



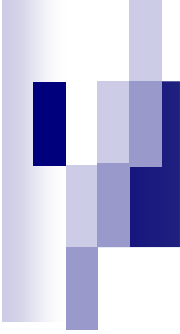
Longitudinal Monitoring of Functional Changes in Irradiated Head and Neck Tumors Using Optical Spectroscopy

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Session: Treatment Response and Monitoring II





Conflicts of Interest

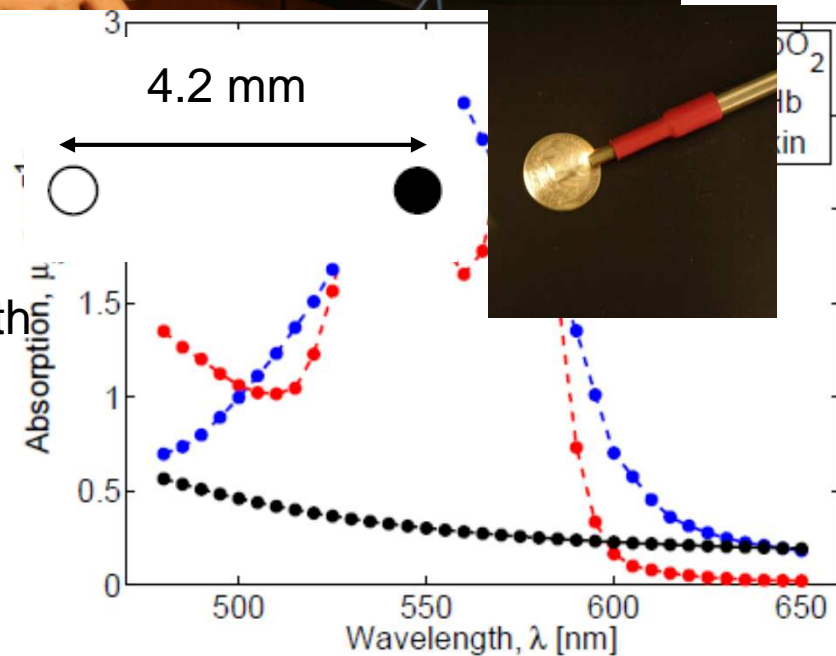
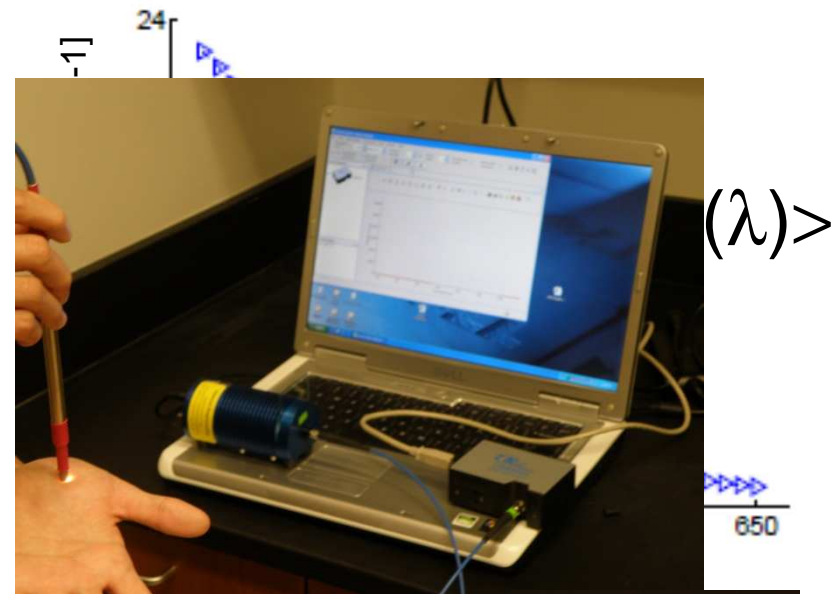
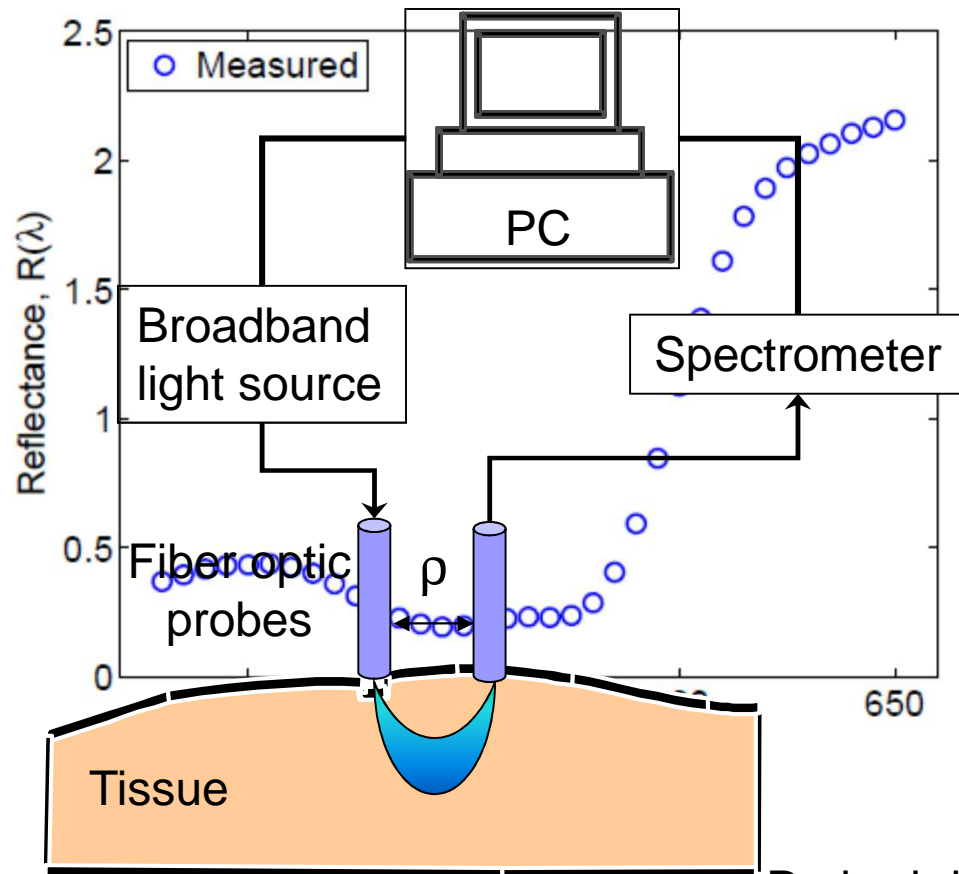
Nothing to disclose

