Prostate cancer detection rate: MRSI directed TRUS biopsy versus increasing number of cores in clinically challenging group of men with PSA in the gray zone of 4-10 ng/ml

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Introduction: Prostate cancer (PCa) is a leading male cancer and to avoid delay in treatment, early diagnosis is vital for patient management. Despite prostate specific antigen (PSA) being the main screening test of PCa detection; it's sensitivity, specificity and the threshold value at which a biopsy should be performed are still unclear (1). Furthermore, elevated PSA is not PCa specific, but can be observed in inflammation, haemorrhage, benign disorders etc. Magnetic resonance spectroscopic imaging (MRSI) is a non-invasive MR technique that determines the likelihood of malignancy based on the changes in metabolites (1). Since, PSA in the range of 4-10 ng/ml has a poor positive predictive (PPV) value for PCa, it results in larger unnecessary biopsies. In the present study, in order to improve PCa detection rate, we evaluated the role of MRSI directed transrectal ultrasound (TRUS) biopsy versus increasing the number of cores (from 6 to 12 cores) during standard TRUS biopsy.

Materials and methods: This is a retrospective case controlled study. The study group included men who underwent MRSI directed TRUS guided biopsy for PSA in the range of 4-10 ng/ml between 2002 and 2011. The control group included men who did not undergo MRSI, i.e. who underwent only standard TRUS guided biopsy for a similar PSA range in the time period between 2005 and 2011. The inclusion criteria in both the groups were similar; normal digital rectal examination (DRE) and a PSA between 4-10 ng/ml. Patients with known causes for PSA increase like prostatitis, urinary tract infection were excluded from both the groups. MR investigations were carried out prior to biopsy at 1.5 Tesla using a whole body MR scanner (SONATA/ AVANTO, Siemens, Erlangen, Germany). The parameters used for MRSI were as follows: TR = 1300 ms, TE = 120 ms, voxel size = 5 x 5 x 5 mm^3, average = 3, total acquisition time = 17 min. An 18G trucut needle was used to obtain the biopsy cores in the study and the control groups. A preliminary TRUS was performed and biopsy was first taken from the abnormal voxels in patients in whom MRSI was positive. The accuracy of MRSI directed TRUS biopsy in sampling the abnormal voxel has been validated and described earlier (2). This was followed by a standard sextant or twelve-core biopsy. All patients in the control group and those in the study group in whom MRSI was negative similarly underwent TRUS guided 6-core or 12-core biopsy. The institute ethics committee approved our study and all patients gave written informed consent before the procedure. The statistical analysis was done using STATA software version 9.2.

Results: A total of 278 men met the inclusion criteria were evaluated. This included 138 men in the control group and 140 men in the study (MRSI) group. The two groups were similar in characteristics that could potentially influence cancer detection like mean age, PSA or prostate volume (Table 1). Our data spans a period of 9 years (2002 to 2011) and during the course of which there was a change in the institutional policy regarding the number of cores for a prostate biopsy (i.e. sextant versus twelve core), which is given in Table 1. Ninety of the 140 men in the MRSI group had voxels suggestive of malignancy that were specifically targeted for additional biopsies. The median number of biopsy cores (MRSI directed + standard biopsy) in these men was 8 in 41 cases (sextant biopsy standard) and 14 in 49 cases (12 cores standard). The pathology findings are provided in Table 2. The overall cancer detection rate in the MRSI group (22/90; 24.4%) was more than two times the control group (14/138; 10.1%). On further analyzing the cancer detection rate based on the number of standard cores (6 versus 12), there was no significant difference between the two groups when the minimum number of cores was six. However, the difference in PCa detection rate was significantly more in the MRSI group when the minimum number of cores was 12. The mean Gleason score of PCa in the MRSI group was lower compared to those in the control group, but the difference was not statistically significant. On comparing the MRSI results with the TRUS biopsy findings, MRSI had 95.6% sensitivity, 41.9% specificity, a PPV of 24.4%, a negative predictive value (NPV) of 98% and an accuracy of 51.4%.

Discussion: Systematic TRUS guided biopsy is the standard procedure for prostate sampling. However, TRUS has low sensitivity to localize PCa. Increasing the number of cores has been proposed as one of the means to improve cancer detection, especially in patients with PSA in the gray zone of 4-10 ng/ml. However, patient discomfort and complication rate increases with increase in number of biopsy cores. The present study comprises of a homogenous group of men with normal DRE and PSA in the range of 4-10 ng/ml. Using logistic regression analysis, it was found that increasing the number of cores from 6 to 12 increased the cancer detection by 10%. However using MRSI guidance as opposed to standard TRUS, increased the likelihood of cancer detection by 2.9 times. This highlights the fact that it is the MR method (i.e. MRSI guidance) and not the number of cores that has made a significant difference in the detection of PCa. However our technique of MRSI directed TRUS guided biopsy does have its limitations like mismatch between abnormal voxel and the biopsy site cannot be completely eliminated (2). MR guided prostate biopsy devices and techniques may help to direct biopsies more accurately (3).

Conclusion: MRSI directed TRUS biopsy increases PCa detection rate compared to standard TRUS biopsy in patients with normal DRE and elevated PSA in the range of 4-10 ng/ml. Larger prospective randomized trials are necessary before it can be incorporated in the management of such patients.

Characteristics	Control group N = 138	Study Group N = 140	P value
Mean age (years)	62.4 ± 10.5	62.96±12.05	0.69
Mean PSA (ng/ml)	6.8 ± 2.25	6.87 ± 2.63	0.89
Mean prostate size (gms)	44 ±14.20	43 ±18.42	0.91
6 core biopsy (n)	31 (22.46%)	79 (56.43%)	0.001
12 core biopsy (n)	107 (77.54%)	61 (43.57%)	

Table 1. Characteristics of study and control groups

Characteristics	Control Group N = 138	MRSI positive group N = 90	P value
Prostate cancer	14 (10.14%)	22 (24.44%)	0.004
- 6 core	4/31 (12.90%)	7/41 (17.07%)	0.588
-12 core	10/107 (9.34%)	15/49 (30.61%)	0.001
Mean Gleason score	6.64 ± 1.20 (5-8)	6.13 ± 1.14 (4-8)	0.208
No. of tumors in TZ	3/14 (21.43%)	8/22 (36.36%)	0.467
No. of tumors in PZ	11/14 (78.57%)	14/22 (63.63%)	
Chronic prostatitis	118	57	<0.001
Atypical small acinar proliferation (ASAP)	0	2	0.155
Prostatic intraepithelial neoplasia (PIN)	1	4	0.081
BPH	5	5	0.521

Table 2. Pathology findings

References: (1) Jagannathan NR *et al*. MAGMA. 2008; 21:393 (2) Kumar V et al. *NMR Biomed*. 2007; 20: 11 (3) Lian J et al. *Med Phys*. 2004; 31: 3087