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● *Original Contribution*

DIAGNOSING BLADDER OUTLET OBSTRUCTION USING NON-INVASIVE DECORRELATION-BASED ULTRASOUND IMAGING: A FEASIBILITY STUDY IN HEALTHY MALE VOLUNTEERS

Muhammad Arif,* Tim Idzenga,* Ron van Mastrigt,* and Chris L. de Korte†
*Department of Urology, Sector Furore, Erasmus Medical Centre, Rotterdam, The Netherlands; and †Medical UltraSound Imaging Center (MUSIC), Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

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Abstract—A feasibility study on the applicability of an ultrasound decorrelation method to urinary flow imaging was carried out in 20 healthy male volunteers, to provide a basis for a non-invasive approach to diagnose bladder outlet obstruction. Each volunteer voided five times in a flow meter in standing position. During each voiding, ultrasound radiofrequency frames were acquired transperineally at different flow rates. The results indicated that the decrease in correlation (decorrelation) of ultrasound radiofrequency signals had no unique relation with flow rate, but decreased distinctively with urinary flow velocity. In most of the healthy volunteers, the decorrelation was small because of the low flow velocity. However, because of the different flow velocities in volunteers, the variation in slope between volunteers was statistically significant. Therefore, it is probably possible to use the decorrelation method to differentiate between healthy persons and patients with obstruction. (E-mail: a.muhammad@erasmusmc.nl) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Decorrelation, Urinary bladder outlet obstruction, Ultrasound, Non-invasive diagnosis.**

INTRODUCTION

Bladder outlet obstruction (BOO) is a common urologic condition in elderly men. Lower urinary tract symptoms (LUTS), including post-void residual volume, low urinary flow rate and nocturia, are common symptoms of BOO. Urodynamic pressure–flow studies are accepted as the standard procedure to diagnose BOO (Griffiths et al. 1997). A major disadvantage of this method is that it involves urethral catheterization, which causes partial obstruction during micturition and may alter the diagnostic results. The invasive nature of the method also causes discomfort and pain to the patients and might result in infection. Therefore, the development of a non-invasive, but accurate urodynamic method of diagnosing BOO has been the goal of many urodynamic experts.

To develop such a clinical urodynamic method, we applied a non-invasive ultrasound (US) decorrelation-based technique to quantify flow velocity and turbulence in silica gel urethra models (Arif et al. 2014b, 2015). This technique estimates the decrease in correlation (decorrelation) between sequentially acquired US radiofrequency (RF) signals reflected by small scattering particles. In urine, various types of crystals such as calcium oxalate, uric acid and amorphous urates have been identified (Elliot and Rabinowitz 1980; Verdesca et al. 2011). These crystalline structures can act as small ultrasound scattering particles in urine. We reported that morning urine contains a sufficient concentration of these scattering materials and is suitable for US imaging of urinary flow using the decorrelation method (Arif et al. 2014a). The studies indicated that the decorrelation depends on the urine flow velocity and turbulence caused by urethral obstruction (Arif et al. 2014b, 2015). Decorrelation also increased with the degree of obstruction (Arif et al. 2015).

On this basis we hypothesized that it might be possible to develop a practical method for non-invasively estimating the degree of obstruction in male patients with lower tract symptoms. For a number of reasons it was necessary to test this hypothesis in healthy volunteers. First, it was not at all obvious if we could acquire images of the lower urinary tract of males during voiding of sufficient quality to enable decorrelation

Address correspondence to: Muhammad Arif, Dr. Molewaterplein 50, Room EE1630, Erasmus MC, 3015 GE Rotterdam, The Netherlands. E-mail: a.muhammad@erasmusmc.nl

analysis and how the tract should be approached, for example, rectally, abdominally or perennially. Second, for practical measurements in patients, it was necessary to develop a procedure and device to image the tract during voiding. Therefore a remote manipulator was developed and repeatedly tested to correctly aim the transducer during voiding. Ethically it would be unacceptable to develop and test this method in patients before a thorough evaluation in healthy volunteers. Additionally, baseline measurements in healthy subjects were required for interpretation of results in patients. In this article we report a study in healthy male volunteers on the applicability and reproducibility of a non-invasive US decorrelation method. For this purpose, we studied the variability in decorrelation values between and within healthy volunteers at maximal and submaximal flow rates and different flow velocities.