Motivation and Background

- Measurements of changes in gross tumor volume does not consider functional changes within lesions
- Treatment efficacy and outcomes have been shown to depend on tumor oxygen levels in HNC
- Obtain non-invasive, longitudinal measurements of changes in tumor hypoxia during treatment

Clinical Options	Cost	Portable	Contrast	Longitudinal Frequency
MR	High	No	Extrinsic	~weeks
CT	High	No	Extrinsic	~weeks-months
PET	High	No	Extrinsic	~weeks
Optical	Low	Yes	Intrinsic	~daily-hourly

Diffuse Optical Spectroscopy



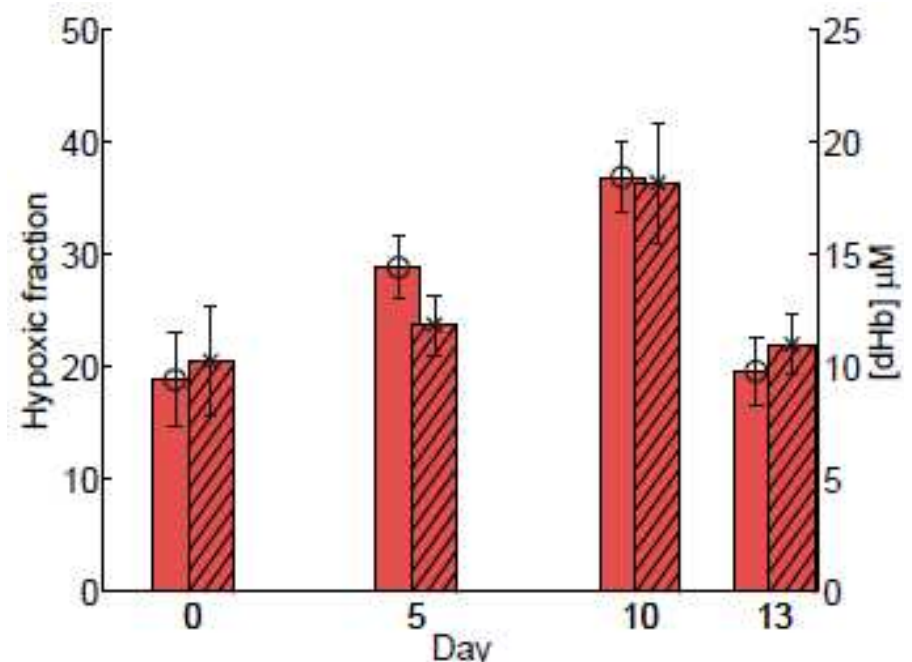
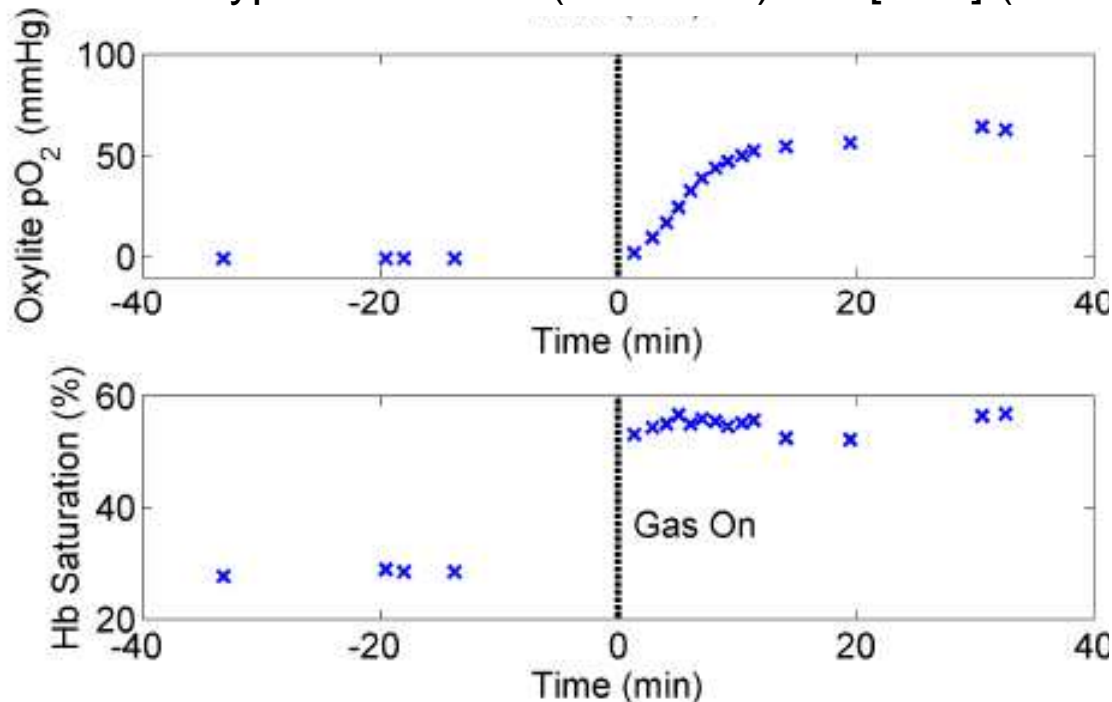
$\mu_a(\text{HbO}_2) \leftrightarrow [\text{HbO}_2]$; $\mu_a(\text{dHb}) \leftrightarrow [\text{dHb}]$ Probed depth $\sim 2-4$ mm

