Rapid monitoring of oxygenation by 19F magnetic resonance imaging : simultaneous comparison with fluorescence quenching

B. F. Jordan[1], G. O. Cron[2], and B. Gallez[1]

[1]Biomedical Magnetic Resonance Unit, Université catholique de Louvain, Brussels, -, Belgium, [2]Magnetic Resonance Imaging, Ottawa Health Research Institute, Ottawa, ON, Canada

Introduction: Methods to determine tumor oxygenation are of crucial importance for the prediction of therapeutic outcome (1). Many current methods are either highly invasive, non quantitative, or lack spatial resolution. Mason et al. have been successfully developing FREDOM MRI (fluorocarbon relaxometry using echo planar imaging for dynamic oxygen mapping) following direct intratumoral injection of the oxygen reporter molecule hexafluorobenzene (HFB) (2). The aim of this study was to develop an MRI fluorocarbon oximetry technique using snapshot inversion recovery (SNAP-IR) and compare it with fluorescence quenching fiber-optic probe oximetry (OxyLite^{TM}) performed simultaneously in experimental mouse tumors.

Materials and Methods: HFB was injected directly into the tumors of TLT bearing mice, along with the insertion of the fluorescent quenching OxyLite^{TM} probe. Tumor pO_2 was modified using carbogen or lethal doses of the anesthetic gas. MRI pO2 maps were generated in 1.5 minutes with an in-plane spatial resolution of 1.88 mm using a SNAP-IR pulse sequence (Bruker, 4.7T with a tunable 1H/19F surface coil). The pulse sequence consisted of a non-selective hyperbolic secant inversion pulse (10 ms length), followed by acquisition of a series of 512 rapid gradient echo images (TR =10.9 ms, TE=4.2 ms, flip angle = 1°, matrix = 32x16, FOV = 60x30 mm, BW = 12.5 kHz, single thick slice [projection]). Calibration of HFB was performed by measuring R_1' in sealed tubes containing HFB respectively bubbled with N_2 (0% O_2), air (21% O_2) and carbogen (95% O_2) for 20 min in a 37° water bath before measurement.

Results:

In vitro data: The respective R1' measurements for HFB in 0, 21, and 95% O2 were 0.105 ± 0.006 s-1, 0.407 ± 0.048 s-1, and 1.56 ± 0.08 s-1 providing a calibration curve of R1' = 0.1048 (± 0.0060) + [0.002000 (± 0.000105)] pO_2 (R1' in s-1 and pO_2 in mmHg). The relation $pO_2 = (R_1' - 0.1048)/0.002$ was used voxel-by-voxel for the remainder of our experiments.

In vivo data: Both MRI and OxyLite^{TM} showed consistent increases in tumor pO_2 during carbogen breathing (Fig.1). However, there was a lack of correlation in the magnitude of response between the two techniques, despite similar baseline and post-mortem values (Fig.2). Color maps show that each region of the tumor responds differently to the respiratory challenge (Fig.3). From the histograms, we observe a clear shift to the right of the median pO_2 value under carbogen breathing conditions (Fig.3).

Discussion:

The SNAP-IR pulse sequence allowed us to sample tumor oxygenation with an effective in-plane spatial resolution (1.88 mm) similar to that of FREDOM (1.25 mm) and with an acquisition time of 1.5 min, which is shorter than that of FREDOM (6.5 min). As the present sequence is more rapid than FREDOM, it could be particularly suitable to monitor acute changes of pO2 in tumors. The quantitative discrepancy might be due to the difference in sampling volumes of the techniques as well as to a 'reservoir' effect of HFB.

Fig.1

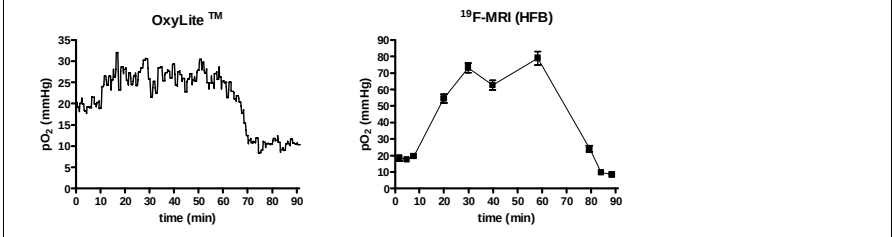

Fig.2

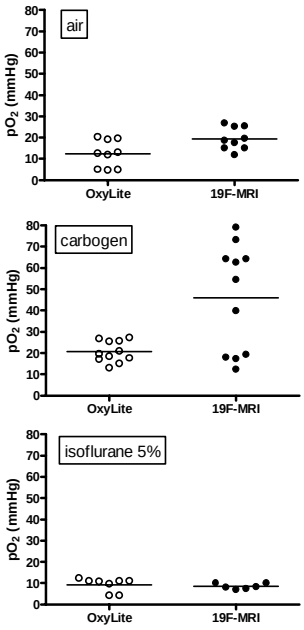

Fig.3

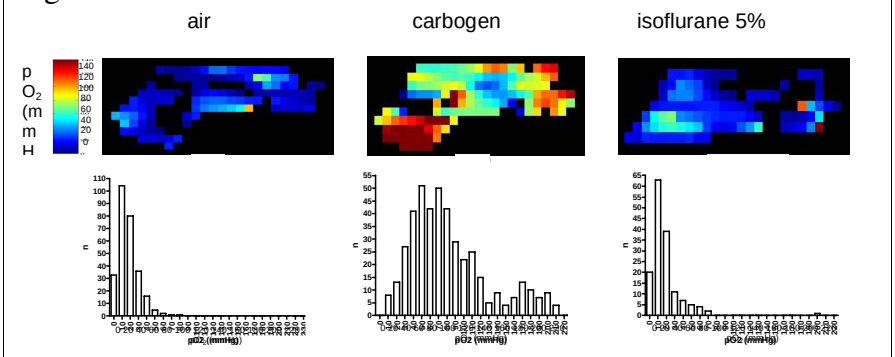

Fig.1 Comparison of the simultaneous monitoring of tumor oxygenation with OxyLite^{TM} (left) and ^{19}F-MRI (right) (typical tumor).
Fig.2 Scatter graphs showing all individual and mean pO_2 values under air, carbogen, and isoflurane 5% breathing conditions.
Fig.3 Typical oxygen maps and histograms of a typical tumor under air, carbogen, and isoflurane 5% breathing conditions.

References: (1) Vaupel P, Harrison L. Oncologist 2004;9:4-9. (2) Hunjan S et al. IJROBP 2001; 49:1097-1108.