}^2/\text{s}$ for normal peripheral zone and $1.43 \pm 0.35 \times 10^{-3} \text{ mm}^2/\text{s}$ for cancer, which are consistent with the literature⁷¹. However, larger studies are needed to determine which DWI sequence is optimal to use for imaging of the prostate.

Recently, with the increased use of 3T in both clinical and research environments, there have been some reports of comparable sensitivity and specificity for prostate imaging using pelvic coils compared to endorectal coils^{8,23,75,76}. The use of pelvic coils as the only receiver does have some advantages and disadvantages. The main advantage for using a pelvic coil is patient comfort, and also “better” anatomical coverage of pelvic structures visualized with the increased FOV. However, there is a trade off in lower SNR and spatial resolution compared to the endorectal coil.

Higher field strengths can mitigate some of the SNR loss and potentially gain some ground in spectral resolution (see below)⁷⁷. But, there are a few technical challenges related to higher fields, for example, increased susceptibility artifacts and greater chemical shifts (water and fat). However, the use of parallel imaging can reduce some of these artifacts by acquiring few phase encoding steps during acquisition, allowing for adjustment of other

parameters (echo spacing and echo train length), and acquiring multiple shots during EPI sequence^{78–80}.

2.2 Magnetic Resonance Spectroscopy

Magnetic resonance spectroscopy (MRS) provides important information about the biochemical and metabolic environment of the tissue and is increasingly being utilized as an intermediate biomarker for detection and for monitoring of treatment response^{37,81–85}. Moreover, MRS can demonstrate differences between normal tissue and tumor environments. In particular, experimental studies using *in vitro* MRS of cancer tissue extracts and cell cultures have detected concentrations of choline (Cho), citrate (Cit), lactate, and creatine (Cr), and lipids^{86–90}. In particular, these studies indicated that increased choline and decreased citrate may be a marker of malignancy in prostate cancer⁹¹. For *in-vivo* MRS in humans, the SNR levels are much lower than those achievable in tissue extracts and cell cultures because of lower field strength of clinical MR scanners, limited scan time in a prostate MR protocol, and the need for localization of the MRS signal to the prostate. MRS localization requires the use of single- or multi-voxel volume selection techniques. The most commonly used MRS method is called Point RESolved Spectroscopy Sequence (PRESS)⁹². PRESS provides increased SNR in prostate. Choline, creatine, and citrate are still observable *in-vivo* in healthy or diseased human prostate tissue (Figures 1–3). The spectroscopic profile for prostate tissue consists of choline (Cho, 3.2 ppm), citrate (Cit, 2.6ppm), creatine (Cr, 3.0ppm), polyamines (2.1–1.8ppm) and lipids (1.3ppm). Choline containing compounds are involved in membrane turnover (phospholipid synthesis and degradation) and consist of several compounds, phosphocholine, (PC), glycerophosphocholine, (GPC) and free choline (Cho).

Increased choline signal or concentration is considered the spectroscopic hallmark of cancer,⁹³. Although, some benign conditions in the prostate have been reported to have increased choline, for example, in prostatitis⁹⁴. Generally, total choline (PC+GPC) signal can be observed as a resonance of the methyl protons at 3.2ppm. Citrate is found in fairly high concentrations (greater than 60mM) in healthy prostate epithelium and in prostatic fluid and in low concentrations elsewhere in tissue^{86,87}. Single-voxel and multi-voxel MRS has been performed in several clinical studies and confirmed that increased choline is associated with prostate cancer^{88,95–97}. Citrate concentration is high in normal prostate tissue but decreases in the presence of cancer with concurrent increases in the choline concentration⁹⁶. A change in the ratio of choline over citrate, or the ratio of (choline+creatine)/citrate may be used as a marker of malignancy in prostate cancer and increases the specificity of diagnosis^{81,97}. It should be noted that the (choline+creatine)/citrate ratio levels are normal in BPH. The current method of evaluating prostate MRS is to use a threshold value greater than 2–3 standard deviations above the mean (~0.22). Peripheral zone voxels where the ratio of (choline+creatine)/citrate is at least two standard deviations above the average ratio in the normal peripheral zone of the prostate are considered likely representative of cancer at 1.5T. When the same ratio is more than three standard deviations above the average, voxels are considered highly suggestive of cancer⁹⁷. False positive results with MRS can be seen with seminal vesicle contamination, when the signal from seminal vesicles contributes to the voxels acquired over the prostate, in prostatitis, as well as in focal prostate atrophy^{94,98}.

