

# The need for QI in Medical Oncology Treatment Guidance and Assessment

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## Disclosures



- **AIQ Solutions**, Founder and President

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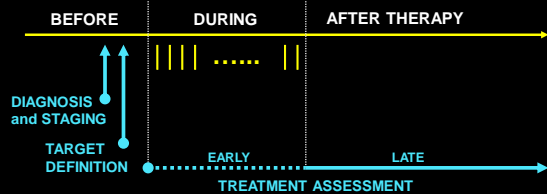
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## Types of imaging



Qualitative imaging (**Diagnostics**)

Quantitative imaging (**Quantitative Imaging Biomarkers**)



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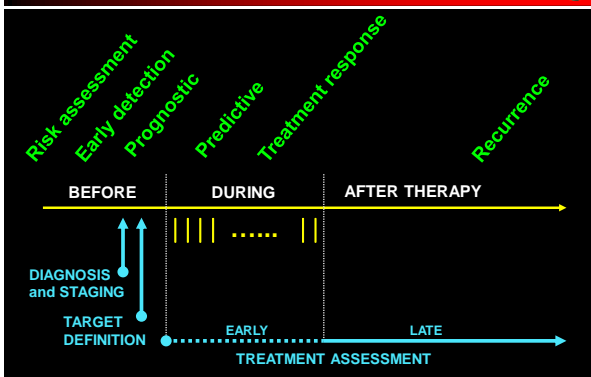
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## QUANTITATIVE IMAGING BIOMARKERS (QIB)

### Biomarkers and surrogate endpoints

- **Biomarkers** are characteristics that are objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention
- **Biomarkers as surrogate endpoints** are biomarkers that are intended to substitute for clinical endpoints. Surrogate endpoints are expected to predict clinical benefit (or harm or lack of benefit or harm) based on epidemiologic, therapeutic, pathophysiologic, or other scientific evidence.

### Types of biomarkers



## What does make imaging biomarkers QUANTITATIVE?



Raunig et al 2015, Stat Methods Med Res 24(1): 27-67

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## Repeatability and reproducibility



- **Repeatability:** The ability of the QIB to repeatedly measure the same feature under identical or near-identical conditions.
  - These studies are often referred to as test–retest, scan–rescan, or coffee-break experiments
- **Reproducibility:** The reliability of the QIB measuring system in different conditions that might be expected in a preclinical study or clinical trial or in clinical practice (e.g. multiple sites)

Raunig et al 2015, Stat Methods Med Res 24(1): 27-67

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## TREATMENT RESPONSE ASSESSMENT




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## Response assessment today



- **WHO** (1979, 1981)<sup>1,2</sup>
  - anatomic
  - bidimensional measurement of lesion
- **RECIST** (2000, 2009)<sup>3,4</sup> – Response Evaluation Criteria In Solid Tumors
  - anatomic
  - CT/MR based
  - unidimensional measurement of lesion
  - 4 response categories (CR, PR, SD, PD)
    - Complete Response: disappearance
    - Partial Response: >30% decrease
    - Stable Disease: in between
    - Progressive Disease: >20% increase

<sup>1</sup> WHO handbook 1979

<sup>2</sup> Miller *et al.* 1981

<sup>3</sup> Therasse *et al.* 2000

<sup>4</sup> Eisenhauer *et al.* 2009

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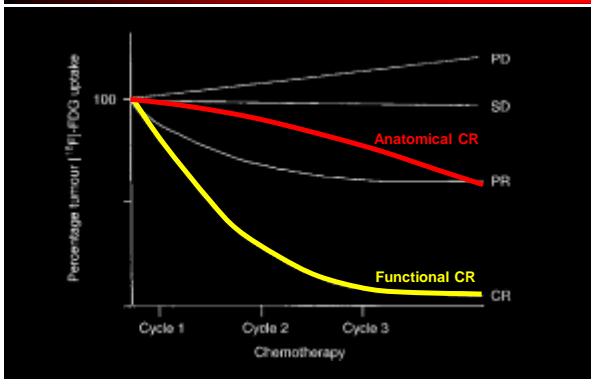
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## Anatomical vs functional response




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## PET-based response assessment



