

Uitgangsvraag 1b: Plaats van (mp)MRI (PET/CT) bij stadiëring van bewezen prostaatacarcinoom (lokaal) en N

Is (mp)MRI geïndiceerd bij de lokale stadiëring van bewezen prostaatacarcinoom?

Systematic reviews

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of review quality
Engelbrecht MR 2002 ¹	<ul style="list-style-type: none"> SR Funding/Col: supported by Dutch Cancer Society, Col not reported Search date: 1/1984-5/2000 Databases: Medline, Embase Study designs: diagnostic studies N included studies: N=146 (71 articles, 5 abstracts) 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer <i>A priori</i> patient characteristics: not reported 	MRI	<p>ROC analysis for studies using per-prostate reference standard (87 studies):</p> <ul style="list-style-type: none"> cT2 vs. cT3: <ul style="list-style-type: none"> Joint max. Se and Sp: 71% At Sp 80%: Se 62% At Sp 95%: Se 29% Extracapsular extension: <ul style="list-style-type: none"> Joint max. Se and Sp: 64% At Sp 80%: Se 64% At Sp 95%: Se 23% Seminal vesicle invasion: <ul style="list-style-type: none"> Joint max. Se and Sp: 82% At Sp 80%: Se 85% At Sp 95%: Se 27% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> Adequate search Quality appraisal performed, but no individual results Heterogeneity not clearly reported

Diagnostische studies

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
Allen DJ 2004 ²	<ul style="list-style-type: none"> • Cohort study • Funding/Col: funding not reported, no Col declared • Setting: single centre, UK • Sample size: N=55 • Duration: 3 years, unclear when 	<ul style="list-style-type: none"> • Eligibility criteria: patients with biopsy-confirmed prostate cancer • Patient characteristics: not stated • Prevalence of disease: 33% of patients had extracapsular extension 	<p><u>Index test:</u> 1.5 T MRI with cardiac phased-array coil; T1W, T2W</p> <p><u>Reference standard:</u> Radical prostatectomy (entire prostate gland was processed in whole-mounted blocks)</p>	<p>Detection of extracapsular extension:</p> <p>General radiologists:</p> <ul style="list-style-type: none"> • Se: 50% • Sp: 84% • PPV: 60% • NPV: 78% • LR+: 3.1 • LR-: 0.6 <p>Specialist radiologists:</p> <ul style="list-style-type: none"> • Se: 72% • Sp: 86% • PPV: 72% • NPV: 86% • LR+: 5.3 • LR-: 0.32 	No significant differences between general and specialist radiologists	<p>Level of evidence: B</p> <ul style="list-style-type: none"> • Moderate risk of bias • Unclear if consecutive patients; selection potentially based on receiving of reference standard • Blinded evaluation of imaging, unclear if blinded evaluation of reference test • <u>Definition of extracapsular extension:</u> low signal infiltration of the periprostatic fat on T1 images, focal bulging of the capsule adjacent to the tumour and loss of signal within the seminal vesicles on T2-weighted images
Brown JA 2009 ³	<ul style="list-style-type: none"> • Retrospective cohort study • Funding/Col: not reported • Setting: unclear, US • Sample size: N=62 • Duration: 3/2002-2/2005 	<ul style="list-style-type: none"> • Eligibility criteria: patients with prostate cancer who underwent radical prostatectomy and had preoperative endorectal MRI staging data available for review • Patient characteristics: <ul style="list-style-type: none"> ○ Mean age: 58y ○ Mean PSA: 9.3 ng/ml • Prevalence of disease: 34% had pT3 	<p><u>Index test:</u> 1.5 T MRI with endorectal coil and pelvic phased-array coil; T1W, T2W</p> <p><u>Reference standard:</u> Radical prostatectomy (46 RALP, 16 open) (completeness not reported)</p>	<p>Detection of T3 disease:</p> <ul style="list-style-type: none"> • Se: 38% • Sp: 83% • PPV: 53% • NPV: 72% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> • Moderate risk of bias • Unclear if consecutive patients; selection based on receiving of reference standard • Blinded evaluation of imaging, unclear if blinded evaluation of reference test
Colleselli D 2011 ⁴ Colleselli D 2010 ⁵	<ul style="list-style-type: none"> • Prospective cohort study • Funding/Col: not reported • Setting: University 	<ul style="list-style-type: none"> • Eligibility criteria: patients with histologically proven prostate cancer and consecutive radical retropubic prostatectomy 	<p><u>Index test:</u> 1.5 T MRI with endorectal coil and body-phased arrays; T2W</p>	<p>Detection of T2a disease:</p> <ul style="list-style-type: none"> • Se: 40% • Sp: 81% • PPV: 27% 	<p>Localisation</p> <ul style="list-style-type: none"> • Dorsal: Se 88%, Sp 100% • Ventral: Se 65%, Sp 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> • Moderate risk of bias • Consecutive patients • Blinding not reported

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	<p>hospital, Germany</p> <ul style="list-style-type: none"> • Sample size: N=69 • Duration: not stated 	<ul style="list-style-type: none"> • Patient characteristics: <ul style="list-style-type: none"> ○ Mean age: 62.4y ○ Mean PSA: 9.2 ng/ml • Prevalence of disease: T2a 14.5%, T2b 4.4%, T2c 66.7%, T3a 7.3%, T3b 7.3% 	<p><u>Reference standard:</u> Radical prostatectomy (whole-mount sections)</p>	<ul style="list-style-type: none"> • NPV: 89% <p>Detection of T2b disease:</p> <ul style="list-style-type: none"> • Se: 0% • Sp: 98% • PPV: 0% • NPV: 96% <p>Detection of T2c disease:</p> <ul style="list-style-type: none"> • Se: 46% • Sp: 57% • PPV: 68% • NPV: 34% <p>Detection of T3a disease:</p> <ul style="list-style-type: none"> • Se: 20% • Sp: 88% • PPV: 22% • NPV: 87% <p>Detection of T3b disease:</p> <ul style="list-style-type: none"> • Se: 20% • Sp: 97% • PPV: 50% • NPV: 88% 	<p>87%</p> <ul style="list-style-type: none"> • Apex: Se 54%, Sp 82% • Mid: Se 76%, Sp 83% • Base: Se 84%, Sp 79% <ul style="list-style-type: none"> • Apex dorsal right: Se 41%, Sp 92% • Apex ventral right: Se 33%, Sp 100% • Apex dorsal left: Se 41%, Sp 89% • Apex ventral left: Se 52%, Sp 100% • Mid dorsal right: Se 60%, Sp 82% • Mid ventral right: Se 43%, Sp 100% • Mid dorsal left: Se 67%, Sp 75% • Mid ventral left: Se 42%, Sp 92% • Base dorsal right: Se 73%, Sp 88% • Base ventral right: Se 47%, Sp 88% • Base dorsal left: Se 79%, Sp 69% • Base ventral left: Se 52%, Sp 83% 	<ul style="list-style-type: none"> • 9/69 patients excluded from contingency table in article because no tumour could be observed by MRI • Outcome 'localisation' is based on lesion-based analysis
Cornud F 2012 6	<ul style="list-style-type: none"> • Prospective cohort study • Funding/Col: funding not reported, no Col declared • Setting: University hospital (N=1), France • Sample size: N=178 	<ul style="list-style-type: none"> • Eligibility criteria: patients with clinically localized prostate cancer (cStage < T3) • Patient characteristics: <ul style="list-style-type: none"> ○ Median age: 63y ○ Median PSA: 7 ng/ml ○ cT1c 83%, cT2 17% 	<p><u>Index test:</u> 1.5 T MRI with integrated endorectal pelvic phased-array coil; T2W, DWI, DCE (gadolinium)</p> <p><u>Reference standard:</u> Radical prostatectomy</p>	<p>Detection of extracapsular extension: direct signs</p> <ul style="list-style-type: none"> • Se: 55% • Sp: 96% • PPV: 78% (seems to be wrongly reported in 	<p>Detection of seminal vesicle invasion:</p> <ul style="list-style-type: none"> • Se: 83% • Sp: 99% • PPV: 83% (seems to be wrongly reported in article) 	<p>Level of evidence: A2</p> <ul style="list-style-type: none"> • Low risk of bias • Consecutive patients • Blinded image and pathology evaluation • Scoring of ECE: 0 – no sign of ECE; 1 – indirect signs of

