

# Advancing an integrated OMRI - PMRI system toward Quantitative Longitudinal studies of Tumor hypoxia and Redox status

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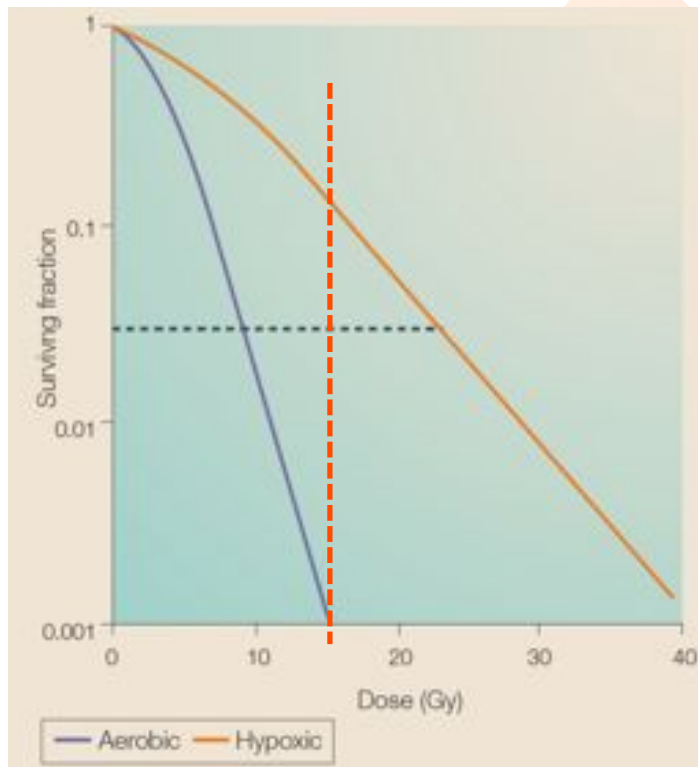
<sup>1</sup>Stanford University, Stanford, CA  
<sup>2</sup>University of California, Berkeley, CA



## OMRI – PMRI collaboration

- ❖ In Vivo Overhauser Development Team (Stanford Radiation Oncology)
  - K. Ahn
  - D. Hristov
  
- ❖ Prepolarized MRI Engineering Team (Stanford EE & Berkeley)
  - P. Stang: MEDUSA Console Development
  - S. Conolly: PMRI Architect
  - G. Scott: PMRI Architect, OMRI development

