

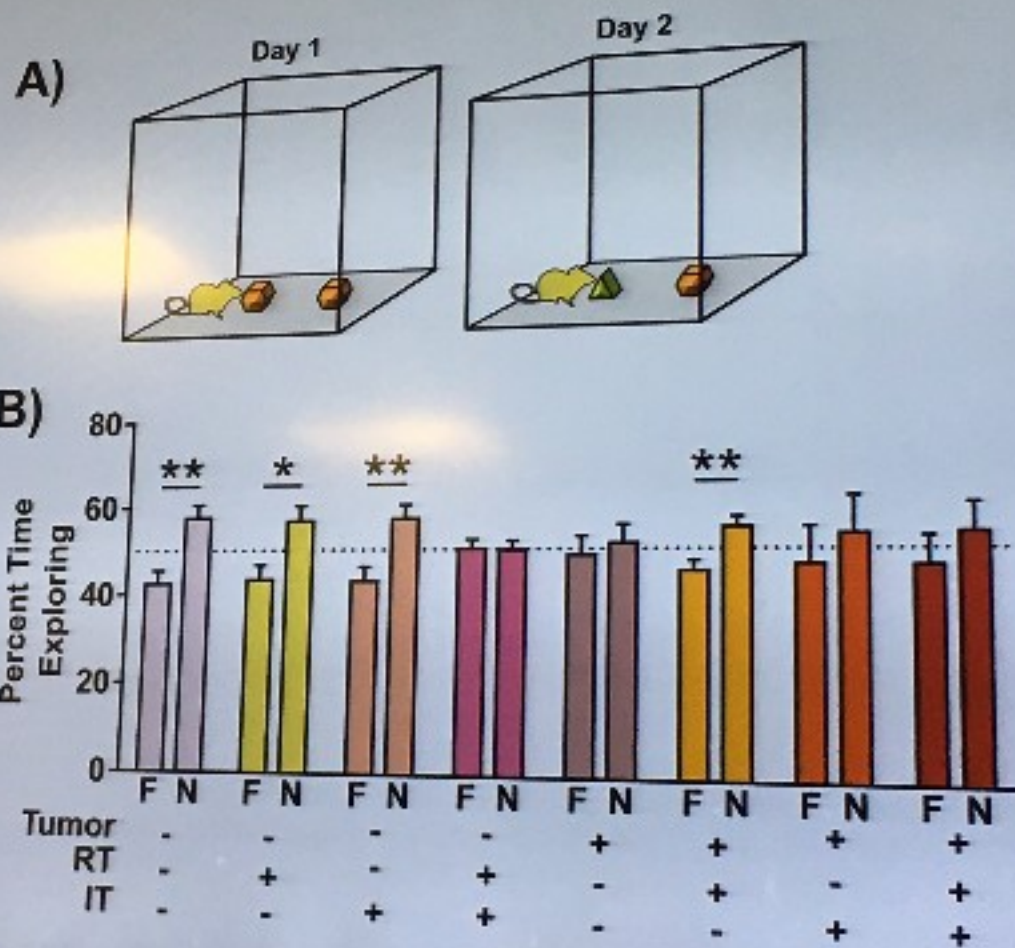








# Combined treatment (CT) and presence of a peripheral tumor impair memory



# Acknowledgements

## Mentorship & Mouse Project Development

Jacob Raber, PhD

Michael Gough, PhD

Charles Thomas, MD

## Mentorship & Human Project Development

Jacob Raber, PhD

Kerri Winters, PhD

Betty Yu

Charles Thomas, MD

## Additional support

Kristina Young, MD, PhD

David Friedman

Eileen Torres

Sydney Weber

Blair Stewart

Tessa Marzulla

Damian Zuloaga PhD

## Funding:

HHMI Medical Research Fellowship

Collins Medical Trust

RSNA Medical Student Research Grant

Tartar Research Fellowship

OSLER TL1 Short Term Research Grant

OHSU Student Senate Funding

Moss-Stevens Radiation Medicine Fund

Development account J. Raber



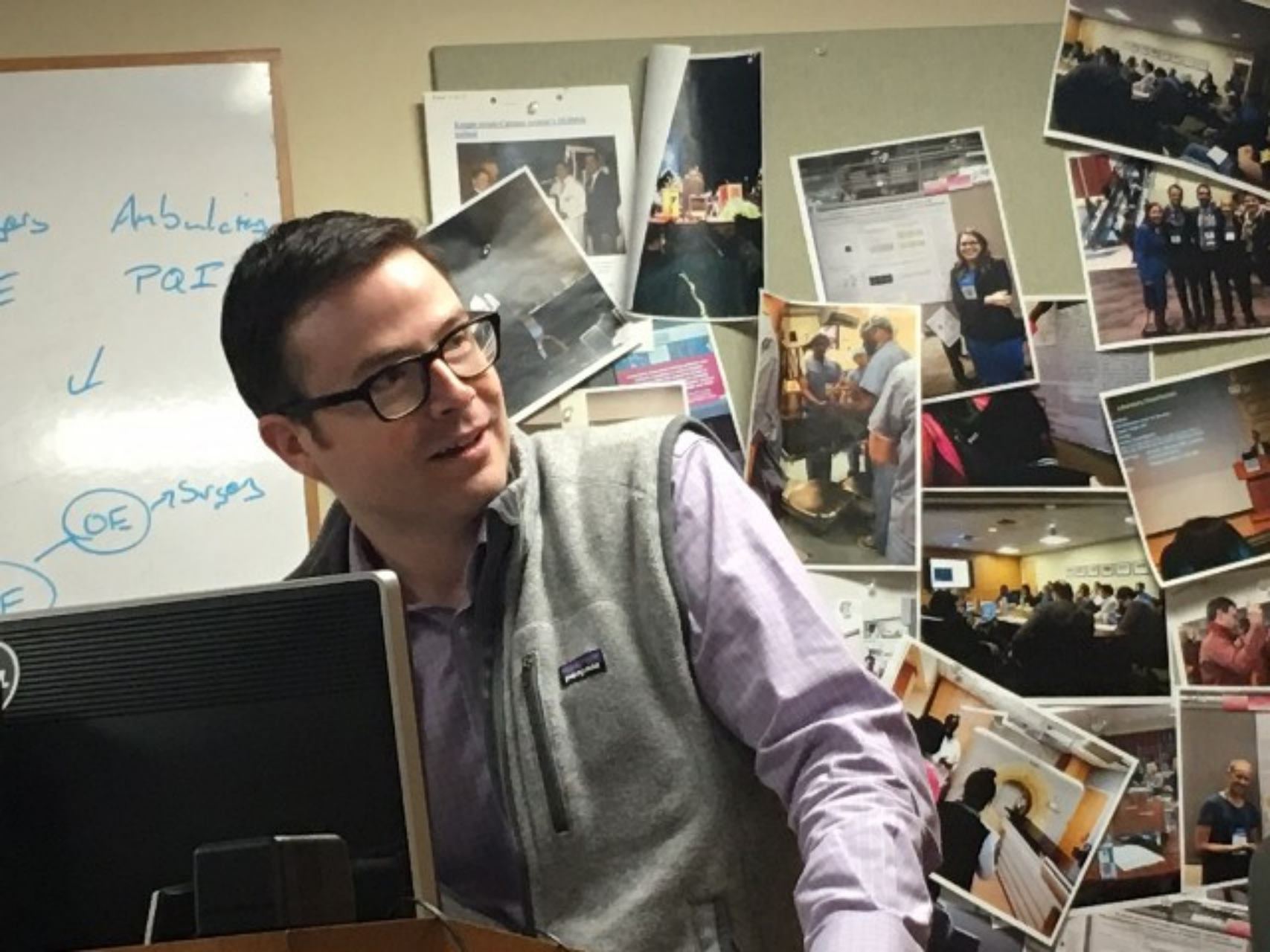


# RESTIMULATION OF TUMOR-SPECIFIC T CELLS USING RADIOTHERAPY IN A MURINE T CELL ANERGY MODEL

Josh Walker, MD/PhD, OHSU Radiation Medicine











OREGON  
HEALTH & SCIENCE  
UNIVERSITY

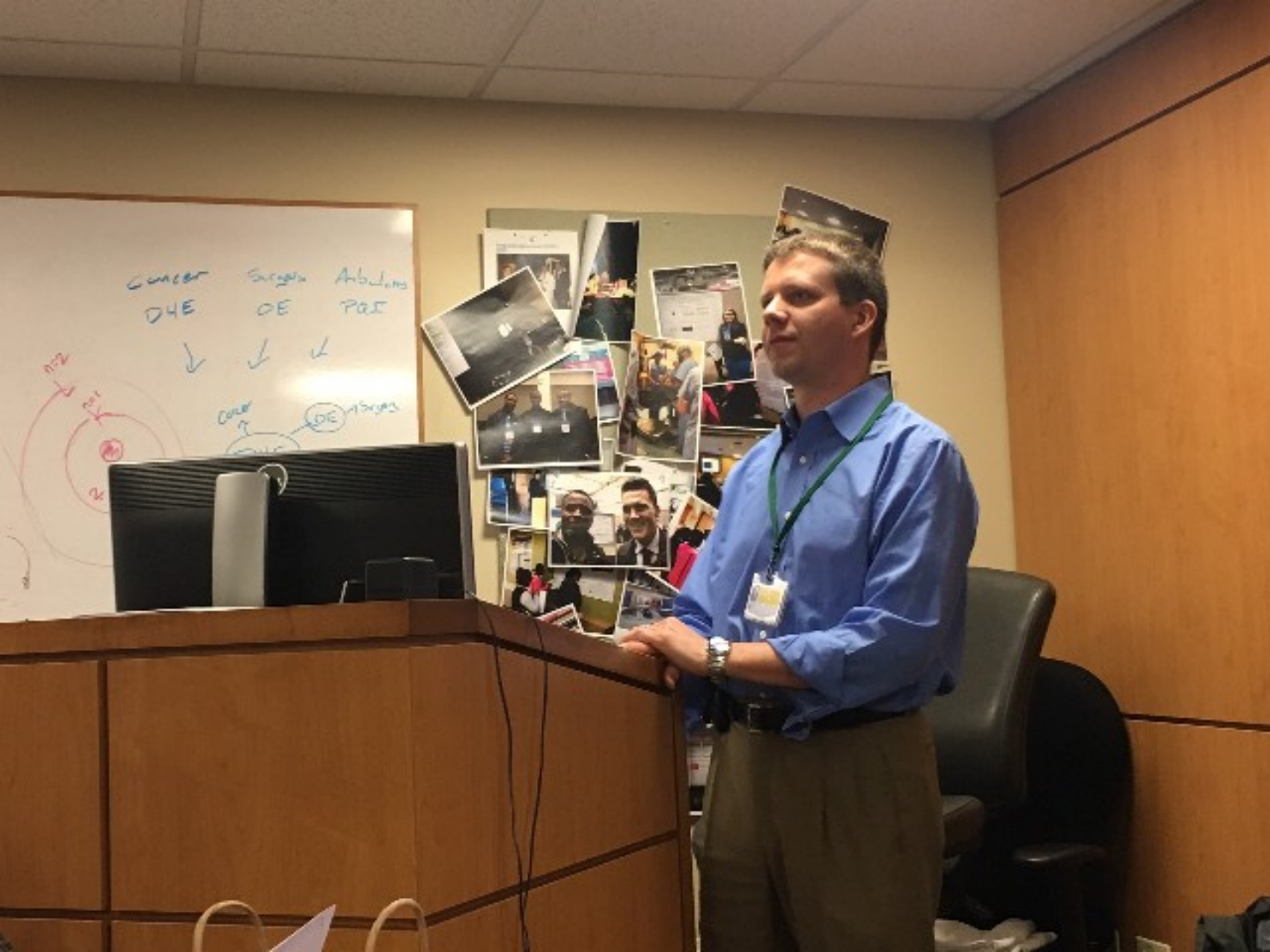
Limited Use of Adjuvant Therapy in US Patients  
with Resected Gallbladder Cancer despite a  
Strong Association with Survival:  
Analysis of the National Cancer Data Base

Timur Mitin, MD PhD

C. Kristian Enestvedt, MD

Ahmedin Jemal, MD

Helmneh Sineshaw, MD

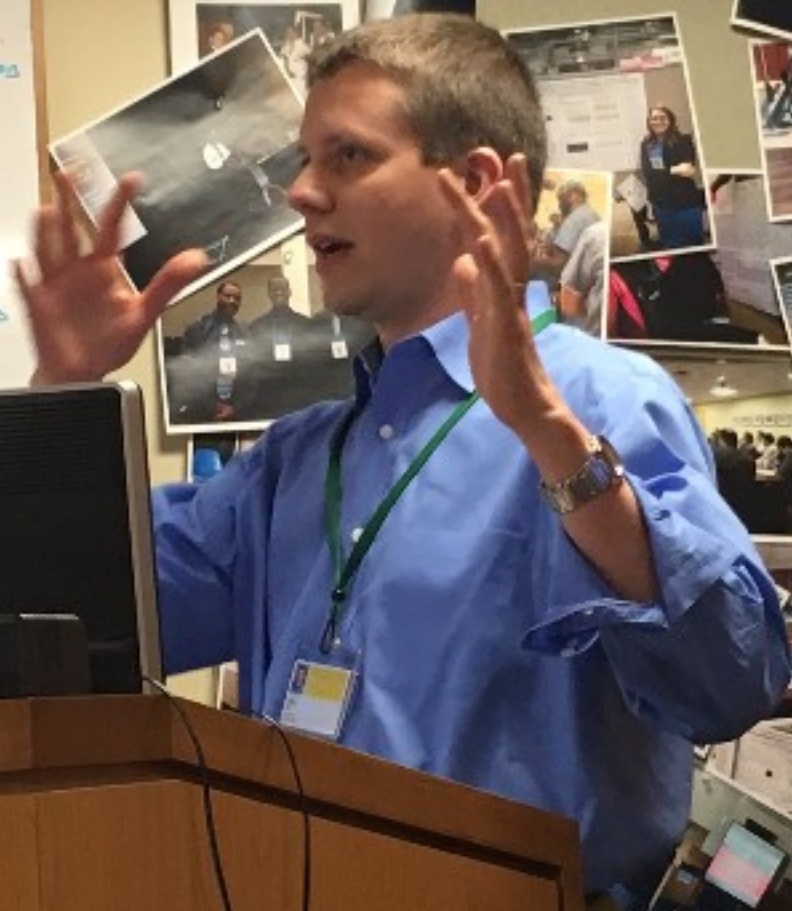


Cancer      Surgery      Antibiotics  
DHE      OE      PGI





Surgery Ambulatory  
OE PAI  
↓ ↓  
Color ↑ (OE) → Surgery  
(DUE)