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	<ul style="list-style-type: none"> Duration: 10/2008-5/2009 	<ul style="list-style-type: none"> Prevalence of disease: 21% had extracapsular extension, 7% had seminal vesicle invasion 	<p><u>(completeness unclear)</u></p>	<p>article)</p> <ul style="list-style-type: none"> NPV: 89% <p>Detection of extracapsular extension: direct + indirect signs</p> <ul style="list-style-type: none"> Se: 84% Sp: 89% PPV: 68% NPV: 95% 	<ul style="list-style-type: none"> NPV: 99% 	<p>ECE; 2 – direct signs of ECE. Indirect signs of ECE were defined by a tumour contact with the capsule and a capsular signal defect with or without capsular bulging of the prostate contour. Direct signs of ECE were defined as the presence of a hyposignal in any periprostatic area (neurovascular bundles, subapical or perivesicular area, rectoprostatic angle and lateral or posterior periprostatic fat)</p> <ul style="list-style-type: none"> Scoring of SVI: 0 – no sign of SVI; 1 – presence of a filling defect within the root of seminal vesicles, or a thickening of the seminal vesicle wall and/or a circumferential thickening of the wall of the vas deferens
Delongchamps NB 2011 7	<ul style="list-style-type: none"> Cohort study Funding/Col: funding not reported, no Col declared Setting: single university centre, France Sample size: N=57 Duration: 11/2008-4/2009 	<ul style="list-style-type: none"> Eligibility criteria: patients with biopsy-proven prostate cancer that underwent MRI before radical prostatectomy Patient characteristics: <ul style="list-style-type: none"> Median age: 63y Median PSA: 7 ng/ml 	<p><u>Index test:</u> 1.5 T MRI with integrated endorectal pelvic phased-array coil; T2W, DWI, DCE (gadolinium)</p> <p><u>Reference standard:</u> Radical prostatectomy (whole-mount sections)</p>	<p>Peripheral zone</p> <p>T2W:</p> <ul style="list-style-type: none"> Se: 63% Sp: 98% PPV: 95% NPV: 80% AUC: 0.81 <p>T2W+DWI:</p> <ul style="list-style-type: none"> Se: 81% (p<0.05 vs. T2W) Sp: 93% PPV: 88% NPV: 88% 	<p>Transition zone</p> <p>T2W:</p> <ul style="list-style-type: none"> Se: 72% Sp: 98% PPV: 84% NPV: 96% AUC: 0.84 <p>T2W+DWI:</p> <ul style="list-style-type: none"> Se: 72% Sp: 98% PPV: 84% NPV: 96% AUC: 0.88 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Consecutive patients, unclear if selection was based on receiving of tests Blinded image review, unclear if pathology review was blinded Region-based analysis

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				<ul style="list-style-type: none"> AUC : 0.92 <p>T2W+DCE:</p> <ul style="list-style-type: none"> Se: 79% (p<0.05 vs. T2W) Sp: 92% PPV: 87% NPV: 87% AUC : 0.91 <p>T2W+DWI+DCE:</p> <ul style="list-style-type: none"> Se: 80% (p<0.05 vs. T2W) Sp: 97% PPV: 95% NPV: 88% AUC: 0.92 	<p>T2W+DCE:</p> <ul style="list-style-type: none"> Se: 48% (p<0.05 vs. T2W) Sp: 77% (p<0.05 vs. T2W) PPV: 23% NPV: 91% AUC: 0.70 <p>T2W+DWI+DCE:</p> <ul style="list-style-type: none"> Se: 52% (p<0.05 vs. T2W) Sp: 83% (p<0.05 vs. T2W) PPV: 31% NPV: 92% AUC: 0.75 	
Fütterer JJ 2007 8	<ul style="list-style-type: none"> Prospective cohort study Funding/Col: supported by Dutch Cancer Society, Col not reported Setting: University hospital (N=1), the Netherlands Sample size: N=81 Duration: 1/1999-5/2002 	<ul style="list-style-type: none"> Eligibility criteria: patients with biopsy-proved prostate cancer who were candidates for radical retropubic prostatectomy; no previous androgen deprivation treatment, positive lymphadenectomy results, incomplete MR examination datasets, or contraindications to MR imaging Patient characteristics: <ul style="list-style-type: none"> Median age: 65.4y Median PSA: 14.1 ng/ml Median Gleason: 6.3 Prevalence of disease: 39% had extracapsular extension, 12% had 	<p><u>Index test:</u> 1.5 T MRI with pelvic phased-array and integrated endorectal-pelvic phased-array coil; T2W</p> <p><u>Reference standard:</u> Radical prostatectomy (transverse whole-mount step-sections), except for 5 patients with positive US-guided seminal vesicle biopsy</p>	<p>Detection of T3 disease: experienced reader, pelvic coil (N=81)</p> <ul style="list-style-type: none"> Se: 56% Sp: 62% PPV: 54% NPV: 64% <p>Detection of T3 disease: experienced reader, endorectal-pelvic coil (N=81)</p> <ul style="list-style-type: none"> Se: 64% Sp: 98% (p=0.0002) PPV: 96% NPV: 77% 	<p>Detection of extracapsular extension: experienced reader, pelvic coil (N=76)</p> <ul style="list-style-type: none"> Se: 50% Sp: 72% PPV: 54% NPV: 69% AUC: 0.57 <p>Detection of extracapsular extension: experienced reader, endorectal-pelvic coil (N=76)</p> <ul style="list-style-type: none"> Se: 57% Sp: 96% (p=0.009) PPV: 89% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Potential selection bias: prospective consecutive inclusion, but exclusion of patients with positive lymphadenectomy or preoperative biopsy-proved seminal vesicle invasion (the latter for evaluation of ECE) One experienced prospective reader with knowledge of clinical data, 2 retrospective readers with knowledge of clinical data, 2 retrospective readers without knowledge of clinical data Blinded pathology review Differential verification

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		seminal vesicle invasion, 44% had T3 disease			<ul style="list-style-type: none"> NPV: 77% AUC: 0.74 (p=0.031) <p>Detection of seminal vesicle invasion: experienced reader, pelvic coil (N=81)</p> <ul style="list-style-type: none"> Se: 50% Sp: 80% PPV: 26% NPV: 92% <p>Detection of seminal vesicle invasion: experienced reader, endorectal-pelvic coil (N=81)</p> <ul style="list-style-type: none"> Se: 90% Sp: 99% (p<0.001) PPV: 91% NPV: 99% 	<ul style="list-style-type: none"> Rating of T3, ECE and SVI: 1 – not present, 2 – probably not present, 3 – possible, 4 – probably present, 5 – definitely present; score 4 and 5 were considered positive
Fütterer JJ 2005 9	<ul style="list-style-type: none"> Prospective cohort study Funding/Col: supported by Dutch Cancer Society, no Col declared Setting: University hospital (N=1), the Netherlands Sample size: N=103 Duration: 3/1999-2/2003 	<ul style="list-style-type: none"> Eligibility criteria: patients with biopsy-proved prostate cancer who were candidates for radical prostatectomy; no previous hormonal treatment, positive lymphadenectomy results, contraindications to MR imaging or endorectal coil Patient characteristics: <ul style="list-style-type: none"> Median age: 63y Median PSA: 7.8 ng/ml Median Gleason: 6 Prevalence of disease: 	<p><u>Index test:</u> 1.5 T MRI with integrated endorectal-pelvic phased-array coil; T2W, T1W-DCE (gadolinium; N=99)</p> <p><u>Reference standard:</u> Radical prostatectomy (transverse whole-mount step-sections)</p>	<p>Detection of T3 disease: experienced reader, T2W (N=103)</p> <ul style="list-style-type: none"> Se: 60% Sp: 97% PPV: 91% NPV: 83% AUC: 0.77 <p>Detection of extracapsular extension: experienced reader, T2W (N=103)</p>	<p>Detection of T3 disease: experienced reader, DCE (N=99)</p> <ul style="list-style-type: none"> Se: 69% Sp: 97% PPV: 92% NPV: 85% AUC: 0.84 <p>Detection of extracapsular extension: experienced reader, DCE (N=99)</p>	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Potential selection bias: prospective consecutive inclusion, but exclusion of patients with positive lymphadenectomy (16/124) or preoperative biopsy-proved seminal vesicle invasion (5/124) One experienced prospective reader, 2 retrospective readers Blinded pathology review