- **EORTC, NCI Recommendations** (1999, 2005)<sup>1,2</sup>
  - SUV-based approach
  - $SUV_{mean}$  and  $SUV_{max}$
  - Response categories with thresholds (CR, PR, SD, PD)
  - Problems
    - $SUV_{mean}$  – collapse information, sensitivity issues
    - $SUV_{max}$  – noise contamination
    - fails to use all available functional data
      - distribution
      - heterogeneity
    - no response threshold validation
    - few sensitivity studies
    - alternative measures
- PET Response Criteria in Solid Tumors (**PERCIST**) (2009)<sup>3</sup>
  - $SUV_{peak}$

<sup>1</sup> Young *et al.* 1999

<sup>2</sup> Shankar *et al.* 2006

<sup>3</sup> Wahl *et al.* 2009

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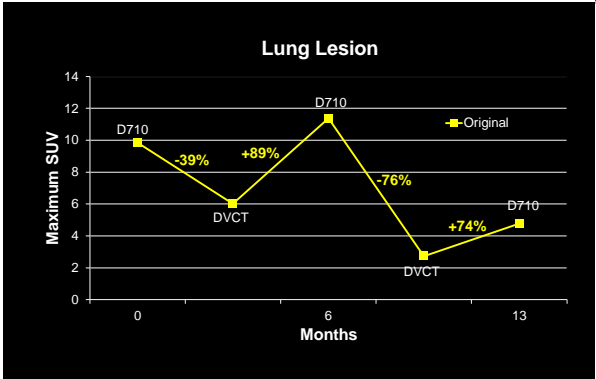
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### What about harmonization?



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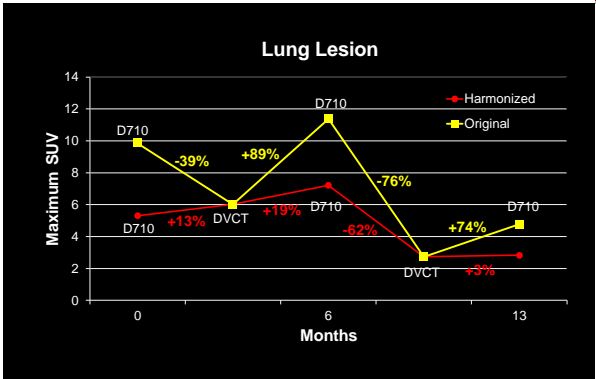
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### What about harmonization?



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### METASTATIC PROSTATE CANCER



METASTATIC PROSTATE CANCER

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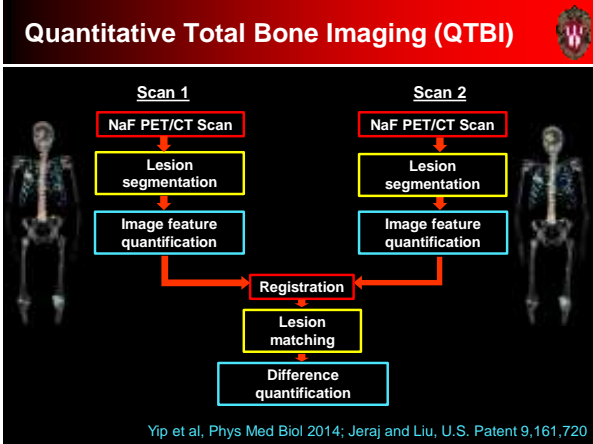
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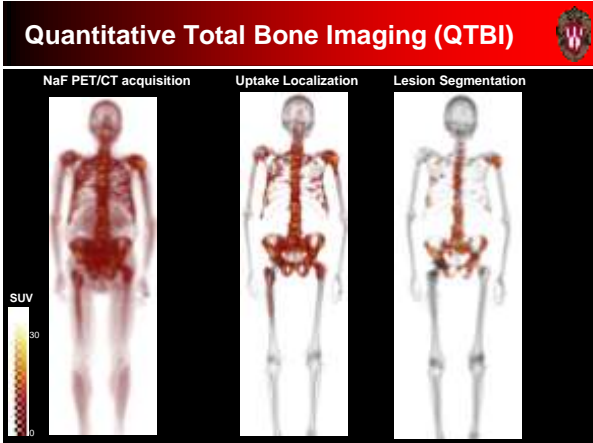
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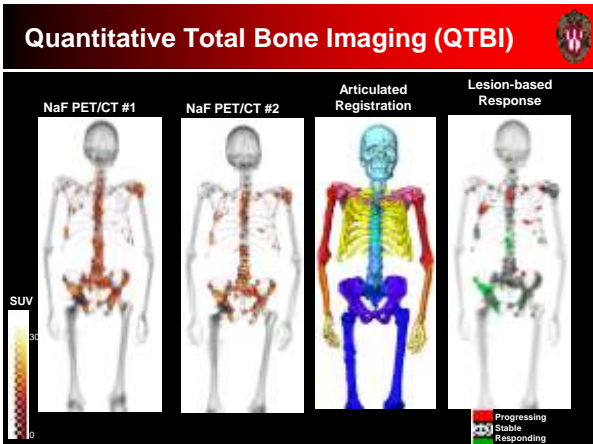
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## Repeatability of QTBI (NaF PET/CT)


