Proton Imaging of Silanes to map Tissue Oxygenation Levels (PISTOL): a new tool for quantitative tissue oximetry

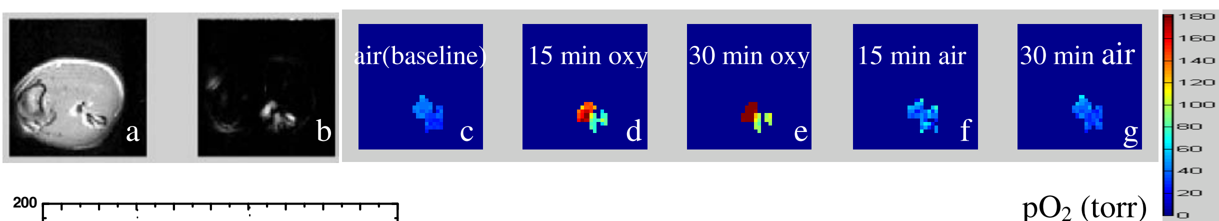
V. D. Kodibagkar[1], R. P. Mason[1]

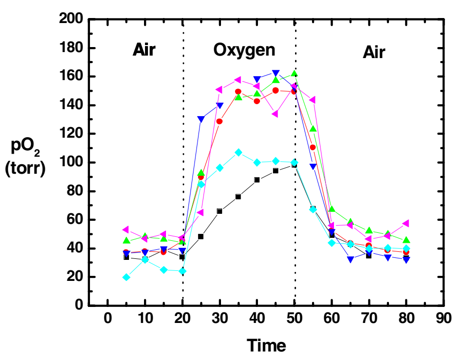
[1]Radiology, UT Southwestern Medical Center at Dallas, Dallas, Texas, United States

Introduction: There is increasing evidence for the importance of tissue oxygenation in development, progression, and response to cancer therapy. Oxygen is required for efficient function by most tissues and hypoxia leads to rapid cellular dysfunction and damage. Thus, the opportunity to measure tissue oxygen tension (pO_2) non-invasively may be significant in understanding mechanisms of tissue function and in clinical prognosis. The potential of hexamethyldisiloxane (HMDSO) as a ^{1}H based pO_2 reporter molecule (by analogy with fluorinated pO_2 reporters) has been previously studied by ^{1}H spectroscopy and linear dependence of R_1 of HMDSO on pO_2 (R_1= 0.12+ 0.00173*pO_2 [torr] at 37°C) was observed (1). We have now extended application to present an imaging based method, PISTOL (Proton Imaging of Silanes to map Tissue Oxygenation Levels), and use HMDSO to map tissue oxygenation in rat thigh muscle in response to oxygen challenge

Materials and Methods: A spin-echo EPI based pulse sequence was used for imaging and measuring T_1 values using a Varian 4.7 T scanner. The sequence consisted of a) 20 non-selective saturation pulses followed by a delay *tau* for magnetization recovery, b) 3 CHESS pulses for selective saturation of water and fat immediately followed by c) spin-echo EPI detection with a slice selective 90° pulse and a frequency selective 180° pulse. T_1 datasets were obtained using this sequence with the ARDVARC (*A*lternating *R*elaxation *D*elays with *V*ariable *A*cquisitions for *R*eduction of *C*learance effects) protocol (2), by varying *tau* (requiring a total of 3 min. per T1 map). Reference images were also obtained using a spin echo sequence. T_1 and pO_2 maps were computed using homebuilt software based on the Matlab programming language.

Results and Discussion:





Monitoring changes in oxygenation of rat thigh muscle in vivo with respect to oxygen challenge. Top: (a) spin-echo image of rat thigh muscle and (b) chemical shift selective spin-echo image of silane injected into thigh muscle, (c-g) *time course* pO_2 *maps (scale: torr) during an air-oxygen-air challenge. Bottom: time-course mean* pO_2 *values in rat thigh muscle during this gas challenge. Imaging reveals different rates and magnitudes of response depending on location.*

PISTOL successfully monitored the modulation of tissue oxygenation in response to oxygen challenge. The short total acquisition time (3 min per pO_2 measurement) reveals dynamic response to oxygen intervention. This study further validates the use of HMDSO as a pO_2 reporter molecule. We believe that PISTOL has great potential for application in the clinic being a proton MRI approach using techniques, which can be implemented on clinical scanners. Lack of toxicity and commercial availability add to the promise of HMDSO as a pO_2 reporter molecule.

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References

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