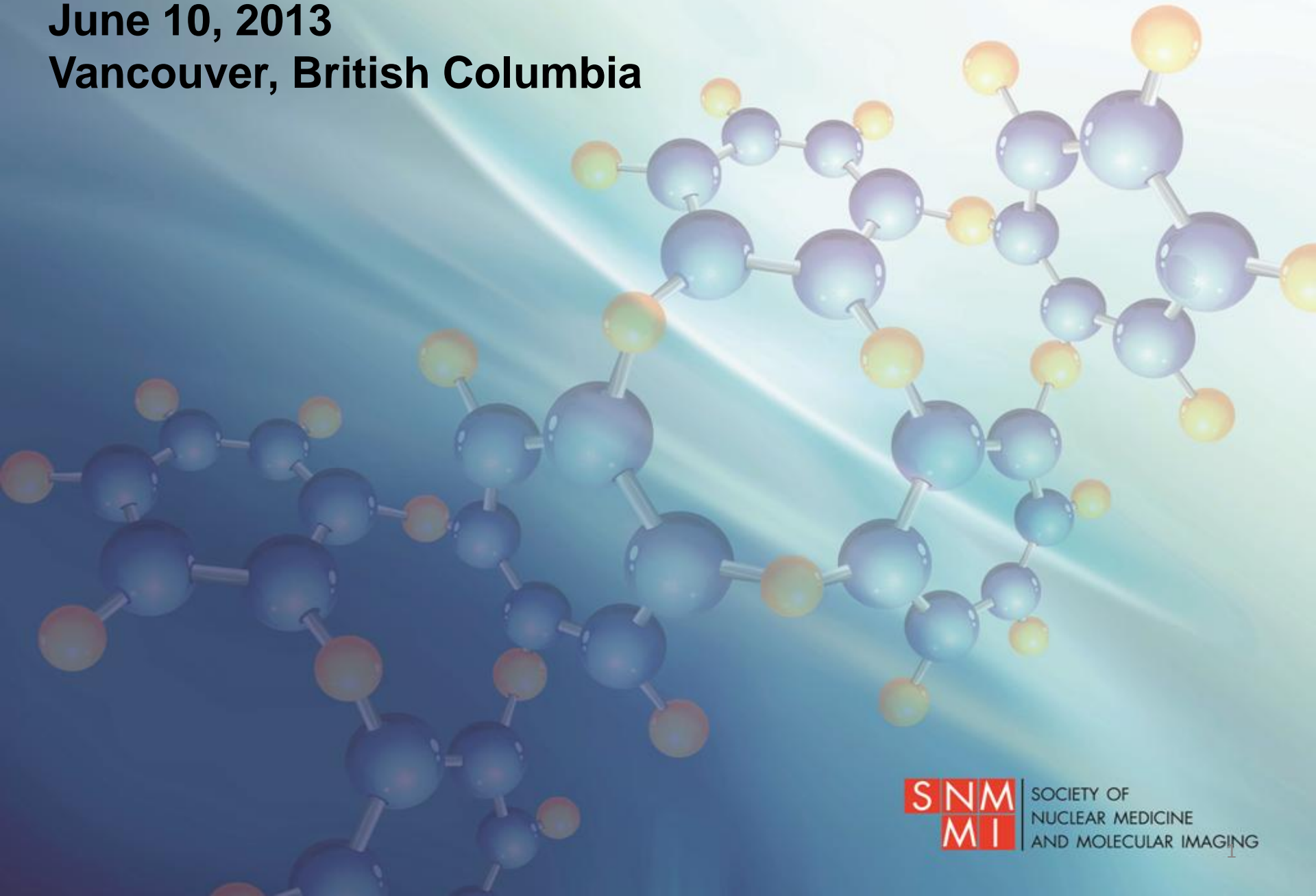


# SNMMI 2013 Annual Meeting Press Conference

June 10, 2013

Vancouver, British Columbia



# Frederic Fahey, DSc

## SNMMI 2012-2013 President

Associate Professor of Radiology  
Harvard Medical School  
Boston, Mass.

# Scientific Research Highlights

# High Sugar Intake Linked to Low Dopamine Release in Insulin Resistant Patients

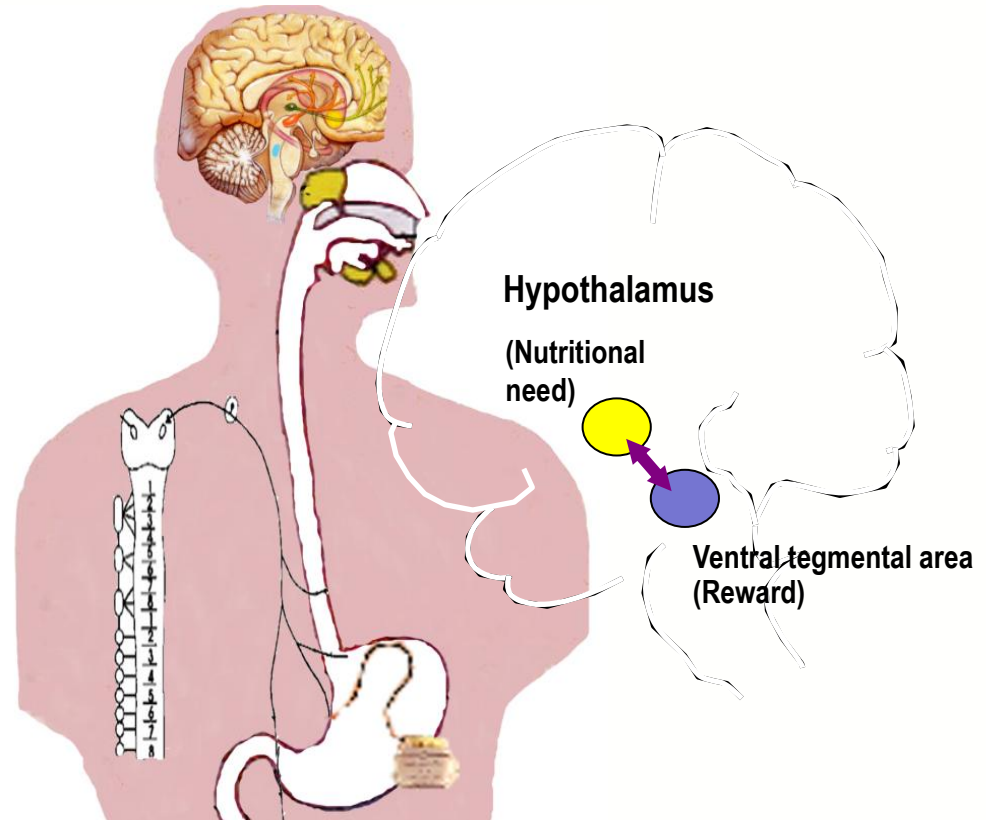
G.J. Wang, J. Logan, E. Shumay, J. Fowler, A. Convit,  
T. Dardo, N. Volkow