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		33% had extracapsular extension, 7% had seminal vesicle invasion, 34% had T3 disease		<ul style="list-style-type: none"> Se: 59% Sp: 96% PPV: 87% NPV: 83% <p>Detection of seminal vesicle invasion: experienced reader, T2W (N=103)</p> <ul style="list-style-type: none"> Se: 71% Sp: 99% PPV: 83% NPV: 98% 	<ul style="list-style-type: none"> Se: 65% Sp: 95% PPV: 88% NPV: 84% <p>Detection of seminal vesicle invasion: experienced reader, DCE (N=99)</p> <ul style="list-style-type: none"> Se: 71% Sp: 100% PPV: 100% NPV: 98% 	<ul style="list-style-type: none"> Rating of T3, ECE and SVI: 1 – not present, 2 – probably not present, 3 – possible, 4 – probably present, 5 – definitely present; score 4 and 5 were considered positive Potential overlap with Fütterer 2007
Giusti S 2010 10	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: not reported Setting: single university centre Sample size: N=52 Duration: 6/2006-4/2007 	<ul style="list-style-type: none"> Eligibility criteria: patients with US biopsy-proven prostate carcinoma who were referred for endorectal MRI prior to radical prostatectomy; no previous hormone/ radiation therapy treatment Patient characteristics: <ul style="list-style-type: none"> Median age: 65y Median PSA: 10.37 ng/ml 	<p><u>Index test:</u> (1) 1.5 T MRI with endorectal and pelvic phased-array coil; T2W, T1W (2) MR spectroscopy</p> <p><u>Reference standard:</u> Radical prostatectomy (whole-mount step-section pathological specimens)</p>	<p>Lobar localization (peripheral zone):</p> <p>MRI</p> <ul style="list-style-type: none"> Se: 84% Sp: 89% PPV: 97% NPV: 53% <p>MRS</p> <ul style="list-style-type: none"> Se: 84% Sp: 78% PPV: 95% NPV: 50% <p>MRI+MRS</p> <ul style="list-style-type: none"> Se: 91% Sp: 78% PPV: 95% NPV: 64% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Selection bias: unclear if consecutive patients or if selection was based on receiving of reference test No information on blinding Per-lesion analysis (86 malignant locations)
Goris Gbenou 2012 11	<ul style="list-style-type: none"> Retrospective cohort study 	<ul style="list-style-type: none"> Eligibility criteria: patients with localized prostate 	<p><u>Index test:</u> (1) 1.5 T MRI with</p>	<p>Localisation (1760 regions):</p>	<ul style="list-style-type: none"> Apex: Se 48% Base: Se 46% 	<p>Level of evidence: B</p>

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	<ul style="list-style-type: none"> Funding/Col: not reported Setting: single centre, Belgium Sample size: N=220 Duration: 3/1999-10/2006 	<p>cancer that underwent laparoscopic radical prostatectomy or RALP and preoperative endorectal MRI; no prior hormonal or neoadjuvant radiotherapy, significant post-biopsy haemorrhage, and use of technique other than DCE-MRI</p> <ul style="list-style-type: none"> Patient characteristics: <ul style="list-style-type: none"> Median age: 62.4y Median PSA: 6.36 ng/ml 	<p><u>endorectal and pelvic phased-array coil; T1W, T2W, DCE (2) MR spectroscopy</u></p> <p>Reference standard: <u>Radical prostatectomy (whole-mount sections)</u></p>	<ul style="list-style-type: none"> Se: 47% Sp: 74% PPV: 87% NPV: 28% 	<ul style="list-style-type: none"> Mid: Se 52% Transition zone: Se 40% 	<ul style="list-style-type: none"> Moderate risk of bias Consecutive patients, but 287/507 patients excluded Selection bias: inclusion based on receiving of reference standard Image evaluation blinded for localisation; blinded pathology review not reported Region-based analysis
Graser 2007 12	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: not reported Setting: single university centre, Germany Sample size: N=106 Duration: 4/1995-12/2003 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer that underwent MRI before radical prostatectomy and whose prostatectomy specimens were reviewed in a whole-mount step fashion Patient characteristics: <ul style="list-style-type: none"> Mean age: 63y Mean PSA: 11.5 ng/ml Prevalence of disease: 39% had extracapsular extension 	<p>Index test: <u>1.5 T MRI with combined endorectal-pelvic phased array coil; T1W, T2W</u></p> <p>Reference standard: <u>Radical prostatectomy (whole-mount)</u></p>	<p>Diagnosis of T3 disease: reviewer 1</p> <ul style="list-style-type: none"> Se: 91% Sp: 78% 	<p>Localisation: reviewer 1</p> <ul style="list-style-type: none"> Se: 82% Sp: 70% PPV: 84% NPV: 68% AUC: 0.802 <p>Diagnosis of extracapsular extension: reviewer 1</p> <ul style="list-style-type: none"> Se: 71% Sp: 90% PPV: 65% NPV: 92% AUC: 0.793 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Selection bias: unclear if consecutive patients; inclusion based on receiving of reference standard Blinded image review; pathology review not blinded 636 sextants reviewed: results based on per-lesion analysis for localisation and ECE 2x2 tables for T3 disease not reconstructable
Hwii Ko Y 2011 13	<ul style="list-style-type: none"> Cohort study Funding/Col: funding not reported, no Col declared Setting: University hospital (N=1), Korea Sample size: N=121 	<ul style="list-style-type: none"> Eligibility criteria: patients with localized or locally advanced prostate cancer (clinical stage T1c to T3c) diagnosed by transrectal prostate biopsy who underwent robotic radical 	<p>Index test: <u>3.0 T MRI with pelvic array coil; T1W, T2W, DWI</u></p> <p>Reference standard: <u>RALP (completeness)</u></p>	<p>Detection of extracapsular extension:</p> <ul style="list-style-type: none"> Se: 30% Sp: 81% PPV: 31% NPV: 80% 	<p>Detection of seminal vesicle invasion:</p> <ul style="list-style-type: none"> Se: 17% Sp: 92% PPV: 18% NPV: 91% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Potential selection bias: unclear if consecutive patients, inclusion probably based on receiving of

