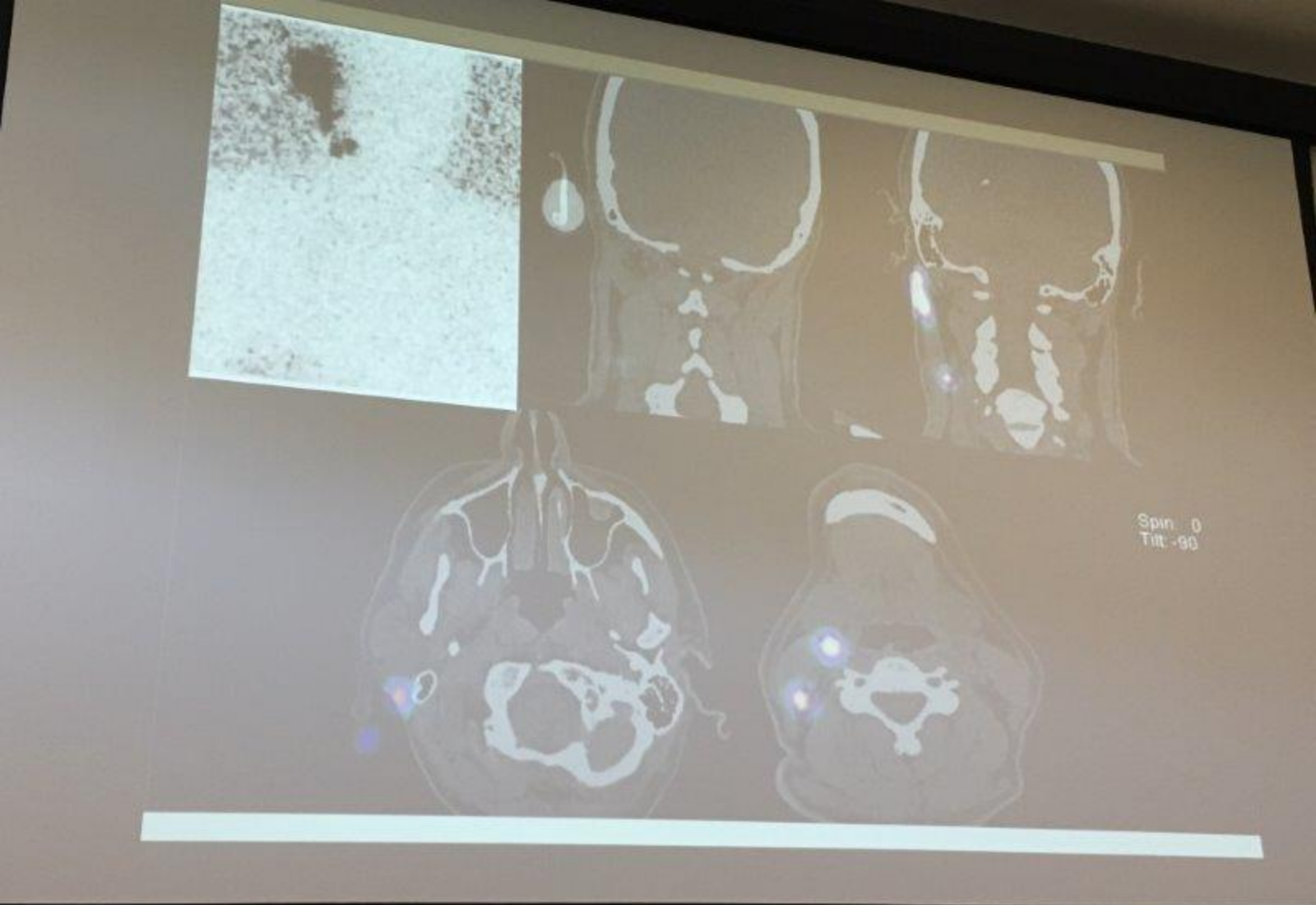

Spin 0
Tilt -90

Piggyback on your therapy trial

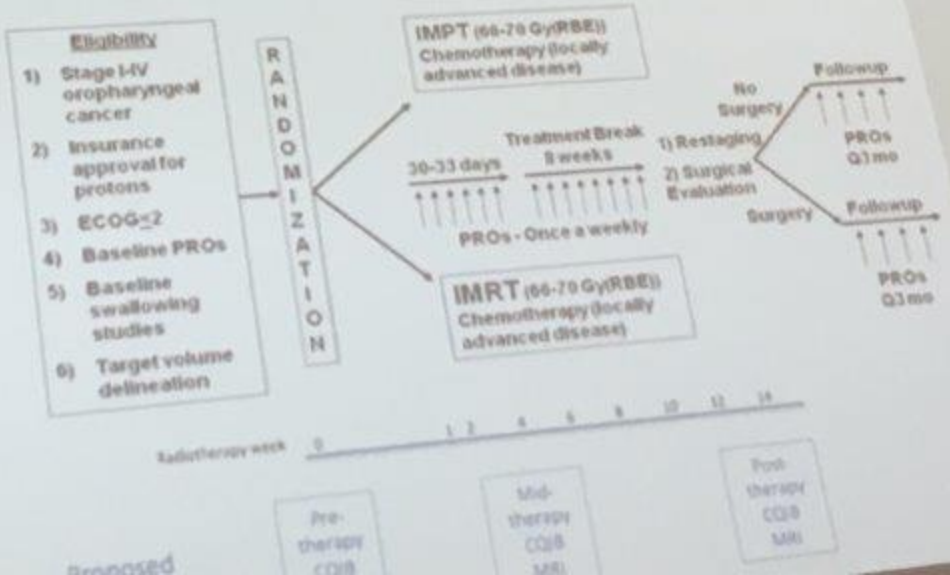
HYPOTHESIS AND SPECIFIC AIMS (1 page)

Primary Study Specific Aim

To assess and to characterize the kinetics of candidate quantitative imaging biomarkers (CQIBs) associated with normal tissue injury before, during, and after therapy by using serial multiparametric MRI for patients enrolled on protocol MDACC 2012-0825, "Phase II/III Randomized Trial of Intensity-Modulated Proton Beam Therapy (IMPT) versus Intensity-Modulated Photon Therapy (IMRT) for the treatment of Oropharyngeal Cancer of the Head and Neck."

Identified Imaging Hypothesis for Primary Specific Aim

Specifically, we hypothesize that IMPT will result in a 10% difference in normalized post-therapy voxel-by-voxe organ-at-risk (OAR) region of interest (ROI) apparent diffusion coefficient (ADC) and the DCE-MRI parameter K^{trans} and v_e at follow-up imaging as compared with those values after IMRT, as detected by 3T MRI acquisition for uninvolved parotid and submandibular glands.



Piggyback on your therapy trial

. HYPOTHESIS AND SPECIFIC AIMS (1 page)

