



## Review – Prostate Cancer

# How Good is MRI at Detecting and Characterising Cancer within the Prostate?

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### Abstract

**Objectives:** As well as detecting prostate cancer, it is becoming increasingly important to estimate its location, size and grade. We aim to summarise current data on the efficacy of magnetic resonance imaging (MRI) in this setting.

**Methods:** Literature review of original research correlating MRI and histologic appearances.

**Results:** Estimates of the sensitivity of MRI for the detection of cancer vary widely depending on method of analysis used and the definition of significant disease. Recent estimates using T2-weighted sequences and endorectal coils vary from 60% to 96%. Several groups have convincingly shown that dynamic contrast enhancement and spectroscopy each improve detection and that the sensitivity of MRI is comparable to and may exceed that of transrectal biopsy. Specificity is not yet good enough to consider the use of MRI in screening. High-grade and large tumours are detected significantly more often with both T2 sequences and spectroscopy. Estimation of size is improved by dynamic contrast and spectroscopy, but errors of >25% are common.

**Conclusions:** The sensitivity of MRI has improved to the point that it has potential in several new areas: targeting of biopsies, monitoring of disease burden both during active surveillance and after focal therapy, and exclusion of cancer in patients with a raised prostate-specific antigen level.

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## 1. Introduction

Local staging of prostate cancer is important for treatment planning and prognosis, and there is

much work (including two meta-analyses [1,2]) on the accuracy of magnetic resonance scanning in this setting. The different but related subject of our review is the ability to detect and characterise

cancer within the gland where the diagnosis has not necessarily been made. Or, put more formally, in men with localised cancer of the prostate, to what extent can magnetic resonance imaging (MRI) characterise its location, size, and grade? The answer is important for at least four reasons.

First, MRI may increase our confidence in excluding cancer in patients with a negative set of biopsies. In a screening population these have a negative predictive value of 80–90% [3,4], meaning that patients with persistently raised prostate-specific antigen (PSA) levels often undergo rebiopsy. There may be some cases in which MRI is so predictive of a negative result that this can be avoided.

Second, if MRI has reasonable specificity and sensitivity for detecting prostate cancer it would serve as a useful baseline test for men considering treatment of small-volume, low-grade disease by active surveillance [5]. Moreover, tumour progression by MRI criteria might prove to be a useful trigger for a more active form of therapy.

Third, standard strategies for prostate biopsy, whether transrectal [3] or transperineal [6], miss a proportion of significant cancers, and although sensitivity increases with the number of cores, so does morbidity, cost, and the need for anaesthesia [6]. A more effective approach might involve targeting areas associated with a high probability of prostate cancer by imaging criteria in addition to standard sector sampling.

Finally, focal treatment of prostate cancer is on the horizon. There is currently little to offer patients between the extremes of active surveillance and radical prostatectomy, with its high risk of urinary and sexual morbidity [7], but recent work has shown that prostate hemiablation is feasible [8] and surveys of radical prostatectomy specimens show that in at least a third of patients the significant cancer is confined to one focus [9]. Several different techniques—microwave ablation [10], cryotherapy [11], high-intensity focused ultrasound (HIFU) [12], and photodynamic therapy [13]—have the potential to be used to treat the cancer but preserve the external urethral sphincter and the nerves responsible for erection that lie just posterolateral to the prostatic capsule. Accurate detection of intraprostatic disease will be vital for focal therapy, both in treatment planning and in follow-up to detect recurrent disease.

## 2. Methods

Original studies correlating MR scan appearances with histology in prostate cancer were found initially by a search of abstracts on Medline with the following criteria: (magnetic

resonance *and* prostate *and* [carcinoma or cancer]). References in the papers found by this initial search were then checked for further relevant publications. Abstracts from meetings of the Radiological Society of North America and American Urological Association over the last 3 yr were also examined.