*Scientific Paper 29: "Peripheral insulin resistance affects brain dopaminergic signaling after glucose ingestion"*

# High Sugar Intake Linked to Low Dopamine Release in Insulin Resistant Patients

## Background

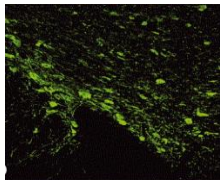
- Signals that control food consumption:
  - Dopamine, Cannabinoids, Serotonin, Opioids
- Homeostatic factors:
  - Insulin, Leptin, Ghrelin, PYY



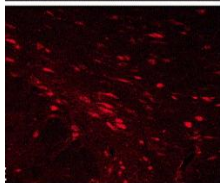
# High Sugar Intake Linked to Low Dopamine Release in Insulin Resistant Patients

## Midbrain DA neurons express insulin receptors

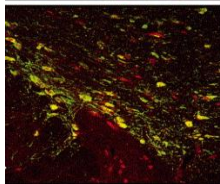
*Fluorescence immunocytochemistry*



Tyrosine hydroxylase (TH), marker for DA neuron



Insulin receptors

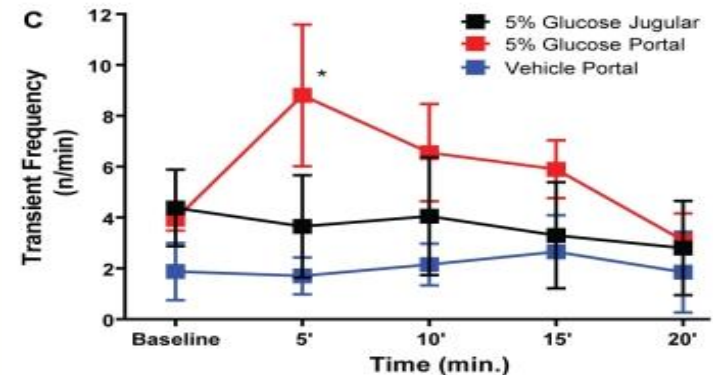


Merge image of TH/insulin receptor (yellow)

DA neurons in VTA and SN mediate insulin's effects on food-seeking behavior.

*Figlewicz DP et al, Brain Res, 2003*

## Glucose increases DA in NAc (independent of taste)



*Oliveira-Maia et al PLOS ONE 2011*

Postingestive mechanisms participate in sugar-induced DA release in Nac.

Insulin modulates glucose-induced DA increases in Nac

Insulin resistance would impair this

# High Sugar Intake Linked to Low Dopamine Release in Insulin Resistant Patients

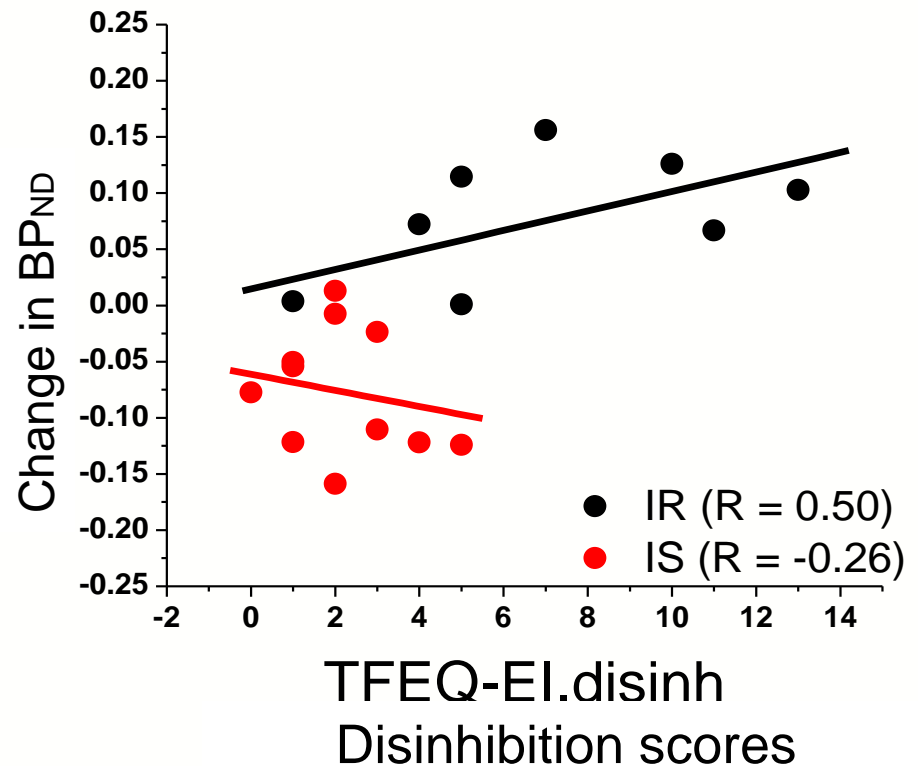
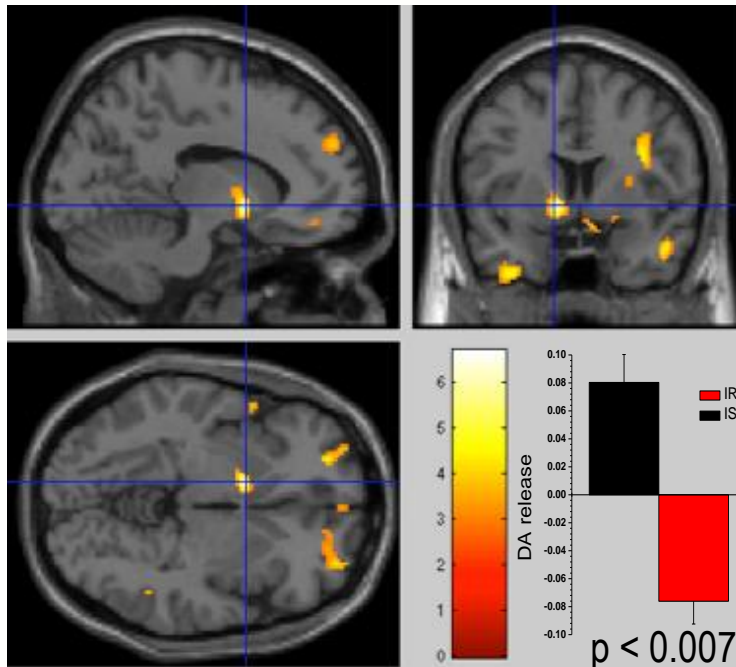
## Methodology

