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Title: Fatty Liver – measuring fat content for noninvasive imaging with MARS spectral
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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a major public health concern within New Zealand. It can lead to severe complications such as liver cirrhosis and even liver cancer. In order to improve the health outcomes, early and accurate detection is crucial. Currently the most accurate diagnostic method is by taking a liver biopsy, however this method is undesirable since it is invasive meaning there is a risk of causing more harm than good. The most effective non-invasive method is through an MRI scan, however this can be expensive, time consuming and there are limited resources.

In order to address this issue there has been development of new technology – the MARS CT scanner, a new type of X-ray imaging. This scanner has multiple x-ray energies, which means that it has the potential to identify and accurately quantify between different materials within tissue. It also has the advantage of reduced time exposed to radiation.

The MARS CT scanner is currently a small animal model prototype and the first of its kind, but has the potential of detecting and measuring fat within the cells of the liver.

Aim

- To develop stable homogenous fat and water phantoms to represent fat found in the liver
- To see if the MARS scanner is able to identify and accurately measure the different concentrations of fat in the phantoms
- Measure the unknown fat content in excised fatty mice livers

Impact

Successful findings with MARS CT can potentially help in the future non-invasive diagnostic testing for NAFLD with improved earlier detection. Accurate fat quantification can assist with appropriate treatment measures allowing for individual tailored treatment.

Method

In radiology, a phantom consists of simulated tissue to evaluate the scanner before the actual tissue is assessed. In this study the phantoms need to be a mixture of fat and water – to represent the fat found within liver tissue. These consisted of peanut oil, water and an emulsifying agent, with the amount of oil varying in order to get fat percentages from 0-60% and one at 100%. The phantoms were homogenised to get a stable emulsion and then scanned using MARS CT with the human energy range. The output CT number (Hounsfield Units) was plotted against the fat concentration to form a calibration curve in order to identify the linear trend. MARS material decomposition, a method of separating individual materials within a mixture, was also used to assess the ability of the scanner to quantify the concentration of the oil within the phantoms.

Following this, four genetically modified mice livers that developed fatty livers were scanned. The output CT numbers were used to identify the unknown fat content using the calibration curve.

A second set of phantoms was developed repeating the emulsion method but adding 0.1g of fresh homogenized animal liver tissue to each of the different fat concentrations to improve the phantom simulation of liver tissue.

Results

The first set of phantoms appeared homogenous and remained stable for up to three weeks, upon which the oil and water phases separated.
The scanner was successfully able to detect the different ranges of fat concentrations within the phantoms and a strong linear trend was formed with a $R^2 > 0.98$. The lowest amount of fat detected was 5%.
The MARS-MD was able to separate the phantoms into their constituent materials however there was some noise resulting in slight underestimation in the measured fat concentrations.

Unfortunately none to little fat was detected in the mice livers. This was thought to be due to the storage of these livers in formalin, a chemical compound that preserves biological tissue. As the livers were kept in formalin for quite some time it was believed that the fat had degraded into lipid peroxides, which meant that the scanner was unable to detect the presence of fat. However there were small regions that showed fat – possibly areas that were unaffected by formalin.

In order to study the effect of formalin a new set of phantoms were made repeating the same method as the second set – involving fat emulsions as well as fresh liver tissue but this time adding the same amount of formalin to each. These were also scanned to confirm the effect of formalin. The results of these showed an underestimation of fat, especially by MARS-MD.

The biochemical analysis of one of the liver samples confirmed the effect of formalin, showing there was only 0.07% fat in the liver. However, the other livers still need to be analysed to further validate these findings.

Conclusion

The method of the fat phantom preparation can be recommended for the future imaging studies of fatty liver.

Formalin should not be used as a storage material for fat samples. This has been an important finding for future MARS imaging research. However this finding will need further biochemical analysis to validate the results.

Overall the MARS scanner has been able to identify and quantify different concentrations of fat in both the phantoms and small areas of the mice liver tissue. Future work is still required to assess the accuracy of the MARS scanner by using fresh liver samples so this can progress onto its clinical application.