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Multiparametric MRI/TRUS Fusion Prostate Biopsy: Advantages of a Transperineal Approach

PIETRO PEPE[1], ANTONIO GARUFI[2], GIAN DOMENICO PRIOLO[2] and MICHELE PENNISI[1]

[1]*Urology Unit – Cannizzaro Hospital, Catania, Italy;*
[2]*Imaging Department – Cannizzaro Hospital, Catania, Italy*

Abstract. *Background/Aim: To evaluate the detection rate for clinically-significant prostate cancer (PCa) of transperineal (TP) vs. transrectal (TR) multiparametric MRI/TRUS (magnetic resonance imaging/transrectal ultrasound) fusion targeted-biopsy. Patients and Methods: From January 2016 to December 2016, 150 men underwent repeat saturation transperineal prostate biopsy (SPBx; median 30 cores) combined with targeted mpMRI/TRUS TR and TP fusion biopsies (4 cores for each procedure) of suspicious MRI lesions (PI-RADS 3/5). Results: Overall, in 55/150 (36.6%) men a clinically-significant PCa was found and in 49 (89.1%) of them mpMRI was positive. SPBx, mpMRI/TRUS TR and TP fusion targeted-biopsy diagnosed 52 (94.5%), 43 (78.1%) and 49 (89.1%) PCa, respectively; TR fusion biopsy missed 8 (53.3%) while TP missed 2 (13.3%) cancers of the anterior zone. Conclusion: Multiparametric MRI/TRUS TP in comparison to TR fusion biopsy detected a greater percentage of small but clinically significant PCa of the anterior zone (86.7% vs. 46.7%; p=0.0001).*

Prostate cancer (PCa) is the most frequent tumor diagnosed in elder men with about 1 million biopsies performed in the United States annualy (1). The rate of overdiagnosis in men enrolled in screening protocols is equal to 50% of the cases (2). Moreover, the transrectal biopsy approach is associated with an increased risk of infection with an estimated hospital admission and sepsis equal to 2.5% (3) and 3.5% (4), respectively. Therefore, the main goal is to reduce the number of unnecessary biopsies and diagnose only clinically significant PCa. In this respect, multiparametric magnetic resonance imaging (mpMRI) combined with TRUS (transrectal ultrasound) fusion targeted biopsy has improved the accuracy of standard biopsy schemes in detecting clinically-significant prostate cancer (PCa), especially, in case of a repeat biopsy (5-7) and in the reevaluation of men enrolled in active surveillance (AS) programs (8-10). Although the accuracy of mpMRI/fusion targeted biopsy has been evaluated in a lot of series, very few papers have compared the detection rate for PCa or/and complications of the different MRI/TRUS fusion platforms in the same population (11-14). On the other hand, the standard transperineal biopsy approach in comparison with the transrectal procedure has demostrated a higher accuracy in diagnosing PCa located in the anterior zone of the gland (15) resetting the risk of sepsis (16).

In this report, the detection rate for clinically-significant PCa (17) performing transperineal (TP) *vs.* transrectal (TR) mpMRI/TRUS fusion targeted-biopsy has been prospectively evaluated in men submitted to repeat prostate biopsy.

Correspondence to: Dr. Pietro Pepe, Urology Unit - Cannizzaro Hospital, Via Messina 829, Catania, Italy. Tel: +39 957263285, Fax: +39 957263259, e-mail: piepepe@hotmail.com

Key Words: Prostate cancer, multiparametric MRI, transrectal fusion biopsy, transperineal fusion biopsy, saturation prostate biopsy.

Patients and Methods

From January 2016 to December 2016 150 men (median age 62 years; range=47-78 years) with negative digital rectal examination underwent repeat saturation transperineal prostate biopsy (SPBx) for the persistent suspicion of cancer (increasing or persistent elevated PSA values). All the patients 10 days before SPBx underwent pelvic mpMRI; SPBx (median 30 cores; range=28-34 cores) was performed transperineally by a GE Logiq P6 ecograph (General Electric; Milwaukee, WI) supplied with a bi-planar trans-rectal probe (5-7.5 MHz) using a tru-cut 18 gauge needle (Bard; Covington, GA) under sedation and antibiotic prophylaxis (18). All mpMRI examinations were performed using a 3.0 Tesla scanner, (ACHIEVA 3T; Philips Healthcare Best, the Netherlands) equipped with surface 16 channels phased-array coil placed around the pelvic area with the patient in the supine position; multi-planar turbo spin-echo T2-weighted (T2W), axial diffusion weighted imaging (DWI), axial dynamic contrast enhanced (DCE) and spectroscopy were performed for each patient. The mpMRI lesions characterized by a PI-RADS (Prostate Imaging-Reporting and Data System) score of 3/5 were considered suspicious for cancer (5,7); two radiologists blinded to pre-imaging clinical parameters evaluated the mpMRI data separately and independently. Informed consent was obtained from all individual participants included in the study. In the presence of mpMRI lesions suggestive of cancer, mpMRI/TRUS TR and TP fusion guided-biopsies (4 cores for each procedure) were