- Hypothesis: insulin resistance in pre-diabetic subjects will result in decreased striatal DA signaling.
- Compared DA increases triggered by glucose between insulin-sensitive (n=11) and insulin-resistant pre-diabetic subjects (n=8).
- Imaged subjects with PET and [11C]raclopride, a ligand sensitive to changes in DA.
- Compared the differences in binding between glucose (calorie content) and sucralose (sweetener without calories) in insulin-sensitive and insulin-resistant subjects.



# High Sugar Intake Linked to Low Dopamine Release in Insulin Resistant Patients

(-12, 6, -8)



Statistical parameter mapping that compared the difference of [C-11] raclopride scan after oral ingestion of glucose and after oral sucralose (artificial sweetener) drinks between insulin resistance subjects and control subjects.



# High Sugar Intake Linked to Low Dopamine Release in Insulin Resistant Patients

## Summary Results

- Insulin-resistant subjects have less brain dopamine release in Nac when given glucose than insulin-sensitive subjects (PFWE < 0.013).
- Disinhibition scores and glucose-induced DA increases in Nac were negative for subjects with insulin-resistance but positive for insulin-sensitive.

# High Sugar Intake Linked to Low Dopamine Release in Insulin Resistant Patients

## Broader Implications of the Study

- Lesser dopamine release in Nucleus Accumbens (main reward region in brain) after glucose in insulin-resistant subjects indicates decreased sensitivity of the DA reward circuit to calorie content.
- Insulin-resistant subjects with greater disinhibition (i.e. prone to eat upon food exposure, stress or negative moods) have less dopamine release in Nac after glucose ingestion.
- The reduced DA release in NAc to the reinforcer (food) in Insulin Resistant subjects is equivalent to the reduced DA release in Nac to drugs in addiction, which might drive overeating to compensate for this deficit (difference between expectation and actual response).

# Molecular Imaging Enlists Prostate Enzyme To Detect Prostate Cancer And Metastases

S. Vallabhajosula, J. Osborne, A. Nikolopoulou,  
I. Lipai, S. Tagawa, D. Scherr, S. Goldsmith,  
J. Joyal, T. Armor, J. Babich

*Scientific Paper 281: "PSMA targeted SPECT imaging biomarker to detect local and metastatic prostate cancer (PCa): Phase I studies with 99mTc-MIP-1404."*

# Molecular Imaging Enlists Prostate Enzyme To Detect Prostate Cancer And Metastases

## Background

- According to the American Cancer Society, approximately 238, 600 new prostate cancer diagnoses will be reported in 2013.
- One in six men will develop prostate tumors within their lives.
- Screening based on:
  - Prostate specific antigen (PSA)
  - Digital Rectal Exam (DRE)
- Confirmation by biopsy
  - Trans-rectal Ultrasound (TRUS) Guided Biopsies
- Imaging studies include CT, MRI and bone scan

# Molecular Imaging Enlists Prostate Enzyme To Detect Prostate Cancer And Metastases

## Methodology

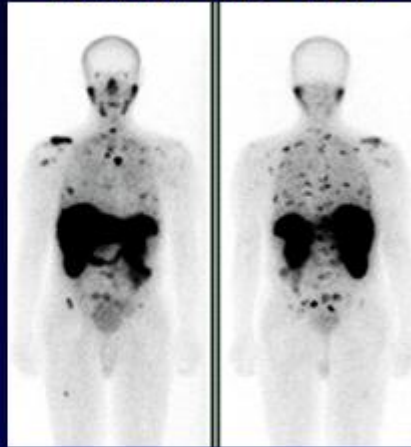
- Prostate Specific Membrane Antigen (**PSMA**) is a surface antigen expressed virtually on all prostate cancer cells.
- **Tc-99m labeled MIP-1404** is a small molecule with specific binding to an enzyme site on PSMA.
- Researchers performed planar imaging and single photon emission computed tomography (SPECT) following intravenous injection of Tc-99m-MIP-1404 in patients with prostate cancer and in patients with metastasis.
- Imaging scans were evaluated to map where the novel agent was bound to PSMA enzyme in primary prostate cancer and metastatic prostate cancer tumors throughout the body.

