

Value of preoperative MRI for prostate cancer staging and continence outcomes prior to prostatectomy: A review of the literature

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where the cohort population underwent pre-operative MRI followed by prostatectomy. Keywords used in the PubMed literature search included: MRI, prostate cancer, prostate cancer staging, multiparametric MRI and incontinence. Papers were included for review if they discussed use of MRI prior to prostatectomy and had corresponding pathologic data, staging, incontinence, and surgical outcomes. Primary information noted was MRI sensitivity, specificity and overall accuracy for detecting extracapsular extension (ECE) and seminal vesicle involvement (SVI). Secondary information derived included assessing the surgical influence of staging information, and identifying predictors of urinary incontinence recovery. Review of the literature showed that in regards to extracapsular extension the reported MRI accuracy ranged from 76%-98%, sensitivity from 20%-90% and specificity from 82%-99%. As for seminal vesicle involvement the reported MRI accuracy ranged from 76%-98%, sensitivity from 20%-90% and specificity from 82%-99%. There is a widely varying sensitivity and specificity for both ECE and SVI and the wide variability in the MRI technology used in the literature supports that use of MRI technology for prostate cancer remains investigational.

Key words: Magnetic resonance imaging; Metastasis; Urinary incontinence; Prostate cancer; Seminal vesicle invasion; Extracapsular extension

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Abstract

Pelvic imaging in newly diagnosed prostate cancer is primarily used for staging prior to definitive treatment. Over the past decade use of magnetic resonance imaging (MRI) for pre-surgical planning has increased, as well has the technology and methods for performing prostate MRI. To investigate and define the different MRI technologies available and further assess MRI technology ability to predict pathologic stage. Searching PubMed, we identified current published literature,

Core tip: Over the past decade use of magnetic resonance imaging (MRI) for pre-surgical planning has increased, as well has the technology and methods for performing prostate MRI. To investigate and define the different MRI technologies available and further assess MRI technology ability to predict pathologic stage. We evaluated the current literature to identify MRI sensitivity, specificity and overall accuracy for detecting extracapsular extension and

seminal vesicle involvement. Primary information noted was MRI sensitivity, specificity and overall accuracy for detecting extracapsular extension and seminal vesicle involvement. Secondary information derived included assessing the surgical influence of staging information, and identifying predictors of urinary incontinence recovery.

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INTRODUCTION

Pelvic imaging in newly diagnosed prostate cancer patients is used to stage biopsy-proven prostate cancer. Accurate staging may identify men with pelvic lymphadenopathy or locally extensive disease who are less likely to benefit from an attempt at definitive treatment. Accurate staging may also potentially guide intraoperative decisions about the ability to perform neurovascular bundle sparing. Historically, pelvic imaging has been performed by computerized tomography (CT) scan but, over time, the utilization of magnetic resonance imaging (MRI) imaging has increased based on expectation of improved accuracy.

With advances in MRI technology, pre-surgical MRI is gaining favor, as evidenced by a 6.2% increase in usage of MRI between 1999-2006^[1]. Endorectal MRI (ER-MRI) can be used to identify suspicious areas within the prostate that may influence therapeutic decisions as well as the operative approach to nerve sparing. The purpose of this review is to evaluate the accuracy of preoperative MRI in regard to identifying extracapsular extension (ECE), seminal vesicle involvement (SVI) and lymph node metastasis. Secondly, we assess MRI's influence on surgical outcomes (positive margins) and ability to predict biochemical recurrence.

CURRENT RECOMMENDATIONS ON PELVIC IMAGING IN PROSTATE CANCER

The majority of men with a prostate cancer diagnosis may not require pelvic imaging prior to definitive treatment. Studies have shown that the vast majority of prostate cancers are low risk, localized, stage T1-T2 tumors, with an average prostate specific antigen (PSA) of 6.7 ng/mL^[2] and thus do not meet the requirement for pelvic imaging. Due to concerns for overuse there have been quality improvement efforts to decrease the use of imaging in low risk prostate cancer patients^[3].