Despite the high concentration of citrate in normal prostate tissue, the detection of the MRS signal is not straightforward. The citrate signal represents a strongly coupled AB spin system, where the signals of magnetically identical CH₂ moieties are split by strong magnetic interactions with neighboring protons into four peaks, separated by 15–17 Hz⁹⁹. The extent of the split, the J coupling, and the small difference in chemical shift between the coupled CH₂, can make the phase and amplitudes of the central two and outer two peaks vary with the MRS sequence used for localization, the echo time of the sequence, and the

magnetic field strength¹⁰⁰. Several methods for optimizing the detection of the citrate signal have been published^{101–105}.

Figure 4 demonstrates the relative signals of the inner (top) and outer (bottom) peaks of the citrate quartet as a function of the timing of the second refocusing pulse in a PRESS sequence at 3T, with the first refocusing pulse fixed at TE=10ms. The total TE is the sum of TE₁ and TE₂. The solid line is the actual part of the signal, i.e., the signal component that is in phase with the rest of the ¹H-MRS spectrum. Desirable signals have a maximum actual inner peak signal (with the dotted line of the dispersion signal at zero), and outer peak signals that are either in-phase or nulled. Another confounding problem is the presence of strong lipid signals in tissues immediately adjacent to the prostate. Strong signals such as the water signal can sometimes create false metabolite signals or distort the baseline of the spectrum in such a way that determination of the choline to citrate ratios becomes unreliable¹⁰⁶. The water signal is routinely suppressed in all *in-vivo* MRS.

The problems caused by strong lipid signals can be overcome by outer volume suppression pre-pulses and by using advanced water and fat suppression techniques¹⁰⁷. When the MRS methods are carefully optimized to yield readily observable citrate, creatine and choline signals, the metabolite ratios can be extracted from the spectra using specialized MR spectral data fitting algorithms^{101,105}. Careful and consistent uses of any of the available methods that have in the past been applied to prostate MRS should yield a reliable test, but the data processing requires a lot of extra attention.

In general, MRS demonstrates increased sensitivity and specificity at both 1.5T or 3T in cancer detection. Some authors have used either (choline+creatine)/citrate (>0.75) or choline/citrate ratio to characterize the different regions of the prostate⁹⁷. In fact, an MRS “score,” based on the number of standard deviations above a mean MRS level, has been introduced¹⁰⁸. Jung, et al., using this method, assigned a score of 1 to voxels with a Cho-Cr/Citrate ratio that was one standard deviation from the mean normal value (0.22), a score of 2 to voxels more than one but less than two or fewer standard deviations above the mean normal value, a score of 3, more than 2 but 3 or fewer standard deviations above the mean normal value, a score of 3 to voxels more than two but three or fewer standard deviations above the mean normal value, a score of 4 to voxels more than three but four or fewer standard deviations above the mean normal value, and finally, a score of 5 to voxels more than four standard deviations above the mean normal value¹⁰⁸. A recent meta-analysis of MRI and MRS studies demonstrated that MRS can increase sensitivity and specificity when combined with MR methods (Table 2 and Figures 2–3). Umber et. al. reported that several studies in the meta-analysis that studied patients suspected of prostate cancer had a sensitivity and specificity of 82% (95% CI, 59–94%) and 88% (95% CI, 80–95%), respectively; in a low-risk group, the sensitivity and specificity was 75% and 91%, respectively¹⁰⁹. Recent publications have demonstrated the feasibility of prostate MRS at 7T, which will extend this modality to further investigate the pathophysiology of prostate cancer and may provide a true non-invasive measure for risk stratification¹¹⁰. Indeed, at 7T, there a major increase in SNR, spectral resolution (various polyamines, maybe more visible), and near histological features in prostate tissue can be visualized (Figure 5). This will provide visualization of changes in prostate tissue with the advanced MR methods. However, there are several technical challenges at 7T for robust prostate imaging to be investigated before, it becomes routine. Nevertheless, 7T will provide a platform for new discovery. Although clearly a lot of work is still to be done before MRS of the prostate can be a routine clinical test, the potential of this technique that gives us a direct insight into the metabolic changes in the prostate tissue justifies further research efforts needed to optimize the technique. The expected end-result will be an addition to the prostate MR exam that can