# Molecular Imaging Enlists Prostate Enzyme To Detect Prostate Cancer And Metastases

Standard Bone Scan

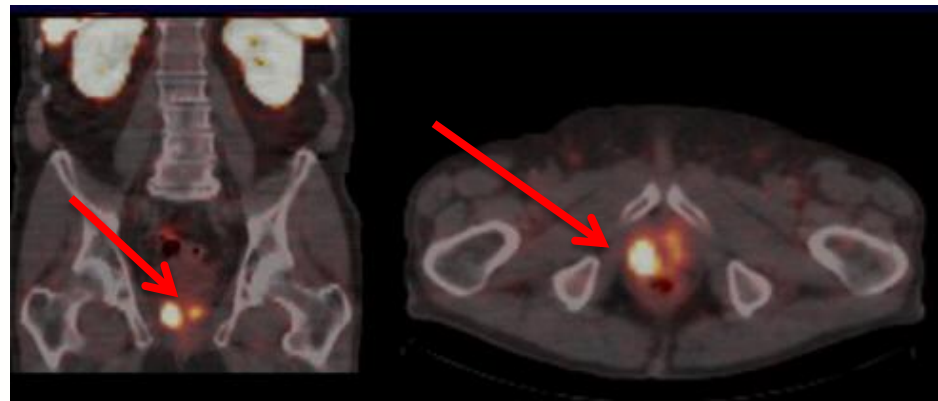
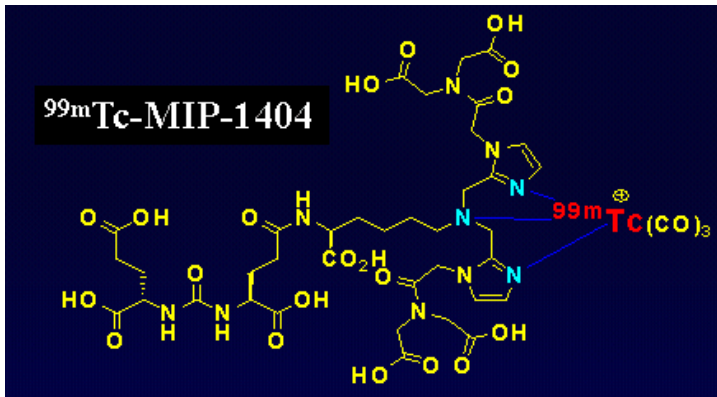


Tc-99m-MIP-1404



Tc-99m-MIP-1404  
Whole body planar scan

Tc-99m-MIP-1404  
SPECT scan



Cancer in prostate gland 14



# Molecular Imaging Enlists Prostate Enzyme To Detect Prostate Cancer And Metastases

## Results

- Tc-99m MIP-1404 was quickly distributed in the body and ready for imaging as soon as one hour after injection for localization of cancer lesions in prostate gland, bones and lymph nodes.
- Higher the PSMA expression in the cancer, greater is the binding of Tc-99m-MIP to PSMA, and better is the detection.
- More lesions detected by this novel agent than in standard bone imaging.

# Molecular Imaging Enlists Prostate Enzyme To Detect Prostate Cancer And Metastases

## Broader Implications of the Study

- Molecular imaging biomarker could one day be used for screening prostate cancer patients and for monitoring the response to therapy.
- MIP-1404 molecule has the potential to also be formulated as a therapeutic radioactive drug.
- Represents a more commercially and clinically viable option because easy to manufacture and has a faster rate of distribution and clearance from the body. SPECT scanners are more readily available through out the world.

# Dose Analysis Predicts Progression Free Survival in Non-Hodgkins Lymphoma Patients

Y. Dewaraja, A. Avram, P. Roberson, L. Smith, S. Wilderman, J. Shen, H. Savas, E. Youssef, M. Kaminski, M. Schipper

University of Michigan Medical School

*Work supported through grant EB001994 awarded by NIH*

*Scientific Paper 51: "Tumor absorbed dose predicts progression free survival (PFS) following I-131 radioimmunotherapy (RIT)."*

# Dose Analysis Predicts Progression Free Survival in Non-Hodgkins Lymphoma Patients

## Background

- 69,740 new cases of non-Hodgkins lymphoma (NHL) in 2013
  - A total of 19,020 will die of the disease
- Advanced low-grade NHL patients who undergo chemotherapy and external radiotherapy eventually relapse and die
- Radioimmunotherapy with radiolabeled antibodies, such as  $^{131}\text{I}$ -tositumomab has offered new therapeutic options
- Treatment planning using pre-therapy tumor dosimetry possible
  - Clear association between radiation dose to tumor and outcome not shown previously, hence tumor dose not considered in planning

# Dose Analysis Predicts Progression Free Survival in Non-Hodgkins Lymphoma Patients

## Background

- Long term study goal: A patient specific dosimetry driven approach to deliver an optimal therapeutic dose to the tumor, avoiding critical organ toxicity
  - First step is to establish a strong correlation between radiation absorbed dose to the tumor and outcome of the treatment (focus of present study).

