Magnetic resonance imaging (MRI) for localization of the prostatic apex: comparison to computed tomography (CT) and urethrography

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Abstract

Background and purpose: It is necessary to include the entire prostate in the high dose treatment volume when planning radical radiation for patients with prostate cancer. We prospectively compared magnetic resonance imaging (MRI) to computed tomography (CT) and urethrography as means of localizing the prostatic apex.

Materials and methods: Thirty patients with clinically localized prostate cancer had a sagittal T2-weighted MRI scan and a conventional axial CT scan performed in the treatment position prior to the start of radiotherapy. Twenty of these patients had a static retrograde urethrogram performed at simulation. The position of the MRI and CT apices were localized independently by two radiation oncologists. In addition, the MRI apex was localized independently by a diagnostic radiologist. The urethrogram apex, defined as the tip of the urethral contrast cone, was easily identified and was therefore localized by only one observer.

Results: There was good interobserver agreement in the position of the MRI apex. Interobserver agreement was significantly better with MRI than with CT. There were no systematic differences in the position of the MRI and CT apices. However, the MRI apex was located significantly above and behind the urethrogram apex. There was poor correlation between MRI and CT and between MRI and urethrogram in the height of the apex above the ischial tuberosities. There was 83% agreement between MRI and CT and 80% agreement between MRI and urethrogram in the identification of patients with a low-lying apex. The apex, as determined by MRI, was 2 cm above the ischial tuberosities and therefore potentially under-treated in 17% of the patients.

Conclusions: MRI is superior to CT and urethrography for localization of the prostatic apex. All patients undergoing radiotherapy for prostate cancer should have localization of the apex using MRI or a technique of equal precision to assure adequate dose delivery to the entire prostate and to minimize the unnecessary irradiation of normal tissues. © 1998 Elsevier Science Ireland Ltd. All rights reserved

Keywords: Prostate cancer; Prostatic apex; Radiotherapy; Magnetic resonance imaging

1. Introduction

Prostate cancer is now the most frequently diagnosed malignancy in men in both Canada [10] and the United States [27]. Approximately 65% of men with prostate cancer have localized disease at diagnosis [24] and are potentially curable with radiotherapy. It is necessary to encompass the entire prostate, with or without the seminal vesicles depending on whether or not they are involved by tumor, in the high dose radiation volume in order to maximize the probability of cure [13,14,29]. This implies the need for careful radiotherapy treatment planning and precise definition of the prostatic anatomy. Recent developments in the use of conformal radiotherapy for prostate cancer [9,22,34] further highlight the need for accurate tumor localization [31].

Computed tomography (CT) scan is widely used to plan radiotherapy for prostate cancer [11] but has limitations. The anterior, posterior and lateral borders of the prostate can usually be seen clearly on CT. However, the prostatic
apex is often radiographically indistinct from the urogenital diaphragm and difficult to identify with certainty. Recognizing this limitation, a variety of techniques for accurately localizing the apex have been proposed, including urethrography [6,28,30,33,36,39] and the use of implanted radioopaque markers [7,35,37,42]. However, the general superiority of one technique over another has not been clearly established. Given this uncertainty, it has often been recommended that the inferior radiation field border be routinely positioned at the most inferior aspect of the ischial tuberosities, with the belief that this provides adequate coverage of the prostatic apex in most patients [13,14].

Magnetic resonance imaging (MRI) has several potential advantages over other methods of localizing the prostatic apex. It is a non-invasive technique which allows the direct generation of high definition high contrast images in sagittal and coronal planes that contain the prostatic apex and warrants further evaluation as an alternative to the aforementioned more established techniques [19].

We prospectively evaluated three minimally invasive methods of localizing the prostatic apex and in particular compared MRI to CT and urethrography. The specific aims of the study were (1) to determine the technical feasibility of localizing the prostatic apex using MRI, (2) to evaluate the interobserver variation in the position of the prostatic apex as determined by MRI and CT, (3) to compare the position of the prostatic apex as determined by MRI, CT and urethrography and (4) to estimate how frequently the prostatic apex receives less than the prescribed dose when the inferior field border is positioned at the inferior aspect of the ischial tuberosities.

