Magnetic Resonance Imaging of Post Radical Retropubic Prostatectomy Localised Recurrence

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Summary

Aim
To present our experience in performing body coil magnetic resonance imaging (MRI) of the pelvis in patients presenting biochemical recurrence (BCR) after radical prostatectomy (RP).

Materials and Methods
A group of 18 patients with BCR following RP and 3 patients without evidence of BCR were evaluated by body coil MRI scan in T1 and T2 imaging sequences, both before and after administration of intravenous contrast. Two experienced radiologists described the anatomy of the vesicourethral anastomosis (VUA) and remarked on the significant findings. Finally, all patients with BCR underwent transrectal ultrasound-guided biopsy at the anastomotic site and the correlations between imaging and biopsy findings are discussed herein.

Results
The majority of patients (five out of six) with cancer recurrence shown on the anastomotic biopsy, presented an inhomogeneous thickening at the anastomosis site, yet this description could also be applied to some cases which finally proved local benign prostatic hyperplasia (BPH). Following intravenous gadolinium, cases with local recurrence or local residual benign tissue presented an enhancement in the contrast uptake areas.

Conclusion
Body coil pelvis MRI scan following RP, is a safe, non-invasive technique that can accurately describe the neo-anatomy of the greater area and provide useful information regarding the anastomotic site.

Keywords
Magnetic Resonance Imaging, recurrence, biochemical failure, radical prostatectomy, anastomosis.

Introduction
Over the last decade, radical prostatectomy (RP) has been established as an effective surgical management method for the treatment of localised prostate cancer even with long-term medical results. Recent studies which presented large series of patients, estimated that there is a recurrence-free ten-year period after surgical management with RP in localised cancer, which ranges within 68-74%.

Despite the long-term biochemical recurrence-free...
(BCR-free) survival, in certain cases, Prostate Specific Antigen (PSA) levels were traceable in the follow up period. This fact was considered as a potential clinically detectable disease. A worse prognosis for the cancer progress was when patients presented symptoms at an early stage sequenced by adverse pathological characteristics. There are only a few studies published for second-line treatment following radical management. Two of them report that after RP, 16% of the patients received a second-line treatment for prostate cancer within two years; 22% within three years and over 35% within five years after surgical treatment. Although a larger series of patients has developed BCR, the specific condition is not yet fully understood. There are several alternative guidelines for the evaluation, treatment and follow up of these patients. The major issue for BCR patients is whether they have localised or systematic recurrence and the need, the type and the appropriate time for the application of second-line treatment. Among the optional imaging methods, Magnetic Resonance Imaging (MRI) is widely preferred due to its impeccable technical characteristics yet, it has not been established as the primary choice for BCR cases and currently remains an alternative for testing the aforementioned patients. We herein present our experience, in regard to MRI use in patients who had recently been diagnosed with BCR of prostate cancer (PCa). This period is the landmark for our concerns regarding the applicable treatment of a potential recurrence. It is obvious that, the accuracy in the differential diagnosis at that crucial moment can determine the timely practice of the applicable second-line treatment and thus increase the ratio of cancer management.

**Materials and Methods**

21 male patients were studied, all of which had undergone RP during 1996-2002, using pelvis MRI. All patients had had their surgery in the same hospital and by the same surgeon. Their follow up period was fully observed and included a survival protocol especially for patients with a medical history of RP. The protocol demanded postoperative PSA and digital rectal exam (DRE) tests on a quarterly basis for the first two years, semesterly for the next year and annually from then on. All PSA measurements were performed on AxSym Total PSA List No. 3C19 (Abbott Laboratories).

The patient selection criteria for the BCR group (including 18 out of 21 patients) in our study were: a) pathological stage T1,N0,M0 as this was diagnosed on the RP preparation, b) no post-RP medical or adjuvant treatment or post-BCR second-line treatment, c) postoperative PSA level should have been undetectable prior to its rise, d) First diagnosis of BCR and always in a four week period prior to the enrolment in the study, e) Upon recurrence, PSA levels should have been minimum -indication of localised recurrence, f) Post-BCR restaging test (CT scan and whole body bone scintigraphy) should have been negative for metastases. Moreover, MRI was used in 3 more patients without indication of PSA level increase (control group). All patients with detectable PSA level were initially investigated with CT scan and Bone Scintigraphy. The diagnosis of BCR was defined by measuring PSA levels above
0.2ng/ml (minimum limit). The interval period between BCR diagnosis and pelvis MRI scan never exceeded four weeks time. All patients were informed of the risks and benefits of their participation in the study and signed the relative form of consent.