Table I. *Biopsy histological findings in the 55 men with clinically significant prostate cancer (PCa) diagnosed by mpMRI/TRUS transperineal (TP) vs. transrectal (TR) fusion biopsy*

Biopsy histological findings and mpMRI results	TRUS/mpMRI TR fusion targeted biopsy	TRUS/mpMRI TP fusion targeted biopsy
mpMRI: true positive	49 (89.1%)	49 (89.1%)
mpMRI: false negative	6 (10.9%)	6 (10.9%)
mpMRI: false positive	16 (22.5%)	16 (22.5%)
Clinically significant PCa* (overall: 55cases)	43 (78.1%)	49 (89.1%)
Anterior zone PCa (overall: 15 cases)	7 (46.7%)	13 (86.7%)
PCa of peripheric zone (overall: 40 cases)	36 (90%)	36 (90%)
Gleason score		
3+4	25	29
4+3	15	17
4+4	2	2
5+4	1	1
Diameter of mpMRI lesion** (range: millimeter)	12 (9-20)	8 (5-20)
Number of positive cores** (range)	2 (1-4)	3.2 (1-4)

TRUS: Transrectal ultrasound; mpMRI: multiparametric magnetic resonance imaging; *Clinically significant PCa (prostate cancer): >2 positive cores with Gleason score >6; **Median.

added to SPBx using a GE Logiq E9 and Hitachi 70 Arietta ecograph (Hitachi Medico, Chiba, Japan), respectively (12,19). The GE Logiq E9 and Hitachi Arietta 70 platforms allowed processing of a software-based rigid registration of pelvic mpMRI and TRUS (end-fire probe and biplanar probe, respectively) by the use of a fusion device; moreover, an electromagnetic tracking system showed the needle localization (Figure 1).

The accuracy of TP *vs*. TR mpMRI/TRUS fusion targeted biopsy in diagnosing clinically significant PCa (Gleason score > 6 and/or more than 2 positive cores) were prospectively evaluated (20) and compared with SPBx results. For statistical analysis the Student's T test was used; a p-value<0.05 was considered statistically significant.

Results

All patients had a negative TRUS (median prostate weight 45 g; range=25-95g) and median PSA was 9.2 ng/ml (range=4.5-31 ng/mL); mpMRI showed a suspicious lesion (PI-RADS 3/5) in 71 (47.3%) cases. Overall, in 55/150 (36.6%) men a clinically significant PCa was found and in 49 (89.1%) of them mpMRI was positive (PI-RADS 3=18 cases; PI-RADS 4= 6 cases; PI-RADS 5=15 cases); in the remaining 12 (8%) and 78 (52%) patients a cancer at risk for indolent disease and a normal parenchyma was detected, respectively. In 55 men with clinically significant PCa 392 targeted biopsies (196 cores for TR and TP fusion procedure) were performed in the mpMRI suspicious lesions; in 40 (72.7%) and 15 (27.3%) cases, PCa was found in the peripheric and anterior zone of the gland, respectively. None had significant complications from prostate biopsy that needed hospital admission; moreover, the mpMRI procedure was well tolerated and successfully performed in all cases.

The biopsy quantitative histology (*i.e.*, number of positive cores, greatest percentage of cancer "GPC"), Gleason score and mpMRI findings in the presence of PCa are listed in Table I. SPBx, mpMRI/TRUS TR fusion and TP fusion targeted biopsy diagnosed 52 (94.5%), 43 (78.1%) and 49 (89.1%) clinically-significant PCa, respectively. SPBx, TR fusion and TP targeted biopsy missed 3 (20%), 8 (53.3%) and 2 (13.3%) cancers of the anterior zone and 0, 4 (10%) and 4 (10%) of the peripheric gland, respectively. The TR fusion approach missed 6/49 clinically significant PCa that were diagnosed by TP fusion biopsy; in detail, all the PCa were located only in the anterior zone of the gland and were provided of a GS, GPC and mpMRI diameter equal to 7, 50% and 8 millimeter, respectively.

The detection rate of cancer for each core performing SPBx, TR and TP targeted biopsy was 12%, 30% and 55%, respectively. Sensitivity, specificity, positive predictive value, negative predictive value (NPV) and diagnostic accuracy of TP-fusion *vs*. TR-fusion targeted biopsy were equal to 89.1 *vs*. 78.2%, 86.3 *vs*. 77.2%, 69 *vs*. 60.5%, 94 *vs*. 88.7%, 87.2 *vs*. 84.2%, respectively.

