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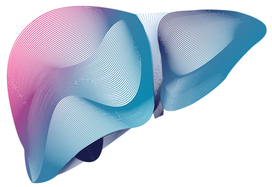

Thermoacoustic assessment of fatty liver disease - an early clinical feasibility study

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Introduction

Thermoacoustics (TA) is a non-invasive, non-ionizing, molecular-sensitive imaging technology based on the absorption of radio frequency waves combined with low cost ultrasound. Unlike purely ultrasonic approaches (such as backscatter and attenuation) that are sensitive to changes in the speed of sound, and tissue density, that may be confounded by fibrosis, **TA signals are similar to Magnetic Resonance Proton Density Fat Fraction (MRI-PDFF)** as they both represent stoichiometric mixing of adipose and lean tissue and thus provide a high diagnostic value.

Aim

The Thermo-Acoustic Enhanced Ultrasound (TAEUS) Fatty Liver Imaging Probe (FLIP) is a hand-held, point-of-care system that quantitatively assesses liver fat content. This work describes an early clinical feasibility study with TAEUS-FLIP and a comparison to MRI-PDFF for demonstrating the potential of TA for assessing fatty liver disease.

Method

16 subjects with suspected Non-Alcoholic Fatty Liver Disease (NAFLD) were scanned at Rocky Vista University (Ivins, UT), Ultrasound Research medical center, USA. For each subject after fasting 6-8 hours, an anatomic B-mode ultrasound scan was obtained by a trained ultrasound operator to determine the locations of the liver capsule and overlying tissue (muscle, fat and skin), as shown in fig. 1, followed by up to 10 consecutive FLIP scans over a **5-8 minute procedure,** as shown in fig. 2. Three subjects were excluded from the analysis based on FLIP measurements that were not concordant with the study subject's muscle thickness obtained by B-mode ultrasound. MRI-PDFF measurements were obtained to assess liver fat fraction. The median value of their individual FLIP scans was used to avoid outlier acquisitions. Linear regression, as well as unpaired t-test, were used to compare the estimated FLIP metric with liver fat fraction as measured by MR-PDFF. In a 2nd study, a trained operator of the FLIP system performed 12 separate study participant exams, each consisting of 6-8 measurements per exam, to determine intra-operator variability.

Conclusions

This early feasibility liver fat fraction study comparing TAEUS-FLIP to MRI-PDFF and provides insight into the potential of thermoacoustic methods to stage NAFLD at the point of care, at a fraction of the cost. **The key advantage of thermoacoustic measurements in estimating liver fat fraction is that it is sensitive to the chemical composition of tissue,** rather than structural changes in tissue (fat droplets) that may be affected by fibrosis.

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Results

Figure 3 shows the median **FLIP metric for each subject compared to MRI-PDFF.** The two methods are strongly correlated, with **a Pearson correlation coefficient of r=0.79**. Linear regression reveals that the FLIP metric of only 3 out of 13 subjects falls out of the 95% confidence interval, indicating a clear relation between the FLIP-derived measurements and MRI-PDFF values with 85% of the subjects staged the same by both methods.

To assess the FLIP method's **ability to discriminate early stages of NAFLD (S0 & S1) from later stages (S2 & S3)**, an unpaired t-test was performed on the FLIP metric with **p<0.02.**

In a second study involving one operator performing 12 FLIP exams, **intra-operator variability was 9.4% (S.D. 4.5%)**.

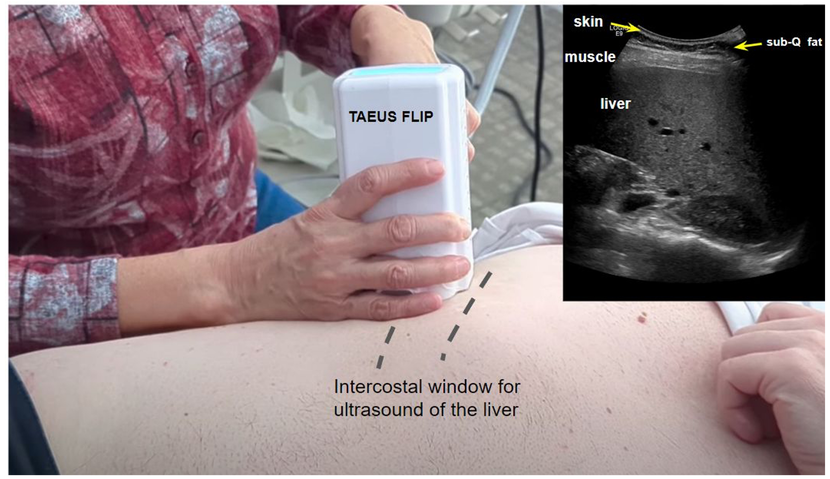

Fig. 2 Conventional B-mode ultrasound is used identify the measurement locations using the 'intercostal liver ultrasound access window' (top right). The optimal measurement location has a clear view of the liver, without interference from bowel or lung. The operator positions the TAEUS - FLIP probe in the intercostal space, at the measurement location determined by B-mode ultrasound. A series of 6 - 10 thermoacoustic measurements are obtained for each study participant.

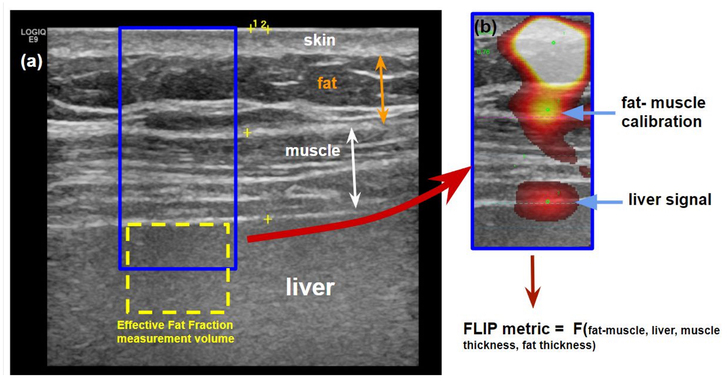

Fig. 1 Conventional ultrasound images obtained with a linear probe are able to delineate the relevant tissue structures in measurement location (skin, subcutaneous fat, intercostal muscle, and liver). The liver tissue measurement is obtained from a 16mm cylindrical region below the liver capsule as shown in (a) with the yellow dashed box. The thermoacoustic calibration and liver signals are shown in (b) overlayed onto the conventional ultrasound image. The FLIP metric incorporates acquired thermoacoustic signals and patient specific tissue depths.

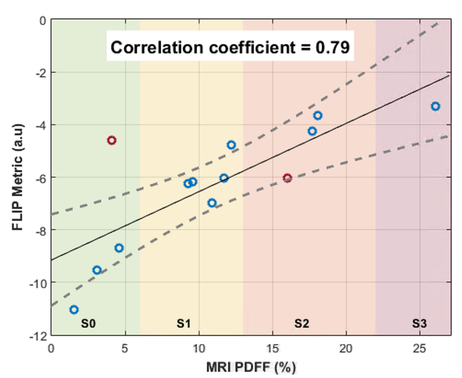

Fig. 3 The median FLIP metric for each of the 13 study participants is plotted vs. their MRI-PDFF score. TAEUS-FLIP was successful in correctly classifying mild fatty liver (S1) from moderate-severe fatty (S2-S3), in all but one subject.