We used a 1.5 Tesla (Philips ACS III) MRI scan to obtain T2 sequences (turbo-spin echo) for the axial plane and T1 sequences for the axial and coronal plane, slice thickness 4mm. Taking T2 sequences was succeeded with and without fat suppression and T1 sequences before and after administration of intravenous contrast (gadolinium, 0.2ml/kg). All BCR patients further underwent transrectal ultrasound (TRUS) guided prostate biopsy of the affected area, two weeks post-MRI testing. On biopsy, tissue blocks were sampled from the ultrasonographically suspicious sites as well as from four random areas adjacent to the anastomotic ring. Attempts were made to ultrasonographically detect areas assessed as suspicious during the MRI and sample selective tissue blocks. Our aim was not to directly compare the imaging studies or the results received from the two different imaging tests (MRI vs. TRUS) but rather to successfully differentiate scar tissue from local recurrence based on biopsy confirmation.

Our initial experience with the MRI scan for testing BCR, led us to stratify the VUA area as "Normal" when a thin outline with a well-defined low tension signal is uniformly amplified on the respective imaging T1. The "Suspicious" category for local recurrence is characterized by either a) a thickened, irregular anastomotic "ring", which appears strong on T2 sequences being disparately enhanced after contrast injection on T1 sequences or b) sites adjacent to the anastomotic “ring” but inside the prostatic bed, also receiving a high signal on T2 sequences and ‘suspicious’ aid after contrast injection on T1 sequences or c) seminal vesicle (SV) remains. Two MRI experienced investigators examined the imaging studies unaware of the patients’ medical history and information such as tissue blocks pathological findings, PSA increase levels or anastomosis biopsy results. The intensity of T-signal was compared to the signal strength of adjacent muscle groups. Tissues with similar characteristics to the adjacent muscles were classified as postoperative scar tissues, whilst tissues which received a higher signal than the muscles were considered as potential tumors. Furthermore, the post-gadolinium administration tissue signal was evaluated whether it was reduced or nonexistent. This was described as scar tissue and in cases where there was moderate or high contrast, it was assessed as suspicious recurrence.

Results

Table 1 contains full details of all our study patients. In every case, tests for secondary localizations (CT scan or Bone Scintigraphy) were negative. We randomly chose patients with PSA levels increase in their follow up period. Pre-operative PSA level was 10.31 ng/ml (average value), (variance 1.33-27), ± Standard Deviation (SD) 6.85, and average value 8.65. Follow up period until the manifestation of BCR was 25.72 months (average value) (variance 9-58) ± SD 12.42 average value 21 months. PSA levels in
BCR were 0.87 (average value) (variance 0.24-2.5) ± SD 0.56, average value 0.78ng/ml. In the BCR group, 12 out of 18 of the cases were classified as pathological display according to the aforementioned criteria. Furthermore, in two cases with abnormal MRI results, the biopsy revealed a benign prostate tissue. Comparing to TRUS, in eight “suspicous” cases, we reported three out of eight (30%) confirmed positive biopsies.

MRI scans on biopsy-confirmed local recurrence cases have been described as isodense on T1 sequences at the anastomosis and then with a different intensity on T2 sequences. In addition, these areas received contrast enhancement (gadolinium) compared to the levator ani and other muscles of the area. Among the cases with biopsy-confirmed local recurrence and abnormal MRI findings based on the above criteria (see Materials and Methods), 5 out of 6 patients (83%) showed abnormal thickening in the anastomotic "ring", while one out of six (16%) exhibited a suspicious area in the prostatic bed remotely of the anastomosis site. Where fibromuscular dysplasia (FMD) was manifested, no increased enhancement was present after contrast injection. For patients whose biopsy revealed hyperplastic tissue (2 out of 18), our findings established less enhancement compared to prostate cancer regions. All control group patients had “normal” DRE, MRI or TRUS findings and had maintained their undetectable PSA levels even 12 months after the initial assessment, demonstrating their validity as control group. Image 1 (a, b, c) presents examples of three different cases with normal (a) and suspicious (b, c) MRI findings.