lead to better targeted biopsies, as well as better assessment of prognosis and treatment monitoring capabilities.

3. Metastatic Prostate Cancer

In general, metastatic prostatic lesions usually present with clinical symptoms of pain and or abnormal serum results, such as, continuing elevations of PSA after prostatectomy or systemic therapy. If metastatic prostate disease is present, the usual sites are in bones, liver, brain, and lung. Typically, the axial skeleton (~90%), e.g., vertebrae, pelvis, ribs, femur, and skull are regions preferentially targeted by metastatic prostate cancer (MPC)^{21,111,112}. The types of metastatic lesions that can arise within the bony structures are osteoblastic (bone formation-usually in the cortical or trabecular structure), osteolytic (bone reabsorption-usually in the marrow), or mixed¹¹³. Metastatic prostate cancers are usually osteoblastic and the metastatic tumor growth replaces the bone marrow. Determination of MPC is accomplished using Tc99m bone scintigraphy, Computed Tomography (CT), Positron Emission Tomography (PET) and MRI¹¹¹. These radiological procedures are performed to detect the presence of metastatic lesions, and, if possible, to assess the type of lesion and the extent and localization of metastatic sites, as shown in Figure 6. Positron emission tomography imaging is detecting metastasis with near whole body coverage and has moderate to high sensitivity and moderate specificity in tumors¹¹⁴. A quantitative measure of glycolic activity in tumors can be obtained using a metric called Standardized Uptake Value (SUV) from PET data. In general, a normal SUV is low (~1) and any change above 2.5 is considered suspicious and requires correlation with clinical and other radiological findings¹¹⁵. However, MRI is the most sensitive method for detection of metastatic disease, but it was limited to localized imaging of organs. New paradigms for metastatic lesion detection and monitoring are emerging, such as the whole-body imaging using MR imaging. Recent developments in the field of MR technology, including gradient systems, RF coils, and “rolling bed” methods allow whole-body coverage. Indeed, conventional and advanced MR imaging sequences can be used such as, inversion recovery T₁-weighted imaging, T₂-weighted imaging, and DWI^{31,116–118}. Whole body MR imaging (WB-MR) will enable better spatial resolution and soft tissue delineation for more accurate assessment of MPC. More importantly, through the use of WB-DWI a better estimation of treatment response in MPC maybe possible. Indeed, as noted above, DWI and MRS provide functional cellular information that would complement routine anatomical imaging with T₁- and T₂-weighted sequences. By capitalizing on these methods in a “whole body imaging setting”, an excellent platform to investigate metastatic disease and to correlate with other biomarkers will be created¹¹⁹.

4. Conclusion

Newer MR sequences to a standard prostate MR imaging protocol, such as DWI and spectroscopy, will generate much needed molecular and metabolic information about prostate lesions; which has been shown to increase specificity in prostate cancer diagnosis and monitoring treatment effect. DWI with ADC mapping will provide information on the cellular status of the tissue, while spectroscopy will provide biochemical information about the intracellular presence of choline and citrate, which has been regarded as a potential marker for diagnosing prostate cancer. Combining these data together with DCE-MRI into a multiparametric prostate model will enable us to further investigate the biophysical environment of the prostate tissue and study the tumor microenvironment in the clinical setting.

