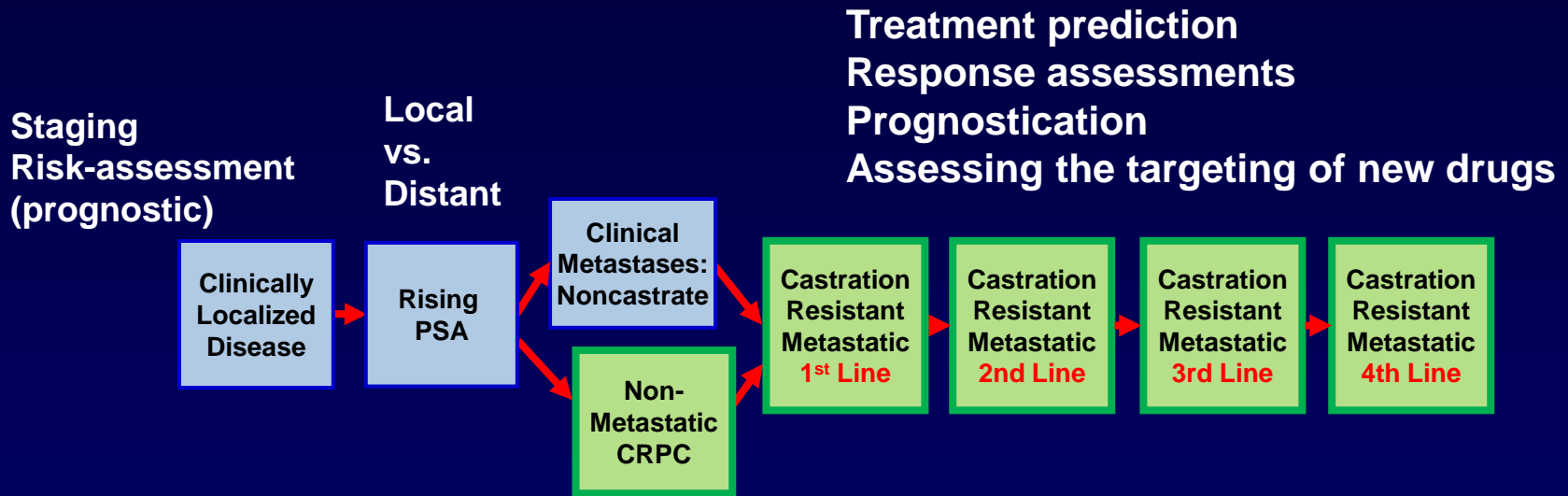


# Imaging the Unseen in Metastatic Prostate Cancer

