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Combined Magnetic Resonance Imaging and Magnetic Resonance Spectroscopy Imaging in the Diagnosis of Prostate Cancer: A Systematic Review and Meta-analysis

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Abstract

Context: Magnetic resonance imaging (MRI) combined with magnetic resonance spectroscopy imaging (MRSI) emerged as a promising test in the diagnosis of prostate cancer and showed encouraging results.

Objective: The aim of this systematic review is to meta-analyse the diagnostic accuracy of combined MRI/MRSI in prostate cancer and to explore risk profiles with highest benefit.

Evidence acquisition: The authors searched the MEDLINE and EMBASE databases and the Cochrane Library, and the authors screened reference lists and contacted experts. There were no language restrictions. The last search was performed in August 2008. Evidence synthesis: We identified 31 test-accuracy studies (1765 patients); 16 studies (17 populations) with a total of 581 patients were suitable for meta-analysis. Nine combined MRI/MRSI studies (10 populations) examining men with pathologically confirmed prostate cancer (297 patients; 1518 specimens) had a pooled sensitivity and specificity on prostate subpart level of 68% (95% CI, 56–78%) and 85% (95% CI, 78–90%), respectively. Compared with patients at high risk for clinically relevant cancer (six studies), sensitivity was lower in low-risk patients (four studies) (58% [46–69%] vs 74% [58–85%]; $p > 0.05$) but higher for specificity (91% [86–94%] vs 78% [70–84%]; $p < 0.01$). Seven studies

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examining patients with suspected prostate cancer at combined MRI/MRSI (284 patients) had an overall pooled sensitivity and specificity on patients level of 82% (59–94%) and 88% (80–95%). In the low-risk group (five studies) these values were 75% (39–93%) and 91% (77–97%), respectively.

Conclusions: A limited number of small studies suggest that MRI combined with MRSI could be a rule-in test for low-risk patients. This finding needs further confirmation in larger studies and cost-effectiveness needs to be established.

Keywords

Prostate cancer; MR imaging and MR; spectroscopy imaging; Diagnosis

1. Introduction

In 2007, the American Cancer Society indicated that prostate cancer is the most commonly diagnosed cancer in the United States, and with an estimated 27 050 prostate cancer-related deaths, prostate cancer is the second leading cause of cancer-related fatality [1]. This is described in a more meaningful way by Walsh et al [2], who wrote that approximately one out of six men in the United States received a diagnosis of prostate cancer in his lifetime, and 1 out of 34 men died from it. Current statistics show that prostate cancer incidence rates are decreasing since 1992, after reaching a peak in the mid-1990s due to the implementation of the prostate-specific antigen (PSA) screening in the late 1980s [3]. Whether this is a sustained decrease is questionable. Data on demographic changes clearly show that the population of the developed world is aging rapidly. For example, Yancik et al predicted a doubling of the population at the age of ≥ 65 yr by the year 2030 in the United States [4]. Because almost two-thirds of new prostate cancer cases occur in the elderly, it can be expected that prostate cancer incidence will rise again. British researchers predict that cancers of the prostate gland could overtake lung cancer as the most common form of the disease in Britain within 20 yr [5].

Arguably, the continuing increase in prostate cancer detection may be attributable to increased screening through PSA testing. However, both in screening and diagnostic work-ups, PSA levels appear to be of low accuracy: using a threshold of <4 ng/ml one misses 15% of prostate cancers [6] and only 33% of patients with PSA values between 4 ng/ml and 10 ng/ml actually have cancer [7]. Moreover, rule-in diagnosis with transrectal needle biopsy has been shown to be remarkably inaccurate [8–10], with a cancer-missing rate of up to 20% using a traditional sextant biopsy schema; indeed, an approach with a 10- to 12-needle prostate biopsy schema leads to a 30% improvement in cancer detection [11]. Over the last decade, imaging technologies, such as combined magnetic resonance imaging (MRI) and magnetic resonance spectroscopy imaging (MRSI) have shown promise for improving the detection and characterisation of prostate cancer. However, these technologies have not yet entered into routine clinical care, and their clinical role remains debated.

The aim of this systematic review and meta-analysis was to establish the current role of combined MRI and MRSI in the diagnosis of prostate cancer and to explore risk profiles with the highest benefit.

2. Evidence acquisition

We used methods recommended by the Cochrane Methods Group for the Systematic Review of Screening and Diagnostic Tests [12].

2.1. Identification of studies

We searched MEDLINE, Cochrane Library, and EMBASE to identify diagnostic studies evaluating the accuracy of combined MRI and MRSI in the diagnosis of prostate cancer. The last search was performed in August 2008. Checking the reference lists of included studies and contacting experts in the field complemented electronic searches. The detailed search strategy for MEDLINE can be found in the Appendix.

2.2. Study selection

We included studies if they compared MRI in combination with MRSI results and potentially other imaging methods (eg, diffusion and contrast-enhanced MRI) with the results of prostate biopsies or prostatectomy specimens in patients with either previously diagnosed or suspected prostate cancer. The minimum requirement for inclusion was enough information to fill the two-by-two table. All papers considered potentially eligible by one of the two observers were ordered, and a checklist was used to determine final eligibility. Disagreements about inclusion or exclusion were resolved by consensus.

We initially included 31 studies (Fig. 1) [8,13-42]. For the meta-analysis we excluded six studies (two with additional diffusion-weighted MRI [23,28], one with additional diffusion-weighted and contrast-enhanced MRI [30], and three others without use of an endorectal coil [24,32,39]) involving a standard MRI/MRSI protocol defined as MRI using an endorectal coil and combined with MRSI on a 1.5 Tesla MR scanner (see Table 1 for technical details of imaging methods). We also excluded seven studies using MRI just as an anatomical reference for MRSI-interpretation [17,18,26,27,36,41,42] without using the morphological information from MRI in the interpretation (see Fig. 2 for selection details).

We grouped the remaining 18 studies first into reports based on cancer status (proven cancer vs suspected cancer) at the time of imaging and secondly into reports based on degree of pathologic correlation (cancer anywhere in the prostate vs a more exact pathologic correlation, eg, hemiprostate, sextant). Typically, studies including men with proven cancer were those studying a part of prostate as single pathologic correlative, and studies including men with suspected cancer were those using the whole prostate as a single pathologic correlative. All but two studies followed this pattern [16,31]. For meta-analysis we excluded two further studies: the study of Shukla-Dave et al [31] because they compared significant versus insignificant cancer instead of cancer versus noncancer and the study of Costouros et al [16] because it focused on developing a MRSI scoring system and did not measure accuracy of cancer detection (Fig. 2). Therefore, the final meta-analysis contained seven reports on men with suspected prostate cancer [8,13-15,37,38,40] and 10 populations (nine studies) analysing correlations of parts of the prostate within men with proven cancer [19-22,25,29,33-35]. The study by Kaji et al [22] contained two separate populations (with and without previous hormone treatment). We treated them as two separate studies. We excluded three further studies [43-45] because they used a diagnostic case-control design which is prone to show overly optimistic accuracy [46].

