An oxygen consuming phantom for simulating oxygen perfusion in tissue using ^{19}F MRI oximetry

S. H. Baete[1,2], and Y. De Deene[1,2]

[1]1Laboratory for Quantitative Nuclear Magnetic Resonance in Medicine and Biology, ECNURAD, Ghent University, Ghent, Oost-Vlaanderen, Belgium, [2]Medisip-IBBT, Ghent University, Ghent, Oost-Vlaanderen, Belgium

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 animal studies to image tumor oxygenation [3]. However, validation of pO_2-measurements in vivo is difficult. In this study a reproducible phantom, simulating well perfused oxygen consuming tissue, is presented. The phantom consists of a hemodialysis filter of which the outer compartment is filled with a gelatin matrix containing viable yeast cells.

Materials and Methods

A hemodialysis filter (DIAPES® HF800, Membrana GmbH, Wuppertal, Germany; BLS819SD, Bellco S.p.a., Mirandola, Italy) is used in this study to simulate oxygen consuming tissue which is perfused (fig. 1). 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, using a standard syringe, to simulate blood flow and oxygen supply.

The tissue itself 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) [4% (w/w)] in tap water [90% (w/w)] 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 [3.92% (w/w)] at room temperature and left for one hour. After heating the gelatin solution to 45°C in order to obtain a sol and successive cooling down to 35°C the yeast solution is added.

The perfluorocarbon hexafluorobenzene (HFB)(Fluorochem, Old Glossop, Derbyshire, UK), used in this study, has the advantage that it has only one ^{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 [4].

For T_1-imaging a fast 2D Look-Locker imaging sequence has been implemented on a 3T clinical MR scanner (Siemens Trio) [5]. In this sequence, an inversion pulse is followed by 32 groups of small flip angle read out pulses. Each group consists of 8 read out pulses probing different k-space lines. One T_1-image, with a resolution of 1.6 mm in-plane and 10 mm out of plane, is acquired in 4 minutes.

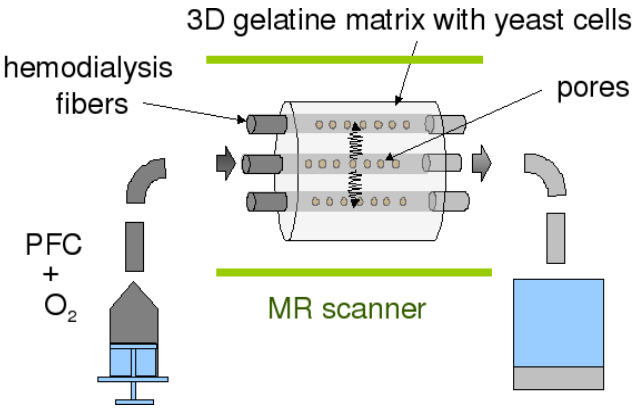

Figure 1: The dialysate compartment of a hemodialysis filter was filled with a gelatin matrix containing viable yeast cells. An oxygen rich perfluorocarbon (PFC) was pumped through the fibers of the blood compartment of the hemodialysis filter, using a syringe. The entire setup was positioned in a Siemens Trio 3T scanner.

Results and discussion

The evolution of the phantom after injecting a bolus of oxygen rich HFB in the fibers is shown in figures 2 and 3. pO_2-images of a cross-section of the hemodialysis filter at subsequent times show the distribution of the oxygen rich HFB over the hemodialysis filter volume (fig. 2). The HFB preferentially flows through the central fibers. After the injection of the oxygen rich HFB the yeast cells in the phantom start consuming oxygen and in a time span of one hour the oxygen levels drop to a hypoxic level (fig. 3). The phantom, presented in this study, can be used in a wide range of applications to simulate living vascularized tissue for validating ^{19}F-oximetry.

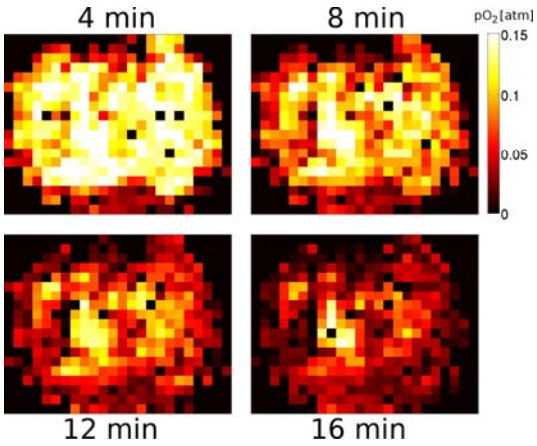

Figure 2: pO_2-images of a cross-section of a hemodialysis filter at four subsequent times post O_2-injection. ^{19}F T_1-images, recorded with a fast T_1 sequence on a 3T scanner, were used to calculate the pO_2-images.

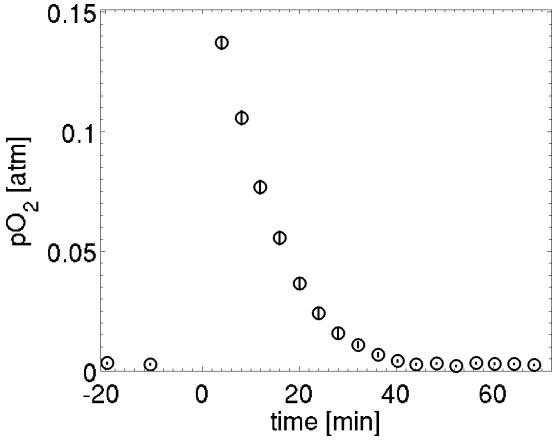

Figure 3: Time evolution of pO_2 of a ROI in the hemodialysis filter. At time 0 a bolus of oxygen rich hexafluorobenzene was injected in the blood compartment of the filter.

Conclusion

A phantom designed to simulate living vascularized tissue is presented. The fibers in the hemodialysis tissue represent blood vessels while the addition of viable yeast cells to a gelatin gel permits the simulation of oxygen consuming tissue. Transverse pO_2-images of the phantom are shown illustrating the oxygen consumption by the yeast cells in the phantom after injection of a bolus of hexafluorobenzene. The phantom can be used to simulate oxygen consumption by somatic cells in vivo and for validating ^{19}F-oximetry.

References

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