Improving non-invasive detection of prostate cancer using diffusion-weighted MRI

Michelle Leech1*, John Gaffney2, Laure Marignol1

1Applied Radiation Therapy Trinity, Discipline of Radiation Therapy, School of Medicine, Trinity College, Dublin, Ireland
2Radiotherapy Department, Galway University Hospital, Galway, Ireland

Abstract: Prostate cancer represents 11% of all cancers in the European Union and 9% of all cancer deaths. Standard MRI for prostate cancer includes high-resolution T2-weighted images, which allow for the assessment of the prostate and the tumour, as tumours arising from the peripheral zone appear dark compared to the expected normally bright peripheral gland tissue. Over the past number of years, the application of diffusion-weighted MRI (DW-MRI) has progressed to include both diagnostic and prognostic roles in oncology. DW-MRI images should be analysed together with the T2-weighted images and the corresponding apparent diffusion coefficient (ADC) maps. We searched PubMed, Cochrane, and Science Direct for relevant journal articles and reviews published up until April 2015 using the search terms “functional MRI” OR “multiparametric MRI” OR “MRSI” AND “diagnosis” AND “prostate cancer” OR “prostate”. The literature indicates that DW-MRI is an important parameter in the identification of prostate cancer. It has the ability to improve sensitivity and specificity, relative to T2-weighted images alone, and has been demonstrated to correlate with tumour grade.

Keywords: prostate cancer detection; diffusion-weighted magnetic resonance imaging


Introduction

Prostate cancer represents 11% of all cancers in the European Union and 9% of all cancer deaths[1]. The introduction of prostate Magnetic Resonance Imaging (MRI) has recently become more prevalent in order to localise any abnormalities that may indicate prostate cancer (CaP). The current European Society of Urogenital Radiology (ESUR) guidelines recommend the use of multiparametric MRI (mpMRI), that is, T2-weighted imaging with at least two functional techniques of diffusion-weighted MRI (DW-MRI), dynamic contrast-enhanced MRI (DCE-MRI) or MR spectroscopy (MR-Spect)[2].

Traditional biopsy in prostate cancer

After an initial negative standard Trans Rectal Ultrasound (TRUS) biopsy, many men exhibit persistently increased prostate specific antigen (PSA) levels[3]. This may be due to the low positive predictive value of PSA, which accounts for a high proportion of unnecessary biopsies[4–6]. However, the negative predictive value (NPV) of TRUS-guided biopsy has been reported as between 36% and 89%[7], with some patients being intolerant of this invasive procedure[8]. Where a negative biopsy is associated with continued suspicious clinical symptoms (continued rising PSA > 4.0 ng/mL, suspicious digital rectal examination, abnormal PSA velocity), repeat biopsies pose an even greater risk of negative rate for cancer detection than the initial biopsy (81%–83%)[9], with second, third, and fourth re-biopsies detecting cancer in only 25% to 27%, 5% to 24%, and 4% to 21% of cases, respectively[10]. Efforts to improve the rates of
cancer detection of the traditional sextant biopsy have resulted in the initiation of extended biopsies, where attention is given to the lateral peripheral zone as well as the anterior apex\(^\text{[11]}\).

**Diffusion-weighted MRI (DW-MRI) in prostate cancer diagnosis**

Diffusion-weighted magnetic resonance imaging (DW-MRI) was first introduced in 1985 and began with intracranial imaging\(^\text{[12]}\). Over the past number of years, the application of DW-MRI has progressed to include both diagnostic and prognostic roles in oncology. Its benefits include speed of acquisition (1–5 minutes to perform) and excellent soft tissue definition without the requirement of intravenous or oral contrast media\(^\text{[13]}\). It also provides qualitative and quantitative information that is used in the assessment of various tumours\(^\text{[14]}\).

DW-MRI examines the random motion of water molecules in the body. The image contrast in DW-MRI reflects the difference in rate of diffusion between tissues. It is known that there is restriction of water molecule movement in tissues due to the disruption of their motion, a process thought to be related to interactions with cell membranes and macromolecules\(^\text{[15]}\), and that this relationship between restriction to water diffusion and that of tissue cellularity and cell membrane integrity in biological tissue is inverse in nature\(^\text{[16–19]}\).

