Dynamic ratio $\Delta R_{2GE}/\Delta R_{2SE}^{3/2}$ in DSC perfusion imaging reveals the relative arterial and venous blood volume fraction

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Introduction: The characterization of the cerebral microvascular morphology, which is of great interest for the research of cerebral diseases such as stroke and brain tumor, can be achieved by assessing the ratio between the transverse relaxation rate measured by gradient echo (GE) R_{2GE} and spin echo (SE) $R_{2SE}^{3/2}$ during dynamic bolus passage. Rather than following a reversible line, the ratio $\Delta R_{2GE}/\Delta R_{2SE}^{3/2}$ often displays a difference between the increase and decrease of the contrast agent (CA) concentration in the tissue, thus forms a loop. Interestingly, the curve of the loop has always been counter-clockwise in ROIs of normal brain tissue during observation (see Fig. 1 and [1]). In this work, we simulate the dynamic involvement of microvasculature --arterioles, capillaries and venules-- during bolus passage to understand the formation of the loop.

Methods: Simulation: The tissue model and signal simulation proposed by [2] are used here. The vascular structure is simplified to be arterioles, capillaries and venules with radii (and volume fractions) 100 µm (0.5%), 4 µm (2%) and 100 µm (1%), respectively. **MRI measurement:** A healthy subject (Female, 40y) and an acute ischemic stroke patient (Male, 55y, time from symptom onset 3h) were examined with a hybrid single-shot GE and SE EPI sequence at a 3.0 Tesla clinical scanner (Tim Trio, Siemens AG) with 50 repetitions ($TE_{GE/SE}$ = 23 /85 ms; TR = 1880ms; FOV 230mm; slice thickness 5mm; matrix size 64×64). A dose of 0.13mL 1 M Gadobutrol /kg bw was injected at 5 mL/s.

Result: We approach the result by a gradual change of the bolus shape from completely unrealistic to a realistic one (Fig.2 from a to b, left). Consider such a long delay in the blood transport and no dispersion, so that the bolus passage in arterioles is completed before the passage in capillaries and so on Fig. 2a. Each of three pools follows their reversible line in this case. Given the fact that the ratio $\Delta R_{2GE}/\Delta R_{2SE}^{3/2}$ is proportional to the main vessel radius in the pool, the slope of capillary pool is much smaller than the other two. Slight difference between arterial and venous pool is due to the presence of deoxyhemoglobin in venules. Note that the maximal ΔR_{2GE} and ΔR_{2SE} for each pool reached at the maximal CA concentration is proportional to their volume fraction.

When bolus passages in three pools overlap each other, shown as the blue line in Fig 2b, the dynamic ratio $\Delta R_{2GE}/\Delta R_{2SE}^{3/2}$ forms a loop by following the slope of the arterial pool at the very beginning, then transiting to the capillaries, and returning back to the venous pool. Since the arterial blood fraction is significantly smaller than venous proportion, i.e. the ascending branch is lower than the descending one, the loop is counter-clockwise. The dispersion in capillary and venous pool (Fig 2b, Dispersion 1 and 2) reduces the area of the loop, because the peak of CA concentration in capillary and venous pool turns smaller due to the dispersion. This can compensate for the smaller volume fraction of arterioles, which results in a counter-clockwise loop with an intersection between the ascending and descending branch.

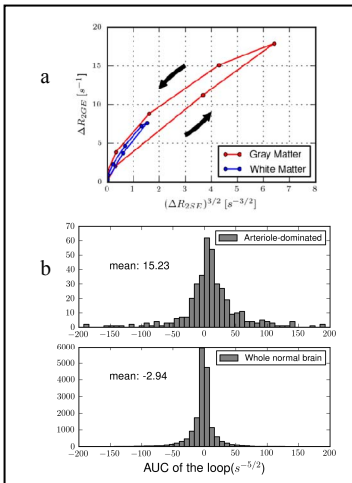

Fig 1. Result from the healthy subject. a. Dynamic ratio ΔR_{2GE} / $\Delta R_{2SE}^{3/2}$ in the white matter and gray matter. Both curves are traversed in a counter-clockwise direction. b. Histograms of the AUC of the loop from arteriole-dominated voxels (top) and the whole normal brain (bottom).

