

Local Staging of Prostate Cancer Using Three Dimensional (3D) Transrectal Ultrasound Assisted with Power Doppler Capability

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Abstract: *Introduction:* The ability to differentiate between carcinoma confined to the prostate and the extra-capsular extension (ECE) of the tumor is the key point for management. ECE of prostate cancer can lead to failure of radical prostatectomy and every attempt should be made to localize the tumor and assess its extensions preoperatively. The study aimed to evaluate the value of three dimensional (3D) Transrectal ultrasound (TRUS) assisted with power Doppler in local staging of prostate cancer.

Methodology: -3D TRUS assisted with the power Doppler capability was performed for 120 patients were complaining of burning urination, difficult urination or blood in urine, among them 95 patients were subjected to 3D TRUS guided biopsies.

Results: 33 patients showed prostatic carcinomas, 2 patients showed prostatic sarcoma. In patients with proven prostate cancer 3D TRUS showed an estimated sensitivity 85.7% and specificity 90% with a positive predictive value 83.3%, negative predictive value 91.5% and total accuracy 90.9%. 77% of our cancer patients (27/35) showed hypervascularity by power Doppler ultrasonography while 8 patients (23%) showed no abnormal high vascularity. Power Doppler increased the sensitivity of 3D TRUS in the detection of prostate cancer from 85.7% to 88.5% 3D TRUS clearly identified the extra-prostatic spread in 15 out of 18 patients of an estimated sensitivity (83%).

Conclusion: 3D TRUS aided with power Doppler is a valuable tool in local staging of prostate cancer .The expected benefits in local staging of prostate cancer from the combination of 3D TRUS, power Doppler and 3D TRUS guided biopsy as one sitting exam, will be highly promising.

Keywords: Prostate cancer, Transrectal ultrasound, Three dimensional.

INTRODUCTION

The ability to differentiate between carcinoma confined to the prostate and the extra-capsular spread of tumor is the key point for management. Radical prostatectomy is the most popular management modality for carcinoma localized to the prostate but if the tumor extends beyond the prostatic capsule, other treatment options like radiotherapy, external beam irradiation, Brachytherapy or Hormonal therapy will be tried [1,2].

Previous studies predict extra-capsular spread of tumor through elevated serum PSA > 20 ng/ml, increased number of positive cores in guided biopsies which means increased tumor volume, detection of perineural invasion in biopsy samples and Gleason score = 8 or more [3,4].

MRI showed moderately high specificity and sensitivity in the judgment of local staging of prostate cancer using an endorectal coil [5-9].

When T2 weighted endorectal MRI was compared with Elastography in the detection of prostate cancer, both techniques give similar sensitivity and negative predictive values [10]. When Elastography targeted

biopsy was compared with systematic biopsy, the former gave a higher detection rate of prostate cancer than the later (12.7% vs 5.6%) [11].

ECE of prostate cancer can lead to failure of radical prostatectomy and every attempt should be made to localize the tumor and assess its extensions preoperatively [12, 13].

It is very disappointing to inform the patient that he has recurrent cancer after he performed radical prostatectomy and after he was exposed to all operative and postoperative risks including impotence and urinary incontinence [14].

Our current study is an attempt to localize the prostate cancer and to assess its local extensions prior to surgery using 3D transrectal ultrasound assisted with power Doppler, comparing with 3D TRUS guided biopsy results and post radical prostatectomy histopathology reports as a reference standard.

The Aim of the Work

To evaluate the value of three dimensional (3D) Transrectal ultrasound assisted with power Doppler in local staging of prostate cancer

METHODOLOGY

3D TRUS assisted with the power Doppler capability using 3D transrectal multi- frequency probe,

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GE Logiq 7 (Milwaukee, WI, USA), Voluson 530 D (Kretz technique, Austria) ultrasound machines, was performed by an experienced radiologist in an endorectal ultrasound for 120 patients referred to the radiology department of our institute and were complaining of burning urination, difficult urination or blood in urine. Their age ranged from 45 to 70 years old with the main age 63 years.

Biopsies were performed for 95 cases showing any of the following criteria :- Focal area of abnormal echo pattern within the prostate during 3D TRUS, abnormal hypervascularity with power Doppler ultrasonography ,when the digital rectal exam revealed abnormal hardness of the prostate and if the serum PSA and % free PSA >4 ng/ml and < 10% respectively .

