

Diurnal Pattern of Hepatic Fat Content measured by Magnetic Resonance Imaging in Human Subjects

M. Shieh-morteza¹, Y. Lee¹, G. Hamilton¹, M. Schroeder¹, I. Mwangi¹, J. Collins¹, M. Bydder¹, T. Yokoo¹, and C. B. Sirlin¹

¹Radiology, University of California San Diego, San Diego, CA, United States

Purpose: To determine whether MR imaging measurement of hepatic fat content is influenced by the time of the day or in response to transitions from fasting to fed states.

Introduction: MR imaging is a non-invasive alternative to biopsy for hepatic fat quantification. An important uncertainty in current scientific knowledge is whether the known oscillations in lipid metabolic pathways throughout the day and in response to fasting-fed transitions could lead to diurnal variation of hepatic fat content. To address this uncertainty, we prospectively measured hepatic fat content by MR sequentially over 24 hours in human subjects with known or suspected fatty liver disease (FLD).

Materials and Methods: Seven adult subjects (2 men, 5 women; mean age 39.0 years; range 29-59 years) with known or suspected FLD were enrolled in this HIPAA-complaint, IRB-approved, prospective pilot study. On day 1, subjects underwent ten 30-minute MR scans at 60-minute intervals, starting at 0800 (Fig. 1). On day 2, subjects underwent an additional 30-minute scan at 0800. Subjects were fasting for the first MR scan on day 1 and for the day 2 scan. Subjects had three ad-lib meals on day 1, with four MR exams performed between meals. All subjects were scanned supine with a phased-array coil centered over the liver at 3T. Hepatic fat content was calculated using a modified Dixon technique, *LIPO-Quant* (Liver Imaging of Phase-related signal Oscillation and Quantification). This technique employs a T1 independent, T2* corrected multi-echo spoiled GRE sequence[1]. Six TEs were acquired in a single TR with a minimum TE 1.15 ms and inter-echo spacing 1.15 ms; TR 150 ms; bandwidth 142 kHz; matrix size 192x192; field of view 350x240 mm and slice thickness 8 mm. Fat fraction (FF) was calculated from T2*-corrected fat and water signals using a 5-peak fat spectral model. *LIPO-Quant* was repeated three times at each MR scan. FF maps, which display the pixel-by-pixel spatial distribution of hepatic fat content, were generated. The mean hepatic fat percentage was calculated from six regions of interest (ROIs) co-localized across scans. Within-subject variability in FF across time was assessed. To test for diurnal patterns in FF variability, each subject's FF was standardized, and raw and smoothed trends were analyzed informally. A simulation of 3000 replicate datasets also was performed and analyzed informally.

Results: At baseline (0800 on day 1), the seven subjects had FF's of 1%, 4.5%, 8.5%, 13.4%, 14.4%, 18.2%, and 40.7% (mean 13.8%). At subsequent time points, all subjects showed some variability in hepatic FF. The range in FF (maximum-minimum over 24 hours) varied from 0.6% fat (for the subject with 1% fat) to 3.4% fat (for the subject with 40% fat). The standard deviation in hepatic FF between time points varied from 0.20% (for the subject with 1% fat) to 1.1% (for the subject with 40% fat). Fig.2 shows each subject's standardized FF over time; the thick black line is the average trend-line across subjects. As shown in Fig.2, the FF for most subjects fluctuated by 1-2 standard deviations. Fig 3. shows the same data as Fig 2 smoothed over time. As shown in Fig.2, there is a

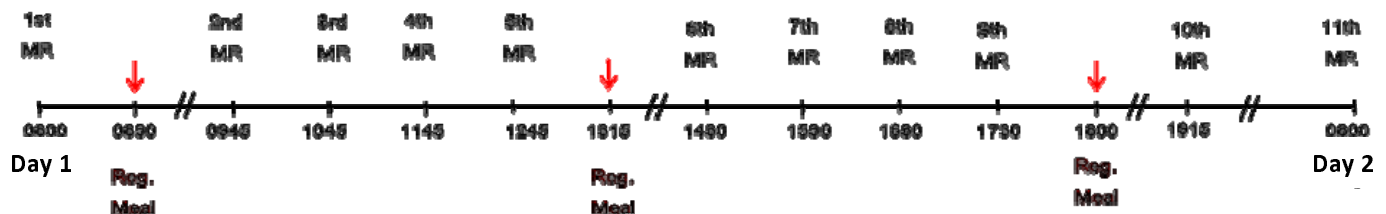
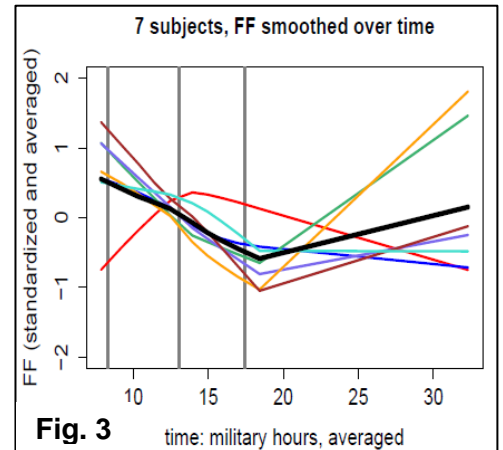
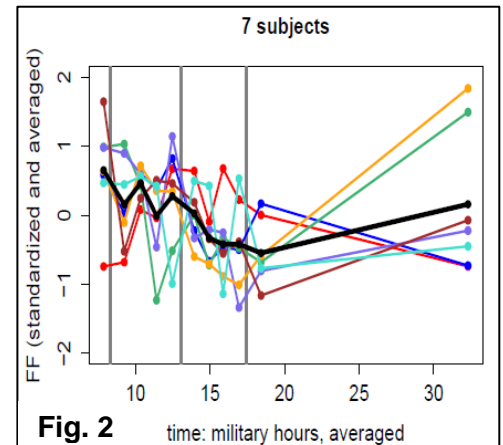


Fig. 1

cyclic trend with a mean overall reduction in FF of 0.78 standard deviations from baseline (morning) to nadir (evening). A simulation informally suggested that the observed trend (reduction from morning to evening) was not due to random sampling (data not shown). There was no observable change in hepatic FF in response to meals.

Conclusion: Hepatic FF varied by 1-4% across a 24-hour observation period. Variability was greater in subjects with higher baseline FF. Informally, we observed a diurnal trend with FF tending to diminish from morning (baseline) to evening (nadir). Formal testing of this trend will require further study. If this trend is confirmed, it will have implications for studies assessing longitudinal changes in MR imaging FF. As opposed to the diurnal variation, meals do not appear to influence the MR imaging FF; if this observation is confirmed, it will suggest that fasting is not necessary for accurate measurement of hepatic FF.

References: [1] Yokoo et al. Hepatic Fat Quantification by Low Flip-Angle Multi-Echo Gradient-Echo MR Imaging: A Clinical Study with Validation with MR Spectroscopy. ISMRM, 2007.