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THE ROLE OF T2W PULSE SEQUENCE AND DIFFUSION WITH ITS NUMERICAL ADC MAP IN PROSTATE CANCER DIAGNOSIS

Masha Kostova [1], Elizabeta Stojovska Jovanovska [2, 4], Ace Dodevski, Dimitar Veljanovski [1, 4], Sandra Dejanova Panev [1, 4], Biljana Prgova Veljanova[1, 4]

[1]Department of Radiology, City General Hospital "8th September", Skopje, North Macedonia
[2]University Institute of Radiology, Skopje, North Macedonia
[3]Institute of Anatomy, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, North Macedonia
[4]Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, North Macedonia

Abstract

In patients with increased PSA (prostate-specific antigen), the next diagnostics tool is transrectal ultrasound-guided biopsy-TRUS. Multiparametric magnetic resonance imaging (mp MRI) as non invasive diagnostic tool is used as a triage test to avoid biopsy, as well as to improve the diagnostics.

In our study we want to prove the clinical meaning of T2W pulse sequence and diffusion as a part of mp MRI in prostate malignant lesions detection and their distinction from the benign lesions.

This cohort prospective study included 100 patients with increased levels of PSA from 4 ng/ml to 76 ng/ml. The MRI equipment used was Siemens Essenza1,5T with body coil.

The results from the T2W pulse sequence and diffusion are correlated with the values of diffusion and ADC map, in which the suspected zones are marked on a template. Patients undergo biopsy depending on the PIRADS (prostate-imaging and reporting data system) classification. The MRI results and the pathohistological findings are then compared.

Clinically significant cancer is considered to be a cancer with a Gleason score 6, diameter > 6mm.

The values of diffusion with its numerical ADC map are considerably lower for malignant nodules compared to benign ones. Hyposignal of T2W pulse sequence is characterized with score 2 and 3 in benign changes, and 4 and 5 in malignant changes using the PI RADS score system for differentiation.

T2W pulse sequence combined with diffusion is a powerful tool for non-invasive differentiation of benign prostatic hyperplastic nodule and prostatitis from a malignant nodule.

Key words: prostate carcinoma, multiparametric MRI, T2W pulse sequence, diffusion with ADC.

Introduction

Prostate carcinoma is the second most frequently found carcinoma in male population [1]. PSA and digital rectal examination are included in the prostate carcinoma screening. The diagnostic problem rises because increased levels of PSA are also found in prostate inflammation, as well as in benign prostatic hyperplasia (BPH) [2].

Prostatitis, hemorrhaging, atrophy and post-radiation changes can also mimic carcinoma in the periphery zones of T2W pulse sequence [3, 4]. MRI is a non-invasive diagnostic tool for evaluation of the changes responsible for higher levels of PSA. Most often the MRI is focused on the lateral zones changes because they are more prone to carcinoma, but in around 20-30% PC is found in the transitory zone [5] and they are thought to have a lower degree of biological aggression.

The transitory zone is the area around the proximal urethra and is a zone which can undergo hypertrophy during the lifetime with consecutive appearance of BPH. BPH, i.e. stromal hypertrophy and PC look similar on MRI, are presented as a hypersignal on T2W pulse sequence, because of which there can be a diagnostic problem in differentiating of BPH carcinoma nodule.

T2W pulse sequence shows the prostate anatomy and the morphology of the changes. Diffusion (DWI) is a method with which a signal is generated based on the differences in the Brownian motion. The diffusion evaluates the microarchitectural of the body based on molecular function and is a revolutionary method in MRI development [6].

Around 60-70% of the human body contains water. Diffusion is an accidental Brownian motion of the water molecules caused by warming. In an ideally homogenic medium, the diffusion is randomized and isotropic (equal probability of motion in all directions).

In a complex medium such as the human body, water is divided in two media – extracellular and intracellular, which implies different movement of molecules. In the extracellular compartment the movement is free, free diffusion, and in the intracellular compartments the diffusion is limited, restricted diffusion. Different tissues in the human body have different intra- and extracellular compartment ratio – different diffusion. In pathological conditions this ratio changes, as well as the amount of water, so, for example, in higher grade neoplasms the intracellular proportion is reduced, which consecutively [7] causes restriction of diffusion, movement, of the water molecules.

