Simultaneous OEF and Haematocrit assessment using T2 Prepared Blood Relaxation Imaging with Inversion Recovery

Esben Thade Petersen[1,2], Jill De Vis[1], Thomas Alderliesten[3], Karina J Kersbergen[3], Manon Benders[3], Jeroen Hendrikse[1], and C. A. T. van den Berg[2]

[1]*Department of Radiology, UMC, Utrecht, Netherlands,* [2]*Department of Radiotherapy, UMC, Utrecht, Netherlands,* [3]*Neonatology, Wilhemina Children's Hospital, Utrecht, Netherlands*

INTRODUCTION: Oxygen metabolism and the bloods degree of oxygen saturation are important parameters not only for the evaluation of patients such as stroke or asphyxiated newborns but also within neuroscience. Here, information about the oxygen extraction fraction (OEF) is important for the interpretation of the blood oxygenation level dependent effect. Techniques such as TRUST [1] have been developed for measuring T2 of the venous blood and by using a prior known relationship between T2 and the oxygen saturation (Y) the global OEF can be calculated. One caveat of this method is the fact that the T2 versus Y relationship depends on bloods haematocrit (Htc) [2], a parameter which is not always available. In addition, bloods T1 depends on haematocrit [3] and this has implications for perfusion quantification using Arterial Spin Labeling (ASL) which is also an important part in the nutritive supply and metabolism assessment of the brain. In healthy volunteers and most patients under normal conditions, a relative normal OEF and Htc can be assumed. This is however not the case in e.g. the neonatal population, where Htc often is outside the normal adult range (38-46%) [4]. Large variations in the arterial oxygen saturation can also be observed and need to be taken into account when estimating the OEF. Another group is cancer patients undergoing radio- and chemotherapy which can result in altered haematocrit.

In this work we present a robust method which simultaneously measures T1 and T2 of the venous blood using a "T2 Prepared Tissue Relaxation Inversion Recovery" (T2-TRIR) sequence from where both OEF and haematocrit can be estimated.

METHODS: The T2-TRIR sequence is shown in Fig. 1. In brief, it presaturates the image region (Fig. 2b) after which the longitudinal magnetization is T2 prepared using a standard MLEV preparation [1]. Subsequently, an inversion pulse is applied (Fig. 2b) and multiple readouts at flip angles large enough to saturate the surrounding tissue are performed. The inversion recovery of venous blood, entering the image slice from the superior part of the sagittal sinus, can thereby be measured. The sequence is repeated in groups of 4, each with an effective MLEV TE preparation of 0, 40, 80 or 160 ms. This corresponds to 0, 4, 8 and 16 refocusing pulses using an interpulse time (τ_{CPMG}) of 10ms. In this work the sequence is used for measuring bloods T1 and T2, however the technique works equally well for simultaneous T1 and T2 mapping in tissue, as long a low flip angle Look-Locker readout is used instead.

For fitting bloods T1b and T2b, the signal from the four inversion recovery curves (Fig. 2a) were fitted simultaneously using:

$M_b(TI) = M_{0b}[1-(1.0+e^{-\frac{eTE}{T_{2b}}} \cdot IE) \cdot e^{-\frac{TI}{T_{1b}}}]$ where TI is the inversion times, M_{0b} is bloods equilibrium magnetization, eTE, the effective MLEV echo time, and IE is the inversion efficiency. Magnetization is allowed to fully recover between repetitions. Estimation of Htc was done using the equation in Fig. 6 of [3] and subsequently OEF by the use of eq.1 in [2].

Four healthy volunteers and 5 neonates were scanned (3T Philips Achieva) using T2-TRIR according to institutional guidelines. The scan parameters were: TR/TE/ΔTI/TI1=15000/20/150/130ms, phases=60 160x160 matrix, FOV=240x240 or 160x160 for neonates, flip-angle=95°, 2mm slice, SENSE=2.5 and eTE=0,40,80 and 160ms. Total scan time 2:15.

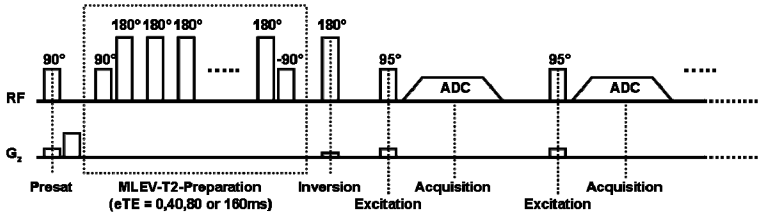

Figure 1. Sequence for simultaneous T1 and T2 blood measurements. The sequence is repeated 4 times, each with a different T2-preparation, resulting in effective TEs of 0,40,80 and 160ms.After the T2-prep, inversion of the blood in the sagittal sinus region followed by multiple readouts allows acquisition of four different inversion recovery curves from where venous blood T1 and T2 can be estimated.