# Dose Analysis Predicts Progression Free Survival in Non-Hodgkins Lymphoma Patients

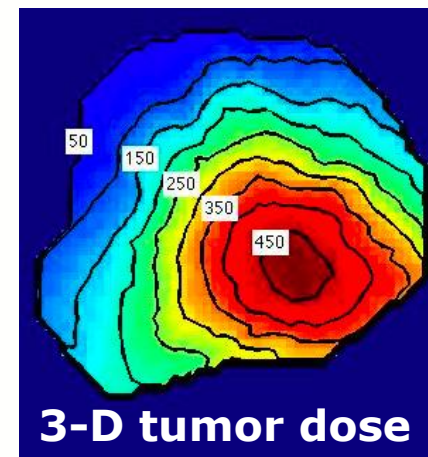
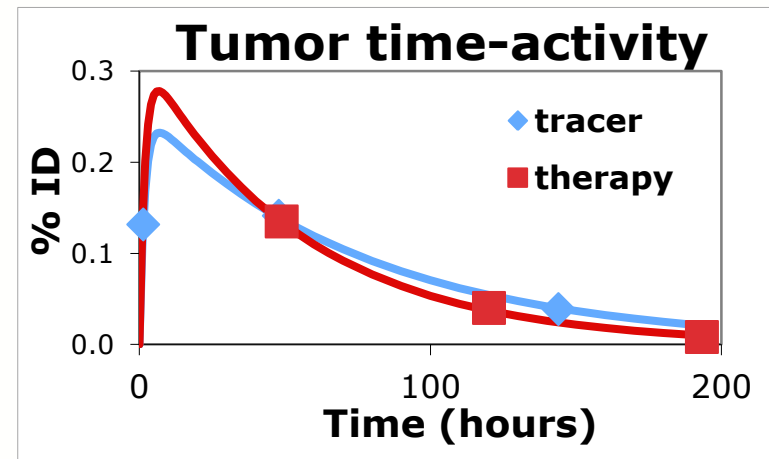
## Methodology

- A total of 39 patients (130 tumors) receiving  $^{131}\text{I}$  radioimmunotherapy included in this prospective study
- To improve on previous studies, accurate tumor dose calculation based on SPECT/CT imaging at multiple time points
- Outcome measured based on follow-up PET/CT imaging
  - Tumor shrinkage
  - Time after therapy that the patient is free of disease progression



# Dose Analysis Predicts Progression Free Survival in Non-Hodgkins Lymphoma Patients

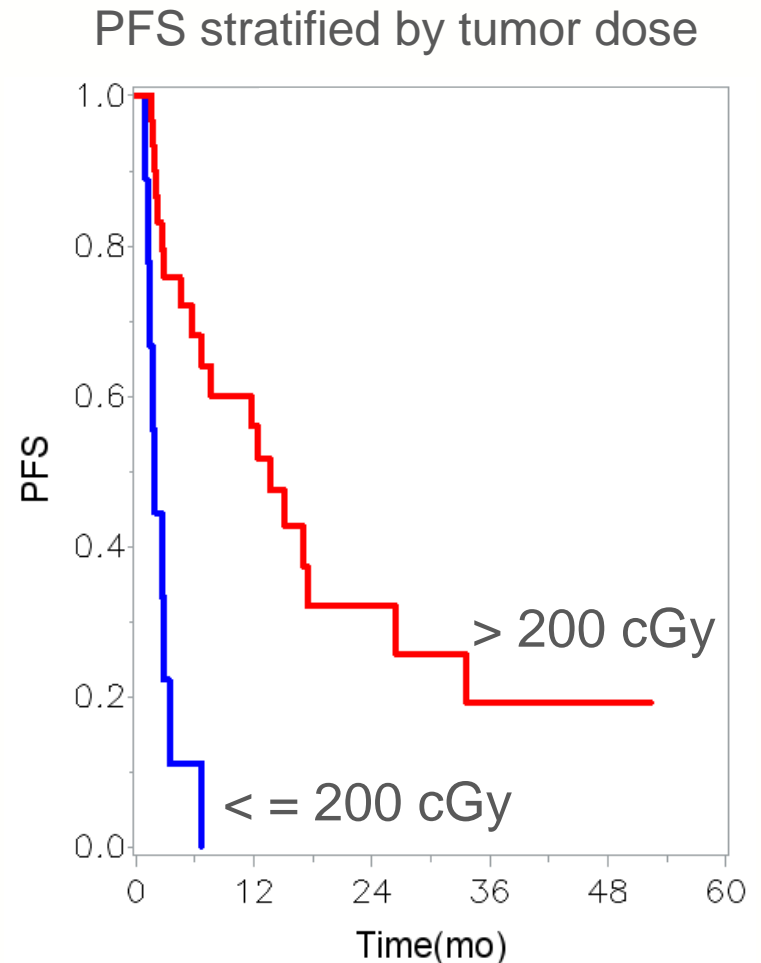
## SPECT/CT Imaging based Estimation of Tumor Dose



## Dose Analysis Predicts Progression Free Survival in Non-Hodgkins Lymphoma Patients

### Research Findings

- Longer progression-free survival (PFS) was seen in patients receiving more than 200 centigray of tumor absorbed dose (median PFS of 14 months). Median PFS was only 2 months for patients receiving less than 200 centigray.
- Patients receiving less than 200 cGy can benefit from a tumor dosimetry driven treatment approach.



## Dose Analysis Predicts Progression Free Survival in Non-Hodgkins Lymphoma Patients

### Broader Implications of the Study

- Tumor absorbed dose, which can be estimated before the therapy, can be used to customize the treatment to achieve marked improvement in progression free survival
  - Additional studies are needed to assess the absorbed dose to the bone marrow to limit toxicity to this sensitive tissue
- Sequential SPECT/CT imaging useful for dosimetry

# Breast Cancer: PET and MR Predict Chemotherapy's Ability to Prolong Life

J. Park, I. Lim, B. Byun, B. Kim, C. Choi, S. Lim,  
W. Noh, H. Kim, E. Kim, S. Lee

*Scientific Paper 76: "Prediction of the disease free survival in patients with advanced breast cancer after first cycle of neoadjuvant chemotherapy using parallel PET/MR"*