Total Hemoglobin, $[\text{THb}] = [\text{HbO}_2] + [\text{dHb}]$

Oxygen Saturation, $\text{SO}_2 = 100 \times [\text{HbO}_2]/[\text{THb}]$

Diffuse Optical Spectroscopy

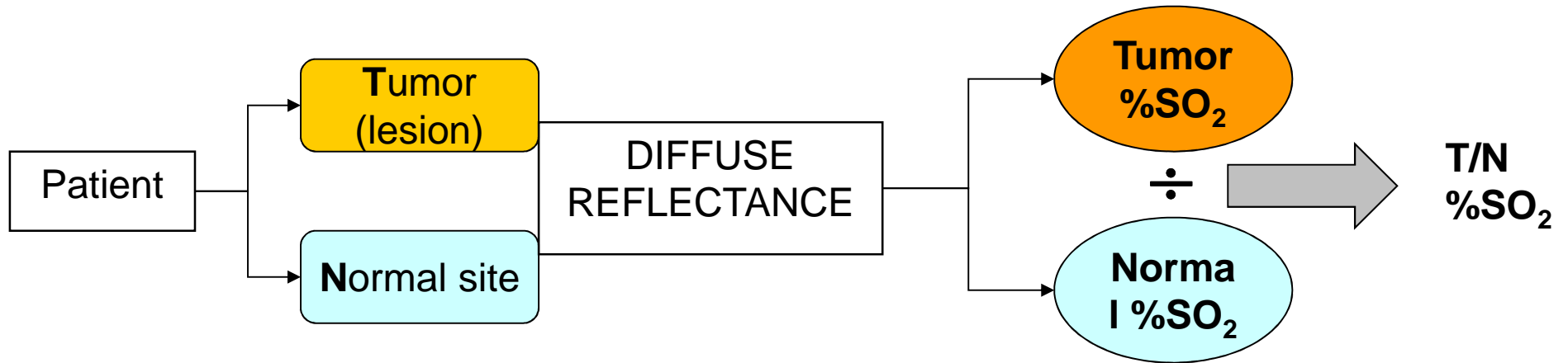
- Optical method has been validated to extract [THb] (1-60 μM) and the relationship between SO_2 and pO_2 (measured using a microelectrode) in optical phantoms (Bender et.al; IEEE Trans. BME; 56(4): p. 960-968; 2009)
- In 4T1 preclinical models we have observed concordance between:
 - pO_2 (microelectrode) and SO_2 (optical) during carbogen breathing
 - Hypoxic fraction (from IHC) and [dHb] (deoxy-Hb concentration) longitudinally