# Radiation Therapy

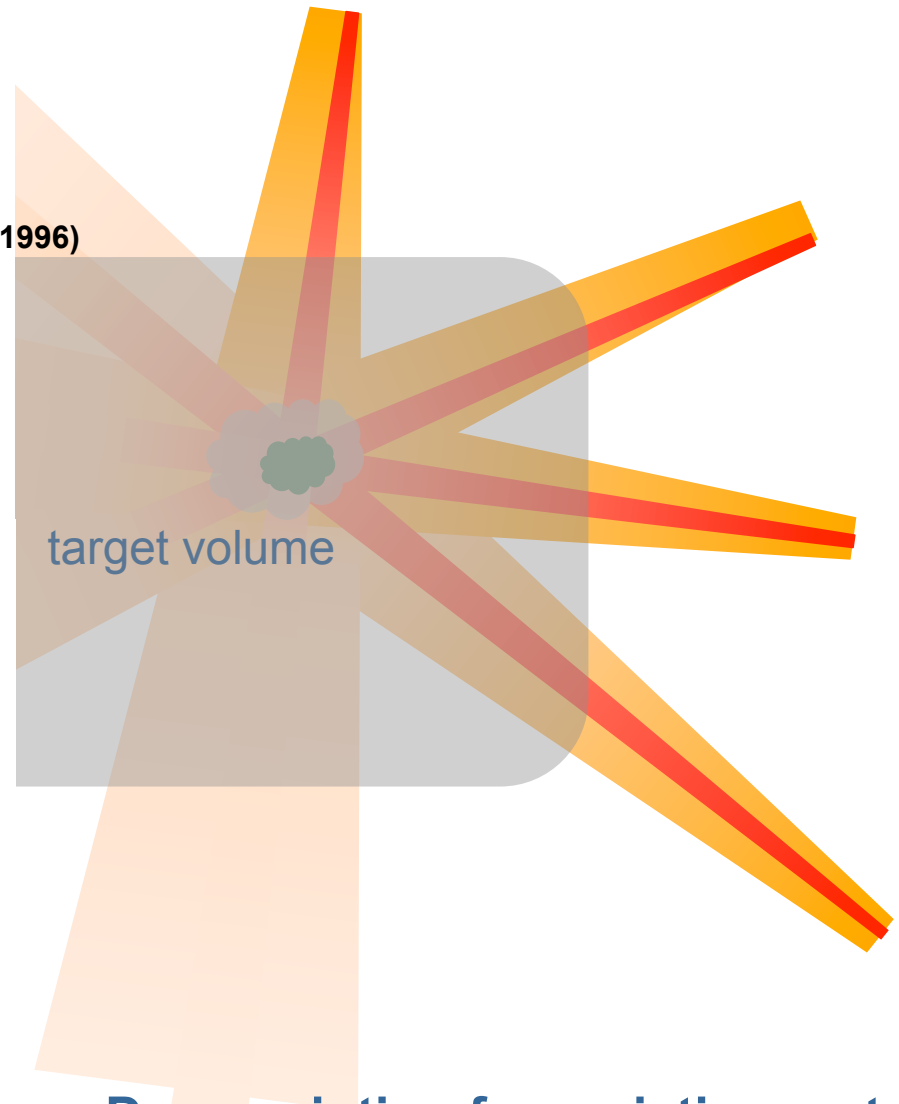
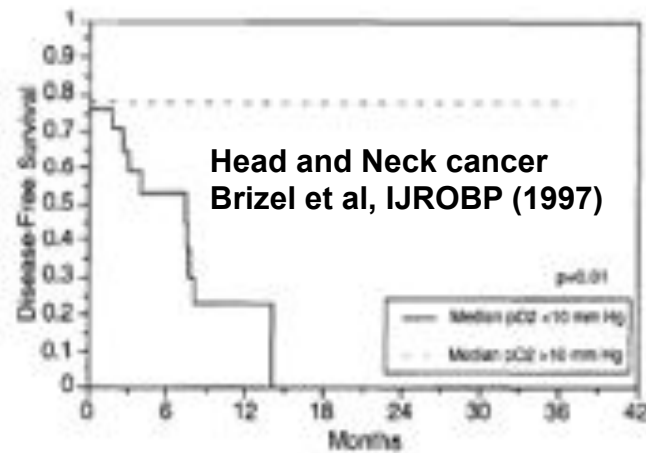
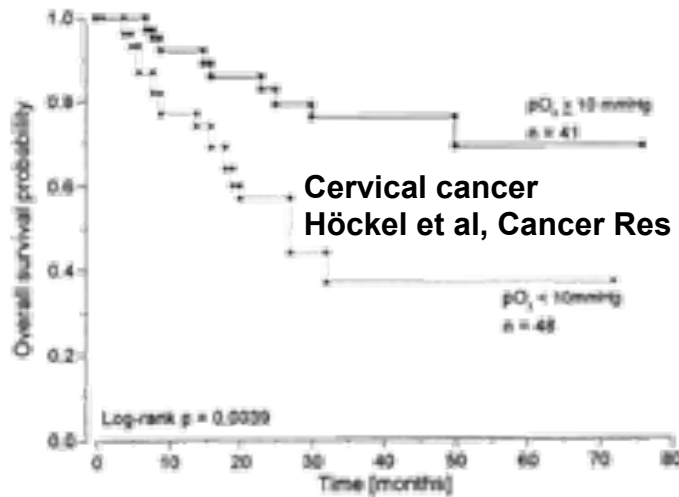