2. Materials and methods

Patients with pathologically proven clinically localized prostatic adenocarcinoma, in whom a decision to treat radically with conventional (non-conformal) external beam radiotherapy was previously made, were eligible for the study. This included patients with T1–3, N0, M0 tumors as per the 1992 UICC TNM classification [17], regardless of histologic grade or PSA level. Patients with a history of urethral stricture requiring dilatation, allergy to radiographic contrast, or a contraindication to MRI (such as an implanted metallic foreign body, a cardiac pacemaker, or severe claustrophobia) were ineligible. Staging investigations included PSA determination, chest X-ray, bone scan and CT scan of the abdomen and pelvis. Pelvic lymphadenectomy was not performed routinely.

After informed consent was obtained, patients underwent an MRI scan, CT scan and a static retrograde urethrogram to localize the apex. All imaging was done with the patients supine in the treatment position. The legs were either slightly flexed and supported on a pillow or positioned in a non-customized foam rubber form [5]. Patients were asked to drink 500 ml of water 30 min before each study to assure a full urinary bladder. All studies were completed before the start of radiotherapy.

Sagittal fast spin echo T2-weighted MR images of the pelvis were obtained using a 1.5 T Signa General Electric machine and a phased-array pelvic coil. The image slice thickness was 4 mm. The matrix was 256 × 256 and the field of view was 24 cm. A mid-sagittal image as well as two or three images 5 mm apart on either side of the midline were obtained. The MRI apex was defined as the most inferior extent of tumor or prostatic tissue in any of these images. Sagittal images were used because, as shown in Fig. 1, the contour of the more superior aspects of the prostate is clearly delineated and can be followed inferiorly to aid in identifying the apex.

Axial CT images of the pelvis were obtained at 1 cm increments from the level of the mid-sacrum to below the ischial tuberosities in accordance with the protocol that is presently used to plan conventional radiotherapy for prostate cancer at this institution. No oral, intravenous, urethral, or bladder radiographic contrast was used. The axial CT images were compared to the sagittal MRI and lateral urethrogram films using a lateral CT scout film. The CT apex was defined as the most inferior extent of tumor or prostatic tissue in any of the axial images.

A static retrograde urethrogram was performed at the time of simulation according to a modification of the technique of McCallum and Colapinto [23]. A size 14 Foley catheter was inserted approximately 2 cm into the penile urethra using aseptic techniques and without lubricant or topical anesthetic. The balloon of the catheter was inflated in the fossa navicularis until the patient experienced mild discomfort and 10–20 ml of sterile diatrizoate sodium (Hypaque®) was injected. The urethrogram apex was defined as the tip of the urethral contrast

Fig. 1. Mid-sagittal fast spin echo T2-weighted MRI of the prostate gland. The arrow indicates the position of the MRI prostatic apex.
column as seen on a lateral simulator film. A typical urethrogram is shown in Fig. 2.

In most cases the MRI apex was identified in either the mid-sagittal image, or in the immediately adjacent sagittal images that were displaced from the midline by 5 mm. For the purpose of the analysis, the prostatic apex was therefore assumed to lie in the mid-sagittal plane. A two-dimensional coordinate system was defined in this plane with the origin at the sacral promontory. The superior–inferior (SI) axis was defined as being parallel to the treatment couch and the anterior–posterior (AP) axis as perpendicular to this. Positive coordinates in the SI and AP directions were defined as those superior and anterior to the origin, respectively. The ability to accurately map points from MRI, CT and urethrogram to this coordinate system was evaluated by comparing the position of a bony reference point that was easily identified using each of the three techniques. This point was defined by the intersection of two lines which were tangent to the most anterior and superior aspects of the symphysis pubis and parallel to the SI and AP axes, respectively. Measurements from the MRI, CT and urethrogram films were scaled by the appropriate magnification factors to yield anatomic dimensions before mapping to this coordinate system.

The MRI and CT apices were localized independently by two radiation oncologists who treat prostate cancer (M.M. and P.W.). The MRI apex was also localized independently by an experienced diagnostic radiologist (R.B.). In contrast to MRI and CT, urethrography yielded a well defined point representative of the prostatic apex (Fig. 2) that was not subject to the same degree of observer interpretation. The urethrogram apex was therefore localized by only one observer (M.M.).