Clinical Study: Recruitment

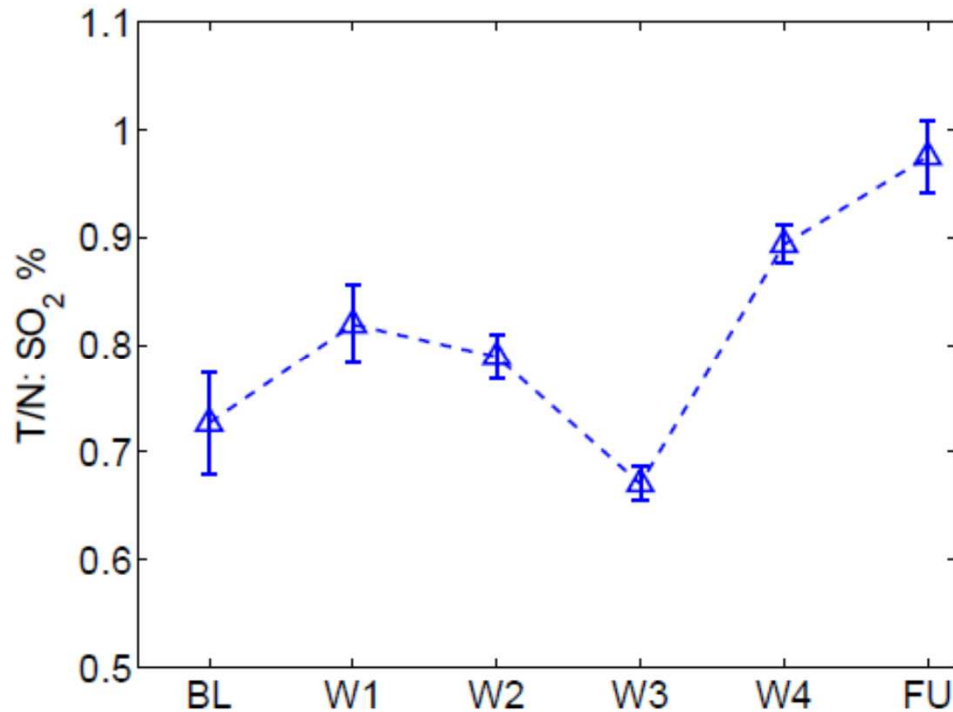
<u>Patient</u>	<u>Treatment</u>	<u>HPV</u>	<u>Clinical outcome</u>	<u>Pathological outcome</u> (@ <u>Neck Node</u>)
P1	Cetuximab + RT	-	Complete clinical response	Negative for SCC
P2	Cisplatin + RT	+	Complete clinical response	NA
P3	RT only	-	Complete clinical response	NA
P4	Cisplatin + RT	-	Complete clinical response	NA
P5	Cisplatin + RT	-	Persistent disease	Positive for SCC
P6	Cisplatin + RT	+	Complete clinical response	NA
P7	RT only	+	Progressive disease	NA
P8	RT only	+	Complete response at primary	NA

