

Assessment of the pancreatic shear stiffness in healthy volunteers with MR Elastography

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Target audience: Physicians, scientists, and physicists interested in performing Magnetic resonance elastography (MRE) of the pancreas.

Purpose: The pancreas is a unique organ with complex anatomy and physiology which sits deep in the retroperitoneum. Histologically, chronic pancreatitis (CP) is associated with periductular fibrosis and acinar destruction with inflammatory cells [1]. Pancreatic ductal adenocarcinoma, or PDAC, which is by far the most common type of pancreatic malignancy is characterized by the presence of ‘desmoplasia’, a process in which fibrous tissue infiltrates and envelops neoplasms [2]. Conventional cross-sectional abdominal imaging has proven to be unreliable for detecting the early-stage of both CP and PDAC [1, 2, 3]. MRE is a phase-contrast MRI technique for measuring the stiffness of biological tissues in vivo by analyzing shear wave propagation in soft tissues. MRE has been shown to accurately assess hepatic fibrosis in patients with chronic liver diseases [4]. Moreover, inflammation has also been shown to elevate stiffness values [5]. Theoretically, both CP and PDAC with histological fibrotic tissue and inflammatory changes might have higher stiffness than normal pancreas. Hence, the goal of this study was to 1) assess the feasibility of 3D EPI MRE using a soft passive driver delivering low-frequency (40-, 60-Hz) vibrations; 2) compile normative values for the shear stiffness of the tail, body, neck, head and uncinate of the normal pancreas; and 3) evaluate the inter-rater agreement of the stiffness measurements of the pancreas.

Methods: Eighteen healthy volunteers (9 men, 9 women) with no history of personal or familial pancreatic disease were enrolled in the study. The study was approved by our Institutional Review Board with written informed consent obtained from all volunteers. The mean age was (33.56 ± 7.03) years [range: (23-48) years], and mean BMI was (22.76 ± 3.06) kg/m² [range (18.25-42.16) kg/m²]. All examinations were performed on a 1.5T MR Scanner (HDx, GE Healthcare, Milwaukee, WI, USA) with an 8-channel, phased-array torso coil. Low-amplitude mechanical waves at 40 Hz and 60 Hz were generated in the upper abdomen using an active acoustic generator. An ergonomic soft pancreatic driver (14 cm×19 cm×2cm) was designed as a pillow-like mechanical transducer which conformed to the abdomen. It was centered at the epigastrium, close to the pancreas and secured by a 20-cm wide elastic band wrapped around the abdomen (Fig.1). The propagating shear waves were imaged with a 3D EPI pulse sequence with the inclusion of motion-encoding gradients (MEGs) in 3 directions (Fig.1, 40 Hz). The imaging parameters were: TR/TE = 1875/39.6 ms (40 Hz), 2084/39.4 ms (60 Hz); phase offsets = 3; FOV = 38.4 cm; acquisition matrix = 96×96; number of signal averages = 1; frequency-encoding direction = RL; parallel imaging acceleration factor = 3; number of slices = 50; slice thickness = 3 mm. The acquisitions were performed at the end of expiration. The acquisition time for each frequency was split into six periods of suspended respiration of 15 seconds. The elastogram was calculated using a 3D DI (direct inversion) algorithm with twenty evenly spaced 3D directional filters and was used for measuring pancreatic stiffness. At least one flexible ROI was drawn on each main part of the pancreas separately by two raters (5 main pancreatic parts: the tail, body, neck, head and uncinate process), as shown in Fig. 2 (40 Hz).

Results: The intraclass correlation coefficient (ICC) for inter-rater measurement agreement for the 40-Hz data was 0.90 (95% confidence interval [CI]: 0.85-0.93), better than that at 60 Hz (0.84, 95%CI, 0.76-0.89). Bland-Altman analysis showed that the mean bias for the two raters was 0.7% (95% limits of agreement: -13.2%~14.6%) at 40 Hz and 0.0% (95% limits of agreement: -18.6%~18.6%) at 60 Hz. Compared with the surrounding retroperitoneal fat, the elastograms delineated the pancreas more clearly due to better shear wave penetration at 40 Hz than 60 Hz, especially for obese subjects with higher BMI (e.g., Fig. 3). The mean shear stiffness of the pancreas tail, body, neck, head and uncinate were lower at 40 Hz; (1.21 ± 0.12) , (1.18 ± 0.15) , (1.02 ± 0.18) , (1.14 ± 0.18) , (1.18 ± 0.17) , and (1.15 ± 0.17) kPa, respectively; compared with (2.15 ± 0.21) , (2.18 ± 0.31) , (1.93 ± 0.33) , (2.02 ± 0.43) , and (2.09 ± 0.32) kPa at 60 Hz. Likewise, the coefficients of variation (CV) for the main pancreatic parts were also lower at 40 Hz (mean:13.2%) than at 60Hz (mean:18.0%) (Fig. 4). The shear stiffness for each individual subject and

each pancreatic part was consistent among the subjects (approximately 1.0-1.5 kPa at 40 Hz and 1.5-2.5 kPa at 60 Hz).

Discussion: This study showed that pancreatic MRE using 3D-EPI MRE is feasible in healthy volunteers at low frequencies. The data from each main part of the pancreas was consistent among the volunteers, corresponding to the histological homogeneity of the pancreas. The pancreas is a narrow and tortuous organ, snaking behind the stomach and is inclined to be compressed by a full stomach; hence a fasted state is strongly recommended. Due to the geometric complexity of the pancreas, 3D imaging using an EPI acquisition with a 3D inversion was used to produce a more accurate measurement with a relatively short acquisition time [6]. Using 40-Hz vibrations might be more suitable for pancreatic MRE than 60-Hz motion based on the lower CV and higher ICC for inter-rater agreements, due to better shear wave penetration. The pancreas stiffness at 60 Hz was similar or a little lower than the reported liver stiffness at 60 Hz [4, 5], and approximately 1kPa higher than at 40 Hz. For obese subjects, the waves are less likely to penetrate through the whole pancreas, especially at 60 Hz, causing noise biases and false stiffness estimates. The normal pancreatic gland is often very soft, and both CP and PDAC can cause fibrosis and inflammation which might increase the stiffness significantly. So MRE could be useful for early detecting and monitoring of CP and PDAC. Our results provide robust data that will enable future investigations of this technique as a clinical tool.

Conclusions: 3D EPI pancreatic MRE at 40 Hz can provide promising and reproducible stiffness measurements throughout the pancreas.

References: [1]. Chari ST. *J Gastroenterol*, 2007.42 Suppl 17:p.58-9. [2]. Bachem MG, et al. *Gastroenterology*, 2001.128(4): p.907-21. [3]. Coté GA, et al. *Gastroenterology*, 2013.144(6):p.1262-71.e1. [4]. Venkatesh SK, et al. *JMRI*. 2013. 37(3):p.544-55. [5]. Wang Y, et al. *AJR*. 2011.196(3):p.553-61. [6]. M. Yin, *ISMRM* 2627, . 2008.

