

# Correlation of Transrectal Ultrasonography and Core Biopsies with Pathology Results in Radical Prostatectomy Specimens

Levent Türkeri,<sup>1\*</sup> Tufan Tarcan,<sup>1</sup> Tuğrul Biren,<sup>2</sup> Sevgi Küllü,<sup>3</sup> and Atif Akdaş<sup>1</sup>

Departments of <sup>1</sup>Urology, <sup>2</sup>Radiology, and <sup>3</sup>Pathology, Marmara University School of Medicine, Istanbul, Turkey

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**Background:** We compared preoperative tumor location, as identified by transrectal ultrasonography (TRUS), and TRUS-guided core biopsies with the final histopathological examination of radical prostatectomy specimens.

**Methods:** Thirty patients who had radical retropubic prostatectomy after evaluation with TRUS are included in the study. Diagnosis of prostate cancer was established with TRUS-guided systematic (3 cores from base, mid and apex of the peripheral zone, and 1 core from the transition zone of each side of the prostate) and lesion-directed core biopsies in all cases. Each prostate gland was halved for histopathological examination and results are reported in terms of "sides".

**Results:** Histopathological examination of the prostatectomy specimens revealed prostate cancer bilaterally in 29 glands (58 sides) and unilaterally in 1 gland. Preprostatectomy TRUS examinations missed cancer in 29 sides, and core biopsies were negative for cancer in 14 sides.

**Conclusion:** This study revealed that 49% of prostate cancer lesions (n = 29 sides) were not recognized on TRUS and 52% of those (n = 15 sides) were diagnosed only by additional systematic biopsies. Furthermore, even with TRUS-guided systematic core biopsies, failure to detect the prostate cancer lesions may be as high as 24% (n = 14 sides).

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**Key words:** transrectal ultrasonography, core biopsies, radical prostatectomy, prostate cancer

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## INTRODUCTION

Since its introduction by Watanabe and associates in 1971, transrectal ultrasonography (TRUS) has rapidly progressed to a front-line position as a diagnostic tool for prostate cancer.<sup>1</sup> Although it lacks specificity in diagnosing the disease it provides objective images of the gland with detailed anatomical information. It also provides more accurate lesion-directed and systematic biopsies.<sup>2,3</sup> Even in the absence of high levels of prostate-specific antigen (PSA) and positive results from a digital rectal examination (DRE), a hypoechoic lesion on TRUS may indicate a need for biopsy.<sup>2,3</sup> Even without hypoechoic lesions on TRUS, PSA levels high enough to suggest prostate cancer (PCa) should be investigated by TRUS-guided systematic biopsies.<sup>2</sup> In this study, we correlated the final pathological results with the PCa prediction of TRUS hypoechoic lesions and the systematic biopsies of ultrasound-normal sides of the prostate in order to assess the accuracy of TRUS as a diagnostic tool.

## PATIENTS AND METHODS

Tumors located preoperatively by TRUS in 30 patients were compared with the postoperative pathological specimens (a total of 60 left and right halves, hereafter called "sides") after the patients had radical retropubic prostatectomy for clinically organ-confined PCa. The algorithm of Cooner was used in the diagnosis of the disease.<sup>4</sup> The prostate gland of patients with positive DRE and/or elevated PSA and/or hypoechoic lesions on TRUS were biopsied using the TRUS-guided technique. Three cores, one each from base, mid and apex of the peripheral zone, and 1 core from the transition zone of each side of the prostate were taken as part of the systematic biopsy. A Bruel and Kjaer 1849 or 1846 ultrasound unit with 7.0MHz multiplane endosonic transducer was used in ultrasonographic evaluation and for biopsy guidance in all cases. The transrectal route was used for all biopsies, and tissue samples were obtained through an 18 gauge needle with the Bard Biopsy gun. The same staff radiologist performed all TRUS examinations and TRUS-guided biopsies. Patients were given 400 mg/day ofloxacin the day before biopsy and the treatment continued for 3 days. No infectious complications were observed. Histopathological examination of the radical prostatectomy specimens was done according to the step sectioning technique with 0.5 cm intervals.<sup>5</sup>

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## RESULTS

In the evaluation of 30 patients according to the algorithm of Cooner, 22 had suspicious DRE with or without PSA elevation; the remaining 8 patients had elevated PSA levels. Of the 8, 3 had normal TRUS but PSA density higher than 0.15, and 5 had a positive TRUS examination. Histopathological examination of the prostatectomy specimens revealed pT1-2 disease in 9, pT-3 A or B in 7, pT-3 C in 12, and pT-4 A in 2 patients according to the 1992 UICC staging system.<sup>6</sup> The median PSA level of the organ-confined group (pT1-2) was 9.1 (range, 0.2 to 17) and of the extracapsular group (pT3-4) was 10.0 (range, 2.6 to 35). PCa was found bilaterally in 29 glands (58 sides) and unilaterally in 1 gland. Preprostatectomy TRUS examinations revealed hypoechoic lesions in 30 sides of the prostates and they were all proven to be adenocarcinoma on histological examination of lesion-directed core biopsies. Of 30 sides with no hypoechoic lesions on TRUS, 15 were found to have PCa according to systematic biopsies. Systematic and lesion-directed core biopsies together revealed PCa in 45 and nodular hyperplasia (NH) in 15 sides. However, histopathological examination of the radical prostatectomy specimens revealed cancer in 14 of these 15 sides with initial NH diagnosis in TRUS-guided biopsies. As a summary of final histopathological results, all sides (30 out of 30) with hypoechoic lesions were found to have PCa, while 97% (29 out of 30) of the ultrasound normal sides had also PCa.