Taking all this into consideration, we can conclude that diffusion gives us both qualitative and quantitative data for the tissue structure, and because of this the MRI now can give us not only anatomical, but also functional information.

With the DWI sequence the diffusion gradients are applied on any side of a 180* refocusing pulse. The B parameter determines the diffusion degree and is measured in mm^2/s. This way we get qualitative information about the tissues [8].

We get the quantitative data on the ADC map (Apparent Diffusion Coefficient of water). Tissues that cause diffusion restriction are presented as hypointense on the ADC map and have accordingly low values. The malignant changes differentiate in their cellularity and the bio aggressiveness which can be quantified on the ADC map [9].

ADC is an indicator for water movement, and it gives us quantification of speed and distance of water movement. Decreased ADC means reduced, lowered movement or diffusion of water molecules, while high ADC means that there is no restriction in water movement.

More studies have shown the sensitivity and specificity of diffusion and the ADC map in differentiation of malignant from benign prostatic tissue combined with standard MRI of the lesser pelvis, especially the T2W pulse sequence. In general, the ADC map values differentiate depending on the localization and the composition of the tissue, and the malignant lesions have about 20-40% lower values compared to normal tissue.

These is also a small variation in normal values of ADC in different prostate zones, for example, in the periphery zones the values are higher (1.5 to $2\times10^{-3}mm^2/s$), compared to the central zone ($1.4–1.7\times10^{-3}mm^2/s$) [10].

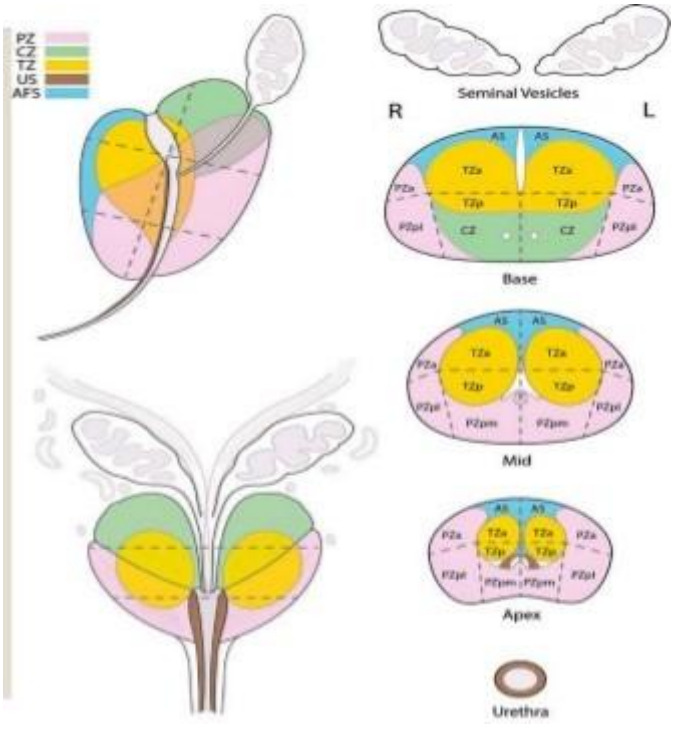

Figure 1. Template of the prostate and marking of changes according to location

Materials and methods

Patients with increased levels of PSA, higher than 4 ng/ml, are analyzed in this study.

They are previously observed by a urologist. Some has also undergone digital rectal examination.

The results from the T2W pulse sequence and diffusion are correlated with the values of diffusion and the ADC map, whereupon with mapping of the suspect zones (Fig.1) the patients undergo a biopsy depending on the PI RADS (prostate imaging and reporting data system) classification (Table 1). The examination is done with MRI Siemens Essenza 1,5T with standard body coil.

