

Perilesional region detection in pancreatic adenocarcinoma (PDA) tumors using Harmonic Motion Elastography (HME)

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Background, Motivation, and Objective

Accurate assessment of regression occurrence of pancreatic ductal adenocarcinoma (PDA) tumors before tumor volume changes, and reliable delineation of tumor margins are essential in PDA patients with typically dismal prospect upon diagnosis (Kluger et al. *J. Gastro. Surg.* 2018).

Methods

Harmonic motion elastography (HME) is based on a harmonic motion at 50 Hz frequency generating by an amplitude modulated (AM) focused ultrasound (FUS) beam, while a confocally aligned imaging transducer records the channel data at the sampling rate of 1000 Hz. To estimate the resulting displacement, 1-D cross correlation is applied on the reconstructed RF data and the shear waves are filtered using a 2D directional filter for left to right wave extraction. In order to generate a 2D Young's modulus (E) map, the speed of shear wave propagation in the lateral direction at a known distance of 8 wavelengths is measured using 1D cross correlation. The resulting shear wave speed, C_s is used to estimate E, $E=3\rho C_s^2$ in which, $\rho=1000 \text{ kg/m}^3$.

In the non-invasive, *in vivo* study, we used 32 post-surgical human pancreatic specimens with (n = 14) and without chemo-radio therapy history (n=18), in which three different (tumor, perilesional, and non-cancerous) regions within each specimen were delineated using HME. A quantitative microscopic staining method (Picrosirius red) was used as a validation method in a subset of specimens. PSR stains for collagen I and II found to be elevated in PDA (Rice A. et al. *Oncogenesis* 2017, 6 (7)).

Results and Conclusion

Figure 1 shows two examples of specimens, one with and one without chemo-radio therapy history in Figs.1A and 1B, respectively. The measured stiffness by HME shows that the tumor region has the highest stiffness value, $E > 40 \text{ kPa}$, while the normal region has the lowest one, $E < 10 \text{ kPa}$ and the perilesional region exhibits intermediate values, $10\text{kPa} < E < 30 \text{ kPa}$. E and PSR are found to be highly correlated in all three regions. Finally, no significant stiffness difference was found

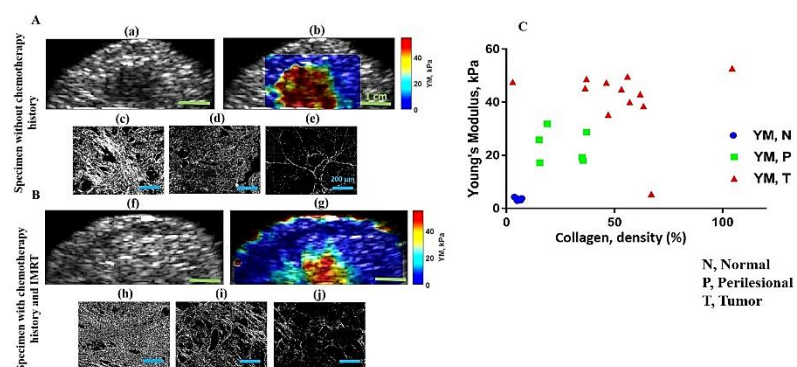


Figure 3. (A) Post-surgical pancreatic human specimens with no chemotherapy history. (a) B-mode image of PDA tumor and its surrounding tissue. (b) 2D Young's modulus map overlaid on B-mode image. The estimated median Young's modulus for tumor part, red/orange/yellow part is (YM = 44.9 kPa). The estimated median Young's modulus for perilesional part, light blue part, is (YM = 19.2 kPa). The estimated median Young's modulus for normal part, dark blue part is (YM = 3.8 kPa). (c) Picrosirius red slide of PDA tumor part with 20x magnification (PSR, density = 53.2 %). (d) Picrosirius red slide of perilesional part of PDA tumor surrounding with 20x magnification (PSR, density = 35 %). (e) Picrosirius red slide of normal part of PDA tumor surrounding with 20x magnification (PSR, density = 4.6 %). (B) Post-surgical pancreatic human specimen with chemotherapeutic history. Chemo-radiation (Gemcitabine /Abraxane, 3 months, accompany with oral Chemo (IMRT over around 28 fractions 50.4 Gy)). (f) B-mode image of PDA and its surrounding tissue. (g) 2D Young's modulus map overlaid on B-mode image. The estimated median Young's modulus for tumor part, red/orange/yellow part, is (YM = 40 kPa). The estimated median Young's modulus for perilesional part of PDA tumor surrounding, light blue area, is (YM = 17.2 kPa). The estimated median Young's modulus for normal part of PDA tumor surrounding, dark blue, is (YM = 2.9 kPa). (h) Picrosirius red slide of PDA tumor part with 20 x magnification (PSR, density = 57 %). (i) Picrosirius red slide of perilesional part of PDA tumor surrounding with 20x magnification (PSR, density = 23.6 %). (j) Picrosirius red slide of normal part of PDA tumor surrounding with 20x magnification (PSR, density = 5 %). (C) Estimated median Young's modulus values vs. PSR density (%) using Picrosirius red staining of post-surgical human specimens. The number of T: tumor samples using PSR analysis is n = 11 with mean and standard deviation of (51.4 ± 23.3) %, for perilesional samples, P, using PSR analysis, n = 6 with mean and standard deviation of (26.1 ± 9.8) %, and the number of none-neo plastic or normal samples, N, using PSR on them, n = 7 with mean and standard deviation (5.3 ± 1.1).

between the specimens that received chemo-radio therapy versus those that did not potentially in line with the shortcomings associated with clinical treatment of PDA tumors.