Interobserver variation in the position of the MRI and CT apices was evaluated by calculating the pair-wise SI and AP differences in the position of the MRI and CT apices in each patient and the mean pair-wise differences and 95% confidence intervals for the entire cohort. Interobserver variation is reflected in mean SI and AP differences significantly greater or less than zero, indicating a systematic tendency of one observer to locate the apex differently than the other observer, and large standard deviations about the means, indicating randomly distributed differences in how the apex was localized by the two observers. Mean differences were compared using the Student’s t-test, and standard deviations were compared using the F-test [32].

The true prostatic apex was, for the purpose of this study, considered to have been inadequately treated if it was <2 cm above the inferior field border. This margin was chosen to allow for subclinical extra-prostatic extension of tumor, day-to-day set-up variation [4,5,8,12,16,38], internal prostate movement [7,40] and treatment beam penumbra. It is consistent with the requirements of ongoing clinical trials of conventional (non-conformal) radiotherapy for prostate cancer [1,2]. The Pearson correlation coefficient was used to compare the distance of the MRI and CT, and MRI and urethrogram apices above the ischial tuberosities [32].

3. Results

The prostatic apex was localized in 30 patients using MRI and CT. Twenty of these patients also had urethromgrams. The median age was 68 years (range 56–80 years). There were eight T1 tumors, 20 T2 tumors and two T3 tumors. The Gleason score was ≤5 in five patients, 6–8 in 24 patients and 9–10 in one patient. The median PSA was 10.3 (range 0.1–54.0). Six patients received neoadjuvant hormone therapy that was started prior to referral for radiotherapy. Six patients had previously undergone transurethral resection of the prostate.

The position of the bony pelvic reference point at the symphysis pubis was compared among MRI, CT and urethrogram in a pair-wise fashion as an indication of the accuracy and transferability of the coordinate system. There were no systematic differences and the standard deviation of the differences ranged from 0.33 to 0.48 cm in the SI direction and from 0.60 to 0.72 cm in the AP direction. Interobserver variation in the position of the MRI apex is shown in Fig. 3. There was good SI agreement between the diagnostic radiologist (observer 1) and one of the radiation oncologists (observer 2). However, the second oncologist (observer 3) located the apex 0.34 ± 0.17 cm higher than

![Fig. 2. Static retrograde urethrogram. The arrow indicates the position of the urethrogram prostatic apex at the tip of the urethral contrast cone.](image)
did observer 1 and 0.25 ± 0.17 cm higher than did observer 2. The standard deviation in the SI direction was between 0.42 and 0.47 cm for all three comparisons. There were no systematic differences in the AP direction and the standard deviation was between 0.51 and 0.57 cm.

Interobserver variation in the position of the CT apex between the two radiation oncologists is shown in Fig. 4. Observer 2 located the apex 0.60 ± 0.28 cm inferior to that of observer 3. There was no systematic difference in the AP direction. For comparison, Fig. 4 also shows the interobserver variation in the position of the MRI apex for the two oncologists. The systematic difference in the SI direction was significantly smaller with MRI than with CT (0.25 versus 0.60 cm, \( P < 0.04 \)). There was also significantly less variability about the mean with MRI than with CT in both the SI (standard deviations 0.47 and 0.75 cm, respectively, \( P < 0.01 \)) and AP directions (standard deviations 0.53 and 0.81 cm, respectively, \( P < 0.03 \)).

The means of the two and three CT and MRI observations, respectively, in each patient were used to compare the position of the apex among the techniques and to the ischial tuberosities. As illustrated in Fig. 5, there were no systematic differences in how the apex was localized by MRI and CT. However, random differences existed in some patients, as reflected by standard deviations of 0.80 and 0.72 cm in the SI and AP directions, respectively. The distance of the MRI and CT apices above the ischial tuberosities correlated poorly (\( r = 0.3, P = 0.07 \)), which also indicates random variation in individual patients.