## Breast Cancer: PET and MR Predict Chemotherapy's Ability to Prolong Life

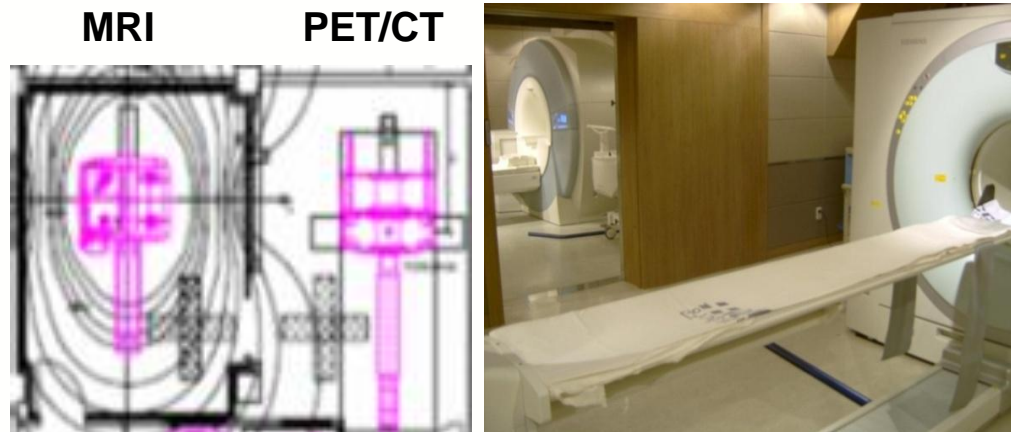
### Background

- In 2013, approximately 232,000 new cases of invasive breast cancer are expected to be diagnosed in women in the United States.
- As many as 39,620 American women will die from the disease this year.
- One in eight American women will develop breast cancer in their lives, according to the American Cancer Society.

# Breast Cancer: PET and MR Predict Chemotherapy's Ability to Prolong Life

## Methods

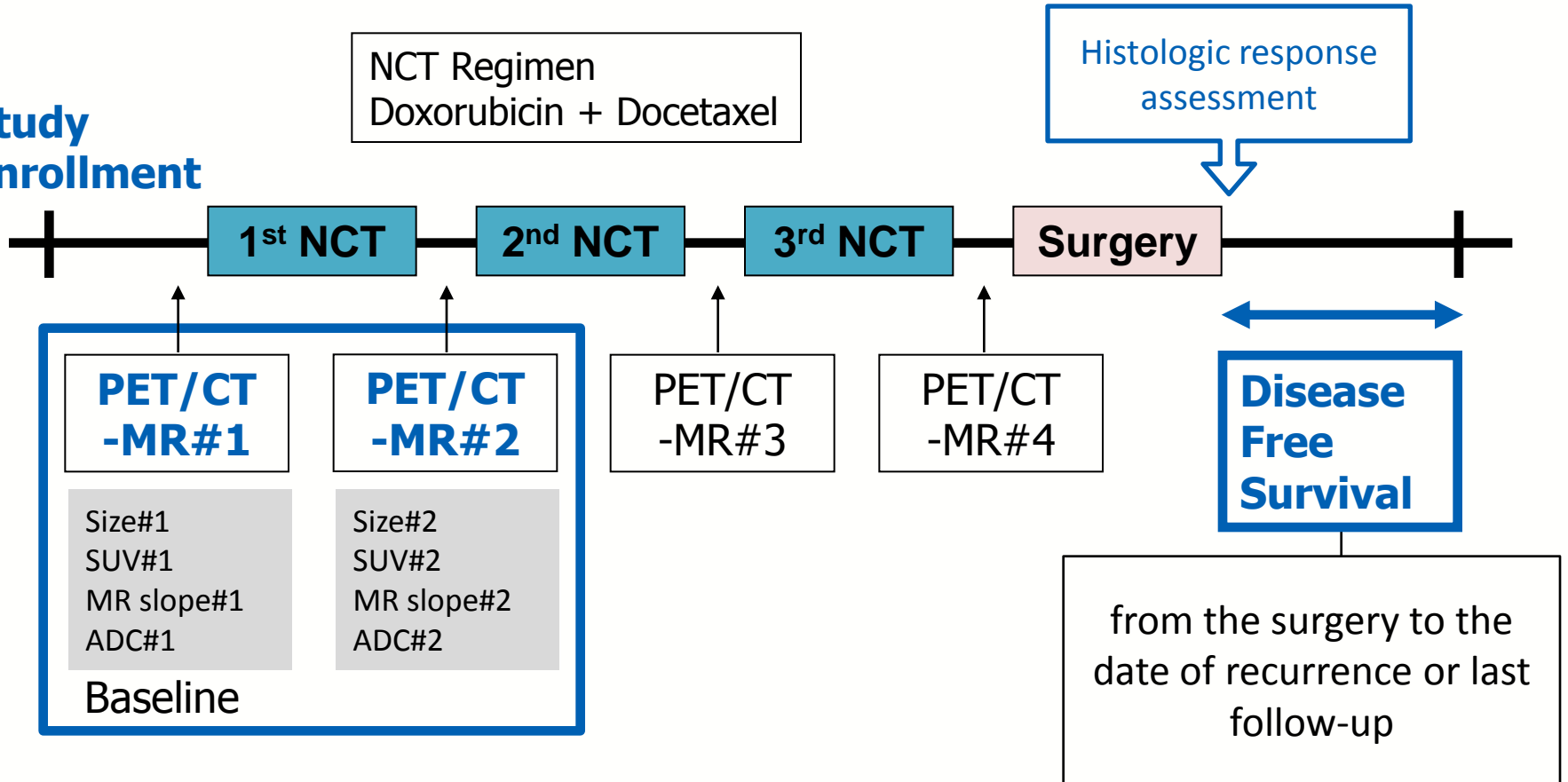
- Fifty-four women with advanced breast cancer
- Imaging conducted before and after one cycle of pre-operative chemotherapy.