Ultimately, the motion of water molecules is more restricted in tissues with high cellular density associated with numerous intact cell membranes, such as tumour tissue\(^\text{[20]}\). This decrease in water diffusion has been attributed to the increased cellularity of the malignant tumour, with a reduction of the extracellular space and restriction of the motion of extracellular water\(^\text{[8]}\).

In DW-MRI, images are generated by applying a diffusion-sensitising gradient, and the strength of this gradient can be manipulated by changing the ‘\(b\)-value’ on the MRI scanner. Higher \(b\)-values indicate higher diffusion weighting. Typical \(b\)-values for prostate imaging are in the range of 0–1500 s/mm\(^2\). In a high \(b\)-value MRI image, areas with impeded diffusion, such as a tumour, will often appear to have a higher signal intensity than that of the surrounding tissues\(^\text{[21]}\).

Performing DW-MRI with two or more \(b\)-values allows for the calculation of the apparent diffusion coefficient (ADC), which quantifies the slope of the line that describes the logarithm of the measured signal intensity and the \(b\)-value. DW-MRI is most often performed using echo planar imaging-based techniques. Image acquisitions with \(b\)-values of 800–1000 s/mm\(^2\) are commonly used while on some scanners, high values of up to 1500 s/mm\(^2\) can be achieved. Endorectal coils provide superior signal-to-noise ratio compared to pelvic phased-array coils but cause reduced patient compliance and increase susceptibility artefacts\(^\text{[21]}\). No standardised DW-MRI techniques currently exist and a large variety of imaging parameters exist for DW-MRI including the number and size of \(b\)-values, diagnostic threshold, and the type of coil\(^\text{[8]}\).

Standard MRI for prostate cancer includes high-resolution T2-weighted images, which allow for the assessment of the prostate and tumour, as tumours arising from the peripheral zone appear darker compared to the normally bright peripheral gland tissue. DW-MRI images should be analysed together with T2-weighted images and ADC maps. A prostate tumour will typically illustrate high signal intensity because of diffusion limitation on high \(b\)-value images and will yield a low ADC value, meaning that it will appear darker on ADC maps. This correlates with higher cellularity of prostate tumours than normal prostate tissue on histology. ADC maps can be useful because the T2 “shine through” from the normal high signal peripheral zone on the DW-MRI images can be problematic. The variances in reported ADC values for normal prostate tissue are due to the use of different \(b\)-values, field strengths, imaging protocols, and MRI scanners.

**Aims and objectives**

The aim of this article is to review the contribution of DW-MRI in the detection of clinically significant prostate cancer.

The objectives are:

- To discuss whether the sensitivity and specificity of prostate cancer detection increases with the addition of DW-MRI relative to standard T2-weighted MRI alone
- To identify if DW-MRI can be correlated with specific Gleason grade
- To describe the use of DW-MRI in conjunction with other functional MRI sequences
- To recognise the limitations of the use of DW-MRI in the detection of prostate cancer

**Materials and methods**

We searched PubMed, Cochrane, and Science Direct for relevant journal articles and reviews published until April 2015 using the search terms “functional MRI” OR “multiparametric MRI” OR “MRSI” AND “diagnosis” AND “prostate cancer” OR “prostate”. Following the initial search, a review of titles and abstracts was performed to avoid duplicated results. Each reference list was reviewed
to help identify any additional papers that were relevant.

The primary search targeted articles in the English language which focused on the use of functional MRI in prostate cancer diagnosis. Papers related to other primary sites and those which used other means to diagnose prostate cancer were omitted. The included publications reported a variety of outcomes.

**Results and discussion**

The studies included in this review are summarized in Table 1.