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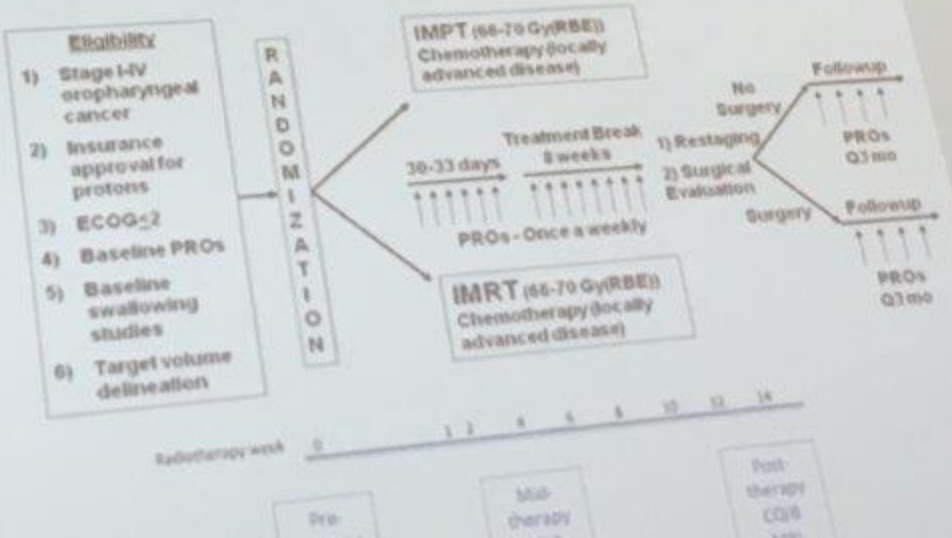
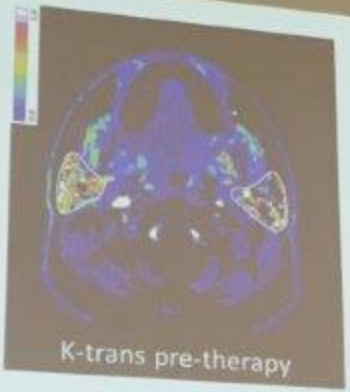
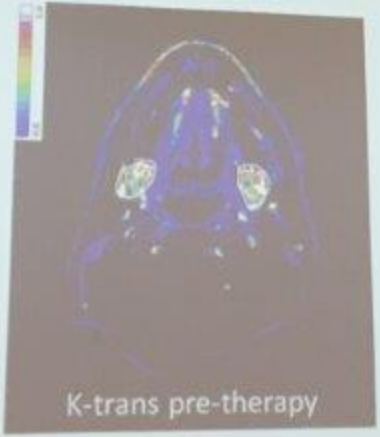
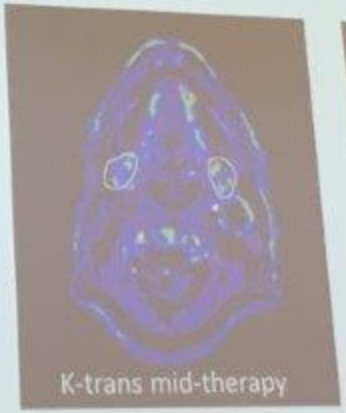


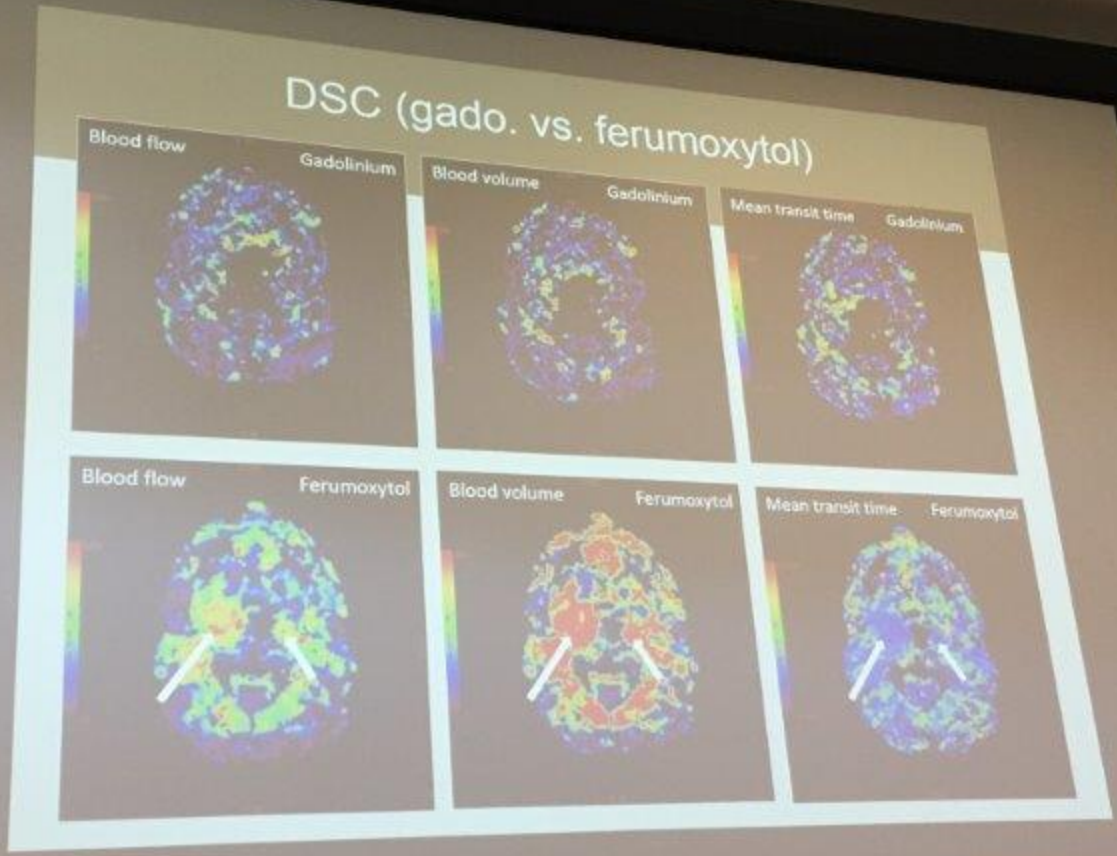

OHSU Department of
Radiation Medicine
www.ohsu.edu/radmedicine

Multi-parametric MRI - DCE (Glands)

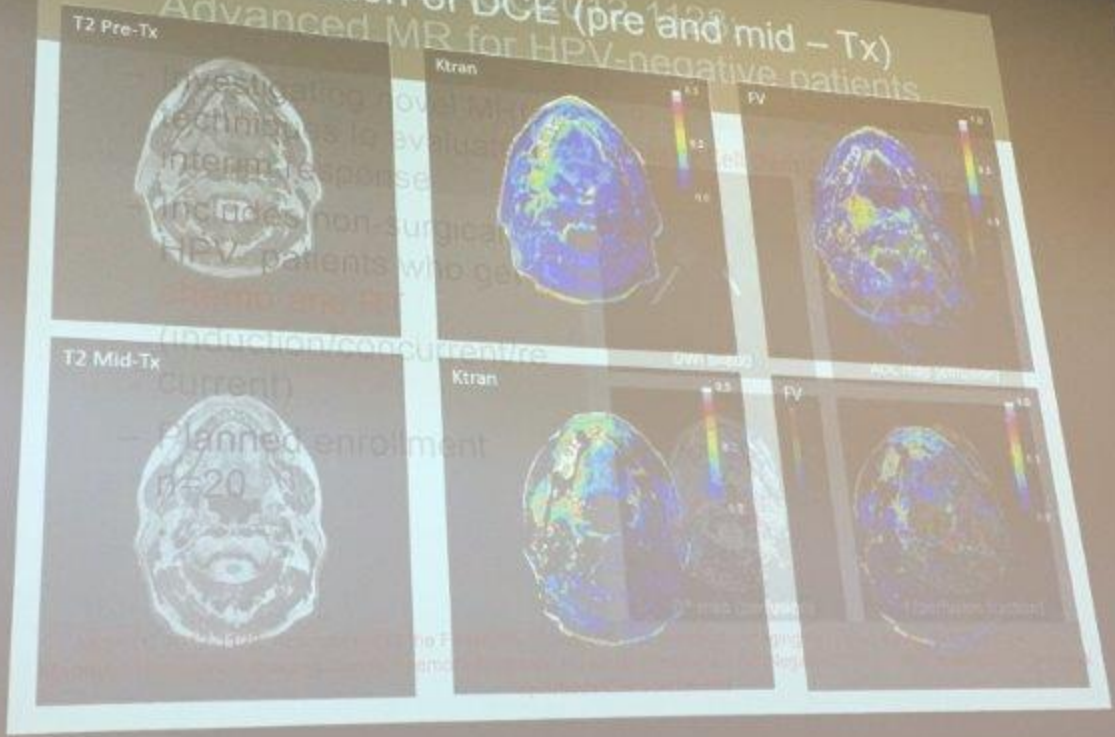






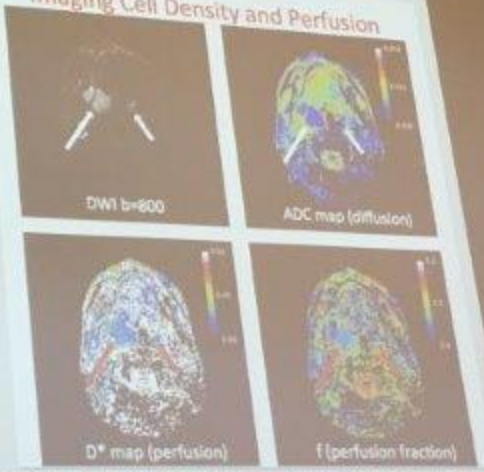

DSC (gado. vs. ferumoxytol)
Blood flow
Gadolinium
Blood volume
Gadolinium
Mean transit time
Gadolinium
Blood flow
Ferumoxytol
Blood volume
Ferumoxytol
Mean transit time
Ferumoxytol