The MRI apex was located 0.57 ± 0.39 cm above and 0.72 ± 0.30 cm behind the urethrogram apex, reflecting the thickness of the urogenital diaphragm which anatomically separates these points [41]. The distance of the MRI and urethrogram apices above the ischial tuberosities correlated poorly (\( r = 0.3, P = 0.2 \)). The apparent thickness of the urogenital diaphragm, defined as the SI separation between the MRI and urethrogram apices, varied in individual patients from -0.8 cm (implying that the urethrogram apex was above the MRI apex) to 3.2 cm (mean thickness 0.57 ± 0.39 cm).

As shown in Fig. 6, the MRI and CT apices were <2 cm above the ischial tuberosities in five (17%) of 30 and eight (27%) of 30 patients, respectively. There was 83% agreement between MRI and CT in the identification of patients with a low-lying apex. CT failed to identify a low-lying apex in one patient and falsely identified a low apex in four patients relative to MRI.

Fig. 7 shows the position of the MRI and urethrogram apices relative to the ischial tuberosities for the 20 patients in whom both studies were performed. The urethrogram apex was <1.5 cm above the ischial tuberosities in four (20%) of 20 patients and <1 cm above the ischial tuberosities in three (15%) of 20 patients. There was 80–85% agreement between MRI and CT in the identification of patients with a low-lying apex. CT failed to identify a low-lying apex in one patient and falsely identified a low apex in four patients relative to MRI.
agreement between MRI and urethrogram in the identification of patients with a low-lying apex, depending on whether the urethrogram cut-off was selected at 1 or 1.5 cm above the ischial tuberosities. Urethrogram failed to identify a low-lying apex in two patients and falsely predicted a low apex in one or two patients (1 and 1.5 cm urethrogram cut-off, respectively) relative to MRI.

4. Discussion

The normal prostate is pyramidal in shape and situated between the base of the bladder and the urogenital diaphragm. Historically, it was felt that the prostatic apex rested atop the urogenital diaphragm and was distinct from it [41]. However, recent surgical series have demonstrated an anatomical continuum between these structures making precise demarcation difficult [25,26]. The urogenital diaphragm is nominally 1 cm thick [23,30], although it has been reported to range from 0.5 to 2 cm [6].

The optimal method of localizing the prostatic apex, which we have defined as the most inferior extent of normal prostatic tissue or tumor, is controversial [3,6,7,28,30,33,35–37,39,42]. This is as a result of the aforementioned uncertainty about the anatomic relationship between the prostatic apex and the urogenital diaphragm and limitations in imaging technology. The latter has, in theory, been partially overcome as a result of improvements in MRI, which has better soft tissue definition than CT and allows the direct generation of images in sagittal and coronal planes that contain the prostatic apex. Although there are theoretical reasons to expect that MRI would have significant advantages over other techniques for localizing the prostatic apex, this has not previously been rigorously evaluated.

A technical obstacle to the widespread use of MRI in radiotherapy treatment planning is the accuracy with which coordinates can be mapped from MRI to CT or simulator films. Factors such as the lack of signal from cortical bone and image distortion near tissue–air interfaces and fatty tissues [19] may reduce the accuracy of MRI if not adequately addressed, and detract from its other benefits. To evaluate this, we compared the position of an easily identified bony reference point among the MRI, CT and simulator films and demonstrated that the simple mapping technique employed in this study is sufficiently accurate to be of value in planning conventional radiotherapy for prostate cancer. No systematic mapping errors were identified and the standard deviations (SI 0.33–0.48 cm, AP 0.60–0.72 cm) were less than the expected uncertainties associated with subclinical extension of tumor, day-to-day set-up variation [4,5,8,12,16,38] and prostate movement during treatment [7,40]. Greater accuracy may be achieved with more sophisticated image analysis and comparison algorithms [18–20], which may be used to advantage when planning conformal radiation for prostate cancer [9,22,34] and other tumors [21].

