Assessing Tissue Oxygen Response to Radiation Therapy Using Spatially-Resolved Oxygen-Enhanced MRI

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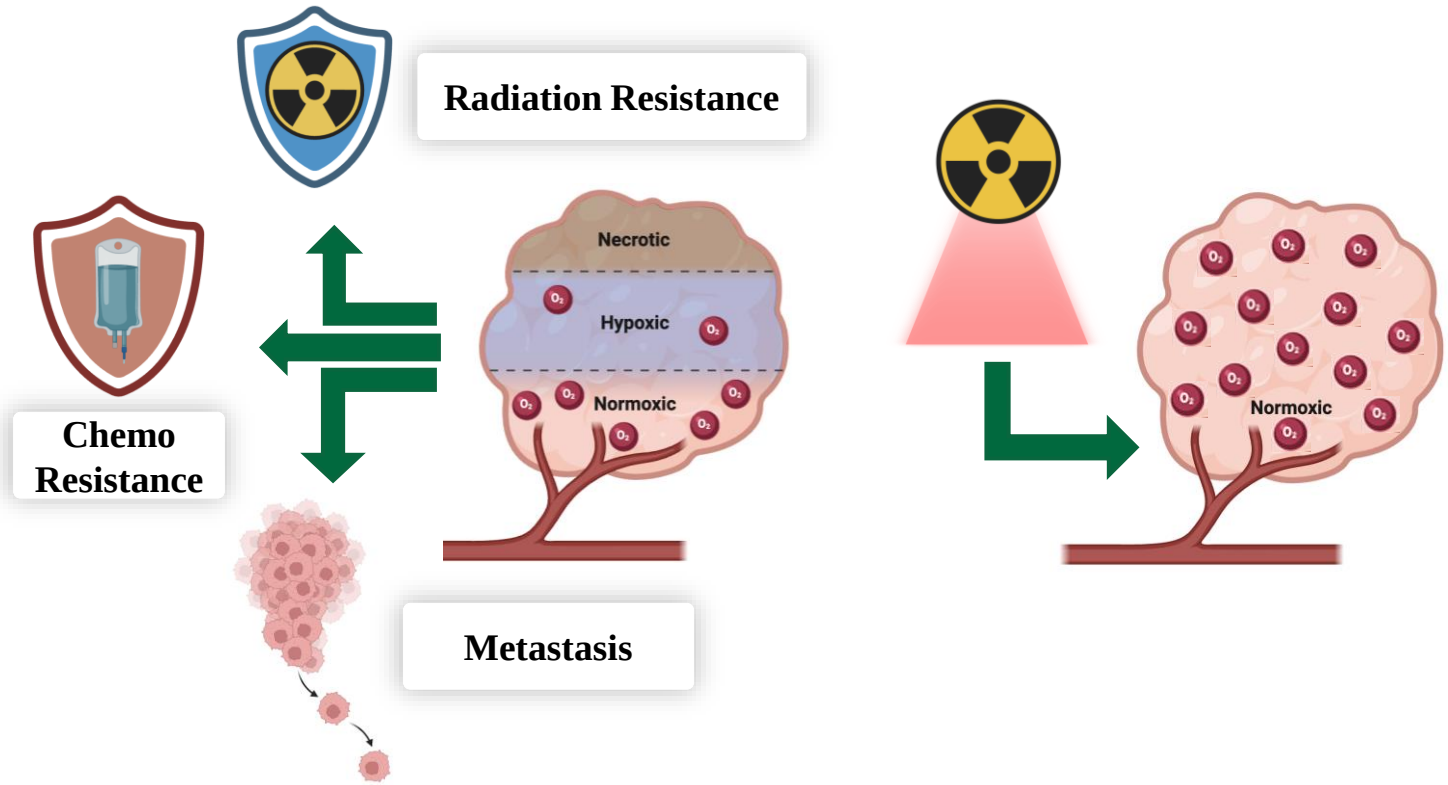
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Disclosure

I have no conflicts of interest to disclose.

Hypoxia is a Significant, Unmeasured Barrier to Effective RT

- Tumor hypoxia mediates resistance to radiotherapy
- Effective radiation treatment results in decreased tumor hypoxia



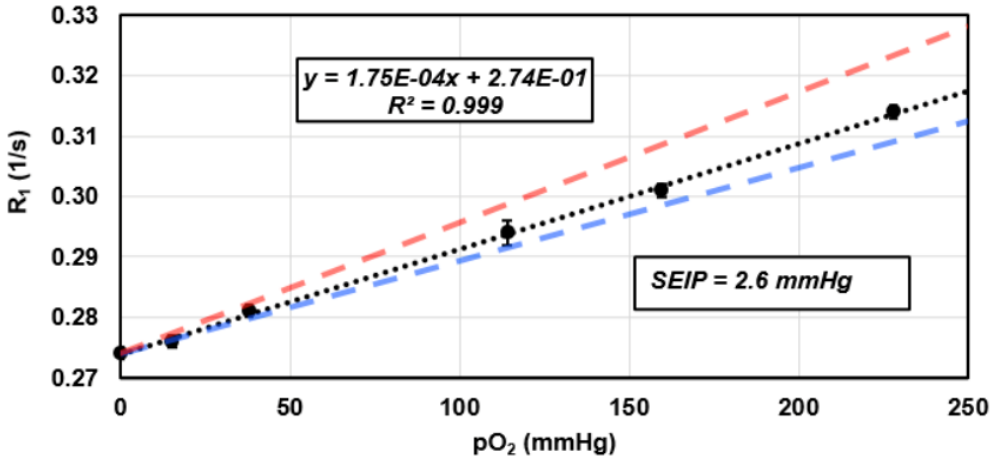
Opportunity
Assessing tumor oxygenation before, during, and after treatment could inform adaptive strategies.