The patients were adequately prepared and were asked to give a consent prior to the biopsy procedure.

3D guided biopsies after confirming the pathway of the biopsy needle in relation to the targeted regions with multi-planar image analysis in 3 orthogonal planes. 6 random biopsies were obtained from the para-median regions of the prostate (3 from each side at the apex, middle zone and basal zones) and one additional biopsy obtained from each lateral lobe.

Targeted biopsies also were taken from an area demonstrating abnormal echo pattern within the prostate, from periprostatic zone if tumor extension was demonstrated with power Doppler as an area of hypervascularity penetrating the prostate capsule into the periprostatic fat planes or as an area of abnormal echogenicity associated with capsular disruption with 3D ultrasound.

Targeted biopsy was taken from the seminal vesicles if there was an obliteration of the angle between the Seminal vesicle and the prostate or abnormal unilateral enlargement or if one of them showed heterogeneous echo pattern.

In cancer patients the final diagnosis was reached based on the result of the true-cut prostatic biopsies, targeted biopsies of the region of interest, post radical prostatectomy pathological reports in 12 patients who were subjected to radical prostatectomy, cystoscopy and biopsy of the urinary bladder in cases with suspected urinary bladder infiltration, and targeted seminal vesicles biopsies in cases with suspected seminal vesicles infiltration.

RESULTS

3-D TRUS with its multi-planar image analysis and volume rendering aided with power Doppler was performed for 120 patients, the final diagnosis was reached in 95 patients who were subjected to TRUS guided biopsies.

33 patients showed prostatic carcinomas, 2 patients showed prostatic sarcoma. 40 patients showed benign prostatic hyperplasia (BPH), 20 patients was diagnosed as prostatitis.

3D TRUS identified 36 patients with lesions suspicious of cancer (Figure 1), among them 30 patients proved to have a malignancy after histopathology assessment. 6 patients were wrongly diagnosed as disease positive and 5 patients were falsely diagnosed as disease free (Table 1).

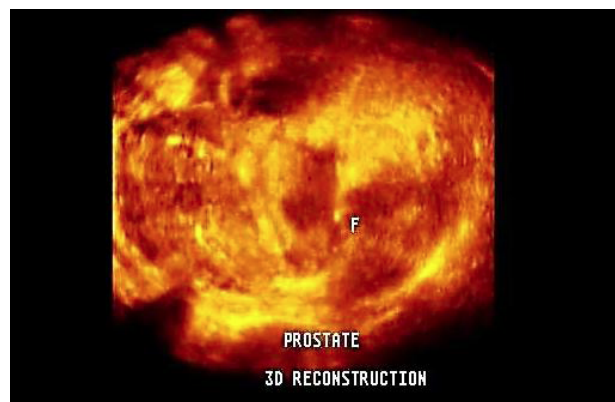


Figure 1: 3D TRUS volume rendering of hypoechoic tumor involving both sides of the prostate (T2c).

Table 1: Summarizes the Results of 3-D TRUS in Detecting Biopsy Proven Prostatic Cancer

	Biopsy		Total
	Positive	Negative	
3D TRUS			
Positive	30 (True positive)	6 (False Positive)	36 (all test positive)
Negative	5 (False Negative)	54 (True Negative)	59 (all test negative)
Total	35 (all diseased)	60 (all disease free)	95 (grand total)

Table 2: Accuracy of 3-D TRUS in Detecting Biopsy Proven Prostatic Cancer

Sensitivity	85.7 %
Specificity	90 %
Positive predictive value	83.3%
Negative predictive value	91.5 %
Total accuracy	90.9%

In patients with biopsy proven prostate cancer, 3-D TRUS showed an estimated sensitivity 85.7 % and

specificity 90 % with a positive predictive value 83.3%, negative predictive value 91.5% and total accuracy 90.9% (Table 2).

3D TRUS clearly identified the extra-prostatic spread in 15 out of 18 patients with an estimated sensitivity 83.3% in detection of tumor ECE, extension to the periprostatic fat was detected in 6 out of 6 patients (Figure 2a, b), infiltration to the seminal vesicles in 3 out of 4 patients (Figure 3), infiltration of the base of urinary bladder (Figure 4) in 2 out of 2 patients and also the presence of capsular breaks (Figure 5) in 4 out of 6 patients (Table 3).