At least two previous studies evaluated the use of MRI for localizing the prostatic apex. Algan et al. [3] reported on 17 patients who had axial and coronal MRI images, retrograde urethrograms and CT-urethrograms. The MRI apex was located a mean distance of 0.58 cm superior to the urethrogram apex and 0.31 cm superior to the CT-urethrogram apex. In no case was the MRI apex inferior to the urethrogram apex. However, the MRI apex was inferior to the CT-urethrogram apex in three patients. Kagawa et al. [18], in a similar study, found the MRI apex to be 1.50 cm superior and 0.71 cm posterior to the urethrogram apex. Both studies concluded that MRI was more accurate than CT or urethrography for localizing the true position of the apex.

We also believe that MRI is the best technique currently available for defining the prostatic apex and should be considered the standard to which other techniques are com-

Fig. 6. Distance of the MRI and CT apices above the inferior ischial tuberosities. Points to the left of and below the lines represent patients with inadequate coverage of the prostatic apex as determined by MRI and CT, respectively, with the inferior field border at the bottom of the ischial tuberosities.

Fig. 7. Distance of the MRI and urethrogram apices above the inferior ischial tuberosities. Points to the left of and below the lines represent patients with inadequate coverage of the prostatic apex as determined by MRI and urethrogram, respectively, with the inferior field border at the bottom of the ischial tuberosities.
pared. Our results suggest that it is superior to the axial CT technique that is presently used to plan conventional radiotherapy for prostate cancer at this institution. We found no systematic difference in how the apex was localized using MRI and CT (Fig. 5), nor is there any anatomic basis to expect a difference. However, the large standard deviations (SI 0.80 cm, AP 0.72 cm) indicate that randomly distributed differences of potential clinical relevance existed in some patients. These random differences may theoretically be due to errors in localization of either the MRI or CT apex relative to the true prostatic apex. However, interobserver variation was significantly greater with CT than with MRI (standard deviations: SI 0.75 versus 0.47 cm, respectively; AP 0.81 versus 0.53 cm, respectively), suggesting that the imprecision of CT was mainly responsible. In theory, the accuracy of CT localization may be improved by reducing the slice thickness, optimizing the scan parameters (KV, ma, scan time) for best soft tissue definition, using reconstructed sagittal or coronal CT images in a plane that contains the apex, or using urethral contrast [3]. We are currently comparing MRI to optimized CT, which has the potential advantage of being more readily available and cost-effective than MRI and therefore more generally applicable to routine radiotherapy treatment planning.

Our results also suggest that MRI is superior to static retrograde urethrography, which is the urethrogram technique most frequently used by radiation oncologists to plan treatment for prostate cancer [7,28,30,33,36,39]. Urethrography does not identify the prostatic apex directly, but rather a point that is usually anterior and inferior to the true apex as determined by the anatomy of the urogenital diaphragm [41]. Therefore, the use of urethrography in treatment planning is based on the assumption that the urogenital diaphragm is of uniform and predictable thickness from patient to patient. However, we found wide variation in the apparent thickness of the urogenital diaphragm, ranging from ~0.8 to 3.2 cm. A similar result was reported by Crook et al. [7], who compared the position of the apex as localized using radio-opaque seeds and urethrography. These findings may reflect not only variability in the true thickness of the urogenital diaphragm but also limitations in the technique of static urethrography. Static urethrograms do not reliably show the membranous or proximal bulbous urethrae [23], which are closest to the urogenital diaphragm and therefore of greatest interest when attempting to localize the prostatic apex. Cox et al. [6] pointed out that contraction of the urethral sphincters after injection but before imaging may ‘milk’ the contrast distally in the urethra away from the urogenital diaphragm, yielding a falsely low estimate of the position of the apex. This effect may be magnified by patient anxiety, discomfort associated with inflation of the catheter balloon in the urethra, or the use of a penile clamp. Dynamic retrograde urethrography [6,23] with constant injection of contrast during imaging may overcome these problems but is not routinely practiced by radiation oncologists.

Implanted radio-opaque markers have been advocated by many as the preferred way to localize the prostatic apex [7,35,37]. They provide a permanent indication of the position of the apex that is visible on portal images obtained during radiotherapy, thereby contributing to treatment quality assurance [37] and facilitating the adjustment of beam position to compensate for prostate movement [7]. However, the advantage of seeds, whether implanted via a trans-perineal approach [37] or trans-rectally under ultrasound guidance [7,35], is potentially offset by the need for expertise in these techniques to assure that the seed is positioned at the true apex. A comparison of MRI to seed localization of the apex is required to evaluate the relative merits of these two techniques.