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	<ul style="list-style-type: none"> Duration: 7/2007-12/2009 	prostatectomy <ul style="list-style-type: none"> Patient characteristics: <ul style="list-style-type: none"> Mean age: 62.8y Mean PSA: 9.6 ng/ml Mean Gleason: 6.7 Prevalence of disease: 22% had extracapsular extension, 10% had seminal vesicle invasion 	<u>of sections not clear</u>			reference test <ul style="list-style-type: none"> Blinded image and pathology review Definition of ECE: tumour tissue in the extraprostatic tissue; obliteration of the rectoprostatic angle; bulging of the prostate contour caused by the tumour; asymmetry or direct involvement of the neurovascular bundles; thickening, retraction or irregularity of the prostate capsule; disruption of the prostatic capsule adjacent to the tumour; and stranding of the periprostatic fatty tissue Definition of SVI: abnormal asymmetric low signal intensity within the lumen or dilatation with or without asymmetry of the seminal vesicles on T2-weighted images
Jung DC 2008 14	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: funded by Korean Research Foundation, Col not reported Setting: University hospital (N=1), Korea Sample size: N=217 Duration: 11/2003-3/2006 	<ul style="list-style-type: none"> Eligibility criteria: patients with clinically localized prostate cancer that underwent MRI before radical prostatectomy; none of the patients received neoadjuvant hormonal or radiation therapy before surgery Patient characteristics: <ul style="list-style-type: none"> Mean age: 64.5y Median PSA: 18.2 (SVI+) vs. 7.0 (SVI-) 	<u>Index test:</u> <u>1.5 T MRI with endorectal coil, T2W, T1W</u> <u>Reference standard:</u> <u>Radical prostatectomy (step-section pathologic maps)</u>	Detection of seminal vesicle invasion: class 4 and 5 = positive <ul style="list-style-type: none"> Se: 71% Sp: 97% PPV: 59% NPV: 98% 		Level of evidence: B <ul style="list-style-type: none"> Moderate risk of bias Retrospective inclusion, potentially based on receiving of reference test Blinded image evaluation Definition of SVI: Class 0 (normal MRI appearance of seminal vesicle), Class 1 (normal seminal vesicle, but abnormal signal intensity [SI] in the lumen of the seminal

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		ng/ml • Prevalence of disease: 7% had seminal vesicle invasion				vesicle), Class 2 (symmetric low SI due to focal wall thickening), Class 3 (diffuse symmetric wall thickening), Class 4 (focal asymmetric low signal intensity lesion within the seminal vesicle, but no definite mass), and Class 5 (apparent mass lesion with destructive architecture)
Katahira K 2011 15	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: not reported Setting: unclear, Japan Sample size: N=201 Duration: 11/2004-3/2008 	<ul style="list-style-type: none"> Eligibility criteria: patients with biopsy-proved prostate cancer; prostatectomy performed within 2 months after MRI; needle biopsy performed at least 1 month before MRI; no history of hormone therapy and radiation therapy before MRI Patient characteristics: <ul style="list-style-type: none"> Median age: 70y Median PSA: 8.6 ng/ml 	<u>Index test:</u> 1.5 T MRI with pelvic phased-array coil; T2W, DWI <u>Reference standard:</u> Radical prostatectomy, step-section pathological maps	Peripheral zone T2W: <ul style="list-style-type: none"> Se: 57% Sp: 75% PPV: 55% NPV: 76% T2W+DWI: b-value = 2 <ul style="list-style-type: none"> Se: 73% Sp: 91% PPV: 81% NPV: 86% 	Transition zone T2W: <ul style="list-style-type: none"> Se: 47% Sp: 86% PPV: 60% NPV: 79% T2W+DWI: b-value = 2 <ul style="list-style-type: none"> Se: 74% Sp: 89% PPV: 75% NPV: 89% 	Level of evidence: B <ul style="list-style-type: none"> Moderate risk of bias 201 out of 435 consecutive patients; selection based on receiving of tests Blinded imaging and pathology review Per-lesion analysis (1608 segments); results of 3 readers are added up
Kim BS 2012 16	<ul style="list-style-type: none"> Cohort study Funding/Col: funding not reported, no Col declared Setting: University hospital (N=1), Korea Sample size: N=151 Duration: 1/2005-5/2010 	<ul style="list-style-type: none"> Eligibility criteria: patients with biopsy-proven prostate cancer that underwent radical prostatectomy; no contraindications for MRI or severe claustrophobia, no neoadjuvant hormonal therapy or radiotherapy after MRI, no prostate biopsy and MRI within 3 weeks of each other Patient characteristics: <ul style="list-style-type: none"> Mean age: 64.8y (ER) 	<u>Index test:</u> 3.0 T MRI with either endorectal coil (N=63) or pelvic phased-array coil (N=88); T2W <u>Reference standard:</u> Radical prostatectomy (open 33/151, RALP 118/151) (whole-mount sections)	Endorectal coil Detection of extracapsular extension: <ul style="list-style-type: none"> Se: 33% Sp: 97% PPV: 92% NPV: 57% Detection of seminal vesicle invasion: <ul style="list-style-type: none"> Se: 46% 	Pelvic phased-array coil Detection of extracapsular extension: <ul style="list-style-type: none"> Se: 31% Sp: 98% PPV: 94% NPV: 54% Detection of seminal vesicle invasion: <ul style="list-style-type: none"> Se: 43% 	Level of evidence: B <ul style="list-style-type: none"> Moderate risk of bias Consecutive patients, but inclusion probably based on receiving of reference test Blinded pathology review, but unclear if image review was blinded Diagnostic criteria for ECE: bulge in contour of prostate, obliteration of retroprostatic angle, thickening or disruption of prostatic capsule, infiltrative

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
		<ul style="list-style-type: none"> vs. 66.8y (PA) <ul style="list-style-type: none"> Mean PSA: 11.7 (ER) vs. 12.4 (PA) ng/ml Prevalence of disease: 54% with extracapsular extension (52% endorectal coil, 55% pelvic coil), 23% with seminal vesicle invasion 		<ul style="list-style-type: none"> Sp: 92% PPV: 60% NPV: 87% 	<ul style="list-style-type: none"> Sp: 93% PPV: 64% NPV: 84% 	<ul style="list-style-type: none"> strand in periprostatic fat, asymmetry in neurovascular bundle Diagnostic criteria for SVI: presence of abnormal tissue with low signal intensity within the seminal vesicle or dilatation of the seminal vesicle with asymmetry on T2W images
Kim JK 2005 17	<ul style="list-style-type: none"> Cohort study Funding/Col: not reported Setting: single university centre, Korea Sample size: N=53 Duration: 5/2003-6/2004 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer that underwent radical prostatectomy with preoperative DCE-MRI Patient characteristics: <ul style="list-style-type: none"> Mean age: 64.9y Mean PSA: 13.7 ng/ml 	<p><u>Index test:</u> 1.5 T MRI with surface coil: T2W, DCE (gadopenetate), wash-in rate</p> <p><u>Reference standard:</u> Radical prostatectomy (whole-mount sections)</p>	<p>Localisation: wash-in rate</p> <p>Entire prostate:</p> <ul style="list-style-type: none"> Se: 96% Sp: 82% PPV: 82% NPV: 96% <p>Peripheral zone:</p> <ul style="list-style-type: none"> Se: 96% Sp: 97% PPV: 97% NPV: 96% <p>Transitional zone:</p> <ul style="list-style-type: none"> Se: 96% Sp: 51% PPV: 62% NPV: 94% 	<p>Localisation: T2W</p> <p>Entire prostate:</p> <ul style="list-style-type: none"> Se: 65% Sp: 60% PPV: 57% NPV: 67% <p>Peripheral zone:</p> <ul style="list-style-type: none"> Se: 75% Sp: 53% PPV: 57% NPV: 72% <p>Transitional zone:</p> <ul style="list-style-type: none"> Se: 45% Sp: 73% PPV: 58% NPV: 61% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Selection bias: unclear if consecutive patients; selection based on receiving of reference test Blinded image and pathology review Segment-based analysis (N=954)
Li H 2006 18	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: not reported Setting: single university centre Sample size: N=116 Duration: 4/1999- 	<ul style="list-style-type: none"> Eligibility criteria: patients with untreated prostate cancer that underwent MRI; no drug allergy history, no serious obstructive voiding symptoms Patient characteristics: <ul style="list-style-type: none"> Mean age: 65y 	<p><u>Index test:</u> 1.5 T MRI with pelvic phased-array coil: T1W, T2W, DCE (gadolinium)</p> <p><u>Reference standard:</u> Radical prostatectomy (completeness of</p>	<p>Transition zone cancer</p> <p>Base criteria:</p> <p>Uniform low intensity on T2W:</p> <ul style="list-style-type: none"> Se: 50% Sp: 51% PPV: 62% 	<p>Transition zone cancer</p> <p>Combination of 2 criteria:</p> <p>Uniform low intensity on T2W + Homogeneous enhancement on DCE:</p> <ul style="list-style-type: none"> Se: 43% Sp: 88% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Consecutive patients Blinded image review; unclear if pathology review was blinded Per-lesion analysis