The studies found can be broadly categorised into two groups by the method used as gold standard: multiple biopsies or whole-mount analysis of radical prostatectomy specimens. Multiple biopsies are easier to perform, but a large body of evidence confirms that they are inaccurate for the estimation of both size and grade of tumour [14], mainly due to sampling error. Whole-mount histology is not without problems, particularly with fixation artefact and misregistration [15–17], but must be considered superior. For estimations of sensitivity (Tables 1–3), only studies that included incidental cancers and used whole-mount histology are included.

Confidence intervals are important for all of the quoted figures for sensitivity and specificity but are rarely given in the original papers. Instead, the number of patients in each study and the total number of tumours found on histology are summarised. Predictive values are not included because they are dependent on the population studied.

Where techniques are new, whole-mount correlation may not yet be available and we also describe the correlation with biopsies.

## 3. Results

### 3.1. Tumour localisation

Most of the initial studies using MRI to detect prostate cancer used T2-weighted sequences to detect low-signal areas of tumour within the relatively high-signal and homogenous peripheral zone. Although change after biopsy, prostatitis, and hyperplasia can all mimic tumour [18–20], reducing specificity (to ~50%), the sensitivity for the detection and correct localisation of peripheral zone disease using T2 sequences has been between 37% and 96% (Table 1). Much of the difference probably lies in the definition of cancer (several studies excluding “clinically insignificant” cancer <0.5 ml in volume), the criteria used for a positive MRI finding, exclusion of transitional zone disease, and the number of segments used for analysis. The ability of one reader to find 96% of tumours in the study by Hricak et al. [21] study is impressive, but must be viewed in context. First, transitional zone cancers were excluded, and second, the analysis was by presence or absence of tumour in a half prostate, accounting for the poor specificity of 36%.

Detection is much worse in the transitional zone. Although tumours here tend to be less aggressive [22], they may account for up to 30% of cancers [23] and their distinction from the heterogenous signal of benign prostatic hyperplasia (BPH) in most studies

**Table 1 – Studies using unenhanced T2-weighted magnetic resonance imaging and whole-mount histology correlation to detect intraprostatic disease**

Study	No. of patients (no. of tumours assessed), no. of segments used for analysis	Coil type	Study design and exclusions	Sensitivity (specificity) and further findings
Rifkin 1990 [72]	185 (299)	Body coil	Incidental cancers >0.5 cm in diameter included Prospective	60% 56% for <1 cm, 71% for >1 cm
Parivar 1991 [73]	12 (26)	Endorectal	All cancers included Prospective	77%
Quint 1991 [20]	26 (54)	Body coil	All cancers included Prospective	54% for cancers >0.1 ml 37% if all included
Carter 1991 [74]	53 (84) 4 segments	Not stated	All cancers included Retrospective	96% for the clinically palpable tumors 58% (43%) for the impalpable 85% sensitivity for posterior impalpable tumours 15% for anterior
Quinn 1994 [75]	69 (134)	Endorectal	All cancers included Prospective	50% 79% of missed tumours were at least partly anterior
Ellis 1994 [24]	320 (484)	Body coil	Incidental cancers >0.5 cm in diameter included Prospective (patients included in Rifkin 1990 study)	62% 78/79 anterior gland cancers were missed
Hricak 1994 [21]	71 (126 positive halves) 2 segments (see note in text)	Endorectal and pelvic phased array	TZ cancers not included Prospective	96% (36%) endorectal coil 92% (21%) pelvic phased array
Jager 1996 [53]	34 (52)	Endorectal	All cancers included Prospective	67% 14/18 missed tumours were in the central zone (sensitivity 92% for peripheral)
Ikonen 1998 [25]	51 (324 positive segments) 10 segments	Endorectal	All cancers included Retrospective	60% (63%) overall 55% (67%) anterior gland 77% (38%) posterior gland
Scheidler 1999 [19]	53 (155 positive segments) 6 segments	Endorectal and pelvic phased array	TZ cancers not included Retrospective	77% (61%) reader 1 81% (46%) reader 2
Only studies including incidental tumours are included. TZ = transitional zone.				

