Alternative Career Opportunities for Medical Physicists

Robert Jeraj
Professor of Medical Physics, Human Oncology,
Radiology and Biomedical Engineering
Director of Translational Imaging Research Program
University of Wisconsin Carbone Cancer Center, Madison, WI
rjeraj@wisc.edu

Medical physics TODAY…

	Development	Translation	Application
	Algorithms	Tools	Clinical

IMAGING CT, MRI, PET, US, Image Analysis…

THERAPY Dosimetry, Linacs, TPS, IMRT…

Clinical Medical Physics

Medical physics TOMORROW…

	Development	Translation	Application
	Algorithms	Tools	Clinical

IMAGING CT, MRI, PET, US, Image Analysis…

THERAPY Dosimetry, Linacs, TPS, IMRT…

Development	Translatio…	…ation	Analysis
Algorithms	Tools	…linical and Basic	

Clinical Medical Physics

Views on medical physics

Lessons learned through interviews

- **Interviews conducted in 2011/12**, involving multiple institutions, disciplines constituting or related to medical physics:
  - **Harvard/MIT:** MGH/BWH Rad Onc, MGH/BWH Radiology, MGH/BWF Nuc Med, Martinos center, Steele lab, Wellman labs, Center for Evidence Based Imaging, Surgical Planning Lab, BIDMC Rad Onc, Harvard SEAS, Harvard/MIT HST program, Biophysics, Systems biology
  - **MD Anderson:** Medical Physics, Radiation Oncology, Radiology
  - **University of Wisconsin:** Medical Physics, Radiology, Human Oncology, UW Carbone Cancer Center

Lessons learned through interviews

- **Anthony Zietman, MD:** Medical physics has a unique position:
  - It will always be needed in the clinics (vs. radiation oncology, which might be "swallowed" by other professions)
  - Medical physics should be guiding research in the departments – "we (oncologists) don't really have time, and are not well trained for that"

Lessons learned through interviews

- **Kian Ang, MD:** Medical physics is in trouble for two reasons:
  - Medical physics has too much too well educated workforce for what it does in the clinics – this should be resolved with technologists – but that is not in the interest of the professional organizations (AAPM)
  - Medical physics has not delivered what we (oncologists) have been asking for years

Lessons learned through interviews

- **Bruce Chabner, MD:** Medical physics has definitely a role (I don't really know what), but that role has to be defined better
  - Medical physicists – "fixing blackberry"
  - What has medical physics done to cure cancer?

Lessons learned through interviews

- **Andrzej Niemierko, PhD:** Medical physics should look well beyond current applications in radiation therapy and imaging
  - There is so much to do for medical physicists in clinical trials – from data analysis to modeling
  - Medical physicists have unique skills that can help in other fields, e.g., systems biology
  - Having basic medical physics training and exposure to clinics helps to better understand clinical problems

Lessons learned through interviews

- **Søren Bentzen, PhD:** If medical physics does not reinvent itself, it risks of being extinct
  - Medical physics has put too much emphasis on development and translation of technology, but not enough on application of it
  - Medical physics should exploit unique “multi-level” modeling expertise (combining heuristic data-based and analytical model based approaches)
  - Medical physics should be trans-disciplinary (connecting) not inter-disciplinary (between)

Lessons learned through interviews

- **Bert van der Kogel, PhD:** The key to the future is to find out what the current problems are
  - Medical physicists have a lot to contribute to biology with their unique modeling skills and their unique approach to solving problems
  - Radiobiology made a big mistake by not responding to the new reality (molecular biology), which made radiobiology practically disappear – the same can happen to med phys
  - Training should present interdisciplinary problems as attractive, not something for people who can not do anything better

Where should we look for alternative career opportunities?

Where is medicine going?