Table 1. Grading of tumor formation through PI RADS classification

PI RADS classification	Definition	Total Score T2W, ADC diffusion, post contrast series, MRI spectroscopy
1	most propably bening	4,5
2	probably benign	6-8
3	indetermined	9-12
4	probably malignant	13-16
5	highly suspicous malignant	17-20

T2W pulse sequence (Fig. 2) is used to characterize the regions suspect of cancer. The periphery zones are normally characterized with a hypersignal. The prostatic cancer is presented as hypo signal, and in rare cases as iso signal [11,12,13].

The standard protocol parameters for T2W pulse sequence for the sagittal and transversal plane are TP/TE 5000/80-149 , FOV (field of view) 14-20 cm, slice thickness 3 mm, and imaging matrix 256x256. The prostate tumors in the central zone are presented as hypo signal, which makes them harder to differentiate from the changes in BPH and that lowers the sensitivity of the T2W sequence to 60-70% [14].

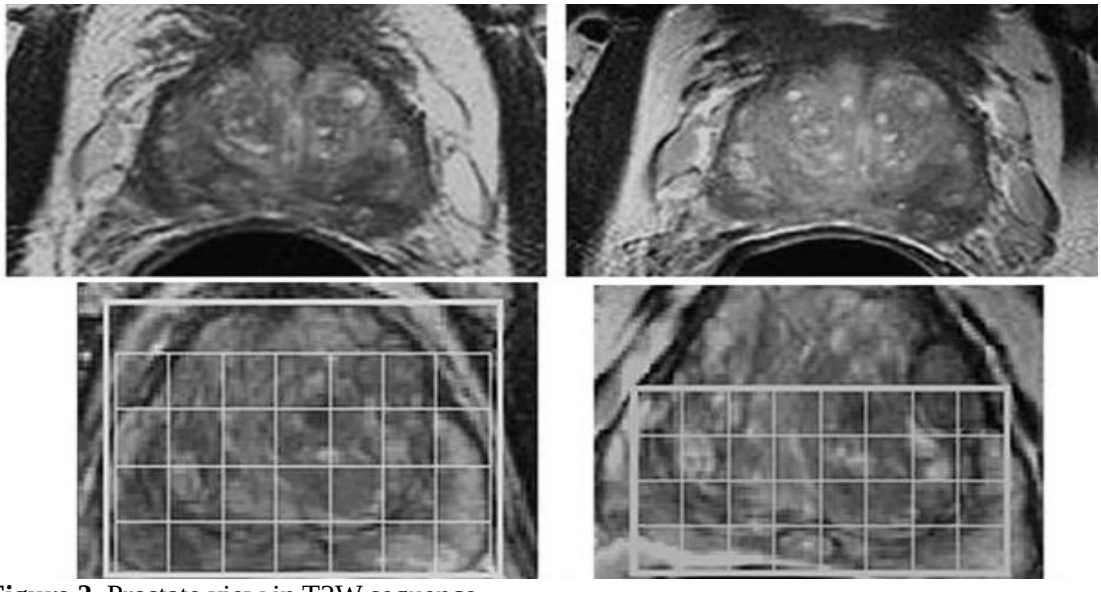

Figure 2. Prostate view in T2W sequence

The T2W pulse sequence gives us information about the tissue morphology, but for diagnosis of cancer we need specifics about the cellularity of the tissues.

Different pulse sequences can be used to realize the diffusion, but for a prostate the standard is to use EPI (Echo Planar Imaging), always in transversal plane, with suppression of fat (FS), minimal repetition time (TR) and at least three b values.

The standard parameters for DWI for magnetic field of 1,5T are TP/TE -3900/78 ms, ST=4 mm, 1–2 mm gap, b value -0,500,1000 s/mm². What we get on diffusion allows us to form the ADC map as a quantitative map which pixel by pixel marks the zones of different diffusion of water molecules in tissues. The ADC values are conveyed in mm²/s.

Results

In the study were included 96 patients, ranging from 48 to 83 years of age, with a median age of 65.9±7.2 years. The levels of PSA ranged from 4ng/mg to 76 ng/mg, the median level being 9.8±10.5 ng/mg. According to the pathohistological findings, 41 (42.71%) patients had benign prostate changes, in 55 (57.29%) patients the biopsy confirmed presence of a malignant lesion (Table 2). According to the PI RADS classification, the most frequently detected score was 4 (40.62%).