Surgeons Ambulances  
OE PQI  
↓ ↓  
Cover n (OE) → Surge





# Prediction Model for Estimating the Survival Benefit of Adjuvant Radiotherapy for Gallbladder Cancer

Samuel J. Wang, C. David Fuller, Jong-Sung Kim, Chuan F. Seng, Charles R. Thomas Jr, and Peter M. Harkin

J Clin Oncol. 2008; 26(14):1776-1781.  
DOI: 10.1200/JCO.2007.13.1153

2008 SSAT PLENARY PRESENTATION

## National Trends in the Management and Survival of Surgically Managed Gallbladder Adenocarcinoma Over 15 years: A Population-Based Analysis

Steve C. Mayo, Andrew B. Shoen, Hart Nathan, Barish Edil, Christopher L. Wolfgang, Kruse Hesse, Joseph Herman, Richard D. Schulick, Michael A. Choti, Timothy M. Pawlik

JOURNAL OF CLINICAL ONCOLOGY

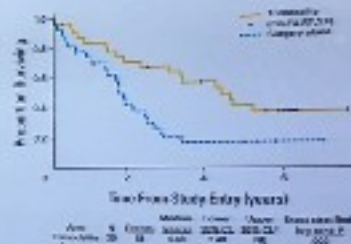
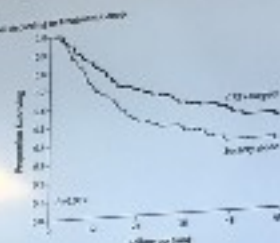
ORIGINAL REPORT

## Nomogram for Predicting the Benefit of Adjuvant Chemoradiotherapy for Resected Gallbladder Cancer

Samuel J. Wang, Andrew Lavinia, Jayashree Kalpathy-Cramer, Celine B. Orl, Gary V. W. C. David Fuller, Jong-Sung Kim, and Charles R. Thomas Jr

# Multi-modality therapy for locally-advanced esophageal cancer

- Surgery has been the cornerstone of definitive therapy
- Multiple studies have tested the value of the addition of chemoradiation to improve LC and OS
- Multimodality therapy has rapidly become the standard of care
  - Multiple RCT and meta-analyses showing better OS



Jeppert, JCO, 2018,  
Van Hagen, NEJM, 2012.



Surgeons Ambulances  
OE PQI  
↓ ↓  
Cover  
OE → Surgeons



## Funding sources and acknowledgements

- ASCO Young Investigator Award
- Radiological Society of North America (RSNA) Seed Grant
- Daira Melendez
- Carol Halsey
- Patrick McLaren
- Sharlene D'Souza
- Brintha Enestvedt
- Radiation Medicine nurses





## Radiation Medicine

### Differential radiation dose-specific microRNA regulation in colorectal cancer

Shushan Rana, MD

PGY-4 Radiation Medicine Resident

Anand Lab



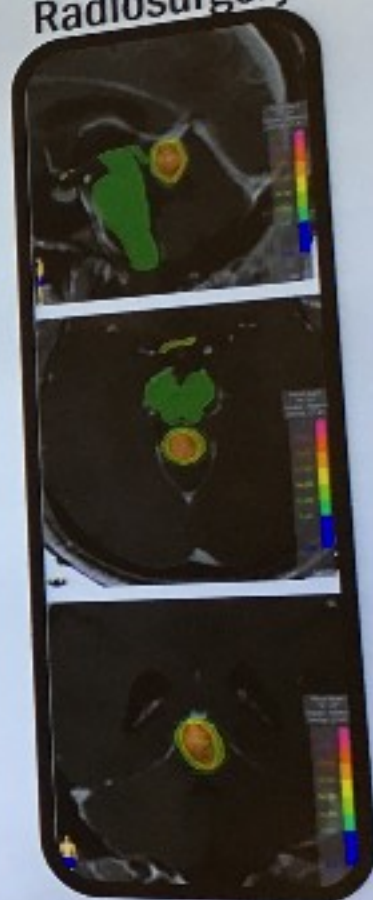
## Standard Fractionated Radiation Therapy



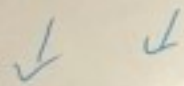
## Stereotactic Body Radiation Therapy



## Stereotactic Radiosurgery



Surgeons Ambulances  
OE PQI



Color  
↑  
OE → Surge









Monitor: Primary Monitor

Use Presenter View

Monitors:

Grant submitted



OHSU Foundation

Medical Research Foundation of Oregon

**CONQUER  
CANCER**  
FOUNDATION

of the American Society of Clinical Oncology

ASCO Young Investigator Award

Grant applications in process

**RSNA**

Radiological Society  
of North America

Research Resident/Fellow Grant

**ASTRO**

TARGETING CANCER CARE

ASTRO Residents/Fellows in Radiation Oncology  
Research Seed Grant

## Research Team



Cell, Developmental & Cancer Biology



Anand Lab



Radiation Medicine

Sudarshan Anand  
Cristina Espinosa  
Namita Chatterjee  
RaeAnna Wilson  
Rebecca Ruhl  
Clay Hudson

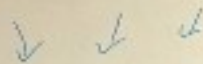
Shushan Rana

Charles Thomas

# Enhanced delivery of antisense oligonucleotides into cancer cells using sublethal dose of radiation to silence MGMT

NAME	:Prakash Ambady, M.D.
DEPARTMENT	:Neurology, :Blood brain barrier & Neuro-Oncology program, OHSU
TITLE	:Assistant Professor
DEGREE, INSTITUTION AND YEAR	:MBBS, Pondicherry University, 2003
SPECIALTY TRAINING	:Neurology; Drexel University College of Medicine, 2012 :Neuro-Oncology; Johns Hopkins University, 2013 National Institutes of Health, 2014
CURRENT AREAS OF EXPERTISE	: Neuro-Oncology

Cancer      Surgery      Ambulatory  
DHE      DE      PRI



Core  
↑  
DE surgery





# Applications of Inorganic Nanoparticles in Radiation Medicine

October 1<sup>st</sup>, 2016

10th Annual Research Retreat Department of Radiation Medicine

**Anna Brown**, Post Doctoral Scholar  
Ph.D. Portland State University 2013

PI: Conroy Sun, Assistant Professor

Oregon State University/Oregon Health and Science University  
College of Pharmacy



# Future Directions

- **Biological clearance metal nanoparticles**
- Radiation dose enhancement effects
- Radiation responsive materials
- Spectral Molecular Imaging (SMI) contrast agents

Fellowships applied for:

PhRMA (DSPE-PEG biocompatibility)

Burroughs Wellcome Fund (heavy metal nanoparticles)

Manuscripts: Anna Brown, Marc Kai, Allison DuRoss, Conroy Sun

**Synthesis and biocompatibility of DSPE-PEG micellular platinum nanoparticles** *in preparation*



# Precision Oncology

## *A Road Map, In Brief...*

Annual Research Retreat (10/1/16)

Reid F. Thompson

*(MD PhD @ Einstein, 2011; RadOnc residency @ Penn 2016)*

Oregon Health & Science University / Portland VA Medical Center

Assistant Professor

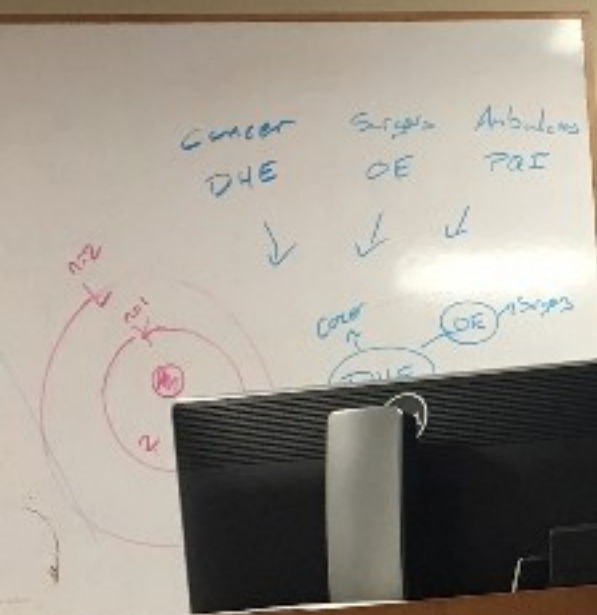
Dept. of Radiation Medicine, Computational Biology

Cancer      Surgery      Ambulances  
DHE      OE      PAI



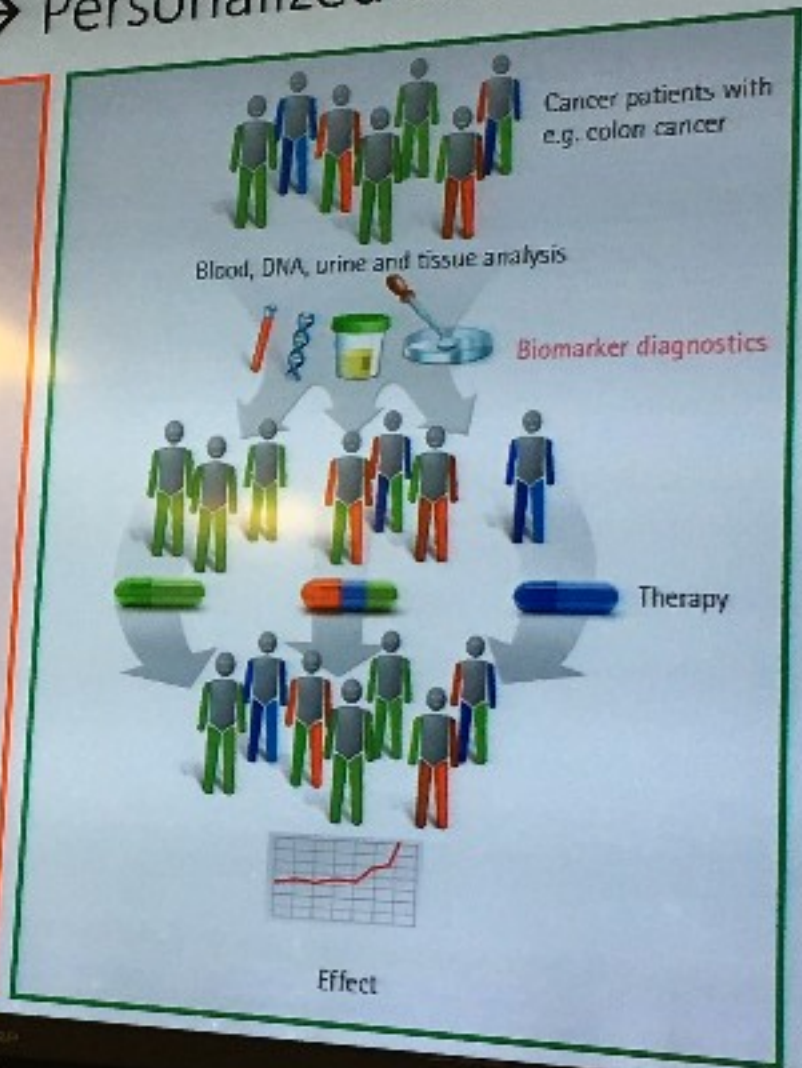
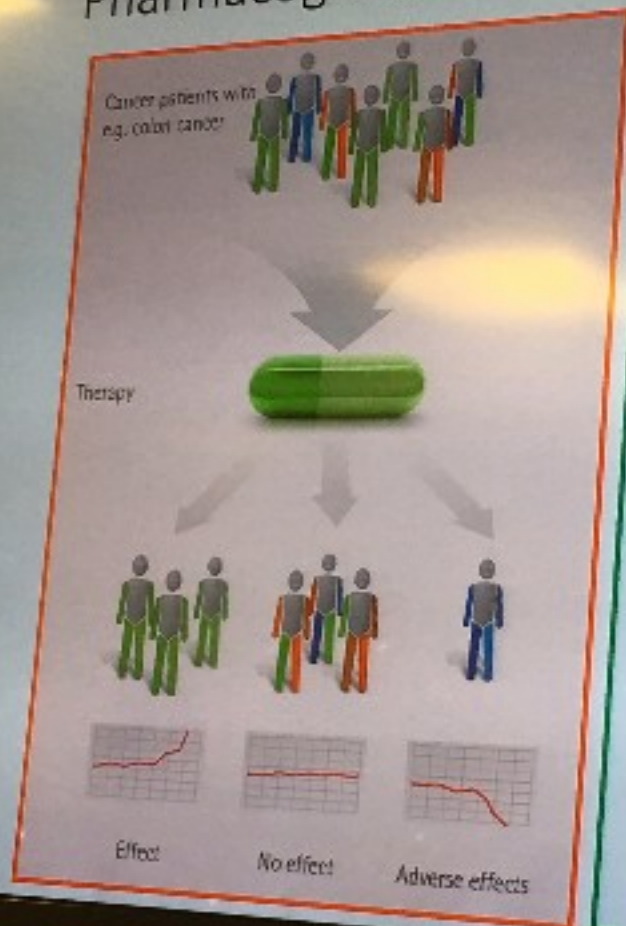
Color      (OE) surgery  
↓      ↓  
TIME