**Table 2 – Studies using dynamic magnetic resonance scans and whole-mount histology correlation to detect intraprostatic disease**

Study	No. of patients (no. of tumours assessed) No. of segments used for analysis	Sensitivity, (specificity) and further findings	Study design	No. of slices Temporal resolution
Jager 1997 [17]	57 (102 positive segments) 4 segments	57% (80%) T2 73% (81%) with dynamic contrast 6 patients: major improvement in detection or staging with contrast	Incidental cancers included Prospective	One slice, 1.25, 2.5 s
Ogura 2001 [35]	38 (85 positive segments) 7 segments	59% (88%) PZ: 81% (79%) TZ: 37% (97%)	Incidental cancers included Prospective	Gland covered, 30 s
Preziosi 2003 [29]	11 (17) 7 segments	76% (one 5-mm anterior lesion and three 1-mm lesions missed) 9 patients had PZ tumour, 4 TZ 2/9 cases did not have an equivalent low-density T2 area	Incidental cancers included Prospective	Gland covered, 30 s
Schlemmer 2004 [32]	28 (28)	79% T2 (PZ) 68% dynamic (PZ) 89% (both) Signal enhancement started earlier in high-grade tumors	Incidental and TZ cancers not included Retrospective	10 slices, 13 s
Nakashima 2004 [50]	95 (186)	58% (85% for >1-cm diameter tumours)	Incidental cancers included Prospective	Not stated

All studies used endorectal coils.  
TZ = transitional zone; PZ = peripheral zone.

using T2-weighted sequences has been almost impossible unless they are large or distorting. One large series of anterior gland cancers showed that 78 of 79 tumours >0.5 ml in volume were missed [24],

although others have had more success by using different criteria. In particular, by identifying areas of “ground glass-like, homogenous low signal intensity areas,” Ikonen et al. achieved a sensitivity

**Table 3 – Studies using magnetic resonance spectroscopy to detect intraprostatic disease, with whole-mount correlation**

Study	No. of patients (no. of tumours assessed) No. of segments used for analysis	Study design	Sensitivity and (specificity)
Scheidler 1999 [19]	53 (155 positive segments) 6 segments	Incidental cancers included, but TZ cancers excluded Retrospective	63% (75%) or 86% (46%) depending on criteria Up to 95% (41%) (MRI or spectroscopy positive) 52% (91%) (both positive)
Wefer 2000 [38]	47 (162 positive segments) 6 segments	Incidental cancers included, but TZ excluded Prospective	76% (57%) spectroscopy 50% (82%) for histology 67% (69%) for T2 sequences
Coakley 2002 [54]	37 (51)	Incidental cancers included, but TZ and tumors <0.5 ml excluded Prospective	69% and 76% for MRI and spectroscopy combined (2 readers)
Zakian 2003 [39]	16 (16)	Only TZ tumours >1 cm Retrospective	56% (100%) (by one voxel having a choline- only peak)
Akin 2006 [26]	148 (223) 6 segments	Only TZ tumours, all sizes included Retrospective	75% (87%) reader 1 80% (78%) reader 2

All used endorectal coils.  
MRI = magnetic resonance imaging; TZ = transitional zone; PZ = peripheral zone.

of 55% with a specificity of 67% for cancers in the anterior half of the gland [25]. A recent paper has suggested that homogenous low signal, lenticular shape, and invasion of the anterior fibromuscular stroma can all be used to identify transitional zone cancer [26].

### 3.1.1. MRI with contrast

Initial studies on the use of MRI contrast for the detection of cancer used delayed spin-echo T1 sequences and suggested that it did not improve on T2-weighted sequences [27]. Later studies using a variety of dynamic imaging techniques have shown that, similar to the behaviour of breast tumours, the enhancement curve of prostate tumours is different to both peripheral zone and BPH, although there is considerable overlap in the latter [15,16,28,29]. The explanation is a difference in microvessel density and permeability within the tumour [30].

It is possible to calculate many different parameters for the enhancement curves according to multicompartiment models [15,31], but the most reliable finding is that prostate tumours enhance earlier than peripheral zone, and in many cases earlier than BPH [28], with the best time for discrimination occurring 30–90 s after injection [15,16,28,29,31], and the differences becoming less marked after 3–5 min. Dynamic sequences are always a compromise between spatial and temporal resolution, and it is not yet clear which of these two factors is most important [16].