J Brown and W R Wilson, Exploiting Tumor Hypoxia in Cancer Treatment, *Nature Reviews*, 4 (2004) 437-447

target volume

**Accurate radiation delivery to the target volume**

# Radiation Therapy



Assessment of early response, Dose painting for resistive part

# Detection of Tumor Hypoxia

## Invasive technique

- Polarographic electrode (Eppendorf)
- Optical probe (Oxylite)

## PET

- $^{18}\text{F}$ -FAZA, FMISO, FDG
- $^{64}\text{Cu}$ -ATSM

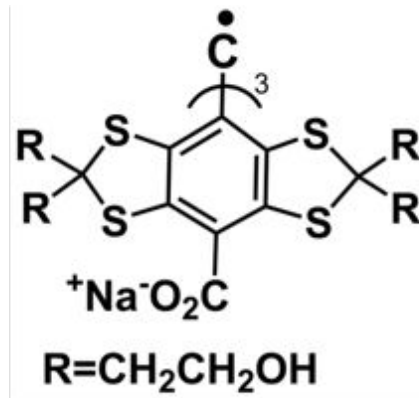
## Magnetic resonance

- BOLD (Hb, HbO<sub>2</sub>)
- EPRI, Overhauser MR

## Immunohistochemistry

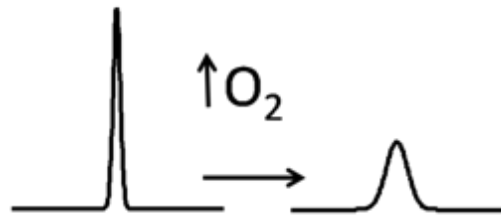
- Misonidazole
- Pimonidazole
- HIF-1 $\alpha$
- VEGF

# Free radical Spin Probes



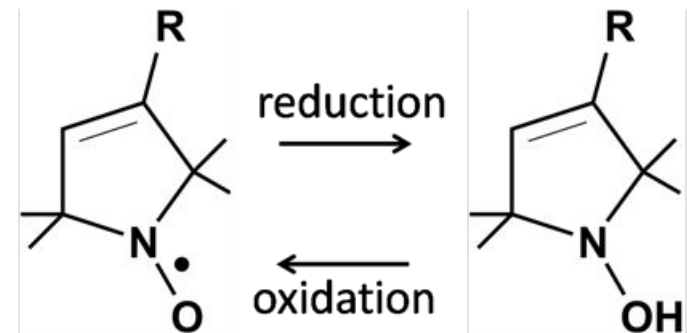
## Trityl

oxygen-sensitive line broadening



## Nitroxide

redox potential similar to tissue



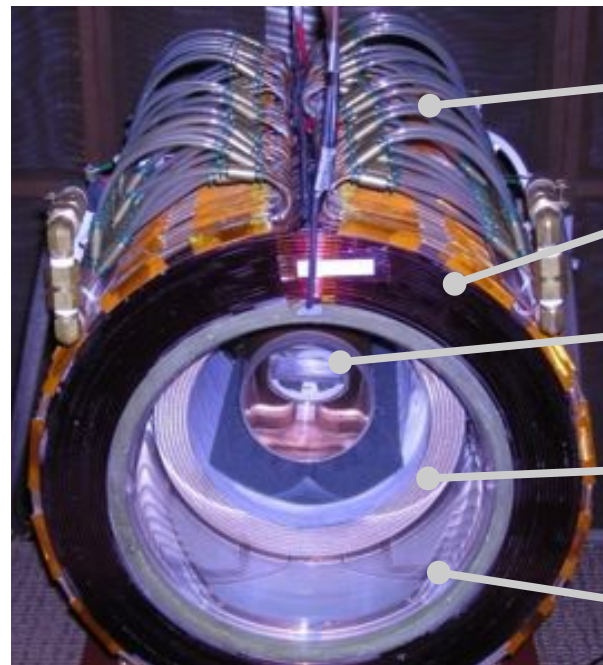
Nitroxide  
(paramagnetic)