Evaluation of DCE (pre and mid – Tx)

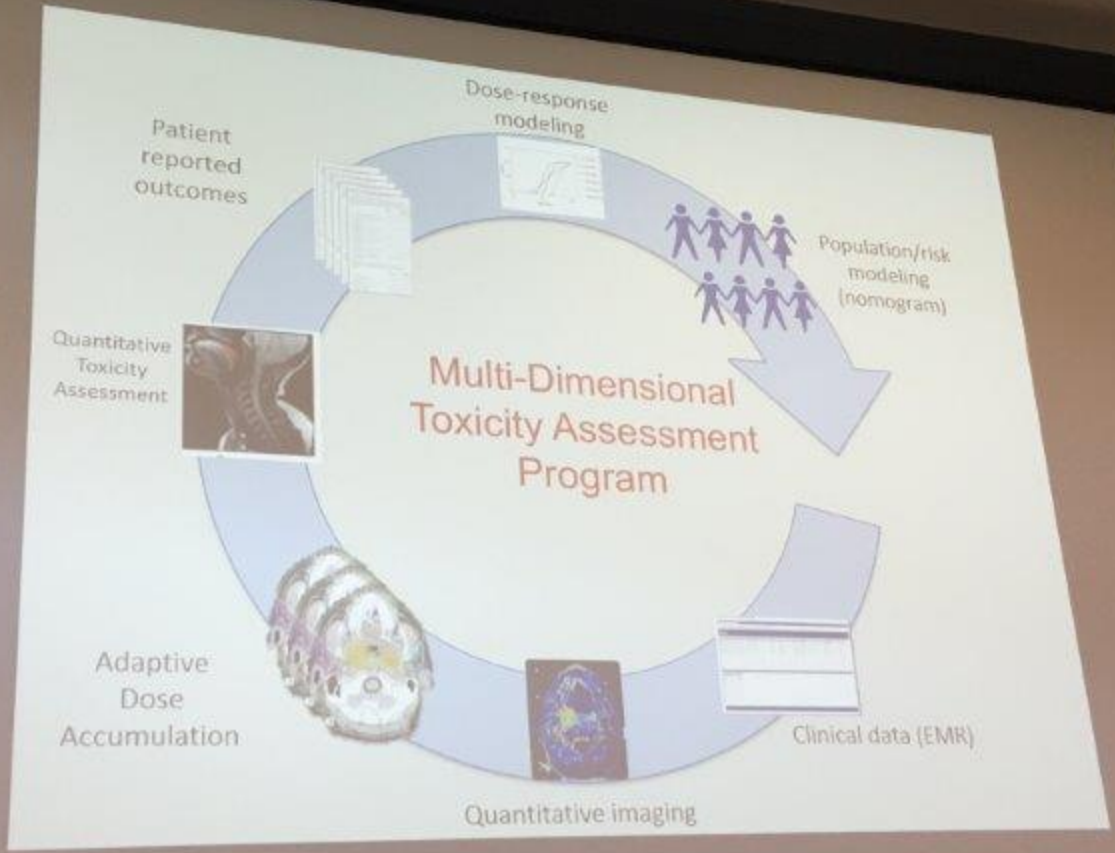


MDACC2012-1128: Advanced MR for HPV-negative patients

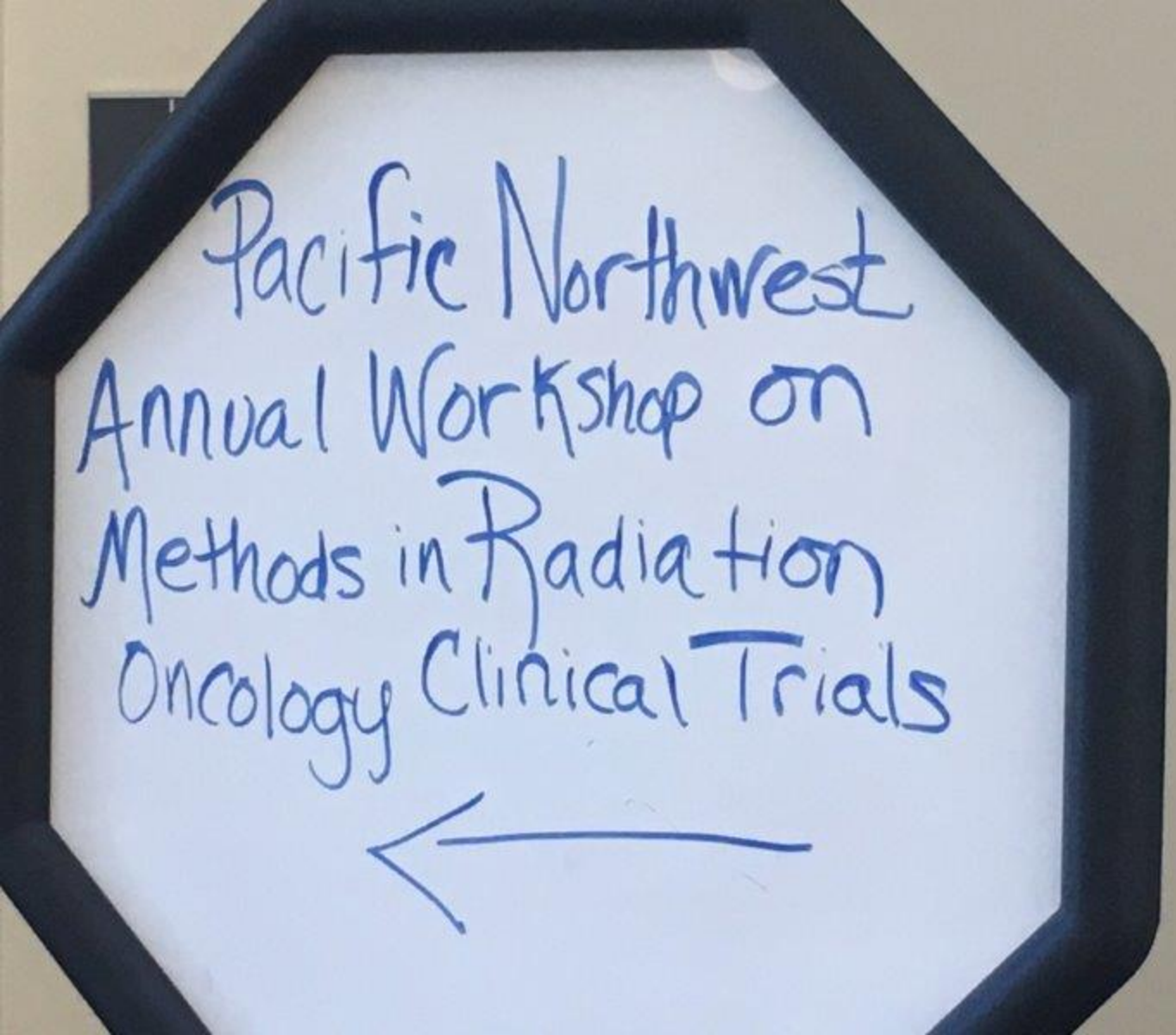
- Investigating novel MRI techniques to evaluate interim response
- Includes non-surgical HPV- patients who get chemo and RT (induction/concurrent/recurrent)
- Planned enrollment n=20



MDACC 2012-1128: Assessment of the Feasibility of Acquisition of Candidate Imaging Biomarker Kinetics of Multiparametric Magnetic Resonance Imaging During Chemoradiotherapy in Human Papilloma Virus-Negative/HPV-non-Associated Head and Neck Squamous Cell Carcinomas