# Pharmacogenomics → Personalized Medicine



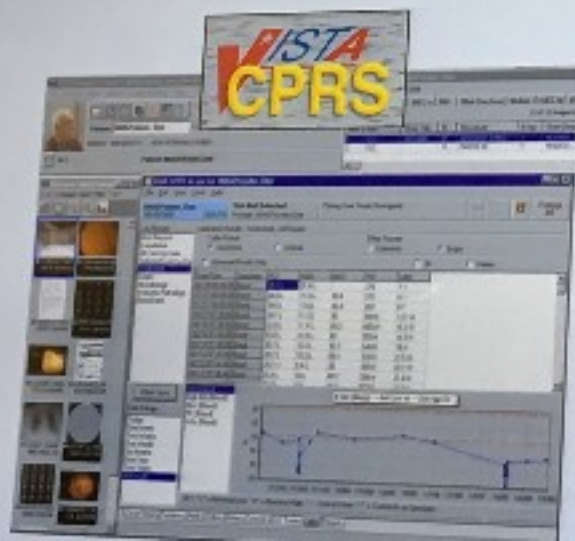
# Opportunities @ the VA

## Enormous, integrated clinical database

- >8 million veterans
- >150 hospitals, ~1000 clinics
- >20 years of EMR data
- Comprehensive **health information**
  - Labs, imaging, medications, procedures, diagnoses, observations/outcomes

## Million Veterans Program (MVP)

- Massive biorepository
- Genome-scale genetic data
- Extensive phenotypic data
  - VistA
  - Questionnaires (e.g. lifestyle)
- Re-contact potential (follow-up)







# VA

## **Million Veterans Program (MVP)**

- Massive biorepository
- Genome-scale genetic data
- Extensive phenotypic data
  - VistA
  - Questionnaires (e.g. lifestyle)

Re-contact potential (follow-up)



# Local Antigen in Non-Lymphoid Tissue Promotes Resident Memory CD8<sup>+</sup> T cell Formation During Viral Infection

Jeff Nolz

Department of Molecular Microbiology and Immunology

Surge's Ambulatory  
OE PQI

↓ ↓

OE Surge's  
PQI

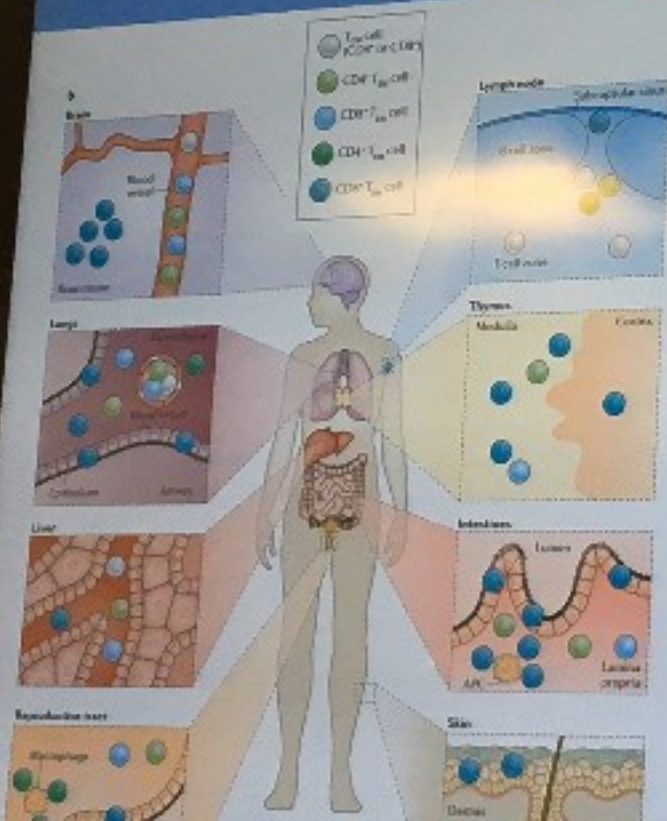
THE  
**PRIDE**



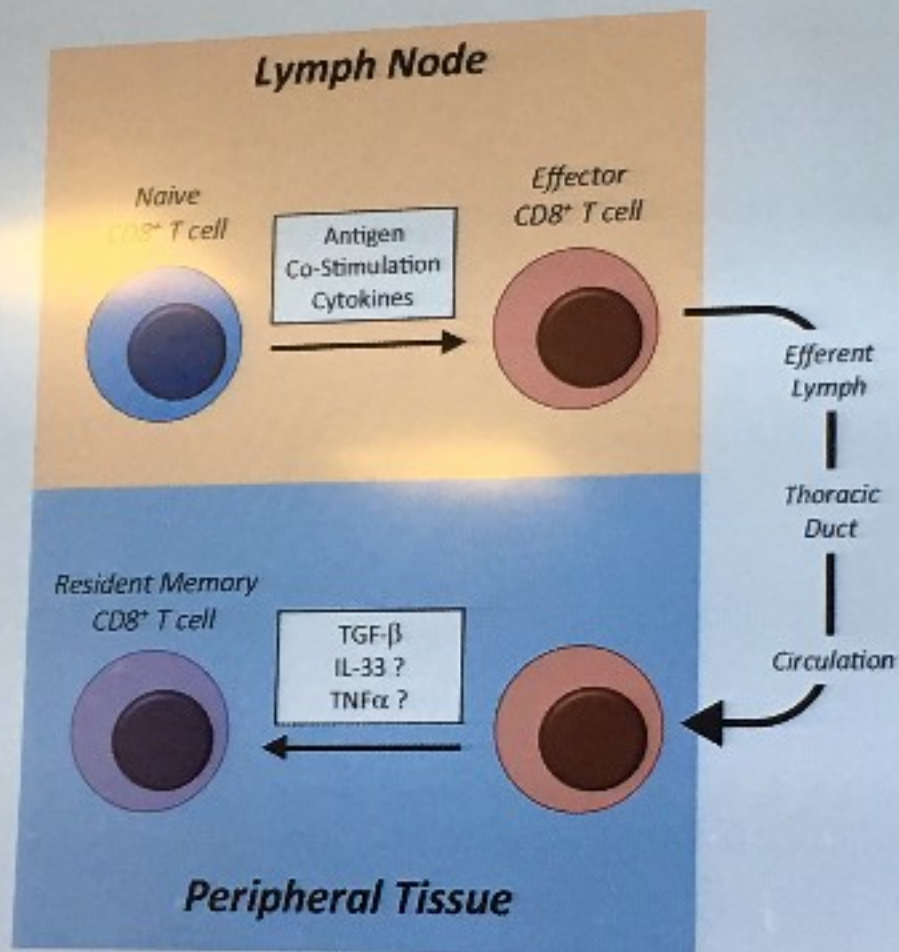
of the Dakotas



# Tissue-Resident Memory CD8<sup>+</sup> T cells



- Have been identified in a number of non-lymphoid tissues such as the skin, gut, lung, and female reproductive tract
- **Do Not** re-enter the circulation following the resolution of infection
- Provide robust protection against re-infection
- Vaccines, Host Defense, Atopic Dermatitis and Contact Hypersensitivity



# Acknowledgements

## Meitz Lab

### *Present Members*

Jana Monster

Josief Onbom

### *Past Members*

Tahsin Khan

Gus Kilgore

Josief

Jana



Gus

Tahsin



KNIGHT  
CANCER INSTITUTE  
Oregon Health & Science University



Medical Research  
Foundation





# Detection of Novel Circulating Tumor Cell Populations in Cancer Patients

Vidya Perera

Bornstein Lab

Department of Radiation Medicine

Portland State University 2015 ( MSc)

Microbiology, Molecular Biology

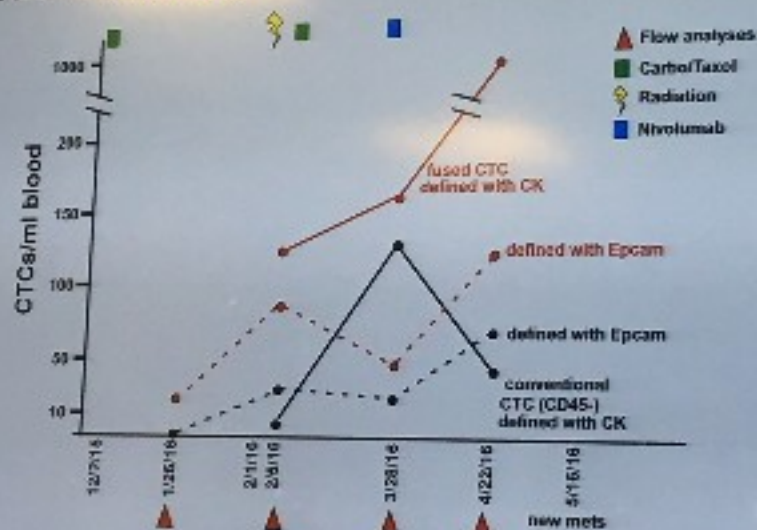






- Correlate Number of CTCs (CD45+ and CD45-) with treatment outcome

## Longitudinal study



# Acknowledgments

## Wong Lab

- Melissa Wong
- Charlie Gast
- Laura Riegler
- Mark Schmidt
- Nick Smith
- John Swain
- Luai Zarour