The results for studies using dynamic contrast-enhanced MRI with whole-mount histology correlation are shown in Table 2. Jager et al were the first to significantly improve detection of cancer, increasing their sensitivity from 57% using T2-weighted sequences alone to 73% when dynamic contrast-enhanced sequences were used, with no reduction in a specificity of 80% [17]. Schlemmer et al. confirmed this finding, with an increase in sensitivity from 79% to 89% for peripheral lesions [32], and several studies using biopsy specimens for correlation have demonstrated high sensitivities [33,34].

As with T2-weighted sequences, findings in the transitional zone vary, with one study detecting tumour with high specificity in 37% [35] and another, using biopsy correlation, showing sensitivity and specificity of 68% and 86%, respectively, changing to 96% and 46% if the method of analysis was different [33]. Muramoto's group recently showed a sensitivity of 100% and specificity of 85% using a dual-echo dynamic contrast technique to measure mean enhancement gradient in 34 patients who had a

mix of BPH and prostate cancer [36]. It would be fascinating to see if these results could be replicated in a prospective study using radical prostatectomy specimens for correlation.

### 3.1.2. MR spectroscopy imaging

Prostate cancers usually have an increased choline and reduced citrate content. MR spectroscopy imaging (MRSI) can characterise this metabolic change in voxel sizes as small as 0.24 ml (and potentially less in 3T magnets), but Coakley points out that, assuming a spherical tumour and the same centre, the volume of cancer required to completely fill a voxel and avoid partial volume effects is nearly double this, a finding that has implications for the ability of spectroscopy to detect small tumours [37].

The studies that have used whole-mount specimens for correlation are shown in Table 3. Scheidler et al. showed that spectroscopy alone is less sensitive than T2-weighted MRI in the detection of cancer in the peripheral zone, but that it was more specific [19]. The largest study is by Wefer et al. who found a higher sensitivity for spectroscopy (76%) than T2-weighted sequences (67%), but who noted that spectroscopy was less specific [38]. The difference in these findings can be almost completely explained by differences in the criteria used to define cancer, and whether "possible" cases are included. Both authors find that the two techniques are complementary and that if the criterion for cancer is positivity on both, specificity can be improved considerably. Zakian et al. showed that identification of a voxel with choline as the only detectable peak might detect half of transitional zone cancers with high specificity [39], and further recent work by the same group has shown that spectroscopy can be used to detect transitional zone cancers with sensitivity and specificity around 80% [26], an impressive result that exceeds the results for T2 and contrast-enhanced techniques in this part of the prostate.

Spectroscopy may be particularly useful for the detection of cancer in glands previously treated with ablative techniques, where posttreatment change obscures cancer on conventional MRI and ultrasound. One study of 25 patients showed that MRSI identified all recurrent foci of tumour that were found on prostate biopsy [40], and in a recent series both spectroscopy and contrast-enhanced MRI were better than biopsy at detecting recurrent disease after radiotherapy [41], although the specificity for the former (78%) was lower than for the latter (>90%), with several areas of benign change being interpreted as cancer.

### 3.1.3. Emerging MRI techniques

Apart from choline and citrate, several potential metabolic markers for prostate cancer can be measured spectroscopically [42], although none has yet been demonstrated to be clinically useful. The emergence of 3T and higher field strength scanners will improve spectral resolution, as well as improving anatomic detail and temporal resolution in contrast-enhanced MRI. This is likely to improve, if not revolutionise, results [43].

Several studies have shown an decreased apparent diffusion coefficient (ADC) in peripheral zone prostate cancer [44,45], and in contrast to initial findings showing poor discrimination [44], transitional zone tumours also have a significantly lower ADC than their surroundings [46]. New work is showing promising results in the transition zone, and one group suggests that varying the b factor can increase tumour conspicuity [47], but prospective data on sensitivity and specificity of the technique are still awaited.

