



# Is quantitative diffusion-weighted MRI a valuable technique for the detection of changes in kidneys after extracorporeal shock wave lithotripsy?

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## ABSTRACT

**Objective:** The aim of this study was to evaluate the capability and the reliability of diffusion-weighted imaging (DWI) in the changes of kidneys occurring after extracorporeal shock wave lithotripsy (ESWL) treatment for renal stones.

**Materials and Methods:** A total of 32 patients who underwent ESWL treatment for renal stone disease between June and December 2011 were enrolled in this prospective study. Color Doppler ultrasonography (CDUS) and DWI were performed before and within 24 hours after ESWL. DWI was obtained with b factors of 0, 500 and 1000 s/mm<sup>2</sup> at 1.5 T MRI. Each of Resistive index (RI) and ADC values were calculated from the three regions of renal upper, middle and lower zones for both of the affected and contralateral kidneys. Paired sample t test was used for statistical analyses.

**Results:** After ESWL, the treated kidneys had statistically significant lower ADC values in all different regions compared with previous renal images. The best discriminative parameter was signal intensity with a b value of 1000 s/mm<sup>2</sup>. The changes of DWI after ESWL were noteworthy in the middle of the treated kidney (p<0.01). There were no significant difference between RI values in all regions of treated and contralateral kidneys before and after treatment with ESWL (p>0.05).

**Conclusion:** DWI is a valuable technique enables the detection of changes in DWI after ESWL treatment that may provide useful information in prediction of renal damage by shock waves, even CDUS is normal.

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## INTRODUCTION

The prevalence of stone disease shows an increase in the developing world. The invention and development of extracorporeal shock wave lithotripsy (ESWL) in the last 25 years has brought an effective perspective to the treatment of urinary stone diseases as a non-invasive method. It is an optimal technique that may save time and resources and decrease the suffering of patients espe-

cially in the emergency department. Shock waves are non-linear waves characterized by high pressure and low frequency. When the shock waves encounters the stone, a part of energy is absorbed, a part of energy is reflected and the rest of energy is transmitted through stone. These destructive forces that are called cavitation and spalling cause stone fragmentation. The shock waves traverse renal parenchyma before reaching renal calculi and this causes some pathologic changes in the kid-

ney. The side effects of shock waves are intra renal hematomas, subcapsular hematomas, subcapsular fluid collections, perinephric soft tissue stranding, cardiac arrhythmias, fascial thickening and loss of corticomedullary junction. Histopathologic changes are observed in the form of diffuse interstitial fibrosis, focal calcification, glomerular hyalinization and sclerosis, damaged capillary vessels and acellular scars ranged from cortex to medulla. These changes results in 0.01-20% loss of renal function (1-4). Color Doppler ultrasonography (CDUS) has been used to detect the effects of ESWL on the kidneys as a noninvasive technique (5). Also, the kidney is a suitable organ for diffusion studies because of its high blood flow and its fluid transport function. Besides, it's a noninvasive technique with no need of contrast agents. Recent ultrafast sequences made diffusion studies more applicable with shorter examination times and fewer motion artifacts (6, 7). The purpose of our study was to detect the changes of kidneys after ESWL treatment by diffusion weighted imaging (DWI) and CDUS and to evaluate whether DWI has advantages in prediction of renal damage due to shock waves.

## MATERIALS AND METHODS

The study protocol was approved by the local Ethics Committee. Written informed consents were obtained from all participants. During the period of June to December 2011, a total of 32 consecutive patients 23-68 years old (mean age,  $41 \pm 0.6$  years old), diagnosed with nephrolithiasis by abdominal X-ray and US, underwent ESWL and were enrolled in the study group. Exclusion criteria included urinary system infection, marked collecting system dilatation, renal parenchymal disease such as diabetes mellitus and hypertension.

