Single Breath-Hold MR Spectroscopy for Diffusion-Weighted Lipid Droplet Size Estimation

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SU-315-GPD-D-35

INTRODUCTION

- Lipid droplet (LD) size may be an important parameter in characterizing normal and pathological fatty tissue
- Recent work has shown that diffusion-weighted MR can estimate LD diameter[1-2]
- Prior techniques have not focused on the rapid acquisitions required for body applications where physiological motion may bias the LD diameter estimates
- Signal contrast for LD size for a short scan duration is theoretically possible (Fig. 1)

Purpose: To assess diffusion-weighted spectroscopy for estimating lipid droplet (LD) diameter with short acquisition times (<30 s)

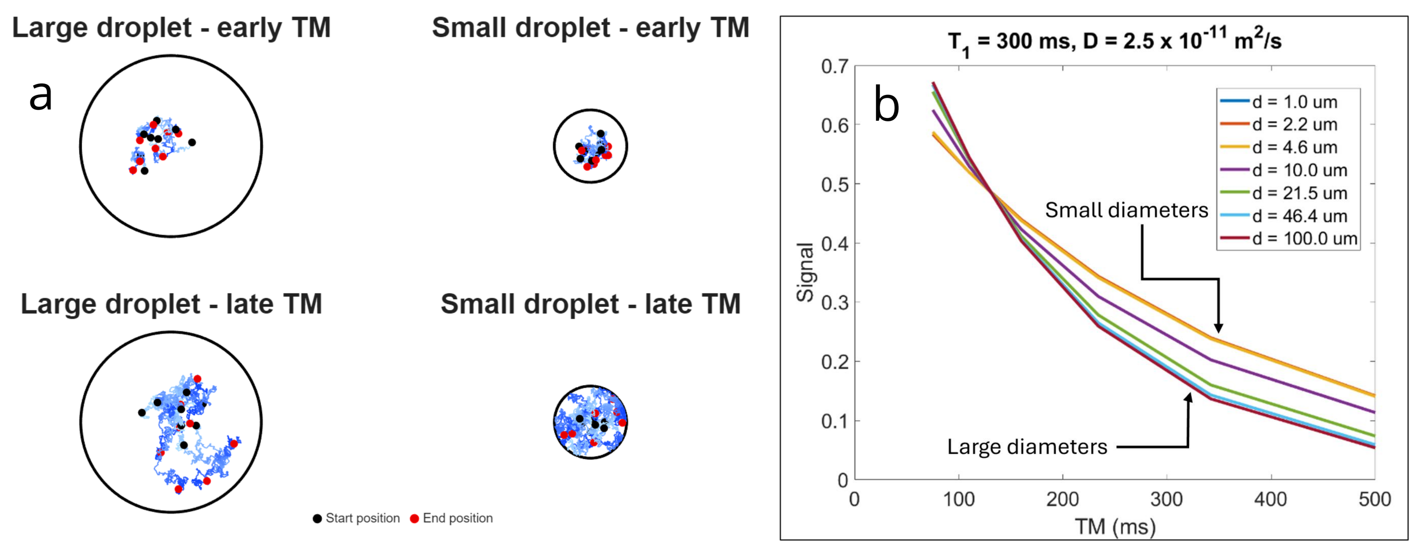

Fig. 1. Illustration of restriction of triglyceride self-diffusion trajectories within different diameter LDs at early and late mixing times (TM) during a diffusion-weighted stimulated echo pulse sequence (a). Restriction creates dispersion in normalized signals across TM as a function of diameter for a given T_1 and self-diffusion coefficient (D) (b).

METHODS AND MATERIALS

- Single-direction diffusion-weighted stimulated echo single-voxel MR spectroscopy (DW-STEAM) used for LD diameter encoding
- Murday–Cotts model of restricted diffusion used for numerical simulation and data fitting (MATLAB 2025b)
- Rapid (<30 s) DW-STEAM using six log-spaced mixing times (TM = 75 to 500 ms; NSA = 4) and long DW-STEAM (~4 min) using 10 mixing times (TM = 50 to 500 ms; NSA = 16)
- Cramér-Rao bound analysis estimated theoretical parameter uncertainty for both DW-STEAM sequences
- Rapid and long DW-STEAM LD diameter estimates were compared in five sunflower oil lipid droplet phantoms
  - Phantoms were homogenized at different rates (12,000-35,000 rpm) and durations (30-120 s)
  - Droplet size assessed by optical microscopy
- Monte Carlo approach (N = 10,000) used to estimate Pearson and Spearman Rank Correlations between rapid and long DW-STEAM – rejecting oil phantom due to estimation constraints
- Rapid DW-STEAM estimated small LD diameter in aqueous gel (1.5% agarose) Intralipid 20 (soybean oil; Sigma-Aldrich) and in pure sunflower oil phantoms