- **Multicenter** trial of metastatic castrate-resistant prostate cancer patients
  - received pre-treatment test-retest <sup>18</sup>F-NaF PET/CT scans

Site	Patients	Bone lesions
University of Wisconsin Carbone Cancer Center	18	265
Memorial Sloan Kettering Cancer Center	11	78
National Cancer Institute	6	68
<b>All</b>	<b>35</b>	<b>411</b>

**Test/retest scans  
(3-5 days apart)**



**Standardized Uptake Value (SUV)  
metrics extracted from an ROI**



SUV<sub>max</sub> – maximum uptake  
SUV<sub>mean</sub> – average uptake  
SUV<sub>total</sub> – total uptake

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## What is our quantitative accuracy?

**Test**



**Retest**





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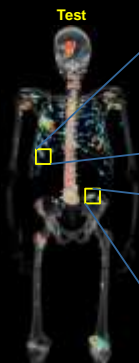
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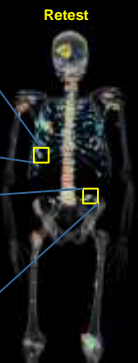
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## What is our quantitative accuracy?

**Test**



**Retest**




**Low repeatability**

SUV	Feature	SUV
48.2	SUV <sub>max</sub>	28.8
22.8	SUV <sub>mean</sub>	19.4
286.4	SUV <sub>total</sub>	92.7

**High repeatability**

SUV	Feature	SUV
64.5	SUV <sub>max</sub>	63.7
29.7	SUV <sub>mean</sub>	28.9
453	SUV <sub>total</sub>	478



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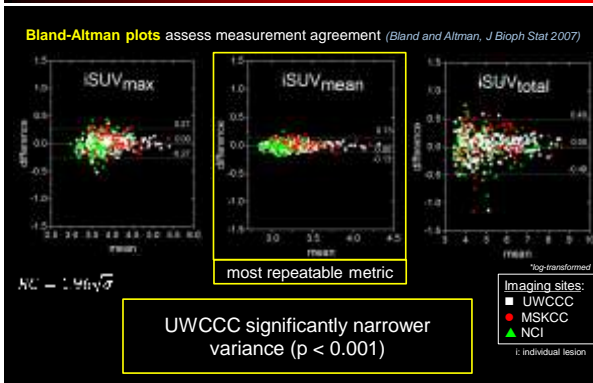
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## How much is repeatability?




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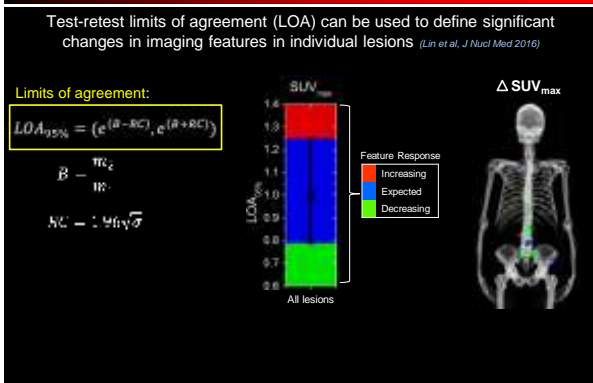
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## Defining limits of agreement




