New bullets for PISTOL: linear and cyclic reporter molecules for ^{1}H MR oximetry

P. K. Gulaka[1], and V. D. Kodibagkar[1,2]
[1]Biomedical Engineering, UT Arlington and UT Southwestern Medical Center at Dallas, Dallas, Tx, United States, [2]Radiology, UT Southwestern Medical Center at Dallas, Dallas, Tx, United States

Introduction:

Oxygen is essential for tissue health and survival and is also an important variable in the treatment of many medical conditions including tumors, peripheral vascular disease, and stroke. Therefore, the ability to measure tissue oxygen tension non-invasively may have a significant impact in understanding mechanisms of tissue function and in clinical prognosis of disease. Previous research demonstrated hexamethyldisiloxane (HMDSO) as a ^{1}H based pO_2 reporter molecule by *in vivo* spectroscopy [1] and imaging using Proton Imaging of Siloxanes to map Tissue Oxygenation Levels (PISTOL) technique [2]. Here we investigate linear and cyclic siloxanes of different chain lengths as pO_2 sensing reporter molecules for use in conjunction with PISTOL.

Materials and Methods:

The linear siloxanes used in the study were hexamethyldisiloxane (HMDSO), octamethyltrisiloxane (OMTSO), decamethyltetrasiloxane (DMTSO) and dodecamethylpentasiloxane (DDMPSO) where as the cyclic siloxanes used were octamethylcyclotetrasiloxane (OMCTSO) and decamethylcyclopentasiloxane (DMCPSO). Each of the chemicals were put into four gas-tight NMR glass tubes (Wilmad Taperlok 528SJH; Buena, NJ, USA) and saturated by bubbling for 15 min with varying standard gases including 0%, 5%, 10% and 21%O_2 (balance N_2), respectively. Each sealed tube was wrapped in a D_2O filled circulating water pad maintained at 37^{0}C and fit under a 1 cm i.d. surface coil. A spin-echo-based pulse sequence was used to measure T_1 values. The sequence consisted of an initial pulse-burst saturation recovery (PBSR) preparation pulses combined with frequency-selective excitation of HMDSO. T_1 values were obtained using this sequence with the ARDVARC (alternating relaxation delays with variable acquisitions for reduction of clearance effects) protocol [3].

Compound	Intercept A (s^{-1})	Slope B ($s^*torr)^{-1}$	η ($X10^{-3}$) = B/A	BP (^{0}C)	Relative signal
HMDSO	0.1126	0.0013	11.5	101	1.00
OMTSO	0.1352	0.0014	10.4	153	0.98
DMTSO	0.1808	0.0014	7.7	194	0.97
DDMPSO	0.2129	0.0016	7.5	230	0.97
OMCTSO	0.2842	0.0016	5.6	176	0.91
DMCPSO	0.3192	0.0015	4.7	90	0.91

Table 1: *Summary of calibration constants and boiling points of the compounds used.*

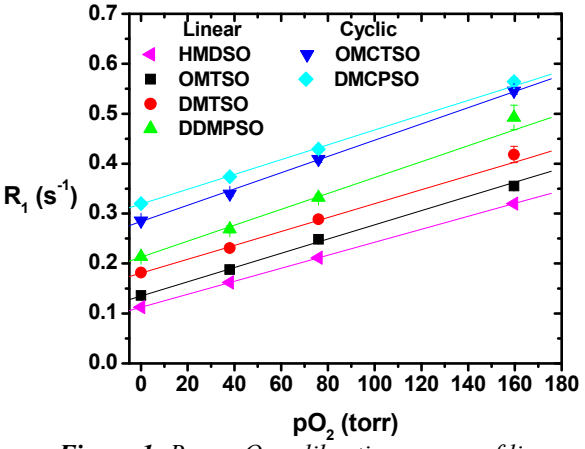

Figure 1: *R_1 vs pO_2 calibration curves of linear and cyclic siloxanes of different chain lengths.*

Results and Discussion:

Molecular oxygen is paramagnetic and it shortens the T_1 of the samples. At a fixed temperature (37°C), the R_1 of all the siloxanes showed a linear dependence on pO_2 (R^2>0.99) given by the equation: R_1 [s^{-1}] = A+ B* pO_2 (torr) where A and B are calibration constants (Table 1) which represent anoxic R_1 and sensitivity of R_1 to pO_2 respectively. In the linear siloxanes it is observed that with increasing chain length, the R_1 of the samples became longer but the slopes of the linear fits were almost similar (Fig. 1). Bi-exponential T_1 behavior was not observed in all the agents suggesting that the availability of oxygen to all the protons (end chain vs backbone) of the long chains was unhindered. Also the agents had a wide range of boiling points, enabling them to be used for different applications. Future studies involve measuring the changes in the calibration curves with changes in temperature and emulsification of these agents.

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References:

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