Non-invasive assessment of Cerebral Metabolic Rate of Oxygen in neonates.

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Introduction
Preterm birth has a worldwide incidence of 9.6%. Of these infants, 25-50% develops cognitive deficits and 5-10% motor deficits. White matter disease plays an important role here. Underlying pathogenic mechanisms are hypoxia-ischemia or hyperoxia. For optimal titration of oxygen supply, one should be able to measure Cerebral Metabolic Rate of Oxygen (CMRO2).

In addition, there may be a relation between CMRO2 and tissue viability after an ischemic event such as perinatal arterial ischemic stroke or asphyxia. Positron Emission Tomography (PET) has been used to evaluate CMRO2 in neonates. However, the invasiveness of this approach urges the need for a non-invasive technique to assess CMRO2. Recently, MR techniques have been developed which enable measurement of oxygen extraction fraction (OEF)1-7. Here we propose a combined approach of OEF-and perfusion measurements to obtain estimates of CMRO2 non-invasively. The T2 Prepared Blood Relaxation Imaging with Inversion Recovery (T2-TRIR) sequence2 was used to measure the OEF and brain perfusion was measured with Arterial Spin Labeling (ASL) MR imaging. Preliminary results are shown and compared to the existing literature. In addition, CMRO2 was measured in infants with asphyxia.

Materials & Methods
MR Imaging was performed in line with institutional guidelines (3T, Philips). Subject characteristics of the 11 included neonates are given in Table 1. Scan parameters of the pulsed ASL experiment were; matrix 40x40, FOV 240x240 mm, SENSE=2.5, voxel 3x3x6mm, gap 1mm, TR/TE/TI: 2500/20/1500ms, Q=4, TIPS 600 ms and scan time 3:00. Scan parameters of the T2-TRIR sequence were; TR/TE/AT/ATI: 1500/20/150/130 ms, matrix 128x128, FOV 160x160, FA 95°, 2mm slice, SENSE=2.5, eTE=0,40,80 and 160ms and scan time 2:15. Perfusion was quantified on the ∆M images of the ASL scan3. The longitudinal relaxation rate of blood (T1b) and the transverse relaxation rate of blood (T2b) were fitted from the four inversion recovery curves obtained in the superior sagittal sinus with the T2-TRIR sequence, using the formula: M0(TI) = M0 [1-(1.0 + e^(-T1b/TE) ) e^(-T2b/TI)] and the hematocrit (htc) was estimated: 1/T1b = 0.50 × Htc + 0.37°. Subsequently, venous oxygen saturation (Yv) was estimated from the T2b and htc1 (Figure 1). Arterial oxygen saturation (Ya) was measured using pulse oximetry. Finally, OEF and CMRO2 were calculated: OEF= ((Ya-Yv)/Ya).100 and CMRO2 = CBF (Ya-Yv) × Ca, with Ca = 1.89596. 0.1. Htc5.

Results
Subjects were divided into 3 categories, characteristics are shown in Table 1. For all categories mean cerebral blood flow (CBF), OEF and CMRO2 are shown. Extracted oxygen fraction was on average lower in the asphyxiated infants compared to infants imaged at term age. Cerebral blood flow in both groups was comparable, resulting in a lower oxygen metabolism in the infants diagnosed with asphyxia.

Discussion
A non-invasive approach to assess hemodynamic parameters and in particular CMRO2 in a vulnerable patient population is presented. Cerebral blood flow in neonates has earlier been shown to be low, our results obtained with ASL MR imaging are in line with this. In addition, OEF seems to be realistic. In the past, CMRO2 in neonates has been measured with PET. Values ranging from 2.7 to 24 μmol/100g.min in preterm infants and 0 to 58 μmol/100g.min in infants imaged at term age were shown. Our values are in the higher end of these ranges. Recently, Lu H et al presented another non-invasive approach to measure CMRO2. In their work, TRUST MRI estimates of OEF were combined with perfusion estimates based on volume-flow measurements obtained with phase-contrast MR angiography. A mean CMRO2 of 18.4 μmol/100g.min was measured. We seem to find higher CMRO2 values although we have to point out that our study population is rather small. Interestingly, in our results we find lower oxygen metabolism in asphyxiated infants which opens the door to implementation of this approach in clinical studies.

Conclusion
Non-invasive assessment of CMRO2 in neonates may yield important clinical information especially in neonates with asphyxia or stroke.

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References