Goal
To identify whether Oxygen-Enhanced MRI can be used for spatially-resolved tumor oxygenation response monitoring during radiation therapy.

Oxygen-enhanced MRI (OE-MRI)

Longitudinal relaxation rate ($R_1 = 1/T_1$) is proportional to pO_2 in water

Linearity of R_1 vs. pO_2 at 9.4T in H_2O



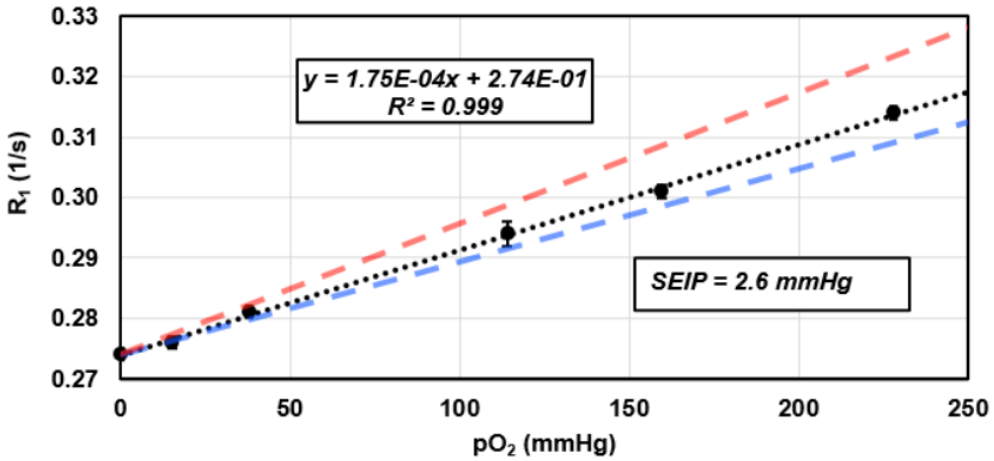
Relaxation Rate vs. pO_2 ⟶ $R_{1,ox} = R_{1,0} + C \cdot r_{1,ox}$

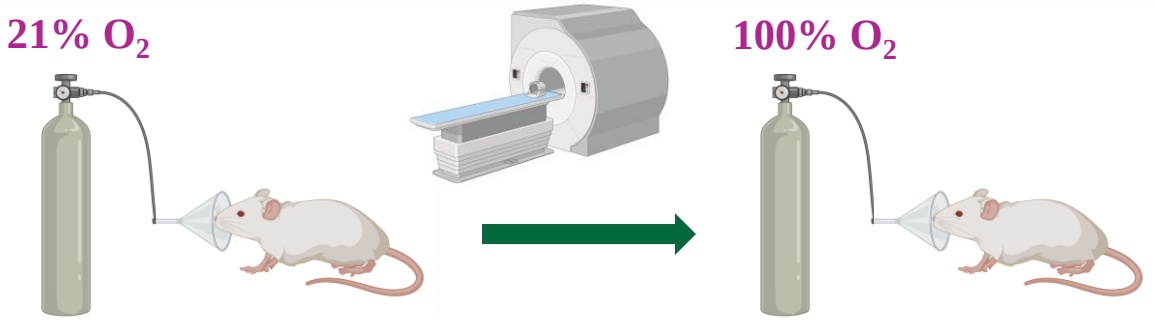
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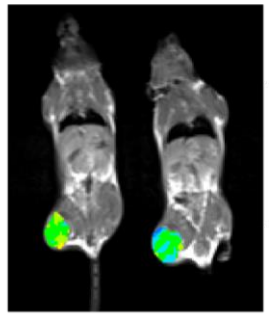
Longitudinal relaxation rate ($R_1 = 1/T_1$) is proportional to pO_2 in water

ΔR_1 in tissue: Surrogate marker for oxygenation capacity
The measured change in R_1 induced after administration of hyperoxic gas is proportional to the change in tissue pO_2 concentration.