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Year</th>
<th>Investigation of this study</th>
<th>Patient cohort</th>
<th>ADC values (if reported) for prostate cancer ($\times 10^{-3}$ mm$^2$/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Franiel et al.</td>
<td>2011</td>
<td>ADC values of prostate cancer</td>
<td>54 patients with a median of at least 2 prior negative TRUS biopsies. Underwent T2W MRI adding different Mp-MRI sequences incrementally. Found that only T2 with all MpMRI sequences (MR Spect, DCE-MRI and DW-MRI) identified all CaPs. T2W and DW-MRI had a detection rate of 85%.</td>
<td>1.03 (Peripheral zone) 0.76 (Transition zone)</td>
</tr>
<tr>
<td>Panebianco et al.</td>
<td>2015</td>
<td>ADC values of prostate cancer</td>
<td>2 groups of 570 patients each. Group A randomized to TRUS biopsy alone. Group B randomized to Mp-MRI, TRUS-targeted and random biopsy. Proportion with clinically significant CaP detected higher in Group B.</td>
<td>1 ± 0.23 (low-grade tumours) 0.7±0.17 (intermediate grade tumours) 0.5 ± 0.13 (high grade tumours)</td>
</tr>
<tr>
<td>AbdelMaboud et al.</td>
<td>2014</td>
<td>ADC values of prostate cancer</td>
<td>36 patients (age range 50–72 years, mean 61 years) underwent DW-MRI. 31 indicated an area of high signal intensity and malignancy.</td>
<td>0.737 ± 0.154</td>
</tr>
<tr>
<td>Chan et al.</td>
<td>2003</td>
<td>ADC values of prostate cancer</td>
<td>15 patients with abnormal PSA levels of &gt; 4 ng/mL and either had at least two negative or normal TRUS biopsies or could not undergo TRUS biopsy due to previous rectal surgery.</td>
<td>1.43</td>
</tr>
<tr>
<td>Sato et al.</td>
<td>2005</td>
<td>ADC values of prostate cancer in transition zone</td>
<td>29 patients with suspected CaP. TRUS biopsy post MR imaging at 1.5T.</td>
<td>1.13 ± 0.42 (Cancerous transition zone) 1.58 ± 0.37 (Benign transition zone)</td>
</tr>
<tr>
<td>Mazaheri et al.</td>
<td>2008</td>
<td>Correlation of ADC values with pathologic findings</td>
<td>38 patients. Median age: 61 years Had 1.5T MR prior to radical prostatectomy. No prior hormonal therapy or radiation therapy. At least one PZ lesion &gt;0.1 cm$^3$ at pathology.</td>
<td>Mean ADC for malignant PZ: 1.39 ± 0.23 Mean ADC for non-malignant PZ: 1.69 ± 0.24</td>
</tr>
<tr>
<td>Panebianco et al.</td>
<td>2015</td>
<td>Efficacy of TRUS-guided biopsy</td>
<td>2 groups of 570 patients each. Group A randomised to TRUS biopsy alone. Group B randomised to Mp-MRI, TRUS-targeted and random biopsy. Proportion with clinically significant CaP detected higher in Group B.</td>
<td></td>
</tr>
<tr>
<td>Arsov et al.</td>
<td>2015</td>
<td>Use of functional MRI in targeted biopsy</td>
<td>With a detection rate of 11/16, targeted biopsies based on functional MRI findings were superior to the traditional transrectal saturation biopsies. Reduction in mean number of biopsy cores required with functional MRI guidance.</td>
<td></td>
</tr>
</tbody>
</table>
Improving non-invasive detection of prostate cancer using diffusion-weighted MRI