Several major organizations have proposed guidelines for appropriate pelvic imaging in patients with prostate cancer. The American Urological Association Best Practice

Statement recommends obtaining pelvic imaging only in high-risk patients: Gleason grade ≥ 8 on biopsy, PSA > 20 ng/mL or digital rectal examination concerning for extra prostatic extension^[4]. The European Association of Urology additionally includes patients with Gleason 7 in their recommendations for pelvic imaging^[5]. Lastly, the National Comprehensive Cancer Network guidelines (version 2.2014) recommend obtaining pelvic imaging for clinically T3, T4 or T1-2 tumors in which nomogram predicts the probability of lymph node involvement at $> 10\%$ ^[6]. All three organizations indicate either CT scan or MRI may be used for pelvic imaging.

MRI TECHNOLOGY

Various MRI technologies are currently in use. A recent evaluation of 36 academic centers reported that 83% were routinely utilizing pelvic MRI for prostate cancer^[7]. Of the 30 programs that responded to a questionnaire, 25% performed imaging using 1.5 T with an endorectal coil, 31% used 3.0T without an endorectal coil and 28% used 3.0 T with an endorectal coil. They also showed that most used diffusion-weighted imaging (95%) and dynamic contrast of enhancement (82%) while only 21% of the centers used MR spectroscopy as part of their standard protocol. The takeaway from this work is that it is important to know what MRI technology each institution has available, as well as its strengths and weaknesses for imaging the prostate.

In the remainder of this section, we will discuss the various MRI modalities and how they affect the ability to visualize the prostate. Notably, T-1 weighed images alone are not useful due to the inability to visualize prostate anatomy. Due to low contrast uptake in the prostate, T-2 weighted images are the main imaging modality used for imaging the prostate because of high spatial resolution and ability to delineate the peripheral zone from the central and transitional zone anatomy. However, T-2 prostate cancer images appear with low signal intensity^[8]. Post-biopsy hemorrhage can also appear as a low uptake region on T2 weighted images. However, T1 imaging can be used to differentiate hemorrhage from prostate cancer, as the former has increased and the latter decreased intensity on T1 imaging.

The use of T2 weight images with other techniques is known as multiparametric imaging. These include dynamic enhanced contrast imaging, diffusion weighted imaging, and MR spectroscopy.

Dynamic enhanced contrast imaging operates on the premise that increased vascularity is present in prostate cancer due to local hypoxia. The mechanism of angiogenesis is felt to be due to influence of vascular endothelial growth factor. This change can be studied by comparing the uptake and washout of gadolinium chelate contrast in normal and cancerous tissues^[9].

Diffusion weighted-proton diffusion uses the properties in water to produce image contrast. The images produced

Table 1 Clinical usefulness characteristics of magnetic resonance imaging for determining extracapsular extension

Ref.	Characteristic
Schiebler <i>et al</i> ^[14]	Asymmetry of the neurovascular bundle Obliteration of the rectoprostatic angle
Outwater <i>et al</i> ^[15]	A bulge in the prostatic contour Gross extracapsular tumor extension into the periprostatic fat

by the reflected protons are then acquired by applying motion gradients that cause phase shifts based on the direction and quality of the proton movement. Healthy prostate tissue is rich in structures that allow for extensive diffusion of water molecules in comparison to prostate cancer, which destroys glandular structure architecture resulting in different diffusion^[10].

MR spectroscopy reflects resonance frequencies unique to protons in the metabolites citrate and choline. When compared to normal prostate tissue, citrate is reduced and choline increased in prostate cancer due to increased cell turnover^[11].

In 2012 the European Society of Urogenital Radiology published guidelines recommending that multiparametric MRI be used for prostate cancer, which they defined as "a combination of high-resolution T2-weighted images (T2WI), and at least two functional MRI techniques, as these provide better characterization than T2WI with only one functional technique"^[12]. Thus, there remains lack of consensus as to the definitive use of all modalities. It is clear based on evidence from pre-biopsy imaging, however, that varying combinations improve the sensitivity for detecting prostate cancer^[13].