## Bornstein Lab

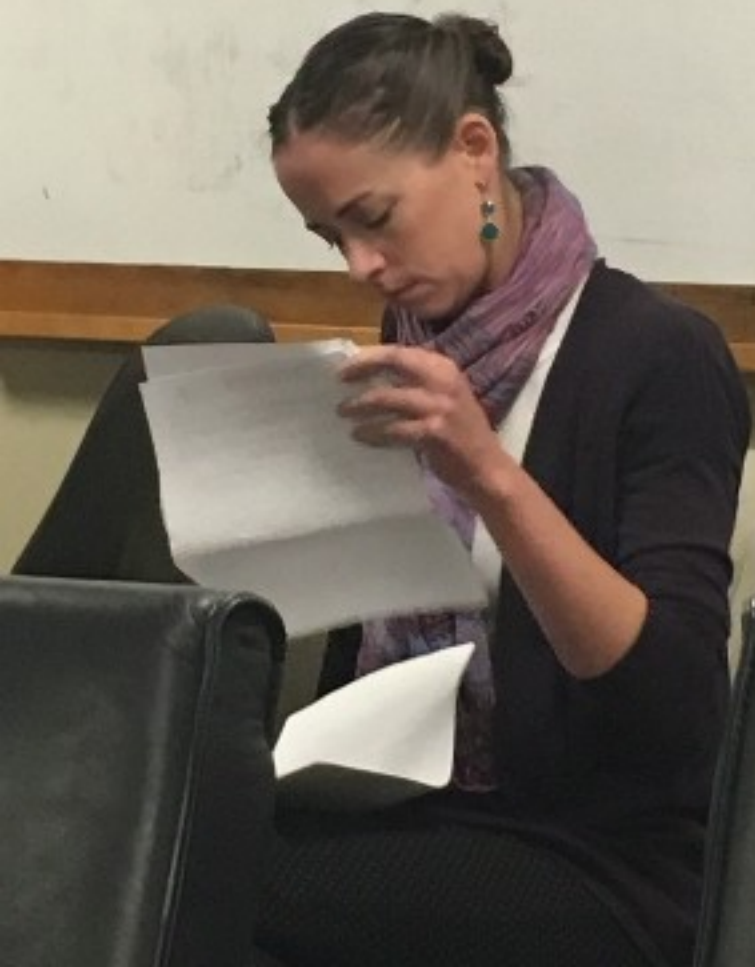
- Sophia Bornstein
- Joanna Filopoulos

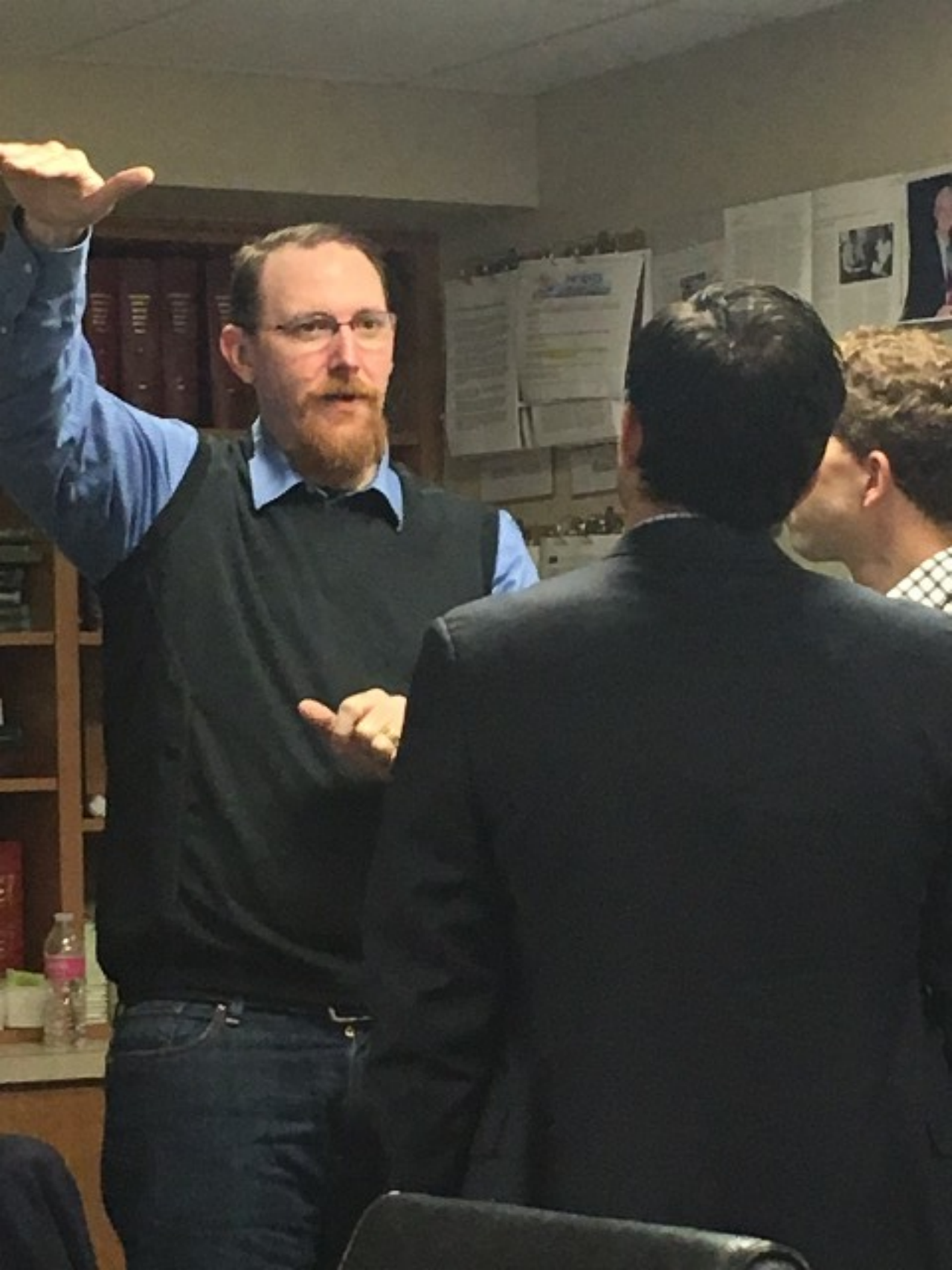
## Department of Radiation Medicine

- Dr. Charles R Thomas Jr
- Arthur Hung, MD
- Charlotte Kubicky MD PhD
- John Holland MD
- Jerry Jaboin MD PhD