# Breast Cancer: PET and MR Predict Chemotherapy's Ability to Prolong Life

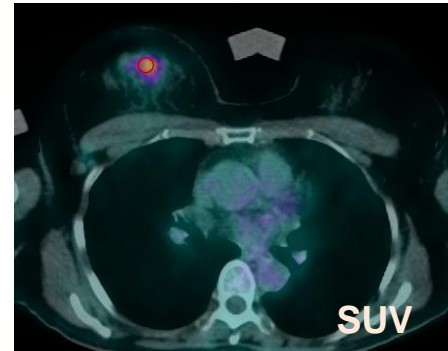
## Study Enrollment



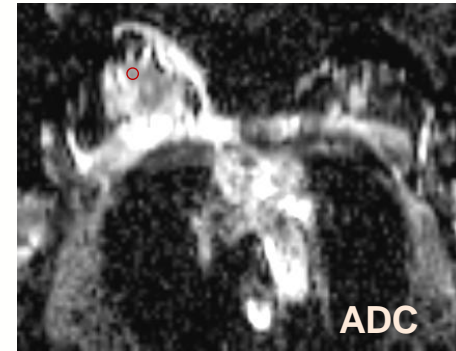
# Breast Cancer: PET and MR Predict Chemotherapy's Ability to Prolong Life

## Methods

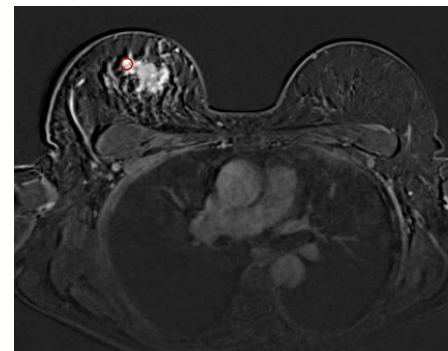
- SUV#1, SUV#2 → SUV ratio
- ADC#1, ADC#2 → ADC ratio
- MRslope#1, MRslope#2 → MRslope ratio



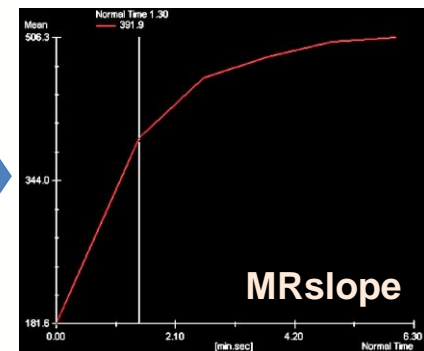
<sup>18</sup>F-FDG PET/CT



Diffusion weighted MRI



DCE MRI

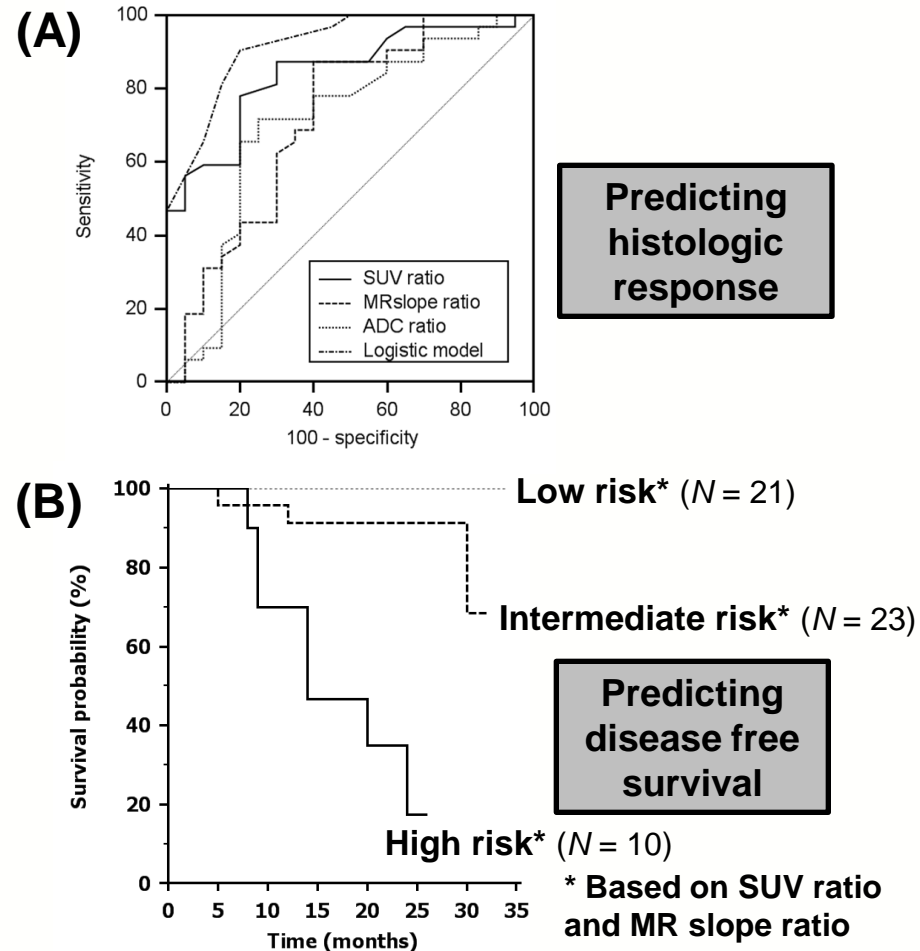


Enhancement curve

# Breast Cancer: PET and MR Predict Chemotherapy's Ability to Prolong Life

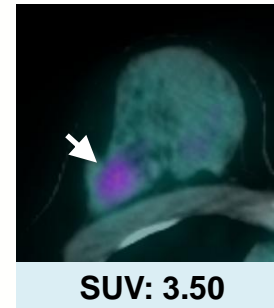
## Results

- A total of 10 patients (19%) experienced disease recurrence during follow-up period.
- Median disease free survival: 21 months (range, 2-34 months)
- Combining PET/CT and MR side by side improves prediction of both histologic response **(A)** and patient survival **(B)**.