2.3. Data extraction and assessment of methodological quality

The methodological quality of all eligible papers was assessed based on published recommendations [46]. Quality assessment involved scrutinising the methods of data collection and patient selection and descriptions of the test and reference standard. Studies were considered to be prospective if the study protocol preceded data collection. Blinding was fulfilled if the person making the definite imaging diagnosis did not know the results of the pathologic examination. One reviewer assessed papers and extracted data using a standardised form (the data extraction form is available on request). This reviewer contacted a second reviewer if an item could not be clearly addressed. Decisions were based on a consensus

between the two reviewers. Papers published in languages other than English, German, or French were translated.

2.4. Risk stratification

We *a priori* defined a set of five parameters (age, PSA level, Gleason score, number of previous negative prostate biopsies, and rate or dimension of detected cancer) to classify study populations into low- or high-risk groups for clinically relevant prostate cancer. For example, we classified patients into the low-risk group if PSA values were low (<10 ng/ml) or if previous needle biopsies had been negative. We classified men >65 yr presenting with a Gleason score >6 and larger tumours (diameter >5 mm) as determined in the prostatectomy specimen or a high positive core rate ($>10\%$) as high risk. The classification was performed separately by two urologists and discrepancies—often due to missing data especially concerning tumour dimensions or positive core rate—were discussed and resolved by consensus.

2.5. Index test

For each study we extracted details about the MR scanner field strength, use of an endorectal or superficial body coil, spectroscopic acquisition parameters and metabolic cut-off values for a positive result. In three studies that assessed different cut-off values, we chose the highest available (>3 SD higher than normal) to optimise the false positive (FP) rate. If studies contained test performance results for experienced and inexperienced spectroscopy readers separately, we only used the data of the experienced examiners. Two urologists separately classified the patient cohorts based on the studies' inclusion criteria. Discrepancies were discussed and resolved by consensus.

2.6. Sensitivity, specificity, and accuracy calculation

We calculated the sensitivity and specificity of the combined positive or negative MRI/MRSI result on patient level within the seven studies including patients with cancer suspicion. In the remaining nine studies (including 10 populations) we calculated sensitivity, specificity of the combined positive or negative MRI/MRSI result not on a patient level but on a prostate subpart level. Unlike studies assessing test performance on patient level, these studies match the cancer status (present/absent) of a prostate subpart with the test result (positive/negative) of that corresponding part of prostate.

2.7. Statistical analysis

For each study, we constructed a two-by-two contingency table consisting of true-positive (TP), false-positive (FP), false-negative (FN), and true-negative (TN) results. For analysis, we called a result TP if both MRI and MRSI were concordant and were in agreement with the pathological findings. We calculated sensitivity as $TP/(TP + FN)$ and specificity as $TN/(FP + TN)$. We plotted results from individual studies in receiver operating characteristic (ROC) space and estimated summary ROC curves using a unified model for meta-analysis of diagnostic test accuracy studies [47]. We also indicated on the ROC figures the confidence and prediction regions. The advantage of doing this is that it provides estimates of average sensitivity and specificity across studies and that it can be used to provide a 95% confidence region for this summary point and prediction regions within which we expect the sensitivity and specificity of 95% of future studies to lie. We performed stratified analyses for studies reporting on cancer status in terms of proven and suspected cancer at the time of the MRI/MRSI exam. In these subgroups we also assessed differences in sensitivity and specificity between low- and high-risk patients in respect to clinically relevant cancer. We pooled results if at least four studies per stratum were available. Following recent recommendations we refrained from pooling positive and negative likelihood ratios because these are sensible parameters to analyse statistically in a meta-analysis [48]. Instead, we calculated the likelihood

ratios from the estimated pooled sensitivities and specificities. All analyses were done using the Stata statistical software package v.9.2 (College Station, TX, USA).

3. Evidence synthesis

3.1. Identification of studies and study quality

Fig. 1 summarises the process of identifying and selecting studies. Thirty-one studies met our primary inclusion criteria. Study characteristics are shown in Table 2.

3.1.1. Study quality—Twelve out of 31 reports had a prospective design [8,15,17-19,^{24,26,28,32,37,38,40}], and 10 studies had a retrospective design [13,14,16,21,^{22,29,31,34,39,42}]. The remaining nine studies did not report details of data collection [20,23,25,30,^{33,35,36,41,49}]. Ten studies had consecutive patient enrolment [8,17-19,29,^{32,37,38,40,42}], and two studies had a case-control design [23,30] comparing test performance among healthy subjects and men with suspected [23] and diagnosed [30] prostate cancer. Seven studies reported that the radiologist was unaware of histologic findings [13,14,16,17,31,37,39]. In one study the most experienced radiologist had 2 yr of experience reading spectroscopic data [49], and in two other studies the most experienced radiologist had 3 yr of experience [18,34]. In 10 studies the most experienced radiologist had at least 4 yr of experience [13,14,16,17,^{21,25,28,31,39,42}]. Ten studies did not specify years of experience but described radiologists as experienced or dedicated [8,19,24,26,32,35-38,40]. Eight studies did not report on the radiologists' level of experience [15,20,22,23,29,30,33,41]. Seven studies reported the exclusion of patients after the imaging exam due to poor imaging quality [13,14,21,26,29,35,36]. The number of excluded patients varied substantially, ranging from 2% [35] up to 41% [21]. The mean percentage of excluded patients within these seven studies was 17%. Ten studies reported the exclusion of prostate subparts after imaging due to poor imaging quality [17,18,21,25,^{28,29,33-35,42}]. The number of excluded prostate subparts varied substantially from 2% [33] up to 73% [21]. The median percentage of excluded prostate subparts in these nine studies was 17%. All studies identified the presence of prostate cancer based on a histologic analysis of tissue. In 11 studies [17,18,21,25,^{29,31,33-35,41,42}] the tissue was obtained at prostatectomy; 17 studies used tissue obtained at prostate needle biopsy [8,13,15,16,^{20,22-24,26,28,32,36-40,49}]; and 2 studies used both tissue from prostatectomy if available or from needle biopsy [14,30]. One study relied on routine histologic reports if structured histologic assessments had not been performed within the study (Table 2) [19].

3.2. Characteristics of the study population

Study populations and settings were heterogeneous (Table 3). The mean age of participants ranged from 56 yr to 72.6 yr; mean PSA level ranged from 5.9 ng/ml (one study [31] reported a median value of 5.4) to 66.4 ng/ml; and mean Gleason scores ranged from 5.3 to 7. Insufficient description of these variables—age, PSA level, and Gleason score—was found in 15 studies [13,14,22,24-^{26,30,32,34-37,41,49}]. Sixteen studies enrolled patients with previously diagnosed prostate cancer [17-22,25,28-^{31,33-35,41,42}]. For imaging interpretation, these studies used the prostatectomy specimen as the standard of reference, with correlation to a specific region of the prostate. Fifteen studies enrolled patients with suspected prostate cancer [8,13-16,23,^{24,26,32,36-40,49}], seven of them involved patients with a prior negative biopsy [8,16,26,37,38,40,49]. For imaging interpretation, these studies used the biopsy as the standard of reference without correlation to a specific region of the prostate (Table 2).