MRI FOR STAGING

The ability to accurately stage prostate cancer prior to prostatectomy would be beneficial in terms of optimizing the aggressiveness of neurovascular bundle sparing and the prevention of positive surgical margins. Studies assessing MRI staging accuracy have primarily focused on ECE and SVI.

STAGING FOR ECE

MRI was first proposed as a potentially useful tool for determining ECE by Schiebler *et al*^[14] in 1992 based on their identification of the characteristic findings of asymmetry of the neurovascular bundle and obliteration of the rectoprostatic angle^[14]. Two years later, Outwater *et al*^[15] added two additional characteristics: bulge in the contour of the prostate and extracapsular tumor gross extension in the periprostatic fat^[15] (Table 1). Using these as indications to determine extracapsular extension, studies were done looking into the accuracy of various MRI modalities and comparing their ability to identify ECE on prostatectomy specimens.

Several studies using the above criteria have looked at the accuracy, sensitivity, and specificity of predicting ECE. The accuracy ranged from 59%-95%, sensitivity from 14%-86% and specificity from 70%-99% (Table 2). Notably, several studies confirmed that an endorectal coil improved all three. In addition, studies using multiparametric MRI showed slight improvement. However it is difficult to compare studies due to the variability in technology used, for example: 1.5T vs 3.0T and different definitions of "multiparametric".

STAGING OF SEMINAL VESICLE INVASION

Due to prognostic and management implications, the ability to identify SVI preoperatively would be useful. Studies assessing this have reported MRI accuracy ranging from 76%-98%, sensitivity from 20%-90% and specificity from 82%-99%. The widely varying ranges observed likely stem from the significantly different MRI imaging technologies used. Thus, direct comparison of the accuracy between institutions is difficult. However, as was the case for ECE, many of the studies show that use of T2-weighted images with addition of endorectal coil was superior to T2 weighted images with pelvic phased array (Table 3).

FACTORS INFLUENCING STAGING MRI ACCURACY

Several prostate MRI studies have observed that experience of the radiologist influenced the overall accuracy of staging. For example Latchamestty *et al*^[16] compared their first 40 ER-MRI to their second 40 and noted an overall modest increase in staging accuracy. Bloch *et al*^[17] and Fütterer *et al*^[18] also commented that accuracy changed considerably with radiologist experience. With this in mind, it is important to know the experience of the radiologist at one's institution. Secondly, it has been observed that higher Gleason score on biopsy and on final pathology correlates with increased cancer detection on preoperative MRI^[19]. Thirdly, an abnormal prostate exam increased preoperative MRI accuracy^[20].

IMPACT OF PREOPERATIVE MRI ON SURGICAL TREATMENT

Information from MRI may also be utilized to guide intraoperative decision making. As stated previously, information about ECE or SVI may influence the aggressiveness of nerve sparing during the operation. Knowledge of prostate adenocarcinoma location preoperatively may additionally influence surgical technique and impact the sensitive margin rate.

Roethke *et al*^[21] evaluated the impact of preoperative MRI on nerve sparing and positive surgical margin

Table 2 Accuracy, sensitivity and specificity of predicting extracapsular extension by magnetic resonance imaging