Blood oxygen level dependent (BOLD) imaging uses T2\*-weighted imaging to detect the different magnetic susceptibility of oxyhaemoglobin and deoxyhaemoglobin and has been used both to image a variety of human tumours [48]. A recent report, using whole-mount prostatectomy for correlation and carbogen breathing to determine enhancement showed a significant difference between tumour and normal peripheral zone, although the overlap was large [49]. An interesting finding is that the central zone almost always enhanced strongly and that cancers rarely did, raising the tantalising possibility that BOLD might detect tumours in the transition zone where other techniques have failed.

### 3.2. Tumour burden

Many studies confirm the expected finding that it is easier to detect larger tumours than small ones. Ikonen et al. showed that detection on T2-weighted MRI is highly dependent on size: only 5% of tumours <5 mm in diameter were detected compared with 89% of those >10 mm [25]. Ellis et al. confirm that tumours <1 cm in diameter are much less likely to be detected, but find no significant correlation between detection and volume above this size [24]. Nakashima detected 22 of 84 tumours <1 cm in diameter and 87 of 102 >1 cm using contrast-enhanced MRI [50].

Once tumour has been detected, estimates of its volume show considerable inaccuracy: Kahn et al. [51] showed an average 40% discrepancy for unenhanced MRI, and others have had similar

findings [20,52,53], with overestimates occurring a little more often than underestimates. The studies that have specifically addressed this question are summarised in Table 4. Although accuracy is greater for large tumours, there are many examples of cancer >5 ml in volume being underestimated by at least 50%.

Jager et al. showed a small improvement with dynamic contrast-enhanced MRI, with the proportion of volumes within 25% of actual increasing from 31% to 42% with contrast (the difference was not statistically significant). Finally, Nakashima's study (with 95 patients) used contrast-enhanced MRI and showed a good correlation between radiologic and pathologic findings ( $r = 0.84$ ), with few outliers compared to the studies using T2-weighted imaging.

It is uncertain whether spectroscopy will improve accuracy, with one study showing a range of 3% to 433% in the tumour volume on spectroscopy compared to histology [54], although results using spectroscopy were better than those obtained using T2-weighted sequences.

### 3.3. Tumour aggressiveness

Tumour size at diagnosis correlates with grade, but not strongly [55]. This may, in part, explain the finding that higher grade cancers are more likely to be detected at spectroscopy (44% for Gleason 3+3 tumours in one study, increasing to 88% for tumours  $\geq 4+3$  [56]), but the metabolic change becomes significantly more marked with increasing grade and it is likely that this is a genuine finding. Interestingly, Ikonen et al. found a similar difference in detection using unenhanced MRI (43% for Gleason 4, 94% for Gleason 10) [57], but did not attempt to correct for the influence of the size of the lesion. Ellis et al., in a large series [24], confirmed that high-grade tumours are more likely to be detected on T2 sequences, with a multivariate analysis (the only one of its kind so far attempted) showing significantly increased odds ratios of 1.5 and 2.7 for detection of Gleason score 5-7 and 8-10, respectively, compared to lesions of score  $\leq 4$ . Recent work has shown that carcinoma in situ is difficult to detect on both T2- and dynamic-enhanced series [58], confirming the impression that conspicuity increases with grade.

The finding that microvessel density correlates with Gleason grade [59] suggests that there may be an association between the shape of the dynamic MR enhancement curve and Gleason score. Schlemmer et al. found that the contrast exchange rate constant correlates moderately with microvessel