### ESWL Protocol

ESWL was performed by piezoelectric lithotripter, Wolf Piezolith 3000 with F3 triple focus (2.5 x 16 mm / 4.0 x 25 mm / 6.0 x 30 mm). Outline X-ray and inline ultrasound was used for stone location. The stones ranged in size from 9 x 6 mm to 18 x 14 mm. Three sessions of ESWL (with interval of 3 days) were applied to all patients and the number of pulses ranged between

1600 and 2000 (mean 1880). Main supply of lithotripter was 220-240 V/ 50-60 Hz with power consumption 1000 VA. Energy density and peak pressure applied to all patients ranged from 0.84 to 1.14 mJ / mm<sup>2</sup> (mean 0.98 mJ / mm<sup>2</sup>) and 36 to 112 MPa (mean 88 MPa), respectively. DWI and CDUS were performed before and within 24 hours after 3 sessions of ESWL in all patients.

### Color Doppler Ultrasound (CDUS)

All the Doppler sonographic measurements were performed by the same operator using a Toshiba Aplio SSA-770A/80 ( Toshiba Medical Systems Corporation, Tokyo, Japan ) scanner using with Convex array probe PVT-375AX (1.9-6 mhz) before and after ESWL in the first day. The resistive index ( RI ) measurements were taken at an interlobar or arcuate artery from the three regions of kidney (upper, middle and lower zones) for both the affected and contralateral kidneys.

### Diffusion Weighted Imaging (DWI)

DW images were obtained with a 1.5 T whole body system (Avanto; Siemens, Erlangen, Germany) with a 33 mT/m maximum gradient capability using an eighteen channel phased-array body coil. No specific preparatory measures were required such as fasting or drinking prior to the examination. Also, no oral or intravenous contrast agent were administered. Axial diffusion weighted single-shot spin-echo echo-planar sequence with chemical shift selective fat-suppression technique ( TR/TE 4738/80; matrix 192 x 192; slice numbers 36; slice thickness 5 mm; interslice gap 30%; FOV 40 cm; averages 5; acquisition time approximately 4 minutes; PAT factor 2; PAT mode generalized autocalibrating partially parallel acquisition -GRAPPA-) was performed. DW images were obtained with b-factors of 0, 500 and 1000 sec/mm<sup>2</sup>. The phase encode direction was set antero-posteriorly in both sequences. All slices were acquired from the superior pole to the bottom of the kidneys. All images were obtained without restriction of fluid intake and without breath-holding.

### Imaging Interpretation

CDUS was performed by a single examiner with experience in sonography before and within

24 hours after ESWL. Measurements were taken three times for each region repeatedly in the three different regions of affected and contralateral kidneys ( middle zone, upper, and lower poles). Averaged values were recorded for each region as the RI value.

DW images were interpreted by two readers at random order in consensus. All were of diagnostic quality with no exclusion. The DWI datasets were transferred to an independent workstation (Leonardo console, software version 2.0; Siemens AG Medical Solutions, Forchheim, Germany) for postprocessing, and the ADC maps were reconstructed. The kidneys were prospectively evaluated quantitatively with the DW sequences before and after ESWL. We measured DWI signal intensity to quantify visual conspicuity and the level of detectability. A large circular region of interest (ROI) was placed at the corticomedullary junction for the measurement of ADC values. ADC values were obtained on the different sites of kidneys. For each ADC calculation, 3 ROI measurements were taken and the average value was accepted. All measurements were repeated at different *b* values (0, 500, 1000 s/mm<sup>2</sup>). Each patient's ADC values were recorded in square millimeters per second quantitatively (Figures 1a, 1b, 2a, 2b, 2c and 2d).

