Spin Echoes Underestimate Functional Changes in Microvascular Cerebral Blood Volume

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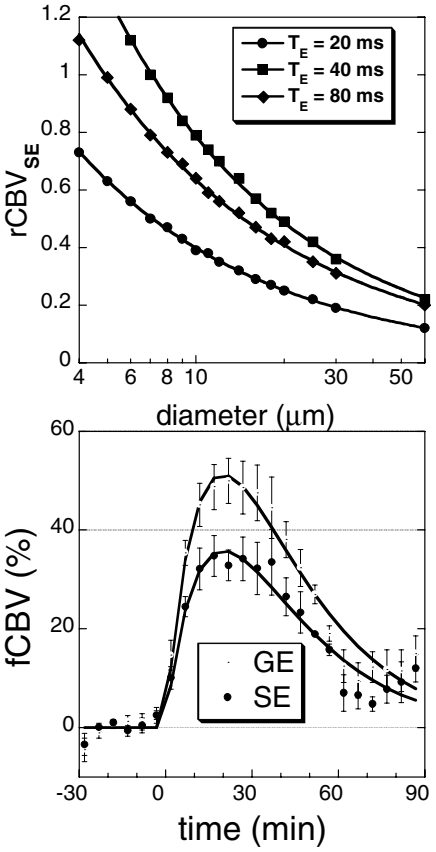
Background: Using iron oxide agents that maintain a nearly steady-state blood concentration for long periods of time, relative regional cerebral blood volume (rCBV) can be calculated from the signal attenuation ($A=S_{POST}/S_{PRE}$) due to agent injection, and relative functional changes (fCBV) can be determined from the ratio of rCBV values.

$$\mathrm{rCBV}(t) = -\ln(\mathrm{A}(t)) \quad , \quad \mathrm{fCBV})(t) = \mathrm{rCBV}(t) \Big/ \mathrm{rCBV}(0) \qquad [1]$$

Extravascular contributions to rCBV have a radial dependence at fixed volume fraction (1). When vessels swell, the voxel concentration of agent increases in proportion to local CBV, but the radial distribution also changes. The extravascular contribution to rCBV is an integral including radial probability (ρ) and sensitivity (S) functions. If sensitivity functions can be represented as inverse power laws of radius, then functional changes in CBV will be underestimated by amounts related to the exponents of these sensitivity functions. This also means that maximal fMRI signal changes will be smaller for spin-echo than gradient-echo acquisitions.

$$\mathrm{rCBV} \propto \int \mathrm{p(r)r^2S(r)dr} \quad \Rightarrow \quad \mathrm{fCBV(t)} \approx (1-\alpha/2)\frac{\Delta \mathrm{V(t)}}{\mathrm{V(0)}} \quad \text{for } \mathrm{S(r)} \propto 1/\mathrm{r}^{\alpha} \qquad [2]$$



Methods: Monte Carlo methods were employed to determine radial dependencies of relaxation rates and to compare simulated values of fCBV to the known (input) values. Methods were similar to those as employed by others (1), in which particles undergo random walks through simulated voxels to acquire phase, and this process is repeated many times to enable calculations of signal.

Measurements were obtained throughout rat brain by adding nitrous oxide (70%) to the inspired gas while maintaining a constant oxygen level (30%). Data were acquired using a multi-echo sequence with a gradient echo time of 5 ms and a spin echo time of 20 ms obtained from one excitation per k-space line.

Results: Simulated SE relaxation rates decreased monotonically versus vessel diameter (> 4 microns) for all echo times less than 100 ms within a range of iron doses from 5 to 50 mg/kg; all reported fMRI results using USPIO agents fall within these ranges. The top figure shows simulated radial response profiles for the EV component of rCBV at echo times using a constant product of echo time and dose. The exponent (α) in Eqs 2 was fit versus echo times and dose. For all combinations of echo time and dose, α was between 0.6 and 0.65 whenever signal attenuation corresponded to rCBV > 0.2 (so that EV dominated IV contributions). Simulations demonstrated that fCBV, as calculated using the standard formula in Eqs 1, reported only about 60% of actual changes in CBV.

Measurements showed a good general agreement with these results. The SE response of CBV in rat caudate (bottom figure) was only 70 ± 6 % as large as the GE measurements, and this result was quite constant across rat brain. The largest deviations from this tissue response was exhibited in very high blood volume regions, were SE values of fCBV matched or exceeded GE values, presumably as a result of low SNR in these regions using the GE method.

Discussion: Spin echo methods have generated interest for fMRI due to the potential to localize signal changes to microvascular beds. When using exogenous contrast agent, spin echoes obtain tissue specificity by applying a low-pass filter in vessel diameter, whereas gradient echoes obtain tissue specificity by applying a band-pass filter in basal blood volume (2). Thus, it's not clear that SE methods should provide better localization, while SE methods possess drawbacks in detection power that cannot be compensated by adjustments in agent dosage, as demonstrated here. Moreover, one cannot interpret the functional physiology of CBV changes without understanding the physics, which demonstrates that SE methods always underestimate actual changes in CBV.

References:

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