"4 P's of medicine": Individuals respond differently to environmental conditions, according to their genetic endowment and their own behavior. In the future, research will allow us to **predict** how, when, and in whom a disease will develop. We can envision a time when we will be able to precisely target treatment on a **personalized** basis to those who need it, avoiding treatment to those who do not. Ultimately, this individualized approach will allow us to **preempt** disease before it occurs, utilizing the **participation** of individuals, communities, and healthcare providers in a proactive fashion, as early as possible, and throughout the natural cycle of a disease process.

Elias A. Zerhouni, M.D.
Director, National Institutes of Health (NIH), 2008

Where is medicine going?

"4 P's of medicine": Individuals respond differently to environmental conditions, according to their genetic endowment and their own behavior. In the future, research will allow us to **predict** how, when, and in whom a disease will develop. We can envision a time when we will be able to precisely target treatment on a **personalized** basis to those who need it, avoiding treatment to those who do not. Ultimately, this individualized approach will allow us to **preempt** disease before it occurs, utilizing the **participation** of individuals, communities, and healthcare providers in a proactive fashion, as early as possible, and throughout the natural cycle of a disease process.

Elias A. Zerhouni, M.D.
Director, National Institutes of Health (NIH), 2008

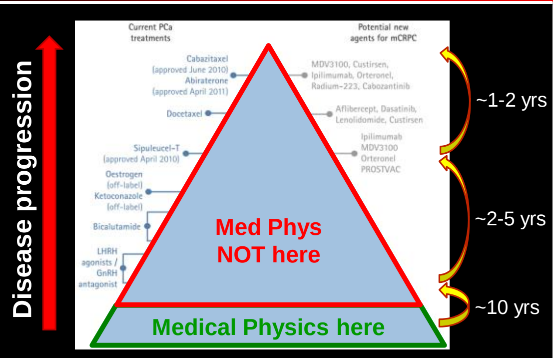
2016: Precision medicine initiative

$215M investment

Tonight, I'm launching a new **Precision Medicine Initiative** to bring us closer to curing diseases like cancer and diabetes—and to give all of us access to the **personalized information** we need to keep ourselves and our families healthier.

THE PRECISION MEDICINE INITIATIVE

What is the major problem today?



Shore et al 2012, Br J Urol Intl, 6: 22

Tumors are heterogeneous

Talmadge 2007, Cancer Res 67: 11471-75

…and they are heterogeneous a lot!

Tumor heterogeneity makes imaging essential

ESTABLISHED IN 1812 MARCH 8, 2012 VOL. 366 NO. 10

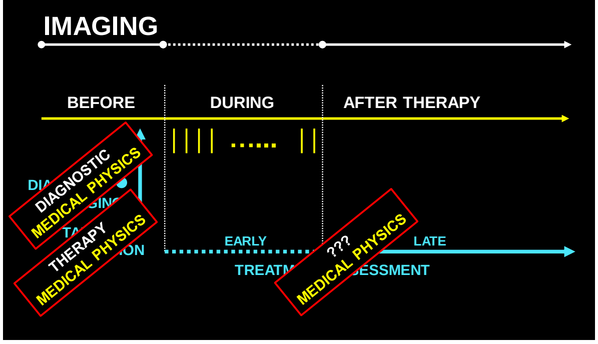
Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing

Marco Gerlinger, M.D., Andrew J. Rowan, B.Sc., Stuart Horswell, M.Math., James Larkin, M.D., Ph.D., …

…branched evolutionary tumor growth, with **63 to 69%** of all somatic mutations not detectable across every tumor region…

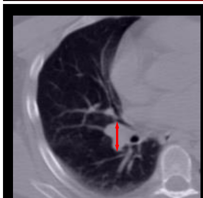
Gerlinger et al 2012, N Engl J Med 366: 883.

Imaging in oncology



Treatment response assessment –
GOLDEN opportunity!

