Contrast-enhanced Ultrasound in Prostate Cancer

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Prostate cancer is the most commonly diagnosed malignancy in men. Greyscale ultrasound (US)-guided systematic biopsy is the standard of care for prostate cancer detection in men with elevated prostate serum antigen (PSA) or an abnormal digital rectal examination (DRE).

Previous reports have demonstrated that contrast-enhanced US (CEUS) investigations of the blood flow of the prostate allow for prostate cancer visualisation and therefore for targeted biopsies. Comparisons between systematic and CEUS-targeted biopsies have shown that the targeted approach detects more cancers with a lower number of biopsy cores. CEUS has also been shown to detect cancers with higher Gleason scores compared with the systematic approach, which seems to improve prostate cancer grading. This article will discuss the value of CEUS in the imaging of prostate cancer.

Newly developed US contrast agents enable improved detection of low-volume blood flow by increasing the signal-to-noise ratio. Therefore, US contrast agents allow for a more complete delineation of the neovascular anatomy by enhancing the signal strength from small vessels (i.e. neovessels). Furthermore, these agents can be used to time the transit of an injected bolus. Unlike radiographic contrast media, which diffuse into the tissue and may obscure smaller vessels, microbubble echo-enhancing agents are confined to the vascular lumen, where they persist until they dissolve. US contrast agents are made of gas bubbles small enough to cross through capillary beds. They have two main important acoustic properties: first, they are many times more reflective than blood, thus improving flow detection; and second, their vibrations generate higher harmonics to a much greater degree than surrounding tissues. The half-life of contrast agents is dependent on bubble construction. Bubbles can be free or encapsulated in soft or hard shells. The duration of enhancement after injection may last from a few seconds to many minutes, depending on the bubble type.

Bree et al. demonstrated the potential use of contrast-enhanced colour Doppler to enhance the diagnostic yield in a group of 17 patients with normal greyscale transrectal US and elevated PSA values. Correlation of biopsy sites with colour Doppler US abnormalities revealed a sensitivity of 54%, a specificity of 78%, a positive predictive value (PPV) of 61% and a negative predictive value (NPV) of 72% for the detection of prostate cancer. Three of the cases with a positive contrast-enhanced biopsy site had negative transrectal US random biopsy within the previous year.

Frauscher et al. examined the use of contrast-enhanced colour Doppler US in 72 patients identified by PSA screening in a previous study. Using a quantitative scale to characterise the degree of vascularity, the technique had a sensitivity of 53%, specificity of 72% and PPV of 70% in distinguishing prostate cancer from benign lesion.

Previous studies reported the value of contrast-enhanced colour Doppler in a prospective study in 230 and 380 male screening volunteers, and found that targeted biopsies based on contrast-enhanced colour Doppler detected as many cancers as systematic biopsies, with less than half the number of biopsy cores.

Bogers et al. evaluated contrast-enhanced 3D transrectal ultrasound imaging of the prostate vasculature with power Doppler. 3D power Doppler images were obtained before and after intravenous (IV) administration of 2.5g Levovist™ (Schering, Berlin). Subsequently, random and/or directed transrectal US (TRUS)-guided biopsies were performed. Prostate vasculature was judged with respect to symmetry and vessel distribution. Eighteen patients with a suspicion of prostate cancer because of either an elevated PSA (greater than 4.0ng/ml); Tandem-R-assay) or an abnormal DRE were included in the study. Prostate cancer was detected in 13 patients. Vascular anatomy was judged abnormal in unenhanced images in six cases, of which five proved malignant. Enhanced images were considered suspicious for malignancy in 12 cases, including one benign and 11 malignant biopsy results. Sensitivity of enhanced images was 85% (specificity 80%) compared with 38% for unenhanced images (specificity 80%) and 77% for conventional greyscale TRUS (specificity 60%). Among six patients who showed no B-mode abnormalities, vascular patterns were judged abnormal in four cases, of which three were malignant. Based on these findings they concluded that contrast-enhanced 3D power Doppler angiography is feasible in patients with suspicion of prostate cancer who are scheduled for prostate biopsies.

Further analyses by the same group suggested that 3D contrast-enhanced power Doppler US is a better diagnostic tool than the DRE, PSA level, greyscale US or power Doppler US alone. The most suitable
The current standard of care for prostate cancer detection – the systematic biopsy – may be replaced by a contrast-enhanced ultrasound targeted approach in the future.

In summary, the detection of prostate cancer with CEUS may be improved relative to baseline TRUS. However, based on the relatively small number of published studies, substantial uncertainty remains in the interpretation of contrast-enhanced TRUS images. In one study, 16% (59 of 360) of contrast-enhanced TRUS images were rated as indeterminate with respect to vascular enhancement. Future studies of contrast-enhanced TRUS should investigate new techniques to optimise the signal from contrast agents in the prostate, and to maximise the difference in signal between benign and malignant tissues. Halpern et al. reported greater enhancement with intermittent imaging and bolus administration of contrast. New imaging techniques may be developed to reduce bubble destruction during imaging. Since the prostate is generally evaluated with a frequency in the range of 5–7.5MHz, newer bubble agents that resonate at higher frequencies may provide a better signal. Alternatively, harmonic imaging at lower frequencies or with subharmonics may be useful with current contrast agents. With these new developments, prostate cancer detection may be significantly improved by the use of CEUS, and the current standard of care for prostate cancer detection – the systematic biopsy – may be replaced by a CEUS targeted approach in the future.

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