The direction of the loop can be changed in simulation by adjusting the relative arterial and venous volume fraction (see Fig2c). When arterioles dominate the blood volume, the ratio of the transition from arterial pool to capillaries, presenting as the ascending branch, is higher than the descending part, while bolus returns from capillaries to the venous pool. In this case, we observe a clock-wise loop.

To validate our observation that the arterial and venous volume contribution affects the direction of the loop, we coregister MRA with the GE image and check the area-under-curve (AUC) of the loop in voxels which are adjacent to the arterioles (diameter < 4mm). As shown in the top histogram in Fig 1b, the majority of those voxels with higher arterial blood fraction has a positive AUC, indicating a clockwise loop. In the bottom histogram in Fig 1b from a healthy brain, more voxels have a negative AUC, which coincides well with global counter-clockwise loops in Fig 1a.

An example of AUC map is shown in Fig 3c from an acute stroke patient. In the ischemic area, identified by MTT hyperintensity, the AUC is more positive compared to the contralateral side. It may be explained by the dilation of arterioles in the ischemic tissue, which results in an increase of arterial blood volume fraction.

Discussion: Although many factors are involved in the formation of the loop, the simulation suggests that the loop results from the chronological transition of the bolus among different blood vessel pools. The inflection point is reached when the bolus passes the capillary tool. The capillary distribution is crucial for a large loop area, since their small radius leads to a large SE relaxation. The direction of the loop is mainly affected by the relationship between arterial and venous blood volume. In normal brain tissue, arterial blood volume is generally 50% smaller than venous blood volume. This explains why the loops in ROIs in Fig1. are all counter-clockwise.

From the majority of clock-wise loop in arteriole-dominated voxel and the increased AUC in ischemic tissue, we suggest that the direction of the loop may indicate the local relative arterial and venous blood contribution. Using AUC is very convenient to appeal the direction of the loop. However, its broad variation is a nature of tissue. In the further study, other parameters may be used to present the loop.

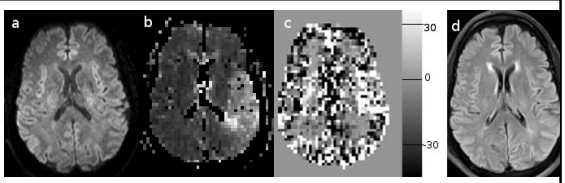

Fig 3. Images of an acute stroke patient. a. DWI b. MTT c.AUC of the loop (unit: $s^{-5/2}$) on day 0 and d. FLAIR on day 6.

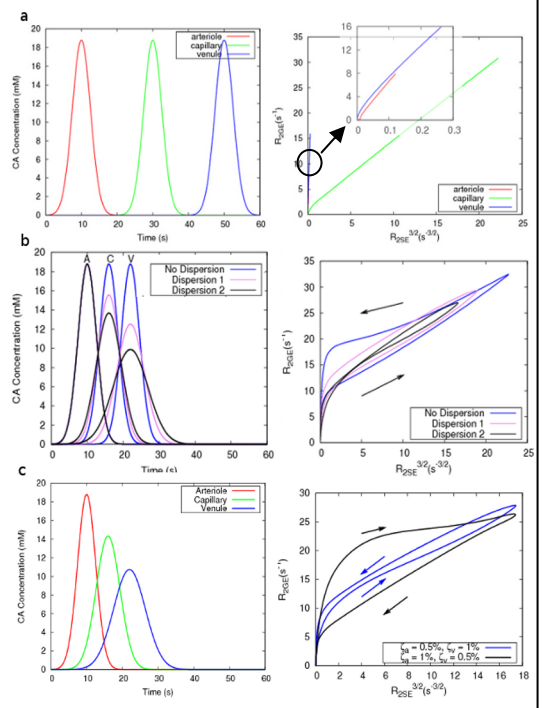

Fig 2. Result of Simulation. a. Individual behaviour of three blood pools. b. Dispersion affects the loop area. A,C,V stand for arteriole, capillary and venule pool separately. c. Arterial and venous contribution affects the direction of the loop. ζ_a is the arterial blood volume fraction, ζ_v venous blood volume fraction

Reference:
[1] Kiselev et. al. (2005) *MRM*
[2] Kiselev (2001) *MRM*