Ref.	Imaging technology	Tesla	n	Accuracy	Sensitivity	Specificity	Comment
Bloch <i>et al</i> ^[17]	T2w imaging combined with dynamic contrast enhancement	1.5	32	95%	86%	96%	Determination of ECE increased by 25% with addition of DCE
Chandra <i>et al</i> ^[30]	T2w imaging with ER-MRI	1.5	38	76	69	82	
Fütterer <i>et al</i> ^[18]	T2w imaging with pelvic phased array and T2w imaging with endorectal coil	1.5	81	76-83 ER-PPA 61-63 PPA	47-63 ER-PPA 43-60 PPA	96 ER-PPA 70-72 PPA	Single reader with conscious readers bc/de?
Park <i>et al</i> ^[31]	3.0 T2w pelvic phase array <i>vs</i> er MRI	3.0 <i>vs</i> 1.5	108 (54 in each group)	72 3T <i>vs</i> 70 1.5T	1.5-T 71% 3.0-T 81%	1.5-T 73% 3.0-T 67%	The 3.0-T MRI had a lower incidence of MR artifacts than the 1.5-T MRI ($P < 0.05$). However, overall imaging quality at both 3.0 and 1.5 T had no significant difference
Zhang <i>et al</i> ^[32]	MRI with endorectal and pelvic multicoil array	1.5	110	91	55	99	
Tan <i>et al</i> ^[33]	T2w- with ERC	1.5	32	59	14	94	
Nepple <i>et al</i> ^[20]	ER-MRI	1.5	94	70	14	88	
Bloch <i>et al</i> ^[34]	T2w imaging with fast spin echo and DCE	3.0	108	86 (80%-91%)	75 (64%-83%)	92 (88%-95%)	NPV/PPV:79/91 Stratified by reader experience
Latchamsetty <i>et al</i> ^[16]	ER-MRI		80	53-73	31-64	71-78	First 40 and second 40. Concluded that experience increases accuracy
Beyersdorff <i>et al</i> ^[35]	T2w ER-MRI <i>vs</i> T2w imaging with torso-array	1.5 <i>vs</i> 3.0	22	73% (both)	1.5T; Extended continuity with capsule-100; Smooth bulging-80; Irregular bulging-80; Direct periprostatic infiltration-20; Asymmetry of NVB-20; Displacement of rectoprostatic angle-0 3-T; Extended continuity with capsule-100; Smooth bulging-60; Irregular bulging-40; Direct periprostatic infiltration-20; Asymmetry of NVB-40; Displacement of rectoprostatic angle-20	1.5T; Extended continuity with capsule-23; Smooth bulging-39; Irregular bulging-50; Direct periprostatic infiltration-83; Asymmetry of NVB-83; Displacement of rectoprostatic angle-100 3-T; Extended continuity with capsule-50; Smooth bulging-44; Irregular bulging-56; Direct periprostatic infiltration-72; Asymmetry of NVB-67; Displacement of rectoprostatic angle-89	Determined that image quality and tumor delineation was better with 1.5T2w ER-MRI
Lee <i>et al</i> ^[36]	ERC <i>vs</i> pelvic phased array	1.5	47 ERC <i>vs</i> 44 PPA	64	32 ERC <i>vs</i> 30 PPA	96 ERC <i>vs</i> 90 PPA	
Hegde <i>et al</i> ^[19]	T2w multiparametric ER-MRI-T2w, T1w, DCE and DW	3.0	118	75	28	91	Presence of a T3 lesion on final pathology was associated with T3 on MRI or higher Gleason score (8-10)
Kim <i>et al</i> ^[24]	T2w pelvic array MRI <i>vs</i> T2w imaging ER-MRI	1.5 <i>vs</i> 3.0	151 63 ER-88 pelvic phase array	61.4 PPA 63.4 ERC	31 PPA 33 ERC	98 PPA 97 ERC	
Tanaka <i>et al</i> ^[22]	T2w pelvic phase array	3.0	67	-	60	86	Specifically mention they did not use an ER-MRI
Roethke <i>et al</i> ^[21]	T2w imaging with ER-MRI	1.5	385	76	42	92	Overstaging occurred in 5.7% and under staged in 17.9% 91.8% sens/41.5%spec in predicting T2 disease dropped to 40.7%sen/92.9%spec for cT3

MRI: Magnetic resonance imaging; ER-MRI: Endorectal MRI; ECE: Extracapsular extension; DCE: Dynamic contrast enhanced; DW: Diffusion weighted; PPA: Pelvic phase array; ER-PPA: Endorectal pelvic phase array; NPV: Negative predictive value; PPV: Positive predictive value; ERC: Endorectal coil; NVB: Neurovascular bundle.