$$6 \times T_{1/2}$$









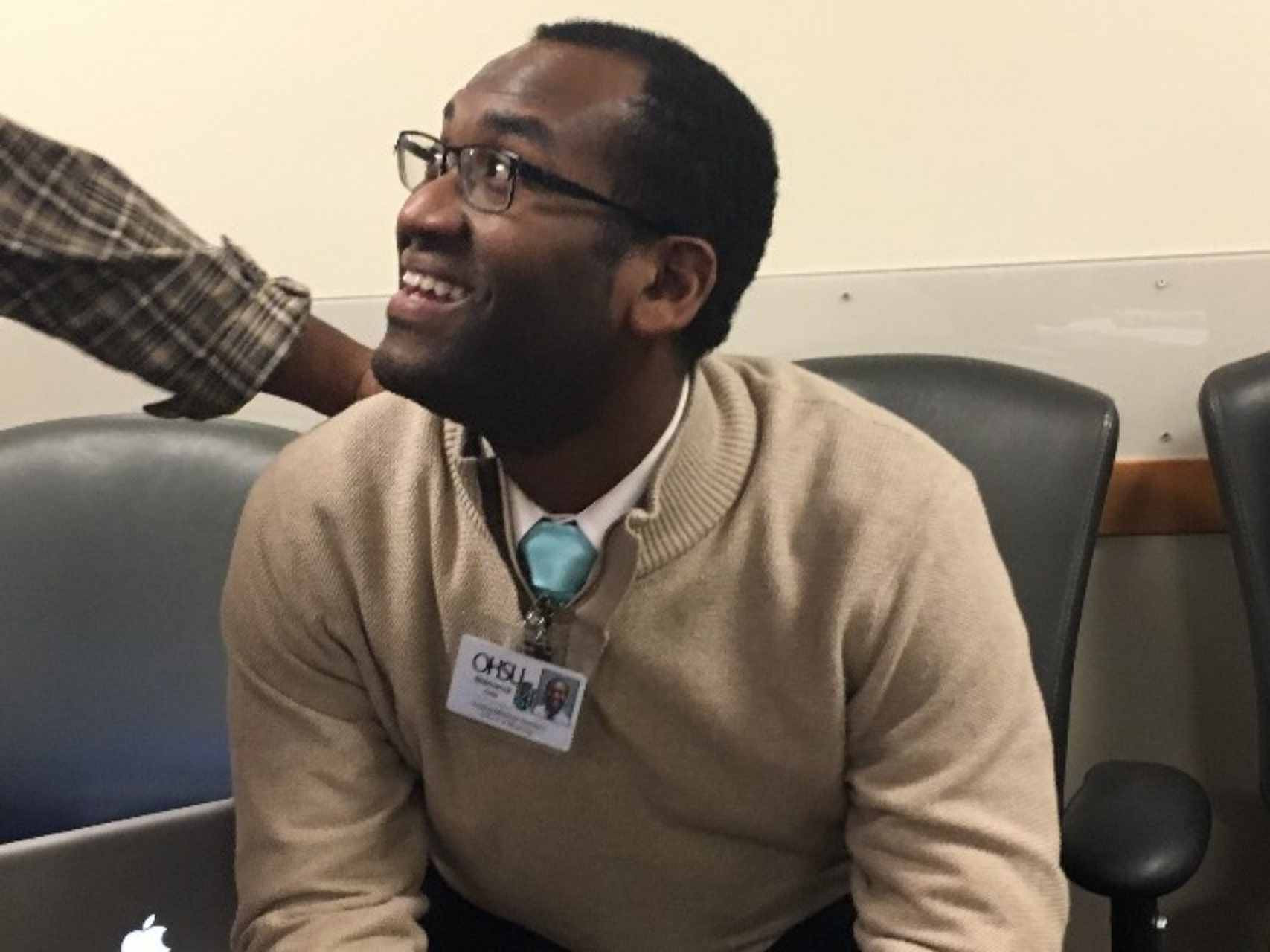








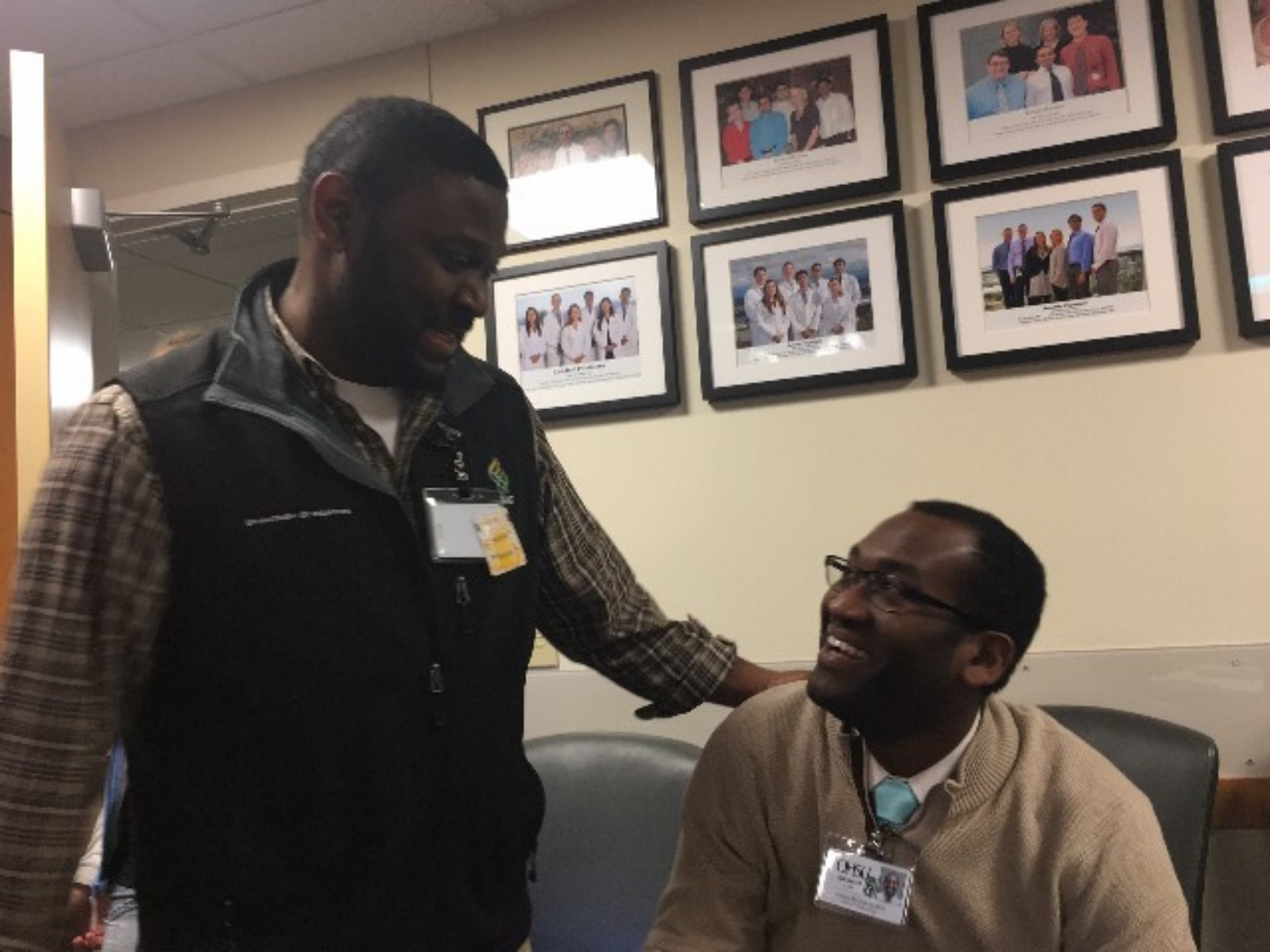


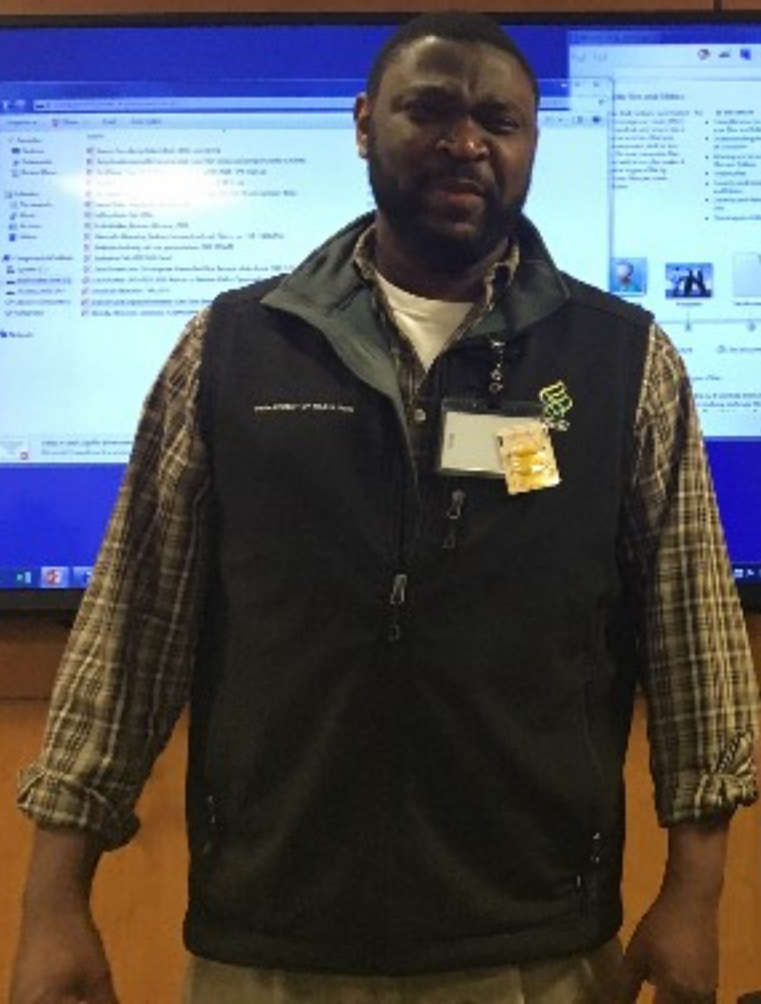




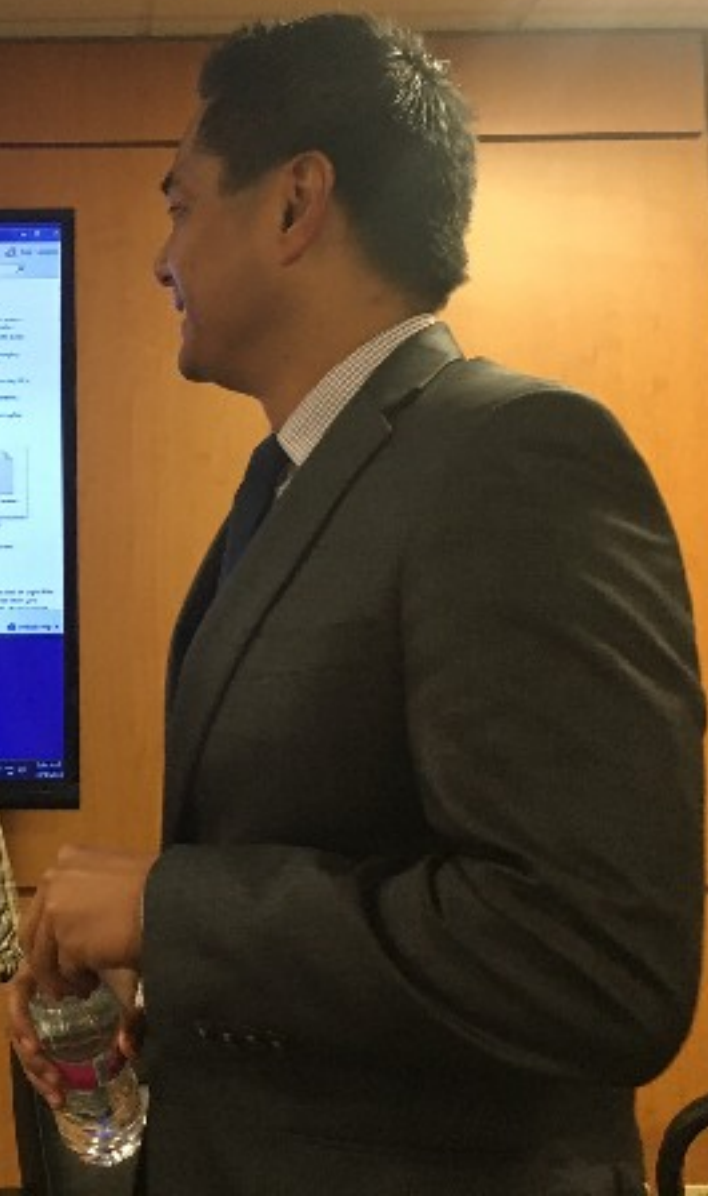
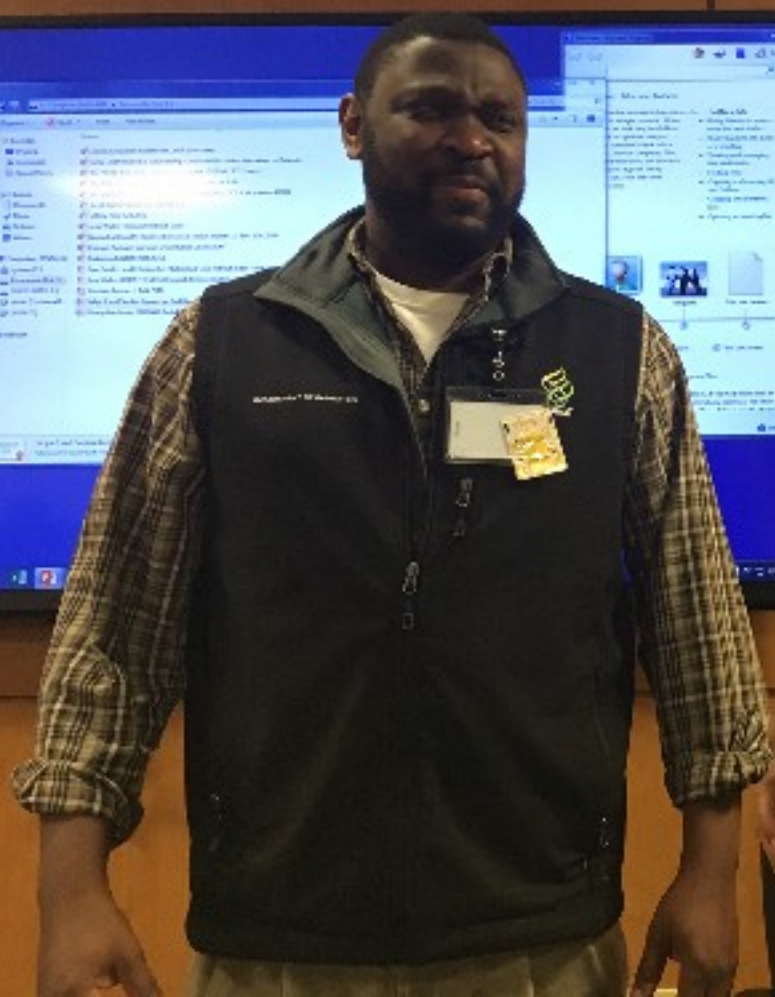
















# **Genetically Engineered Mouse Models for Studying Radiation Biology**

**Phuoc T. Tran**

**October 1, 2016**



**JOHNS HOPKINS**  
MEDICINE

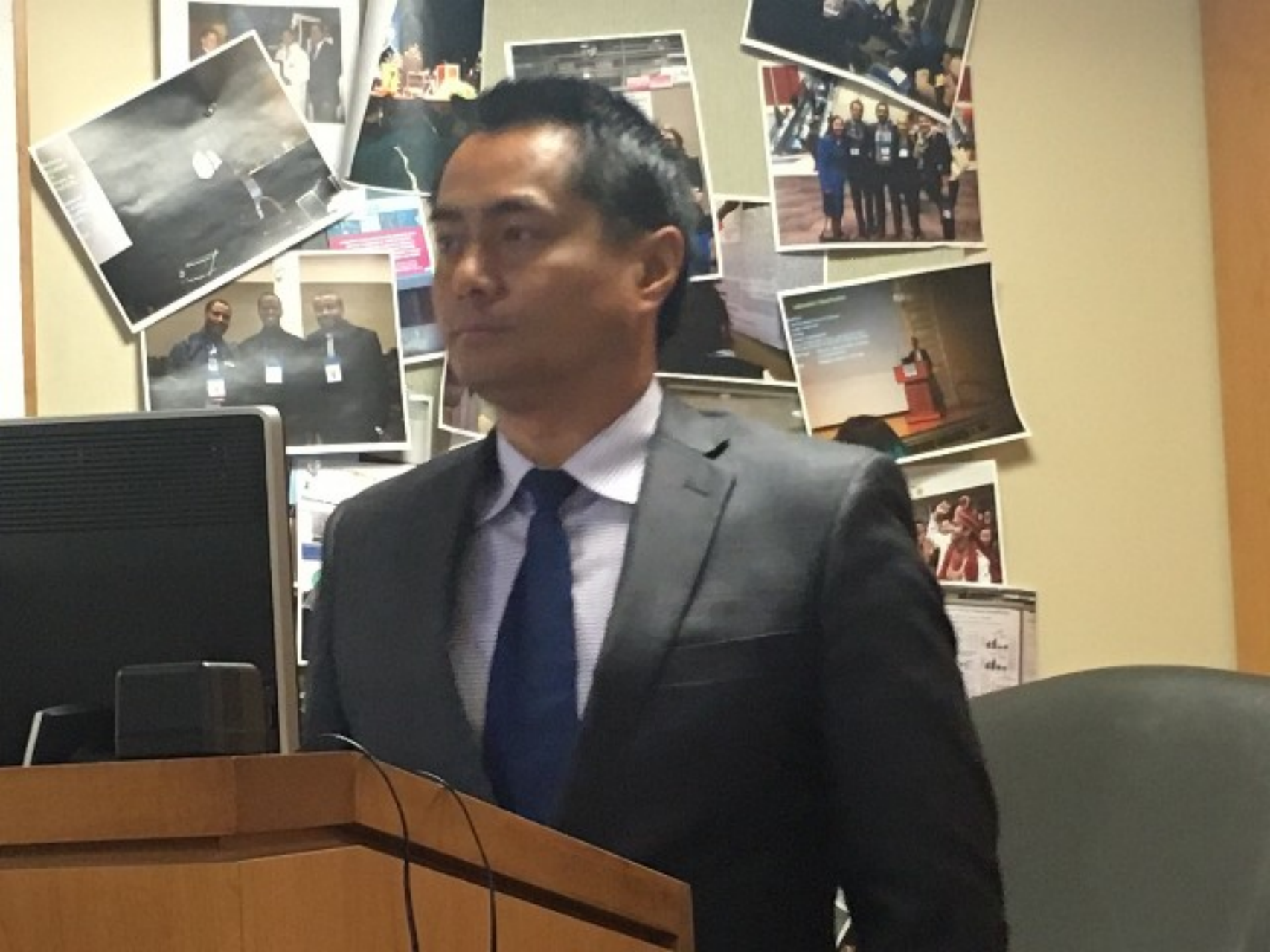
**RADIATION ONCOLOGY &  
MOLECULAR RADIATION SCIENCES**



Customer  
DHE

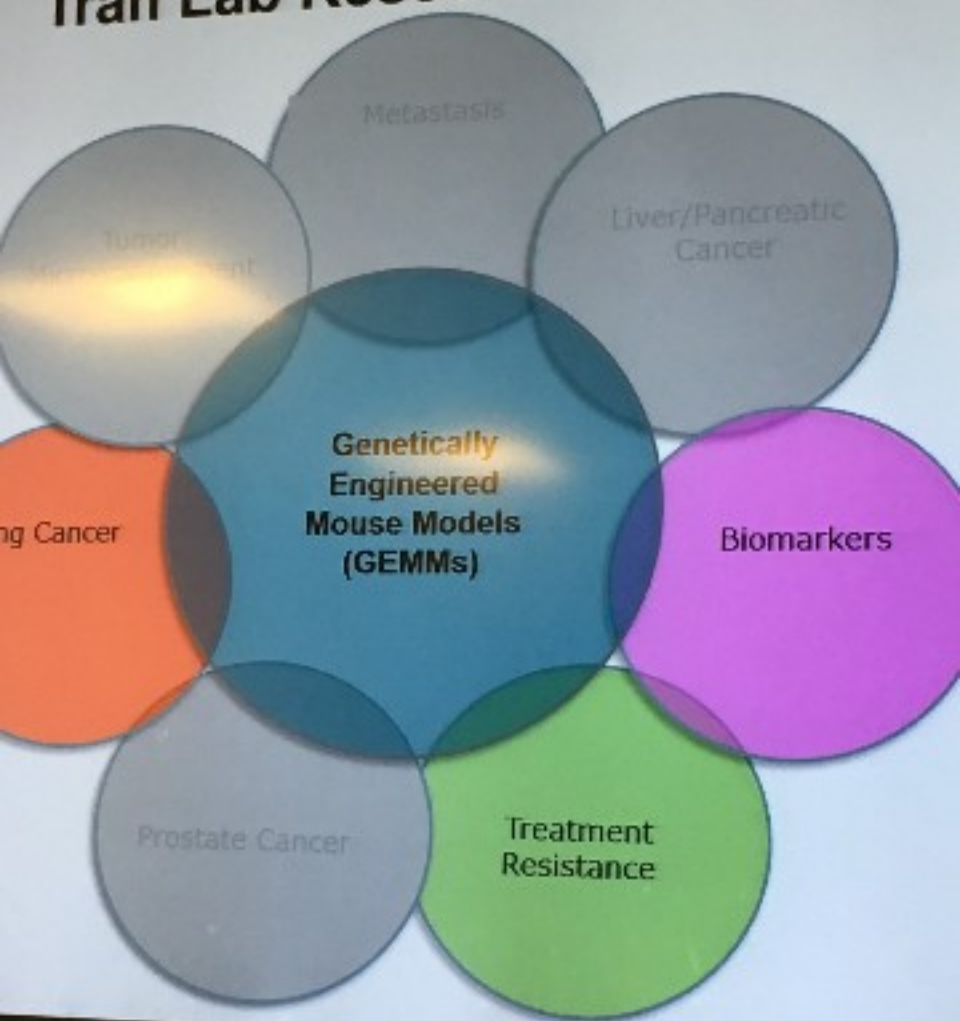
Support  
O







# Tran Lab Research Program



### Directions

and yield approximately 100% conversion of monomer to polymer.

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-Cooping in this manner not only are children  
injected with and subvert the idea of  
peace in migration.



The image shows a collage of scientific posters from the 1997 American Society of Human Genetics meeting. The posters are displayed on a wall, with some showing bar graphs, line graphs, and text. The bottom of the image shows the backs of many people sitting in an audience, looking towards the posters.

**THE EFFECT OF TEMPERATURE ON THE RATE OF ENZYME ACTIVITY**

**HYPOTHESIS**  
The rate of enzyme activity will increase with temperature up to an optimal point, after which it will decrease.

**PROCEDURE**  
1. Prepare a series of test tubes containing a fixed volume of substrate solution.  
2. Add a fixed volume of enzyme solution to each test tube.  
3. Mix the contents of each test tube thoroughly.  
4. Place the test tubes in a water bath at different temperatures.  
5. Measure the rate of reaction using a colorimeter.

**DATA TABLE**

Temperature (°C)	Rate of Reaction (Absorbance)
10	0.15
20	0.35
30	0.55
40	0.75
50	0.95
60	0.85
70	0.65
80	0.45
90	0.25

**CONCLUSION**  
The results of the experiment support the hypothesis. The rate of enzyme activity increases with temperature up to an optimal point of 50°C, after which it decreases.