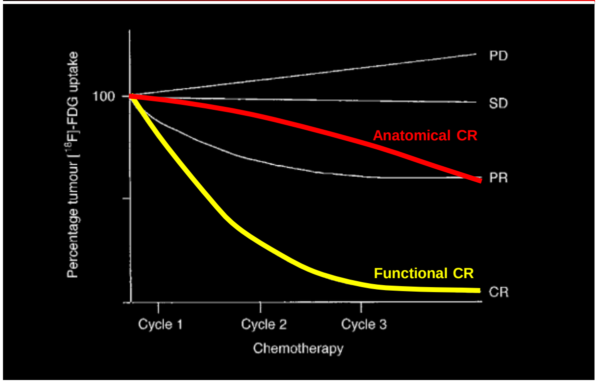
Response assessment today



- **WHO** (1979, 1981)[1,2]
  - anatomic
  - bidimensional measurement of lesion
- **RECIST** (2000, 2009)[3,4] – 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

[1] WHO handbook 1979
[2] Miller *et al.* 1981
[3] Therasse *et al.* 2000
[4] Eisenhauer *et al.* 2009

Anatomical vs functional response



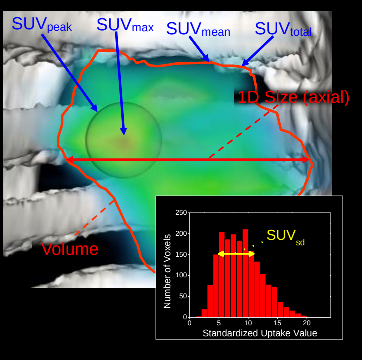
PET-based response assessment

- **EORTC, NCI Recommendations** (1999, 2005) [1,2]
  - 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) [3]
  - SUV_{peak}

[1] Young *et al.* 1999
[2] Shankar *et al.* 2006
[3] Wahl *et al.* 2009

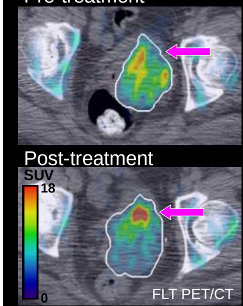
Images are more than just one number!

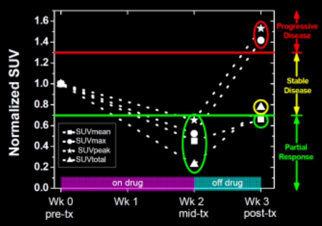
- Size measures
  - Volume
  - 1D size (axial)
- Standardized Uptake Value (SUV) measures:
  - SUV_{mean}
  - SUV_{total}
  - SUV_{max}
  - SUV_{peak}
- Uptake Non-uniformity measure:
  - SUV_{sd}
- …



But ambiguity of information

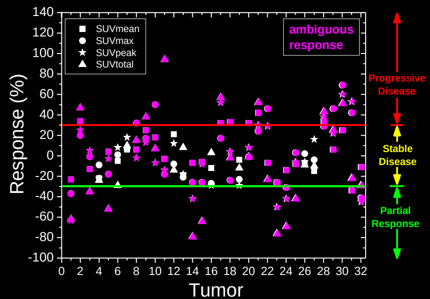
Pre-treatment





Vanderhoek, … Jeraj 2013, J Nucl Med 54: 1188.

But ambiguity of information



Vanderhoek, … Jeraj 2013, J Nucl Med 54: 1188.

Example from medical oncology: Imaging for mCRPC

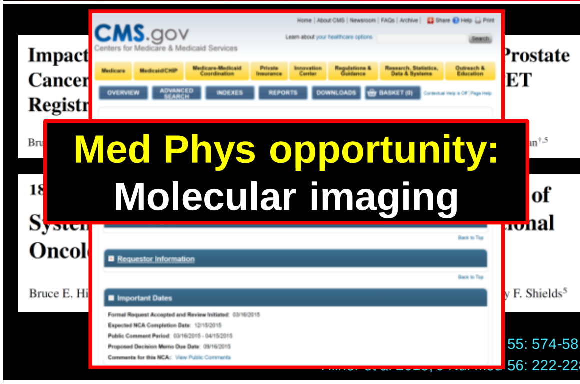
Drug development in mCRPC

- Osseous metastases are found in **85% of patients**
- **No standard tools availabl**... of response in bone met...
  – PCWG2 defi...