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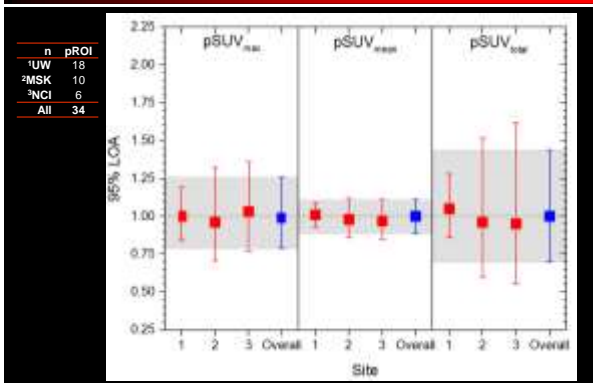
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## Imaging site affects repeatability




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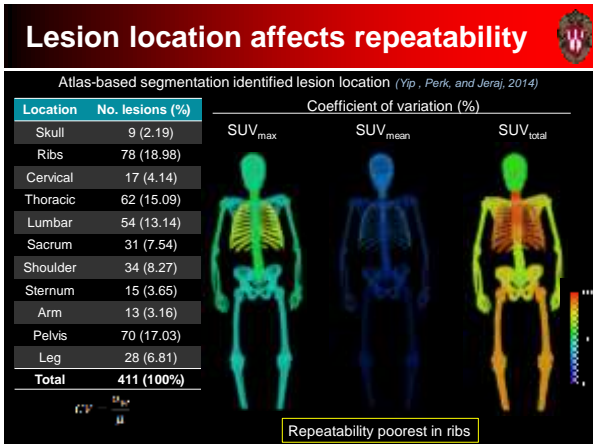
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## CLINICAL IMPLICATIONS OF QIB IN PROSTATE CANCER

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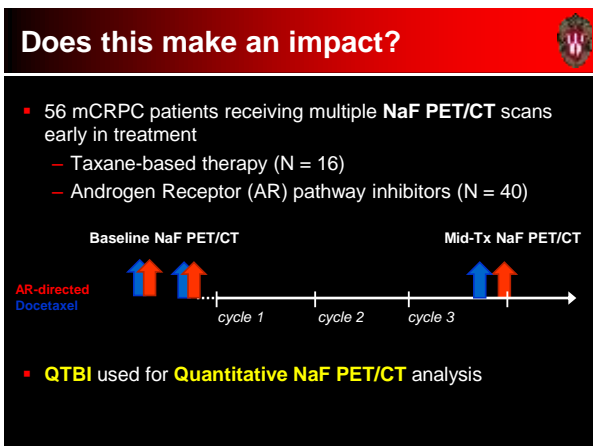
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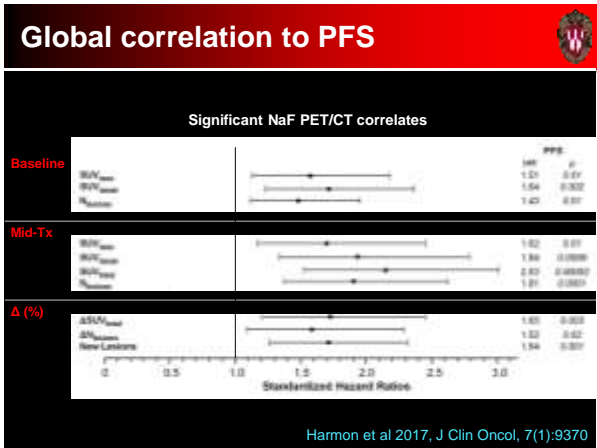
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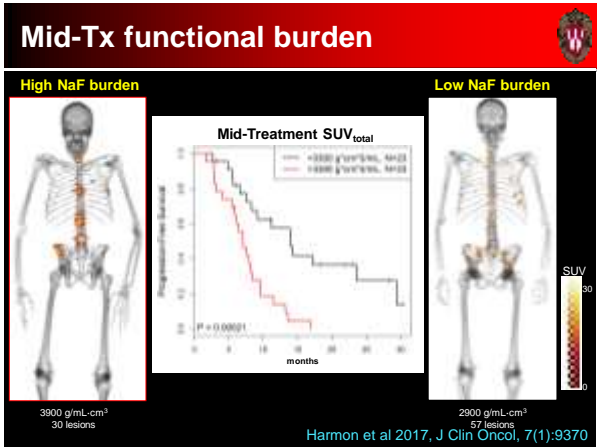
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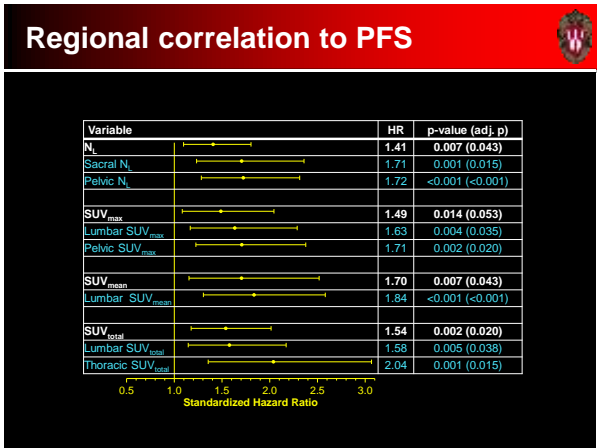
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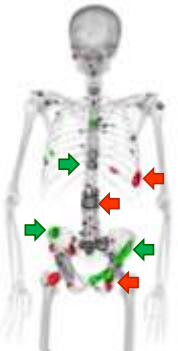
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## Lesion-level heterogeneity