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Figure 1. Demonstration of T2WI and MRS. A) Examples of T2W images at 1.5T and 3T (B, C) Representative spectra at 1.5T and at 3T in different patients without prostate cancer, using the endo rectal coil in two separate sessions in the same patient. The resolution and signal are slightly higher at 3T. (B, C) Voxel prescription and sample spectra at 1.5T. The voxel size is large, and there is a single choline, polyamine, and creatine peak. (C) At 3T, the voxel size is smaller. The choline peak is seen separately from the polyamine and creatine peaks. Adapted from ⁸

Figure 2.

Demonstration of T₂WI, DWI/ADC mapping, and DCE-MR on a 61 year old man with suspected prostate cancer (Gleason score = 6). Multiparametric MR imaging of the prostate glands revealed focal areas of "dark" T₂ signal with corresponding decreased ADC ($0.76 \pm 0.58 \times 10^{-3} \text{mm}^2/\text{s}$), and positive DCE-MR kinetics in the R mid region gland that is correlated to the Gleason score.

Figure 3.

Demonstration of T2WI, DWI/ADC mapping, MRS, and DCE-MR on a 55 year old man with suspected prostate cancer (Gleason score =7). Multiparametric MR imaging of the prostate gland revealed focal areas of “dark” T2 signal bilaterally with corresponding decreased ADC in left mid gland ($0.41 \pm 0.13 \times 10^{-3} \text{mm}^2/\text{s}$) and $0.97 \pm 0.34 \times 10^{-3} \text{mm}^2/\text{s}$ on the right side (although a smaller region). There is positive DCE-MR kinetics, with increased permeability and extra-vascular fraction R and L mid gland that is correlated to the Gleason score 7. Moreover, both sides have evidence of increased choline and decreased Citrate by MRS.

Figure 4.

Relative signals of the inner (top) and outer (bottom) peaks of the citrate quartet as a function of the timing of the second refocusing pulse in a PRESS sequence at 3T with the first refocusing pulse fixed at $TE=10\text{ms}$. The total TE is the sum of $tt1$ and $t2$. The solid line is the real part of the signal, i.e the signal component that is in phase with the rest of the ^1H -MRS spectrum. Desirable signals have a maximum real inner peak signal (with the dotted line of the dispersion signal at zero) and outer peak signals that are either in phase or nulled.

Figure 5.

A.) 1H-MRSI results from phantom and human measurements using the semi-LASER sequence with MEGA water and lipid suppression at 7T.. As can be seen in a 1H MR spectrum of one voxel from the 3D dataset (b) the resonances of the strongly coupled spin systems of citrate are completely in absorption with only minor side lobes of the citrate signals B.) 1H-MRSI of the prostate at 7 T of healthy volunteer showing resonances of citrate, choline, creatine, and polyamines (spermine) from the 3D 1H-MRSI dataset location of this voxel is indicated on a sagittal and coronal TSE image. Adapted from ¹¹⁰.

Figure 6. 64-year-old patient with metastatic disease who underwent WB-DWI at 1.5T. **Right)** Tc99m bone scan. The bone scan demonstrates multiple metastatic areas of increased uptake in the calvarium, sternum, ribs, vertebra, pelvis, and femur. **Middle)** Sagittal image showing the whole-body coverage. **Middle and Left)** Axial diffusion-weighted images ($b=600\text{s/mm}^2$) of corresponding areas of metastatic sites. Note the sternum metastases are clearly seen, as are metastases in the rib and femur.

Table 1
Summary of literature review of diffusion weighted Imaging and ADC mapping in prostate patients.