Can we make imaging a better response tool?

- Ho... we deal with **heterogeneity** of the disease response?

QIB candidates in advanced PC



Med Phys opportunity:
Molecular imaging

55: 574-581
56: 222-228

Clinical protocol

- **NaF PET/CT repeatability, responsiveness, and response assessment in patients with metastatic castrate-resistant prostate cancer to bone treated with either docetaxel-based chemotherapy or**

Med Phys opportunity:
Clinical trials

- Total N = 55 evaluable patients
  – 34 test-retest scans
  – 16 docetaxel-based treatment (Cohort A)
  – 39 AR-directed therapies (Cohort B)

PI: Liu, Jeraj

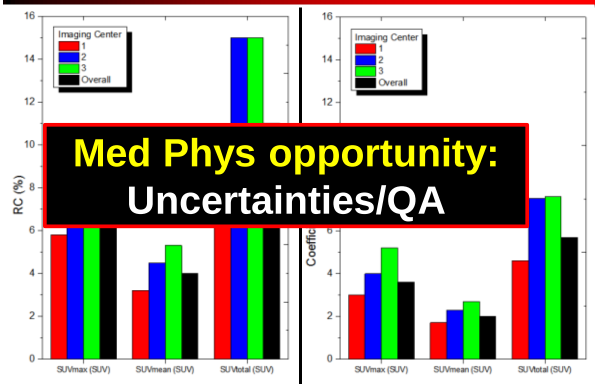
Imaging harmonization

- **Harmonization of acquisition**
  - Minimize limitations due to different scanner hardware and software
- eed

Med Phys opportunity: Harmonization

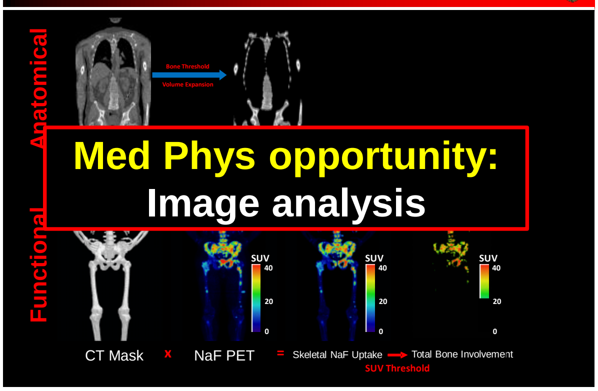
- **Harmonization of image analysis**
  - Unifying image analysis protocols, which often means centralized analysis
- **Harmonization of reporting**
  - Unified reporting, otherwise the data can