T:N Ratio for SO₂: Temporal Trends



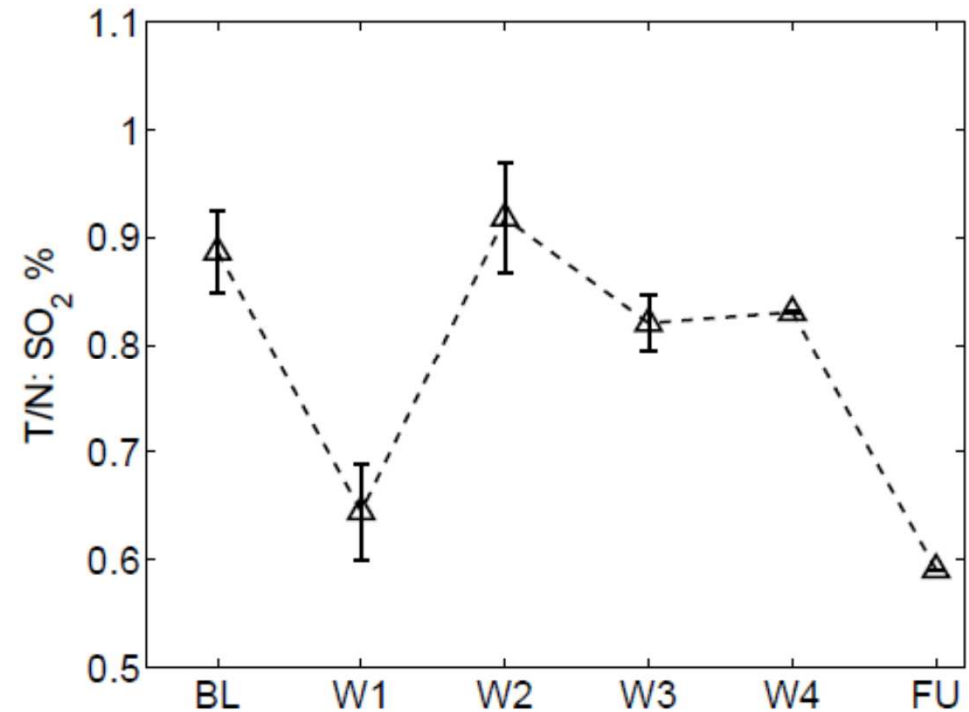
T:N Ratio for SO₂: Temporal Trends

T:N Ratio for Clinical Responders



Mean across P1, P2, P3, P4, P6, P8

T:N Ratio for Clinical Non-Responders