Christie Binder

Radiation Medicine

STUDY CONCEPT: Urine miRNA  
Biomarkers for HCC

MD, PhD, Tufts University, PGY-3



$$F_{No} e^{-\lambda t} = 1.5 \mu g$$

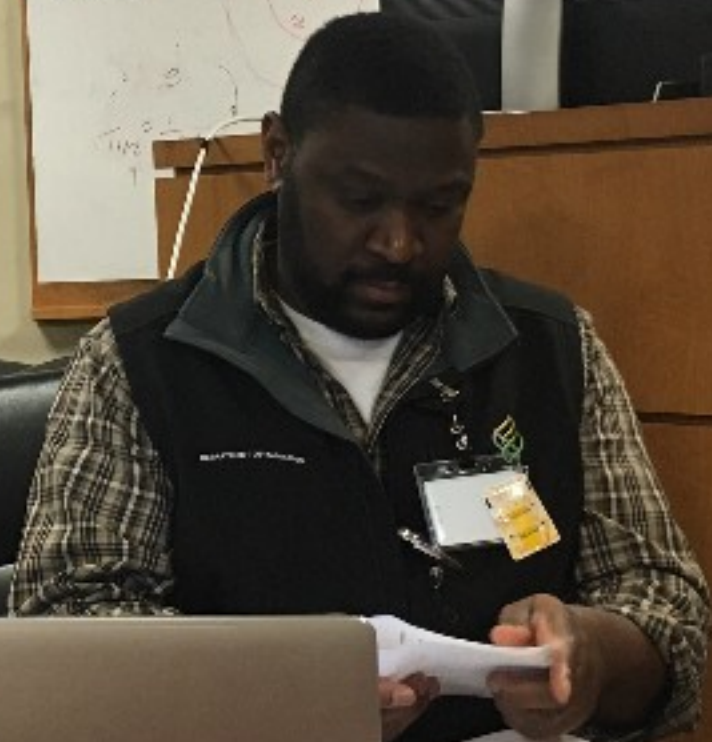
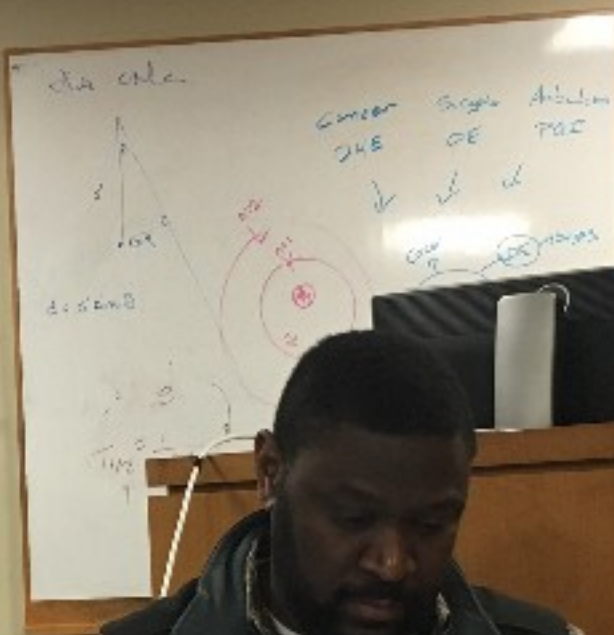
$$t = \frac{\ln 2}{\lambda} = 20 \text{ min}$$

6.7



MACRA

- Med
- Access
- Clinical
- Payment
- And



Surgeons Ambulatory  
OE PQI  
↓ ↓ ↓  
Cover ↑ (OE) Surgeons



## Checkpoint Adaptation in Rhabdomyosarcoma

---

Narendra Bharathy

PhD, National University of Singapore, 2013

Specialty Training: Skeletal Muscle Biology

Current area of expertise: Pediatric Cancer Biology

---



Surgeons Ambulances  
OE PQI



OE → Surgeons  
DHF



DHF

## Checkpoint Adaptation in Rhabdomyosarcoma

---

NarendraBharathy

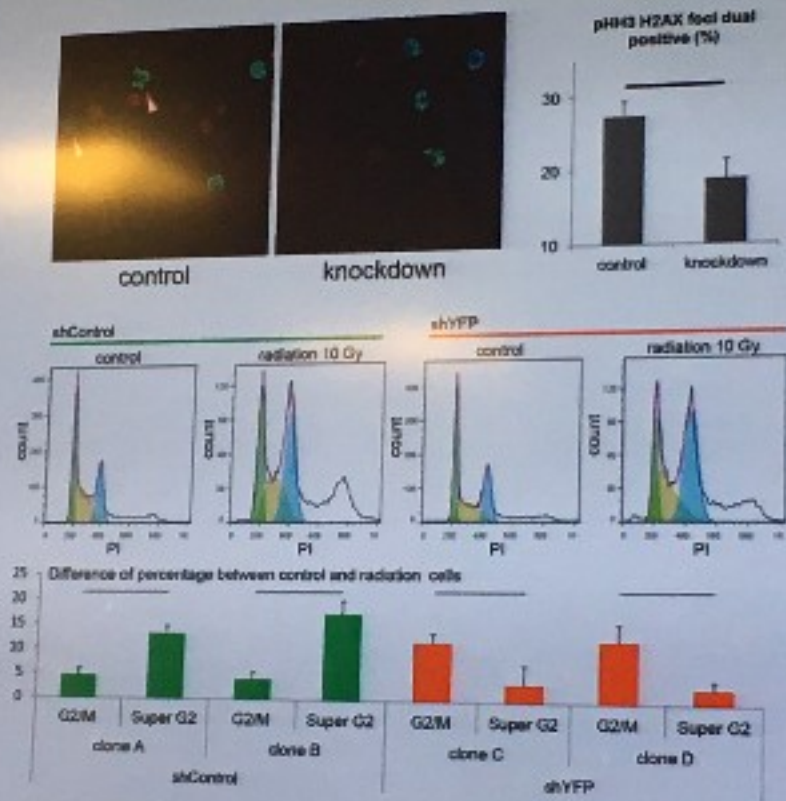
PhD, National University of Singapore, 2013

Specialty Training: Skeletal Muscle Biology

Current area of expertise: Pediatric Cancer Biology

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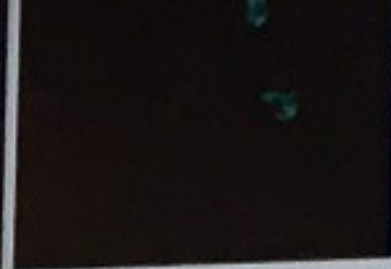
# Pax3:Foxo1a facilitates G2/M checkpoint adaptation



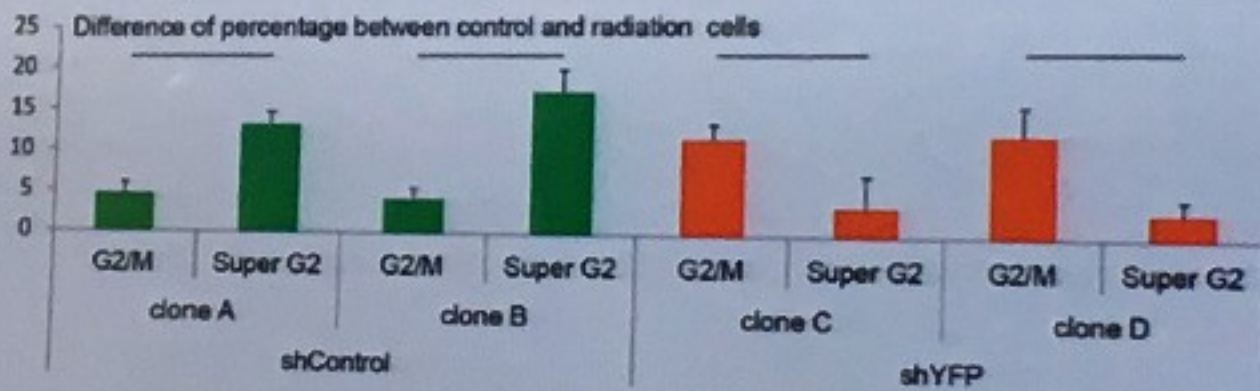
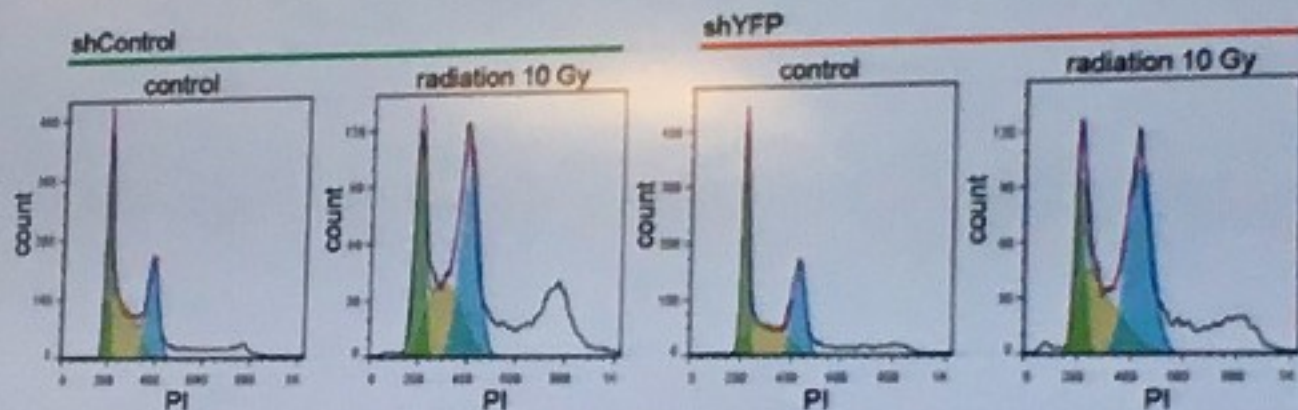
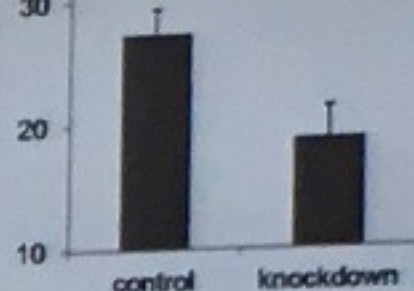




control




knockdown



# empowering phase II: avatar army



ENT 1, 2.5 or 5 mg/kg po QD  
VCR .5, .75, or 1 mg/kg IP Q7D

	RMS Model	Alias	Histology	Harvest site	Disease stage	Diagnosis	Age	Gender
	CTG-1401	PDS-14107	Alveolar	abdomen	IV	recurrent	14	male
	CTG-1211	PDS-13712	Embryonal	vagina	not available	first diagnosis	2	female
	CTG-1115	PDS-13166	Embryonal	neck	not available	first diagnosis	6	male
	CTG-1419	PDS-14094	mesenchymal	orbit	not available	recurrent	9	male
	CTG-1628	PDS-13166B	not available	neck	not available	recurrent	7	male
	CTG-0800	PDS-11074	Pleomorphic	hip	IV	first diagnosis	38	male
	CTG-0129	PDS-10009	Pleomorphic	lung	III	first diagnosis	47	male

# Prognostic implications of skeletal muscle mass depletion in head and neck cancer

Aaron Grossberg, MD, PhD

Resident Physician, PGY-4

Department of Radiation Oncology

MD Anderson Cancer Center

Adjunct Research Instructor

Department of Radiation Medicine

Oregon Health & Science University

KNIGHT RESEARCH APP1: None

KNIGHT SHARED RESOURCES: None

DEGREE, INSTITUTION AND YEAR: MD, PhD OHSU 2013

SPECIALTY TRAINING: Radiation Oncology

CURRENT AREAS OF EXPERTISE: Cachexia, Sarcopenia, Fatigue, Neuroinflammation



# Prognostic implications of skeletal muscle mass depletion in head and neck cancer

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KNIGHT RESEARCH APPT: None

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# Prognostic implications of skeletal muscle mass depletion in head and neck cancer

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KNIGHT SHARED RESOURCES: None