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
	10/2003	<ul style="list-style-type: none"> Mean PSA: 16.9 ng/ml 	<p><u>pathological exam unclear</u></p>	<ul style="list-style-type: none"> NPV: 39% <p>Homogeneous enhancement on DCE:</p> <ul style="list-style-type: none"> Se: 66% Sp: 75% PPV: 81% NPV: 58% <p>Irregular margin:</p> <ul style="list-style-type: none"> Se: 60% Sp: 72% PPV: 78% NPV: 53% <p>Any one criterion:</p> <ul style="list-style-type: none"> Se: 79% Sp: 27% PPV: 63% NPV: 45% <p>All 3 criteria:</p> <ul style="list-style-type: none"> Se: 34% Sp: 91% PPV: 86% NPV: 46% 	<ul style="list-style-type: none"> PPV: 85% NPV: 49% <p>Uniform low intensity on T2W + Irregular margin:</p> <ul style="list-style-type: none"> Se: 42% Sp: 88% PPV: 85% NPV: 48% <p>Homogeneous enhancement on DCE + Irregular margin:</p> <ul style="list-style-type: none"> Se: 52% Sp: 79% PPV: 80% NPV: 51% <p>Any two criteria:</p> <ul style="list-style-type: none"> Se: 68% Sp: 82% PPV: 86% NPV: 61% 	<ul style="list-style-type: none"> Transition zone: 53 cancers, 33 benign lesions
Lim HK 2009 19	<ul style="list-style-type: none"> Retrospective study Funding/Col: Supported by the Korea Research Foundation Grant funded by the Korean government (MOEHRD, Basic Research Promotion Fund) (KRF-2006-E00406) and by the Korea Science and Engineering Foundation 	<ul style="list-style-type: none"> Eligibility criteria: patients that underwent radical prostatectomy for pathologically proved prostate cancer; preoperative MRI Patient characteristics: <ul style="list-style-type: none"> Mean age: 65y Mean PSA: 10.5 ng/ml 	<p><u>Index test:</u> 1.5 T MRI with endorectal and pelvic phased-array coil; T1W, T2W, DWI (with ADC map)</p> <p><u>Reference standard:</u> Radical prostatectomy (completeness of pathological exam unclear)</p>	<p>Localisation: reader 1</p> <p>T2W</p> <ul style="list-style-type: none"> Se: 74% Sp: 79% PPV: 66% NPV: 84% <p>DWI</p> <ul style="list-style-type: none"> Se: 75% Sp: 86% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> Selection based on receiving of reference test; unclear if consecutive patients Blinded image review; unclear if pathology review was blinded Per-lesion analysis (624 segments)

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
	<ul style="list-style-type: none"> grant funded by the Korean government; Col not reported Setting: single university centre, Korea Sample size: N=52 Duration: 3/2005-2/2007 			<ul style="list-style-type: none"> PPV: 75% NPV: 86% <p>T2W+DWI:</p> <ul style="list-style-type: none"> Se: 88% Sp: 88% PPV: 80% NPV: 93% 		
McClure TD 2012 20	<ul style="list-style-type: none"> Prospective cohort study Funding/Col: funding not reported, Col declared in article Setting: single centre, US Sample size: N=104 Duration: 1/2004-4/2008 	<ul style="list-style-type: none"> Eligibility criteria: patients with biopsy-proved prostate cancer undergoing MRI before RALP Patient characteristics: <ul style="list-style-type: none"> Mean age: 60.1y Mean PSA: 6.5 ng/ml Prevalence of disease: 5% with T3 disease 	<p><u>Index test:</u> (1) 1.5 T MRI with endorectal coil: T2W (N=104), DWI (N=88), DCE (N=51) (2) MR spectroscopy (N=91)</p> <p><u>Reference standard:</u> RALP (serially sectioned, not whole mount)</p>	<p>Detection of T3 disease: 208 regions</p> <ul style="list-style-type: none"> Se: 50% Sp: 97% PPV: 50% NPV: 97% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Consecutive patients, but selection potentially based on receiving of reference test Blinded image and pathology review 1/105 patients excluded because of open prostatectomy Only region-based analysis
Morgan VA 2007 21	<ul style="list-style-type: none"> Prospective cohort study Funding/Col: grant from the Royal Marsden NHS Trust Charitable Funds; Col not reported Setting: single centre, UK Sample size: N=54 Duration: unclear 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer, elevated PSA and histology available from sextant biopsies Patient characteristics: <ul style="list-style-type: none"> Mean age: 67.6y Median PSA: 9.8 ng/ml 	<p><u>Index test:</u> 1.5 T MRI: T2W, DWI (with ADC maps)</p> <p><u>Reference standard:</u> Sextant biopsies</p>	<p>T2W:</p> <ul style="list-style-type: none"> Base, right: Se 31%, Sp 89% Base, left: Se 42%, Sp 50% Mid, right: Se 41%, Sp 78% Mid, left: Se 77%, Sp 30% Apex, right: Se 5%, Sp 91% Apex, left: Se 55%, Sp 78% 	<p>T2W+DWI:</p> <ul style="list-style-type: none"> Base, right: Se 31%, Sp 79% Base, left: Se 50%, Sp 53% Mid, right: Se 44%, Sp 59% Mid, left: Se 68%, Sp 39% Apex, right: Se 9%, Sp 91% Apex, left: Se 55%, Sp 81% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Consecutive patients; selection based on availability of reference standard results Blinded image review; unclear if pathology review was blinded Per-lesion analysis (324 sextants)
Nakashima J 2004 22	<ul style="list-style-type: none"> Cohort study Funding/Col: supported by Ministry of Education, Science and 	<ul style="list-style-type: none"> Eligibility criteria: patients with localized prostate cancer who were preoperatively evaluated 	<p><u>Index test:</u> 1.5 T MRI with endorectal coil: T2W, T1W, DCE</p>	<p>Detection of T3 disease:</p> <ul style="list-style-type: none"> Se: 62% Sp: 83% 	<p>Detection of extracapsular extension:</p> <ul style="list-style-type: none"> Se: 57% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Unclear if consecutive