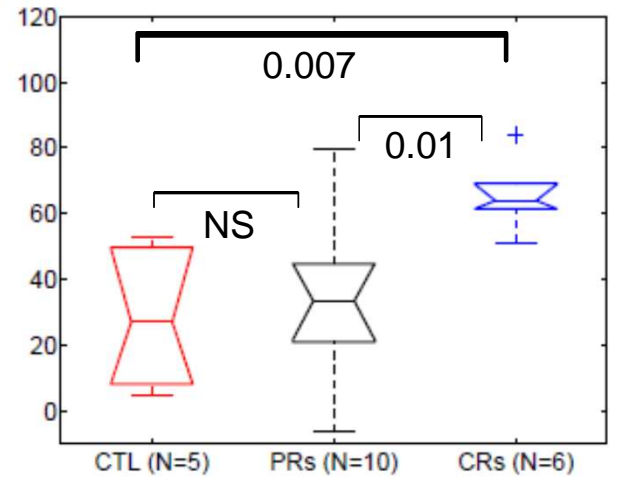
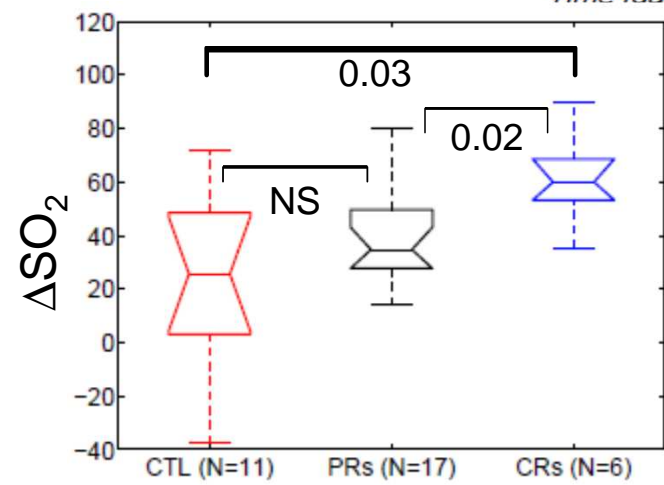
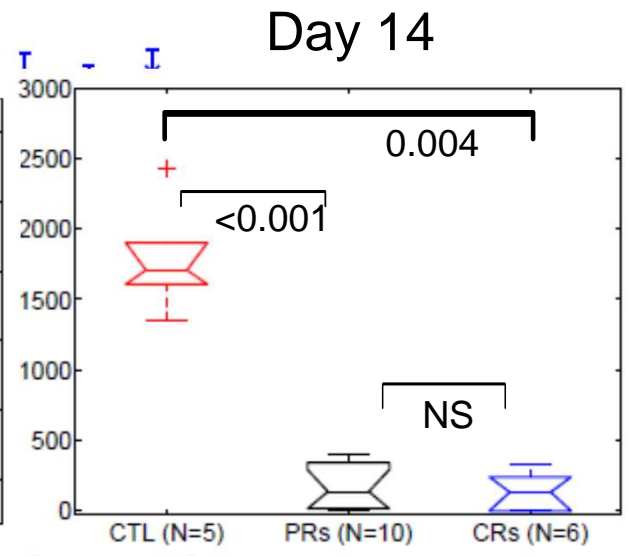
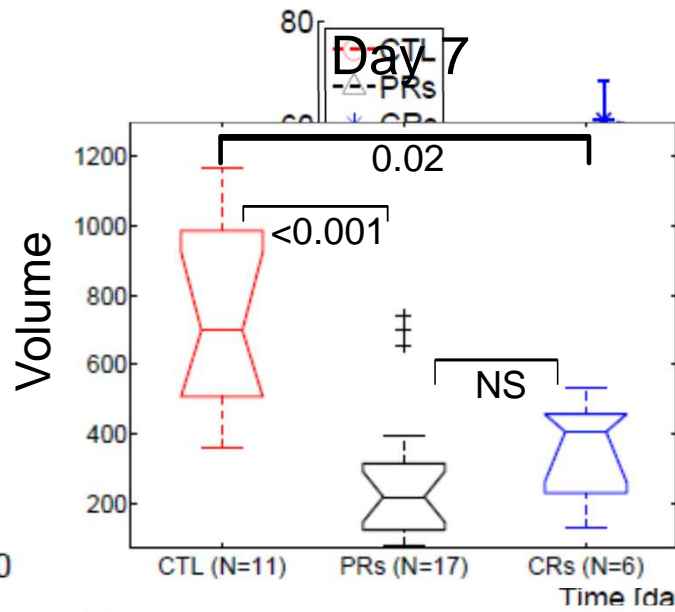
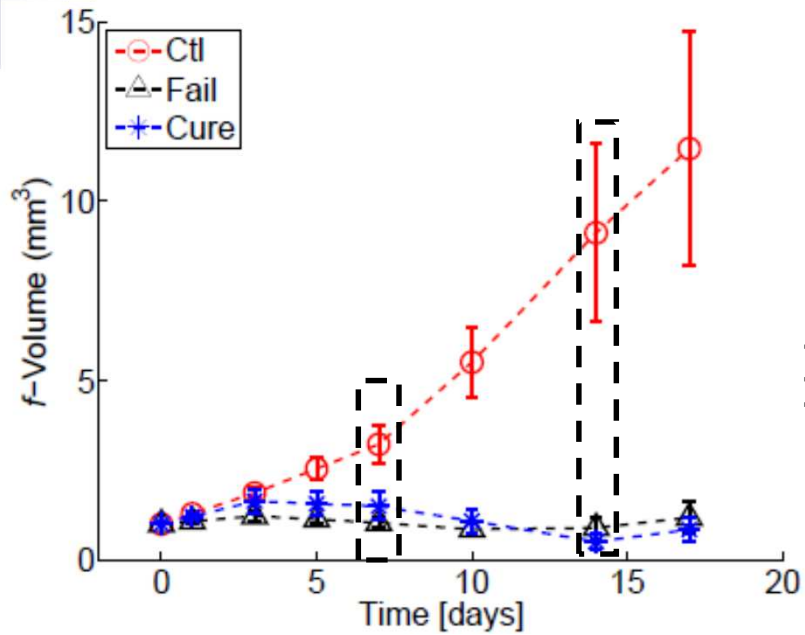
Mean across P5 and P7