Hydroxylamine  
(diamagnetic)

**Electron Paramagnetic Resonance**

**is sensitive to Hypoxia and Redox status.**

# Stanford PMRI system



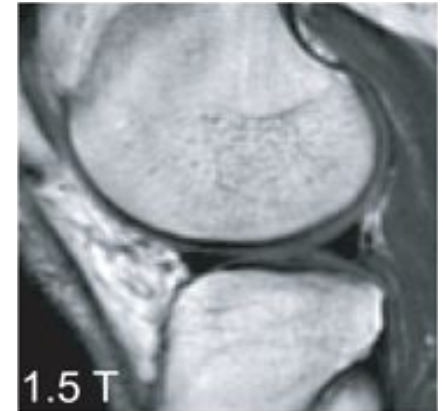
water cooling

33-cm bore  
readout magnet

resonator

13-cm bore  
polarizing magnet

3-axis gradient  
coil set



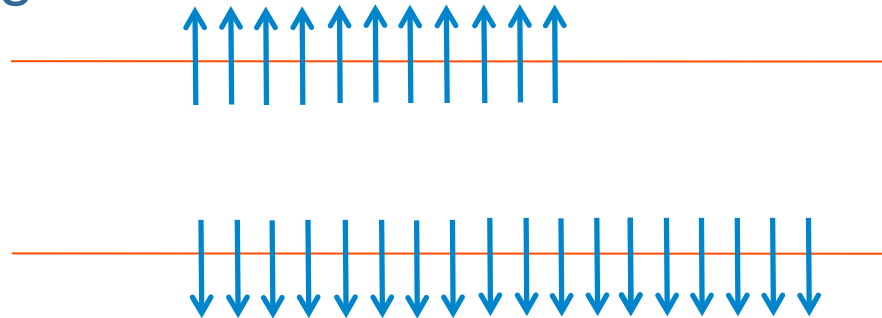
## **prepolarized MRI:**

low-cost MRI with image quality  
comparable to conventional MRI

**PMRI as a development platform for OMRI**

# Overhauser Effect

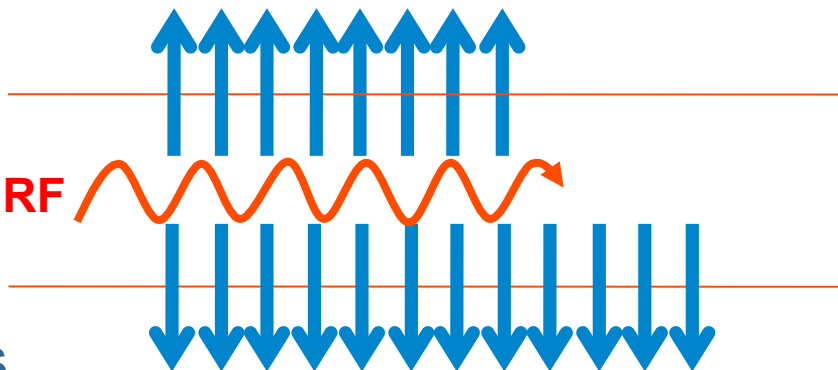
nuclear spins