Table 3 Studies assessing magnetic resonance imaging accuracy in predicting seminal vesicle involvement

	Imaging technology	Tesla	n	Accuracy	Sensitivity	Specificity	Comment
Chandra <i>et al</i> ^[30]	T2w imaging with ER-MRI	1.5	38	76	69	82	
Fütterer <i>et al</i> ^[18]	T2w imaging with pelvic phased array and T2w imaging with endorectal coil	1.5	81	90-98 ER-PPA 76-86 PPA	40-90 ER-PPA 30-50 PPA	92-99 ER-PPA 80-94 PPA	
Latchamsetty <i>et al</i> ^[16]	ER-MRI		80	80-85	20-22	94-100	First 40 and second 40. Concluded that experience increases accuracy
Park <i>et al</i> ^[31]	PPA vs er MRI	3.0	108 (54 in each group)	3-T 98 vs 1.5-T 91%	1.5-T 75% 3.0-T 50%	1.5-T 92% 3.0-T 100%	The 3.0-T MRI had a lower incidence of MR artifacts than the 1.5-T MRI ($P < 0.05$). However, overall imaging quality at both 3.0 and 1.5 T had no significant difference
Zhang <i>et al</i> ^[32]	MRI with endorectal and pelvic multi-coil array	1.5	110	99	80	99	
Lee <i>et al</i> ^[36]	1.5 T ERC vs pelvic phased array	1.5	47 ERC vs 44 PPA	89	50 ERC vs 50 PPA	93 ERC vs 98 PPA	
Nepple <i>et al</i> ^[20]	T2w ER-MRI	1.5	94	93	38	99	
Hegde <i>et al</i> ^[19]	T2w multiparametric ER-MRI-T2w, T1w, DCE and DW	3.0	118	95	50	99	Presence of a T3 lesion on final pathology was associated with T3 on MRI or higher gleason score (8-10)
Kim <i>et al</i> ^[24]	T2w pelvic array MRI vs T2w imaging ER-MRI	1.5 vs 3.0	151 63 ER-MRI vs 88 pelvic phase array	81 PPA 83 ERC	43 PPA 46 ERC	92 PPA 93 ERC	

MRI: Magnetic resonance imaging; ER-MRI: Endorectal MRI; DCE: Dynamic contrast enhanced; DW: Diffusion weighted; PPA: Pelvic phase array; ER-PPA: Endorectal pelvic phase array.

rates. Bilateral nerve sparing was feasible in 48.4% of patients with stage clinical T2 lesions but in only 19.7% patients with clinical T3 or T4 disease on MRI. ER-MRI stage did not impact the possibility for patients to receive a unilateral nerve-sparing procedure, as they were able to accomplish this in 35.1% of patients with ER-MRI stage cT2 tumors and 35.2% of the patients with ER-MRI stage T3/T4 disease. Additionally, they found that positive margin rates were lower (10.8%) for cases noting no ECE on preoperative MRI compared to MRI diagnosed cT3 lesions (32.4%).

Tanaka and associates used 3-T MRI to make the decision on whether to perform nerve sparing vs resection based on evidence for ECE^[22]. Of the cases where preoperative MRI showed no evidence of ECE, 38.7% underwent nerve sparing with an overall positive margin rate of 7.5%. No patients who underwent nerve-sparing had a positive surgical margin identified. When ECE was identified on MRI, only 1 patient of the 28 was able to undergo a nerve sparing surgery. Despite this, the overall positive margin rate was 46.4%. Surgical specimens in the 67 patients identified were 75% pT2 and 25% pT3. From this, their conclusion was that MRI evidence of ECE can be used to guide surgical decision making.

CONTINENCE

Men who undergo a prostatectomy uniformly develop some degree of postoperative urinary incontinence, with

variable rates of recovery and an unknown expected final result. While a majority of men recover satisfactorily, some eventually require surgical correction. Several investigators have identified factors that influence this recovery and expected final continence status by analyzing different anatomical landmarks on preoperative MRI.