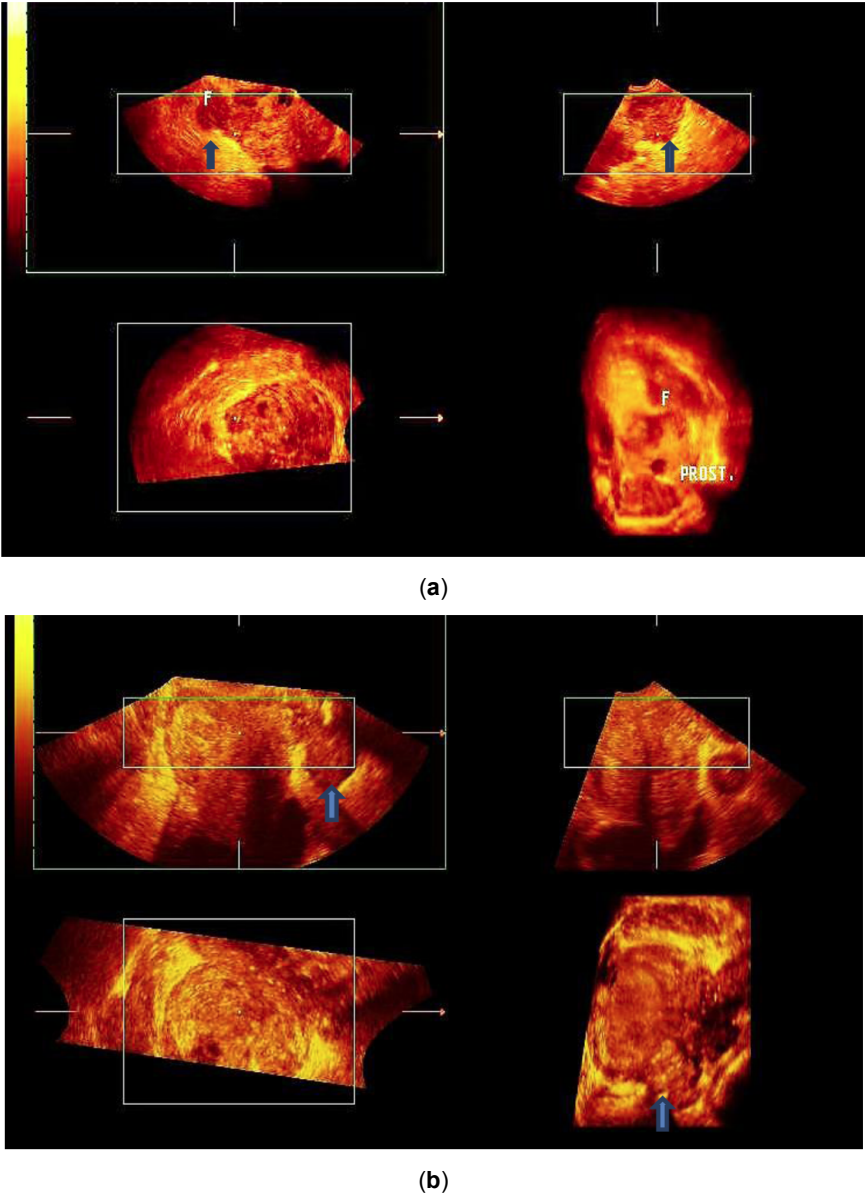


Figure 2: a: 3D TRUS showing multiplanar image analysis with volume rendering of prostate cancer showing periprostatic fat plane infiltration.
b: 3D TRUS with multiplanar image analysis and volume rendering of prostate cancer (arrow) T3a in association with benign prostatic hyperplasia.

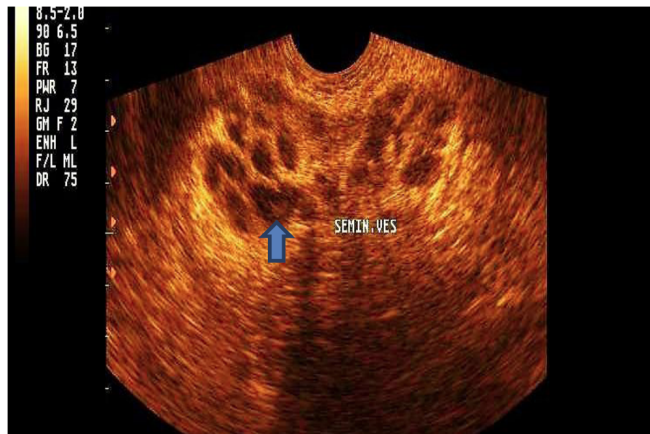


Figure 3: Asymmetrical size of the seminal vesicles in axial scan of a TRUS 3D exam with suspect tumor infiltration.

