Correcting for Imperfect Spin Echo Refocusing in Gas-Free fMRI Calibration

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Introduction

- Calibrated fMRI is typically performed with a hypercapnic gas challenge during BOLD and cerebral blood flow (CBF) imaging[1]
- Eliminating the gas challenge could greatly improve the appeal of calibrated fMRI
- Efforts to calibrate without gases, by quantifying the reversible relaxation rate (R_2') using asymmetric spin echo (ASE) imaging, have tested the hypothesis:[2]

$$M_{ASE} = \ln S_{SE}/S_{ASE} \cong R_2'\tau \qquad (1)$$

- This underestimated the calibration constant (M), relative to hypercapnia
- The underestimation is postulated to arise from incomplete spin echo (SE) refocusing to due diffusion in the extravascular space[2]

Objectives

- Determine how incomplete refocusing of SE and ASE signals affects estimation of the calibration constant, M
- Correct for this when performing ASE-based calibration

Methods: Simulations

- SE and ASE signals were simulated as a function of vessel radius with the following parameters:
  - CBV = 2%
  - Radii = 1–100 µm
  - O_2 saturation = 62%
  - D = 0.8 µm²/ms
  - B_0 = 3 T
  - TE = 4–100 ms
- As shown in Fig. 1, both the SE and ASE signals approximately follow a quadratic-exponential decay initially and transition to linear-exponential decay later
- Considering just the quadratic decay, we propose the ASE signal model can be modified to include SE attenuation from diffusion using a quadratic ASE model (**q-ASE**):

$$S_{ASE} = S_0 e^{-R_2 TE} e^{-R_2'\tau} \underbrace{e^{-(R_{2,diff})^2 (TE-\tau)^2}}_{\text{diffusion-induced spin echo attenuation}} \qquad (2)$$

- The ratio, $\ln S_{SE}/S_{ASE}$, then decreases linearly with TE:

$$\ln \frac{S_{SE}}{S_{ASE}} = R_2'\tau + \left(R_{2,diff}\right)^2 \tau^2 - 2\left(R_{2,diff}\right)^2 \tau TE \qquad (3)$$

- If $\ln S_{SE}/S_{ASE}$ measured at more than one TE, we can estimate R_2' and $\left(R_{2,diff}\right)^2$ from a linear fit to (3)
- Considering M as the maximum possible BOLD signal,[3] it can finally be estimated using