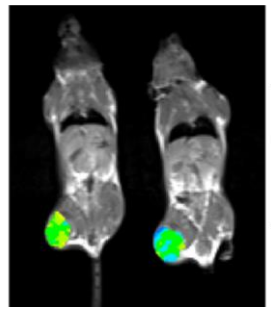
Linearity of R_1 vs. pO_2 at 9.4T in H_2O







R_1(21%)



R_1(100%)

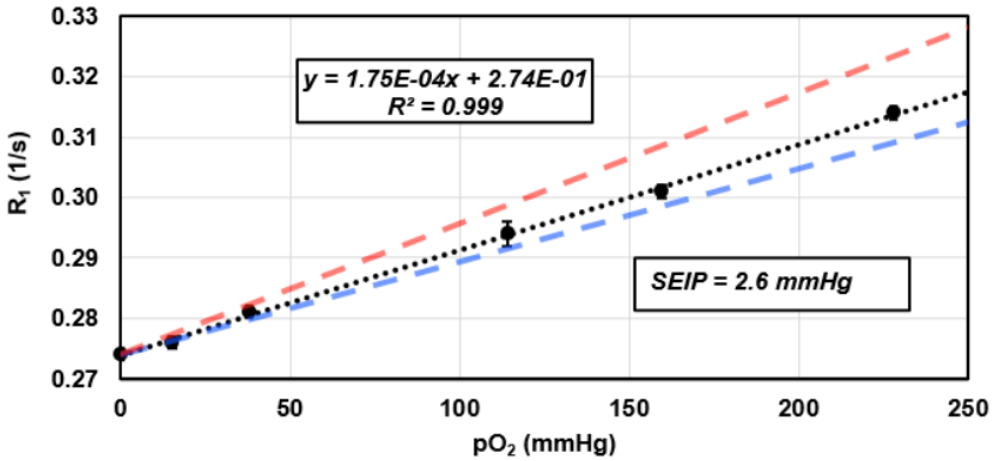
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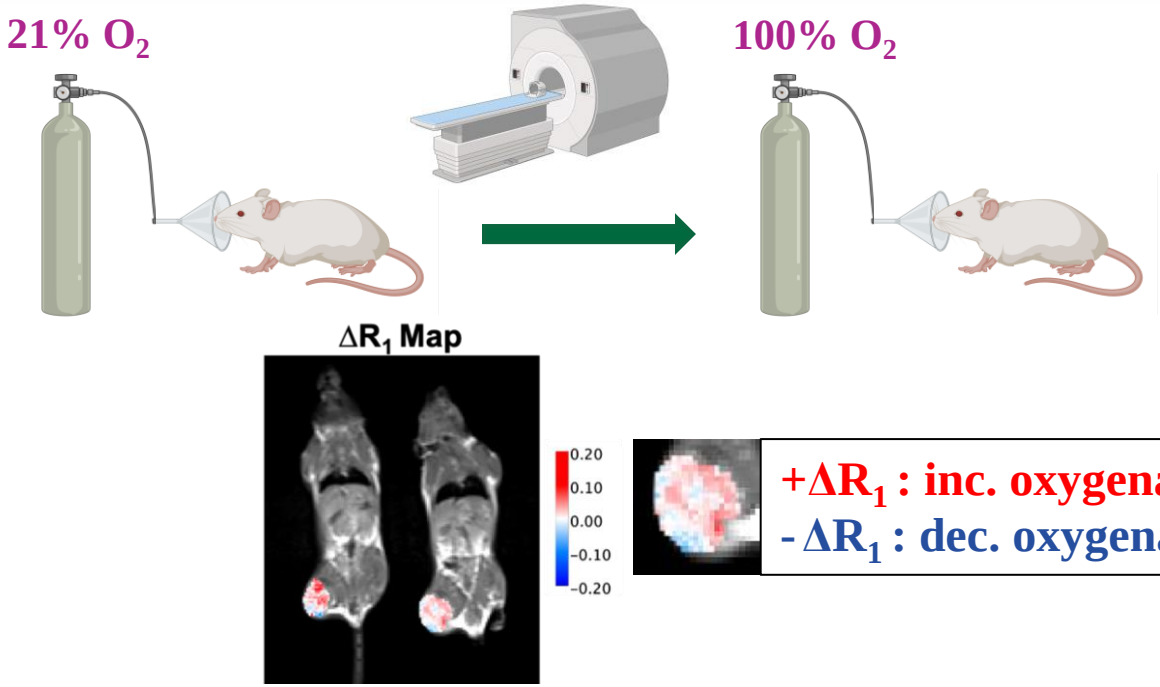
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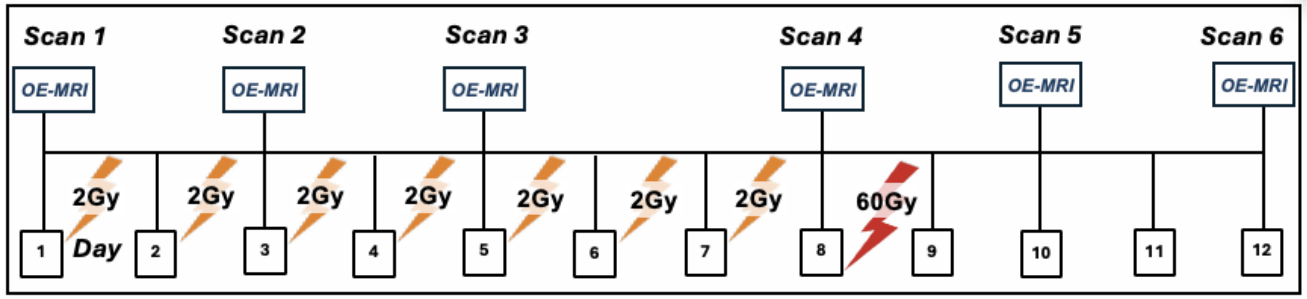
Relaxation Rate vs. pO_2 $\longrightarrow$ $R_{1,ox} = R_{1,0} + C \cdot r_{1,ox}$

