Two-photon microscopy measurement of cerebral metabolic rate of oxygen using periarteriolar oxygen concentration gradients

AUTHOR BLOCK: S. SAKADZIC\textsuperscript{1}, M. A. YASEEN\textsuperscript{1}, R. S. JASWAL\textsuperscript{1}, E. ROUSSAKIS\textsuperscript{2}, A. M. DALE\textsuperscript{3}, R. B. BUXTON\textsuperscript{4}, S. A. VINOGRA DOV\textsuperscript{2}, D. A. BOAS\textsuperscript{1}, *A. DEVOR\textsuperscript{3,1};
\textsuperscript{1}Martinos Ctr. for Biomed. Imaging, MGH/HMS, Charlestown, MA; \textsuperscript{2}Biochem. and Biophysics and Chem., Univ. of Pennsylvania, Philadelphia, PA; \textsuperscript{3}Neurosciences and Radiology, \textsuperscript{4}Radiology, UCSD, La Jolla, CA

Abstract:

Objective. The cerebral metabolic rate of oxygen (CMRO\textsubscript{2}) is an essential parameter for evaluating brain function and pathophysiology. Measurements of CMRO\textsubscript{2} with high spatio-temporal resolution are critically important for understanding how the brain copes with metabolic and blood perfusion changes associated with various clinical conditions, such as stroke, perinfarct depolarizations, and various microvasculopathies (e.g., Alzheimer’s disease, chronic hypertension). CMRO\textsubscript{2} measurements are also
important for understanding the physiological underpinnings of functional Magnetic Resonance Imaging signals. However, the currently available approaches for quantifying CMRO$_2$ rely on complex multimodal imaging and mathematical modeling. Here, we introduce a novel method that allows estimation of CMRO$_2$ based on a single measurement modality - two-photon phosphorescence lifetime microscopy (2PLM) imaging of the partial pressure of oxygen (PO$_2$) in cortical tissue.

**Methods.** We measured the baseline CMRO$_2$ in anesthetized rats, and modulated tissue PO$_2$ levels by manipulating the depth of anesthesia. CMRO$_2$ is estimated by fitting the changes of tissue PO$_2$ around cortical penetrating arterioles with the Krogh cylinder model of oxygen diffusion.

**Results.** Using this method, we obtained a mean baseline CMRO$_2$ of $1.71 \pm 0.16 \mu$mol cm$^{-3}$ min$^{-1}$, within the error bounds of previously reported CMRO$_2$ under similar anesthesia in rats measured by MRI ($2.5 \pm 1.0 \mu$mol cm$^{-3}$ min$^{-1}$) [1]. To experimentally manipulate CMRO$_2$, we modulated the level of anesthesia by applying isoflurane (2%) on top of the ongoing alpha-chloralose anesthesia. Adding isoflurane resulted in the measured CMRO$_2$ decreased from $1.56 \pm 0.07 \mu$mol cm$^{-3}$ min$^{-1}$ (alpha-chloralose only) to $1.38 \pm 0.07 \mu$mol cm$^{-3}$ min$^{-1}$ (combined alpha-chloralose and isoflurane).

**Conclusion.** Our study demonstrates that we can estimate CMRO$_2$ using the Krogh cylinder model based on a single measurement modality - periarteriolar tissue PO$_2$ measurement by two-photon microscopy in a single plane perpendicular to the vessel axis. With this method, no measurements of blood flow are required for the CMRO$_2$ estimation. This method has a spatial resolution of approximately 200 μm and it may provide CMRO$_2$ measurements in individual cortical layers or within confined cortical regions such as in ischemic penumbra and the foci of functional activation.


---

**Presentation Preference (Complete):** Poster Only  
**Nanosymposium Information (Complete):**  
**Theme and Topic (Complete):** I.04.a. Optical methods ; I.04.a. Optical methods  
**Linking Group (Complete):** SilverRed  
**Keyword (Complete):** oxygen metabolism ; oxygen partial pressure ; phosphorescence  
**Support (Complete):**  
  Support: Yes  
  Grant/Other Support: : NIH grant NS091230  
  Grant/Other Support: : NIH grant NS55104  
  Grant/Other Support: : NIH grant NS092986  
  Grant/Other Support: : NIH grant NS057198  
  Grant/Other Support: : NIH grant EB021018  

http://www.abstractsonline.com/cSubmit/SubmitPrinterFriendlyVersion.asp?ControlKey=%7B4652F227%2D2DD9%2D41FF%2DA4E0%2D00499D93F0A0%7D&MeetingActivityKey=%7BA8A513A0%2DDB922%2D...
Grant/Other Support: NIH grant EB00790
Grant/Other Support: NIH grant AG042026
Grant/Other Support: NIH grant EB018464

Special Requests (Complete):
   Would you be interested in being considered for a dynamic poster?: No, I am not interested in presenting a Dynamic Poster
   Is the submitting author of this abstract also a senior author?: Yes

Is the first (presenting) author of this abstract a high school or undergraduate student?: None

Religious Conflict?: No Religious Conflict
   Additional Conflict?: No

Status: Finalized