We found the MRI apex to be <2 cm above the inferior ischial tuberosities in 17% of patients. As shown in Table 1, others have reported potential under-dosing of the prostatic apex in between 0 and 63% of patients if the inferior field border is routinely positioned at the ischial tuberosities [6,7,28,31,33,36,39,42]. The largest series is by Wilson et al. [42] and is comprised of 153 patients with prostate cancer who were treated using a 125I prostate implant. In 133 of these patients, the 125I seeds were positioned via suprapubic surgery with direct visualization of the prostate and the most inferior seed was placed 5 mm or less above the apex. Subsequent imaging showed the apical seed to be <2 cm above the ischial tuberosities in approximately 16% of patients and <1.5 cm above the ischial tuberosities in 5% of patients. These results, which provide the best available surgicopathologic indication of the position of the prostatic apex relative to the ischial tuberosities, are in close agreement with our results and further strengthen the role of MRI as the best non-surgical means of localizing the apex.

From ours and other studies [7,30,33,36,39,42] it is evident that the hitherto often recommended practice of positioning the inferior radiation field border at the bottom of the ischial tuberosities in all patients receiving conventional radiotherapy for prostate cancer [13,14] is inadequate. Precise localization of the apex is necessary in all patients to guarantee the delivery of full radiation dose to the entire prostate and to minimize the volume of normal tissue that is irradiated unnecessarily. In our study, the MRI apex was more than 2 cm above the ischial tuberosities in 25 patients (mean 0.8 ± 0.2 cm, range 0.2–1.9 cm). This implies that, on average, a volume of normal tissue corresponding to a thickness of 0.8 cm would have been irradiated unnecessarily in these patients if the inferior field margin was routinely positioned at the bottom of the ischial tuberosities. Treatment of excessive normal tissue in this area may contribute to greater acute urethral and perianal toxicity [15] and possibly to greater late toxicity in some patients.

In conclusion, pelvic MRI obtained using modern techniques and a phased-array pelvic coil is an accurate non-invasive method of localizing the prostatic apex. It provides better soft tissue definition than CT, which is reflected in greater interobserver agreement. Furthermore, it identifies
the prostatic apex directly, rather than indirectly by means of a remote anatomic point that varies in its relationship to the apex from patient to patient, which is a limitation of urethrography. The high cost of MRI and spatial image distortion are present obstacles to its widespread use in the treatment planning of prostate cancer. However, as the advantages of MRI for this purpose are recognized and with improvements in image analysis and fusion technology that reduce the complexity of combining MR with CT and simulator images, the availability and application of MRI is likely to increase. Presently, MRI should be considered the optimal method of localizing the prostatic apex and the standard to which other methods should be evaluated in the context of clinical studies. All patients undergoing either conventional or conformal radiotherapy for prostate cancer should have localization of the apex using MRI or a technique of equal precision to assure accurate dose delivery to the entire prostate and to minimize side-effects.

References

[1] Intergroup (NCIC CTG, CUOG, ECOG, CALGB, SWOG) phase III randomized trial comparing total androgen blockade versus total androgen blockade plus pelvic irradiation in clinical stage T3–4, N0, M0 adenocarcinoma of the prostate, 1995.


Table 1

Relationship between the prostatic apex and the inferior ischial tuberosities

<table>
<thead>
<tr>
<th>Study</th>
<th>Urethrogram</th>
<th>Seeds</th>
<th>MRI</th>
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<td></td>
<td>&lt;1 cm above</td>
<td>&lt;1.5 cm above</td>
<td>&lt;2 cm above</td>
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<tr>
<td>Schild et al. [36]</td>
<td>8/30 (27)</td>
<td>22/89 (25)</td>
<td>3/20 (15)</td>
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<td>Wilson et al. [42]</td>
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<tr>
<td>Sadeghi et al. [33]</td>
<td>2/20 (10)</td>
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IT, inferior aspect of ischial tuberosities.