example patient



- Does heterogeneity in lesion response impact our prediction?
- 43 patients with paired baseline and mid-Tx
  - 3228 lesions tracked across scans
  - 75.2 lesions/patient (range: 3 – 315)
- Classify lesion response based on local test-retest analysis (volume dependent)
- Record the proportion of lesions contained within each response classification group

Lin et al 2016, J Nuc Med, 57: 1872

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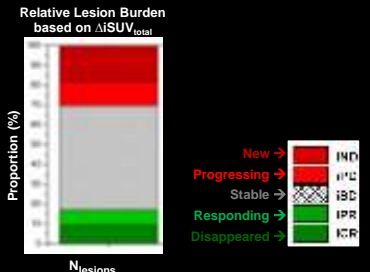
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## Lesion-level heterogeneity



example patient



Lin et al 2016, J Nuc Med, 57: 1872

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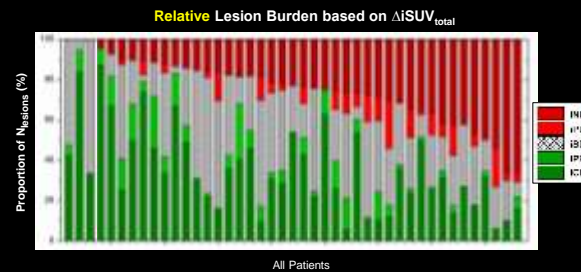
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## Lesion-level heterogeneity



- 40/43 patients exhibit response heterogeneity regardless of burden




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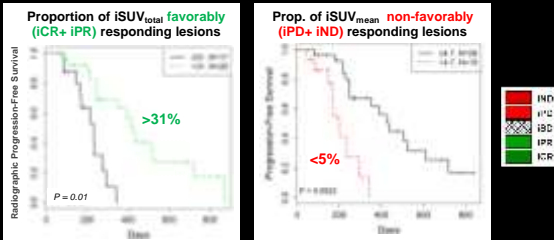
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## Lesion-level heterogeneity

- 40/43 patients exhibit response heterogeneity regardless of burden
- Non-favorable response dominates progression events!**




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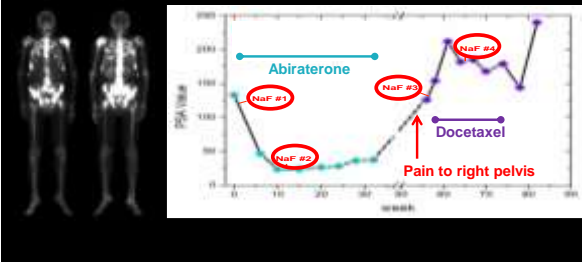
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## Sample patient

- 73 year old, diagnosed in 2/2012 w/ PSA=764 and diffused bony mets (biopsy confirmed)
- Treated with combined androgen blockade; developed CRPC by 12/2012
- Palliative XRT (T6-L1) in 1/2013




