effect of skeletal muscle T1 changes on the determination of perfusion by arterial spin labelling combined to NMR imaging

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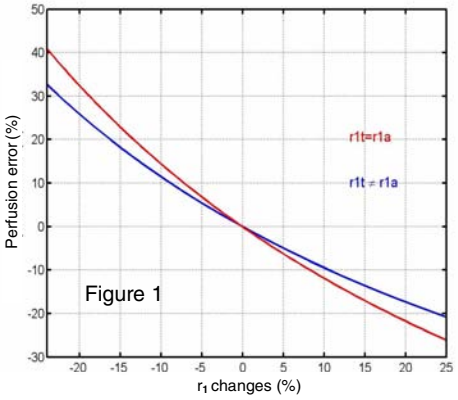
Introduction: Skeletal muscle perfusion can be quantified non-invasively by arterial spin labeling (ASL) combined to NMR imaging. Dynamic testing results in rapid and important changes in perfusion that need a high sampling rate, approximately 1Hz, in order to be properly characterized. This can be achieved with pulsed ASL sequences, such as SATIR developed in our lab, and the acquisitions of pairs of images with a differential labeling. In contrast with other ASL techniques that actually measure the apparent changes in T1 brought in by perfusion but with long acquisitions time incompatible with the time-courses of the perfusion changes, pulsed ASL measurements with pairs of images at fixed labeling time are based on the assumption that skeletal muscle T1 is known and invariant throughout the experiment. However, it is known that dynamic testing can induce T2 and also T1 changes of the skeletal muscle. In this study, we evaluate the impact of T1 changes on the determination of skeletal muscle perfusion with such pulsed ASL sequences when T1 changes are neglected. We also measured the actual T1 changes during reactive hyperemia in a mouse model and corrected the calculated perfusion curves for these changes.

Modelisation: Assuming that blood and muscle tissue could have different relaxation rates, we can consider the following expressions of the magnetisation in the Slice-Selective (SS) and the Non-Selective (NS) images of a pulsed ASL SATIR experiment: $M_{SS}=M_0[1-\exp(-(r_{1t}+f/\lambda)t)]$ et $M_{NS}=M_0[1-(1-2/(r_{1t}+r_{1a}+f/\lambda).\exp(-(r_{1t}+f/\lambda)t)-2/(r_{1t}+r_{1a}+f/\lambda).f/\lambda.\exp(-t/r_{1a})]$, with r_{1t} and r_{1a} the longitudinal relaxation rates of tissue and blood, λ the blood/tissue partition coefficient and f the tissue perfusion. Then, assuming that r_{1a} and r_{1t} are close enough to be considered identical and that r_{1t} is invariant during the experiment allows an analytical expression for f: $f=-\lambda/T_{ev}.\ln[(M_{SS}-M_{NS})/(M_{SS}+M_{NS}).(1-\exp(r_1.T_{ev}))+1]$. To evaluate how ignored changes in r_{1t} value could affect perfusion quantitation by SATIR-NMRI, we can simulate M_{SS} and M_{NS} with different values of r_{1t} while f is kept constant. We have examined two situations: a)a variation of r_{1t} assuming that $r_{1t}= r_{1a}$ (simplified model), b)a variation of r_{1t} independently of r_{1a} (tissue-arterial model). The sensitivity of SATIR to variations in r_{1t} is then assessed by the relative error on f, with respect to r_{1t} values, when f is calculated with the simplified analytical expression, which does not take into account potential r1t changes (figure 1).