**Statistical analysis**

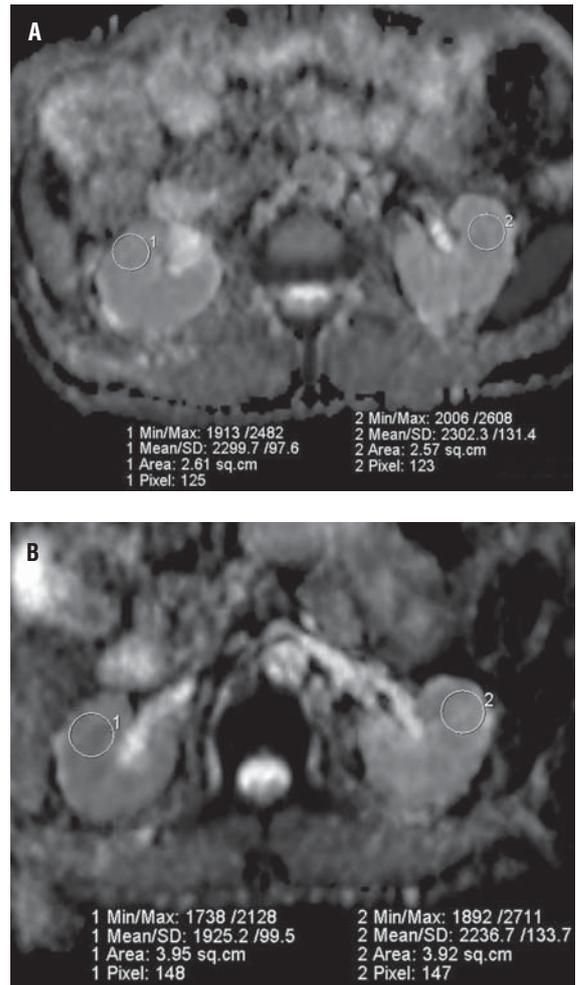
Statistical analysis was performed with the NCSS (Number Cruncher Statistical System) 2007&PASS 2008 Statistical Software (Utah, USA) packages program. The paired sample t-test was used to compare RI and ADC values before and after ESWL. A p value of less than 0.05 was considered statistically significant.

**RESULTS**

**Color Doppler Ultrasound**

Comparison of the mean RI values before and after ESWL showed no statistically significance for both ipsilateral and contralateral kidneys (*p*>0.05). The mean RI values pre and post ESWL were 0.58±0.05 and 0.59±0.04 in the ipsilateral kidney, 0.58±0.05 and 0.59±0.05 in the contralateral kidney, respectively. The changes in the RI

**Figure 1 - 56 years old male patient. Apparent diffusion coefficient (ADC) maps of treated and contralateral kidneys before (Figure-1a) and after (Figure-1b) treatment with ESWL. The ADC value is decreased from 2.29x10<sup>-3</sup> mm<sup>2</sup>/sn to 1.92x10<sup>-3</sup> mm<sup>2</sup>/sn in treated kidney. The ADC values of the contralateral kidney are 2.30x10<sup>-3</sup> mm<sup>2</sup>/sn and 2.23x10<sup>-3</sup> mm<sup>2</sup>/sn before and after ESWL treatment, respectively.**