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Year</th>
<th>Investigation of this study</th>
<th>Patient cohort</th>
<th>ADC values (if reported) for prostate cancer ($\times 10^{-3}$ mm$^2$/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schoots et al.</td>
<td>2015</td>
<td>Use of MRI-targeted biopsies in prostate cancer detection</td>
<td>Systematic review. Patients who had suspicion of prostate cancer following MRI included. No difference in overall detection between targeted and random biopsies. MRI-targeted biopsy had a higher detection of significant CaP and lower rate of detection of insignificant CaP compared to random TRUS biopsy.</td>
<td></td>
</tr>
<tr>
<td>Willis et al.</td>
<td>2014</td>
<td>Use of MRI-targeted biopsies in prostate cancer detection</td>
<td>Comparison of TRUS-guided biopsy with mpMRI, then MRI-targeted biopsy, if positive. Suggests that mpMRI and consequent MRI-targeted biopsy result in increased accuracy and fewer biopsies than TRUS-guided.</td>
<td></td>
</tr>
<tr>
<td>Morgan et al.</td>
<td>2007</td>
<td>Accuracy, sensitivity and specificity measurement of combined T2W and DW-MRI with T2W imaging alone in the detection of prostate cancer</td>
<td>56 patients with raised PSA and available histology from sextant biopsies. Mean age: 67.6 years Median PSA: 9.8 ng/ml. Positive cores on biopsy: 1–6 Gleason grade: 6–8. T1: n = 35 T2: n = 11 T3: n = 8</td>
<td></td>
</tr>
<tr>
<td>Jie et al.</td>
<td>2014</td>
<td>Accuracy, sensitivity and specificity measurement in the peripheral zone relative to rest of prostate gland</td>
<td>Peripheral zone data were analysed separately for 8 studies. Noted that there was significant heterogeneity in the 8 trials chosen for this subgroup analysis.</td>
<td></td>
</tr>
<tr>
<td>Petriollo et al.</td>
<td>2013</td>
<td>Sensitivity of multiparametric MRI in prostate cancer grade determination</td>
<td>136 patients were enrolled in total. PSA 4–10: n = 119 PSA 2.5–4: n = 17</td>
<td></td>
</tr>
<tr>
<td>Ocak et al.</td>
<td>2007</td>
<td>Specificity improvement of DCE-MRI with T2W MRI relative to T2W alone</td>
<td>Showed an improvement in sensitivity of 16% for detection of CaP in the transition zone when DCE-MRI was combined with standard T2W MRI in comparison to T2W MRI alone. Showed a reduction in specificity for peripheral zone detection from 98% to 92%.</td>
<td></td>
</tr>
<tr>
<td>Rud et al.</td>
<td>2014</td>
<td>Sensitivity and specificity of T2W and DW-MRI in detection of prostate recurrence</td>
<td>42 patients with biochemical recurrence after EBRT. Mean age: 67 ± 6 years Median PSA: 4.0 ± 3.0 ng/mL Elapsed time since EBRT: 5.6 ± 2.8 years</td>
<td></td>
</tr>
<tr>
<td>Ren et al.</td>
<td>2009</td>
<td>Seminal vesicle involvement (SVI) detection</td>
<td>283 patients. Had conventional MRI and DW-MRI prior to surgery for prostate cancer 39 patients had SVI and had significantly lower ADC values than those without SVI.</td>
<td></td>
</tr>
<tr>
<td>Ren et al.</td>
<td>2008</td>
<td>Detection of urinary bladder wall invasion (UBWI)</td>
<td>68 patients with proven prostate cancer and UBWI. Mean ADC values for those with UBWI: 0.963 ± 0.155 and with normal bladder wall: 1.517 ± 0.103.</td>
<td></td>
</tr>
<tr>
<td>Mir et al.</td>
<td>2010</td>
<td>Pelvic lymph node detection. Nodal detection between T2W alone and fused T2W and DW-MRI using relative to an identified distribution analysis (RIDIT)</td>
<td>20 patients with pelvic tumours. T2W and fused T2W-DW-MRI at 1.5T. 114 nodes identified with T2W alone. 161 nodes identified with fused T2W + DW-MRI.</td>
<td></td>
</tr>
<tr>
<td>Eiber et al.</td>
<td>2010</td>
<td>Pelvic lymph node detection using DW-MRI at 1.5T</td>
<td>29 patients. 118 lymph nodes &gt; 6 mm in short axis analysed. Mean ADC of malignant nodes was 1.07 ± 0.23 and for non-malignant nodes was 1.54 ± 0.25.</td>
<td></td>
</tr>
</tbody>
</table>
Sensitivity and specificity in the detection of prostate cancer lesions

In an attempt to determine whether sensitivity and specificity were increased when combining DW-MRI with T2-weighted (T2W) imaging relative to T2W imaging alone, Morgan et al.\(^{22}\) compared diagnoses based on imaging with the results of sextant biopsies. Each sextant’s histology was compared with the T2W images alone and then with the T2W and ADC maps together. Sensitivity, specificity, positive, and negative values were calculated and compared. A kappa value for interobserver agreement was calculated for T2W imaging alone and for T2W and ADC maps together. There was an improvement in overall accuracy, sensitivity, and specificity for the most experienced observer with the addition of ADC maps to the T2W images. The sensitivity for tumour detection by an experienced observer improved from 46.5% to 71% on inclusion of ADC maps in the evaluation.

