

## MRI and MRS monitoring of gastrointestinal distribution, physiological effects and absorption of fat emulsions

M. O. Hussein<sup>1</sup>, L. Marciani<sup>2</sup>, M. Stephenson<sup>1</sup>, C. L. Hoad<sup>1</sup>, E. F. Cox<sup>1</sup>, E. Placidi<sup>1</sup>, S. Pritchard<sup>1</sup>, H. Ribeiro<sup>3</sup>, E. Ciampi<sup>3</sup>, P. Rayment<sup>3</sup>, A. Nandi<sup>3</sup>, N. Hedges<sup>3</sup>, P. Sanderson<sup>3</sup>, I. Kruse<sup>3</sup>, R. C. Spiller<sup>2</sup>, and P. A. Gowland<sup>1</sup>

<sup>1</sup>The Sir Peter Mansfield Magnetic Resonance Centre, School of Physics & Astronomy, The University of Nottingham, Nottingham, NG7 2RD, United Kingdom,

<sup>2</sup>Nottingham Digestive Diseases Centre NIHR Biomedical Research Unit, The University of Nottingham, Nottingham, United Kingdom, <sup>3</sup>Unilever Discover, Colworth Science Park, Bedford, United Kingdom

**Background:** Magnetic resonance imaging (MRI) can monitor gastrointestinal (GI) function [1-3] and visualise the water and fat components of food in the GI tract separately and non-invasively. This has allowed the spatial distribution of fat in the stomach to be monitored [4, 5] and related to gastric emptying rates [6], the cholecystokinin (CCK) response from the small bowel and satiety [7]. Proton magnetic resonance spectroscopy (<sup>1</sup>H-MRS) can also be used to monitor the absorption of fat in the liver and skeletal muscle [8]. **Aim:** To combine these MRI and MRS techniques to provide a unique, non-invasive, method of complete, serial monitoring of the delivery to the intestine and absorption of fat in the human skeletal muscle and liver. This abstract describes MRI and MRS development work to investigate the processing of fat in the GI tract and the subsequent arrival of fat in liver and muscle.

**Methods:** Two different emulsions were prepared: a coarse emulsion with a mean diameter of approximately 8  $\mu$ m and a fine emulsion with a mean diameter of approximately 0.4  $\mu$ m. The emulsions contained 79% distilled water, 20% sunflower oil (SFO) with 100mg of <sup>13</sup>C-triolein label, 1% Tween20 emulsifier, 2 Hermesetas mini sweetener tablets and approximately 1.5g Dr. Oetker coffee flavouring. The mixture was blended in the Ultraturrax at 13,500 rpm: fine emulsion for 10 min and coarse emulsion for 16 min. The fine emulsion was then passed through a Microfluidizer at 1 bar corresponding to 233 bars in the interaction chamber.

**Volunteers:** Two healthy male volunteers, aged 18 and 19 years with no history of GI disease, each attended the study site on 2 separate mornings having fasted overnight. The subjects gave informed consent and the study was approved by the local Ethics Committee. Initial baseline, fasted scans were acquired and then the volunteer was given 300g of either the coarse or fine emulsion (60g SFO in total). Scanning was carried out at 2 hourly intervals for up to 6 hours to follow the fate of the fat meals.

**Scanning:** MR data were acquired using a Philips 3.0 T Achieva whole body scanner and SENSE-torso coil. The following MR scans were acquired in approximately 45 minutes: HASTE (30 x 7mm transverse slices, covering the whole abdomen,  $TE_{eff}$ =60ms,  $TR=\infty$ ,  $FOV=400$ mm, SENSE factor=2.0 resolution 0.78x0.78 mm<sup>2</sup>, in 3 breath-holds) to quantify gastric and gall bladder volumes. RARE (22 x coronal 7mm thick slices covering the whole abdomen,  $TE_1=2.30$ ms,  $TE_2=5.74$ ms,  $TR=130$ ms,  $FOV=400$ mm, SENSE factor=2.0, resolution 0.78x0.78 mm<sup>2</sup> in 3 breath-holds) to quantify small bowel water contents (SWBC). Hepatic <sup>1</sup>H MR spectra were acquired from a voxel positioned in the right lobe of the liver, using a respiratory triggered PRESS sequence ( $TE/TR = 40/5000$ ms,  $VOI = 30x30x30$ mm,  $Nave = 16$ ,  $BW = 2000$ Hz, 1024 samples). Two <sup>1</sup>H MR spectra were acquired in muscle; water-suppressed for measurement of intramyocellular lipid (IMCL)/water ( $Nave=32$ ) and non water-suppressed for total calf lipid/water measurement ( $Nave=16$ ). PRESS localization was used ( $TE/TR = 40/7000$ ms,  $VOI = 30x30x50$ mm,  $BW = 2000$ Hz, 1024 samples). Water unsuppressed spectra were post-processed using jMRUI and peak areas were calculated using in-house software built in Matlab. Water-suppressed spectra were post-processed using jMRUI and peak areas were calculated using the AMARES algorithm, fitting to Gaussian curves. Lipid values are given as lipid/water ratios.