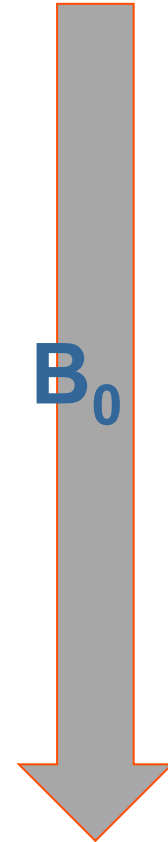
saturation RF



electron spins



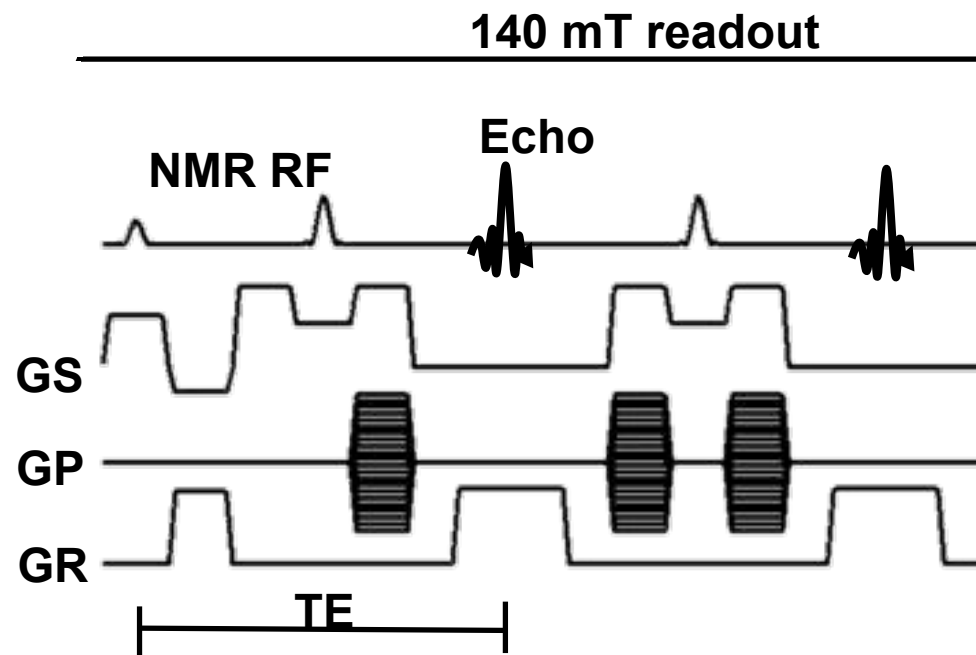
$B_0$



**EPR saturation enhances NMR polarization**

# Pulse sequences

$B_0$

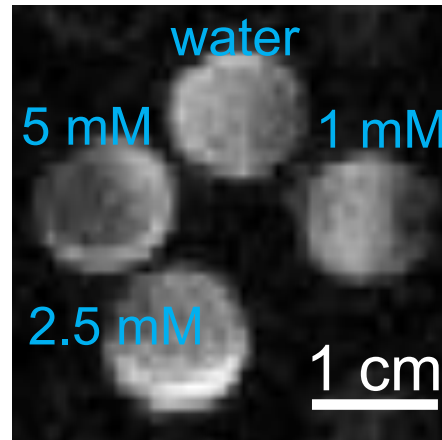


Field-cycling technique for PMRI and OMRI