3.3. Pooled sensitivity and specificity

3.3.1. Confirmed versus suspected prostate cancer at the time of imaging—Table 4 shows for each study population the number of TPs, FPs, FNs, and TNs, as well as sensitivity and specificity. The accuracy parameters in studies assessing patients with suspected cancer

are based on patient level, and in studies assessing patients with previously diagnosed cancer they are based on classification of prostate subpart level. The pooled mean sensitivity of 10 two-by-two tables investigating men with confirmed cancer using a cancer threshold value for MRSI of >3 SD deviations from normal (choline + creatinine)/citrate, was 68% (95% CI, 56–78%) and specificity was 85% (95% CI, 78–90%) (Fig. 3). The corresponding positive and negative likelihood ratios were 4.5 and 0.37. The pooled sensitivity and specificity of five studies investigating men with suspected prostate cancer was 82% (95% CI, 59–94%) and 88% (95% CI, 80–95%) (Fig. 4). The corresponding positive and negative likelihood ratios were 6.8 and 0.15.

3.4. Risk stratification in the confirmed cancer group

For the confirmed prostate cancer studies we performed a risk stratification for patient cohorts with low and high pretest probability of having clinical relevant cancer. Low-risk patients had lower sensitivity [19,21,29,33] (58% [46–69%] vs 74% [58–85%]; $p > 0.05$) but higher specificity (91% [86–94%] vs 78% [70–84%]; $p < 0.01$) than high-risk patients [20,22,25,34,35] for prostate cancer detection (Figs. 5 and 6).

3.5. Risk stratification in the suspected cancer group

We were unable to calculate pooled estimates for the high-risk group. In the low-risk group [8,15,37,38,40] sensitivity was 75% (39% to 93%), and specificity was 91% (77% to 97%) respectively (Fig. 7).

4. Discussion

This is the first meta-analysis examining the combined diagnostic value of MRI and MRSI in the work-up of prostate cancer patients. We found limited evidence indicating a potential role of this technique in the future. At this stage clinical implications of our results remain limited for several reasons. Studies tended to be of limited size, applied different methods, and investigated a broad spectrum of patients. Moreover, study quality and reporting was limited. For example, only seven studies reported that radiologists were blinded for pathological information, and only few gave a detailed description of clinically relevant information of enrolled patients such as PSA levels and Gleason scores. Finally, we found substantial variation in the way spectroscopy findings were used for the identification of prostate cancer indicating a lack of consensus regarding diagnostic criteria and thresholds.

4.1. Our findings in context of existing literature

We found two systematic [50,51] and two nonsystematic reviews [52,53]. In 2002 Engelbrecht et al [51] made a first systematic attempt to summarise the clinical value of the MRI in local staging of prostate cancer. The study also assessed the value of MRSI in that field but failed to perform a meta-analysis due to the limited number of available studies. Their search was limited to the year 2000, and they only searched two databases. Moreover, all but three studies assessing the diagnostic value of MRSI in combination with MRI were published after the year 2000. The other meta-analysis investigated the diagnostic value of MR spectroscopy in the diagnosis of prostate cancer [50] but not the value of combined MRI/MRSI.

4.2. Strength and limitations

Our review was based on thorough literature searches and careful data extraction, and included assessments of the methodological quality of diagnostic test accuracy studies. This is the first study performing a meta-analysis in this diagnostic field. We modelled sensitivity and specificity by simultaneously applying a novel and valid meta-analytic method, which incorporates both within- and between-study variance [47]. In addition we performed stratified

analyses to examine variability of results between subgroups of patients. Reporting of salient clinical features was suboptimal in some of the studies. This could have introduced bias in our results. A further limitation is that many studies used prostate needle biopsy cores as the reference method, which is considered to be a poor gold standard due to the high rate of missing. Moreover, nine studies matched the cancer status (present/absent) of a prostate subpart with the test result (positive/negative) of that corresponding part of prostate to calculate sensitivity and specificity assuming that these figures represent a fair proxy for test performance in clinical practice. Also, due to the fact that some studies excluded substantial numbers of patients or prostate subparts due to poor imaging quality, we cannot fully rule out selection bias in these studies. Although we aimed at quantifying the additional value of combined MRI/MRSI over MRI technology alone, the paucity of such data in our set of studies impeded us from doing a solid analysis. Finally, we performed this systematic review in a rapidly evolving field of research, and we cannot overlook the fact that relevant reports appeared while completing this study.

4.3. Implications for research

We believe that future studies of the diagnostic value of new MR imaging technologies should include recent methodological recommendations for studies evaluating diagnostic tests [54]. Researchers should be encouraged to agree on data acquisition protocols and data analysis algorithms to increase the comparability of studies. Careful reporting of those methods will facilitate the evaluation to the extent that the results are applicable to other clinical settings. For example, in the studies included in this meta-analysis, the pathologic standard of reference for cancer presence varied substantially leading to variability in test performance measures [46].

4.4. Implications for practice

Based on the results of our study we think that it is too early to call for broad application of this method in clinical practice. We speculate that further improvement of the technology will increase its role in the future. For example, higher field strengths will lead to a better spatial resolution, and the combination of existing techniques with diffusion weighted imaging and dynamic contrast-enhanced MRI could provide additional functional information concerning the presence and stage of prostate cancer. A further challenge needing resolution relates to the clinical circumstances for which MRI/MRSI is most useful. Can MRI/MRSI play a role in identifying cancer in men with a rising PSA level but negative prior biopsies, or can it help confirm that a biopsy procedure has not missed a clinically significant tumour?

5. Conclusions

A limited number of small studies suggest that MRI combined with MRSI could be a rule-in test for low-risk patients. This finding needs further confirmation in larger studies, and cost-effectiveness needs to be established.

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Appendix A. Medical Literature Analysis and Retrieval System Online (US National Library of Medicine database; MEDLINE PubMed interface) search terms and strategy. The last search was performed in August 2008

MRI = magnetic resonance imaging; Mesh = medical subheading; MR = magnetic resonance; NMR = nuclear magnetic resonance.