**Results:** Figure 1 show representative RARE images (5 consecutive slices acquired at different times) for both emulsion meals. These illustrate the large amount of water induced in the small bowel by the meals, particularly by the fine emulsion. The HASTE images showed intragastric creaming of the coarse emulsion. Figure 2 shows variation in gastric volume (a), small bowel water content (b) and gallbladder contraction (c). Figure 2 (d) shows <sup>1</sup>H spectroscopic data from the calf muscle and (e) from the liver. The spectroscopy numbers are too small to draw conclusions at this stage.

**Discussion:** The gastric volume data indicates that the coarse emulsion caused the gastric volume to fall more quickly. This is probably due to creaming of the emulsion which would have led to the water component of the meal being delivered to the small bowel earlier than the fat component; fat triggers duodenal receptors which form part of the feedback loop that controls gastric emptying. This is supported by the reduced gallbladder contraction for the coarse emulsion, since gallbladder contractions reflect the release of CCK in response to fat in the duodenum. Such a marked increase in small bowel water content, induced particularly by the fine emulsion, had not been expected. We are performing further experiments to determine whether the droplet size or the creaming is responsible for this effect. MRS showed promise for monitoring postprandial changes in both liver and calf lipid/water ratios. This data will be used to plan experiments to study the effect of droplet size on the bioavailability of fat.

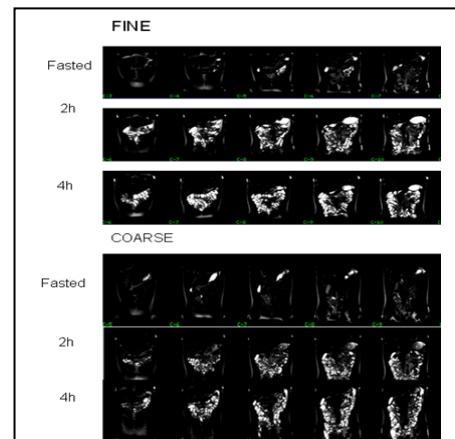


Figure 1: RARE images showing large increase in small bowel water after the volunteers were fed an emulsion.

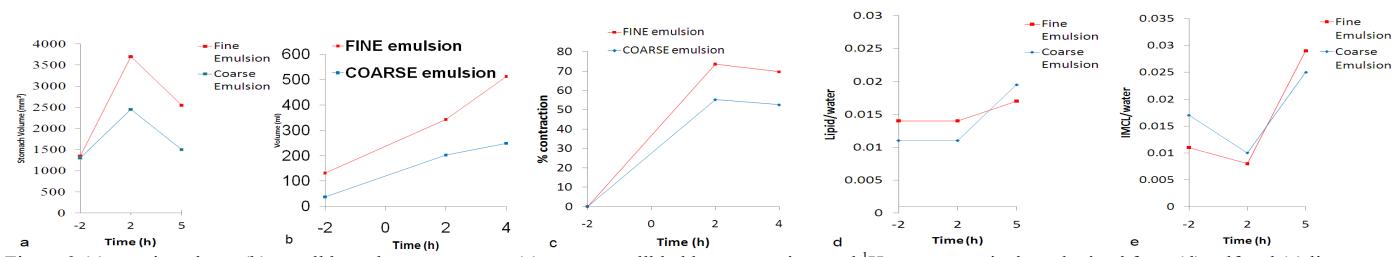


Figure 2 (a) gastric volume (b), small bowel water contents (c) average gallbladder contraction; and <sup>1</sup>H spectroscopic data obtained from (d) calf and (e) liver.

**Conclusion:** Fat emulsions triggered a diverse duodenal response which affected gastric emptying (fine droplets slower), gallbladder contraction (fine droplets greater) and small bowel secretion (fine droplets greater). MRI and MRS can provide comprehensive insight into the body's handling of a fatty meal.

**References:** <sup>[1]</sup> Gowland et al. In "Magnetic resonance in food science, a view to the future" Webb et al, Editors. 2001, The Royal Society of Chemistry: Cambridge. 2001, 85. <sup>[2]</sup> Marciani et al. *JMRI*, 2005, **21**(1): 82-85. <sup>[3]</sup> Marciani et al. *Neurogastro Motil*, 2001, **13**: 511. <sup>[4]</sup> Marciani et al. *BJN*, 2006, **95**:331. <sup>[5]</sup> Marciani et al. *JFS*, 2004, **69**:E290. <sup>[6]</sup> Boulby et al. *Neurogastro Motil*, 1997. **9**:41. <sup>[7]</sup> Marciani et al. *AJP*, 2007, **292**:G1607. <sup>[8]</sup> Shulman, G. I. *Am J Cardiol*, 1999, **84**:3J.