^{19}F MRI oximetry in a phantom simulating oxygen consuming perfused tissue

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I. 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.

II. ^{19}F MRI oximetry

One of the parameters which can be measured quantitatively with magnetic resonance imaging (MRI) is the spin-lattice relaxation rate R_1. The spin-lattice relaxation rate R_1 ($R_1 = 1 / T_1$) of perfluorocarbons is sensitive to changes in oxygen tension pO_2 [4] :

$$R_1 = a_1 + a_2 T + a_3 pO_2 + a_4 T\, pO_2 \quad (1)$$

with a_i calibration constants, T the temperature (°C), pO_2 the oxygen pressure (%atm) and R_1 in s^{-1}. Consequently, pO_2-maps can be calculated from R_1 images with equation (1).

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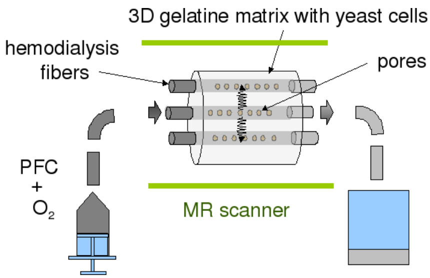

Figure 1. Schematic of a phanthom for the validation of ^{19}F MRI-oximetry methods. The phantom consists of a hemodialysis filter placed in an MR-scanner and an automated syringe pump. The outer compartment of the filter is filled with a gelatin matrix containing viable yeast cells simulating oxygen consuming tissue. The pump is used to circulate a blood substituting fluid through the lumen of the fibers.

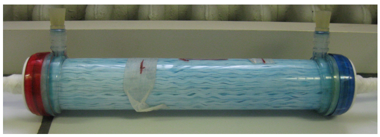

Figure 2. Side view of a hemodialysis filter.

III. Phantom

A hemodialysis filter (DIAPES® HF800, Membrana GmbH, Wuppertal, Germany) is used in this study to simulate oxygen consuming tissue which is perfused (fig. 1, 2). 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 is pumped, using a

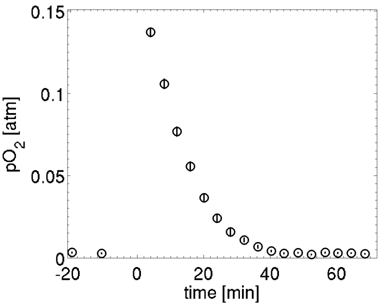

Figure 3. Time evolution of oxygen tension pO_2 in a roi in the phantom following the injection of a bolus of oxygen rich hexafluorobenzene in the inner compartment of the phantom.

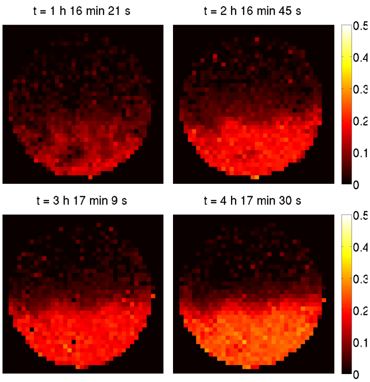

Figure 4. Oxygen tension pO_2-images (pO_2 in atm) of a cross-section of the phantom at four subsequent times during the application of an in-flow of oxygen rich hexafluorobenzene in the inner compartment of the phantom.

syringe pump, to simulate blood flow and oxygen supply. Perfluorocarbon (hexfluorobenzene, HFB; Fluorochem UK) oxygen concentrations can be varied. The tissue itself is simulated by a gelatin gel containing viable yeast cells.

IV. Results and Discussion

The evolution of the oxygen level in the phantom after injecting a bolus of oxygen rich HFB in the fibers is shown in figure 3. 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 back to a hypoxic level (fig. 3). Figure 4 shows pO_2-images of a cross-section of the hemodialysis filter. These images illustrate the distribution of oxygen rich HFB over the hemodialysis filter volume during the application of an inflow of oxygen rich HFB in the inner compartment of the phantom (see fig. 1). The hexafluorobenzene, having a higher density than water, preferentially flows at the bottom of the dialysis filter.

V. Conclusions

Tumor areas with decreased oxygen concentrations (hypoxic tissue) are more resistant to therapy. Identification of hypoxic tumor tissue may improve cancer treatment. The oxygen levels in tissue can be imaged in a non-invase way by ^{19}F-oximetry. The phantom, presented in this study, can be used to simulate living vascularized tissue for validating ^{19}F-oximetry. In this phantom, 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. A steady in-flow of oxygen rich perfluorocarbons simulates blood flow.

Acknowledgments

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