$\Delta R_1 = R_1(100\%) - R_1(21\%)$

OE-MRI Setup and Preparation

Experimental Protocol

- C3H mice, SCC7 tumors
- OE-MRI scans every other day (6)
- 2-Gy fractionation x7d + single dose 60-Gy (TCD95)



OE-MRI Optimization

- 3T Siemens MAGNETOM Prisma Fit
- Variable Flip Angle Relaxometry Parameters:
  - Flip angles were optimized between T_1 sensitivity and signal (19º and 89º with a TR of 500 ms; Deoni et al.)

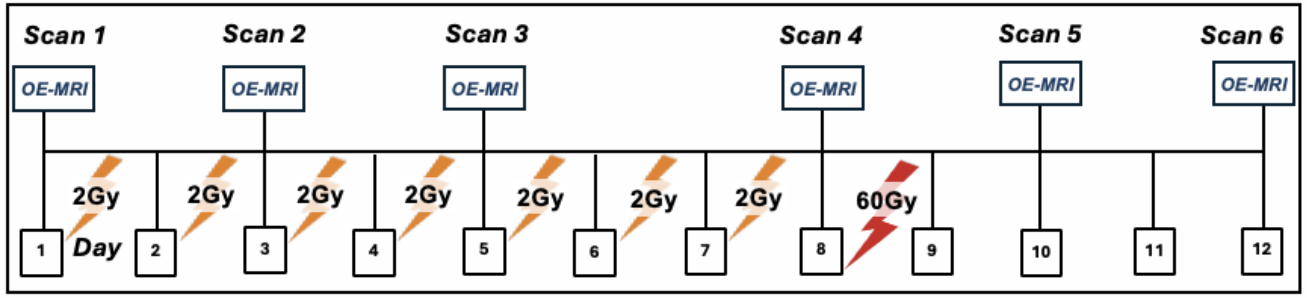
$$\frac{S}{\sin\theta} = E_1 \cdot \frac{S}{\tan\theta} + M_0(1 - E_1)$$

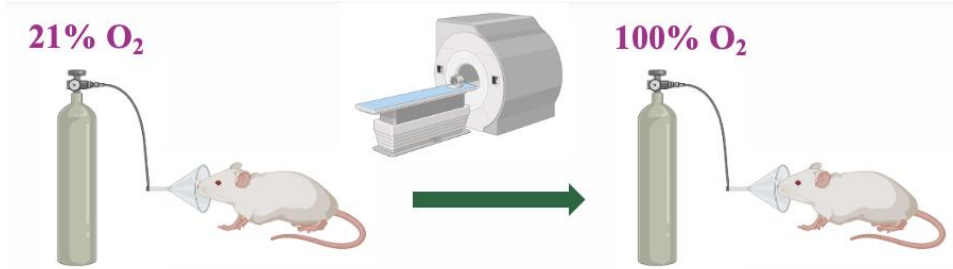
$$\mathrm{DR} \cdot \mathrm{FS} = \left[\frac{S(\theta_2)}{\sin(\theta_2)} - \frac{S(\theta_1)}{\sin(\theta_1)}\right] \cdot \left[\frac{S(\theta_1) + S(\theta_2)}{2 \cdot S(\theta_E)}\right]$$

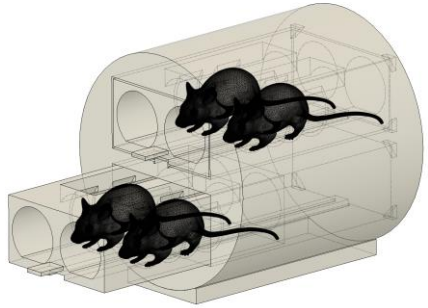
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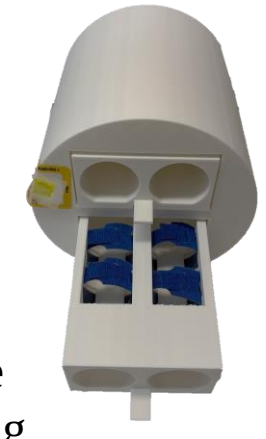
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- OE-MRI scans every other day (6)
- 2-Gy fractionation x7d + single dose 60-Gy (TCD95)
- Optimized Variable Flip Angle Relaxometry Parameters