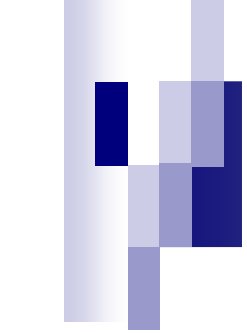
Animal Studies (Single Fraction)

- Nude mice grown with FaDu tumors on right flank
- Treated (N = 23) animals received radiation
- Control (N = 11) received sham radiation
- Optical probe placed on tumor and reflectance measured

		1x RT																	
		D0	39 Gy X 1 (TCD 50)				Week1				Week2				Weeks 3-15				
							X				X				X (once/week)				
Volume	x		x		x			x		x									
Optical	x		x	x	x	x	x	x	x	x	x	x	x						

1X RT: Changes in Tumor SO₂

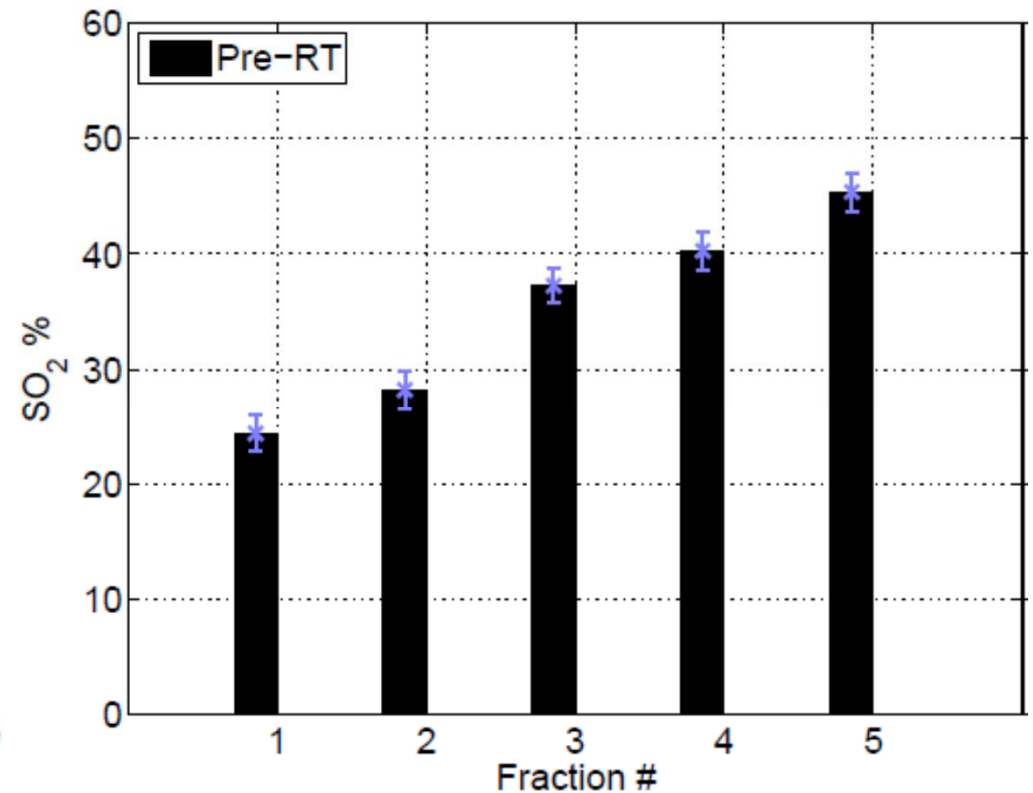
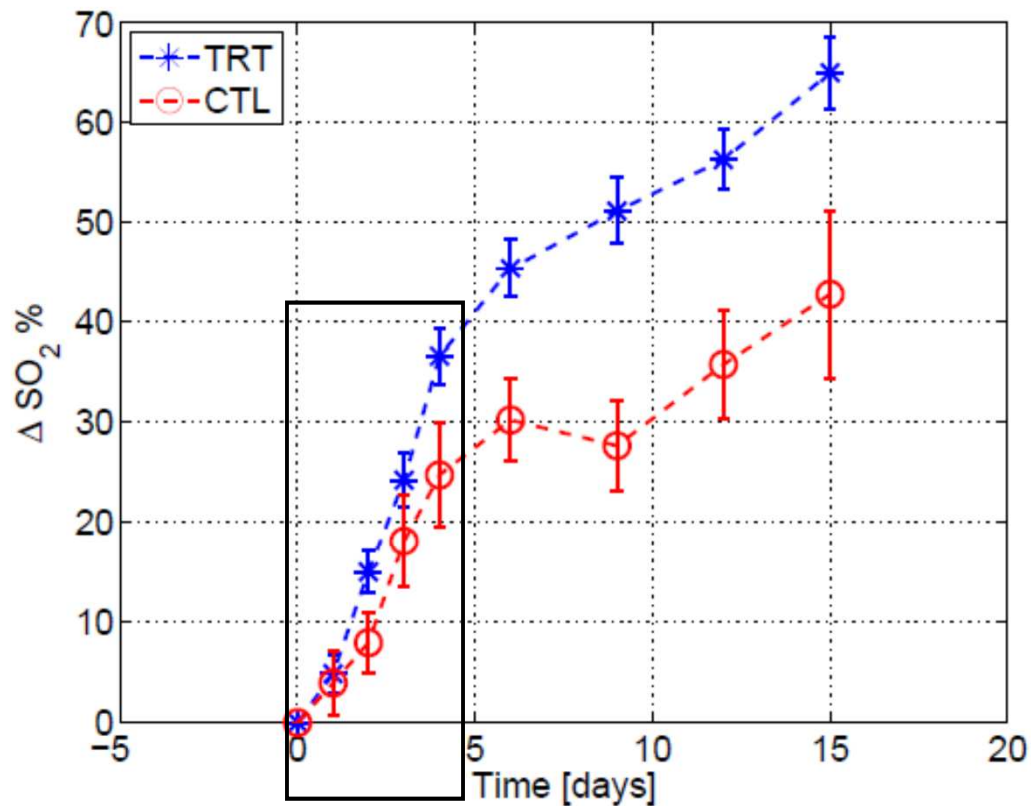




Fractionated (5X) Studies

- We have tested 5X daily-fractions:
 - N = 27 mice (20 Treated, 7 control) with 15.5 Gy/fraction
 - N = 27 mice (20 Treated, 7 control) with 13.5 Gy/fraction
- As before, optical measurements obtained over a period of 2 weeks
- For each dose, optical measurements were obtained just before the animals were irradiated (PRE) and immediately after completion (POST)

Data from Fractionated Studies



Statistically significant ($p < 0.05$) increases post-irradiation in tumor SO_2 , on the order of minutes, were observed each day for each fraction



Summary and Acknowledgements

- Optical spectroscopy can detect changes in vascular tumor oxygenation
- Irradiated tumors show increases in oxygen saturation
- Longitudinal measurements of functional optical endpoints could prove useful to plan treatment

Funding Sources:

