Ultrasound in Med. & Biol., Vol. 41, No. 4, pp. 1112–1118, 2015

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2014.10.014

● *Technical Note*

TRANSABDOMINAL CONTRAST-ENHANCED ULTRASOUND IMAGING OF THE PROSTATE

Massimo Mischi,* Libertario Demi,* Martijn Smeenge,† Maarten P. J. Kuenen,*† Arnoud W. Postema,† Jean J. M. C. H. de la Rosette,† and Hessel Wijkstra*†

*Electrical Engineering Department, Eindhoven University of Technology, Eindhoven, The Netherlands; and †Urology Department, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

(*Received* 30 *June* 2014; *revised* 22 *October* 2014; *in final form* 24 *October* 2014)

Abstract—Numerous age-related pathologies affect the prostate gland, the most menacing of which is prostate cancer (PCa). The diagnostic tools for prostate investigation are invasive, requiring biopsies when PCa is suspected. Novel dynamic contrast-enhanced ultrasound (DCE-US) imaging approaches have been proposed recently and appear promising for minimally invasive localization of PCa. Ultrasound imaging of the prostate is traditionally performed with a transrectal probe because the location of the prostate allows for high-resolution images using high-frequency transducers. However, DCE-US imaging requires lower frequencies to induce bubble resonance and, thus, improve contrast-to-tissue ratio. For this reason, in this study we investigate the feasibility of quantitative DCE-US imaging of the prostate via the abdomen. The study included 10 patients (age = 60.7 ± 5.7 y) referred for a needle biopsy study. After having given informed consent, patients underwent DCE-US with both transabdominal and transrectal probes. Time–intensity contrast curves were derived using both approaches and their model-fit quality was compared. Although further improvements are expected by optimization of the transabdominal settings, the results of transabdominal and transrectal DCE-US are closely comparable, confirming the feasibility of transabdominal DCE-US; transabdominal curve fitting revealed an average determination coefficient $r^2 = 0.91$ ($r^2 > 0.75$ for 78.6% of all prostate pixels) compared with $r^2 = 0.91$ ($r^2 > 0.75$ for 81.6% of all prostate pixels) by the transrectal approach. Replacing the transrectal approach with more acceptable transabdominal scanning for prostate investigation is feasible. This approach would improve patient comfort and represent a useful option for PCa localization and monitoring. (E-mail: M.mischi@tue.nl) **© 2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Prostate cancer, Contrast-enhanced ultrasound, Ultrasound contrast agents, Dilution curve, Transabdominal ultrasound, Transrectal ultrasound, Perfusion.**

INTRODUCTION

Prostate problems are a major age-related burden in men. Three in four men in their sixties present with lower urinary tract symptoms, which are often the result of benign prostate hyperplasia (Wei et al. 2008), but generate concerns for prostate cancer (PCa) and thus require special investigations (Brown et al. 2003). PCa is the cancer with the highest incidence in Western men (Siegel et al. 2014). Twenty-seven percent of all new malignancies diagnosed in men in 2014 in the United States are expected to be prostate cancer (Siegel et al. 2014). Standard PCa diagnosis comprises digital rectal examination, assessment of serum prostate-specific antigen levels and transrectal ultrasound (TRUS) imaging. All have serious limitations: digital rectal examination is subjective and assesses only a part of the gland (the posterior part), whereas the prostate-specific antigen test is not disease specific, producing about two in three false-positive results (Draisma et al. 2003; Schröder et al. 2009). Ultrasound is the most used clinical instrument for pre- and peri-operative visualization of the prostate gland. It permits estimation of the prostate volume, as well as guidance for systematic biopsies. In addition, gray-scale and Doppler imaging may provide diagnostic information on intraprostatic abnormalities, although its poor sensitivity and specificity make this approach unreliable (Aarnink et al. 1998; Sedelaar et al. 2001).

