# Temporal Evolution of Cerebral Oxygen Extraction Fraction Using MRI in a Middle Cerebral Artery Occlusion Stroke Rat Model

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## Introduction

It has been suggested that the balance between oxygen delivery, indicated by cerebral blood flow (CBF) and oxygen demand, reflected by oxygen extraction fraction (OEF) is of critical importance in determining the status of tissue viability during acute cerebral ischemia (1). Beyond the threshold for cerebrovascular autoregulation, a reduction in cerebral perfusion pressure (CPP) results in decreased CBF, accompanied by an increase in OEF in order to maintain a normal cerebral oxygen cerebral metabolic rate of oxygen utilization ($CMRO_2$) and neuronal function. At maximal oxygen extraction, any further reduction in CBF results in a decline of $CMRO_2$, leading to a cascade of cellular events that inexorably progresses to neural cell death. Therefore, a non-invasive means to assess cerebral oxygenation status in vivo may be potentially useful in delineating the ischemic tissue viability. It has been demonstrated that both T2* and T2 can be utilized to indirectly reflect the change of tissue oxygenation (2, 3). Recently, we have demonstrated that OEF can be obtained based on T2* (T2') BOLD contrast in normal human subjects under normocapnia and hypercapnia (4, 5). In this study, a similar approach is utilized in a middle cerebral artery occlusion (MCAO) rat model to gauge the temporal evolution of brain tissue oxygenation under acute cerebral ischemia.

## Materials and Methods

In total, five male Long Evans rats weighting 250-300 g were studied. The rats were anesthetized using isoflurane mixed with medical air and oxygen (5% and 1.5% isoflurane for induction and maintenance, respectively). Cerebral ischemia was induced using the suture model while rats were inside the magnet bore. All animal protocols were approved by the Institutional Animal Research Committee of the University of North Carolina at Chapel Hill. All images were acquired on a Siemens 3T Allegra head only scanner (Siemens Medical Inc., Erlangen, Germany) with a maximum gradient strength of 40 mT/m and a slew rate of 400 mT/msec. A small animal birdcage coil (Nova Medical Inc., Ma. USA) was used as the transmit/receive coil. A two-dimensional multi-echo asymmetric spin echo/spin echo sequence (MEGESE) with was utilized to obtain estimates of R2*, R2, R2', vCBV and OEF (3). Apparent diffusion coefficient (ADC) maps was obtained from segmented EPI diffusion weighted images (DWI) with b=0 and 1200 s/mm2. Acquisition time of MEGESE and DWI sequences were about five minutes each. MEGESE and DW images were acquired prior to MCAO and continued up to three hours post MCAO. A tracer dynamic perfusion weighted imaging (PWI) was utilized to assess CBF deficit at the end of the entire study so as to avoid the contamination of contrast agent induced susceptibility for the oxygenation measurements. Since a permanent MCAO was achieved, CBF should remain constant throughout the entire post MCAO experimental period. T2 images were acquired at 21 to 29 hrs after MCAO to define the final lesion. Data with obvious motion artifacts were excluded from analysis. ROIs were defined in both ipsilateral and contralateral hemisphere to obtain percent ADC, ΔR2*, ΔR2, ΔR2' and OEF changes.

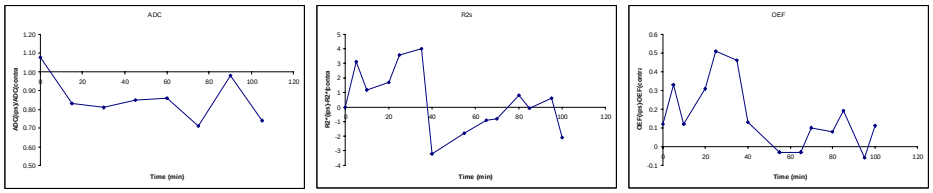


Figure 1. Representative temporal evolution of ADC (left), R2* (middle) and OEF (right) changes between ipsilateral and contralateral ROIs from one rats. The x axis is time in minutes. ADC change is presented as ADC(ipsilateral)/ADC(contralateral), R2* change is R2*(ipsilateral)-R2*(contralater) in Hz and OEF change is OEF(ipsilateral)-OEF(contralater).

## Results

In all five rats, before MCA occlusion, ADC, R2*, R2, R2' and OEF were not statistically different in the ipsilateral and contralateral hemisphere ROIs. Immediately after MCAO, ADC reduced, while both R2* and OEF increased. As lesion progresses, the initially elevated R2* and OEF return back to or below the baseline, while the ADC might further decrease or has little change. Representative results from one rat are shown in Figure 1 to demonstrate the ADC, R2* and OEF temporal evolution. The ADC remains low throughout the entire experimental condition. In contrast, an elevation of OEF was observed, reached to a maximum ~20 min after MCAO, persisted for 20min and started to return to the baseline value ~40 min after onset. Importantly, the observed temporal evolution of OEF coincides with that observed for T2*. As shown in Figure 2, the dynamic susceptibility contrast studies reveal that no apparent signal changes were observed in the ipsilateral hemisphere, suggesting that CBF is substantially compromised and the CMRO2 (the product between OEF and CBF) is marked decreased. Therefore, our results suggest that the brain tissue may not be viable as early as 40 min post-MCAO in this rat. This rat died premature (16 hrs after the induction of ischemia), consistent with a severe ischemic injury.

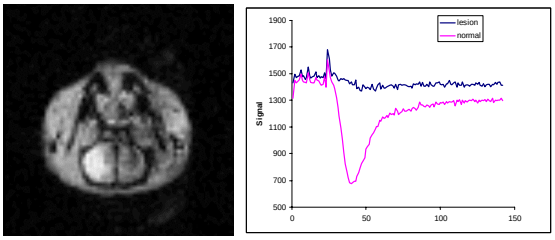


Figure 2. A perfusion image show the entering of contrast agent into brain tissue (left). The hyperintensity region indicates that little signal change was induced by contrast agent in lesion. Signal curve from lesion and contralateral brain region was plotted (right).

## Discussion and Conclusion

With a multiple echo gradient echo and spin echo approach, we have demonstrated that quantitative measures of OEF can be obtained. With a MCAO rat model, our results demonstrate the temporal biphasic behavior of OEF with an initial increase and followed by a returning toward baseline values, consistent with the reported results in the literature using PET (6). In addition, given the fact that quantitative measures of CBF are readily available using MRI, the combination of OEF and CBF allow a direct measure of CMRO2, which offer a direct means to assess brain viability during acute ischemia.

## References

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