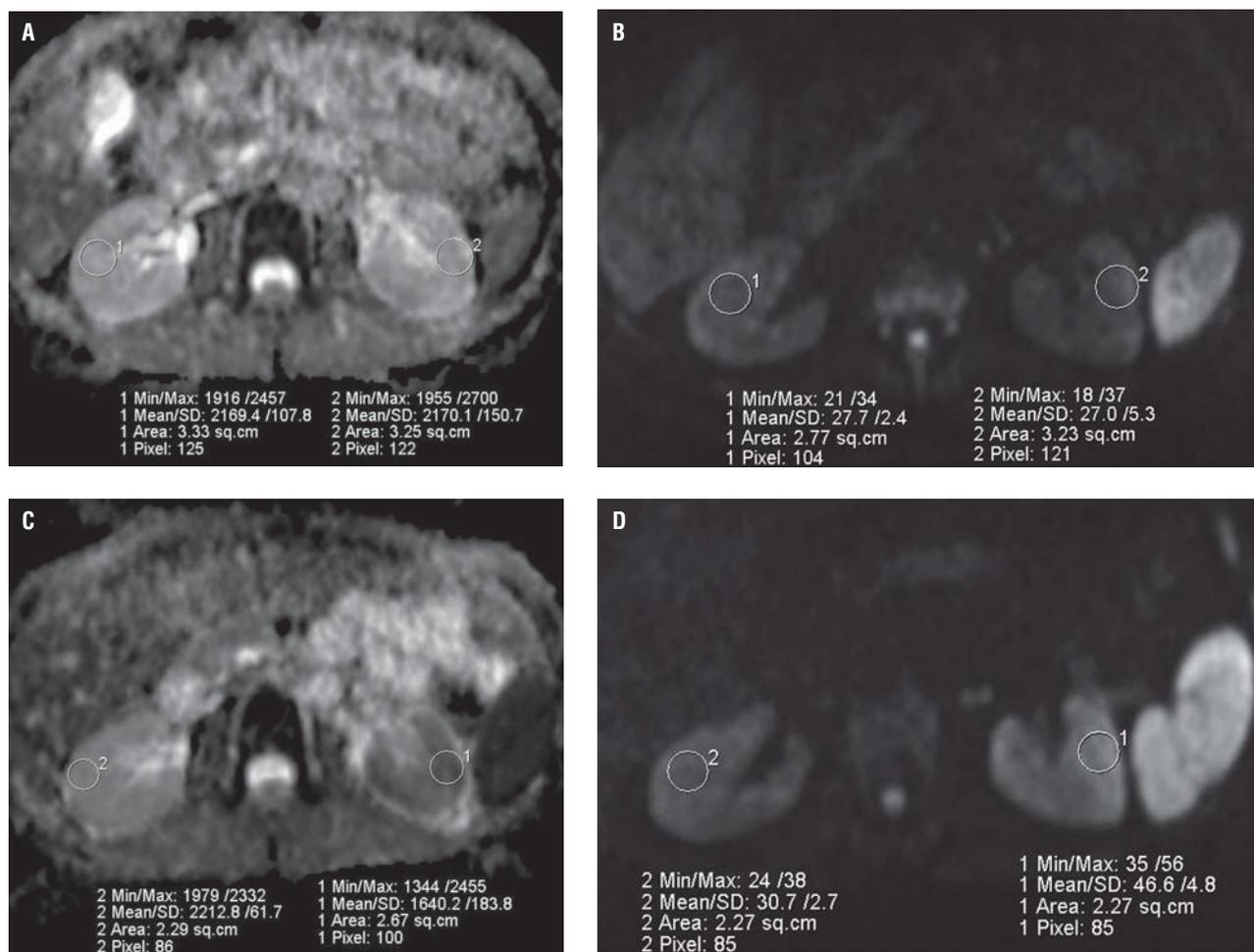
values before and after ESWL in certain regions are shown in Table-1.

**Diffusion weighted imaging**

The mean ADC values of ipsilateral kidneys with *b*=0, *b*=500 and *b*=1000 values before and after ESWL treatment are shown in Table-2.

Ipsilateral kidneys had statistically significant lower ADC values in all different regions compared to contralateral kidneys after ESWL (Figure-3). The changes after ESWL were conspi-

**Figure 2 - 44 years old male patient. Apparent diffusion coefficient (ADC) maps and signal intensities (with b values of 1000 s/mm<sup>2</sup>) of treated (left) and contralateral kidneys before (Figures 2a and 2b) and after (Figures 2c and 2d) treatment with ESWL. The ADC value decreased from 2.17x10<sup>-3</sup> mm<sup>2</sup>/sn (Figure-2a) to 1.64x10<sup>-3</sup> mm<sup>2</sup>/sn (Figure-2c) in the treated kidney. Signal intensity of the treated kidney with b values of 1000 s/mm<sup>2</sup> increased from 27.0 s/mm<sup>2</sup> (Figure-2b) to 46.6 s/mm<sup>2</sup> (Figure-2d). The ADC values of the contralateral kidney are 2.16x10<sup>-3</sup> mm<sup>2</sup>/sn (Figure-2a) and 2.21x10<sup>-3</sup> mm<sup>2</sup>/sn (Figure-2c) before and after ESWL treatment, respectively. Signal intensities of the contralateral kidney with b values of 1000 s/mm<sup>2</sup> are 27.7 s/mm<sup>2</sup> (Figure-2b) and 30.7 s/mm<sup>2</sup> (Figure-2d) before and after ESWL treatment, respectively.**



cuous in the middle zone ( $p < 0.01$ ). The best discriminative parameter was signal intensity with a b value of 1000 (Figure-4).