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
	<p>Culture, Japan; Col not reported</p> <ul style="list-style-type: none"> • Setting: University hospital (N=1), Japan • Sample size: N=95 • Duration: not stated 	<p>by endorectal MRI with a pelvic phased-array coil, underwent radical prostatectomy, and did not receive neoadjuvant therapy before surgery; patients who had definite findings of extracapsular extension and/or seminal vesicle involvement on preoperative evaluation were not included</p> <ul style="list-style-type: none"> • Patient characteristics: not reported • Prevalence of disease: 31% had T3 disease, 29% had extracapsular extension, 6% had seminal vesicle invasion 	<p><u>(gadopentetate)</u></p> <p><u>Reference standard: Radical prostatectomy (whole-mount sections)</u></p>	<ul style="list-style-type: none"> • PPV: 60% • NPV: 84% 	<ul style="list-style-type: none"> • Sp: 82% • PPV: 57% • NPV: 82% <p>Detection of seminal vesicle invasion:</p> <ul style="list-style-type: none"> • Se: 33% • Sp: 99% • PPV: 67% • NPV: 96% 	<p>patients; inclusion potentially based on receiving of reference test; patients with definite ECE or SVI on other test were excluded</p> <ul style="list-style-type: none"> • Blinding not clearly reported • Diagnostic criteria for ECE: localized bulge, an irregular margin, disruption of the prostatic capsule, infiltration of the periprostatic fat, darkening of the periprostatic veins, and the involvement of a neurovascular bundle • Diagnostic criteria for SVI: focal wall thickening or a low-signal intensity area within the seminal vesicles
Nepple KG 2011 23	<ul style="list-style-type: none"> • Retrospective cohort study • Funding/Col: not reported • Setting: University hospital (N=1), US • Sample size: N=94 • Duration: 2003-2008 	<ul style="list-style-type: none"> • Eligibility criteria: patients with prostate cancer undergoing open radical prostatectomy and preoperative endorectal MRI • Patient characteristics: <ul style="list-style-type: none"> ○ Mean age: 61y ○ Mean PSA: 7.0 ng/ml • Prevalence of disease: 24% had extracapsular extension, 9% had seminal vesicle invasion 	<p><u>Index test: 1.5 T MRI with endorectal coil; T1W, T2W</u></p> <p><u>Reference standard: Radical prostatectomy (completeness of pathological exam unclear)</u></p>	<p>Detection of extracapsular extension: gross</p> <ul style="list-style-type: none"> • Se: 14% • Sp: 88% • PPV: 27% • NPV: 76% <p>Detection of extracapsular extension: gross + suspicious</p> <ul style="list-style-type: none"> • Se: 55% • Sp: 64% • PPV: 32% • NPV: 81% 	<p>Detection of seminal vesicle invasion:</p> <ul style="list-style-type: none"> • Se: 38% • Sp: 99% • PPV: 75% • NPV: 94% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> • Moderate risk of bias • Selection out of 309 consecutive patients; selection probably based on receiving of reference test • In 3 patients no RP was done because of positive LN on frozen section • Blinding not clearly reported • Definition of ECE and SVI not clearly provided: gross ECE yes/no, suspicion of ECE based on smooth or irregular capsular bulge
Park BK 2007 24	<ul style="list-style-type: none"> • Retrospective cohort study 	<ul style="list-style-type: none"> • Eligibility criteria: patients undergoing radical 	<p><u>Index test: (1) 3.0 T MRI with</u></p>	<p>3.0 T MRI</p>	<p>1.5 T MRI with endorectal coil</p>	<p>Level of evidence: B</p>

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
	<ul style="list-style-type: none"> Funding/Col: not reported Setting: University centre (N=1), Korea Sample size: N=108 Duration: 5/2005-3/2006 for 3.0 T MRI, 4/2003-3/2005 for 1.5 T MRI 	<p>prostatectomy because of prostate cancer</p> <ul style="list-style-type: none"> Patient characteristics: <ul style="list-style-type: none"> Median age: y Median PSA: ng/ml Prevalence of disease: T3 disease 39% (3.0 T) vs. 30% (1.5 T), extracapsular extension 39% vs. 26%, seminal vesicle invasion 4% vs. 7% 	<p><u>phased-array coil; T2W, T1W (N=54)</u> <u>(2) 1.5 T MRI with endorectal coil; T2W, T1W (N=54)</u></p> <p><u>Reference standard: Radical prostatectomy (transverse whole-mount sections)</u></p>	<p>Detection of T3 disease:</p> <ul style="list-style-type: none"> Se: 81% Sp: 67% PPV: 61% NPV: 85% <p>Detection of extracapsular extension:</p> <ul style="list-style-type: none"> Se: 81% Sp: 67% PPV: 61% NPV: 85% <p>Detection of seminal vesicle invasion:</p> <ul style="list-style-type: none"> Se: 50% Sp: 100% PPV: 100% NPV: 98% 	<p>Detection of T3 disease:</p> <ul style="list-style-type: none"> Se: 75% Sp: 68% PPV: 50% NPV: 87% <p>Detection of extracapsular extension:</p> <ul style="list-style-type: none"> Se: 71% Sp: 73% PPV: 48% NPV: 88% <p>Detection of seminal vesicle invasion:</p> <ul style="list-style-type: none"> Se: 75% Sp: 92% PPV: 43% NPV: 98% 	<ul style="list-style-type: none"> Moderate risk of bias Selection bias: only patients receiving RP were included; many exclusion stated in article; unclear if consecutive patients Blinded image and pathology evaluation Criteria for ECE: irregular contour bulging, asymmetric neurovascular bundle, obliterated rectoprostatic angle, overt extracapsular tumor, and periprostatic infiltration Criteria for SVI: hypointense seminal vesicle mass on T2W without evidence of hemorrhage on T1W Scoring system: 1, definitely not present; 2, probably not present; 3, possibly present; 4, probably present; and 5, definitely present; 4 and 5 were considered positive
Park SY 2010 25	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: funding not reported, no Col declared Setting: University hospital (N=1), Korea Sample size: N=54 Duration: not stated 	<ul style="list-style-type: none"> Eligibility criteria: patients who underwent radical prostatectomy for clinically localized prostate cancer; patients who received neoadjuvant treatment after the endorectal MRI examination and patients who had undergone a prostate biopsy and endorectal MRI within 3 weeks of each other were 	<p><u>Index test: 1.5 T MRI with endorectal coil; T2W, T1W, DCE (gadopentetate)</u></p> <p><u>Reference standard: Radical prostatectomy (completeness of pathological exam unclear)</u></p>	<p>Detection of extracapsular extension:</p> <ul style="list-style-type: none"> Se: 50% Sp: 83% PPV: 33% NPV: 90% 	<p>Detection of seminal vesicle invasion:</p> <ul style="list-style-type: none"> Se: 75% Sp: 92% PPV: 43% NPV: 98% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Selection bias: only patients receiving RP were included; unclear if consecutive patients Blinding not reported Criteria for ECE: localized bulge of the prostatic contour, a thickening or disruption of the prostatic capsule, an infiltrative strand in the periprostatic fat, or asymmetry

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
		<p>excluded</p> <ul style="list-style-type: none"> • Patient characteristics: <ul style="list-style-type: none"> ○ Mean age: 63.5y ○ Mean PSA: 7.35 ng/ml ○ cT1 59.3%, cT2 40.7% • Prevalence of disease: 15% had extracapsular extension, 7% had seminal vesicle invasion 				<ul style="list-style-type: none"> • of the neurovascular bundle • Criteria for SVI: abnormal tissue with low signal intensity within the seminal vesicle or dilatation of the seminal vesicle with asymmetry
Ren J 2009 26	<ul style="list-style-type: none"> • Retrospective cohort study • Funding/Col: not reported • Setting: University hospital (N=1), China • Sample size: N=283 • Duration: 1/2007-11/2008 	<ul style="list-style-type: none"> • Eligibility criteria: patients with clinically localized prostate cancer that underwent MRI before radical prostatectomy; none of the patients received neoadjuvant hormonal or radiation therapy before surgery • Patient characteristics: <ul style="list-style-type: none"> ○ Mean age: 68y ○ Mean PSA: 12.87 ng/ml ○ Median Gleason: 6 • Prevalence of disease: 14% had seminal vesicle invasion 	<p><u>Index test:</u> 3.0 T MRI with pelvic phased-array coil; TW1, T2W, DWI</p> <p><u>Reference standard:</u> Radical prostatectomy (transverse pathological step sections)</p>	<p>Detection of seminal vesicle invasion: 4 and 5 = positive</p> <p>T2W:</p> <ul style="list-style-type: none"> • Se: 69% • Sp: 74% • PPV: 30% (incorrect in article) • NPV: 94% • AUC: 0.779 <p>DWI:</p> <ul style="list-style-type: none"> • Se: 62% • Sp: 76% • PPV: 29% • NPV: 93% • AUC: 0.757 <p>T2W and DWI:</p> <ul style="list-style-type: none"> • Se: 74% • Sp: 89% • PPV: 52% • NPV: 96% • AUC: 0.897 (p<0.05 vs. T2W and DWI alone) 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> • Moderate risk of bias • Selection bias: only patients receiving RP were included; unclear if consecutive patients • Blinding not reported • Criteria for SVI: disruption or loss of the normal architecture of the seminal vesicle, focal or diffuse areas of low signal intensity within the seminal vesicle, low signal intensity within the seminal vesicle causing mass effect, enlarged ejaculatory ducts with low signal intensity, direct extension of the low signal intensity of tumour from the base of the prostate to the seminal vesicle on T2W images, and high signal intensity within the seminal vesicle on DWI • Scoring system: 1 indicating no SVI; 2, probably no SVI (SVI cannot be ruled out, although there is no clear evidence); 3, possible SVI