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RESULTS

Theoretical LD diameter estimation uncertainty

- Cramér-Rao lower bound coefficient-of-variation (COV) calculations for SNR = 100
- T_1-constrained (independently estimated or known)
- Both long and rapid DW-STEAM show comparable, narrow range of low LD diameter estimation uncertainty
- At small and large diameter, TM selection reduces sensitivity to LD diameter

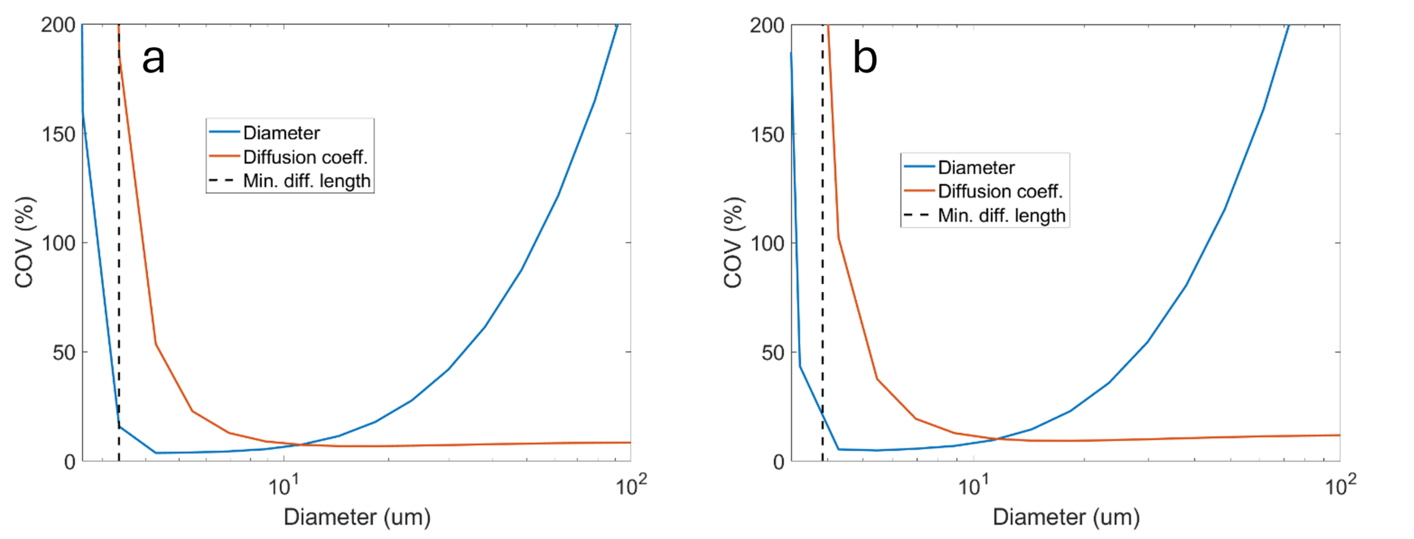

Fig. 2. The theoretical coefficient of variation (COV) of simultaneous lipid droplet diameter and triglyceride self-diffusion coefficient estimation for the long (a) and rapid (b) DW-STEAM sequences. The vertical dotted line is the RMS length of unrestricted fat molecule diffusion at minimum mixing time.

Phantom LD diameter estimates from the two sequences:

- Optical microscopy-based volume-weighted LD diameter estimates ranged from 10 to 19 μm
- Long and rapid DW-STEAM estimates qualitatively agreed with microscopy (Fig. 3)
- LD diameter estimates from both DW-STEAM techniques were positively biased relative to volume-weighted microscopy (Fig. 3)
- While MRS LD diameter estimates from long and rapid sequences agreed within margins of error, they were weakly correlated (Table 1)