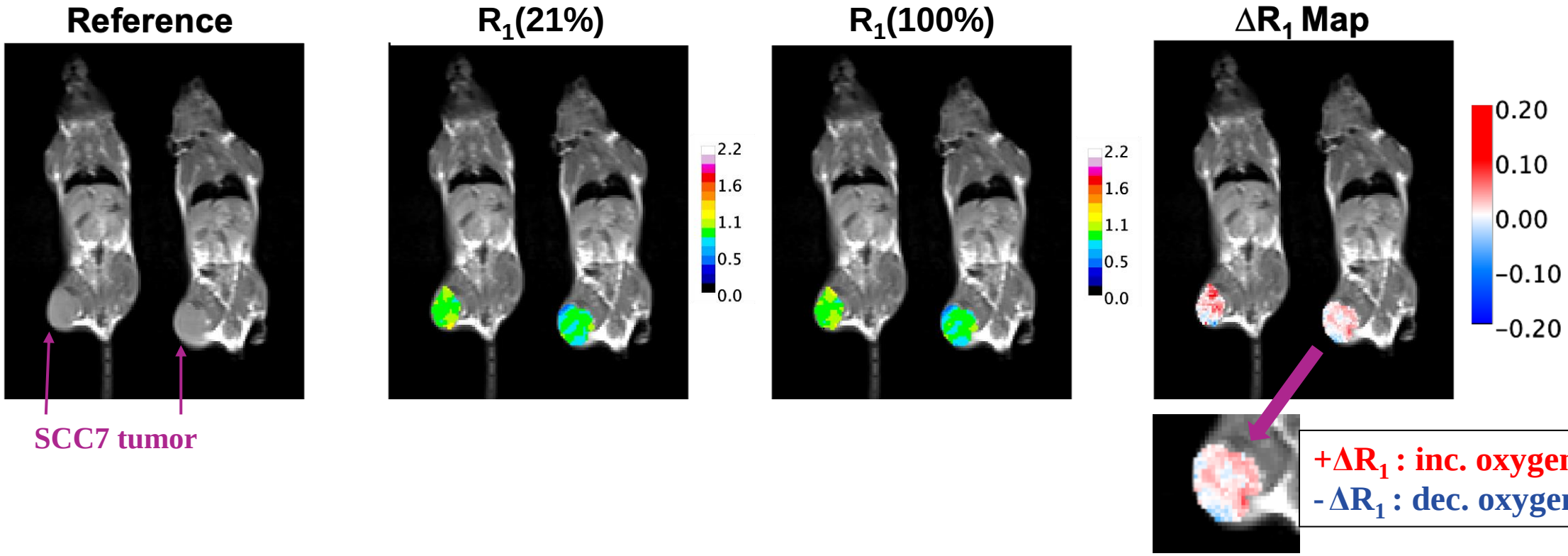


3D-printed MR- and CT- compatible platform for high-throughput imaging

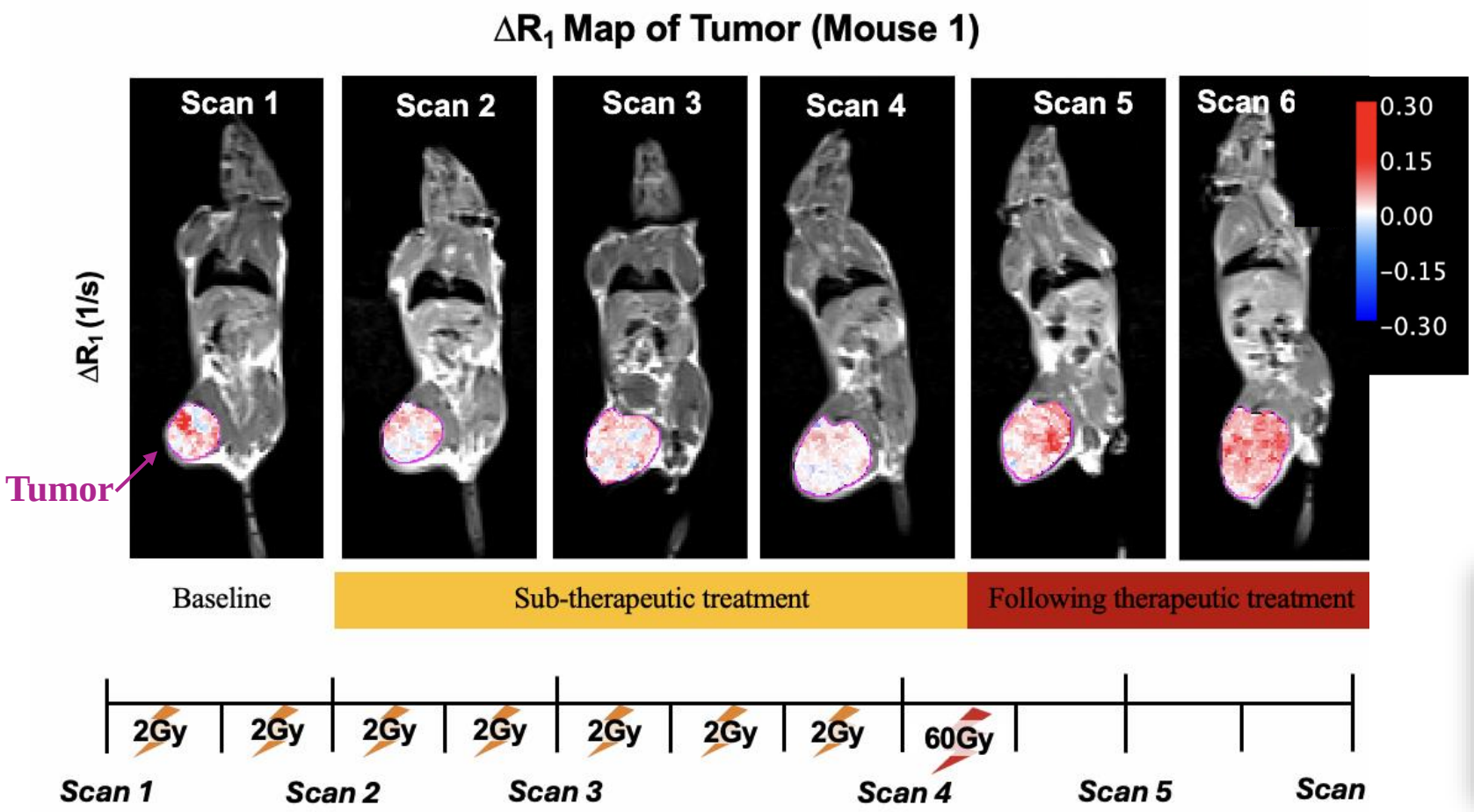
OE-MRI Protocol	
21% O_2	1. Localizer
	2. B_1 Field Map
	3. VFA T_1 Mapping (21%)
100% O_2	4. Anatomical Scan
	5. VFA T_1 Mapping (100%)