$$M = e^{-R_2' TE_{fcn}} - 1 \qquad (4)$$

TE_{fcn} : echo time in functional imaging after calibration

Results

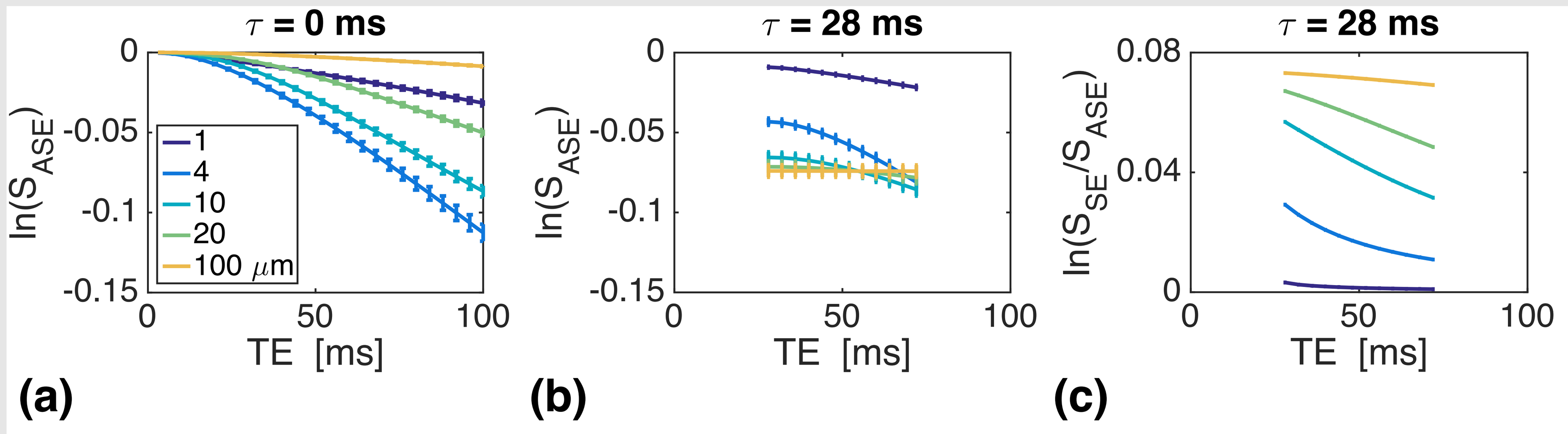
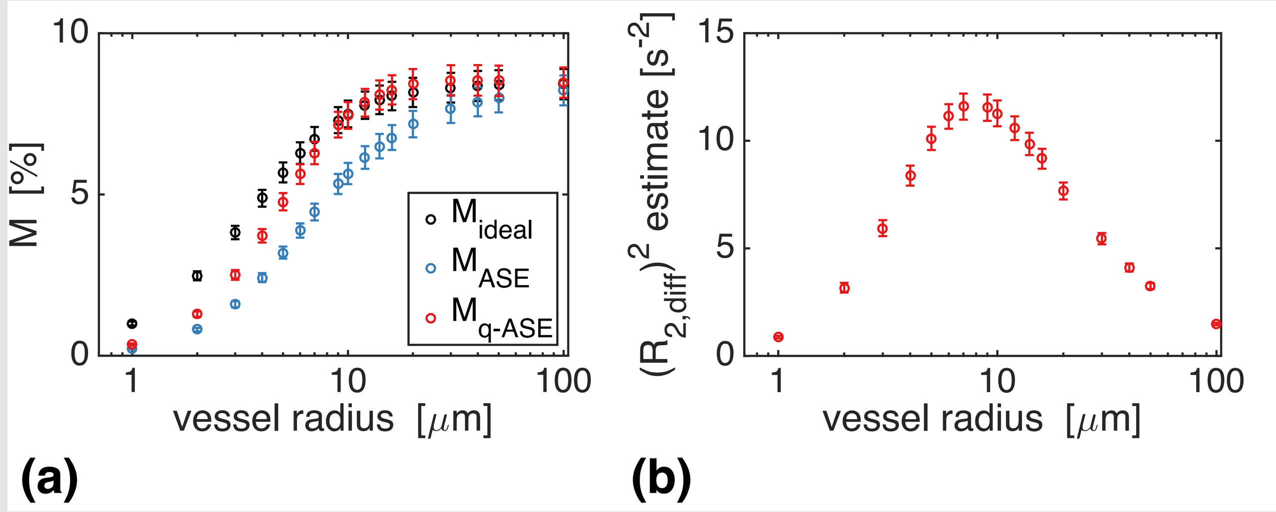


Figure 1: (a) and (b) Simulated ASE signals vs. echo time and vessel radius. The lines pass through the mean signal at each echo time. In (a), τ = 0 ms corresponds to a pure SE signal. **(c)** The ratio of the SE and ASE signals with τ = 28 ms

Key Findings: The SE and ASE curves initially decay quadratically and transition to linear decay. Larger vessels transition later. This results in the ratio, $\ln S_{SE}/S_{ASE}$, decaying linearly for early TE and later plateauing.

Figure 2: (a) Comparison of the ideal M value and M calculated from simulated ASE signals as a function of vessel radius. The ideal M (M_{ideal}) was calculated as the maximum possible percent gradient echo signal change at a TE of 30 ms (i.e. TE_{fcn} = 30 ms). Using Eq. (1), M_{ASE} was calculated at a single TE of 40 ms with τ = 30 ms, as in [2]. Using the SE and ASE signals at TEs of 40 and 50 ms, M was calculated using the q-ASE model by fitting for R_2' and $\left(R_{2,diff}\right)^2$. **(b)** The estimated $\left(R_{2,diff}\right)^2$ values from the q-ASE fits for each radius.