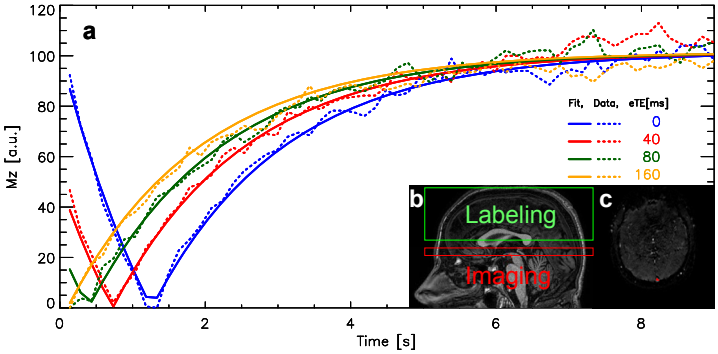

Figure 2. a) *Single voxel example fit to the four inversion recovery curves with effective echo times of 0,40,80 and 160ms respectively. The difference in T2 preparation gives rice to four sufficiently different recovery curves which allows for robust fitting of both T1 and T2 simultaneously. The blood inversion recovery arises from the inversion of venous blood, while sampling at multiple inversion times* ***(b)****. Repeated and appropriately spaced acquisition at a high flip angle ensures saturation of surrounding tissue while allowing only "fresh" blood to be imaged. Automatic localization of the sagittal sinus* ***(c)*** *can be done using the later phases where blood signal is high and static tissue suppressed. The current fit results in a T1 of 1.71s, T2 of 56ms which can be translated into a haematocrit of 43%, a venous oxygen saturation of 59% and an oxygen extraction fraction of 40%.*

Table 1.*(H=Healthy Adult, N=Neonatal Patient, Values in brackets were assumed)*

Subject	T1 [s]	T2 [ms]	T1-Htc [%]	Htc [%]	Oxy.Sat. [%]	OEF [%]
1 (H)	1.66	63	47	-	(98)	34
2 (H)	1.71	50	43	-	(98)	43
3 (H)	1.68	58	45	-	(98)	37
4 (H)	1.65	65	47	-	(98)	37
5 (N)	1.80	75	37	-	93	30
6 (N)	1.71	42	43	40	86	44
7 (N)	1.78	80	38	42	89	23
8 (N)	1.89	92	32	-	94	29
9 (N)	1.92	93	31	29	88	25

RESULTS and DISCUSSION: Figure 2a shows an example fit to a single voxel in the sagittal sinus, typically 5-10 voxels are averaged for the final result. The region of interest is automatically extracted (Fig.2c) and the least noisy fits from within that region are chosen. Table 1 shows the corresponding T1, T2, Htc and OEF estimated from the healthy volunteers as well as the neonates. Oxygen saturation using pulse oximetry and Htc from blood samples was also available in some of the neonates. The observed values are in line with literature values and separate T1 and T2 mapping using the techniques from [1] and [3] (data not shown), indicating that robust T1 and T2 mapping in blood is possible within 2:15 min. This is crucial for correcting perfusion estimates using ASL in neonates and possibly cancer patients, while at the same time gathering information about the global OEF. Global metabolic rate of oxygen can be estimated by combining the technique with full brain ASL or velocity mapping of the feeding vessels.

CONCLUSION: A robust T1 and T2 tissue mapping method has been developed and when applied on the venous blood it allows for non-invasive assessment of both haematocrit and OEF simultaneously. Further validation work is ongoing in healthy subjects using a reactivity challenge as well as in neonates where it is compared to near infrared spectroscopy and blood drawn heamatocrit. However these initial results pinpoints the heterogeneity of T1 (Htc) and T2 (OEF) in neonates as compared to adults which necessitates mapping of bloods T1 e.g. to correct cerebral blood flow quantification using ASL or for calibrating the OEF estimate.

REFERENCES: [1] Lu H et al, MRM 2008;60:357-63 [2] Lu H et al, MRM 2011 (Online) [3] Varela M et al, NMR Biomed 2011;24:80-88 [4] Lu H et al, JMRI 2004;52:679-82

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