**Discussion**

Usually, the cause detection of PSA increased levels constitutes a challenge for modern depiction techniques. Cher and Bianco have reported that the lowest PSA value for patients with positive Bone Scintigraphy was 46mg/ml, whereas Kramer et al. concluded that the CT scan could indicate local recurrence should the tumor size be above 2cc. Patients who undergo RP are frequently investigated for PSA levels. PSA level increase usually occurs at low levels reflecting small-sized tissues, thus complicating our efforts to timely start second-line treatment. Our decision process was assisted by several factors such as the characteristics of PSA levels increase and pathological findings from RP tissue blocks. Unfortunately, due to statistics, these variables are difficult to apply on each patient individually. Moreover, previous experience in performing DRE or TRUS on these patients shows reduced sensitivity which, in one large study, has been estimated as 44% and 76% respectively, while the biopsy detection rate was around 44%.

Period and treatment method for BCR patients also remains a subject matter. Mehta et al. presented data from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) showing that only 33.7% of BCR patients received second-line treatment and this occurred 1 year after BCR confirmation on average. Where a localized recurrence is detected, radiotherapy application may be curative. Several studies demonstrate a better response if radiation is applied while the PSA levels are limited (usually <1.1 or 2 ng/ml). Although more well-designed prospective randomized studies are
Table 1. Patients Characteristics

<table>
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<th>No. Patients</th>
<th>PSA Pre-operative (ng/ml)</th>
<th>T-stage</th>
<th>Gleason Sum</th>
<th>Disease-free survival</th>
<th>PSA During Relapse (ng/ml)</th>
<th>Guided anastomotic Biopsy results</th>
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The normal bladder-ureteral anastomosis is depicted as a thin and well-defined annular structure. Enhancement after administration of intravenous contrast material is equally distributed in the tissue (arrow).

Thickening of the anastomotic ring (arrow). Enhancement after administration of intravenous contrast material is abnormally diffused to the surrounding tissues. This finding suggests local recurrence that was confirmed by biopsy in this particular case.

A neoplastic mass emerges on the left front compartment of the prostatic bed (right arrow). The anastomotic ring is completely disturbed while the enhancement of the neoplastic tissue after administration of intravenous contrast material extends to the pubic symphysis (left arrow).

necessary to estimate the appropriate starting point of second-line treatment, it is evident that the sooner we conclude based on evidence, the better results we get.

MRI scan continues to evolve in the prostate cancer field. MRI is primarily used for staging purposes providing useful information, given the diagnosis of prostate cancer precedes. It has been reported that MRI offers the highest sensitivity in detecting extra-capsular extension in patients who had undergone RP. Also, a recent meta-analysis of more than 70 articles reported overall sensitivity and specificity ranging from 71 to 74% and estimated deviation between 51-93% and 53-84%, respectively. The main advantage of using MRI for staging purposes is the excellent contrast. Therefore, the method appears promising for other indications, such as confirmation of post-RP local recurrence. Silverman
et al. studied the use of rectal MRI scan after RP in forty-one patients. Most of them (35 out of 41) manifested a strong clinical suspicion of local recurrence. The authors reported that in all cases of local recurrence (100%), MRI was able to highlight suspicious nodules in the prostatic bed albeit the authors admit that there was a statistical error in the study. While there were confirmed cases of local recurrence, there was no reference of a BCR-free survival group of patients. In another recent study by Sella et al., the same method was followed (41 clinically confirmed local recurrences) with the same excellent results (95% sensitivity and 100% specificity). Unlike previous studies, we tried to evaluate patients with MRI immediately after the diagnosis of BCR. We have also used a new description of the anastomotic “ring” estimating tissue thickness and contour details of imaging studies in an effort to second the method’s diagnostic accuracy. Indeed, in our study, despite the lack of strong clinical suspicion, “suspicious” MRI findings were successfully correlated with local presence of prostatic tissue in all cases (8 out of 12). However, there is number of patients (4 out of 12) with “abnormal” MRI findings where the local recurrence has not been proved on biopsy and therefore MRI resolution was better compared to TRUS. Also, early results showed MRI findings of uncertain significance between cases with hyperplastic and neoplastic tissue at the anastomosis. Although the total number of cases with hyperplastic tissue was small to draw firm conclusions, according to our initial experience, “benign” cases presented lower contrast enhancement compared to the cases of neoplasia. The contrast differences, however, were clearer between fibromuscular and prostate tissue.