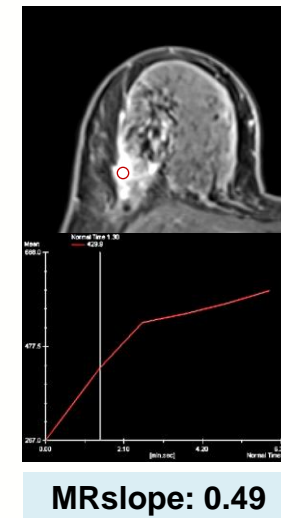
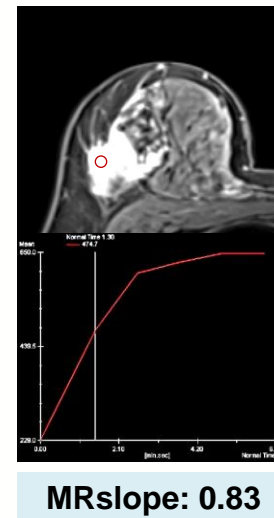


# Breast Cancer: PET and MR Predict Chemotherapy's Ability to Prolong Life

- F/43, Invasive lobular carcinoma
  - Histologic response: **poor**
  - PET/MRI-based risk assessment: **low risk group**
- This patient has been alive without evidence of recurrence for 31 months.



SUV ratio  
= 0.49



MRslope  
ratio = 0.58

Before treatment

After 1 cycle of  
preop. chemotherapy

## Breast Cancer: PET and MR Predict Chemotherapy's Ability to Prolong Life

### Broader Implications of the Study

- Using both FDG PET and MR imaging to predict disease-free survival allows clinicians to apply more aggressive therapies that could potentially halt patients' cancers and extend lives.
- The study provides evidence that fused PET/MR utilizing both metabolic and vascular perfusion imaging can benefit patients.

# Gary Dillehay, MD, FACNM, FACR

SNMMI 2013-2014 President

Professor of Radiology  
Northwestern Memorial Hospital  
Chicago, Ill.



# SNMMI 2013 Image of the Year

Peter Herscovitch, MD  
2013-2014 President-Elect

## SNMMI 2013 Image of the Year

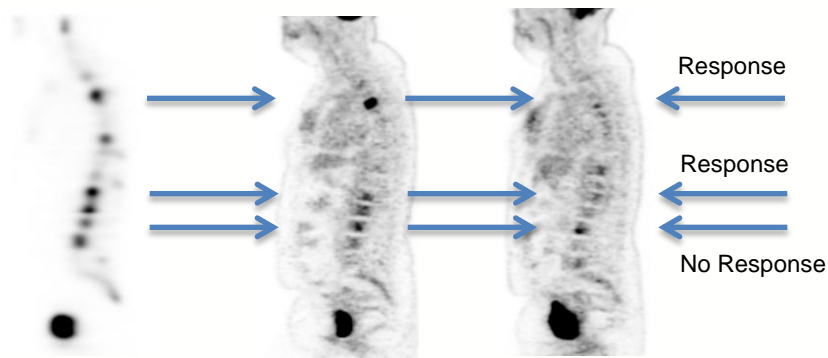
# **Scientific Paper #647: [ $^{18}\text{F}$ ] FDG PET: Changes in uptake as a method to assess radium-223 dichloride (Ra-223) response in bone metastases of breast cancer patients with bone-dominant disease**

Patrick Flamen, MD, PhD  
Institut Jules Bordet, Brussels, Belgium

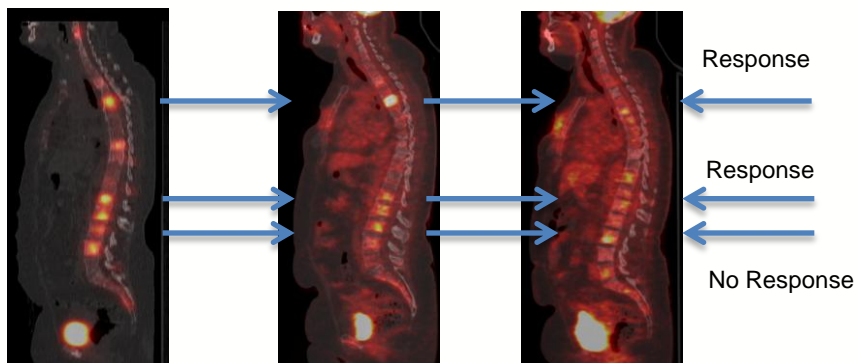
R. Coleman, B. Naume, G. Jerusalem, C. Garcia, A.  
Aksnes, M. Piccart

# [<sup>18</sup>F] FDG PET/CT at Baseline and After 2 Injections of Ra-223

**Baseline Bone Scan**      **Baseline [<sup>18</sup>F] FDG PET**      **[<sup>18</sup>F] FDG PET After 2 Injections of Ra-223**



**Baseline Fused SPECT/CT**      **Baseline Fused [<sup>18</sup>F] FDG PET/CT**      **Fused [<sup>18</sup>F] FDG PET/CT After 2 Injections of Ra-223**



Images obtained after 2 injections of Ra-223 showed a significant decrease ( $\geq 25\%$  decrease of  $SUV_{max}$  from baseline) in [<sup>18</sup>F] FDG uptake intensity in multiple bone mets located in the thoracic and lumbar spine, indicating a partial metabolic treatment response at the level of the tumor cells early during Ra-223 therapy.

**Thank You!**

**Questions?**