Inter-site repeatability

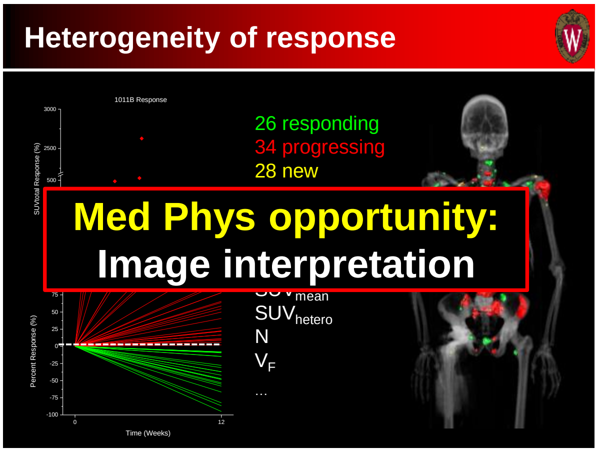


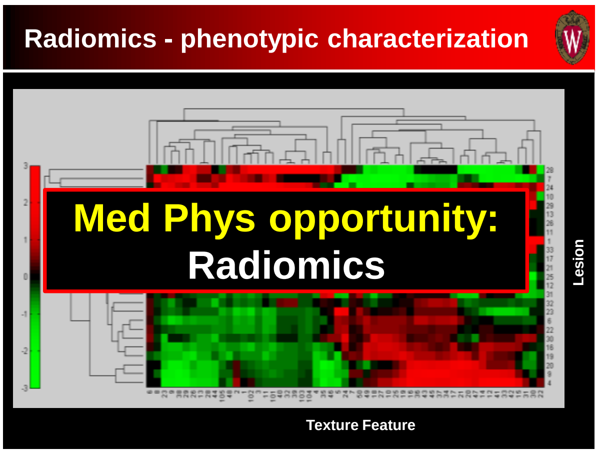
Med Phys opportunity: Uncertainties/QA

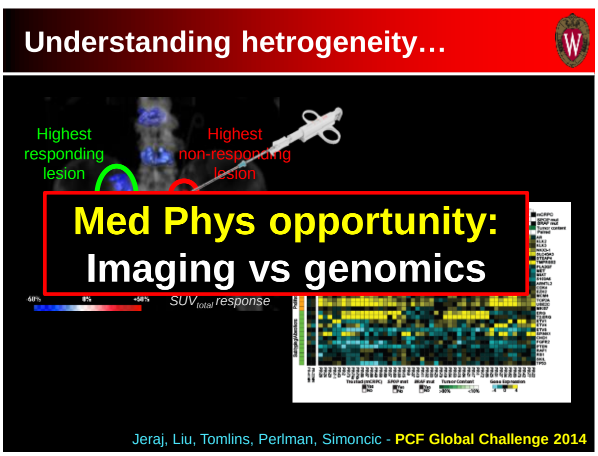
Quantitative Total Bone Imaging (QTBI)



Med Phys opportunity: Image analysis


Heterogeneity of response
1011B Response
26 responding
34 progressing
28 new
Med Phys opportunity:
Image interpretation
SUVhetero
N
VF
...
Time (Weeks)
Percent Response (%)


Radiomics - phenotypic characterization
Med Phys opportunity:
Radiomics
Lesion
Texture Feature


Understanding hetrogeneity…
Highest responding lesion
Highest non-responding lesion
Med Phys opportunity:
Imaging vs genomics
SUVtotal response
Jeraj, Liu, Tomlins, Perlman, Simoncic - PCF Global Challenge 2014

Understanding hetrogeneity…

Jeraj, Liu, Tomlins, Perlman, Simoncic - **PCF Global Challenge 2014**

Medical physics TOMORROW…

Development	Translation	Application	
Algorithms	Tools	Clinical	

IMAGING CT, MRI, PET, US, Image Analysis…

THERAPY Dosimetry, Linacs, TPS, IMRT…

?

Development	Translation	Application	Analysis
Algorithms	Tools	Clinical and Basic	

Medical physics TOMORROW…

Development	Translation	Application	
Algorithms	Tools	Clinical	

IMAGING CT, MRI, PET, US, Image Analysis…

THERAPY Dosimetry, Linacs, TPS, IMRT…

QIB

Development	Translation	Application	Analysis
Algorithms	Tools	Clinical and Basic	

Lessons learned…

- **Precision medicine** is uncovering complexity of cancer and other diseases
  - Medical physics has to be at the forefront of activities – jobs in the future!
- **Quantitative imaging** is ideally suited to address the challenge
  - Medical physics has the knowledge and skills
    - QA of the QI chain
    - Image analysis
    - Data analysis
- **Medical physics needs to expand** beyond diagnostic radiology and radiation oncology
  - Treatment response assessment
  - Medical oncology
  - …

Research vs Clinics

Optimal medical physics chain

Time [y]	
20	**Cutting edge research**
10	
5	**Translational research**
2	**Technology improvement**
Now	**Clinical implementation**