Image Processing

R_1 maps: Generated from optimized VFA maps + B_1 field inhomogeneities
ΔR_1 maps: calculated by subtracting the $R_1^{21\%}$ from the $R_1^{100\%}$ map



OE-MRI Gives Indication of Oxygen Response to Radiation



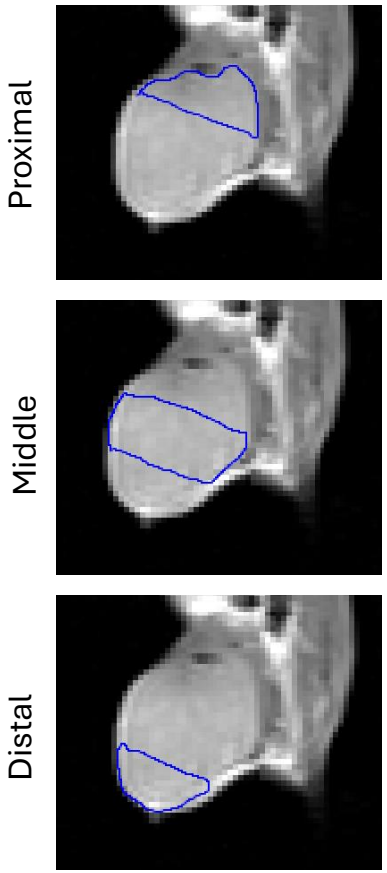
+ΔR_1 : increased oxygenation
- ΔR_1 : decreased oxygenation

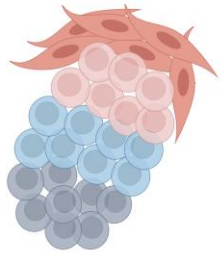
- Increasing tumor size
- During sub-therapeutic treatment, *no change in R_1*
- Following therapeutic treatment, there is a *large + change in R_1*

Tumor Subregions

- Spatially resolved subregions within R_1 maps of oxygenation status may be clinically informative

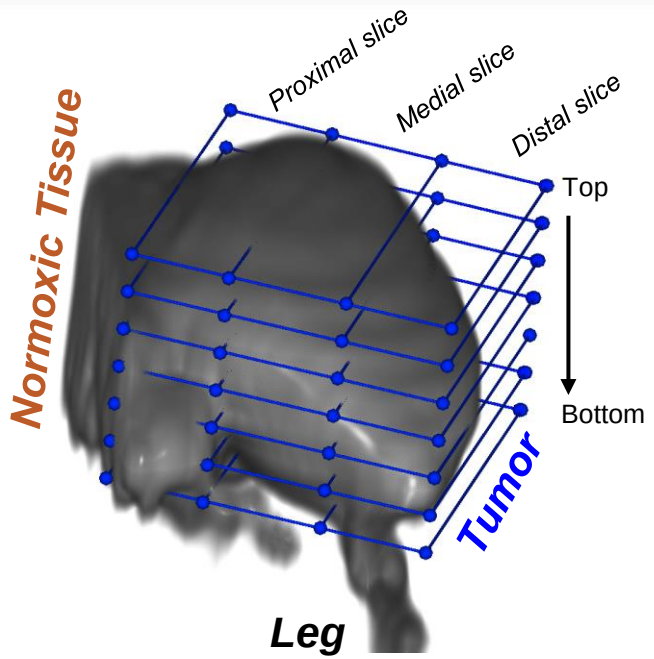
Approach for spatial analysis based on tumor physiology

