Background: Hepatic fibrosis is a progressive disease caused by incessant irritation of the liver tissue, which results in the formation of scar tissue. Fibrotic progression and subsequent scar tissue formation is correlated to changing liver mechanical properties. This correlation may be used to assess the state of the disease, and hence methods to determine the elastic modulus of the liver are of considerable interest. In order to assess the diseased state of the liver accurately, controlled experiments to establish baseline modulus values for healthy livers as well as diseased livers must be conducted.

Aims: The focus of this work is the development of a protocol for mechanical testing combined with finite element modeling to allow for the evaluation of normal and fibrotic murine livers using multiple testing methods. This system can potentially be utilized for tissue characterization. In addition, current techniques are being developed to assess tissue stiffness, and this testing assay could be utilized for verification of the assessment technique.

Methods: The developed system employs a portion of liver tissue suspended in a cylindrical gel for CT imaging and mechanical testing. A finite element model is built from the CT images, and boundary conditions are imposed in order to simulate the testing conditions of the gels. The resulting model surface stress is compared to that obtained during mechanical testing, which subsequently allows for direct evaluation of the liver modulus. In addition, a separate mechanical indentation test was performed on each liver specimen, and histological analysis was performed for fibrosis staging. This system was used to study a total of fourteen livers: eight livers which were chemically-induced to develop fibrosis, three control livers, which were given placebo injections, and three normal livers, which were not subjected to any injections or treatment. The eight challenged mice were sacrificed at differing time points to study the fibrosis degree with modulus. The fibrotic livers are referred to as the diseased group, and the control and normal livers are collectively referred to as non–diseased.

Results: Though the sample sizes for this initial work were small, the preliminary results indicate that the livers can be identified within the gel, and the fibrotic livers can be identified as having a higher modulus than the control livers. The moduli evaluations for non–diseased livers were estimated as 0.62 ± 0.09 kPa, and 0.59 ± 0.09 kPa for indenter and model–analysis tests, respectively. Moduli estimates for diseased liver ranged from 0.85 to 1.64 kPa and 1.10 to 1.88 kPa for indenter and model–analysis tests, respectively. For diseased mice, scores ranged from 2–4 on the Ishak scale of 0–6 with 6 being the most severe (i.e. cirrhosis).

Conclusions: The model–calculated modulus was well correlated to the indenter modulus, excluding one presumed outlier. The results also showed a clear difference between non–diseased and diseased livers with qualitative agreement between disease scores and mechanical properties. Further testing is necessary to corroborate these initial results, but the preliminary implication is that the developed gel–tissue assay system could be utilized for controlled evaluation of soft–tissue moduli.

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