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
						(lesion is suggestive of SVI); 4, probable SVI (lesion is highly suggestive of SVI); and 5, definite SVI
Renard-Penna R 2011 27	<ul style="list-style-type: none"> Prospective cohort study Funding/Col: not reported Setting: University hospital (N=1), France Sample size: N=101 Duration: 3/2009-3/2010 	<ul style="list-style-type: none"> Eligibility criteria: patients with biopsy-proven prostate cancer, radical prostatectomy as the treatment plan performed within 1 month after imaging, needle biopsy performed at least 8 weeks before MRI, patient able to undergo MRI with a pelvic phased array, patient had no history of the use of hormonal blockade prior to surgery Patient characteristics: <ul style="list-style-type: none"> Median age: 60y Mean PSA: 8 ng/ml Mean Gleason: 6.4 Prevalence of disease: 16% had extracapsular extension 	<p><u>Index test:</u> 1.5 T MRI with pelvic phased-array coil; T1W, T2W, DCE (gadoterate)</p> <p><u>Reference standard:</u> Radical prostatectomy (open or RALP) (transverse pathologic step sections)</p>	<p>Detection of extracapsular extension: reader 1</p> <ul style="list-style-type: none"> Se: 81% Sp: 94% PPV: 72% NPV: 96% 	<p>Detection of extracapsular extension: reader 2</p> <ul style="list-style-type: none"> Se: 44% Sp: 92% PPV: 50% NPV: 90% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Consecutive patients; inclusion probably on receiving of reference test: only men for whom whole mount step section histopathologic maps from pathologic surgical specimen were available for comparison with imaging findings were included Blinded imaging review; unclear if pathology review was blinded Criteria for ECE: (1) capsular irregularity, (2) bulging of the capsule, (3) capsular retraction, (4) obliteration of the recto-prostatic angle, (5) extracapsular tumour, (6) enhancement of extracapsular tumor, (7) asymmetry or direct involvement of the neuro-vascular bundles, (8) asymmetric enhancement of neurovascular bundles Criteria for SVI: (1) focal low signal intensity mass within the lumen, (2) focal wall thickening, (3) asymmetric enhancement within the lumen; however, no

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
						diagnostic accuracy data provided
Roethke 2012 28	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: funding not reported, no Col declared Setting: single centre, Germany Sample size: N=385 Duration: 7/2003-2/2008 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer that underwent radical prostatectomy Patient characteristics: <ul style="list-style-type: none"> Mean age: 62.7y Mean PSA: 8.9ng/ml Prevalence of disease: 17% with extracapsular extension 	<p><u>Index test:</u> 1.5 T MRI with endorectal coil; T2W, T1W</p> <p><u>Reference standard:</u> Radical prostatectomy (whole-mount sections)</p>	<p>Detection of extracapsular extension:</p> <ul style="list-style-type: none"> Se: 42% Sp: 92% PPV: 69% NPV: 78% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Unclear if consecutive patients, inclusion based on receiving of reference test No blinding Criteria for ECE: Low-intensity lesions on T2W images within the peripheral zone of the prostate were considered suspicious for tumour. In the transitional zone, areas with homogeneous low-signal intensity, ill-defined margins and/or lack of capsule were interpreted as tumour foci. Asymmetric bulging, irregular margin or direct extension of the lesion in the periprostatic fat or neurovascular bundle was graded as capsular penetration Criteria for SVI: low intensity in one or both seminal vesicles
Wang 2007 29	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: Supported by National Institutes of Health grant R01 CA76423 Setting: single centre, US Sample size: N=255 Duration: 3/2004-1/2005 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer that underwent radical prostatectomy Patient characteristics: <ul style="list-style-type: none"> Mean age: 59y Prevalence of disease: 5% with seminal vesicle invasion, 27% with extracapsular extension 	<p><u>Index test:</u> 1.5 T MRI with pelvic phased-array and endorectal coil; T2W</p> <p><u>Reference standard:</u> Radical prostatectomy (whole-mount sections)</p>	<p>Detection of extracapsular extension:</p> <p>Reviewer 1 - 2, no cross-referencing:</p> <ul style="list-style-type: none"> Se: 43% - 40% Sp: 94% - 93% <p>Reviewer 1 - 2, cross-referencing</p>	<p>Detection of seminal vesicle invasion:</p> <p>Reviewer 1 - 2, no cross-referencing:</p> <ul style="list-style-type: none"> Se: 23% - 31% Sp: 83% - 91% <p>Reviewer 1 - 2, cross-referencing</p>	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Potential overlap with Wang 2010 Consecutive patients; inclusion based on receiving of reference test Blinded image review, unclear if pathology review was

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
				<ul style="list-style-type: none"> Se: 57% - 59% Sp: 100% - 98% 	<ul style="list-style-type: none"> Se: 46% - 54% Sp: 93% - 95% 	<ul style="list-style-type: none"> blinded Criteria for ECE: capsular irregularity, bulging of the capsule, capsular retraction, obliteration of the rectoprostatic angle, and asymmetry or direct involvement of the neurovascular bundles Criteria for SVI: focal low-signal-intensity mass or diffuse enlargement with low signal intensity and loss of the perceptible vesical wall on both T1- and T2-weighted sequences
Wang L 2010 30	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: funded by National Institutes of Health; no Col declared Setting: single centre, US Sample size: N=176 Duration: 1/2001-7/2004 	<ul style="list-style-type: none"> Eligibility criteria: patients who underwent endorectal MRI followed by radical prostatectomy; no neoadjuvant hormonal or radiation treatment received before RP; and at least one pathologically confirmed capsule-abutting lesion Patient characteristics: <ul style="list-style-type: none"> Mean age: 58.9y Prevalence of disease: 29% had extracapsular extension 	<p><u>Index test:</u> 1.5 T MRI with endorectal coil and pelvic phased-array coil; T1W, T2W</p> <p><u>Reference standard:</u> Radical prostatectomy (whole-mount step sections)</p>	<p>Detection of extracapsular extension (per-patient analysis):</p> <ul style="list-style-type: none"> Se: 69% Sp: 90% 	<p>Detection of extracapsular extension (per-lesion analysis):</p> <ul style="list-style-type: none"> Se: 67% Sp: 91% PPV: 57% NPV: 93% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Retrospective inclusion out of 455 consecutive patients; inclusion based on receiving of reference test Probably blinded imaging review; unclear if pathology review was blinded Definition of ECE: irregular capsular bulge, periprostatic fat infiltration, obliteration of the retroprostatic angle, and asymmetry or direct involvement of the neurovascular bundles
Wang L 2004 31	<ul style="list-style-type: none"> Retrospective cohort study Funding/Col: not reported Setting: single centre, 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer that underwent endorectal MRI before radical prostatectomy; none of 	<p><u>Index test:</u> (1) 1.5 T MRI with endorectal and pelvic phased-array coil; T1W, T2W</p>	<p>Detection of extracapsular extension:</p> <ul style="list-style-type: none"> Se: 42% Sp: 95% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Consecutive patients; inclusion based on receiving

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
	US <ul style="list-style-type: none"> • Sample size: N=344 • Duration: 5/1999-1/2003 	the patients received neoadjuvant hormonal or radiation therapy prior to surgery <ul style="list-style-type: none"> • Patient characteristics: <ul style="list-style-type: none"> ○ Mean age: 57.5y ○ Mean PSA: 7.64 ng/ml ○ cT1c 56.7%, T2a/b 33.7%, cT2c 9.6% • Prevalence of disease: 24% had extracapsular extension 	<u>(2) MR spectroscopy</u> <u>Reference standard: Radical prostatectomy (whole-mount sections)</u>	<ul style="list-style-type: none"> • PPV: 74% • NPV: 84% 		of reference test <ul style="list-style-type: none"> • Blinding not clearly reported • Definition of ECE: irregular capsular bulge, periprostatic fat infiltration, obliteration of the retroprostatic angle, and asymmetry or direct involvement of the neurovascular bundles • Potential overlap with Wang 2010

Abbreviations: 95%CI: 95% confidence interval; ADC: apparent diffusion coefficient; AUC: area under the curve; Col: conflict of interest; DCE: dynamic contrast-enhanced; DRE: digital rectal examination; DWI: diffusion-weighted imaging; ECE: extracapsular extension; LR+: positive likelihood ratio; LR-: negative likelihood ratio; MRI: magnetic resonance imaging; MRS: magnetic resonance spectroscopy; NPV: negative predictive value; PPV: positive predictive value; PSA: prostate-specific antigen; RALP: robotic-assisted laparoscopic prostatectomy; ROC: receiver operator curve; RP: radical prostatectomy; Se: sensitivity; Sp: specificity; SR: systematic review; SVI: seminal vesicle invasion; T: tesla; T1W: T1-weighted; T2W: T2-weighted; TRUS-GB: transrectal ultrasound-guided biopsy; UK: United Kingdom; US: United States.

