A Fast Look-Locker Imaging Technique for Quantitative Tissue Oximetry

Rohini Vidya Shankar[1] and Vikram D Kodibagkar[1]
[1]*Biomedical Engineering, Arizona State University, Tempe, AZ, United States*

Introduction: Hypoxia or low oxygen tension (pO_2), commonly observed in tumor cells, leads to tissue damage and dysfunction, and contributes to the malignant progression of solid tumors[1]. Mapping pO_2 non-invasively *in vivo*, using magnetic resonance imaging (MRI), may be vital in the detection, treatment, and surveillence of cancer. Quantitative tissue oximetry studies may facilitate a better understanding of the pathophysiology and prognosis of various diseases, and help to determine the extent of hypoxia in tumors[2]. PISTOL (**P**roton **I**maging of **S**iloxanes to map **T**issue **O**xygenation **L**evels)[3] is a recently-developed oximetry technique that maps the T_1 of administered hexamethyldisiloxane (HMDSO, ^{1}H NMR pO_2 reporter molecule), and hence maps the tissue pO_2 at various locations. The objective of this study was to accelerate PISTOL acquisitions by developing a HMDSO-selective Look-Locker[4] imaging sequence with echo planar imaging (EPI) readout (refered to here as PISTOL-LL) for faster oximetry.

Materials and Methods: All oximetry experiments were conducted on a horizontal-bore Bruker BioSpec® 7 Tesla preclinical MRI scanner housing actively shielded gradients. A cohort of six (n = 6) healthy Fischer F344 rats was used to demonstrate the application of the PISTOL-LL sequence *in vivo*. 50 µL of HMDSO was injected into the left thigh muscle of each rat for the *in vivo* pO_2 experiments. A HMDSO-selective spin echo sequence was initially used to locate the reporter molecule; a cross section through the thigh at the desired slice location was subsequently imaged. To introduce modulation in the tissue oxygenation, the rats were subjected to respiratory challenge by supplying air (~20 min) – oxygen (~30 min) – air (~30 min)[3]. Both the PISTOL (3 min 45 s) and PISTOL-LL (55 s) imaging sequences were run in an interleaved manner, and a set of T_1 datasets was collected every 5 min. Sixteen pO_2 maps were generated for each of the PISTOL and PISTOL-LL sequences over a time interval of ~80 min. All datasets were subsequently processed offline using custom built Matlab fit routines to generate pO_2 maps from the R_1 values.

Results:

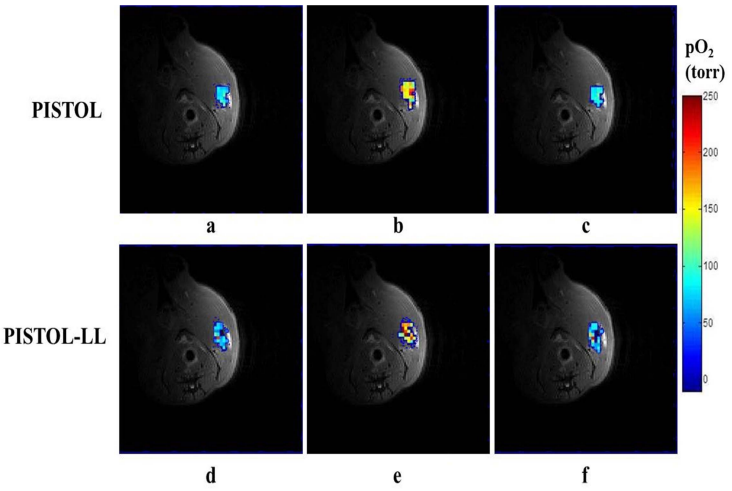

Figure 1: Time course PISTOL (**a, b, c**) and PISTOL-LL (**d, e, f**) pO_2 maps, respectively, in response to gas intervention - Baseline air (**a, d**), after 30 mins O_2 breathing (**b, e**), 30 mins after return to air breathing (**c, f**).

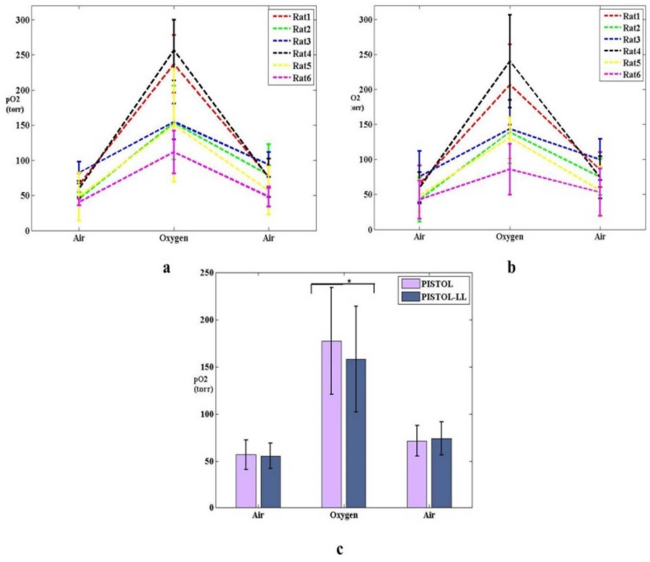

Figure 2: Dynamic changes in rat thigh muscle pO_2 values: (a) PISTOL, (b) PISTOL-LL. (c) Mean pO_2 values for all rats (n=6) over the time course air-O_2-air (*$p<0.05$). The two methods give similar mean pO_2 in air, slight difference under O_2.

Conclusion: PISTOL-LL enabled T_1 and subsequently pO_2 mapping of the HMDSO reporter molecule in under a minute (4X faster than PISTOL) while retaining data fidelity. This is particularly significant as the T_1 of HMDSO ranges from ~2.5 s (160 Torr, hyperoxia) to ~11 s (0 torr, anoxia) at 7T, leading to long scan times in MR oximetry. This sequence can also be used with other siloxanes[5] with shorter T_1s, resulting in even lower scan times and has the potential for adaptability for ^{19}F based oximetry[6] as well.

References: [1] Tatum et al, *Int. J. Radiat. Biol*., 2006; **82**(10): 699-757. [2] Chapman et al, *Radiat Res*, 1991; **126**: 73-79. [3] Kodibagkar et al, *NMR in Biomedicine*, 2008; **21**(8): 899-907. [4] Gowland et al, *MRM*, 1993; **30**(3): 351-354. [5] Gulaka PK et al. *Proc. Intl. Soc. Mag. Reson. Med*., 2010; **18**: 1883. [6] Zhao D et al, *Methods Enzymol*, 2004; **386**: 378–418.