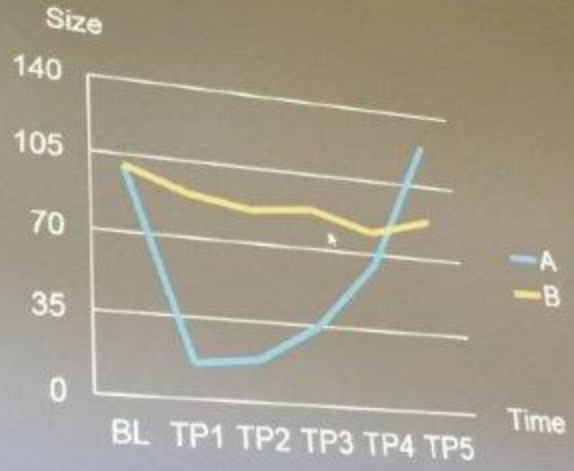

Dose-response modeling
Patient reported outcomes
Population/risk modeling (nomogram)
Quantitative Toxicity Assessment
Multi-Dimensional Toxicity Assessment Program
Adaptive Dose Accumulation
Clinical data (EMR)
Quantitative imaging


LEARNING STUDIO


Pacific Northwest
Annual Workshop on
Methods in Radiation
Oncology Clinical Trials

Clinical Endpoints

« Vertical »
Response Rate



« Horizontal »
Time to Progression


« Vertical »
Response Rate
CLSB


CLSB

WHO Criteria - 1981

SPD: Sum of product of diameters

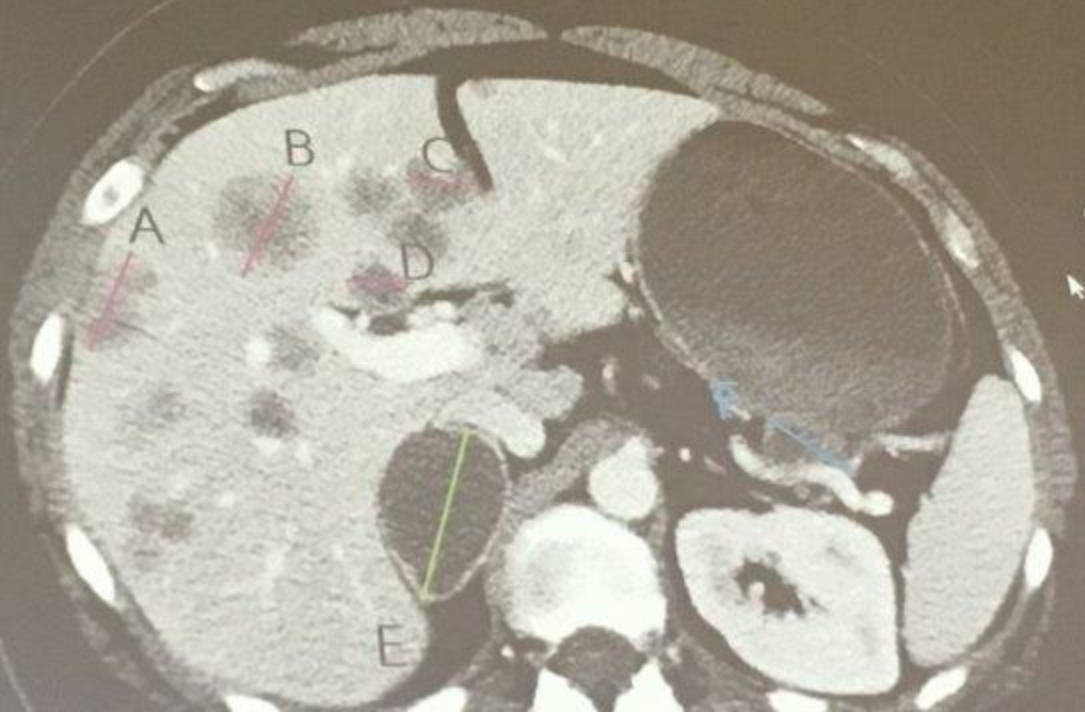
AxB + CxD

- Tumor response assessed by change in SPD of >2 lesions
- No minimum size of lesions
- No specification of number of lesions

...to small changes in tumor size**

RECIST – 2000

(Response Evaluation Criteria in Solid Tumors)



SLD = Sum of
diameters

A+B+C

When RECIST doesn't work

Infiltrative tumor and tumor in hollow organs is hard to measure

Using RECIST 1.1 in targeted therapy trials:

1) can lead to declaration of progressive disease (PD) too early, when the treatment effect is not yet fully evident or there is “flare effect”.

2) does not consider change in enhancement/density or FDG avidity, which may be the only relevant changes.

irRECIST (immune-related): Ca

PERCIST (PET): Uses change

Immune-related (ir)

irRC

Based on WHO (2D)
Up to 10 targets
Sum of Long Axis x Short Axis

irRECIST

- Based on RECIST (1D)
- Up to 5 targets
- Sum of Long Axis

- Main difference
  - New Lesions are integrated into the tumour burden.

Immune-related (ir)

irRC

Based on WHO (2D)

Up to 10 targets

Sum of Long Axis x Short Axis

irRECIST

- Based on RECIST (1D)
- Up to 5 targets
- Sum of Long Axis

PROVIDENCE
Cancer Center

hat is your hypothesis?

lways be mindful when selecting
ndpoints

- You need to address you hypothesis
- You need to be realistic in what you are asking of your patients
  - How many blood draws, biopsies, and trips to


DELL

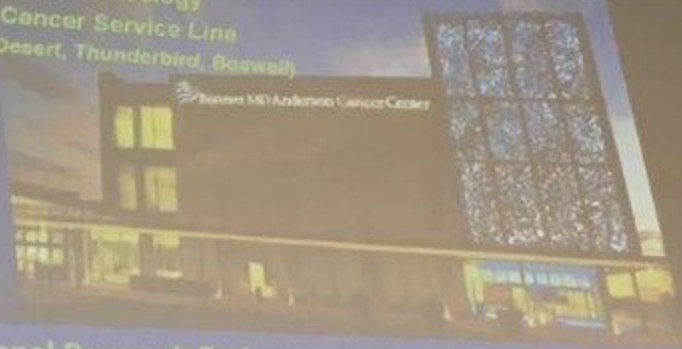
Statistical Considerations

PROVIDENCE Cancer Center

- If this is the first time being tested
  - Training set
  - Validation set
- Continuous variable, ordinal measure, binary cut-off?

Mohamed Khan, MD, PhD, MBA
Division Chief of Radiation Oncology
Banner MD Anderson Cancer Service Line
(BMDACC-Gilbert & BMDACC-Desert, Thunderbird, Boswell)

Banner
MD Anderson
Cancer Center
Making Cancer History®



Incorporation of Novel Translational Research Endpoints in Clinical Trials

Mohamed Khan, MD, PhD, MBA

Division Chief of Radiation Oncology

Banner MD Anderson Cancer Service Line

(BMDACC-Gilbert & BMDACC-Desert, Thunderbird, Boswell)

Banner
MD Anderson
Cancer Center

Making Cancer History®

corporation of Novel Translational Research Endpoints i


Post-it
Post-it


Post-it
Post-it

PROVIDENCE
Cancer Center

s tissue parameters


Post-it
Post-it

Clifton (Dave) Fuller,
MD, PhD

Assistant Professor

Head & Neck Section

UNIVERSITY OF TEXAS

ID Anderson

ncer Center

ncer History®

Post-it

Clifton (Dave) Fuller,
MD, PhD
Assistant Professor
Head & Neck Section

Innovatio
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Clifton (Dave) Fuller,
MD, PhD
Assistant Professor
Head & Neck Section

THE UNIVERSITY OF TEXAS
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cer History®