## Progress - nitroxide phantom image

Feb 2009

PMRI

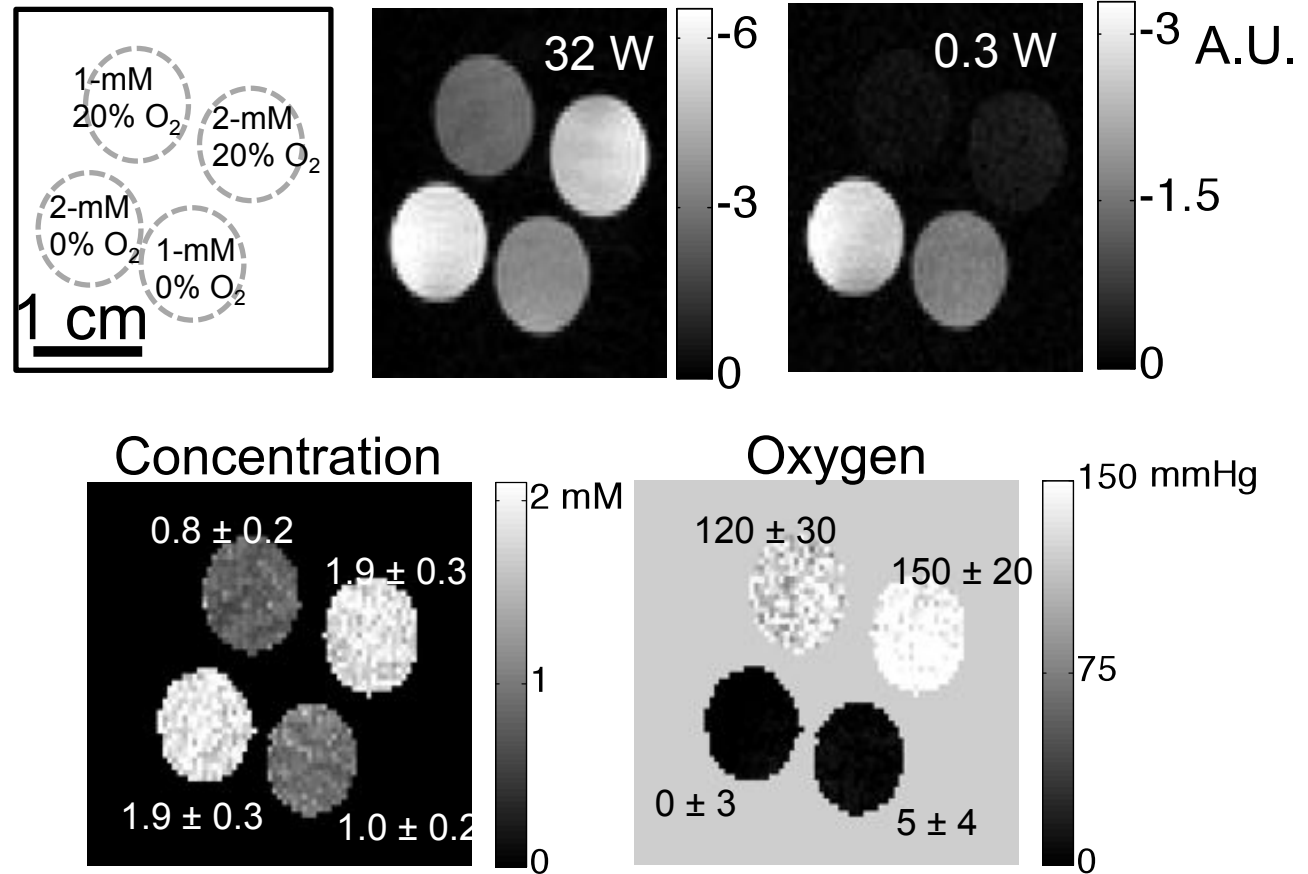


OMRI



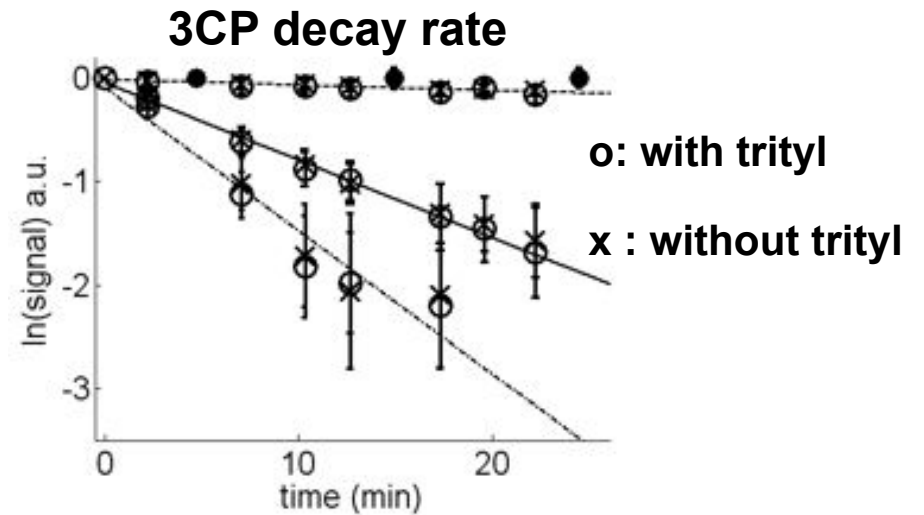
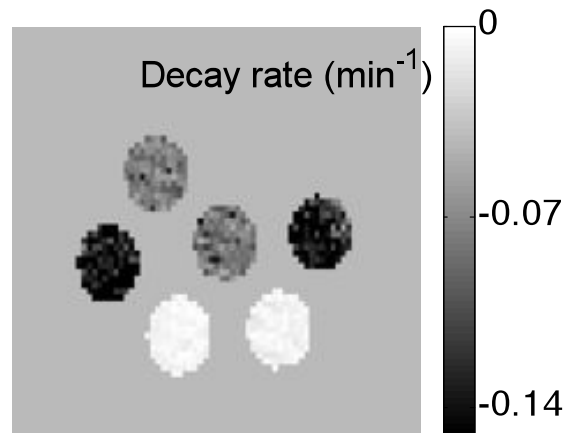
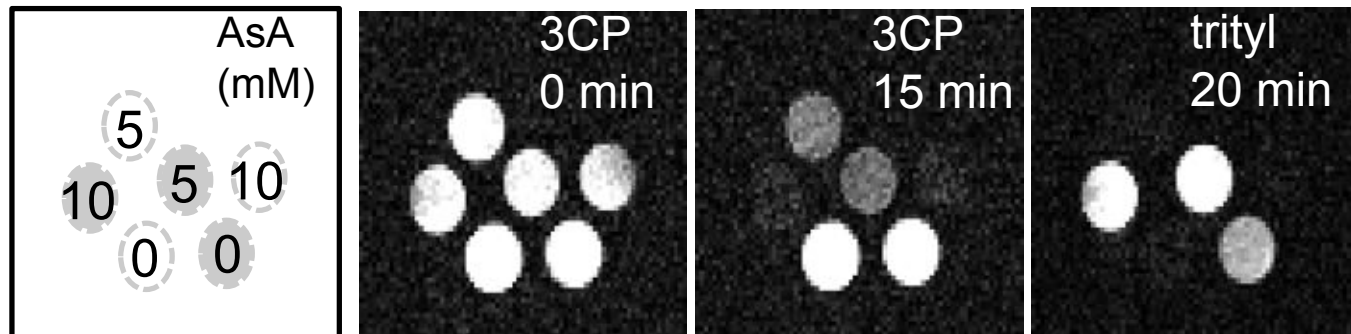
- Upgrade of EPR and NMR coils
- Multi-spin echo pulse sequences