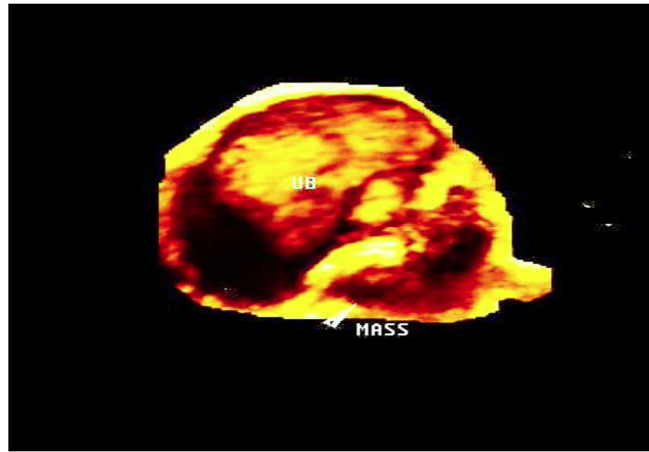


Figure 4: 3D volume rendering of prostate tumor seen invading the urinary bladder base.

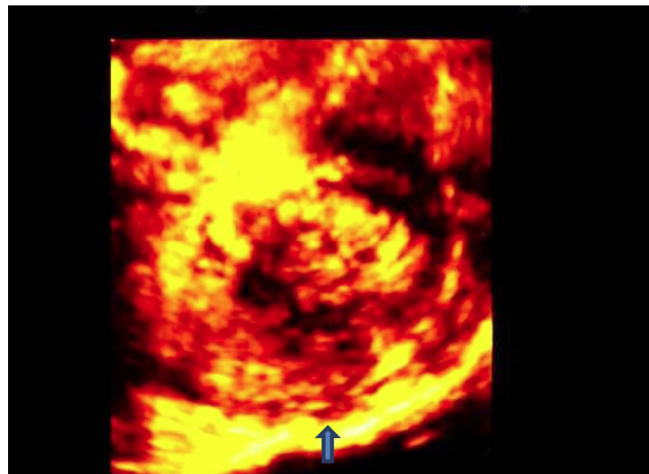


Figure 5: 3D TRUS volume rendering of prostate tumor with capsular breaks (arrow).

77% of our cancer patients (27/35) showed abnormal high vascularity by power Doppler

ultrasonography while 8 patients (23%) showed no abnormal high vascularity.

Table 3: Demonstrate the Sensitivity of 3D TRUS in the Detection of Extra-Prostatic Spread of Cancer Prostate

Lesions	Sensitivity% of 3D TRUS
Capsular breaks	67%
Spread to the periprostatic fat	100%
Infiltration to urinary bladder	100%
Infiltration to seminal vesicles	75%

Power Doppler ultrasound showed an estimated sensitivity 70.5% in the detection of organ confined cancer (12 out of 17 organ confined tumors), and an estimated sensitivity 83.3% in the detection of extra-capsular extension of tumor (15 out of 18 tumors) with an overall sensitivity 77% in the cancer detection

Power Doppler increased the sensitivity of 3D TRUS in the detection of prostate cancer from 85.7% to 88.5% as 1 patient with false negative results during 3D TRUS showed high vascularity with power Doppler and warrant further targeted biopsy

Both techniques failed to diagnose 2 patients with biopsy proven organ confined transitional zone carcinoma and 3 patients with extra-capsular extension of the disease, among them 2 patients detected with capsular penetrations and 1 patient detected with unilateral seminal vesicle infiltration proved with histopathology assessment, possibly due to the isoechoic nature of the lesions and the lack of hypervascularity in the later and the similarity of the lesion to benign hyperplasia in the former.

DISCUSSION

Prostate cancer is the 2nd commonest cause of death in men from cancer [15].

Radical prostatectomy when performed for an organ confined disease carries a potential cure with a life expectancy >10 years [16].

However 24 -42% of patients may show positive surgical margins and nearly 1/3 of the patients showed seminal vesicles infiltration [4].

Accurate prediction of surgical outcome is extremely urged to avoid the postsurgical recurrence.