Discussion

The improvement of diagnostic imaging by mpMRI has allowed to perform targeted biopsies of suspicious areas increasing the accuracy in the diagnosis of clinically-significant PCa (21, 25) resulting in predictive of definitive Gleason score with a higher detection rate of cancer for each core in comparison to standard prostate biopsy schemes. The detection rate for PCa of mpMRI is between 39% and 59% (26, 27) with an incidence of cancer located only in the anterior zone equal to 20% (16, 28). Although mpMRI is strongly recommended in men who are candidates to repeat biopsy or enrolled in AS protocols (8-11), still today, extended or SPBx should always be combined with mpMRI/TRUS fusion biopsy because of the false negative

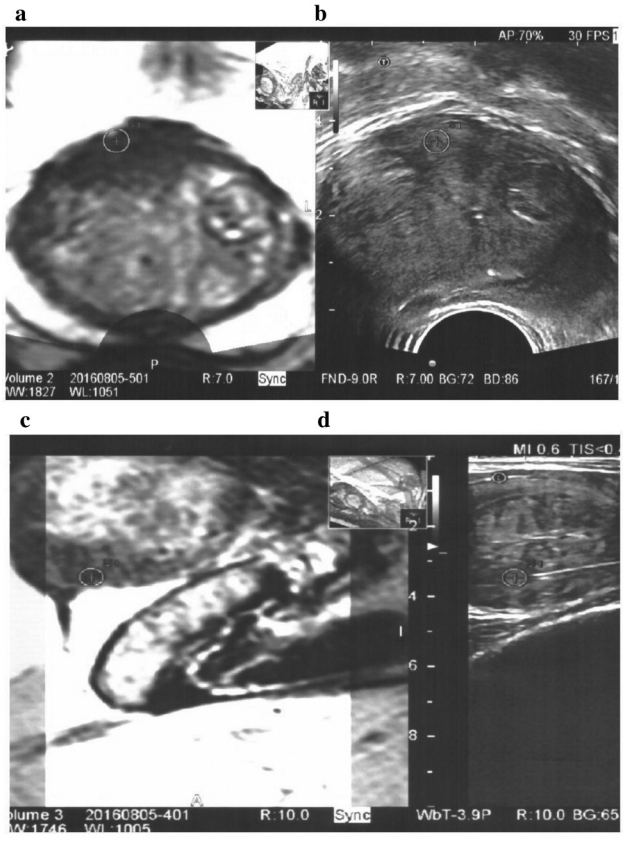

Figure 1. *Multiparametric MRI/TRUS fusion image (caliper) of a prostate cancer located in the anterior zone (a: axial T2W - PI-RADS 4; b: axial TRUS). Transperineal mpMRI/TRUS fusion targeted biopsy of the suspicious lesion (c: sagittal mpMRI; d: sagittal TRUS during fusion targeted biopsy).*

rate of mpMRI (15-20% of PCa with low volume and GS >7) and the variable diagnostic accuracy reported using the different mpMRI/TRUS fusion biopsy platform (12, 22-24). The targeted biopsy of mpMRI suspicious areas could be performed using "in-bore" mpMRI-guidance, real-time mpMRI/TRUS imaging fusion or by performing cognitive mpMRI/TRUS biopsies (29, 30). Recently, many papers have demonstrated a higher accuracy in favour of the fusion technique; conversely, few data have been reported regarding the accuracy of TR *vs*. TP mpMRI/TRUS fusion approach in diagnosing clinically significant PCa (12, 13). In this respect, standard TP and TR prostate biopsies are provided of a superimposable detection rate for PCa (4-17), but, at the same time, the transperineal approach allows to easily and better reach the anterior zone of the gland (15) resetting the risk of sepsis (16).

In our series, the detection rate for clinically significant PCa was lower performing the TR (78.1%) *vs*. TP (89.1%) fusion approach. In detail, the TP targeted biopsies diagnosed more PCa (86.7%) located in the anterior zone of the prostate in comparison with TR approach (46.7%; p=0.0001) and SPBx (80%). Moreover, clinically significant PCa detected by TR mpMRI/TRUS fusion biopsy had a greater mpMRI lesion diameter in comparison with the TP approach; 12 *vs*. 8 millimeter, respectively. In definitive, TP and TR fusion biopsy diagnosed the same percentage of PCa located in the peripheric zone of the gland (90% of the cases), conversely, the TP fusion targeted approach allowed to diagnose a greater number of clinically significant PCa of the anterior zone (6 out 15 equal to 40% of the cases) charaterized by a small volume showing a NPV for PCa equal to 94%. These data could be useful in the planning of a mpMRI/TRUS fusion targeted biopsy of small mpMRI lesions located in the anterior prostate near the pubic bone.

Regarding our results certain considerations should be made. Firstly, an "in-bore" approach could improve the detection rate for PCa; secondly, biopsy histological findings should be compared with the whole prostate specimen to evaluate the false positive mpMRI results (about 20% of cases). Finally, a greater number of patiens submitted to TR *vs*. TP mpMRI/TRUS fusion biopsy should be compared.

In conclusion, although SPBx diagnosed the majority of clinically-significant PCa (94.5% of the cases), mpMRI/TRUS TP in comparison with TR fusion biopsy detected a greater percentage of small, but clinically-significant PCa of the anterior zone (86.7% *vs*. 46.7%; p=0.0001).

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