Using a murine metastatic liver model to investigate the relationship between shear wave speed and survival during chemotherapy

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Background, Motivation and Objective

Gemcitabine is a standard drug used to treat patients with locally advanced or metastatic pancreatic cancer. Researchers have demonstrated a strong correlation between low tissue pressure and patient survival in many cancers[1], but this has never been demonstrated for pancreatic cancers with liver metastasis. Although tissue pressure is difficult to measure with current *in vivo* techniques, we have previously[2] demonstrated that shear modulus is good a surrogate. In this work, we used a metastatic liver murine model and plane wave single track location shear wave elasticity imaging[3] (pSTL-SWEI) to investigate the relationship between shear wave speed (SWS) and survival of rodents undergoing chemotherapy (Gemcitabine).

Statement of Contribution/Methods

Injecting KCKO-luc cells into the hemispleen produced liver metastases in mice (n = 22), which we divided into two groups: untreated and treated by Gemcitabine. Mice were imaged under anesthesia with pSTL-SWEI and optical bioluminescence imaging (BLI) two times per week for seven weeks. For pSTL-SWEI, which we implemented on a Vantage 256 scanner with L11-5v probe (10 MHz), a total of 41 laterally-spaced push beams, each with four rapid multi-focal zones, were transmitted followed by compounded plane wave tracking. To suppress respiration motion, we implemented a novel automated gating using real-time cross-correlation of plane wave images achieving one push-detect ensemble per respiration beat.

Results/Discussion

Fig A and B show the SWS and BLI maps of a mouse liver at two time points, respectively. Fig C shows the survival curve of 22 mice. Fig D shows the longitudinal stiffness and BLI measurements in one mouse. Liver stiffness was consistently high (>3 m/s) before demise. Scatterplots of data (12 mice at 14 timepoints) shows (Fig E) that SWEI and BLI measurements have a good (R^2=0.39) correlation. The correlation, however, is stronger (R^2=0.54) in more established tumors (Fig F) indicating that SWEI measurements are more sensitive to macro-scale structural changes than cell growth.

References:
[1] Haider, M. A. *et al.*, *Int J Radiat Oncol*, **62**, (2005).
[2] Wang, H. *et al.*, *Ultrasound Med. Biol.*, **43**, (2017).
[3] Ahmed, R. *et al.*, *IEEE UFFC*, **65**, (2018).