Bortfeld and Jeraj 2011, Br J Rad 84: 485

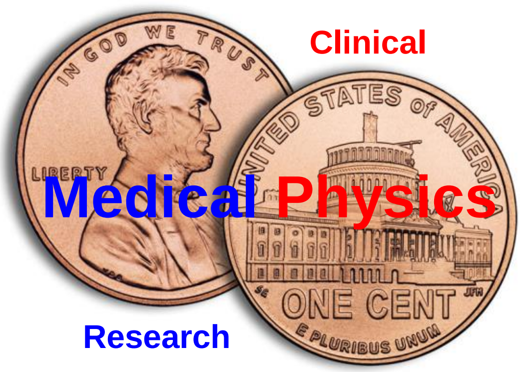
WG FUTURE

- **Charge:** To initiate, coordinate and lead activities to **secure sustainable growth and improvement** in the long-term future environment for **high quality** research and academic training of physicists in medicine
- **Goals:**
  - To prepare a strategic plan and coordinate activities for **improvement of research environment**
  - To prepare a strategic plan and coordinate activities for **improvement of academic training and educational environment**

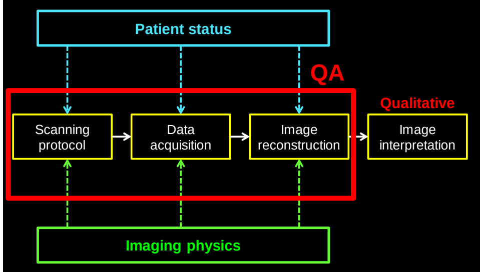
WG FUTURE - Professional

- **Charge:** To initiate, coordinate and lead activities to **secure sustainable growth and improvement** in the long-term future environment for **high quality** and **well-respected** medical physics profession
- **Goals:**
  - To prepare a strategic plan and coordinate activities for **improvement of professional environment**
  - To prepare a strategic plan and coordinate activities for **improvement of professional training**

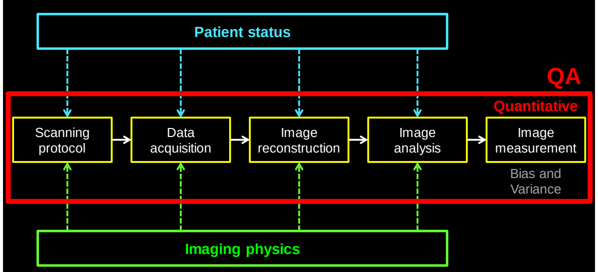
Medical physics: E pluribus unum



Qualitative imaging chain



Quantitative imaging chain



WG FUTURE - Research

- **WG FUTURE retreat on Research (2012):**
  - Defining research activity roadmap for WG FUTURE
- **Expanding Horizons meetings:**
  - Medical physics laboratory of the future (2011)
  - The physics of cancer (connecting with PS-OCs) (2013)
  - Bridging the scales (connecting with BPS)
- **Grant challenges of medical physics (2015):**
  - Modeled after "NCI's provocative questions"
  - Defining roadmap for future Horizon's meetings

WG FUTURE - Research

- **Specialized scientific sessions at AAPM:**
  - 2014: The physics of cancer (Science Council Symposium)
  - 2015-: The physics of cancer (regular sessions)
- **Multiple symposia at AAPM:**
  - 2014: Industrial partnerships (together with Vendor relations committee)
  - 2015: Modeling Cancer Complexity (with PS-OCs)
  - 2015: Bridging the scales from molecules and cells to clinical applications (with BPS)
- **Multiple training sessions at AAPM:**
  - 2013-15: Grantsmanship and funding symposium (with Grantsmanship committee)

WG FUTURE - Research

- **Engagement of junior medical physicists:**
  - Student research WG (with Research Committee)
    - Travel grants ($20k) for travel to non-AAPM sponsored meetings
    - Reaching to undergraduate physics students to increase recruitment
- **Research webpage** (with Research Committee)
  - Increasing visibility of research within AAPM
  - Student research corner