In contralateral kidneys, minimum and maximum ADC values of renal parenchyma ranged from 1.98 to 2.47x10<sup>-3</sup> mm<sup>2</sup>/sn.

## DISCUSSION

ESWL has dominated the treatment of renal stone disease since its introduction in 1980. It

has been a major advance in Urology which is the fragmentation of stone by means of acoustic shock waves created by an extracorporeal source. It is non-invasive, effective and very well tolerated. The shock waves generated by ESWL cause fragmentation of renal calculi by exerting on the brittle calculi mechanical stresses sufficient to exceed the tensile strength of the stone (1-4). Although the focal point of the shock wave is centered on the renal stone, the waves must pass through the soft tissues of the back and the renal parenchyma-

**Table 1 - The RI values of treated kidneys before and after ESWL in certain regions.**

	RI		p
	Pre-ESWL	Post-ESWL	
	Mean±SD	Mean±SD	
Upper Pole	0.58±0.05	0.59±0.04	0.375
Middle Zone	0.58±0.05	0.59±0.04	0.204
Lower Pole	0.58±0.04	0.59±0.04	0.307

**Table 2 - The mean ADC values of ipsilateral kidneys with b-0, b-500 and b-1000 values before and after ESWL treatment.**

		Pre-ESWL		Post-ESWL		p
		Mean±SD		Mean±SD		
<b>Upper Pole</b>	b0	244.47±44.99	254.03±43.41	0.107		
	b500	67.37±7.01	72.15±13.98	0.075		
	b1000	26.87±5.84	31.18±11.55	0.014*		
	ADC	2.173±0.112	2.099±0.243	0.049*		
<b>Middle Zone</b>	b0	255.06±43.95	266.34±40.70	0.006**		
	b500	68.47±9.38	75.37±13.72	0.005**		
	b1000	27.15±5.81	33.40±11.60	0.001**		
	ADC	2.189±0.125	2.053±0.244	0.004**		
<b>Lower Pole</b>	b0	241.12±47.75	254.97±46.31	0.003**		
	b500	65.43±9.28	69.72±11.64	0.015*		
	b1000	25.56±6.95	30.56±11.26	0.012*		
	ADC	2.201±0.129	2.115±0.204	0.023*		

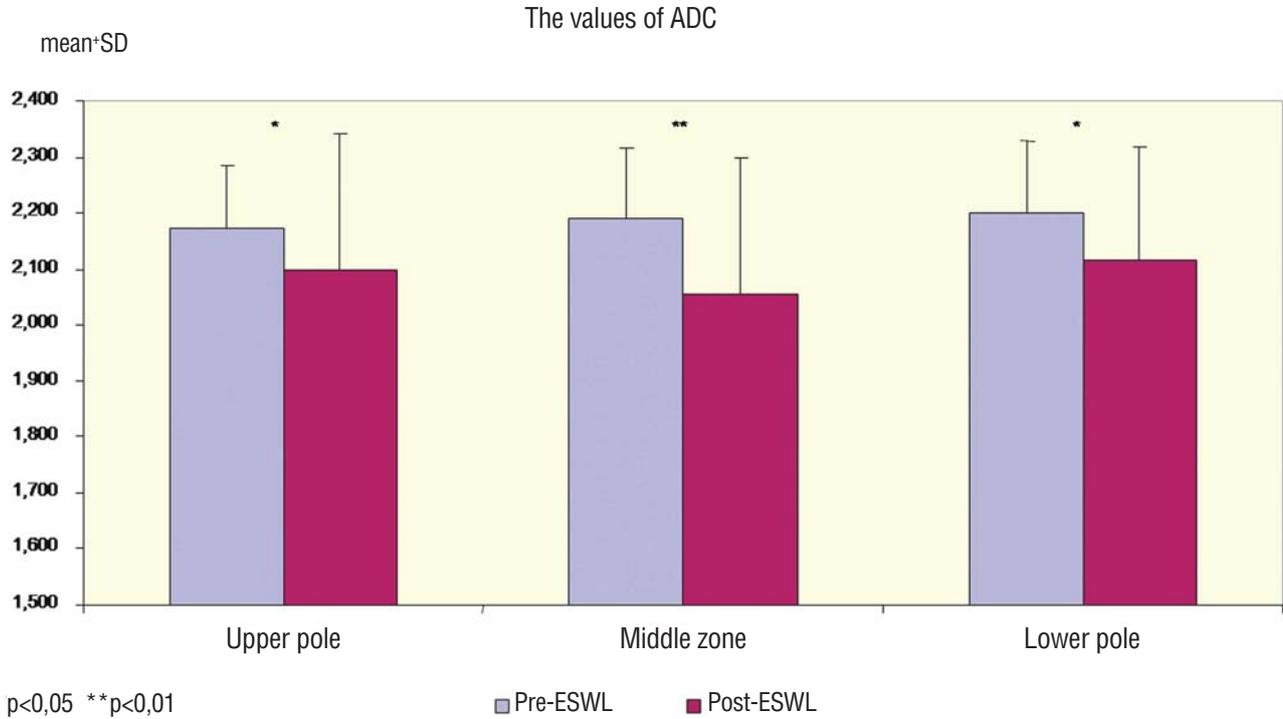
ADC ( $\times 10^{-3}$  mm<sup>2</sup>/sn)