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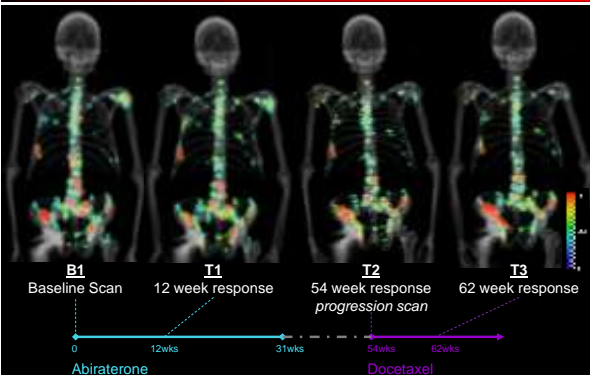
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## Sample patient




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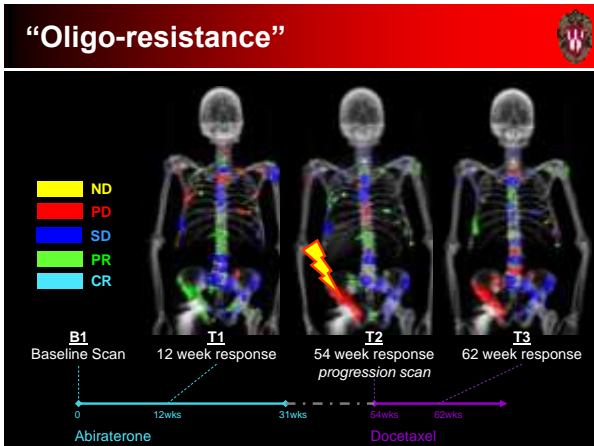
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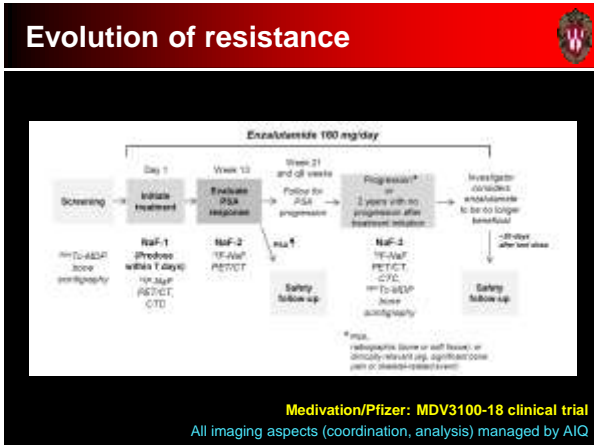
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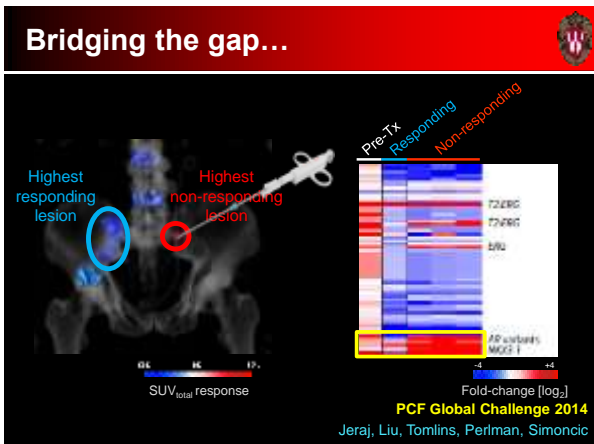
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## Summary



- **Quantitative Imaging Biomarkers (QIB)** require:
  - Characterization of **instrument+analysis** variability
    - Repeatability and Reproducibility
  - Analysis of **performance characteristics**
    - Limits of Agreement  $\Rightarrow$  Response Thresholds
- QIB enable **radically different approach** to treatment response evaluation
  - Impact on **clinical decision making**
  - Impact on **drug development**

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## Thanks to:



- **Image-guided Therapy Group (UW)**
  - Enrique Cuna
  - Peter Ferjancic
  - Daniel Huff
  - Christie Lin
  - Mauro Namias
  - Tim Perk
  - Alison Roth
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  - Urban Simoncic
  - Marusa Turk
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- **Medical Oncology/Hematology**
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  - Doug McNeel
  - Ryan Mattison
  - Mark Albertini
  - Ruth O'Regan
  - ...
- **Radiology**
  - Scott Perlman
  - Tyler Bradshaw
  - Chris Jaskowiak
- **Human Oncology**
  - Paul Harari
  - Mark Ritter
- **Medical Physics**
  - Ed Jackson
- **UWCCC TIR, CTD2, DOTs**
- **UW WONIX, NIX**

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