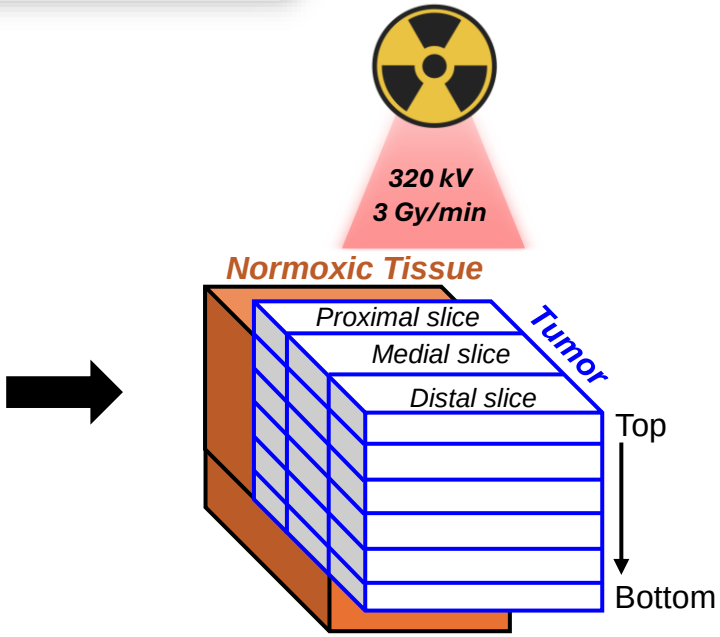




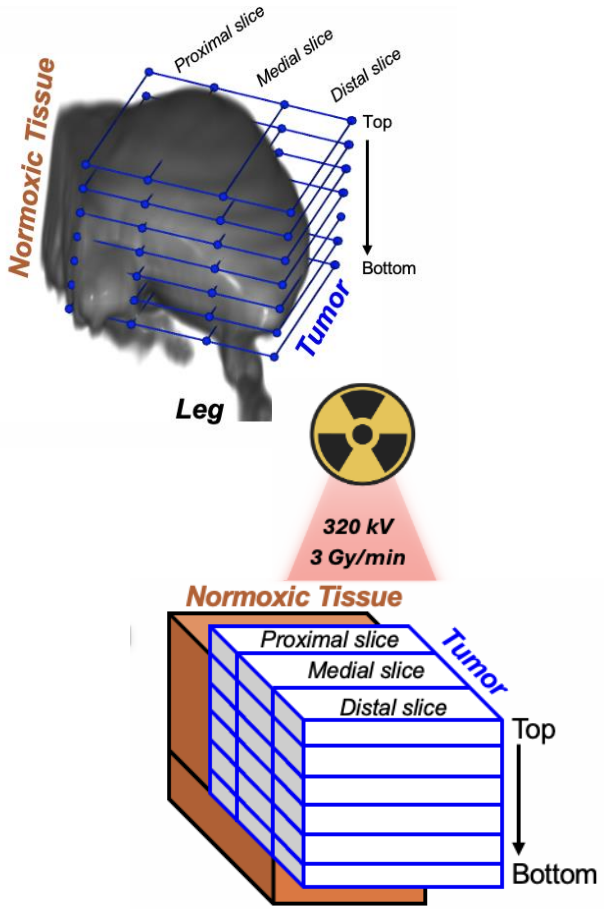
Proximal to Distal - "Jenga"

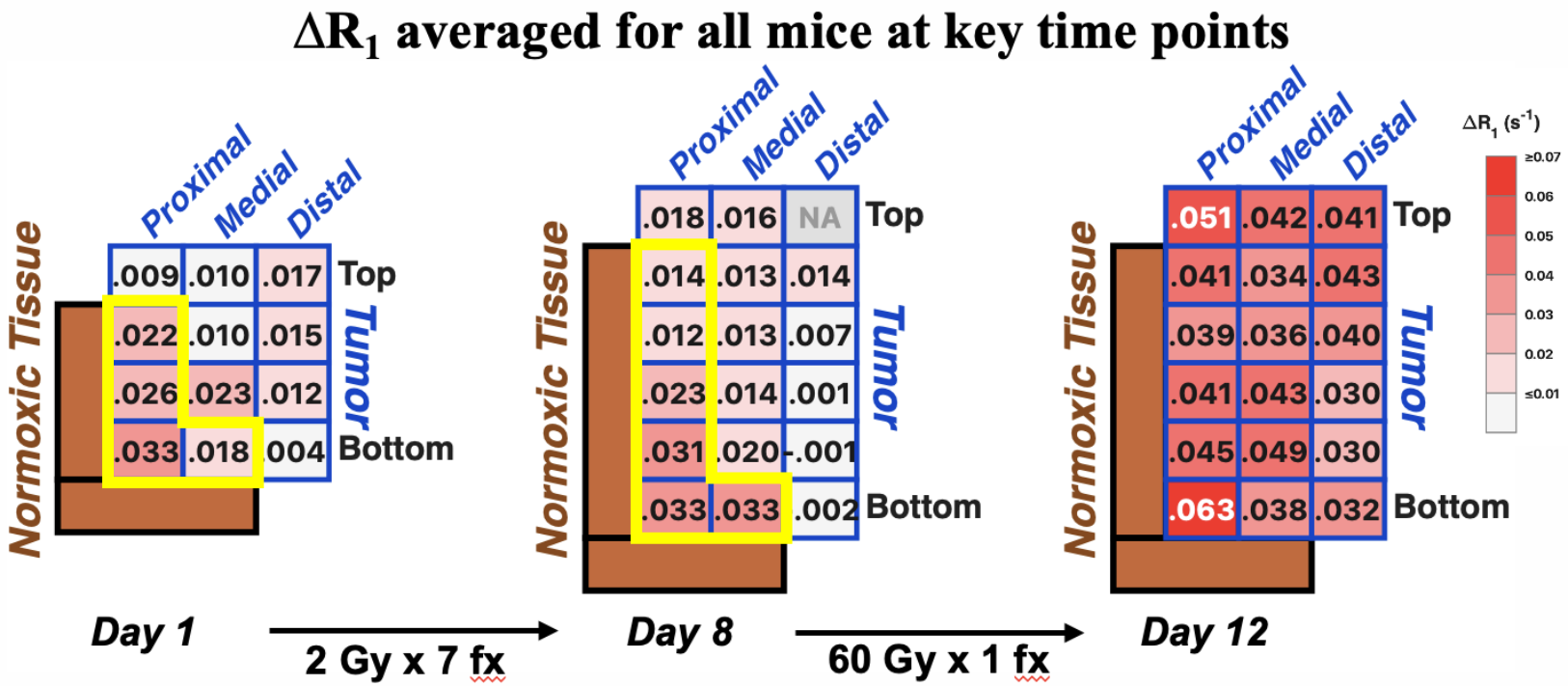
- Division into proximal, middle, distal regions
- Vertical slices