And
Innovation in Rad
Oncology

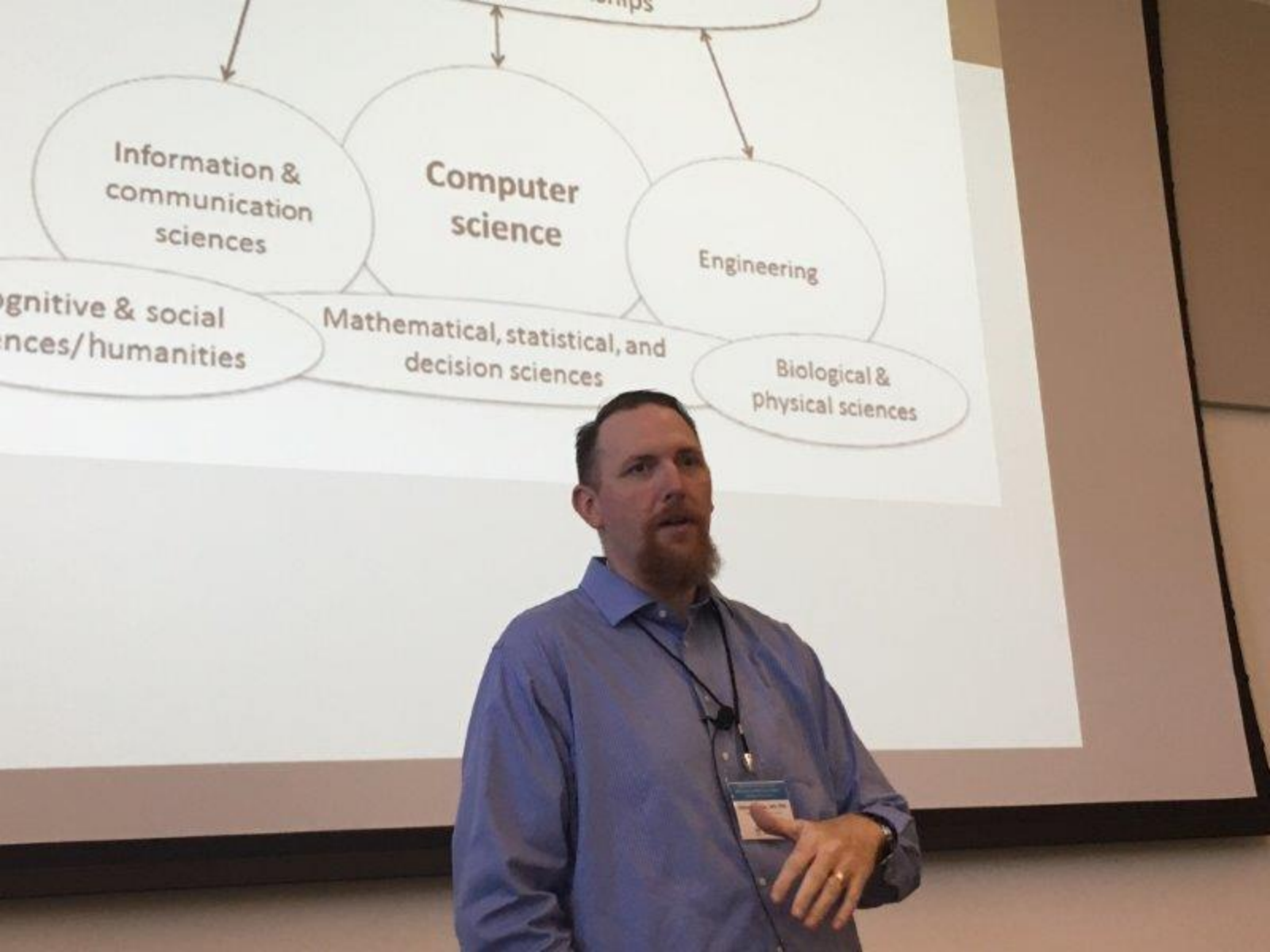
Informatics And Innovation in Radiation Oncology

LET'S SOLVE THIS PROBLEM BY USING THE BIG DATA NONE OF US HAVE THE SLIGHTEST IDEA WHAT TO DO WITH


LET'S SOLVE THIS PROBLEM BY USING THE BIG DATA NONE OF US HAVE THE SLIGHTEST IDEA WHAT TO DO WITH


WHAT TO DO


IDEA WHAT TO DO

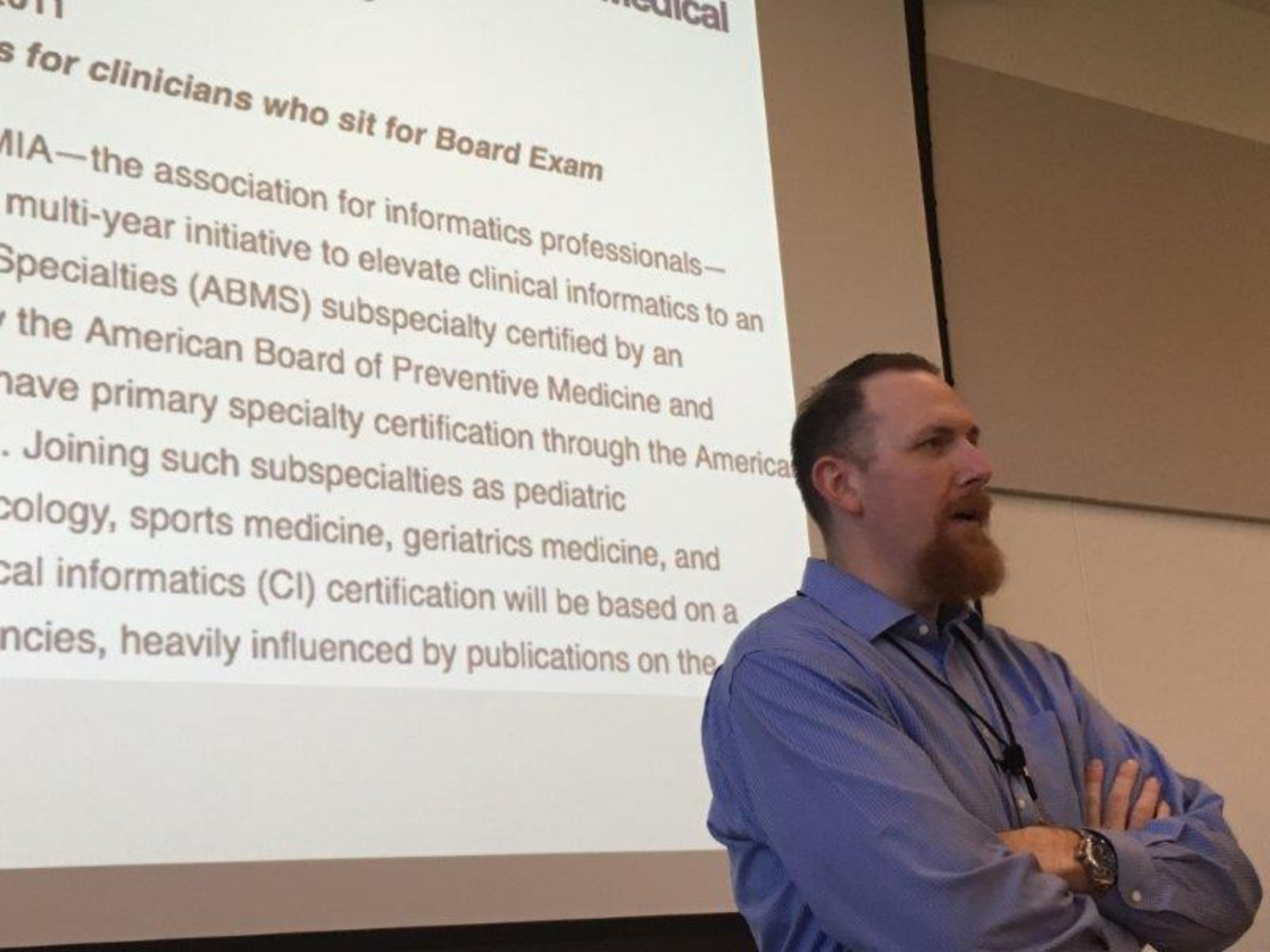

Information & communication sciences
Computer science
Engineering
gnitive & social nces/humanities
Mathematical, statistical, and decision sciences
Biological & physical sciences

Clinical Informatics Becomes a Board-certified Medical Subspecialty Following ABMS Vote