#1	MRI
#2	"Magnetic Resonance Imaging" [Mesh]
#3	"Magnetic Resonance Imaging"
#4	"Magnetic Resonance Spectroscopy" [Mesh]
#5	"Magnetic Resonance Spectroscopy"
#6	"MR Spectroscopy"
#7	MRS
#8	"MR Imaging"
#9	"NMR Tomography"
#10	"NMR Imaging"
#11	#4 OR #5 OR #6 OR #7
#12	#1 OR #2 OR #3 OR #8 OR #9 OR #10
#13	#11 AND #12
#14	"Prostatic Neoplasms" [Mesh]
#15	Prostate carcinoma
#16	Prostatic Cancer
#17	Prostate Cancer
#18	Prostatic Carcinoma
#19	#14 OR #15 OR #16 OR #17 OR #18
#20	#13 AND #19

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. *CA Cancer J Clin* 2007;57:43–66. [PubMed: 17237035]
2. Walsh PC, DeWeese TL, Eisenberger MA. Clinical practice. Localized prostate cancer. *N Engl J Med* 2007;357:2696–705. [PubMed: 18160689]
3. National Cancer Institute. SEER cancer statistics review: surveillance, epidemiology, and end results. http://seer.cancer.gov/statfacts/html/prost_print.html. Accessed August 28, 2008
4. Yancik R, Ries LA. Aging and cancer in America. Demographic and epidemiologic perspectives. *Hematol Oncol Clin North Am* 2000;14:17–23. [PubMed: 10680069]
5. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000: the global picture. *Eur J Cancer* 2001;37(Suppl 8):S4–66. [PubMed: 11602373]
6. Thompson IM, Pauler DK, Goodman PJ, et al. Prevalence of prostate cancer among men with a prostate-specific antigen level ≤ 4.0 ng per millilitre. *N Engl J Med* 2004;350:2239–46. [PubMed: 15163773]
7. Djavan B, Milani S, Remzi M. Prostate biopsy: who, how, and when. An update. *Can J Urol* 2005;12 (Suppl 1):44–8. discussion 99–100. [PubMed: 15780165]
8. Amsellem-Ouazana D, Younes P, Conquy S, et al. Negative prostatic biopsies in patients with a high risk of prostate cancer: is the combination of endorectal MRI and magnetic resonance spectroscopy imaging (MRSI) a useful tool? A preliminary study. *Eur Urol* 2005;47:582–6. [PubMed: 15826747]
9. Norberg M, Egevad L, Holmberg L, Sparen P, Norlen BJ, Busch C. The sextant protocol for ultrasound-guided core biopsies of the prostate underestimates the presence of cancer. *Urology* 1997;50:562–6. [PubMed: 9338732]
10. Presti JC Jr, Chang JJ, Bhargava V, Shinohara K. The optimal systematic prostate biopsy scheme should include eight rather than six biopsies: results of a prospective clinical trial. *J Urol* 2000;163:163–6. discussion 6–7. [PubMed: 10604337]

11. Eichler K, Hempel S, Wilby J, Myers L, Bachmann LM, Kleijnen J. Diagnostic value of systematic biopsy methods in the investigation of prostate cancer: a systematic review. *J Urol* 2006;175:1605–12. [PubMed: 16600713]
12. Irwig, L.; Glasziou, P. Cochrane Methods Group on Systematic Review of Screening and Diagnostic Tests: recommended methods. Cochrane Collaboration; Oxford, UK: 1996.
13. Casciani E, Polettini E, Bertini L, et al. Prostate cancer: evaluation with endorectal MR imaging and three-dimensional proton MR spectroscopic imaging. *Radiol Med (Torino)* 2004;108:530–41. [PubMed: 15722999]
14. Casciani E, Polettini E, Bertini L, et al. Contribution of the MR spectroscopic imaging in the diagnosis of prostate cancer in the peripheral zone. *Abdom Imaging* 2007;32:796–802.
15. Chrzan R, Urbanik A, Dobrowolski Z, Lipczynski W. Morphological MRI and 3D proton spectroscopy using endorectal coil in the diagnostics of prostate cancer—preliminary experience. *Polish J Radiology* 2006;71:42–7.
16. Costouros NG, Coakley FV, Westphalen AC, et al. Diagnosis of prostate cancer in patients with an elevated prostate-specific antigen level: role of endorectal MRI and MR spectroscopic imaging. *AJR* 2007;188:812–6. [PubMed: 17312072]
17. Fütterer JJ, Heijmink SW, Scheenen TW, et al. Prostate cancer localization with dynamic contrast-enhanced MR imaging and proton MR spectroscopic imaging. *Radiology* 2006;241:449–58. [PubMed: 16966484]
18. Fütterer JJ, Scheenen TW, Heijmink SW, et al. Standardized threshold approach using three-dimensional proton magnetic resonance spectroscopic imaging in prostate cancer localization of the entire prostate. *Invest Radiol* 2007;42:116–22. [PubMed: 17220729]
19. Goeb K, Engehausen DG, Krause FS, et al. MRI spectroscopy in screening of prostate cancer. *Anticancer Res* 2007;27:687–93. [PubMed: 17348461]
20. Hasumi M, Suzuki K, Taketomi A, et al. The combination of multi-voxel MR spectroscopy with MR imaging improve the diagnostic accuracy for localization of prostate cancer. *Anticancer Res* 2003;23:4223–7. [PubMed: 14666629]
21. Jung JA, Coakley FV, Vigneron DB, et al. Prostate depiction at endorectal MR spectroscopic imaging: investigation of a standardized evaluation system. *Radiology* 2004;233:701–8. [PubMed: 15564406]
22. Kaji Y, Kurhanewicz J, Hricak H, et al. Localizing prostate cancer in the presence of postbiopsy changes on MR images: role of proton MR spectroscopic imaging. *Radiology* 1998;206:785–90. [PubMed: 9494502]
23. Kumar V, Jagannathan NR, Kumar R, et al. Correlation between metabolite ratios and ADC values of prostate in men with increased PSA level. *Magn Reson Imaging* 2006;24:541–8. [PubMed: 16735174]
24. Manenti G, Squillaci E, Cariani M, Mancino S, Di Roma M, Simonetti G. Magnetic resonance imaging of the prostate with spectroscopic imaging using a surface coil. Initial clinical experience. *Radiol Med (Torino)* 2006;111:22–32. [PubMed: 16623302]
25. Mueller-Lisse UG, Vigneron DB, Hricak H, et al. Localized prostate cancer: effect of hormone deprivation therapy measured by using combined three-dimensional 1H MR spectroscopy and MR imaging: clinicopathologic case-controlled study. *Radiology* 2001;221:380–90. [PubMed: 11687679]
26. Portalez D, Malavaud B, Herigault G, et al. Predicting prostate cancer with dynamic endorectal coil MR and proton spectroscopic MR imaging. *J Radiol* 2004;85:1999–2004. [PubMed: 15692410]
27. Prando A. Prostatic biopsy directed with endorectal MR spectroscopic imaging findings in patients with elevated prostate specific antigen levels and prior negative biopsy findings: early experience: editorial comment. *Int Braz J Urol* 2005;31:494–6.
28. Reinsberg SA, Payne GS, Riches SF, et al. Combined use of diffusion-weighted MRI and 1H MR spectroscopy to increase accuracy in prostate cancer detection. *AJR* 2007;188:91–8. [PubMed: 17179350]
29. Scheidler J, Hricak H, Vigneron DB, et al. Prostate cancer: localization with three-dimensional proton MR spectroscopic imaging—clinicopathologic study. *Radiology* 1999;213:473–80. [PubMed: 10551229]