\*p&lt;0.05; \*\*p&lt;0.01

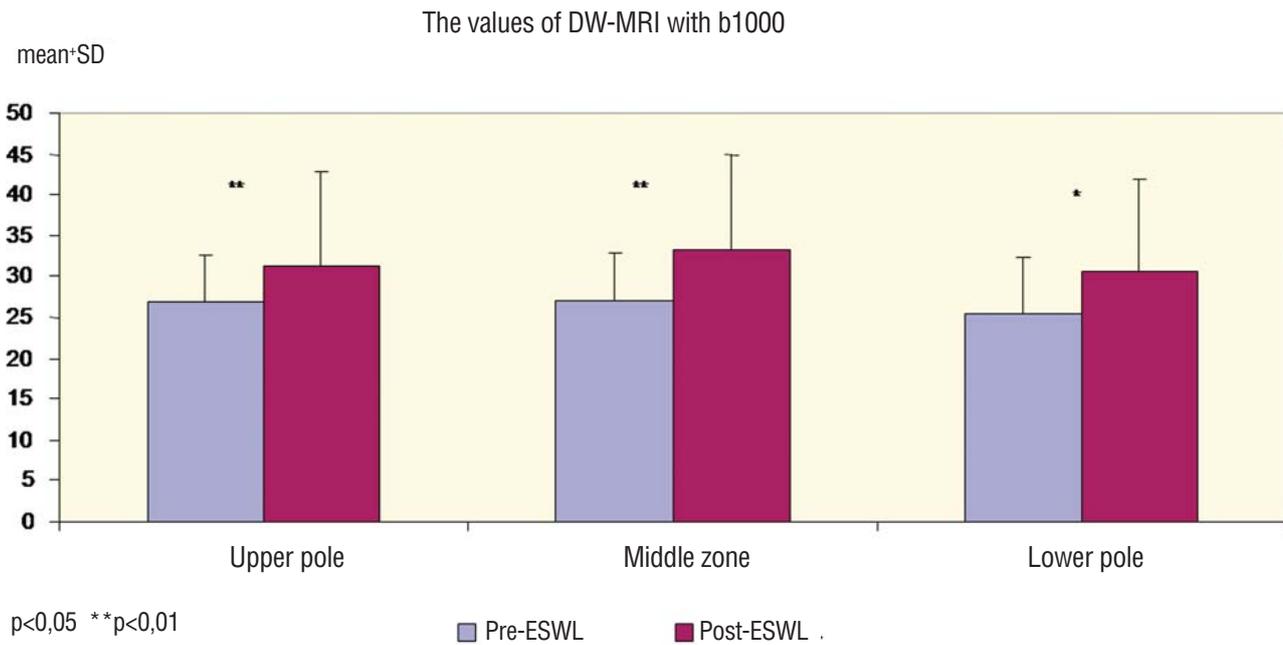
ma before reaching the calculus. Therein lies the potential for damage to these tissues. Kaude and co-workers (8) hypothesized that the spherical shock waves passing through the kidney during ESWL produce renal contusions. Lang et al. (9) have defined renal contusion as interstitial extravasation of small amounts of urine and blood and interstitial edema. However, the treatment with shock waves carries the risk of acute injury with the potential for long-term adverse effects (8-12). Many techniques have been used to show the effects of ESWL on the kidneys, such as US, CT, MRI, laboratory findings.