DEGREE, INSTITUTION AND YEAR: MD, PhD OHSU 2013

SPECIALTY TRAINING: Radiation Oncology

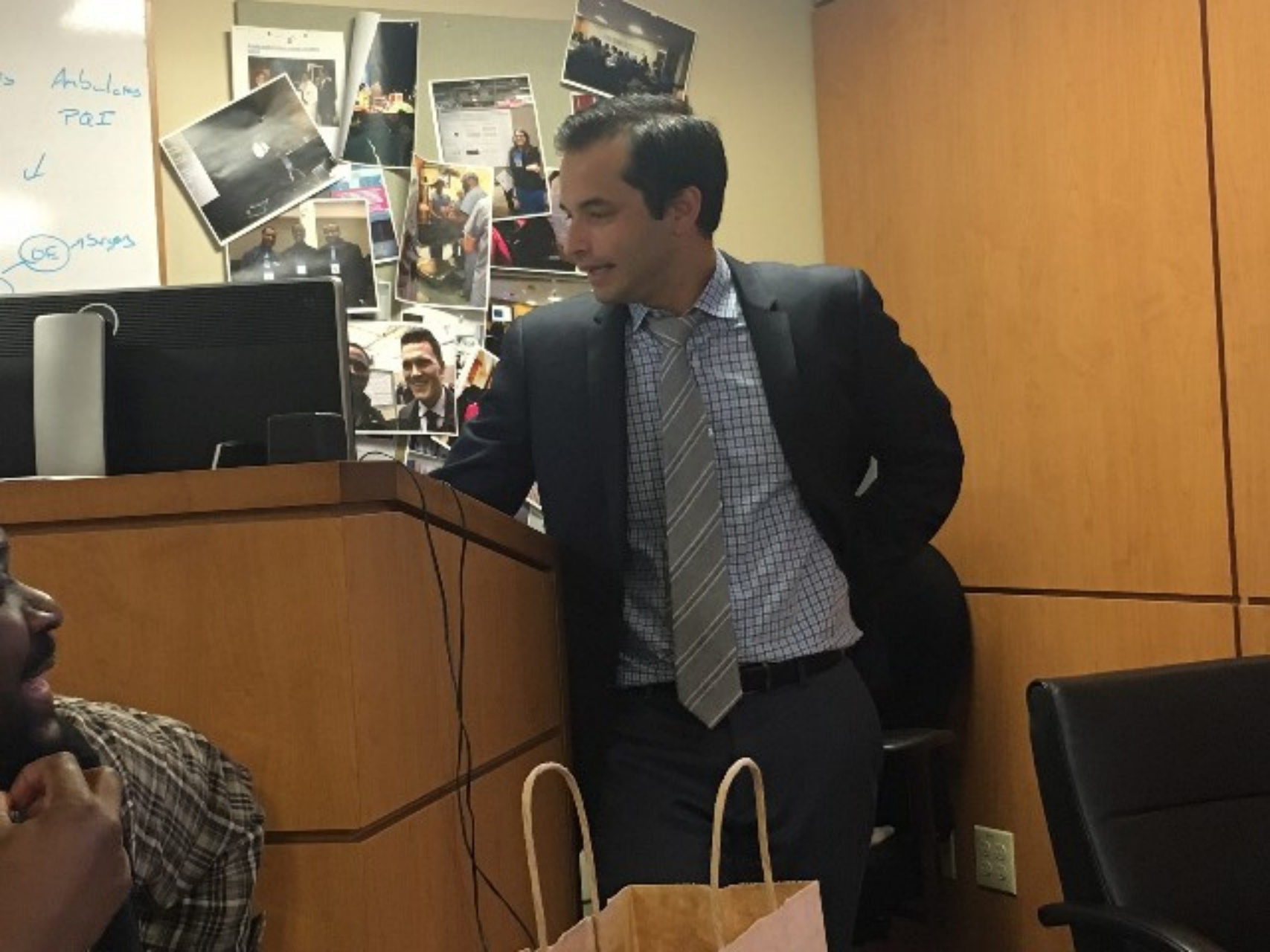
CURRENT AREAS OF EXPERTISE: Cachexia, Sarcopenia, Fatigue, Neuroinflammation













# Optical Coherence Tomography Angiography (OCTA) for eyes with intraocular tumors

Alison H. Skalet, MD PhD

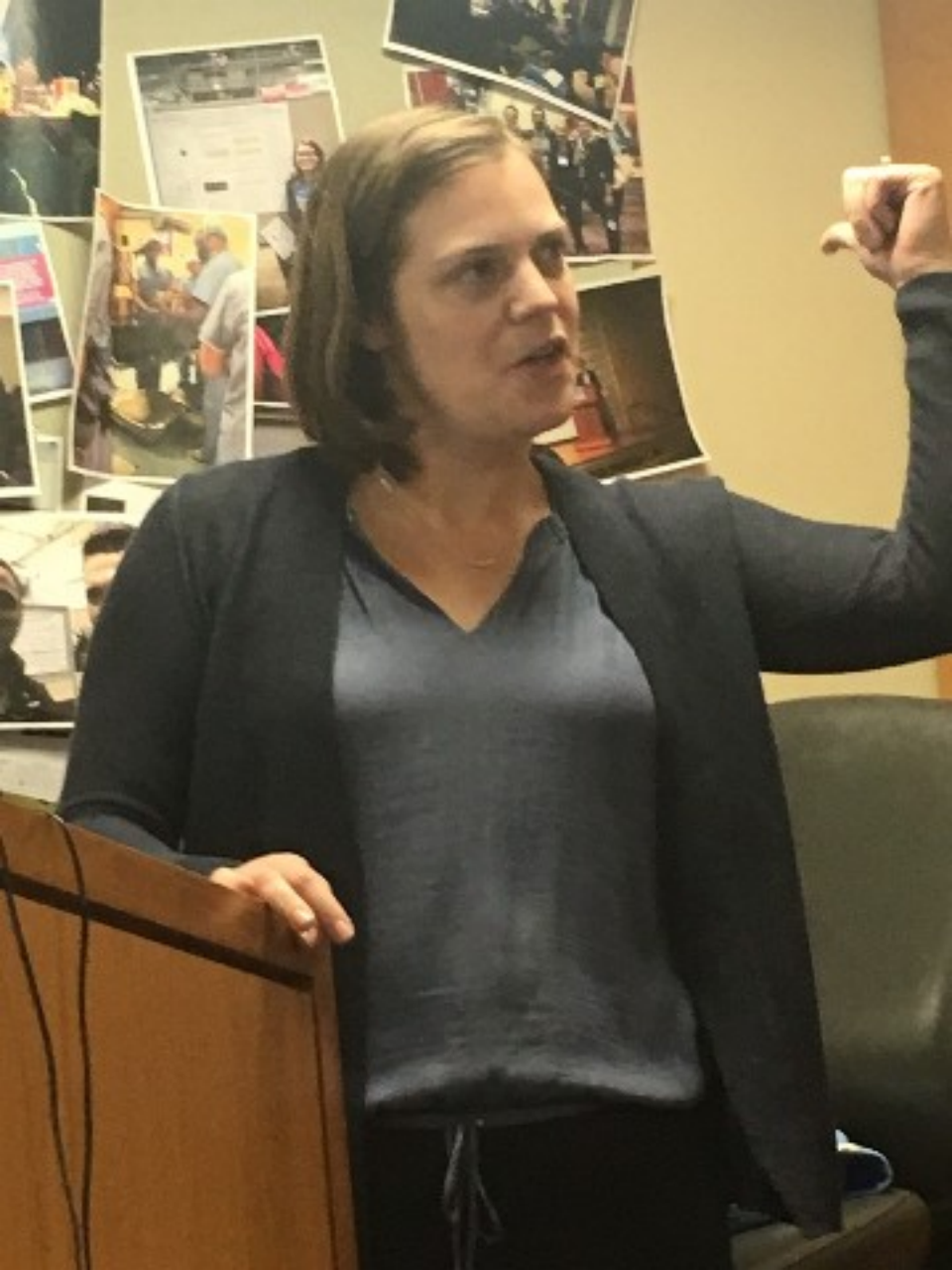
Assistant Professor of Ophthalmology

Adjunct Assistant Professor of Radiation Medicine

University of Pennsylvania School of Medicine, MSTP, 2006

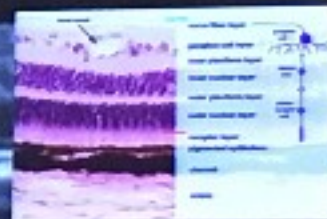
Ocular oncology and pathology







# Optical Coherence Tomography



# Collaborators

- COOL Lab

- David Huang, Yan Li, Yali Jia, Liang Liu
- <http://www.coollab.net>

- Radiation medicine: Charles Thomas, Arthur Hung
- Ophthalmology: David Wilson





# CREDITS AND FUNDING

## Collaborating investigators:

Charles R. Thomas, Jr, MD

Sara J. Walker, PhD

## Funding:

Time and other resources for this project are funded by the OHSU Department of Radiation Medicine

## Resources:

1. NCI Website: <http://www.cancer.gov/about-cancer/what-is-cancer/statistics>
2. McCabe et al, 2013
3. Salz, McCabe, Onstad et al, 2013

## BACKGROUND: PSYCHOLOGICAL STATE/TRAIT AND SPIRITUAL WELL-BEING

- Change in psychological state (i.e., current anxiety, depression, etc) is common among people with cancer
  - E.g., **depression during treatment** associated with:
    - Lower health related quality of life
    - Higher health resource utilization and healthcare costs
    - Higher functional impairment
- **Personality trait** factors also play role **health and QOL**
  - "Big five" personality traits: Neuroticism/Emotional Instability, Extraversion, Openness, Agreeableness, Conscientiousness
    - High levels of neuroticism, particularly introverted, also associated with Neuroticism associated with lower psychological QOL, is particularly detrimental in individuals
- **Spiritual well-being**
  - Significant associations with QOL and coping in life-threatening illness
  - Receiving spiritual support from one's medical team associated with improved QOL

Chen et al., 2002; Eklund et al., 2010; Dugan et al., 2012; Herwig et al., 2016; Hurd et al., 2010; Kyrle et al., 2010; McNeil & Eklund, 2002; Tak-Poon et al., 2014; Walsh et al., 2006, 2009; Schell et al., 2000; Zwaan et al., 2011



CONCEPT  
DUE

STRATEGY  
OF

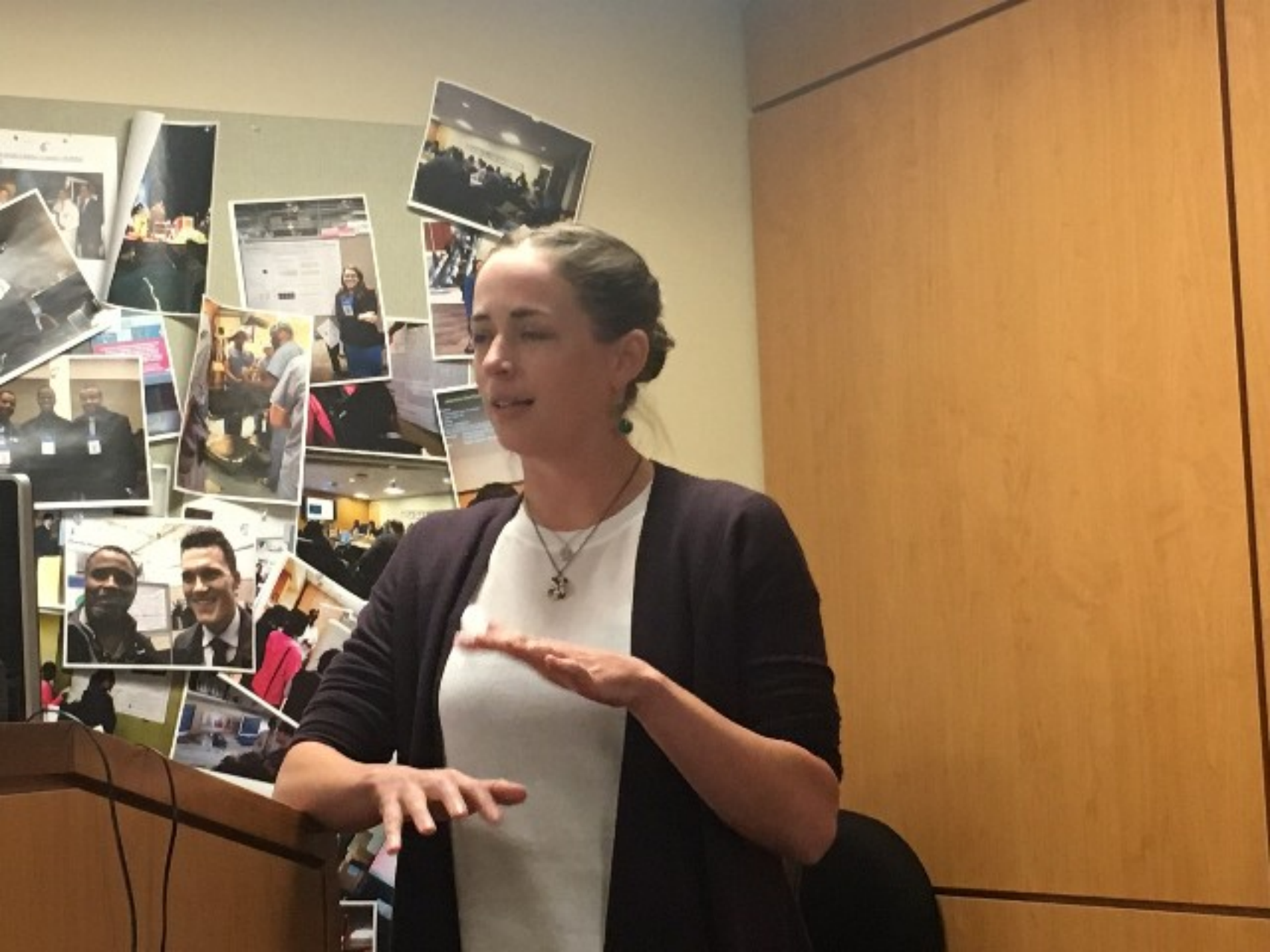
ANALYSIS  
P&L



ONE  
DUE

ONE  
DUE







# CO-INVESTIGATORS AND ACKNOWLEDGEMENTS

- Study supported by Departments of Radiation Medicine and Psychiatry
- Charles Thomas, Jr., MD  
Professor & Chair, Department of Radiation Medicine  
OHSU Knight Cancer Institute
- Jeffrey Robinson, PhD  
Professor & Chair, Department of Communications  
Portland State University
- Biostatistician: Yiyi Chen, PhD  
Assistant Professor, Department of Public Health Admin.  
OHSU Knight Cancer Institute

Acknowledgement and many thanks also to:

Jenn Lockhart

Jo Price

Daphne Baracena

Ramon Sison

Scott Madsen

KJ Paik

Carrie North

Bonnie Luedloff

Alexis Fields

Amy Leatherwood

Feather Coates

Sole Avila



# FUTURE DIRECTIONS

- Abstracts to be submitted for poster/presentation:
  - ASCO Cancer Survivorship Symposium, January 2017
- Manuscripts in preparation:
  - Pre-treatment state/trait associations with illness-related stigma
  - Role of pre-treatment depression and anxiety on post-treatment QOL
- Collaborations with survivorship investigations
  - Effect of premorbid PTSD on post-treatment service utilization and QOL
- Long-term goals:
  - Investigate/understand/address the role of cognitive functioning in QOL, treatment satisfaction, adherence
  - Investigate/understand/address the spiritual needs
  - PCORI mechanism, foundation funding

## MEANING-CENTERED GROUP PSYCHOTHERAPY FOR PATIENTS WITH ADVANCED CANCER



A Treatment Manual

WILLIAM S. BREITBART  
SHANNON POPPITO

OXFORD

DSC

OHSU Retreat 2016



Clifton (Dave) Fuller, MD, PhD

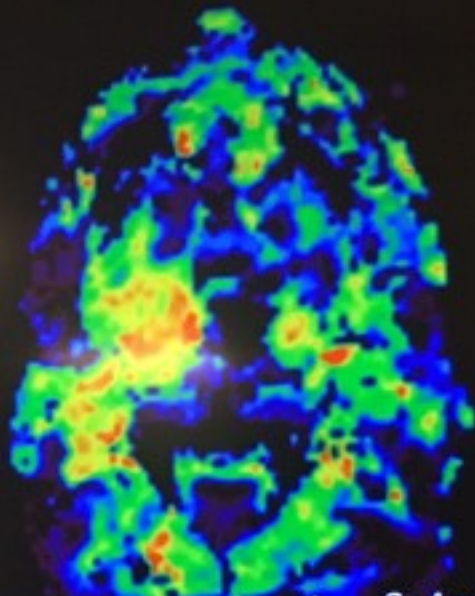
Assistant Professor  
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Assoc. Director,  
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THE UNIVERSITY OF TEXAS

MD Anderson  
Cancer Center

Making Cancer History®



*From Tumor Quantification & Assessment  
toward  
Minimization of Normal Tissue Injury*



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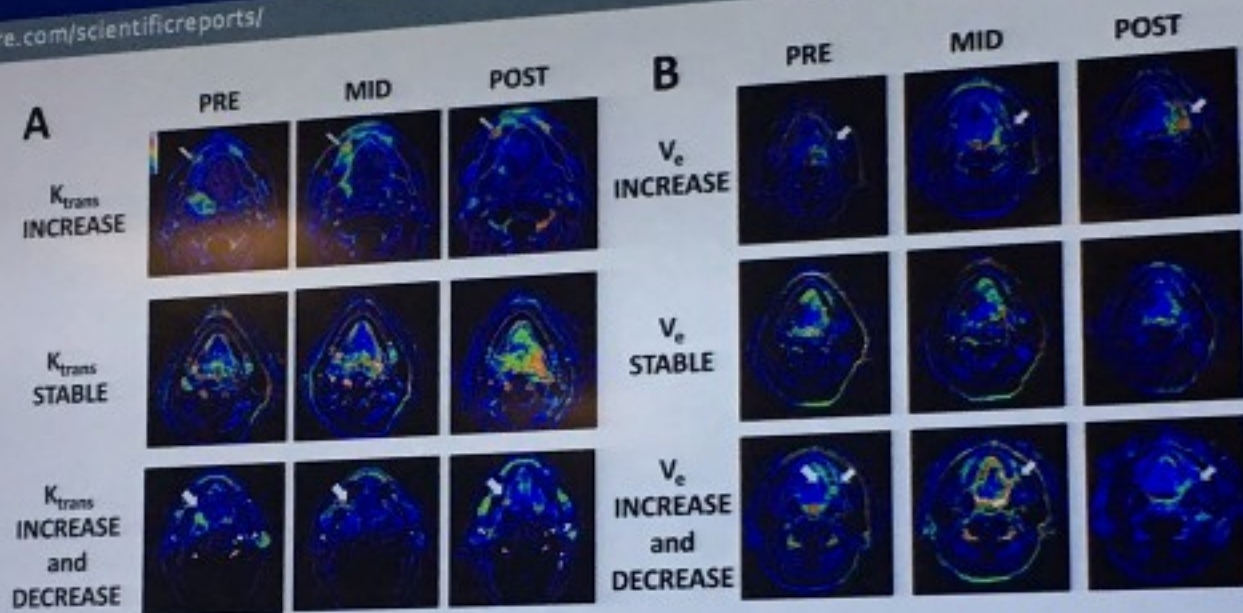
IVIM

*From Tumors*

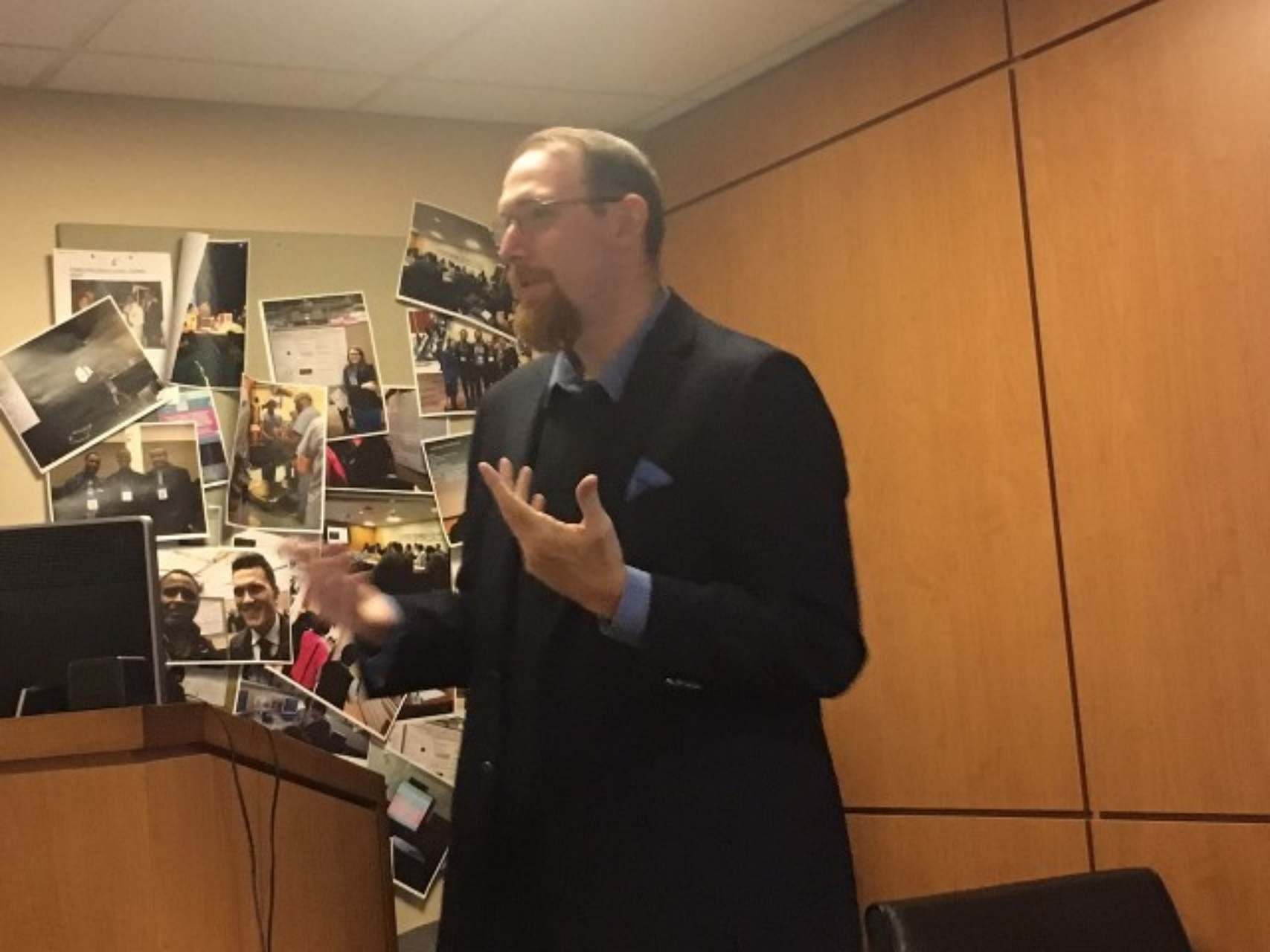
*Minimizing*







**Figure 2. DCE-MRI Detects Focal Vascularity Changes During EBRT.** Evaluation of DCE-MRI acquired  $K_{trans}$  across the entire mandibular volume allows for identification of geographically distinct perturbations which can then be correlated to the dosimetric map for each individual patient. **(A)** Arrows in top and bottom rows identify the area of altered  $K_{trans}$ . Middle row demonstrates no appreciable change in  $K_{trans}$  across the entire mandibular volume regardless of administered EBRT dose. **(B)** Arrows in top and bottom rows identify the area of altered  $V_e$ . Middle row demonstrates no appreciable change in  $V_e$  across the entire mandibular volume regardless of administered EBRT dose. Panels A and B represent distinct patients.







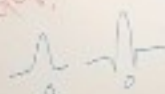


$$N = N_0 e^{-\lambda t} = 1.5 N_0$$

$$t = 20 \text{ min}$$

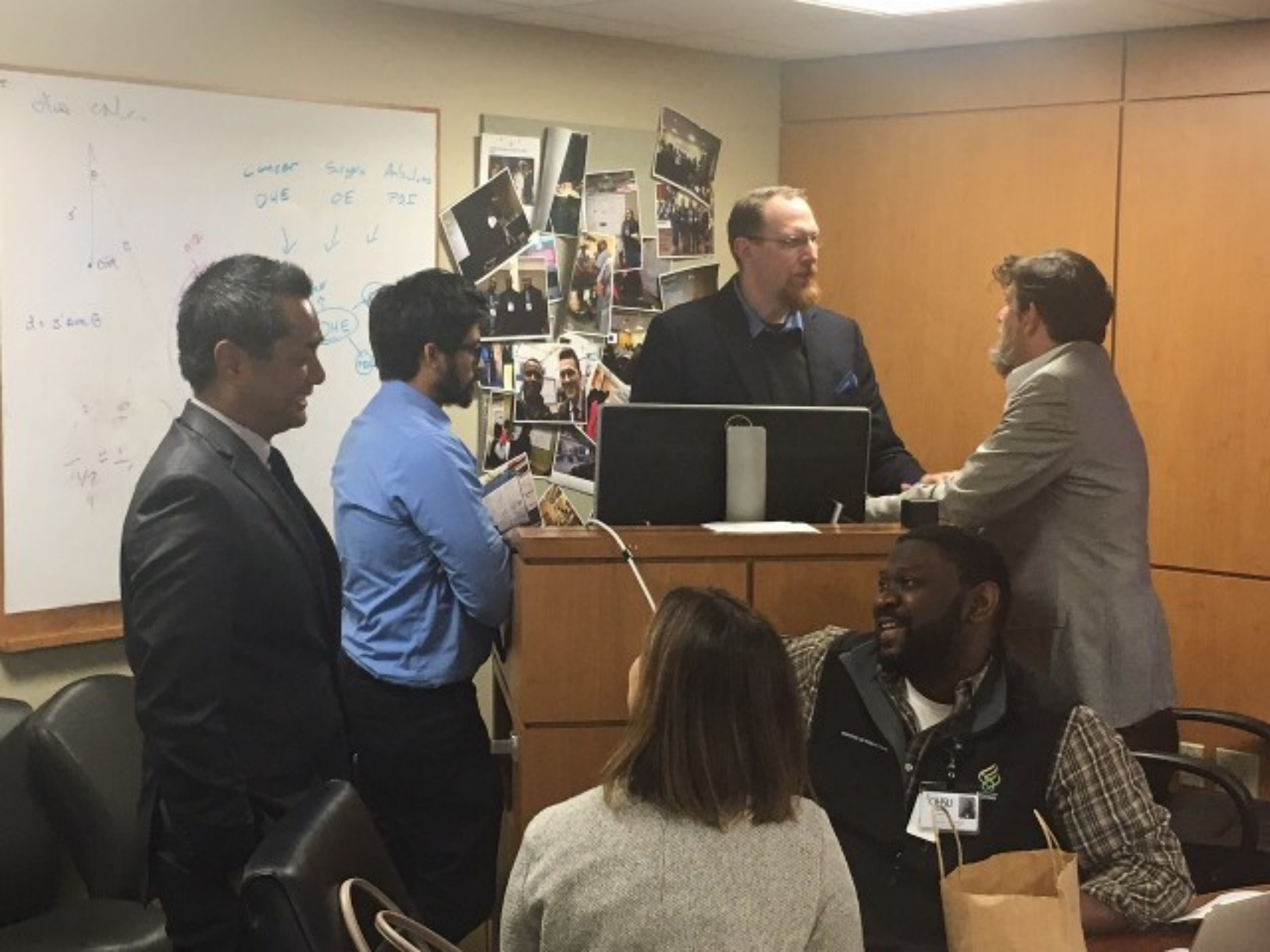
$$N = N_0 e^{-\lambda t}$$

$$t = T_{1/2}$$

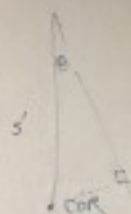


MACRA  
 Mac  
 Cap  
 Ray



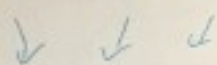


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$$d = s \sin \theta$$

Cancer Surgery Ambulans  
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