30. Shi H, Wu LB, Ding HY, et al. Prostate cancer: diagnostic value of dynamic contrast-enhanced MRI, diffusion weighted imaging and 3D (1)H-MR spectroscopy. *Chinese J Radiology* 2006;40:678–83.
31. Shukla-Dave A, Hricak H, Kattan MW, et al. The utility of magnetic resonance imaging and spectroscopy for predicting insignificant prostate cancer: an initial analysis. *BJU Int* 2007;99:786–93. [PubMed: 17223922]
32. Squillaci E, Manenti G, Mancino S, et al. MR spectroscopy of prostate cancer: initial clinical experience. *J Exp Clin Cancer Res* 2005;24:523–30. [PubMed: 16471314]
33. Swanson MG, Vigneron DB, Tabatabai ZL, et al. Proton HR-MAS spectroscopy and quantitative pathologic analysis of MRI/3D-MRSI-targeted postsurgical prostate tissues. *Magn Reson Med* 2003;50:944–54. [PubMed: 14587005]
34. Testa C, Schiavina R, Lodi R, et al. Prostate cancer: sextant localization with MR imaging, MR spectroscopy, and 11C-choline PET/CT. *Radiology* 2007;244:797–806. [PubMed: 17652190]
35. Wefer AE, Hricak H, Vigneron DB, et al. Sextant localization of prostate cancer: comparison of sextant biopsy, magnetic resonance imaging and magnetic resonance spectroscopic imaging with step section histology. *J Urol* 2000;164:400–4. [PubMed: 10893595]
36. Wetter A, Hubner F, Lehnert T, et al. Three-dimensional 1H-magnetic resonance spectroscopy of the prostate in clinical practice: technique and results in patients with elevated prostate-specific antigen and negative or no previous prostate biopsies. *Eur Radiol* 2005;15:645–52. [PubMed: 15627189]
37. Yuen JS, Thng CH, Tan PH, et al. Endorectal magnetic resonance imaging and spectroscopy for the detection of tumour foci in men with prior negative transrectal ultra-sound prostate biopsy. *J Urol* 2004;171:1482–6. [PubMed: 15017203]
38. Bhatia C, Phongkitkarun S, Booranapitaksonti D, Kochakarn W, Chaleumsanyakorn P. Diagnostic accuracy of MRI/MRSI for patients with persistently high PSA levels and negative TRUS-guided biopsy results. *J Med Assoc Thai* 2007;90:1391–9. [PubMed: 17710982]
39. Chen M, Dang HD, Wang JY, et al. Prostate cancer detection: comparison of T2-weighted imaging, diffusion-weighted imaging, proton magnetic resonance spectroscopic imaging, and the three techniques combined. *Acta Radiol* 2008;49:602–10. [PubMed: 18568549]
40. Cirillo S, Petracchini M, Della Monica P, et al. Value of endorectal MRI and MRS in patients with elevated prostate-specific antigen levels and previous negative biopsies to localize peripheral zone tumours. *Clin Radiol* 2008;63:871–9. [PubMed: 18625351]
41. Saito K, Kaminaga T, Muto S, et al. Clinical efficacy of proton magnetic resonance spectroscopy (1H-MRS) in the diagnosis of localized prostate cancer. *Anticancer Res* 2008;28:1899–904. [PubMed: 18630478]
42. Shukla-Dave A, Hricak H, Moskowitz C, et al. Detection of prostate cancer with MR spectroscopic imaging: an expanded paradigm incorporating polyamines. *Radiology* 2007;245:499–506. [PubMed: 17890357]
43. Mazaheri Y, Shukla-Dave A, Hricak H, et al. Prostate cancer: identification with combined diffusion-weighted MR imaging and 3D 1H MR spectroscopic imaging—correlation with pathologic findings. *Radiology* 2008;246:480–8. [PubMed: 18227542]
44. Scheenen TW, Heijmink SW, Roell SA, et al. Three-dimensional proton MR spectroscopy of human prostate at 3T without endorectal coil: feasibility. *Radiology* 2007;245:507–16. [PubMed: 17848681]
45. Westphalen AC, Coakley FV, Qayyum A, et al. Peripheral zone prostate cancer: accuracy of different interpretative approaches with MR and MR spectroscopic imaging. *Radiology* 2008;246:177–84. [PubMed: 18024434]
46. Lijmer JG, Mol BW, Heisterkamp S, et al. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 1999;282:1061–6. [PubMed: 10493205]
47. Harbord RM, Deeks JJ, Egger M, Whiting P, Sterne JA. A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics* 2007;8:239–51. [PubMed: 16698768]
48. Zwinderman AH, Bossuyt PM. We should not pool diagnostic likelihood ratios in systematic reviews. *Stat Med* 2008;27:687–97. [PubMed: 17611957]
49. Prando A, Kurhanewicz J, Borges AP, Oliveira EM Jr, Figueiredo E. Prostatic biopsy directed with endorectal MR spectroscopic imaging findings in patients with elevated prostate specific antigen levels and prior negative biopsy findings: early experience. *Radiology* 2005;236:903–10. [PubMed: 16118169]

50. Qiang YQ, Guo YM, Wang P, et al. A meta-analysis for assessing the value of MR spectroscopy in the diagnosis of prostate cancer. *J Med Colleges PLA* 2006;21:401–7.
51. Engelbrecht MR, Jager GJ, Laheij RJ, Verbeek AL, van Lier HJ, Barentsz JO. Local staging of prostate cancer using magnetic resonance imaging: a meta-analysis. *Eur Radiol* 2002;12:2294–302. [PubMed: 12195484]
52. Kirkham APS, Emberton M, Allen C. How good is MRI at detecting and characterising cancer within the prostate? *Eur Urol* 2006;50:1163–75. discussion 75. [PubMed: 16842903]
53. Shah N, Sattar A, Benanti M, Hollander S, Cheuck L. Magnetic resonance spectroscopy as an imaging tool for cancer: a review of the literature. *J Am Osteopath Assoc* 2006;106:23–7. [PubMed: 16428685]
54. Bachmann LM, ter Riet G, Weber WE, Kessels AG. Multivariable adjustments counteract spectrum and test review bias in accuracy studies. *J Clin Epidemiol*. In press. doi:10.1016/j.jclinepi. 2008.02.007.

Fig. 1.
Study flow.
MRSI = magnetic resonance spectroscopy imaging.

Fig. 2.

Final study selection.

MRI = magnetic resonance imaging; MRSI = magnetic resonance spectroscopy imaging.

Fig. 3.
 Diagnosed prostate cancer—single pathologic correlative: part of prostate (cut-off value MRSI >3 SD).
 HSROC = hierarchical summary receiver operating characteristic.

Fig. 4.
 Suspected prostate cancer—single pathologic correlative: whole prostate (cut-off value MRSI >3 SD).
 HSROC = hierarchical summary receiver operating characteristic.