Thursday, September 22, 2011

AMIA to offer prep courses for clinicians who sit for Board Exam

Washington, DC—Today, AMIA—the association for informatics professionals—announces the success of a multi-year initiative to elevate clinical informatics to an American Board of Medical Specialties (ABMS) subspecialty certified by an examination administered by the American Board of Preventive Medicine and available to physicians who have primary specialty certification through the American Board of Medical Specialties. Joining such subspecialties as pediatric anesthesiology, medical toxicology, sports medicine, geriatrics medicine, and cardiovascular disease, clinical informatics (CI) certification will be based on a rigorous set of core competencies, heavily influenced by publications on the


s for clinicians who sit for Board Exam
MIA—the association for informatics professionals—
multi-year initiative to elevate clinical informatics to an
Specialties (ABMS) subspecialty certified by an
the American Board of Preventive Medicine and
have primary specialty certification through the America
. Joining such subspecialties as pediatric
cology, sports medicine, geriatrics medicine, and
cal informatics (CI) certification will be based on a
ncies, heavily influenced by publications on the


NIH
NATIONAL CANCER INSTITUTE
Informatics Technology for Cancer Research
Funding Opportunities
ITCR has issued four Funding Opportunity Announcements aimed at successive stages of informatics technology development.
Algorithm Development
PAR-15-334 Development of Innovative Informatics Methods and Algorithms for Cancer Research and Management (R21)
Prototyping & Hardening
PAR-15-332 Early-Stage Development of Informatics Technologies for Cancer Research and Management (U01)
Enhancement & Dissemination
PAR-15-331 Advanced Development of Informatics Technologies for Cancer Research and Management (U24)
Sustainment
PAR-15-333 Sustained Support for Informatics Resources for Cancer Research and Management (U24)

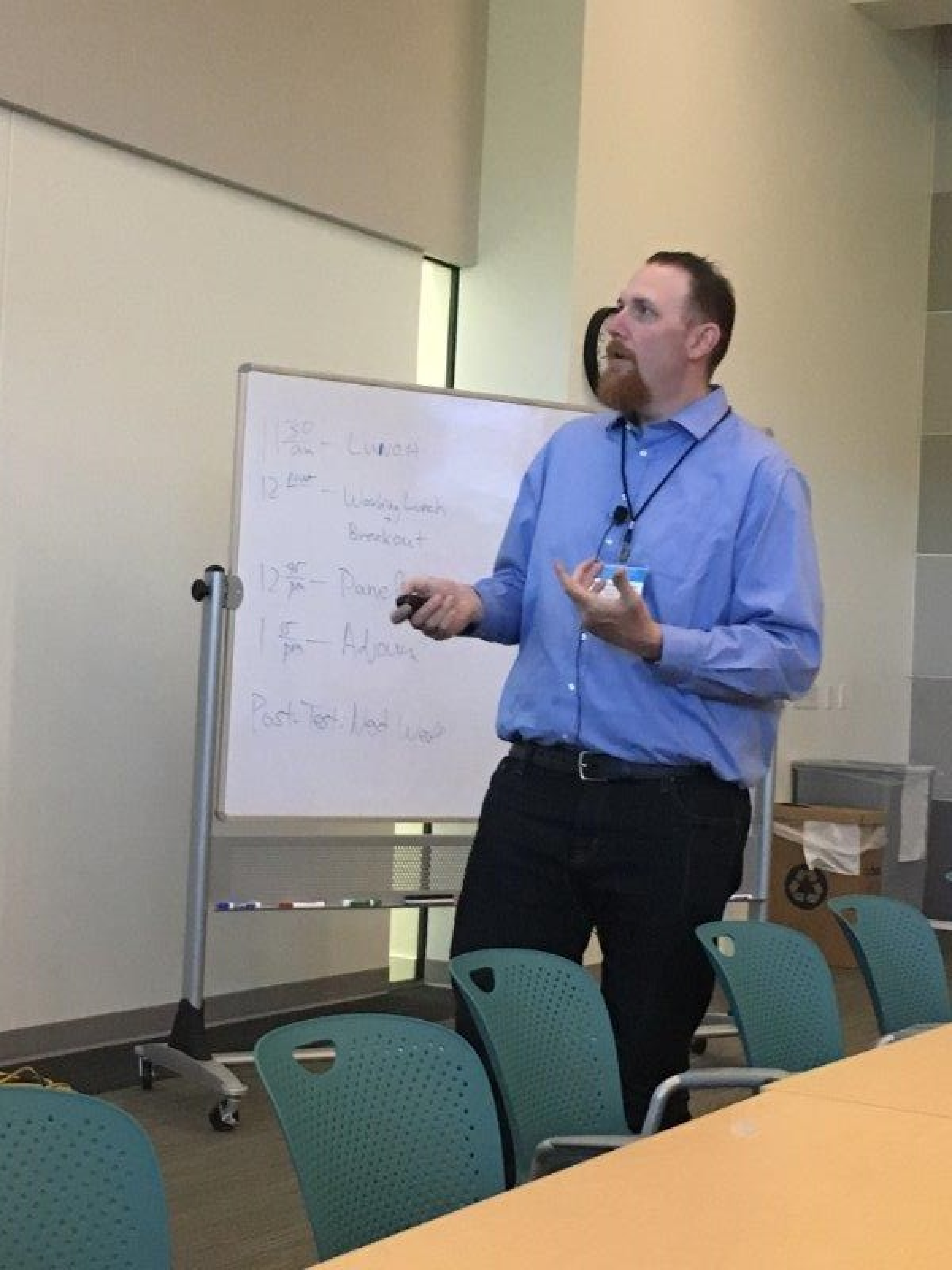
Fellowship in Clinical Informatics: Radiation Oncology Track

Fellowship in Clinical Informatics: Radiation Oncology Track

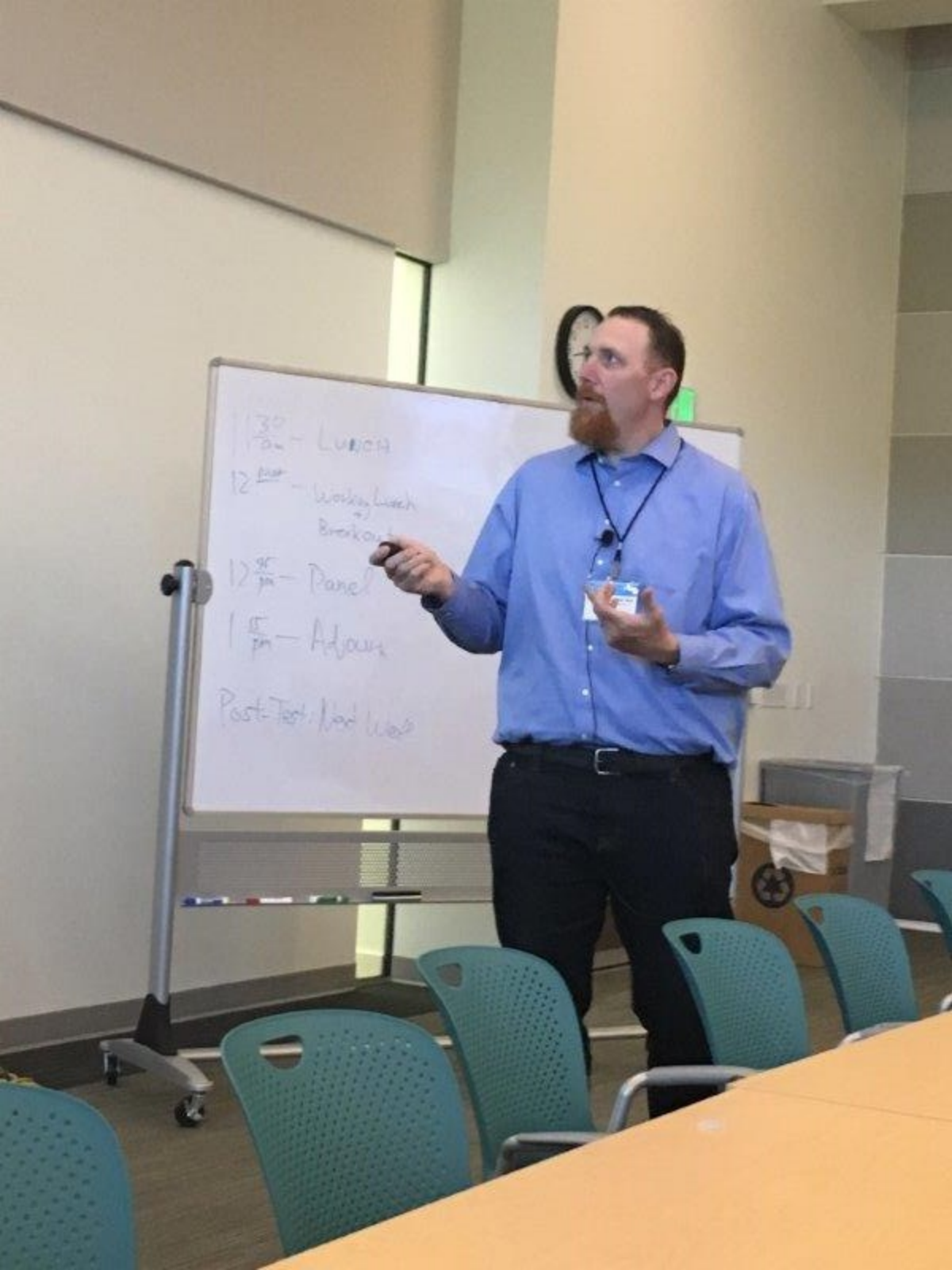
Clinical informatics is the subspecialty of all medical specialties that transforms health care by analyzing, designing, implementing, and evaluating information and communication systems to improve patient care, enhance access to care, advance individual and population health outcomes, and strengthen the clinician-patient relationship.

