Quantitative dynamic 19F MRI oximetry in a phantom simulating hypoxia

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Introduction

Tumor hypoxia is well known to reduce cancer treatment efficacy [1]. Hypoxic tumor cells, which have decreased oxygen levels (pO_2), are more resistant to radiotherapy and chemotherapy. Dissolved oxygen influences the ^{19}F magnetic resonance relaxation times of perfluorocarbons [2]. This property has been used in semi-quantitative animal studies to image tumor oxygenation [3]. In this study a reproducible phantom which mimics oxygen consuming tissue is used for quantitative dynamic ^{19}F MRI oximetry. The phantom consists of a hemodialysis filter of which the outer compartment is filled with a gelatin gel containing viable yeast cells [4]. The gelatin matrix was loaded with perfluorocarbon vesicles to simulate the absorption of perfluorocarbons in tissue from intravenous emulsions.

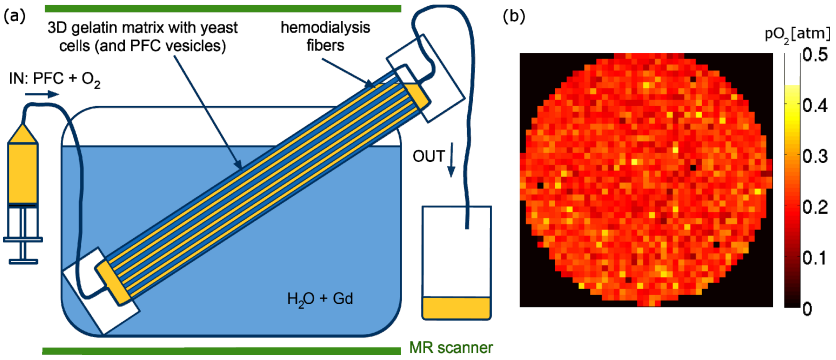

Figure 1 (a) The dialysate compartment of a hemodialysis filter was filled with a gelatin matrix containing viable yeast cells and perfluorocarbon (PFC) vesicles. An oxygen rich PFC was pumped through the fibers of the blood compartment of the hemodialysis filter, using a syringe pump. The entire setup was positioned in a Siemens Trio 3T scanner. **(b)** pO_2-image of a cross-section of a hemodialysis filter. ^{19}F T_1-images, recorded with a fast T_1 sequence, were used to calculate the pO_2-images.

Materials and Methods

A hemodialysis filter (DIAPES® HF800, Membrana GmbH, Wuppertal, Germany; BLS819SD, Bellco S.p.a., Mirandola, Italy) is used to simulate perfused oxygen consuming tissue (fig. 1) [4]. In the hemodialysis filter, the hollow hemodialysis fibers represent blood vessels and the outer compartment, normally used for dialysate fluid, represents tissue. In the fibers of the hemodialysis filter a perfluorocarbon (PFC) with variable concentrations of dissolved oxygen is pumped at variable flow speed, using a standard syringe, to simulate blood flow and oxygen supply.

In the phantom, tissue is simulated by a gelatin gel containing viable yeast cells. The gelatin gel is fabricated by dissolving gelatin (300 Bloom, type A, purchased from Sigma-Aldrich) [3% (w/w)] in tap water at room temperature (approximately 22°C). Fresh yeast cells (Baker's yeast, ALGIST Bruggeman nv., Ghent, Belgium)[2%(w/w)] and glucose (Sigma-Aldrich)[0.08%(w/w)] are dissolved in tap water at room temperature and left for one hour. Perfluorocarbons [40%(w/w)] and tap water are emulsified with the surfactant sodium dodecyl sulfate [0.5%(w/w)]. After heating the gelatin solution to 45°C in order to obtain a sol and successive cooling down to 35°C, the yeast solution and perfluorocarbon emulsion are added.

The perfluorocarbon hexafluorobenzene (HFB)(Fluorochem, Old Glossop, Derbyshire, UK), used in this study, has the advantage that it has a single ^{19}F resonance frequency [3]. The dependence of the longitudinal relaxation time T_1 on oxygen concentration and temperature has been studied extensively in pure HFB samples [5].

For T_1-imaging, a fast 2D Look-Locker imaging sequence [6] has been implemented on a 3T clinical MR scanner (Siemens Trio). In this sequence, an inversion pulse is followed by 32 read out blocks with small flip angle excitation pulses. Each group consists of 16 excitation pulses probing different k-space lines. One T_1-image, with a resolution of 0.94 mm in-plane and 10 mm out of plane, is acquired in 4 minutes.

Results and discussion

Figure 2 shows the evolution of mean pO_2 in a ROI in phantoms during the application of an inflow of oxygen rich HFB. In a first experiment, no PFC vesicles were added to the gelatin matrix (figure 2a). Here, pO_2 increases with increasing oxygen inflow to reach an equilibrium when oxygen supply and consumption balance. Afterwards, pO_2 drops back to a hypoxic level. When PFC vesicles are added to the gelatin matrix (figure 2b), pO_2 starts to increase when the oxygen rich HFB reaches the ROI and continues to increase throughout the experiment. The high pO_2, both at the beginning and at the end of the experiment, indicates the difficulties of the yeast to consume the oxygen dissolved in the PFC vesicles in the gelatin matrix.

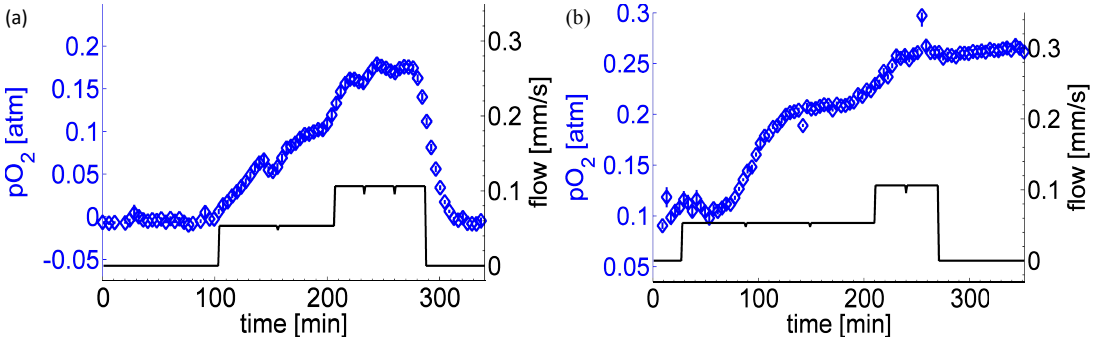

Figure 2 (a) Time evolution of oxygen tension pO_2 in a ROI in the phantom (◊, left axis) in reaction to the inflow of oxygen rich HFB at different flow speeds (-, right axis) in the fibers of the phantom. In **(b)** PFC vesicles, simulating absorbed PFC emulsions in tissue, were added to the gelatin matrix in the phantom.

Conclusion

Quantitative dynamic ^{19}F MRI oxygen measurements of a phantom simulating living vascularized tissue are presented. The phantom consists of a hemodialysis filter of which the outer compartment is filled with a gelatin matrix containing viable yeast cells. Perfluorocarbon vesicles are added to the gelatin matrix to simulate the absorption in tissue of perfluorocarbons from intravenous emulsions. Quantitative dynamic pO_2-measurements in phantoms are shown illustrating the oxygen consumption by the yeast cells in the phantoms during a constant inflow of oxygen. The presented experimental setup can be used to simulate oxygen consumption by somatic cells in vivo and for validating computational biophysical models of hypoxia, as measured with dynamic ^{19}F MRI oximetry.

References

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