	Patient (n)	Field Strength	Normal (volunteer)	ADC values $\times 10^{-3}(\text{mm}^2/\text{s})$						Sensitivity/Specificity	
				Patient (normal)		Tumor		Patient (normal)			Tumor
				Peripheral Zone	Peripheral Zone	Peripheral Zone	Central Zone	Transition Zone	Transition Zone		
Gibbs 47	20	1.5T	1.25±0.23	3.43 ± 0.69	2.73 ± 0.70	1.17 ± 0.18					
Issa 48	26	1.5T	1.91±0.46	1.82 ± 0.53	1.38 ± 0.52	1.63 ± 0.30	1.62 ± 0.41				
Chan 71	11	1.5T		1.61 ± 0.37	1.43 ± 0.35						
Hosseinzadeth 39	10	1.5T		1.61 ± 0.27	1.34 ± 0.38						
Sinha 120	6	1.5T	1.95±0.08			1.53 ± 0.34					
Sato 121	29	1.5T	1.93±0.24	1.80 ± 0.41	1.08 ± 0.39	1.68 ± 0.26	1.58 ± 0.37	1.13±0.42			
Kozlowski 69	14	1.5T		1.57 ± 0.27	0.99 ± 0.16		1.38 ± 0.17		84%/98%		
Manenti 122	19	1.5T	2.08±0.22	1.98 ± 0.23	0.96±0.17	1.57±0.12					
Matsuki 123	15	1.5T		1.85 ± 0.22	1.18±0.21		1.57±0.09				
Reinsberg 51	42	1.5T		1.51 ± 0.27	1.03 ± 0.18	1.31±0.20					
Kitajima 124	26	1.5T		1.69 ± 0.23	0.82 ± 0.27						
Kozlowski 56	15	1.5T		1.99 ± 0.21	1.21±0.25	1.52±0.13			54%/100%		
deSouza 62	33	1.5T		1.71 ± 0.16	1.30 ± 0.30		1.46 ± 0.14				
Yoshimitsu 58	37	1.5T		1.07±0.20							
Ren 59	75	1.5T	1.83±0.07		0.93 ± 0.17	1.35 ± 0.05					
Mazaheri 54	61	1.5T		1.69 ± 0.24	1.39 ± 0.23			0.94±0.21			
Tamada 60	215	1.5T	1.80±0.27		1.02 ± 0.25	1.34 ± 0.14					
Takayama 125	9	1.5T		1.67 ± 0.07	1.07 ± 0.07	1.43± 0.02					
Van as 61	11	1.5T		1.70 ± 0.09	1.30 ± 0.09	1.50 ± 0.06					
de Souza 62	44	1.5T		2.05 ±0.31	1.50 ± 0.27	1.53 ± 0.21			89%/58% 55%/95%		
Langer 126	18	1.5T		1.46		1.15					

Patient (n)	Field Strength	ADC values $\times 10^{-3}(\text{mm}^2/\text{s})$						Sensitivity/Specificity	
		Normal (volunteer)		Patient (normal)		Tumor			
		Peripheral Zone	Peripheral Zone	Peripheral Zone	Central Zone	Transition Zone	Tumor	Transition Zone	Tumor
Kumar 127	1.5T	1.68 $\pm$ 0.31	1.34 $\pm$ 0.30		0.98 $\pm$ 0.22	1.07 $\pm$ 0.25			73%/74%
Tanimoto 128	1.5T	1.72 $\pm$ 0.35			1.46 $\pm$ 0.16				
Riches 65	1.5T	1.66 $\pm$ 0.34			1.72 $\pm$ 0.35				
Kim 129	1.5T		1.57 $\pm$ 0.34			1.44 $\pm$ 0.31	0.96 $\pm$ 0.14		98%/81% 81%/87%
Pickles 50	3T	1.60 $\pm$ 0.25		1.95 $\pm$ 0.50	1.27 $\pm$ 0.14				80%/74%
Gibbs 49	3T			1.64 $\pm$ 0.21					
Kim 67	3T			1.97 $\pm$ 0.25	1.32 $\pm$ 0.24	1.79 $\pm$ 0.19	1.37 0.29		94%/91%, 90%/84%
Gurses 57	3T			1.61 $\pm$ 0.35	1.22 $\pm$ 0.24				62%/97%
Kim 67	3T			1.61 $\pm$ 0.21	0.93 $\pm$ 0.23				
Gibbs 52	3T	1.56				1.21			
Zelhof 64	3T	1.90 $\pm$ 0.33			1.45 $\pm$ 0.26				
Klomp 110	7T	Investigation al							

ADC= Apparent Diffusion Coefficient

Table 2

Summary of literature review of magnetic resonance spectroscopy (MRS) in prostate patients.