Fig. 5.
Risk stratification within the group with diagnosed cancer/part of prostate—high risk of clinically relevant cancer.
HSROC = hierarchical summary receiver operating characteristic.

Fig. 6.

Risk stratification within the group with diagnosed cancer/part of prostate—low risk of clinically relevant cancer.

HSROC = hierarchical summary receiver operating characteristic.

Fig. 7.

Risk stratification within the group with suspected cancer/whole prostate—low risk of clinically relevant cancer.

HSROC = hierarchical summary receiver operating characteristic.

Table 1

Technical characteristics

Study	Year	MRI			MRSI			Additional techniques
		Model	Field strength (Tesla)	Weighting	Coil	Water and lipid suppression	Imaging development technique	
Saito et al [41]	2008	Signa, LX Horizon Echosped, GE Medical Systems	1.5	T1 + T2	Body coil and endorectal coil	PROSE	PRESS	Not described
Chen et al [39]	2008	Magnetom Espree, Siemens	1.5	T1 + T2	Body coil and spine coil	Frequency-selective refocusing technique	3D PRESS CSI STEAM	Diffusion-weighted MRI
Cirillo et al [40]	2008	Signa, GE Medical Systems	1.5	T1 + T2	Pelvic phased array coil Balloon-covered endorectal coil	Selective spatial and frequency suppression pulses	PRESS	0.34
Bhatia et al [38]	2007	CV/i&NV/i, GE Medical Systems	1.5	T1 + T2	Body coil and pelvic-phased array coil Balloon-covered endorectal coil	Done, not described in detail	Not described	0.24–0.34
Shukla-Dave et al [42]	2007	GE Medical Systems	1.5	T1 + T2	Pelvic-phased array coil Endorectal coil	Spectral-spatial pulses + outer Voxel suppression pulses	PRESS	0.33
Testa et al [34]	2007	Signa, GE Medical Systems	1.5	T1 + T2	Body coil Endorectal coil combined with pelvic-phased array coil	PROSE	PRESS	0.34 (PET/CT)
Shukla-Dave et al [31]	2007	Signa Horizon scanner, GE	1.5	T1 + T2	Pelvic-phased array coil Expandable endorectal coil	BASING technique	PRESS	0.12
Casciani et al [14]	2007	Signa, GE Medical Systems	1.5	T1 + T2	Pelvic phased array coil Endorectal coil	Selective spectral 180° refocusing pulses	3D PRESS CSI	0.24–0.70
Goeb et al [19]	2007	Siemens Medical Systems	1.5	T1 + T2	Phased array coil Endorectal coil	Outer volume suppression	3D PRESS CSI	0.125–0.325
Reinsberg et al [28]	2007	Intera Philips Medical Systems	1.5	T1 + T2	Endorectal coil with balloon	BASING technique	PRESS CSI	1.15
Flitterer et al [18]	2007	Magnetom Sonata Siemens Medical Systems	1.5	T1 + T2	Pelvic phased array coil Endorectal coil	BASING technique	PRESS	0.22
Manenti et al [24]	2006	Philips Gyroscan Intera	1.5	T1 + T2	Body coil and surface coil near the pelvis	BASING technique	double spin echo PRESS	0.24

Study	Year	MRI			MRSI			Additional techniques
		Model	Field strength (Tesla)	Weighting	Coil	Water and lipid suppression	Imaging development technique	Voxel size
Kumar et al [23]	2006	Sonata/Avanto Siemens	1.5	T1 + T2	Pelvic-phased array coil Endorectal surface coil	Six outer volume saturation bands and frequency selective suppression	3D PRESS	0.125–0.198
Costouros et al [16]	2006	Signa, GE Medical Systems	1.5	T1 + T2	Body coil and pelvic-phased array coil Expandable endorectal coil	Spectral-spatial pulses for the two 180° excitation pulses and outer voxel saturation	double spin echo PRESS	0.24–0.34
Chrzan et al [15]	2006	Signa Excite, GE Medical Systems	1.5	T1 + T2	Endorectal coil	PROSE	PRESS	Not described
Shi et al [30]	2006	Siemens Sonata Medical Systems	1.5	T1 + T2	Not translated	Not translated	Not translated	Not translated
Flitterer et al [17]	2006	Sonata Siemens Medical Systems	1.5	T1 + T2	Pelvic phased array coil Endorectal coil	BASING technique	PRESS	0.22
Amsellem-Onazano et al [8]	2005	Signa, GE Medical Systems	1.5	T1 + T2	Torso phased array coil Expandable endorectal coil	Not described	3D PRESS CSI	0.32
Squillaci et al [32]	2005	Philips Gyroscan Intera	1.5	T1 + T2	Body coil and surface coil placed on pubic region	BASING technique	PRESS	0.24
Wetter et al [36]	2005	Magnetom Sonata Siemens Medical Systems	1.5	T1 + T2	Combined pelvic-phased array coil Endorectal coil	BASING technique	PRESS	0.45
Prando et al [49]	2005	Signa, GE Medical Systems	1.5	T1 + T2	Body coil and pelvic phased array coil Balloon-covered endorectal coil	Spectral-spatial pulses capable of volume selection and frequency selection	PRESS	0.34
Portalez et al [26]	2004	Gyroscan Intera Philips	1.5	T1 + T2	Endorectal coil	Not described	Not described	Not described
Yuen et al [37]	2004	Signa Tesla LX Scanner, GE	1.5	T1 + T2	Phased-array torso-surface coil Endorectal coil	Not described	3D PRESS CSI	0.328
Casciani et al [13]	2004	Signa Excite, GE	1.5	T1 + T2	Phased array coil placed on the pelvis Endorectal coil	Selective spectral 180° refocusing pulses	3D PRESS CSI	Not described

Study	Year	MRI			MRSI			Additional techniques
		Model	Field strength (Tesla)	Weighting	Coil	Water and lipid suppression	Imaging development technique	Voxel size
Jung et al [21]	2004	Signa, GE Medical Systems	1.5	T1 + T2	Body coil and pelvic-phased array coil Expandable endorectal coil	BASING technique	3D double spin echo PRESS	0.24–0.34
Hasumi et al [20]	2003	Signa Horizon LX, GE	1.5	T1 + T2	Endorectal surface coil	Not described	PRESS	0.59
Swanson et al [33]	2003	Signa, GE Medical Systems	1.5	T1 + T2	Body coil Endorectal/pelvic-phased array coil	BASING technique	3D double spin echo PRESS	0.24–0.34
Mueller-Lisse et al [25]	2001	Signa, GE Medical Systems	1.5	T1 + T2	Pelvic-phased array coil Endorectal coil	BASING technique	PRESS	0.24
Wefer et al [35]	2000	Signa, GE Medical Systems	1.5	T1 + T2	Pelvic-phased array coil Balloon-covered endorectal coil	BASING technique	PRESS STEAM	0.25–0.54
Scheidler et al [29]	1999	Signa, GE Medical Systems	1.5	T1 + T2	Pelvic-phased array coil Endorectal coil	BASING technique	PRESS	0.24–0.70
Kaji et al [22]	1998	Signa, GE Medical Systems	1.5	T1 + T2	Body coil and pelvic-phased array coil Endorectal coil	BASING technique	PRESS	0.24

PET/CT = positron emission tomography/computer tomography; MRI = magnetic resonance imaging; MRSI = magnetic resonance spectroscopy imaging; BASING = band selective inversion with gradient dephasing; PRESS = point resolved spectroscopic sequence; CSI = chemical shift imaging; STEAM = stimulated echo acquisition mode; PROSE = prostate spectroscopy and imaging examination, water and lipid suppressing PRESS technique.