The predictors of surgical outcome as serum PSA, PSA density, the biopsy Gleason score, the number of biopsy positive tissue samples, the age of the patient and the results of DRE don't give a high diagnostic confidence either to the patients or their clinicians [17]. As all have been just predictors and don't depend on the actual imaging of the tumor and its real extension.

MRI was of moderate high sensitivity and specificity in local staging of prostate cancer and the results will depend on the equipment type, the experience of the reader, the protocol used and the coil type. Recently a combination between MRI and ultrasound guided biopsy was achieved, but it was of limited experience and appeared to be promising [18-19].

In our current study 3D TRUS showed promising results in the detection of prostate cancer, with an estimated sensitivity 85.7% and specificity 90 % with a positive predictive value 83.3%, negative predictive value 91.5% and total accuracy 90.9%, the sensitivity in the detection of extra capsular extension was 83.3%, the high specificity is possibly due to an increased number of patients detected with the extra - capsular extension of tumor which is seen mostly in cancer patients.

Using the power Doppler ultrasound in addition to 3D TRUS had resulted in an increased sensitivity of cancer detection from 85.7% to 88.5%.

In the current study, we didn't estimate the overall sensitivity and specificity of the combination between the 3D TRUS and 3D TRUS guided biopsy, as both were performed in the same sitting using the same machine, which will be expected to be high and very promising owing to only 1/3 of our patients had performed radical prostatectomy and as our results need to be confirmed, we utilized the results of guided biopsies from the prostate and the targeted regions as an additional reference standard ,which was a restriction of our work that required a large scale of patients who underwent radical prostatectomy, 18 of our patients were not submitted to radical prostatectomy as they were established to deliver extra-capsular extension, 15 of them with 3D TRUS alone and 18 (51.5% of cancer diagnosed patients) with the combination of 3D TRUS and TRUS guided Biopsy.

Our technique in 3D TRUS guided biopsy can greatly improve the accuracy of local cancer staging, through taking 8 random biopsies from the prostate,

which helped in the detection of the isoechoic hypovascular tumors and cancers of the transitional zone simulating hyperplasia. Taking an additional targeted biopsy from the hypervascular lesion observed with power Doppler study and or of the focal areas of abnormal echoes pattern, in addition to targeted biopsy through the gland capsule where the tumor became in contact with, from the periprostatic fat planes and from the seminal vesicles if suspected with tumor infiltration.

All the targeted biopsies will be in accordance to the ultrasound and power Doppler findings and will help greatly in confirming the diagnosis.

Detection of capsular breaks with extension of the tumor more than 1mm in the periprostatic fat planes using 3D TRUS and targeted biopsy can lead to avoid the positive surgical margin [20].

Detection of the seminal vesicles infiltration observed with an estimated sensitivity 75% in our group of patients examined with 3D TRUS and sensitivity 100% in patients subjected to combined TRUS and targeted biopsy evaluation, is really essential since it predict lymph node metastasis and poor prognosis [21].

3D TRUS can give an accurate volume estimation, so it can be used to estimate the tumor volume, as previous studies showed a correlation between the large tumor volume and the presence of extra capsular extension [22].

3D TRUS guided biopsy has the advantage over 2D TRUS guided biopsy that it can give an accurate targeting of the focal lesions through its multi-planar image analysis.

Targeted biopsies were taken in our current study if extra-capsular extension was suspected from the ultrasound images or from the area of abnormal high vascularity during power Doppler study but to increase the accuracy of the exam in local staging of prostate cancer we suggest that 3D targeted biopsies can be taken from the periprostatic fat planes and from the seminal vesicles even with negative extension concluded from the ultrasound exam, if the patient age was >70ys with elevated PSA density, the tumor volume >0,3cc, the PSA serum level >20, the contact base of the tumor with the prostate capsule >12mm, as all these findings are shown to have an increased risk of extra-capsular extension of the tumor [3,22-24].

For more optimization of the results we suggest using 3D TRUS assisted with Elastography in addition to power Doppler, since previous studies showed that Elastography has similar sensitivity and negative predictive value to that of MRI with an endorectal coil in the detection rate of prostate cancer and will improve the sensitivity of targeted biopsy [11].

CONCLUSION

3D TRUS aided with power Doppler is a valuable tool in local staging of prostate cancer. The expected benefits in local staging of prostate cancer from the combination of 3D TRUS, power Doppler and 3D TRUS guided biopsy as one sitting exam, will be highly promising

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