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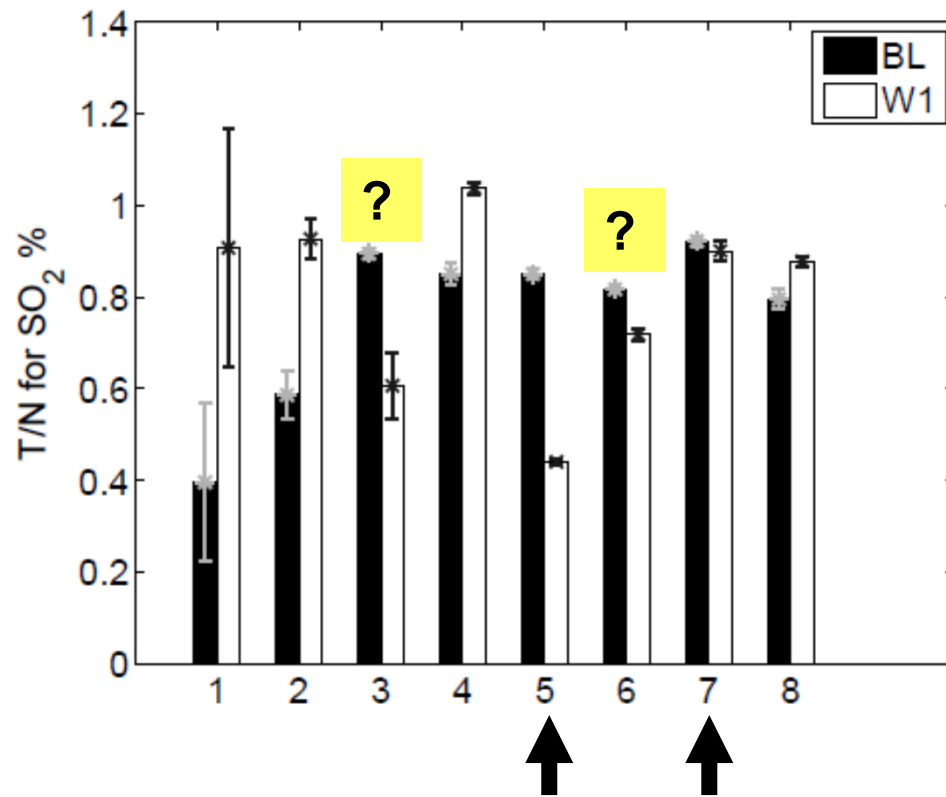
People:

Dr. Joe Salama, Dr. Thies Schroeder, Dr. Yulin Zhao, Kevin Chang, and Daniel Klein



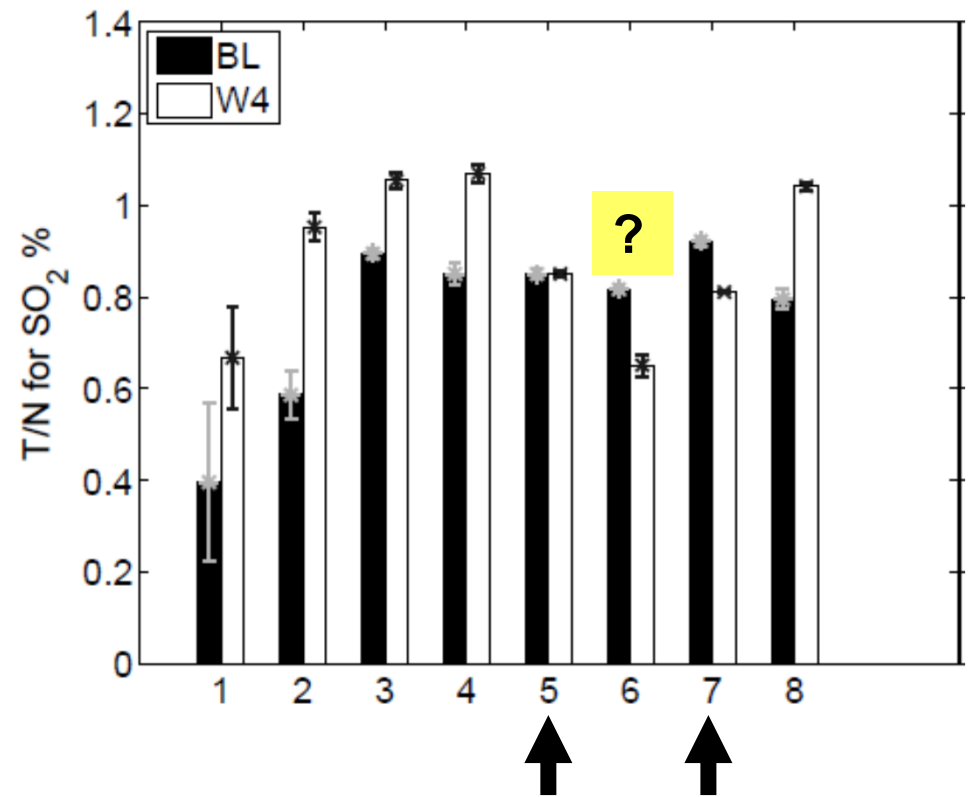
Individual Changes in T:N of %SO₂

Changes 1 week after treatment



Non-Responders

Changes 4 weeks after treatment



Non-Responders