CDUS is an easy, effective, noninvasive method for evaluating changes of after ESWL therapy (5, 13-15). The RI measured by CDUS is a physiologic parameter reflecting the degree of renal vascular resistance and intrarenal edema and is elevated in diseases involving the tubulointerstitial or vascular system. Our study demonstrated no significant differences in the RI of treated kidneys before and after ESWL, as Beduk et al. (13) reported. Aoki et al. (14) showed that the RI of treated kidneys significantly increased at 30 minutes after ESWL. Janetschek et al. (15) found that

**Figure 3 - The mean ADC values before and after ESWL treatment in upper pole, middle zone and lower pole of treated kidneys.**



**Figure 4 - Signal intensities with b=1000 s/mm<sup>2</sup> before and after ESWL treatment in upper pole, middle zone and lower pole of treated kidneys.**



RI values in the treated region within 3 hours after ESWL were significantly higher in the group of patients aged >60 years.

Baumgartner et al. (10) showed the presence of abnormality in 74% of patients studied after ESWL by MR imaging. According to their results, MR imaging may be a very sensitive method to image these pathologic alterations occurring in the kidney.

The results of diffusion-weighted MRI in the kidney are still preliminary, and more research should be done (16). DWI provides information on perfusion and diffusion simultaneously in any organ; it can be used to differentiate normal and abnormal structures of tissues and it might help in the characterization of various abnormalities. Thus, calculating the ADC of low and high *b* values separately provides more specific information on kidney function (17). Thoeny et al. (18) showed the decrease in the ADC values of kidneys in patients with chronic renal failure and pyelonephritis. Chan et al. studied DWI to differentiate between hydronephrosis and pyonephrosis (7). Powers et al. (19) used a spin-echo diffusion-weighted sequence with respiratory triggering in dog kidneys, and found a drop in ADC in the unilateral renal artery stenosis that correlated with renal blood flow. Müller et al. (20) demonstrated that acute ureteral obstruction shows a quick decrease in ADC.

Researches have been processing about the long term side affects after ESWL. These possible adverse effects include a decrease in renal function, an increased rate of new stone formation and an increase in systemic blood pressure. Yokoyama and friends (21) have witnessed 1.5% of new initiative hypertension on normotensive patients after one year of ESWL. It is realized that retrospectively more than 8% of patients have suffered hypertension within the following two years (11). Uozumi et al. (22) determined a decrease of renal blood flow and delay of radionuclide urinary clearance in the affected kidney from ESWL.

In our study, renal changes after ESWL treatment were demonstrated with DWI in spite of a normal CDUS. After ESWL session, ipsilateral kidneys had statistically significant lower ADC values in all certain regions compared to contralateral kidneys. This condition can be explained by the decrease of renal blood flow or renal mi-

crocontusion arising from shock waves. ESWL centers routinely apply shock wave dosages in the range of 1500 to 2500 per treatment session. Since the possibility of an adverse effect of ESWL on the blood pressure and the lack of evidence that efficacy is enhanced by the utilization of such high doses of shock wave energy, such practices should be discouraged.

Our data suggest that DWI may be a very useful method for imaging pathologic alterations occurring in the kidney after ESWL therapy. Additionally, to our knowledge there has been no previous report relating the DWI findings in the kidneys treated by ESWL. One of the limitations of our study is that all images were obtained without any specific preparation of the patients such as fasting or drinking. However it's known that hydration has some effects on the ADC levels even though minimal.

## CONCLUSIONS

DWI is a valuable technique for detection of post-ESWL changes in the kidneys even while the Doppler US is normal. Further studies specifically investigating long-term effects are warranted.

## CONFLICT OF INTEREST

None declared.

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