Table 2. Percentual presentation of pathohistological verification of PI RADS classification

variable	**n(%)**
Prostate lesion	
benign	41 (42.71)
malignant	55 (57.29)
PI-RADS	
2	14 (14.58)
3	24 (25)
4	39 (40.62)
5	16 (16.67)
5/3 тр	1 (1.04)
missing	2 (2.08)

There wasn't any statistically significant difference in PSA concentrations measured in patients with benign lesions. The patients with prostate carcinoma without malignant changes (p=43);median levels of PSA were 8.1±3.9 and 10.9±13.4 ng/mg, in patients with benign and malignant changes; the median PSA levels was 6.51 I 7,6 ng/mg, in patients with benign and malignant lesions (Table 3).

Table 3. Median age of patients and PSA levels

variable		Descriptive Statistics				p-level
		n	mean ± SD	min- max	median (IQR)	
Age	benign	41	64.37 ± 6.8	49 – 77		t=1.9 p=0.06
	malignant	55	67.14 ± 7.3	48 – 83		
PSA	benign	41	8.18 ± 3.9	3.1 – 15.9	6.51(5.1-10.3)	Z=0.8
	malignant	55	10.95 ± 13.4	3.34 – 76	7.6(5.41-11)	p=0.43

T (Student t-test for independent samples); Z (Mann-Whittney test)

In patients with prostate carcinoma the ADC value was significantly lower compared to patients with benign changes (p<0.0001); the median ADC value for malignant changes was 647.7±150.9, for the benign changes was 964.0±265.9 (Table 4, figure 3).

Table 4. Comparing the levels of ADC in benign and malignant changes

Variable		Descriptive Statistics			p-level
		n	mean ± SD	min- max	
ADC	benign	41	964.05 ± 265.9	2 – 1800	t=7.4
	malignant	55	647.74 ± 150.9	364 – 1290	***p=0.00000

t(Student t-test for independent samples) ***sig p<0.0001

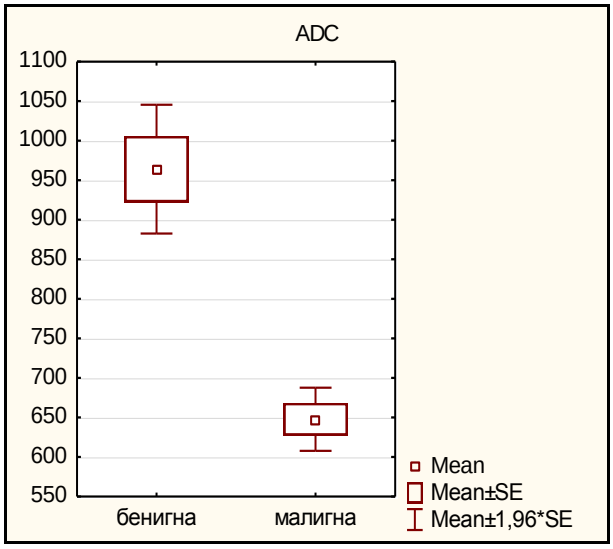

Figure 3. Distinction between benign and malignant lesion according the value of ADC

The T2W parameter was significantly different in the benign and malignant changes of the prostate (p<0.0001). In the benign changes group, the T2W parameter most often had a score of 2 and 3 (48.78% and 43.9%, accordingly), while in the malignant changes group the T2W parameter most often had a score of 4 and 5 (50.91% and 30.91%, accordingly). (Table 5)

Table 5. T2W parameter in benign and malignant changes

T2 W	Prostate lesion			p-level
	n	benign n(%)	malignant n(%)	
1	1	1 (2.44)	0	X^2=56.4
2	24	20 (48.78)	4 (7.27)	p=0.0000
3	24	18 (43.9)	6 (10.91)	
4	30	2 (4.88)	28 (50.91)	
5	17	0	17 (30.91)	

X^2(Pearson Chi-square) ***sig p<0.0001

On Table 6 is shown the diagnostic value of T2W, ADC and the combination of both in prostate carcinoma detection. In accordance with the area under the ROC curve, AUC (Area Under the Curve), both parameters have excellent discriminatory ability to differentiate the malignant and the benign prostate lesions, but still, their combination presents the biggest AUC (0.933). (Table 6, figure 4).