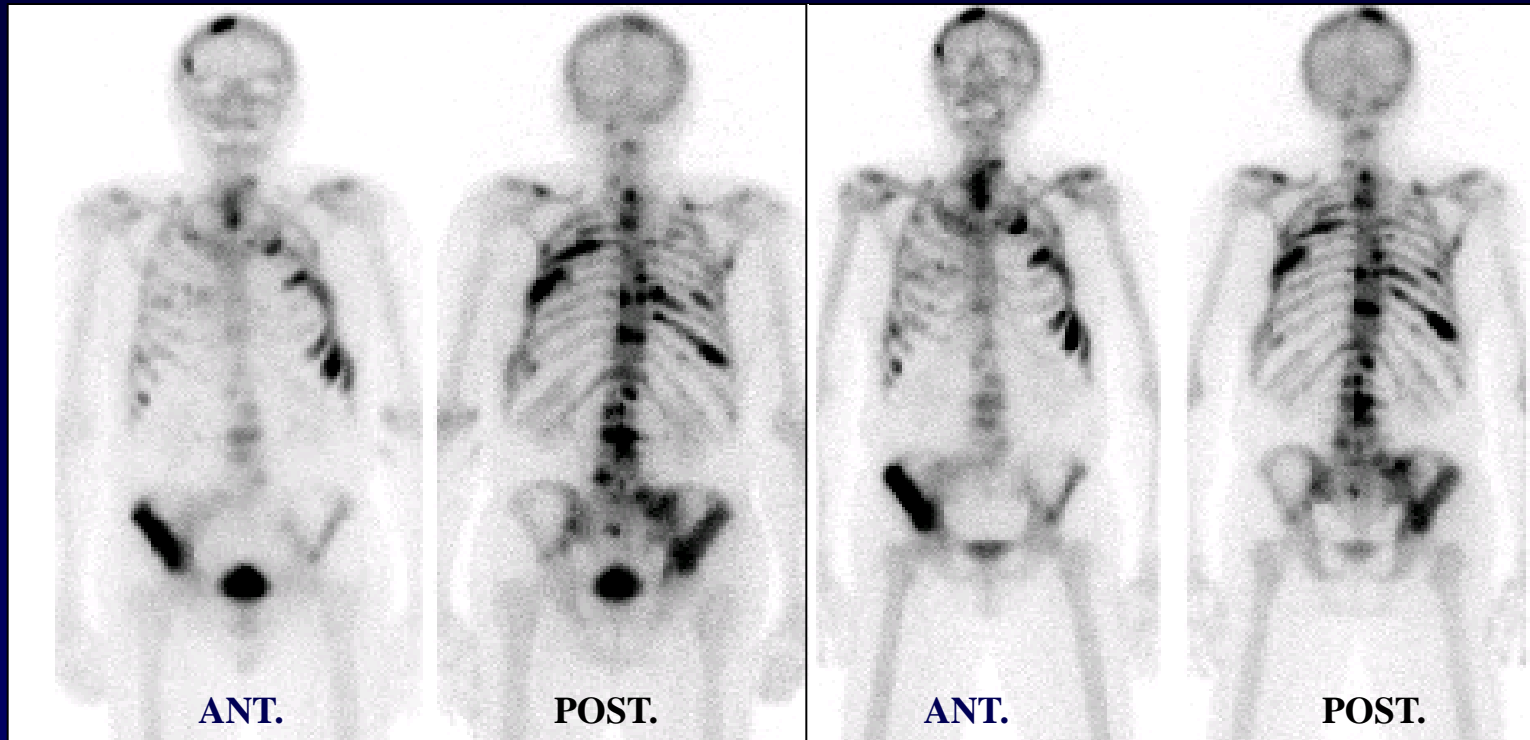
Michael J Morris, MD  
GU Oncology Service  
MSKCC

