

PP-10**Detection of prostate cancer by contrast-ultrasound dispersion imaging****M. Kuenen¹, T. Saidov¹, C. Heneweer², H. Wijkstra³, J. de la Rosette³, M. Mischi¹**¹ *Eindhoven University of Technology, Eindhoven, Netherlands*² *University Hospital Schleswig-Holstein, Kiel, Germany*³ *Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands*

Despite the development of several efficient focal therapies for prostate cancer, treatment options are often restricted to radical treatments, such as a radical prostatectomy. One of the main obstacles preventing a wider application of focal therapies is the lack of reliable imaging methods for prostate cancer. Contrast-ultrasound dispersion imaging (CUDI) is a recently introduced method for detection and localization of prostate cancer, based on dynamic contrast-enhanced ultrasound (DCE-US) imaging. CUDI aims at localizing prostate cancer by detection of angiogenesis, i.e., the development of a chaotic dense microvascular network that has a proven correlation with prostate cancer aggressiveness. Key features of the microvascular structure, such as microvascular density and tortuosity, are characterized by the dispersion of ultrasound contrast agents (microbubbles) through the microcirculation. A twofold validation of CUDI is performed. The ability of CUDI to differentiate between different microvascular structures is evaluated in an animal study using two xenograft models of human prostate cancer that feature different microvascular structures. Furthermore, a preliminary clinical validation is performed to evaluate the value of CUDI for prostate cancer localization in humans. In the animal study, seven mice were injected with cancer cells at the University Hospital Schleswig-Holstein (Kiel, Germany). The adopted cell lines were DU-145 (four mice) and PC-3 (three mice). In each mouse, a 0.1 mL MicroMarker Non-Targeted Contrast Agent Kit (VisualSonics Inc., Toronto, Canada) bolus was injected. DCE-US imaging was performed with a Vevo 2100 imaging system (VisualSonics Inc.). Data acquisition in humans was performed at the AMC University Hospital (Amsterdam, The Netherlands) with an iU22 imaging system (Philips Healthcare, Bothell, WA) after injection of a 2.4 mL SonoVue® (Bracco, Milan, Italy) bolus. In both studies, CUDI analysis was performed based on time-intensity curves that are obtained at each image pixel. Dispersion is estimated by assessment of the local shape similarity between these curves. This analysis results in a parametric dispersion map that highlights angiogenic regions by an increased level of dispersion. The validation in mice was performed by comparing CUDI results with the microvascular density, estimated by tomato-lectin-FITC (Vector Labs) staining. In humans, the resulting dispersion maps from 12 DCE-US recordings obtained from 8 patients were compared with the histology ground truth, obtained after radical prostatectomy. In the animal study, CUDI analysis revealed a significant difference ($p < 0.01$) between the spatial distributions of the microvascular structure in the two cancer lines. In agreement with the histology, the DU-145 xenografts all showed a hypervascular core of the tumor as compared to the periphery, whereas the PC-3 xenografts showed a more homogeneous distribution throughout the tumor. In the preliminary clinical validation, the obtained ROC curve area for pixel classification by CUDI (0.89) was superior to that of all other DCE-US perfusion maps, such as mean transit time, peak intensity, and area under the time-intensity curve. The encouraging results in both the animal study and human study motivate towards a more extensive validation of CUDI for prostate cancer localization. In the future, CUDI may provide support for targeting of biopsies and focal therapies.