Table 6. Diagnostic value in detection of prostate cancer

	AUC (95% CI)	sensitivity	specificity
T2w	0.905(0.843 – 0.967)	81.8%	95.1%
ADC	0.923 (0.858 – 0.988)	89.1%	87.8%
T2w+ ADC	0.933 (0.881 – 0.986)	83.6%	85.4%

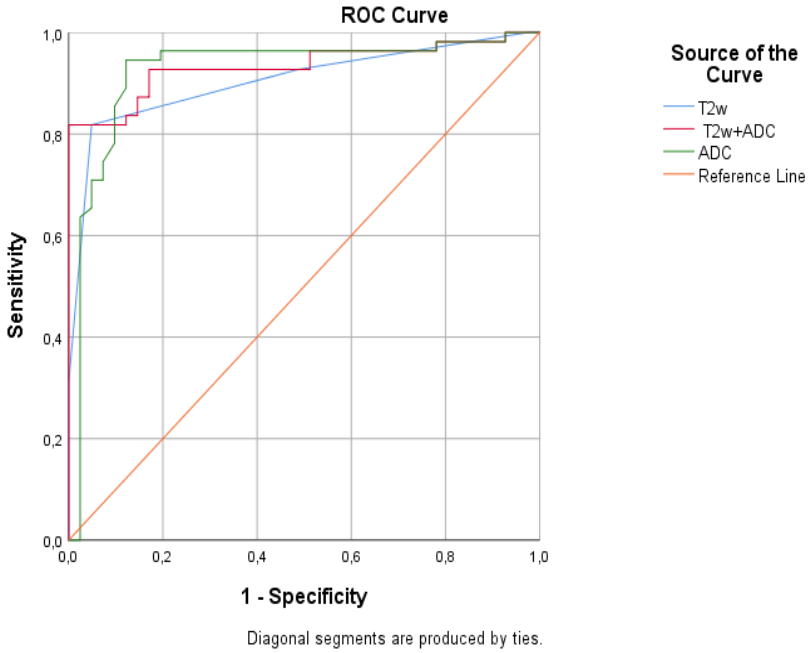

Figure 4. Sensitivity and specificity of T2, diffusion with ADC and combination of both

Discussion

The prostate carcinoma is found most often in patients over the age of 60, but with lower mortality rate compared to the period between 2014 and 2018 [15]. Timely and precise detection and evaluation are essential for further planning of treatment, as well as a follow-up to the therapy response. That's why we use the multiparametric MRI in patients with increased PSA levels as a triage test to avoid biopsy, as well as to improve the diagnostics [16].

The results are graded according to the PI RADS score from 1 to 5, where 1 is a surely benign lesion, and 5 is a surely malignant lesion.

There is a certain discrepancies of lesions shown on the T2W pulse sequence and the diffusion which according to Gibbs et al. [17] is probably due to the diffusional anisotrophy present in different regions in a healthy prostate, too.

With our study we have shown that T2W by itself is not enough for prostate carcinoma detection, apart from advanced carcinomas, but combined with diffusion and ADC map, the sensitivity and the specifics of the method are increased. It's sensitivity id 89,8%, the specificity is 95% and is almost the same compared to some studies where they are 58-71% and 77-98% [18].

In suspect lesions, the carried-out diffusion showed a hypersignal, which represents a restriction of the diffusion. The numerical values are presented on an ADC map, and we measured them in ROI. The lower the values on the ADC map, the higher is the probability for malignancy. There is a certain correlation between the low values on ADC and the aggressiveness of the tumor (high Gleason score), which is also noted in different authors [19, 20]. This can be the subject of further investigations.

Conclusion

In our study the diffusion has shown to be a highly sensitive method with 89,1% and specificity of 87,8% in 96 evaluated patients.

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