Table 2

Study quality characteristics

Study	Year	Study attributes		Index test					Reference test	
		Study design	Data collection	Index test description	Blinding	Cut-off value and level	Region of investigation	Single pathologic correlative		Exclusion due to poor imaging quality
Saito et al [41]	2008	Cohort	Not mentioned	Sufficient	Not described	Prespecified high	Peripheral zone	12th part of prostate	0%	Prostatectomy specimen
Chen et al [39]	2008	Cohort	Retrospective	Sufficient	Yes	Prespecified high	Whole prostate	Sextant	0%	Biopsy (8 cores)
Cirillo et al [40]	2008	Cohort	Prospective	Sufficient	Not described	Prespecified high	Peripheral zone	Patient	0%	Biopsy (10 cores)
Bhatia et al [38]	2007	Cohort	Prospective	Sufficient	Not described	Prespecified high	Whole prostate	Patient	0%	Biopsy (12 cores)
Shukla-Dave et al [42]	2007	Cohort	Retrospective	Sufficient	Not described	Prespecified high	Peripheral zone	Voxel	32%	Prostatectomy specimen
Testa et al [34]	2007	Cohort	Retrospective	Sufficient	No	Prespecified moderate and high	Whole prostate	Sextant	10%	Prostatectomy specimen
Shukla-Dave et al [31]	2007	Cohort	Retrospective	Sufficient	Yes	Prespecified moderate	Whole prostate	Patient	0%	Prostatectomy specimen
Casciani et al [14]	2007	Cross-sectional	Retrospective	Sufficient	Yes	Prespecified moderate	Peripheral zone	Patient	11%	Biopsy + prostatectomy specimen
Goeb et al [19]	2007	Cohort	Prospective	Sufficient	Not described	Prespecified high	Whole prostate	Third of prostate	0%	Prostatectomy specimen + histology reports
Reinsberg et al [28]	2007	Cross-	Prospective	Sufficient	Not described	Optimized	Whole prostate	Voxel	28%	Biopsy (at least 6 cores)
Fütterer et al [18]	2007	Cohort	Prospective	Sufficient	No	Prespecified low	Whole prostate	Tumour nodule	11%	Prostatectomy specimen
Manenti et al [24]	2006	Cohort	Prospective	Sufficient	No	prespecified moderate	Whole prostate	Patient	0%	Biopsy (10 cores)
Kumar et al [23]	2006	Case control	Not mentioned	Sufficient	No	Prespecified low	Peripheral zone	Patient	0%	Biopsy (6 cores)
Costouros et al [16]	2006	Cohort	Retrospective	Sufficient	Yes	Prespecified moderate	Peripheral zone	Half of prostate	0%	Biopsy (6 cores)

Study	Year	Study attributes			Index test				Reference test
		Study design	Data collection	Index test description	Blinding	Cut-off value and level	Region of investigation	Single pathologic correlative	
Chrzan et al [15]	2006	Cohort	Prospective	Not described	Not described	Prespecified high	Whole prostate	Patient	Biopsy (numbers of cores undeclared)
Shi et al [30]	2006	Case control	Not mentioned	Sufficient	Not described	Prespecified	Whole prostate	Patient	Biopsy + prostatectomy specimen
Fütterer et al [17]	2006	Cohort	Prospective	Sufficient	Yes	Prespecified low	Whole prostate	14th part of prostate	Prostatectomy specimen
Ansellem-Onazano et al [8]	2005	Cohort	Prospective	Sufficient	No	Prespecified moderate and high	Whole prostate	Patient	Biopsy (12 cores)
Squillaci et al [32]	2005	Cohort	Prospective	Sufficient	No	Prespecified moderate	Whole prostate	Patient	Biopsy (10 cores)
Wetter et al [36]	2005	Cohort	Not mentioned	Sufficient	Not described	Prespecified moderate and high	Whole prostate	Patient	Biopsy (numbers of cores undeclared)
Prando et al [50]	2005	Cohort	Not mentioned	Sufficient	Not described	Prespecified high	Peripheral zone	Patient	Biopsy (12 cores)
Portalez et al [26]	2004	Cohort	Prospective	Sufficient	Not described	Prespecified moderate	Whole prostate	Patient	Biopsy (12 cores)
Yuen et al [37]	2004	Cohort	Prospective	Sufficient	Yes	Prespecified high	Peripheral zone	Patient	Biopsy (10-14 cores)
Casciani et al [13]	2004	Cohort	Retrospective	Sufficient	Yes	Prespecified moderate	Peripheral zone	Patient	Multiple biopsies
Jung et al [21]	2004	Cross sectional	Retrospective	Sufficient	No	Prespecified moderate and high	Peripheral zone	Voxel	Prostatectomy specimen
Hasami et al [20]	2003	Cohort	Not mentioned	Sufficient	Not described	Prespecified high	Peripheral zone	Half of prostate	Biopsy (numbers of cores undeclared)
Swanson et al [33]	2003	Cohort	Not mentioned	Sufficient	Not described	Prespecified moderate	Whole prostate	Tumour node	Prostatectomy specimen
Mueller-Lisse et al [25]	2001	Cohort	Not mentioned	Sufficient	No	Prespecified moderate and high	Peripheral zone	Sextant	Prostatectomy specimen
Wefer et al [35]	2000	Cross sectional	Not mentioned	Sufficient	No	Prespecified moderate	Peripheral zone	Sextant	Prostatectomy specimen

Study	Year	Study attributes			Index test				Reference test
		Study design	Data collection	Index test description	Blinding	Cut-off value and level	Region of investigation	Single pathologic correlative	
Scheidler et al [29]	1999	Cross sectional	Retrospective	Sufficient	No	Prespecified moderate and high	Peripheral zone	Sextant	Exclusion due to poor imaging quality
									11% of sextants
Kaji et al [22]	1998	Cohort	Retrospective	Sufficient	Not described	Prespecified high	Whole prostate	Tumour module	9% of patients 26% of sextants
									0% Biopsy (4-12 cores)