School of Medicine

Radiation Medicine



LUNCH
Breakout
Post-Test


Post-Test


PROBA
Post-it
Post-it


PROBA


PR
Post-it

ticle Therapy Based Clinical Trial Design: Considerations

Integral dose reduction

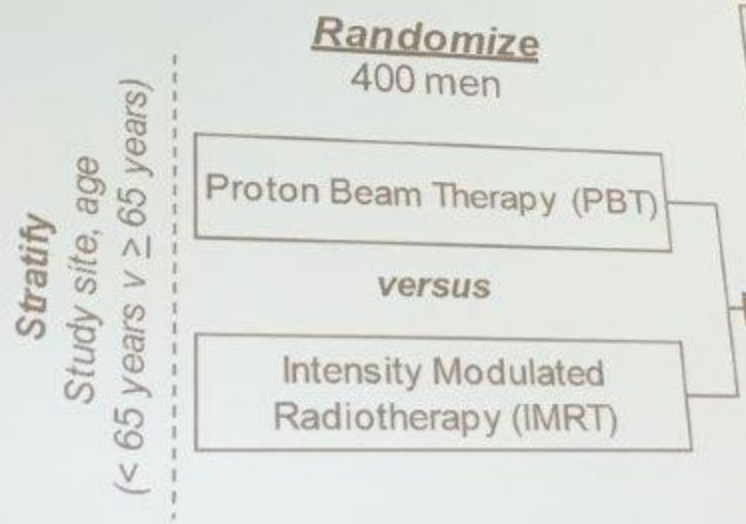
- Patient populations likely to benefit most: pediatrics, lymphoma
- Considerations: Small patient numbers, long-term endpoints

Improved tumor control

- Patient populations likely to benefit most: Soft tissue sarcoma, NSCLC, melanomas
- Considerations:
  - Radioresistant solid tumors historically treated with surgery
  - Dose escalation with low-LET radiation has not been successful (Carbon?)

Phase III Randomized Clinical Trial of Proton Therapy vs IMRT for Low or Low-Intermediate Risk Prostate Cancer

Study Schema



Follow
Months 1, 3, 6, 9, 12, 18, 24, 36, 48, 60

Primary Endpoint
- Bowel function at 24 mo (EPIC)

Secondary Outcomes
- Urinary and erectile function
- HRQOL and Utilities
- Perceptions of care
- Adverse events
- Efficacy endpoints


SB


SB


SB

Considerations when putting toget

- **Statistical analysis plan**
  - Primary or secondary endpoint
  - Power
- **Reporting of results**
  - Inclusion group
  - Intent to treat
  - Data complete?
- **Interpreting the Data**
  - Minimally clinically important difference

- **Number/timing /costs of ass**
  - Balance between brief interva liklihood of detecting changes
  - Baseline assessment
    - To establish pre-existing dif
    - Provides reference point for
  - One or more on-treatment as
    - Frequency will depend on r
    - Timing will depend on when
  - Post-treatment assessments
    - Depends on research ques

Lunch

Clinical Trial Design breakout sessions (disease

Session 1	**GU Radiotherapy** Timur Mitin, M.D., Ph.D.
Session 2	**GI Radiotherapy** Charles Thomas, M.D.
Session 3	**Soft Tissue and Bone Tumor** Arthur Hung, M.D.
Session 4	**Lung Radiotherapy** Ramesh Rengan, M.D., Ph.D.
Session 5	**Head and Neck** Dave Fuller, M.D., Ph.D.
Session 6	**Palliative Radiotherapy** Sophia Bornstein, M.D., Ph.D.
Session 7	**"TBD" as needed**

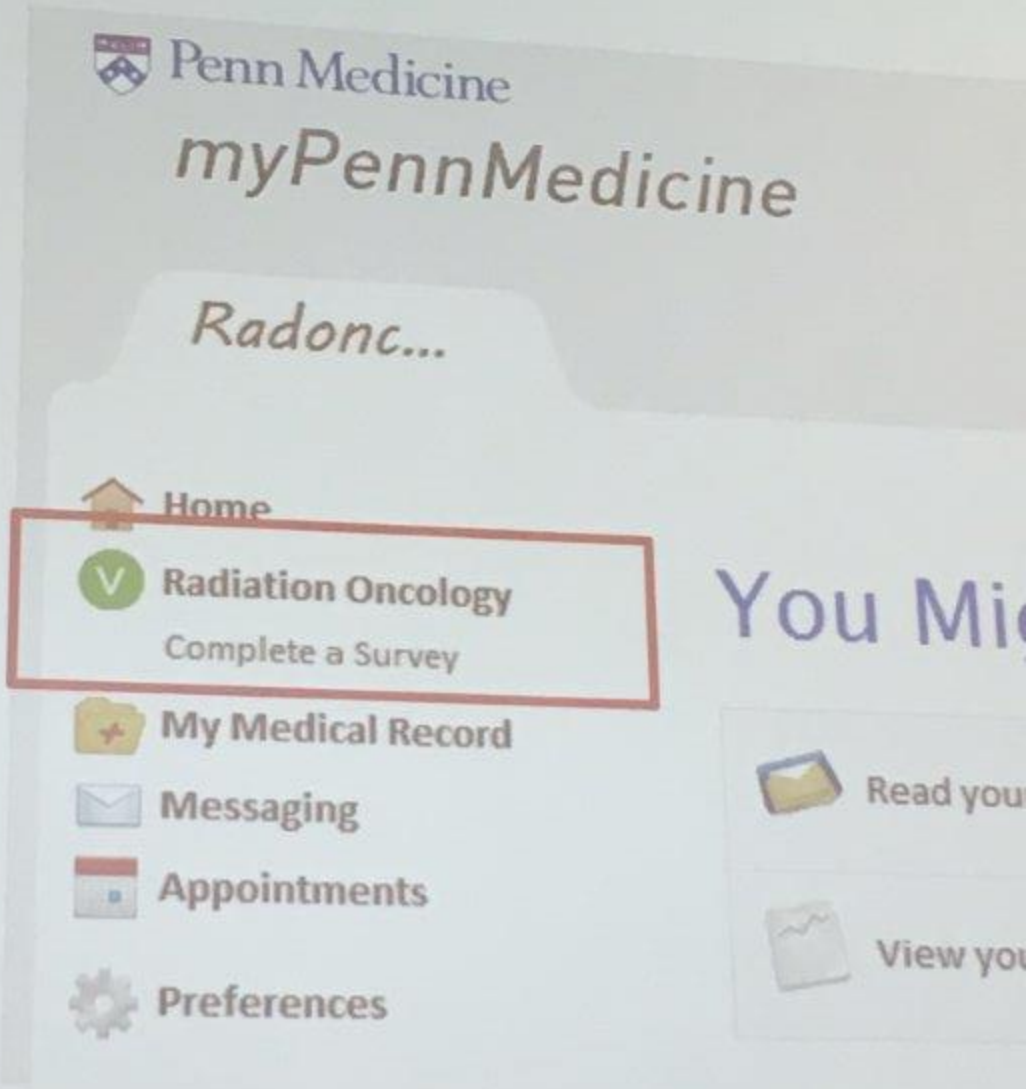
SATURDAY, MAY 7

7:45 a.m.	**Continental breakfast**
8:25 a.m.	**Clinical Informatics in Radiotherapy** Dave Fuller, M.D., Ph.D.
9:05 a.m.	**Particle Therapy-Based Clinical Tri** Ramesh Rengan, M.D., Ph.D.
9:45 a.m.	**QOLife Endpoints in Clinical Trial** Lilie Lin, M.D.
10:25 a.m.	**Mathematical Modeling in Design Time-Dose-Fractionation** Andrew Trister, M.D., Ph.D.