Spatially-resolved OE-MRI





Tumor tissue Adjacent vs. Non-adj. to Normal tissue

- Significant oxygen response difference between adj. and non-adj. tissue
- Reoxygenation throughout the tumor volume after 60-Gy dose

Conclusions

OE-MRI: Tumor Oxygenation Monitoring

- Non-invasive, clinically feasible
- ΔR_1 changes in response to tumor progression, radiation
- Spatially-resolved for the detection of potentially clinically meaningful subregions
- R_1 imaging has the potential to guide treatment modifications to improve the efficacy of radiotherapy

Limitations and Path Forward

- Single tumor model (SCC7; n = 6)
- ΔR_1 reflects dissolved-oxygen change, not absolute pO_2
- Validation across tumor models, direct pO_2 correlation, and clinical OE-MRI are the next steps toward adaptive, hypoxia-targeted treatment monitoring

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Program Director

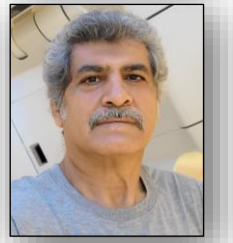

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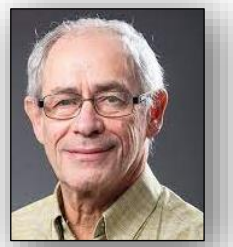

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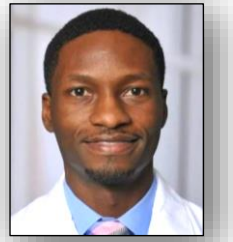

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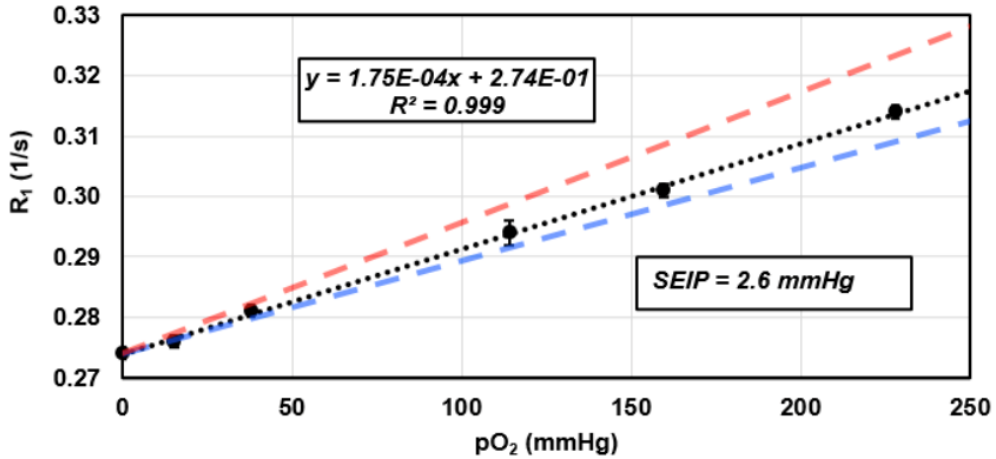
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Oxygen-enhanced MRI (OE-MRI)

Spin-lattice Relaxation Rate is Proportional to pO_2

- The spin-lattice or longitudinal relaxation rate (R_1) is linearly proportional to the amount of dissolved pO_2 in water.
- Paramagnetic oxygen dissolved in water perturbs the local magnetic field which acts to shorten the relaxation time of water protons.

Relaxation Rate vs. pO_2 $\longrightarrow$ $$R_{1,ox} = R_{1,0} + C \cdot r_{1,ox}$$



Linearity of R_1 vs. pO_2 at 9.4T in H_2O