The whole body MRI has a theoretical advantage in examining the anatomical information of the surrounding pelvic area after RP since it does not strongly interfere with the neo-anatomy of the site, as expected in intrarectal coil MRI use. In addition to the increased interference with the tissues, intrarectal MRI scan offers a reduced window compared to in vitro MRI. Intrarectal MRI bears other comparative disadvantages as well: a) image degradation, b) motion point associated with false technical imaging errors (artifacts) and c) intrarectal head insertion issue. With respect to prostate cancer, previous studies that have compared the two MRI types (whole body and transrectal) and their use on pelvic relapses, ruled in favor of the intrarectal method. However, many technical advances have been realized in the field of whole body MRI. Recent studies reported that the aforementioned theoretical advantage of transrectal MRI is no longer that clear, and patients can avoid the impact of a time-consuming and invasive process. Nonetheless, continuous technological evolution, radio- logists’ skills and experience on the method remain very important variables to its value. Contrary to previous reports, in our study, we were able to provide promising new diagnostic data for the MRI method at an earlier stage and with lower PSA levels on relapse. (see Table 1) In BCR cases, the role of the method is presently limited and clearly the method has not been established. Additionally, the inability of real time MRI-guided biopsy can be
regarded as another drawback.

In recent literature there are several studies assessing the contribution of MR spectroscopy (MRS) in detecting prostate cancer cells by measuring different metabolites within the prostate tissue. The role of MRS in the evaluation of residual disease or local recurrence has also been reported in the past. But although it is promising, it has also not been established yet. Moreover, the introduction of 3T imaging systems can improve the assessment of prostatic disease by using advanced imaging techniques, such as dynamic imaging, diffusion imaging and MR Spectroscopy.

In conclusion, according to our experience, there are specific benefits when evaluating patients with suspected local recurrence via MRI and these are: a) Direct imaging of local recurrence that can help us begin applicable treatment earlier, b) MRI findings that can later on direct to ultrasound-guided biopsies and lead to a better diagnostic approach, c) the display of a measurable tumor can help in monitoring treatment response and d) MRI may help in radiotherapy planning. Since state-of-the-art MRIs (e.g. rectal coils, MRS, or 3T) are not widely available, our findings add value to countries like ours and may help in reaching our healing decisions immediately after the detection of BCR.

Conclusion

Whole-body MRI method provides high resolution imaging that can significantly assist in detecting local recurrence in post-RP BCR cases. MRI can detect and depict small minor sites of prostatic tissue in patients with limited PSA level increase and also reveal recurrences located anteriorly or laterally to surgical margins as well as inside the remaining seminal cysts which are undetectable by TRUS. Moreover, it allows for the overall evaluation of the pelvis site including lymph nodes and bones without interfering with the neo-anatomy of the site as opposed to endorectal MRI. Furthermore, randomized prospective studies including more patients are needed to assess the sensitivity and specificity of the method soon after BCR or where there is strong clinical evidence of local recurrence.
τριν και μετά τη χορήγηση ενδοφλέβιου σκιαγραφικού. Δύο έμπειροι ακτινολόγοι περιεγγράφηκαν την ανατομία της κυστοουρηθρικής αναστάμωσης, ανέφεραν τα ευρήματα και κατέγραψαν σημαντικές παρατηρήσεις. Μελλοντικά σε όλους τους ασθενείς με βιοχημική υποτροπή πραγματοποιήθηκε διορθωτική βιοσία καθοδηγούμενη με υπέρχον από την περιοχή της κυστοουρηθρικής αναστάμωσης. Οι συγχρόνες μεταξύ των ευρημάτων του απεικονιστικού ελέγχου και των βιοσίων έγιναν αντικείμενο συζήτησης.

Αποτελέσματα: Οι περισσότεροι ασθενείς (5/6) με υποτροπή της νόσου όπως αποδείχτηκε από τη βιοσία της αναστάμωσης, παρουσίασαν αναμοιβατική πάζυμα της περιοχής της αναστάμωσης. Ωστόσο αυτή η περιγραφή θα μπορούσε να αφορά σε μερικές περιπτώσεις και ασθενείς οι οποίοι είχαν τοπικά καλοήθη προστατική υπερπλασία. Μετά από ενδοφλέβια χορήγηση γαστρικίου, στις περιπτώσεις με τοπική υποτροπή ή παραμονή καλοήθη προστατικού ιστού παρουσιάστηκε αύξηση των περιοχών πρόσληψης του σκιαγραφικού.

Συμπεράσματα: Ο απεικονιστικός ελέγχος με MRI πεύκου μετά από ριζική προστατευτική είναι μια ασφαλής, μη-επεμβατική τεχνική που μπορεί με ακρίβεια να περιγράψει την ανατομία της ευρύτερης περιοχής και να παρέχει χρήσιμες πληροφορίες όσον αφορά την περιοχή της αναστάμωσης.

Αξέζεις ευρετηριασμού
Μαγνητική τομογραφία, MRI, τοπική υποτροπή, ριζική προστατευτική.

References