	Year	MRS	Normal Peripheral Zone	Central Zone	Tumor	Sensitivity/Specificity
Kurhanewicz ⁹⁶	1995	Cit/(Cho + Cr)	1.46 ± 0.28	0.67 ± 0.17	1.21 ± 0.29	
Kurhanewicz ⁹⁷	1996	(Cho + Cr)/Cit	0.54 ± 0.11	2.1 ± 1.30		
Kurhanewicz ¹³⁰	1996	(Cho + Cr)/Cit	0.5 ± 0.10	1.9 ± 0.8	0.6 ± 0.2	
Parivar ¹³¹	1996	(Cho + Cr)/Cit		2.1 ± 1.3	0.56 ± 0.2	
Heerschap ¹³²	1997	Cit/(Cho + Cr)	1.88 ± 0.34	0.94 ± 0.16		
Kim ¹³³	1998	Cit/(Cho + Cr)		1.46 ± 0.11	0.45 ± 0.06	
Kaji ¹³⁴	1998	Cit/(Cho + Cr)			>3*SD of normal	90/64
Garcia-Segura ¹³⁵	1999	Cit/Cho	0.86		0.39 ± 0.28	
		Cit/(Cho + Cr)			0.31 ± 0.23	
Scheidler ¹³⁶	1999	(Cho + Cr)/Cit	0.22	>0.75 >0.86		52/91
Males ¹³⁷	2000	(Cho + Cr)/Cit	0.22 ± 0.13	1.62 ± 2.08		
Mueller-Lisse ¹³⁸	2001	(Cho + Cr)/Cit	0.24 ± 0.13			73/76
Kaji ¹³⁹	2002	(Cho + Cr)/Cit	0.58 ± 0.38	0.72 ± 0.51	4.68 ± 3.95	
	2002	(Cho + Cr)/Cit (phased array)			4.71 ± 4.45	
Zakian ¹⁴⁰	2003	(Cho + Cr)/Cit	0.63 ± 0.2	1.74 ± 1.35		
Shukla-Dave ⁹⁴	2004	(Cho + Cr)/Cit		0.6–7.9 (grade of cancer)		
Jung ¹⁰⁸	2004	(Cho + Cr)/Cit	0.25 ± 0.12		>4–5*SD	69/89 (score 4 or 5) 90/72 (score 3–5)
Squillaci ¹⁴¹	2005	(Cho + Cr)/Cit	<0.75		>0.86	76/91
Wetter ¹⁴²	2005	(Cho + Cr)/Cit	0.39 ± 0.26	2.65 ± 2.37		83/93
Kumar ¹⁴³	2006	Cit/(Cho + Cr)	2.16 ± 0.56	0.31 ± 0.25	1.43 ± 0.58	100/33
Shukla-Dave ¹⁴⁴	2007	(Cho + Cr)/Cit		1.08 ± 0.2	0.59 ± 0.03	70/80
Reinsberg ⁵¹	2007	Cho/Cit	0.07 ± 0.05	0.92 ± 1.28		70/84
Scheenen ⁷⁶	2008	(Cho + Cr)/Cit	0.22 ± 0.12	0.34 ± 0.14		66/95 (MRS<0.41) 78/82 (MRS<0.27)

	Year	MRS	Normal Peripheral Zone	Central Zone	Tumor	Sensitivity/Specificity
Chen ⁵⁵	2008	(Cho +Cr)/Cit		>0.42		
Cirillo ¹⁴⁵	2008	(Cho +Cr)/Cit		>0.86		
Thomas ¹⁴⁶	2008	2D-Cosy				
Ren ¹⁴⁷	2009	Cho/Cit	0.15	1.6		
Klomp ¹¹⁰	2009	7T	Visible			

MRS= Magnetic Resonance Spectroscopy, Cho=choline, Cr=creatine, Citrate-Cit,