Quantitative Imaging Biomarkers

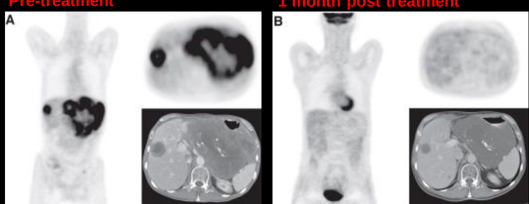
- **QIBA** initiative: create "measuring devices," not "imaging devices" (Kessler, 2014)
  - **Standardize** acquisition and analysis protocols, eliminate systematic error (Shankar, 2006; Boellaard, 2010)
  - **Optimize** accuracy, robustness over expected range in phantom studies (Jallow, 2014)
  - **Quantify** remaining uncertainties under test-retest conditions (repeatability) (Kessler, 2014)

Biomarker validation/qualification

1. **Individual validation (measurement)**
   Successfully measures a quantifiable characteristic both **precisely** and **reproducibly**
2. **Internal validation (study)**
   Correlates with clinical endpoint, adds **accuracy** to precision and reproducibility
3. **External validation**
   Demonstrates similar predictive power in **other populations** or in **other related treatment studies**
4. **Broad qualification**
   Can be used as a **surrogate** in evaluating other classes of disease

Power of molecular imaging

Pre-treatment | **1 month post treatment**

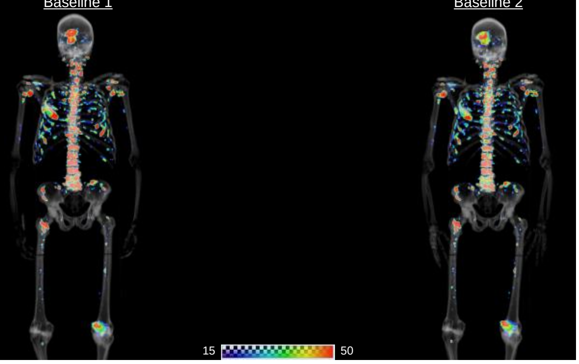


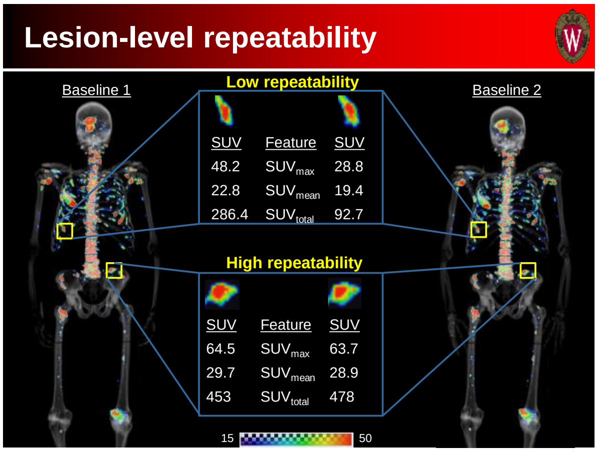
- FDG PET response **correctly predicts response** to Gleevec in majority of patients
- FDG PET response **correctly predicts SD and PD**, while CT does not
- FDG PET response **precedes the CT response** (shrinkage) by several weeks
- FDG PET response is strongly **associated with a longer progression free survival** (92% vs. 12% after 1 year) and closely correlated **with subjective symptom control**

Stroobants et al 2003, Eur J Cancer 39, 2012
Van der Abbelle 2008, The Oncologist 13(suppl 2), 8

Lesion-level repeatability

Baseline 1 | Baseline 2




Lesion-level repeatability
Baseline 1
Low repeatability
Baseline 2
SUV Feature SUV
48.2 SUVmax 28.8
22.8 SUVmean 19.4
286.4 SUVtotal 92.7
High repeatability
SUV Feature SUV
64.5 SUVmax 63.7
29.7 SUVmean 28.9
453 SUVtotal 478
15
50