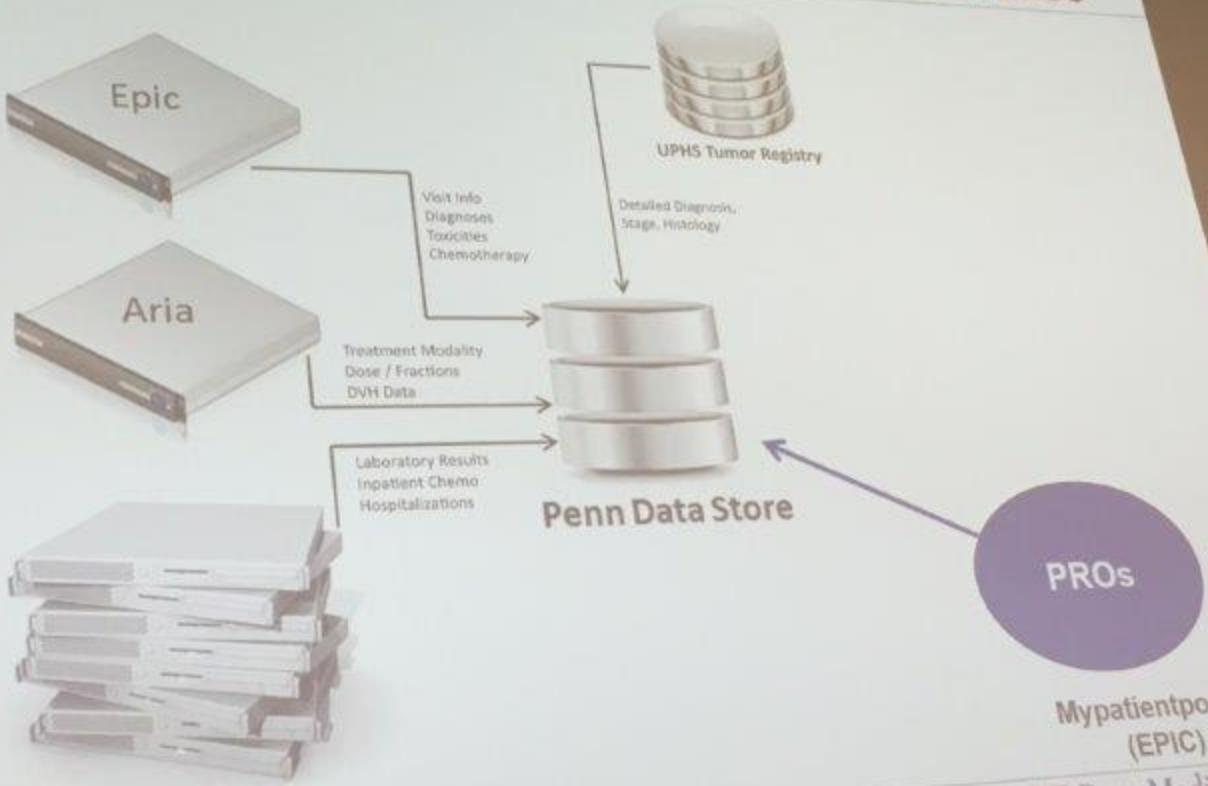
Measurement

- **Reliability and validity depe**
  - Fact-G has 0.87 reliability in
  - Is it still reliable in Botswana
  - Is it reliable measure in Chin
- **If it's to be applied in new p**
- **What's wrong with a low re**
  - Poor measure
  - Implies low validity
  - Want reliability to be above

- Patients login to the MyPennMedici



Adding PROs to Existing Clinical Data Warehouse



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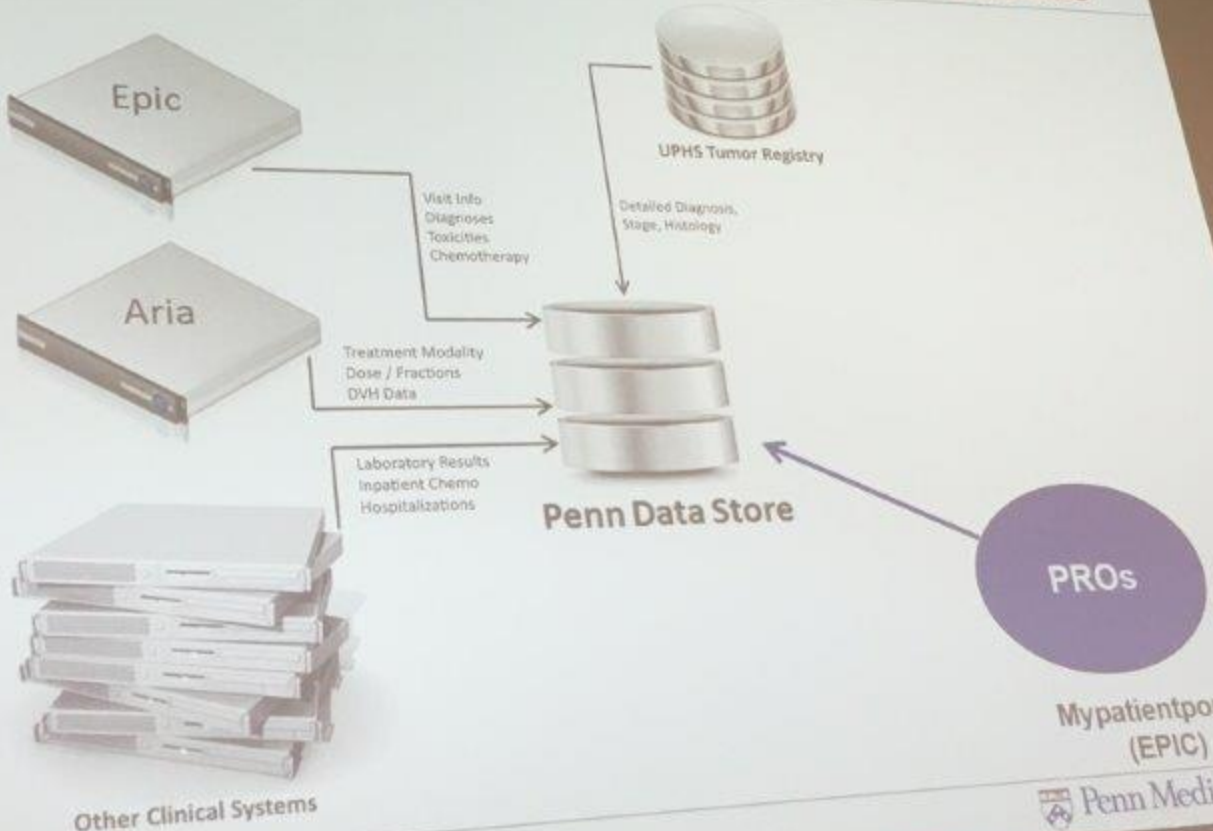


Overview
• Early steps
• Who is picking up the bill?
• Protocol development
• Data safety monitoring
• Case report forms & da
• Privacy & confidentialit
• IRB and supporting docur
• Training


... AND THIS IS THE FORM YOU SEND BACK TO CONFIRM YOU'VE SENT BACK ALL THE OTHER FORMS!
FORM


• Data safet
• Ensure
• Who i
• Establ
• Case rep
• Build
• Deci
CLSB


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