METHODS

Population

After institutional research ethics board approval (MEC-2013-419), we recruited 20 healthy male volunteers to void at least five times at normal desire. At recruitment, the volunteers gave their informed consent and were asked to complete an International Prostate Symptom Score (IPSS) form to quantify their urologic condition (Barry et al. 1992).

Experimental setup

The volunteers voided in a standing position with an ultrasound transducer placed gently against the perineum using a specially designed mechanical transducer manipulator (Fig. 1). To adequately visualize the urethra, the transducer was manually moved in angular and sidewise directions by the investigator using the vertical handle. The vertical position was adjusted by moving the junction C_1. To acquire US RF data of the urinary stream, a BK-Medical US system (Pro Focus UltraView 2202) with a custom-designed RF interface was used. The US system was equipped with a 5-MHz linear array transducer (8670), consisting of 128 transducer elements with a pitch of 0.3 mm. The acquired RF signals were stored on an external PC using a frame grabber (OR-X4 C0-SE-F00, Imago Group, Waalre, Netherlands). The RF data were acquired at a sampling frequency (f_s) of 20 MHz. The flow rate was measured with a rotating disk flow meter (Disa Electronic, Denmark) and stored on a PC using an analogue-to-digital (A/D) converter (PCI 6220, National Instruments, Woerden, The Netherlands) in combination with a custom-written LabView program (National Instruments, Woerden, Netherlands). During US data acquisition, a light-emitting diode on the frame grabber emitted light (flashes) at a frequency of 16 Hz. A photodetector was used to record this signal via the A/D converter and the LabView program to synchronize US data with the flow rate signal. The voided volume was measured at each voiding using a measuring jug.

Data acquisition

We acquired 50 ultrasound frames at the frame rate of 10 frames/s at maximum and sub-maximum flow rates during each voiding of each volunteer. Each US frame contained 10 sequential RF data sets (images). Every RF data set consisted of 144 RF signals acquired at a pulse repetition frequency (PRF) of 0.5 kHz. Each RF signal yielded a single image line in an image. The US frames were stored on an external PC and analyzed using custom-written MATLAB (The MathWorks, Natick, MA, USA) programs.

Data analysis

Correlation coefficients. In healthy volunteers, because of their low flow velocity, the decorrelation between sequential US signals was very small. Therefore, to adequately estimate the decorrelation we calculated the correlation coefficients (ρ) between the RF data sets at an interval longer than that used in our earlier measurements in urethra models (data set 1 with 5, data set 2 with 6, data set 3 with 7, *etc*.), instead of subsequent RF data sets (data set 1 with 2, data set 2 with 3, *etc*.). To do this, segments of data points from two RF lines representing a certain echo depth were taken, and the correlation coefficients between these segments were calculated. This was repeated for all image lines of the full data set, and a correlation coefficient distribution (correlation image) was constructed by using a color code for each correlation value (a detailed description of the correlation coefficient calculation has been given in Arif et al. [2014b]). For each US frame, from 10 ultrasound RF data sets, 6 correlation images were thus constructed. To calculate averages, a normal distribution of the correlation coefficients was obtained by applying the Fisher *Z*-transformation (Lupotti et al. 2002).

After transformation, we calculated the mean $\bar{z}$ in a region of interest (ROI) of length 1.8 cm selected in each correlation image downstream of the prostatic urethra and transformed it back to $\bar{\rho}$ by computing the inverse Fisher *Z*-transformation. Next we calculated the average (ρ_{avg}) of these $\bar{\rho}$ values over the six correlation images for each US frame.

As we acquired US frames at different flow rate values during a complete voiding cycle, we obtained (ρ_{avg}) values at each of these flow rates and flow velocities for each volunteer. The flow velocity v (cm/s) in the urethra corresponding to each measured flow rate Q_m (mL/s) value was calculated using the relation $v = Q_m/A$, where A (cm^2) = the cross-sectional area of the urethra, which