Because of the relatively small size of the prostate and its proximity to the rectal wall, prostate imaging is

Address correspondence to: Massimo Mischi, Electrical Engineering Department, Eindhoven University of Technology, Room PT 3.02, P.O. Box 513, 5600 MB Eindhoven, The Netherlands. E-mail: M.mischi@tue.nl

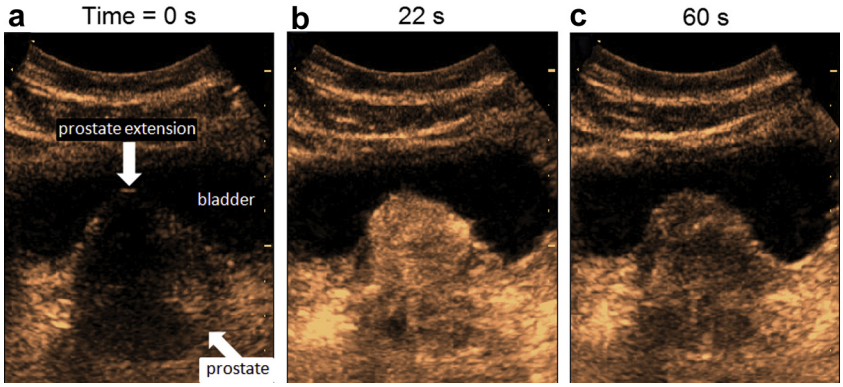

Fig. 1. Three selected frames from the transabdominal dynamic contrast-enhanced ultrasound scan (a) before ultrasound contrast agent wash-in, (b) at peak concentration and (c) during washout, revealing a hypervascularized prostate extension toward the bladder. The bladder, prostate and a prostate extension into the bladder are indicated in (a).

conventionally performed with a transrectal probe that allows use of high-frequency ultrasound (typically >8 MHz) to provide high-resolution images. The quality of the images justifies the patient's discomfort caused by transrectal access.

More recently, the potential of advanced imaging methods, including elastography and dynamic contrast-enhanced ultrasound (DCE-US) imaging, to improve detection and localization of PCa has been reported (Salomon et al. 2008; Wink et al. 2008). Elastography estimates tissue stiffness as a marker for increased cellular density and, therefore, cancer (Salomon et al. 2008). DCE-US can detect signals from the microvasculature and serves as a marker for neoangiogenesis and tumor progression (Halpern et al. 2001; Russo et al. 2012). This relates to the diameter of the microbubbles used as ultrasound contrast agents (UCAs); they are gas microbubbles with a size comparable to that of red blood cells (Schneider 1999) and can therefore flow through the smallest microvessels. A large retrospective study reported that UCAs are tolerable for non-cardiac applications (Piscaglia et al. 2006).

Several methods have been proposed for detection of changes in the microvascular architecture based on the assessment of tissue perfusion by analysis of the time evolution (wash-in and wash-out) of the UCA concentration (Russo et al. 2012). To this end, specific (empirical) features are estimated from UCA time–intensity curves (TICs) measured after a peripheral intravenous injection of an UCA bolus (Eckersley et al. 2002). Typical features extracted are the mean transit time, wash-in rate and area under the curve. More recently, some authors have proposed UCA dispersion as a better marker than perfusion for detection of angiogenic changes in the microvascular architecture (Kuenen et al. 2011). The results obtained in the prostate are promising and have motivated the development of improved algorithms for dispersion analysis (Kuenen et al. 2013b; Mischi et al. 2012).

Driven by established clinical practice and the common thought that a transrectal approach leads to improved spatial resolution, DCE-US has always been performed by TRUS, but this overlooks essential technical aspects of the imaging system. In particular, DCE-US is performed with contrast-specific imaging using dedicated pulse schemes that improve microbubble detectability by suppressing tissue echoes and thus increasing the contrast-to-tissue ratio (Frinking et al. 2000). Commonly used solutions for contrast-specific imaging modes aim at enhancing the non-linear signals produced by UCAs compared with the linear signals produced by tissue (Frinking et al. 2000).

An important feature common to all these methods relates to the chosen ultrasound frequency; to achieve strong contrast signals, the ultrasound frequency should be close to the resonance frequency of the microbubbles used. According to microbubble simulations and dedicated measurements, the resonance frequency of commercially available UCAs is ≤3 MHz (Fillon 2013; Gorce et al. 2000; Schneider 1999). Therefore, when TRUS is used, the high US frequencies that are allowed by the small imaging depth (low attenuation) are lowered to values that are close to the microbubble resonance frequency. This permits achievement of efficient contrast enhancement at the cost of a lower spatial resolution.

In the work described here we evaluated for the first time the feasibility of DCE-US imaging of the prostate via the abdomen, using lower frequencies that are close to the microbubble's resonance and permit achievement of the required, greater depth. To this end, the quality of TICs acquired by transabdominal scanning is evaluated and compared with that of TICs acquired by a transrectal probe. The transabdominal approach avoids patient discomfort and simplifies clinical practice.