Is (mp)MRI geïndiceerd voor het bepalen van de pelviene lymeklierstatus van bewezen prostaatacarcinoom?

Systematic reviews

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of review quality

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of review quality
Hovels AM 2008 ¹	<ul style="list-style-type: none"> SR Funding/Col: not reported Search date: 1980-2003 Databases: Medline, Cochrane Library Study designs: diagnostic studies N included studies: 10 studies on MRI (628 patients) 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer Prevalence of LN metastasis: 7-41% (average 30%) 	MRI, CT	<ul style="list-style-type: none"> Pooled sensitivity: 39% (95%CI 19-56%), range 6-83% Pooled specificity: 82% (95%CI 79-83%), range 65-99% LR+: 2.16 (95%CI 0.89-3.29) LR-: 0.74 (95%CI 0.53-1.02) 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> N included patients per study: 10-185; 9 prospective studies, 1 retrospective study; only one study with blinded evaluation Only English studies included No formal assessment of heterogeneity

Diagnostische studies

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
Harisinghani MG 2002 ²	<ul style="list-style-type: none"> Cohort study Funding/Col: not reported Setting: unclear Sample size: N=50 Duration: not reported 	<ul style="list-style-type: none"> Eligibility criteria: patients with proven primary prostate cancer and scheduled for radical prostatectomy Patient characteristics: not reported Prevalence of disease: unclear (not reported on a patient-basis) 	<p><u>Index test:</u> MR lymphangiography (1.5 T; T1W, T2W; USPIO)</p> <p><u>Reference standard:</u> Histopathology (but no details on how)</p>	<p>Diagnosis of positive pelvic lymph nodes (per-lesion analysis):</p> <ul style="list-style-type: none"> Se: 92% Sp: 93% PPV: 92% NPV: 93% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> High risk of bias Unclear design, unclear if consecutive inclusion Blinded image reading, unclear if blinded evaluation of reference test Potential differential verification Only per-lesion analysis reported (168 lymph nodes) Overlap with Harisinghani 2003?
Harisinghani MG 2003 ³	<ul style="list-style-type: none"> Prospective cohort study Funding/Col: reported in 	<ul style="list-style-type: none"> Eligibility criteria: patients with resectable prostate cancer as determined by 	<p><u>Index test:</u> 1.5 T MRI with pelvic phased-array coil;</p>	<p>Diagnosis of positive pelvic lymph nodes (per-patient analysis):</p>	<p>Diagnosis of positive pelvic lymph nodes (per-lesion analysis):</p>	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
	<p>article</p> <ul style="list-style-type: none"> Setting: 2 centres, USA and The Netherlands Sample size: N=80 Duration: 1999-2002 	<p>conventional imaging methods, DRE, US-guided sextant core biopsy, and measurement of serum PSA levels</p> <ul style="list-style-type: none"> Patient characteristics: <ul style="list-style-type: none"> Mean age: 64y Median PSA: 21 ng/ml All patients had T1-3 disease Prevalence of disease: 41% patients with LN metastasis 	<p>lymphotropic superparamagnetic nanoparticles as contrast agent</p> <p><u>Reference standard:</u> PLND (open: N=60, laparoscopic: N=15) CT-guided biopsy in 5 patients</p>	<p>MRI with contrast:</p> <ul style="list-style-type: none"> Se: 100% Sp: 96% PPV: 94% NPV: 100% <p>Conventional MRI:</p> <ul style="list-style-type: none"> Se: 45% Sp: 79% PPV: 60% NPV: 67% 	<p>MRI with contrast:</p> <ul style="list-style-type: none"> Se: 91% Sp: 98% PPV: 95% NPV: 98% <p>Conventional MRI:</p> <ul style="list-style-type: none"> Se: 35% Sp: 90% PPV: 56% NPV: 80% 	<ul style="list-style-type: none"> Included in Hovels 2008 Unclear if consecutive patients Differential verification Blinded evaluation of index and reference test
<p>Heesakkers RAM 2008 ⁴ Deserno WM 2011 ⁵</p>	<ul style="list-style-type: none"> Prospective cohort study Funding/Col: TASK24, Nieuwegein, Netherlands, partially funded; no Col declared Setting: multicentre study (N=11), The Netherlands Sample size: N=375 Duration: 4/2003-4/2005 	<ul style="list-style-type: none"> Eligibility criteria: patients with prostate cancer, serum PSA concentration of > 10 ng/mL, or Gleason score of > 6, or T3 tumour defined by DRE Patient characteristics: <ul style="list-style-type: none"> Mean age: 67y Median PSA: 15 ng/ml Median Gleason score: 7 Prevalence of disease: 16% patients with LN metastasis 	<p><u>Index test:</u> 1.5 T MRI with pelvic phased-array coil; T2W, T1W, ferumoxtran-10</p> <p><u>Reference standard:</u> PLND (open: 140/375; laparoscopic: 221/375) PLND was omitted in 14 patients: these underwent biopsy</p>	<p>Diagnosis of positive pelvic lymph nodes (per-patient analysis):</p> <ul style="list-style-type: none"> Se: 82% Sp: 93% PPV: 68% NPV: 96% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Consecutive patients No blinding Differential verification: open and laparoscopic PLND (30% more nodes removed with open PLND)
<p>Wang L 2006 ⁶</p>	<ul style="list-style-type: none"> Prospective cohort study Funding/Col: Supported by the National Institutes of Health; Col not reported Setting: single centre, USA Sample size: N=411 Duration: 11/1999-9/2003 	<ul style="list-style-type: none"> Eligibility criteria: patients with clinically localized prostate cancer; no neoadjuvant hormonal or radiation therapy before surgery Patient characteristics: <ul style="list-style-type: none"> Mean age: 57.6y Mean PSA: 7.68 ng/ml cT1c 57.8%, cT2a 23.2%, cT2b 10%, cT2c 	<p><u>Index test:</u> 1.5 T MRI with pelvic phased-array and endorectal coil; T1W, T2W</p> <p><u>Reference standard:</u> PLND</p>	<p>Diagnosis of positive pelvic lymph nodes (per-patient analysis):</p> <ul style="list-style-type: none"> Se: 27% Sp: 98% PPV: 50% NPV: 96% 		<p>Level of evidence: B</p> <ul style="list-style-type: none"> Moderate risk of bias Consecutive patients Unclear blinding

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Results secondary and other outcomes	Critical appraisal of study quality
		9% • Prevalence of disease: 5%				

Abbreviations: 95%CI: 95% confidence interval; Col: conflict of interest; CT: computed tomography; DRE: digital rectal examination; LN: lymph node; LR: likelihood ratio; MRI: magnetic resonance imaging; NPV: negative predictive value; PLND: pelvic lymph node dissection; PPV: positive predictive value; PSA: prostate-specific antigen; Se: sensitivity; Sp: specificity; SR: systematic review; US: ultrasonography; USPIO: ultrasmall superparamagnetic iron oxide.