However, T2W imaging alone showed a moderate overall interobserver agreement (Kappa 0.53), which was surprisingly better than for T2W and ADC maps (Kappa 0.334; \(p < 0.001\)).

A meta-analysis on the value of diffusion-weighted imaging in the detection of prostate cancer speculated that, given the aggressive nature of peripheral zone (PZ) tumours, a separate protocol specific to PZ tumours might lead to improved accuracy\(^{31}\). Such a protocol may have merit, as 70%–75% of CaPs arise in the PZ\(^{23,24}\). The PZ data were analysed separately for eight studies. Sensitivity was increased relative to the entire gland (79% compared to 62%). However, the overall diagnostic accuracy was not improved, as there was still significant heterogeneity among the eight trials chosen for this subgroup analysis.

Sato et al.\(^{25}\) studied prostate cancer detection with T2W MRI and DW-MRI in comparison to those detected by T2W alone and found that the combined imaging modality had an area under the receiver operating characteristic curve (AUC) of 0.89, in comparison to 0.81 of T2W alone. However, the addition of DW-MRI and DCE-MRI to T2-weighted MRI may improve the positive predictive value (PPV) and the specificity of prostate cancer diagnosis, particularly in transitional zones\(^{36}\).

Arsov et al.\(^{27}\) performed a study in patients with prior negative transrectal ultrasound-guided biopsy (TRUS-GB) and increased PSA. It illustrated that targeted biopsies based on functional MRI findings were superior to the traditional transrectal saturation biopsies, which are generally performed for such patients. In 37.9% (22/58) of patients, functional MRI showed evidence of prostate cancer. A total of 16 of the 22 patients underwent TRUS-GB with additional targeted biopsies, and CaP was diagnosed in 68.8% (11/16). The follow-up was 49.1 weeks. There was no significant elevation in PSA or detection of significant PSA increase in patients with normal functional MRI findings. The study showed a reduction in the mean number of biopsy cores required, relative to what would be required for traditional transrectal saturation biopsies.

A meta-analysis\(^ {28}\) showed no difference in overall detection between targeted and random biopsies; however, the MRI-targeted biopsy (MRI-TBx) had a higher rate of detection of significant prostate cancer (sensitivity 0.91, 95% CI 0.87–0.94) compared to TRUS-GB (0.76, 95% CI 0.64–0.84), and a lower rate of detection of insignificant prostate cancer (sensitivity 0.44, 95% CI 0.26–0.64) compared to TRUS-GB (0.83, 95% CI 0.77–0.87). Differentiation between significant and insignificant CaP was ascertained using either Epstein criteria or Gleason score.

Willis et al.\(^ {29}\) compared two diagnostic pathways: TRUS-guided biopsy against multiparametric MRI (mpMRI), followed by MRI-targeted biopsy, if positive. The study suggested that mpMRI and consequent MRI-targeted biopsy might result in biopsies that are more accurate and fewer in numbers as compared to TRUS-guided biopsies. The former not only accurately detects more clinically significant cancers, but also correctly identifies more men without clinically significant disease in probabilistic sensitivity analysis.

Use of ADC maps in prostate cancer detection and grading

The ability to detect a lesion on DW-MRI depends on the tumour site, its size, and composition. Tumours < 5 mm are difficult to detect and inflammatory processes in the prostate can produce low ADC values and mimic prostate cancer, leading to false positives\(^ {30}\). It is particularly difficult to detect tumours in the transition zone, and ADC maps in conjunction with T2W images can improve their detection\(^ {31}\).