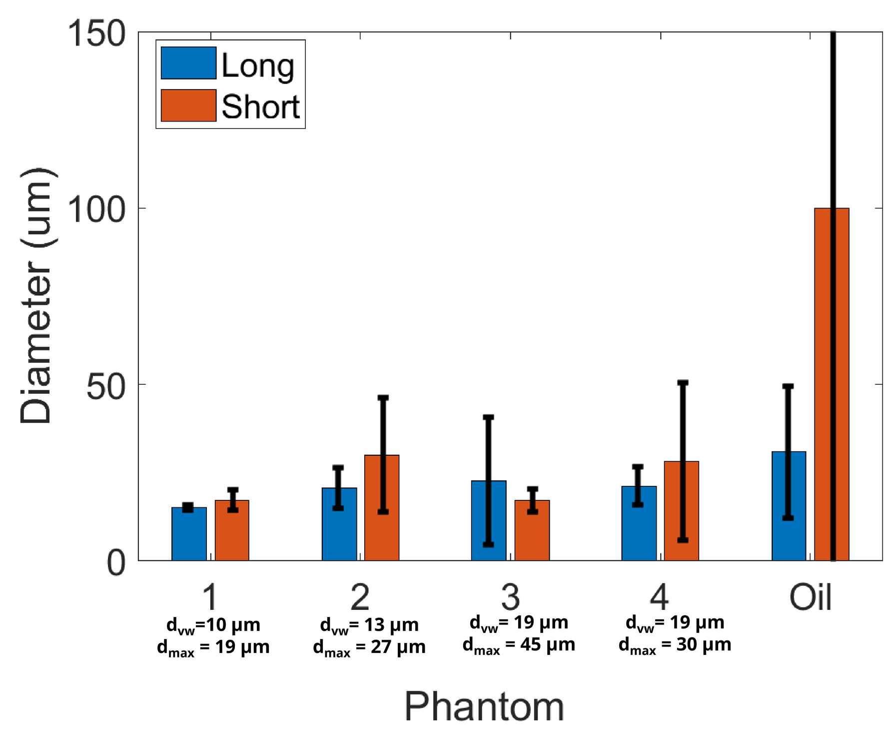

Table 1. Estimated correlations between LD diameter estimates from the two DW-STEAM sequences

Correlation Type	R	CI
Pearson	0.105	[0.095, 0.115]
Spearman	0.121	[0.110, 0.132]

Fig. 3. The estimated lipid droplet diameters from the long and short DW-STEAM sequences with standard errors in fat-water phantoms. Phantom 1 -> 4/Oil is smallest to largest lipid droplet size. Volume-weighted diameter and maximum diameter from microscopy are given below the phantom labels.

RESULTS

LD diameter estimates from the rapid MRS sequence in Intralipid 20 and pure oil

- Gel with Intralipid (IL) fat fraction was ~5%, verified by Dixon imaging
- Rapid DW-STEAM estimated diameters for IL and oil were 7 and 100 μm, respectively
- The true IL diameter <1 μm, indicating positive bias in DW-STEAM diameter estimate
- LD diameter constrained ≤100 μm, so oil LD diameter consistent with expectation

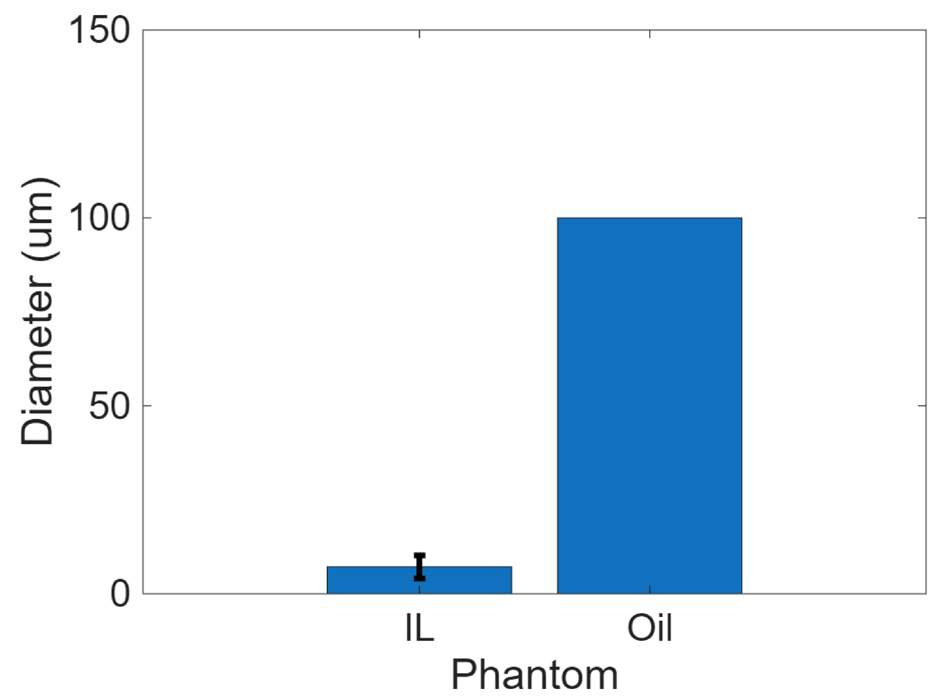

Fig. 4. The rapid DW-STEAM estimated diameters for Intralipid 20 (IL) and vegetable oil. Standard error (SE) is shown for the IL but not for oil, as the SE estimate is biased high for large diameters. Acquisition time for both was the short (<30 s) sequence.

DISCUSSION

- Simulations show that the rapid DW-STEAM has sensitivity to diameter over a narrow range of sizes (~2 to ~20 μm)
- Weak correlation between rapid and long DW-STEAM may be due to narrow dynamic range of droplet sizes
- Evaluation of IL droplet size approaches true diameter but remains positively biased
- Future work is needed to reduce potential phase errors and motion-induced sources of bias[3]
- Future in vivo validation is needed to determine best physiological motion mitigation strategy
- Depending on LD diameter of interest and TM selection, current method may be best for differentiation between small (≲3 μm) and large (≳20 μm) diameter LDs

REFERENCES

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