**Table 4 – Studies assessing the accuracy of tumour volume estimation using magnetic resonance imaging**

Study	No. of patients (tumours detected)	Type of study and exclusions	Imaging method	Volume findings
Sanchez-Chapado 1997 [76]	20 (19)	Incidental cancers not included	Unenhanced (endorectal and pelvic phased array)	$r = 0.84$ MRI volume generally smaller than histologic. Histologic volume = (MR volume*0.51) + 2.07
Ponchiatti 1999 [77]	25 (25)	Incidental cancers not included	Unenhanced (endorectal)	$r = 0.94$
McSherry 1991[78]	25(25)	Incidental cancers not included	Unenhanced (body coil)	$r = 0.44$ ; no significant correlation
Quint 1991 [20]	26 (20)	Incidental cancers not included	Unenhanced (body coil)	5 tumours underestimated by >50%, 7 overestimated by >50%
Sommer 1993 [52]	20 (20)	Incidental cancers not included	Unenhanced (body coil)	$r = 0.81$ Histologic volume = (0.3 + MR volume*1.47)
Jager 1996 [53]	34 (44)	All cancers included	Unenhanced (endorectal)	7 tumours: error <25% 19 overestimated by >25% 8 underestimated by >25%
Lencioni 1997 [79]	24 (24)	Incidental cancers not included	Unenhanced and nondynamic contrast-enhanced (endorectal, 0.5T)	$r = 0.944$ Error >1 cm <sup>3</sup> in only 3 cases. MR overestimates in 58%, underestimates in 42%
Coakley 2002 [54]	37 (51)	Incidental cancers included, but TZ excluded	Unenhanced and spectroscopy (endorectal and pelvic phased array)	MRI: $r = 0.21$ or $0.49$ for >0.5-ml tumours Spectroscopy: $r = 0.44$ or $0.59$ for >0.5-ml tumours Both: $r = 0.32$ or $0.55$ for >0.5-ml tumours
Nakashima 2004 [50]	95 (116)	Incidental cancers included	Unenhanced and contrast-enhanced (endorectal and pelvic phased array)	$r = 0.84$ Histologic diameter = (0.1+ MR maximum diameter*0.97)

TZ = transitional zone;  $r$  = correlation coefficient; MRI = magnetic resonance imaging.

density ( $r = 0.62$ ) but that only the time to onset of the enhancement curve was significantly different with high-grade compared to low-grade tumours, a finding likely to be of limited clinical potential. Padhani et al. failed to find a correlation between enhancement parameters and Gleason grade in a study using prostate biopsies for correlation [15].

## 4. Discussion

### 4.1. Summary of results

Even using similar techniques, the sensitivity of MRI in the detection of prostate cancer varies enormously, from 37% to 96% with unenhanced MRI (Table 1), depending on the criteria for a positive result and exclusion of incidental cancers, “insignificant” disease (itself open to debate [34,60]), and tumours in the transitional zone. Such differences make comparisons between techniques almost impossible unless they are performed by the same authors in the same group of patients. The few studies that have attempted to quantify the benefit of adding a new technique to standard unenhanced sequences are therefore particularly valuable—notably an increase of 16% in sensitivity with dynamic contrast-enhanced sequences [53] and similar improvements in either sensitivity or specificity with spectroscopy [38].

Although retrospective, recent data suggest that spectroscopy can also detect about 80% of transition zone tumours [26]. Diffusion-weighted imaging and possibly BOLD (with the former considerably faster and cheaper to perform) are promising techniques and may add further, independent information, in particular in the transition zone, but we cannot yet quantify how much. Overall, it seems reasonable to hope that an approach using T2 sequences, dynamic contrast enhancement, spectroscopy, and possibly diffusion imaging will achieve sensitivity for significant cancers of around 90%, with acceptable specificity, but no group has attempted such a study, let alone a multivariate analysis. The results showing better detection for aggressive, large lesions suggest that cancers missed would be of limited clinical significance and allow a cautious optimism about the potential adequacy of MRI to exclude cancer in a screening setting.

### 4.2. Methodologic issues

The assessment of specificity—and by extension the likely positive and negative predictive values—of MRI in prostate cancer remain a problem. First, there

is an inevitable, difficult-to-quantify, group selection bias; because it is impossible to perform radical prostatectomy on men without prostate cancer, estimates of specificity are usually from an analysis of uninvolved sectors in men who have already been diagnosed with the disease. An alternative method would be a prospective study of MRI, with extensive transperineal mapping biopsy for histologic correlation in a group of men suspected of having cancer, but this has not yet been performed.