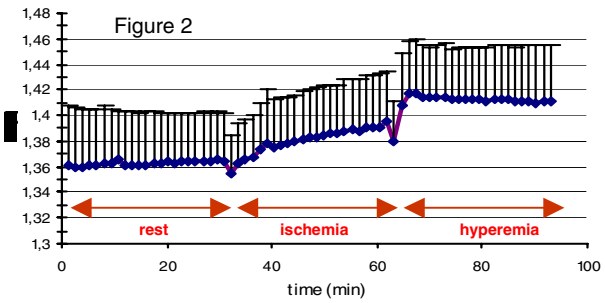


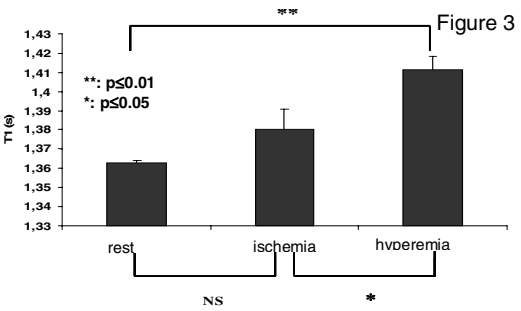
Experiments: Saturation-recovery measurements of T1 and SATIR perfusion imaging measurements were performed in the gastrocnemius muscle of five isoflurane-anesthetised mice during rest (30 min), ischemia (30 min) and reperfusion (30 min). A 4T Bruker Biospec NMR system with a 20 cm diameter 200 mT/m gradient insert was used. SS-FSE sequence parameters were: Tev=1s, TR=8s, TEeff=11.6ms, FOV=5x2cm, Matrix=128x32. Mice were placed supine in a 14 cm long cosine volume coil to allow a whole body tag of the blood and a 8 mm diameter surface coil was used for reception.

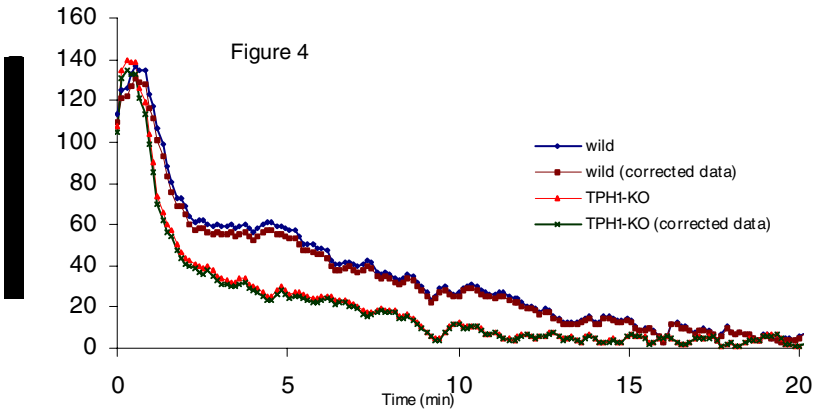
Results and discussion: The simplified model and the arterial-tissue model gave relatively similar results (figure 1) and as expected, the relative error is somewhat lower with the tissue-arterial model. Within the tested range, there is almost a direct proportionality between r1 changes and perfusion relative error.

In the skeletal muscle, the mean rest value of T_1=1,36+/-0,05s was found to increase up to 1,41+/-0,05s at the end of the ischemia and to decrease slowly, remaining at a greater value than at rest after 30 min of perfusion (figure 2). ANOVA statistics (figure 3) show that these values are significantly different, and the model predicts an overestimation of the perfusion values. A correction coefficient has then be defined to improve perfusion measurements accuracy, based on the mean variations of r_1 found in this study. Assuming that T1 changes found in this mouse model could be observed in other models, we applied the correction to a perfusion dataset previously acquired in our laboratory. In the figure 4 are shown the temporal evolution of hyperemic perfusion after 30 min ischemia for two groups of animals with and without correction : Wild type mice and TPH1-KO mice (5HT deficient).

The overestimation induced by the T_{1t} increase during ischemia recovery is minimal. As a consequence, the introduction of correction factors does not modify the conclusion of this physiopathological investigation.







Conclusions: A precise quantitation of skeletal muscle perfusion during dynamic testing requires prior knowledge or actual measurement of the associated T1 changes. However, the error introduced when the relaxation changes are neglected remains very moderate, typically of the order of 10%. When comparing groups or treatments, it is only when the differences in calculated perfusion profiles are low that bias introduced by possible differential T1 changes must be considered.