On the relation between contrast-ultrasound kinetic features and microvascular density by acoustic angiography

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Anastasiia Panfilova[1], Sarah Shelton[2], Ruud JG van Sloun[1], Cristina Caresio[4], Hessel Wijkstra[1,3], Paul Dayton[4], Massimo Mischi[1]
1 Eindhoven University of Technology, Electrical Engineering Dept, Signal Processing Systems Group
2 University of North Carolina at Chapel Hill, USA
3 Academic Medical Center, University of Amsterdam, Urology Dept
4. Polytechnic University of Turin, Italy

Introduction

Cancer growth is supported by angiogenesis. Newly formed tumor vasculature is characterized by a set of abnormalities, exhibiting irregular branching patterns, prevalence of shunts, and elevated tortuosity of vascular segments. This leads to altered blood flow dynamics which can be recognized with dynamic contrast enhanced ultrasound (DCE-US). Typically, two types of parameters are extracted with DCE-US following an intravenous injection of ultrasound contrast agent, quantifying either perfusion or dispersion. In this work, we investigate whether these parameters reflect the underlying microvascular density (MVD), extracted with acoustic angiography (AA). AA is a high resolution technique, requiring a constant infusion of contrast agent, and receiving at a central frequency of 30 MHz. It enables vessel delineation and vascular characterization.

Methods

Fibrosarcoma tumors were implanted in the flanks of 3 rats (Fischer 344). A longitudinal study has been performed, imaging the tumors and the control regions on the contralateral flank with 2D DCE-US and 3D AA. Imaging was initialized 8 days after implantation, with subsequent acquisitions every 3 days, amounting to 4 time points. The longitudinal trends of the DCE-US and AA parameters were evaluated and compared, with the objective of identifying similar trends. Besides this, a tool was developed, helping to identify the DCE-US plane in AA volumes. A skeletonization algorithm was applied to the identified slice in the AA volume and the derived MVD distribution was compared with the corresponding WIR and correlation coefficient maps.

Results and conclusions

MVD and WIR exhibit a similar trend in time, peaking for the youngest tumors, and gradually decreasing as they grow. Moreover, a significant Pearson correlation of 0.86 ($p<0.001$) has been identified between the median WIR of the tumors and their MVD. From the spatial maps we noticed that regions of high WIR highlight large vessels or areas of elevated MVD (Fig.1), giving further confidence to the conclusion that WIR and MVD are related. As for the correlation coefficient, it shows an overall better cancer classification than WIR. Despite this result, no link between MVD and the correlation coefficient was found in this work. We hypothesize that the correlation coefficient reflects properties of smaller vessels (<100-200μ), not visible with AA. In line with this, is the observation that WIR and correlation coefficient maps are complementary (Fig.1) and convey different types of information.

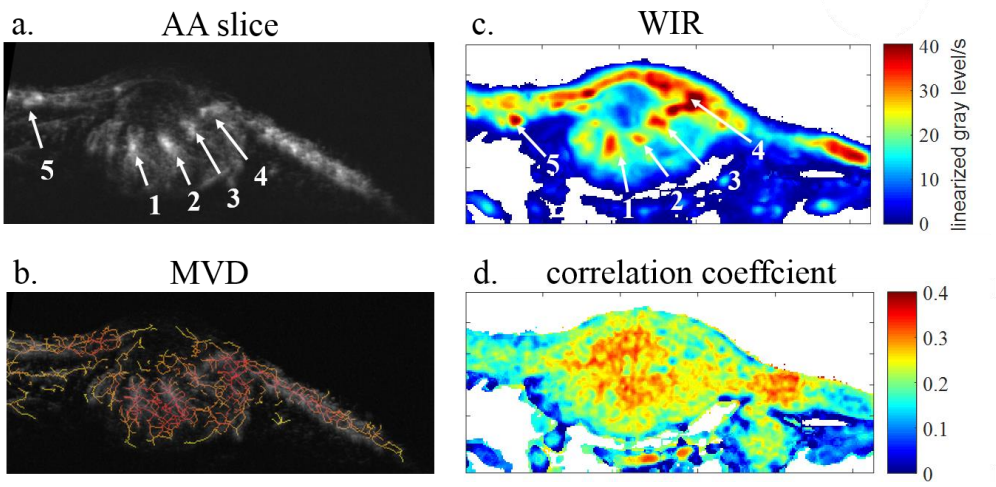

Figure 1. a: Selected AA slice. b: vascular skeleton, color-coded according to the values of vascular density (yellow indicates low values, while red indicates high values. c-d: wash-in-rate and correlation coefficient color maps, respectively. Regions with power below -22 dBs of the maximum intensity are in white. The numbers in a. and c. illustrate the vessels identified in wash-in rate maps, used as markers to locate the right plane in AA volumes.