Paparel *et al*^[23] assessed whether recovery of urinary continence after open retropubic prostatectomy is influenced by preoperative membranous urethral length (MUL) identified on ER-MRI. Sixty-four patients were studied using pre- and postoperative MRI. Twenty-four patients had a MUL greater than 14 mm. They noted that these patients had improved rates of continence as well as time to continence and thus they concluded that longer preoperative MUL was in fact associated with superior continence rates.

Kim *et al*^[24] evaluated both RALP and RRP continence rates, defining continence as pad-free. They noted that longer preoperative MUL on MRI and younger age were independent prognostic factors for continence recovery.

Lim *et al*^[25] looked at anatomical information including MUL, thickness of the levator ani muscle and urogenital diaphragm on preoperative MRI to determine if these factors influenced continence status post retropubic prostatectomy. They further categorized patients into four groups based on the overlying pattern of the prostatic apex and the membranous urethra. They noted that membranous urethral length > 14.24

mm and the type of prostatic apex were significant predictors of continence at 12 mo.

von Bodman *et al.*^[26] studied preoperative MRI predictors of continence recovery. They found that urethral length and urethral volume were statistically significant predictors of regaining continence at both 6 mo and 12 mo.

As stated above, shorter urethral sphincter length on preoperative ER-MRI has been associated with increased risk of postoperative urinary incontinence and longer time to continence. Nguyen *et al* utilized this information to evaluate alternative anatomical reconstruction techniques done at their institution^[27]. They started in 2005 by using a previously described apical dissection and urethrovesical anastomosis in robotic radical prostatectomy. They then moved to an anterior reconstruction with preservation of the puboprostatic collar. In 2007 they started performing a total reconstruction with the addition of posterior reinforcement. This additional reinforcement technique was done by using a reinforcing stitch at the midline suturing of the right and left detrusor flaps behind the bladder neck to create a thick muscular bladder neck and a retrotrigonal flap, sutured into the posterior bladder neck. Based on these techniques, they assessed the overall impact of their techniques on continence and specifically in men with shorter urethral length. They studied 274 patients receiving a 1.5T endorectal MRI prior to robot-assisted laparoscopic prostatectomy. Urethral lengths were measured on the T2-weighted images and all sphincter lengths were measured from the prostatic apex to the penile bulb. They defined short urethral lengths as < 14 mm and continence was defined as zero pads or only a liner for security reasons. They observed that men with a short urethral length had a continence rate of only 47% compared to 80% for men with longer sphincter lengths on MRI. Their surgical modifications also increased the continence rate to 81% for their anterior reconstruction and 90% for a total reconstruction, up from 47%. Men with longer urethral length on MRI had only a 3% increase of continence if they received anterior reconstruction but a 19% increase of continence if they received a total reconstruction for the longer urethral length (up from 80%).

CHANCE OF BIOMEDICAL RECURRENCE BASED ON MRI

Hattori *et al.*^[28] reported that MRI stage T3 predicted for biochemical recurrence. However, long term prostate cancer oncologic outcomes relative to preoperative MRI are not available. While the analogous nature of breast cancer to prostate cancer is not certain, the concept of improved local control by preoperative MRI staging has been evaluated in breast cancer where a recent meta-analysis reported no improvement in local recurrence or distant recurrence in breast cancer

patients who received preoperative breast MRI^[29].

CONCLUSION

Preoperative MRI for prostate cancer has become increasingly utilized since the early 1990s. With advancement in technology and expansion of imaging modalities, prostate cancer detection and staging information can now be more readily ascertained. While the primary current use of prostate MRI is preoperative staging, widely varying sensitivity and specificity for both ECE and SVI and the wide variability in the MRI technology used in reported studies supports that use of MRI technology for prostate cancer remains investigational. While there appears to be a potential role in determining aggressiveness of neurovascular bundle sparing and for assessment of urethral length towards improvement in the prediction of continence recovery, no routine recommendation to use this technology should be made. Instead, the urologist should selectively use this technology based on the equipment and expertise present at their own institution. Future study is needed to further identify the value of preoperative MRI for guiding surgical decision making and evaluating the impact on patient outcomes.

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