In 14 patients where PCa was missed by systematic biopsies of 14 sides but found on final histological examination, diagnosis of PCa was made according to TRUS-guided biopsies of the contralateral sides. The mean PSA in this group was 10.9 ng/mL (range, 0.19 to 33). DRE was normal on 13 of 14 sides missed by biopsies, but DRE was positive in 10 contralateral sides. There was a hypoechoic lesion in 9 of the contralateral sides in this group which all revealed PCa according to lesion-directed biopsies. In the 5 contralateral sides that were normal on TRUS, PCa was diagnosed by systematic biopsies.

According to these results, TRUS had an accuracy rate of 52%, specificity and positive predictive values of 100%, a sensitivity rate of 51% and a negative predictive value of 3% in detecting and locating PCa within the prostate. TRUS-guided (systematic and lesion-directed) biopsies were 77% accurate, 76% sensitive, 100% specific, and had 100% positive and 3% negative predictive values.

According to the histopathological examination of the radical prostatectomy specimens, the median Gleason score, 7, was found in 29 ultrasound normal sides (range, 4 to 10), and also in the 14 sides with

PCa which were missed by TRUS-guided biopsies (range, 4 to 9).

## DISCUSSION

Transrectal ultrasound (TRUS) of the prostate is indicated when there is an elevation in PSA or an abnormal DRE. The low specificity of TRUS makes it inappropriate for routine use in screening for PCa.<sup>1</sup> TRUS is, however, a valuable tool for detecting nonpalpable PCa and guiding needle biopsies, especially in the presence of hypoechoic lesions.<sup>2</sup> A drawback of TRUS is that the hypoechoic lesions it locates are not cancer-specific. In a study of 954 biopsies of hypoechoic lesions, only 35% contained cancer.<sup>7</sup> Also, this issue is further confused by studies showing that isoechoic regions on TRUS may prove tumorous.<sup>8</sup>

Systematic biopsies are of great importance in the diagnosis of the disease, because only 60% of prostate cancers are hypoechoic, 25% of PCa arise in the transition zone which is poorly echogenic, and tumors less than 0.5 mm in diameter are outside the range of the spatial resolution of TRUS.<sup>9</sup> In a group of patients with abnormal DRE, Hodge et al. proved the safety of systematic biopsies.<sup>10</sup> They were able to detect 96% of the cancers by systematic biopsies whereas 17% of the cancers were missed by biopsies directed into hypoechoic defects.<sup>10</sup> Vallancien et al.<sup>11</sup> clearly showed that 6 systematic biopsies, even in a palpably normal prostate, may detect cancer in 14% of patients, which was a 3 times higher detection rate than when 2 biopsies were taken only from the apex of the prostate.<sup>12</sup> In contrast, Cooner et al. had a 9.6% positive rate among biopsies taken only from hypoechoic areas.<sup>13</sup>

However, systematic biopsies miss some prostate cancers. Kabalin et al. reported the presence of unsuspected prostate cancer in 38% of cystoprostatectomy specimens with roughly uniform anatomical distribution in anterior and posterior portions of the gland.<sup>14</sup>

Approximately 30% of prostate cancers arise from the transition zone and some of them may be associated with a relatively poor prognosis (A2 disease), thus requiring early diagnosis and treatment. Terris et al. used a modified systematic biopsy technique which included anteriorly directed biopsies into the transition zone in addition to sextant peripheral zone biopsies.<sup>15</sup> Subsequent studies by Lui et al. indicated that transition zone biopsies did not improve the cancer detection rate in patients with abnormal DRE or sonographic abnormalities.<sup>16</sup> However, in the subset of patients with normal DRE, 33.3% of the cancers could be detected only by additional transition zone biopsies. These authors obtained 4 to 6 cores from the transition zone compared to 2 cores in our study.

Lippman et al. obtained systematic digitally guided biopsies (2 to 4 cores from each lateral lobe and an additional 2 to 3 cores from the palpable lesion) and detected cancer in 30% of their patients.<sup>17</sup>

Clearly an increased number of biopsies result in an increased detection rate of prostate cancer. Recent literature appears to have reached a consensus that systematic sextant biopsies of the peripheral zone and directed biopsies of hypoechoic lesions, if present, with or without transition zone biopsies (2 to 4 cores) are required for the detection of prostate cancer.<sup>11,16,18,19</sup>

Our study revealed that 49% of PCa could not be recognized by TRUS and 52% of these cancers were diagnosed only by additional systematic biopsies. Tumors that were not recognized on TRUS have been found to have a median Gleason score of 7, indicating that these were in fact significant cancer foci. The current study provided strong evidence that a malignancy found in a systematic biopsy specimen may be clinically significant, and this may settle previous arguments about the biological significance of these tumors.<sup>20,21</sup>

Since core biopsies could not detect PCa in 24% of the sides that contained tumors, an argument may be that an increased number of core biopsies is needed in order to achieve higher accuracy in clinical staging.

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