# Oximetry of trityl-OMRI



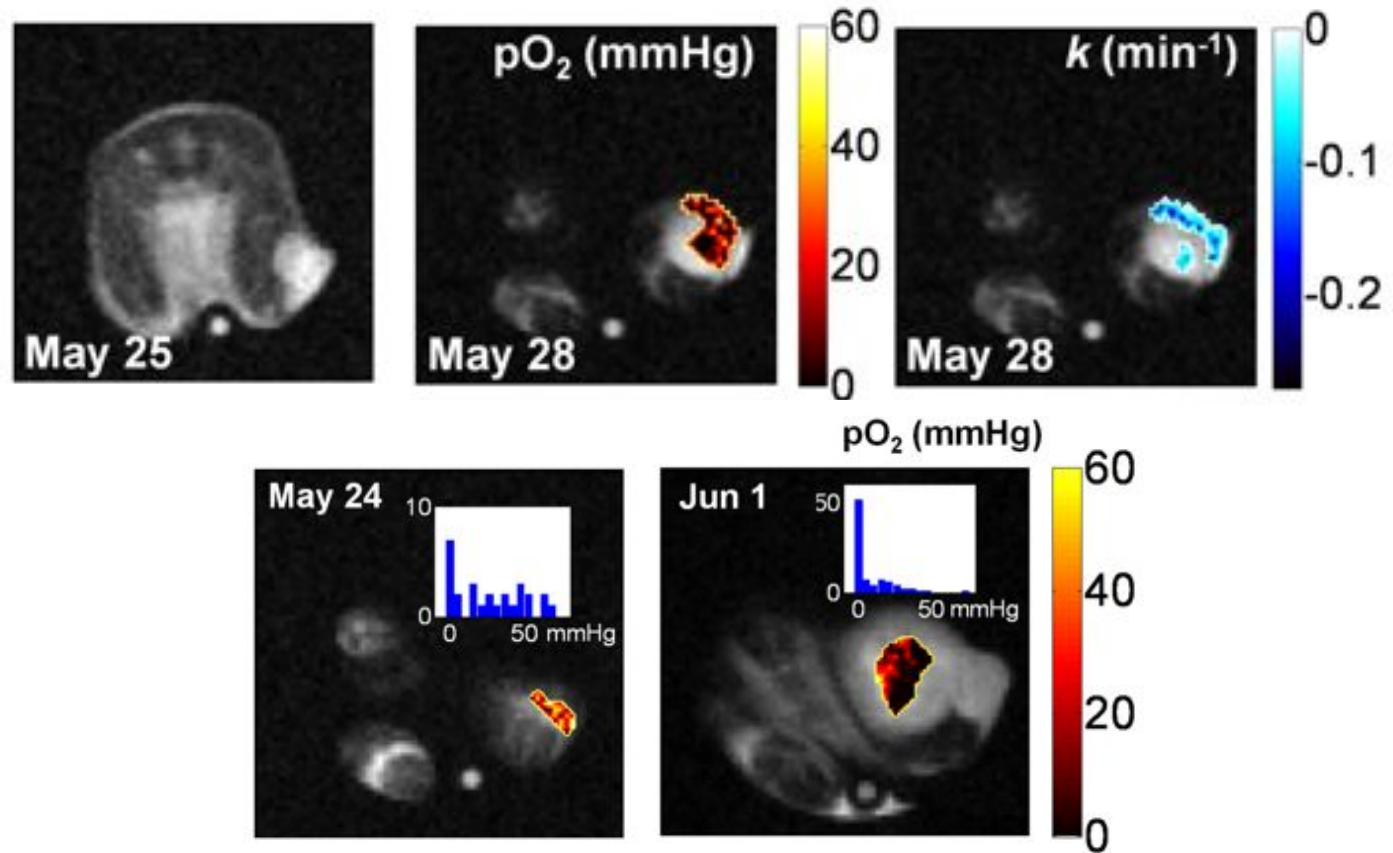
**Oxygen resolution of 3 mmHg achieved for hypoxia**

# Redox imaging of trityl + nitroxide



Nitroxide redox imaging in the presence of trityl

## *in vivo* OMRI-PMRI



**Demonstration of  
multi-parametric imaging and longitudinal study**

# Conclusion

## ❖ Multiparametric Imaging

- $pO_2$  from trityl, redox from nitroxide OMRI
- Proton  $T_1$ ,  $T_2$  from PMRI

## ❖ Longitudinal Study

- Physiologic OMRI with naturally co-registered anatomical PMRI
- Unique opportunity to investigate oxidative stresses as prognostic factors of radiation therapy