Franiel et al.\(^ {39}\) examined 178 areas suspicious for prostate cancer, where the prostate was divided into 20 zones to coincide with histological reporting. 64% of these were at the peripheral zone, with the remainder (36%) in the central gland. 53 areas were positive for prostate cancer; of these, 53% were in the peripheral zone and 47% in the transition zone. A median ADC value of 1.03 × 10\(^{-3}\) mm\(^2\)/sec was measured for prostate cancer in the peripheral zone. In this region, normal prostate tissue had a median ADC of 1.42 × 10\(^{-3}\) mm\(^2\)/sec.
and prostatitis $1.26 \times 10^{-3} \text{ mm}^2/\text{sec}$. For the transition zone, median ADC for prostate cancer was recorded as $0.76 \times 10^{-3} \text{ mm}^2/\text{sec}$; normal prostate tissue was $0.96 \times 10^{-3} \text{ mm}^2/\text{sec}$ and prostatitis was $1.06 \times 10^{-3} \text{ mm}^2/\text{sec}$.

AbdelMaboud et al.\textsuperscript{[32]} reported on 36 patients whose data of T2W and DW-MRI were correlated with histology post-TRUS-guided biopsy and/or prostatectomy. ADC values for the prostate tumours were similarly decreased relative to the healthy prostate tissue ($0.737 \pm 0.154 \times 10^{-3} \text{ mm}^2/\text{sec}$ and $1.484 \pm 0.289 \times 10^{-3} \text{ mm}^2/\text{sec}$, respectively). Afzq et al.\textsuperscript{[21]} reported the highest mean ADC values of $1.54-2.99 \times 10^{-3} \text{ mm}^2/\text{sec}$ in the peripheral zone, followed by the central gland ($0.9-2.14 \times 10^{-3} \text{ mm}^2/\text{sec}$) and prostate cancer ($0.8-1.66 \times 10^{-3} \text{ mm}^2/\text{sec}$). Again, this study noted that there was some overlap between the ADC values for prostate cancer and normal prostate tissue. Chan et al.\textsuperscript{[33]} reported benign mean peripheral zone ADC values as $1.6 \times 10^{-3} \text{ mm}^2/\text{sec}$ and mean ADC values in cancer tissue as $1.43 \times 10^{-3} \text{ mm}^2/\text{sec}$.

An ADC value derived from DW-MRI has the potential to be an important prognostic disease marker in identifying how aggressive the tumour is. Currently, this is conducted using Gleason score on a biopsy specimen only, which has the associated limitations of sampling errors as well as being an invasive procedure. The principle behind using DW-MRI images in this manner is that altered gland formations such as medullary or solid patterns are likely to show impeded water diffusion and be associated with an increased histological Gleason grade\textsuperscript{[31,34]}. ADC values for low-grade tumours have been reported as $1 \pm 0.23 \text{ mm}^2/\text{sec}, 0.7 \pm 0.17 \text{ mm}^2/\text{sec}$ for intermediate-grade tumours, and approximately $0.5 \pm 0.13 \text{ mm}^2/\text{sec}$ for high-grade tumours\textsuperscript{[10]}. Similarly, Turkbey et al.\textsuperscript{[35]} reported that low ADC values were associated with higher grade tumours and therefore higher Gleason scores.

DW-MRI may also be helpful for the assessment of seminal vesicle involvement in the staging process. Seminal vesicles have high signal on T2W imaging, low on DW-MRI and have high ADC values, as they are typically fluid-rich structures\textsuperscript{[36]}. DW-MRI has also been reported to be useful in the detection of bladder wall invasion\textsuperscript{[15]}. Using fused DW-MRI and T2W images can also improve the identification of positive pelvic lymph nodes, relative to T2W alone\textsuperscript{[38]}. Eiber et al.\textsuperscript{[39]} found in a small retrospective study a significant difference between the mean ADC of malignant and benign nodes.

### DW-MRI in conjunction with other MRI acquisition sequences

Petrello et al.\textsuperscript{[40]} focused on 136 intermediate risk patients with PSA 2.5–10. Of these, 119 had PSA scores between 4 to 10 and 17 had scores between 2.5 to 4. Such cases are often a diagnostic challenge due to low, but not negligible, tumour prevalence. Each MRI sequence was given a separate score for each prostate site.