A further problem with using whole-mount correlation to estimate specificity is that results depend on the number of sectors used for analysis, for the following reason. Imagine a small low-signal area that is not cancer but that will be a false-positive diagnosis according to all authors. If the prostate is divided into halves, one of two results will be a false positive, and if into octants, one of eight. The figures for specificity, that is, true negatives/(true negatives + false positives), will be much better using the octant technique. This accounts for the very poor specificity in the study by Hricak et al. study using halves [21] and better figures in a study using decants [25].

Current data estimating the ability of MRI to predict transrectal biopsy results are free of group selection bias, and although the histologic correlation is not ideal, their estimates of specificity and negative predictive value are useful. Vilanova et al. showed a specificity of 76% and a sensitivity of 70% for prediction of positive biopsy using unenhanced MRI in a group of 81 patients with PSA levels ranging from 4 to 20 [61], and Comet-Battle et al. had similar results, with sensitivity of 80% and specificity of 76% using sextant biopsy for correlation [62]. The work by Hara et al. [34] using dynamic contrast enhancement is impressive, with a sensitivity of 93% and a specificity of 96% in a group of 90 patients with PSA levels <10 ng/ml. However, this excellent specificity must be interpreted in the context of the methodology of the study; the prostate was divided into 42 “sub-sectors” and the calculation of specificity, as described above, will be affected by this. Another group has shown that in a set of patients with a single negative set of biopsies, spectroscopy can increase the sensitivity for the prediction of positive biopsy without reducing specificity [63].

Debate continues about the need for an endorectal coil. The improved signal-to-noise ratio certainly improves resolution, with the addition of a pelvic phased array minimising distortion and flare artefact [53,64], and endorectal coils are almost always used for spectroscopy in 1.5 T systems. There are two meta-analyses of staging (rather than cancer detection) accuracy, one showing better results with

endorectal coils [1], the other the opposite [2]. The only data available for cancer detection accuracy are Hricak's from 1994 [21], showing a slight (but not significant) benefit with an endorectal coil. Although it is likely that endorectal coils give better results in 1.5 T systems, they are expensive and may not be necessary in 3 T magnets, an important finding if MRI is to be used for screening [65].

#### 4.3. Implications and future research

No one has yet advocated the replacement of biopsy by MRI, but the study by Wefer et al. indicates that in some cases it might be possible [38] (Table 1). They directly compared the sensitivity of unenhanced MRI, spectroscopy, and sextant biopsy in localising cancer to a specific sextant and found both imaging techniques more sensitive than biopsy in the detection of cancer. The authors state that "when high sensitivity is required, MR spectroscopic imaging is significantly better than biopsy," a finding recently confirmed by another study using T2 sequences and spectroscopy [66]. At the least this suggests that MRI will be useful in the follow up of focally or incompletely treated glands. Onik followed a series of patients having prostate hemi-ablation with repeated biopsies [8], but might MRI not be superior, or at least eliminate the need for rebiopsy in patients without areas suspicious for cancer? More speculatively, it suggests that MRI may be a superior modality for planning focal therapy, where only the cancer and a margin of normal prostate are treated. Once the diagnosis of cancer has been made, treatment might be directed at all suspicious areas on MRI. False positives in this setting are relatively unimportant if they do not markedly increase morbidity, but it is vital that the test be sensitive to ensure that cancers are not missed.

If MRI can detect most cancers, the argument for scanning before biopsy in intermediate-risk patients becomes stronger. Although more expensive (many patients without cancer will be scanned), this has important advantages. First, biopsy artefact from haemorrhage or oedema is eliminated. This undoubtedly makes T2-weighted scans more difficult to interpret and overestimates cancer, a problem that is only partly mitigated by the use of spectroscopy [67].

Second, targeting biopsies should increase the cancer detection rate. Although biopsies targeted at abnormal areas on MRI have a high likelihood of being positive [34,68,69], there are not yet convincing data to show that prospective MRI increases overall biopsy detection of prostate cancer, probably

because a study of sufficient power has not yet been performed. Emerging techniques for image fusion may play a part by improving the accuracy of ultrasound-guided targeting using the MR scanning data [70], whether by pure image processing or coregistration using a positioning marker on the ultrasound probe. Alternatively, several authors have reported MR-guided prostate biopsy [71], but these are time-consuming techniques and will have to demonstrate clear advantages before their cost and complexity can be justified.