Table 3

Patient characteristics

Study	Year	No. of patients	Mean age, yr	Age range, yr	Mean PSA, ng/ml	PSA range, ng/ml	Gleason score, mean	Gleason score, range	Previous neg. biopsies	Cancer status
Saito et al [41]	2008	20 (test pop. 10)	67 (median)	51–77	–	–	–	–	No	Diagnosed
Shukla-Dave et al [42]	2007	50 (test pop. 26)	60 (median)	44–69	5.4 (median)	0.6–24.1	6 (median)	6–9	No	Diagnosed
Testa et al [34]	2007	50	64	51–75	13.9	2.5–70	–	–	No	Diagnosed
Fütterer et al [18]	2007	32	61	51–68	7.8	3.2–19.4	6	5–8	No	Diagnosed
Shukla-Dave et al [31]	2007	220	–	–	max <20	–	–	No one >6	No	Diagnosed
Goeb [19]	2007	46	65.1	49–77	11.24	–	6.5	3–9	No	Diagnosed
Reinsberg [28]	2007	42	69.3	60–78	10.2 (median)	0.45–45	–	6–8	No	Diagnosed
Fütterer et al [17]	2006	34	60	50–69	8	3.2–23.6	6	5–8	No	Diagnosed
Shi et al [30]	2006	125 (32 with cancer)	72.6	58–87	–	7.2–200	–	–	No	Diagnosed
Jung et al [21]	2004	37	56	44–69	5.9	2.2–17.2	6.6	5–8	No	Diagnosed
Hasumi et al [20]	2003	21	70 (median)	52–82	51	3.5–817	–	No one >7	No	Diagnosed
Swanson et al [33]	2003	26	56	44–70	6.5	0.8–15	6.5	5–8	No	Diagnosed
Mueller-Lisse et al [25]	2001	48	60.2	–	–	–	6.5	5–10	No	Diagnosed
Wefer et al [35]	2000	116	58	46–77	–	–	6.1	4–8	No	Diagnosed
Scheidler et al [29]	1999	89	60.2	49–77	8.2	–	5.3	4–10	No	Diagnosed
Kaji et al [22]	1998	49	63.2	–	–	–	–	–	No	Diagnosed
Chen et al [39]	2008	42	63	45–82	11.9 (cancer neg) 52.5 (cancer pos)	4.7–38 7.4–147	–	3–8 (≥)	No	Suspected
Cirillo et al [40]	2008	54	65.4 (median)	(+/-) 6.5	10.8	(+/-) 7.5	6 (median)	4–8	Yes	Suspected
Bhatia et al [38]	2007	21	61.4	50–77	13.1	4.3–46.6	6	No range	Yes	Suspected
Casciani et al [14]	2007	79	68.1	–	9.54	4.5–40.4	–	–	No	Suspected
Chrzan et al [15]	2006	20	61.9	50–72	10.91	2.9–23.58	6.18	4–9	No	Suspected
Manenti et al [24]	2006	39	68.5	55–82	24.15	0.3–44	–	–	No	Suspected
Kumar et al [23]	2006	33	69.4 (PSA >20) 61.4 (PSA 4–20)	–	66.4 (PSA >20) 9.9 (PSA 4–20)	–	–	2–10 (PSA >20) 2–8 (PSA 4–20)	No	Suspected
Costouros et al [16]	2006	45	63	48–80	10.6	5.2–24.1	7 (median)	5–8	Yes	Suspected
Ansellem-Onazano et al [8]	2005	42	62.3	54–74	12	3.87–35	6.6	5–9	Yes	Suspected
Squillaci et al [32]	2005	65	68.5	55–82	24.15	4.3–44	–	–	No	Suspected

Study	Year	No. of patients	Mean age, yr	Age range, yr	Mean PSA, ng/ml	PSA range, ng/ml	Gleason score, mean	Gleason score, range	Previous neg. biopsies	Cancer status
Wetter et al [36]	2005	103	64	46–77	8.6	–	–	–	No	Suspected
Prando [49]	2005	42	63.3	45–75	6.8	4.1–15.3	–	–	Yes	Suspected
Casciani et al [13]	2004	97	–	–	–	–	–	5–9	No	Suspected
Yuen et al [37]	2004	24	64.5	58–69	8.2 (cancer neg) 20.4 (cancer pos)	4–40	–	–	Yes	Suspected
Portalez et al [26]	2004	54	62.9	50–72	10.7	0.95–27.3	–	–	Yes	Suspected

Table 4
True positive (TP) and false positive (FP), true negative (TN) and false negative (FN), sensitivity, and specificity

Author	Year	TP	FP	FN	TN	Sensitivity	Specificity
Included in meta-analysis							
Diagnosed cancer—single pathologic correlative subpart of prostate							
Testa et al [34]	2007	44	5	47	44	48	90
Goeb et al [19]	2007	11	0	17	8	39	100
Jung et al [21]	2004	56	32	25	267	69	89
Hasumi et al [20]	2003	28	1	3	13	90	91
Swanson et al [33]	2003	17	3	7	26	71	90
Mueller-Lisse et al [25]	2001	111	22	41	68	73	76
Wefer et al [35]	2000	91	16	71	72	56	82
Scheidler et al [29]	1999	80	7	75	72	52	91
Kaji et al [22]*	1998	13	3	3	13	81	77
Kaji et al [22]**	1998	36	24	4	42	90	64
Suspected cancer—single pathologic correlative whole prostate/patient							
Cirillo et al [40]	2008	15	6	2	31	88	84
Bhatia et al [38]	2007	2	3	0	16	100	84
Casciani et al [13]	2007	41	5	5	19	89	79
Ansellem-Onazano et al [8]	2005	9	1	6	26	60	96
Chrzan et al [15]	2006	10	2	1	7	91	78
Casciani et al [13]	2004	35	3	2	13	95	81
Yuen et al [37]	2004	1	0	6	17	14	100
Excluded from meta-analysis							
Not combined analysis of MRI and MRSI (MRSI analysis only)							
Saito et al [41]	2008	43	6	28	43	61	88
Shukla-Dave et al [42]	2007	91	69	124	383	42	85
Fütterer et al [18]	2007	76	43	18	259	81	86
Fütterer et al [17]	2006	78	37	20	249	80	87
Prando et al [50]	2005	12	4	5	21	71	84
Wetter et al [36]	2005	5	1	1	13	83	93
Portalez et al [26]	2004	12	2	3	15	80	88

Author	Year	TP	FP	FN	TN	Sensitivity	Specificity
Combined with diffusion weighted MRI							
Reinsberg et al [28]	2007	33	45	14	227	70	84
Kumar et al [23]	2006	18	10	0	5	100	33
Combined with diffusion weighted and contrast-enhanced MRI							
Shi et al [30]	2006	13	4	2	24	89	95
Not standard imaging procedure—no use of endorectal coil							
Chen et al [39]	2008	43	8	4	197	84	98
Manenti et al [24]	2006	14	2	6	17	70	89
Squillaci et al [32]	2005	24	3	9	29	71	90
Exclusion due to heterogeneity within meta-analysis groups							
Shukla-Dave et al [31]	2007	121	48	8	43	93	47
Costouros et al [16]	2006	9	11	18	42	35	79

* Cohort with previous hormonal treatment.

*** Same study, cohort without previous hormonal treatment.