Data were first collected in couples [morphologic (m) MRI/MR-Spect score and mMRI/DW-MRI score] as the sum of each site scores. A multiparametric score (cMRI) was subsequently obtained for every site as the sum of scores from each MRI technique. A significant correlation was seen by comparing cMRI score to the Gleason score ($p < 0.05$). Using Wilcoxon rank sum test, it was shown that significant and insignificant Gleason score tumours had a different cMRI score median value ($p < 0.01$).

The use of cMRI score showed higher sensitivity and higher NPV than either of the single multiparametric MRI techniques (mMRI, DW-MRI, and MR-Spect) or their combination (mMRI/MR-Spect score and mMRI/ DW-MRI score). The authors showed a significant correlation between cMRI score and Gleason score, with all significant Gleason tumours having a cMRI score $\geq 2$. Taking this into account, the cMRI score could reduce the number of negative biopsies in those with PSA $< 10$ because of its high NPV. In essence, it was found that cMRI scores could identify those at high risk of cancer. The technique of DCE-MRI, which involves intravenous injection (IV) of a contrast agent followed by multiphase MRI imaging, is now widely used\textsuperscript{[41]}.

The IV contrast causes earlier tumour enhancement than that of background tissues. This is related to the highly vascular process of angiogenesis observed in tumours\textsuperscript{[42]}. Ocak et al.\textsuperscript{[43]} demonstrated an improvement in specificity of $51\%$ for detection of prostate cancer in the transitional zone when DCE-MRI performed at 3 Tesla was combined with standard T2W MRI in comparison to T2W MRI alone. However, it did show a reduction in sensitivity for peripheral zone detection by $24\%$. In follow-up imaging, Rud et al.\textsuperscript{[44]} found that DW-MRI was equally sensitive and more specific compared to DCE-MRI after EBRT for the detection of local prostate cancer recurrence. However, a recent study of 245 patients\textsuperscript{[45]} has indicated that DCE-MRI may have limited added value to a combination of T2W and DW-MRI for the diagnosis of clinically significant prostate cancer. The use of mpMRI in the diagnosis of prostate cancer requires a validated scoring system. ESUR have developed a structured reporting system called the Prostate Imaging Reporting and Data System (PI-RADS v2.0) with standard subscores depending on the sequence (T2-weighted, DW-MRI, and DCE-MRI). These are then summarised in a final score ranging from 1 to 5 and aid in the identification of intermediate to high grade cancers of small volume\textsuperscript{[46]}. Visschere et al.\textsuperscript{[45]} found that only $19.2\%$ of their...
population of 245 patients actually required DCE-MRI based on the PI-RADS v.20 criteria and, of these, enhancement was incorrect in 30%. Similarly, Vargas et al. found that DCE-MRI provided additional information in only 3% of peripheral zone tumours ≥ 0.5 ml.

Other studies have reiterated how the detection of prostate cancer can be increased when T2-weighted imaging is combined with functional MRI. The result is an improvement in specificity from 68% to 87%. As benign prostatic hyperplasia (BPH) is similar to prostate tumour tissue in that they both strongly enhance, it was previously thought that these could be differentiated on DCE-MRI since BPH regions do not wash out as quickly and that DCE-MRI could play a role in the identification of transition zone cancers from BPH. This benefit in the transition zone has been refuted in a randomised study. Urol 2012; 48: 751–757.

It has the ability to improve sensitivity and specificity relative to T2-weighted images alone, and has a role to play in the identification of tumour grade. Together with other MRI techniques, it can assist in more targeted and accurate biopsies in the detection of prostate cancer, which would lessen the current burden on both prostate cancer patients and health services resources.

**Conclusion**

While not without its limitations, DW-MRI is an important parameter in the identification of prostate cancer. It has the ability to improve sensitivity and specificity relative to T2-weighted images alone, and has a role to play in the identification of tumour grade. Together with other MRI techniques, it can assist in more targeted and accurate biopsies in the detection of prostate cancer, which would lessen the current burden on both prostate cancer patients and health services resources.

**Author contributions**

M Leech and J Gaffney conducted the literature review and drafted the manuscript. L Marignol reviewed the manuscript.

**References**

11. Le JD, Huang J, Marks LS. Targeted prostate biopsy: Value of multiparametric magnetic resonance imaging in...
Improving non-invasive detection of prostate cancer using diffusion- weighted MRI