Key Findings: M_{ASE} significantly underestimates M_{ideal}; $M_{q\text{-}ASE}$ compensated for this underestimation for intermediate to large vessels; The vessel-size dependence of $\left(R_{2,diff}\right)^2$ is very similar to that of SE BOLD.[4]



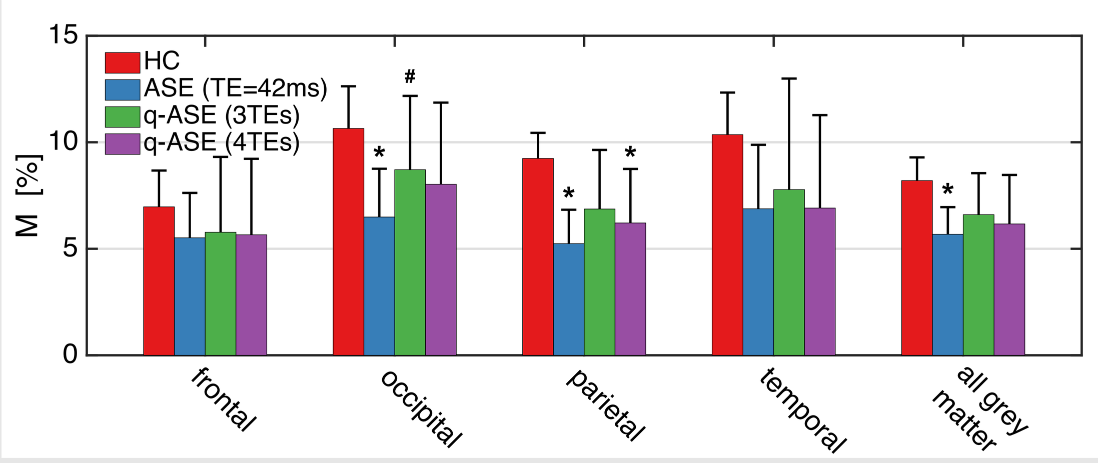


Figure 3: Comparison of M measured *in vivo* from hypercapnia (HC), from the first ASE echo time (ASE (TE=42 ms)), from the q-ASE model fit to the first three TEs (q-ASE (3TEs)), or fit to all four TEs (q-ASE (4TEs)). * denotes the ASE or q-ASE M values were significantly different from the HC values. # denotes the q-ASE M values were significantly greater than the ASE (TE=42ms) M values. Significance tests were performed using false discovery rate-corrected paired t-tests. Bars represent the mean ± standard deviation.

Key Findings: M_{ASE} tends to underestimate M_{HC}; The q-ASE model tends to increase the M_{ASE} values; Regions of severe field inhomogeneity locally limit the method's effectiveness.

Methods: Imaging

- Pairs of CSF-nulled SE and ASE EPI images with FLAIR preparation were acquired in seven healthy subjects at 3 T (GE Discovery 750) using:
  - In-plane resolution = 2.33 mm
  - Slice thickness = 2.0 mm + 1.0 mm gap
  - ASE τ = 30 ms
  - TR / TI = 8 s / 2 s
  - TEs = 42, 50, 60, 70 ms
  - N_{reps} = 15
- Images were registered and corrected for geometric distortion[5] and signal loss from though-plane gradients using a field map
- Signals were averaged across grey matter regions of interest[6,7]
- M_{ASE} was calculated using Eq. (1) at a single TE of 42 ms
- M was also calculated using the q-ASE model by fitting Eq. (3) with either the first 3 echoes or all 4 echoes
- For comparison, M was calculated from a 5% CO_2 fixed-inspired hypercapnia challenge using a dual-echo pseudo-continuous ASL sequence

Conclusions

- Diffusion leads to imperfect spin echo refocusing that can be approximated by quadratic-exponential decay initially and linear-exponential decay at later times (Figs. 1 a & b)
- The quadratic decay can be described by a diffusion decay term, $\left(R_{2,diff}\right)^2$, that depends on vessel size (Figs. 1 & 2)
- This decay leads to M_{ASE} underestimating the expected M, as observed in our simulations (Fig. 2a) and in vivo (Fig. 3), and consistent with previous findings[2]
- Measuring the linear decay of $\ln S_{SE}/S_{ASE}$ permits partial to full compensation of the underestimation of M (Figs. 2a & 3)
- Future studies may benefit from measuring $\left(R_{2,diff}\right)^2$ or using an assumed value to correct M_{ASE} for SE attenuation

Acknowledgements

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References

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