Third, a negative MRI result should increase the negative predictive value of a set of negative biopsies and might eliminate the need for rebiopsy. Here figures for negative predictive value become relevant, and the biases inherent in studies using the cancer-free parts of radical prostatectomy specimens particularly problematic; the best data are probably from groups that have used MR scanning before transrectal biopsy. Comet-Battle et al. showed that in a screening population of 92 patients a negative unenhanced MR scan had a negative predictive value for cancer on subsequent transrectal biopsy of 91% [62]. This is comparable to figures of around 85% negative predictive value for negative octant biopsy (approximately 15% of patients with a negative initial biopsy will have a positive result on rebiopsy [3]). Perrotti et al. found in a group of 35 patients with previous negative biopsies that a low probability MR scan had a negative predictive value of 94% for repeat biopsy, with positive scans having a 40% positive predictive value [68]. These results suggest that a negative MR scan is as reassuring for absence of cancer as a negative repeat sextant biopsy. With the addition of contrast and spectroscopy it should be even more so.

A study of all established and practical MR sequences (T2, dynamic-enhanced, spectroscopy, and diffusion) has not yet been performed and must be one of the major goals of research in this field. It might answer two questions. First, what proportion of cancers can be detected using the four sequences combined? For this study histologic correlation using radical prostatectomy specimens would be ideal. Second, what is the negative predictive value of a scan that is normal using each sequence? Are some cancers invisible regardless of the modality used, and are these cancers likely to be of significant size or grade? To answer this question properly a prospective study in a screening population would be necessary, with correlation by biopsy mapping of the prostate and long-term follow-up. In both cases the multivariate analysis would be fascinating.

## 5. Conclusions

The addition of dynamic contrast enhancement, spectroscopy, and diffusion-weighted imaging to standard T2-weighted sequences is practical and has the potential to improve MRI of the prostate to the point where it has several new applications: the targeting of biopsies, monitoring of disease burden both during active surveillance and after focal therapy, and excluding cancer in patients with a raised PSA level. The precise benefit of each technique in a multisequence scan remains to be quantified.

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### Editorial Comment

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Reliably diagnosing early prostate cancer is a first step in improving the outcome of the management of this disease.

Magnetic resonance imaging (MRI) is accepted as the best imaging modality for detection and staging prostate cancer due to its excellent depiction of the zonal anatomy and the relationship of the prostate gland to the surrounding structures in the pelvis. Moreover, MRI is the most promising imaging modality and it has the greater potential for technical improvement.

Endorectal 1.5 T MR imaging combined with spectroscopic imaging has already demonstrated a potential for improved diagnosis and staging of prostate cancer [1].

The authors summarise the current data on the efficacy of MRI at detecting and characterising cancer within the prostate by analysis of the different MR sequences currently available. In agreement with the authors, we think that the routine use of spectroscopy, dynamic contrast-enhanced and diffusion sequences could increase significantly the sensitivity and the specificity of the T2-weighted sequences in the depiction and characterization of the prostate cancer in the peripheral and the transition zones.

In the last year, we have been using routinely, in our institution, endorectal MR imaging, spectro-

scopy, dynamic contrast enhancement, and diffusion weighted images for the detection of prostate cancer. We have found that the evaluation of metabolites (choline, citrate, and polyamines) at spectroscopy, and the kinetics of gadolinium enhancement (fast and high contrast enhancement and contrast de-enhancement) by the lesion can be of further value, while diffusion weighted images did not add any contribution.

Moreover, 3T MR units are becoming more widely available and offering higher signal-to-noise ratios and increased temporal, spatial and spectral resolution [2–4].

Thus it is right to predict that the 3.0 T MR scanner with adequate endorectal coil will very soon offer a significant improvement in conventional MR images and also in spectroscopic analysis, causing a significant impact in the evaluation of patients with prostate cancer.

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