# Why do we image?



# Standard Bone Scans: Poorly Reflect Anti-Tumor Effects

## Failure to Reflect Response



Baseline

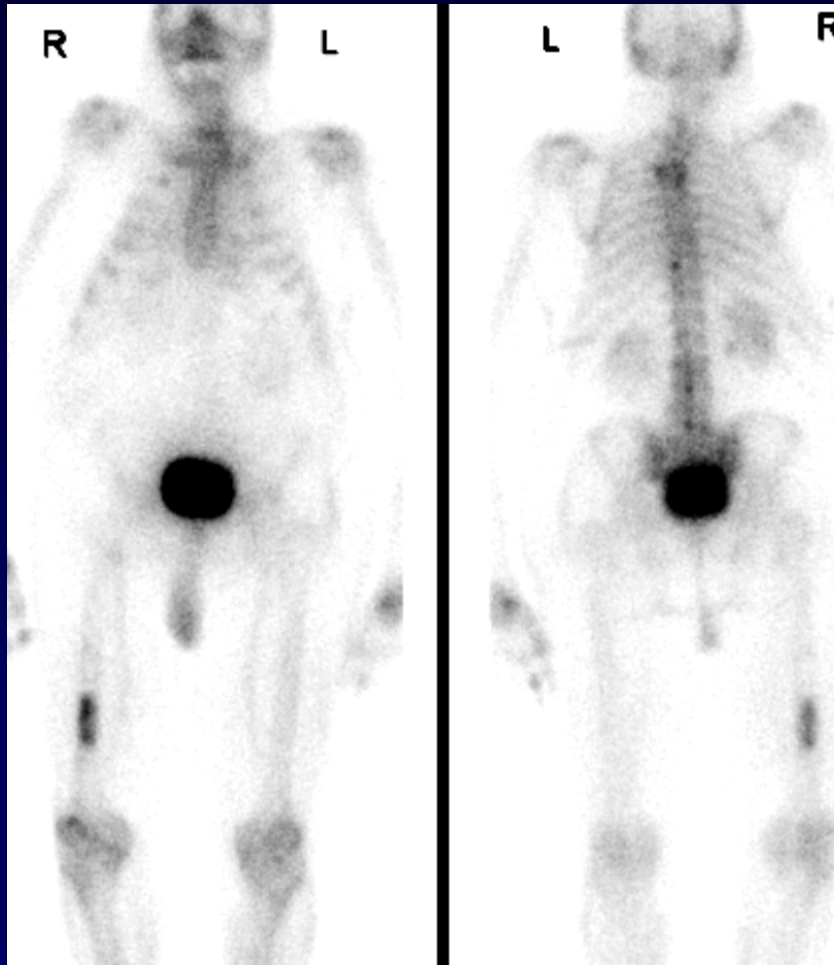
After 3 months of treatment

PSA= 75 ng/ml

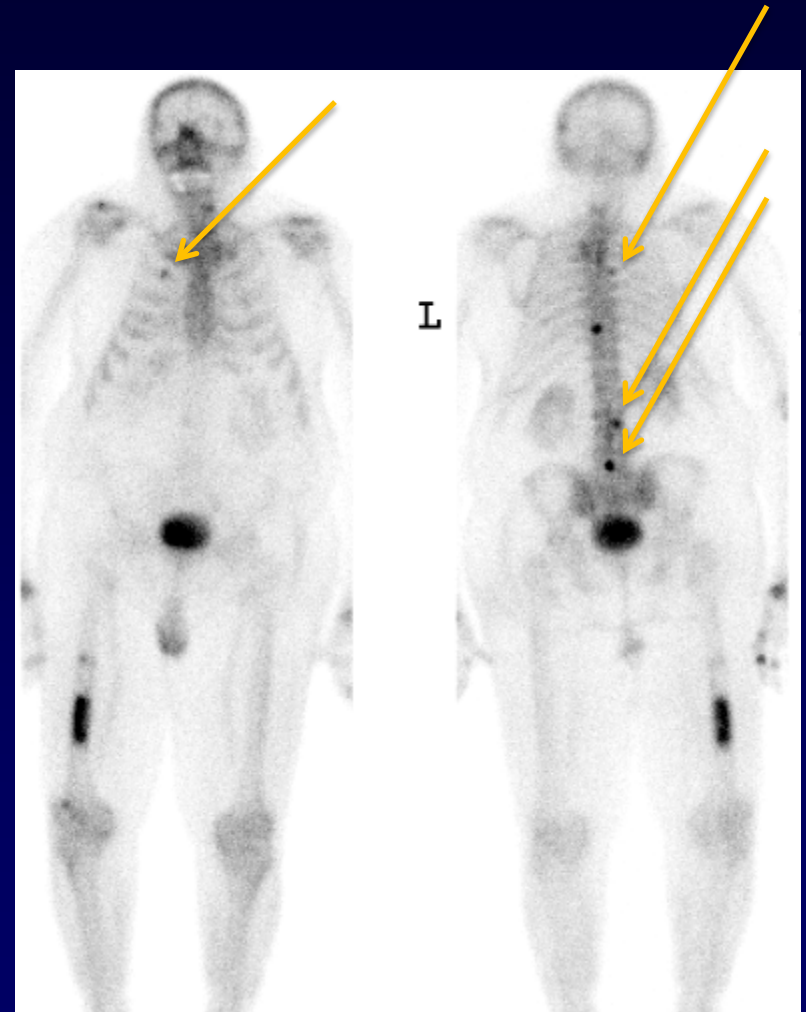
PSA=8.6 ng/ml

# Standard Bone Scans: Flare Phenomena

## Failure to Reflect Response



Baseline  
PSA= 2.6



After 6 weeks of treatment  
PSA=0.52 ng/ml

# The Dangers of Flare

- Can happen in 50% of responders
- Patients discontinue treatment early
- Effective drugs are declared as ineffective
- Focus on drug approval is on survival, rather than changes on scans
  - Current standard is feel, function, or survive

# The real world: When to stop treatment?

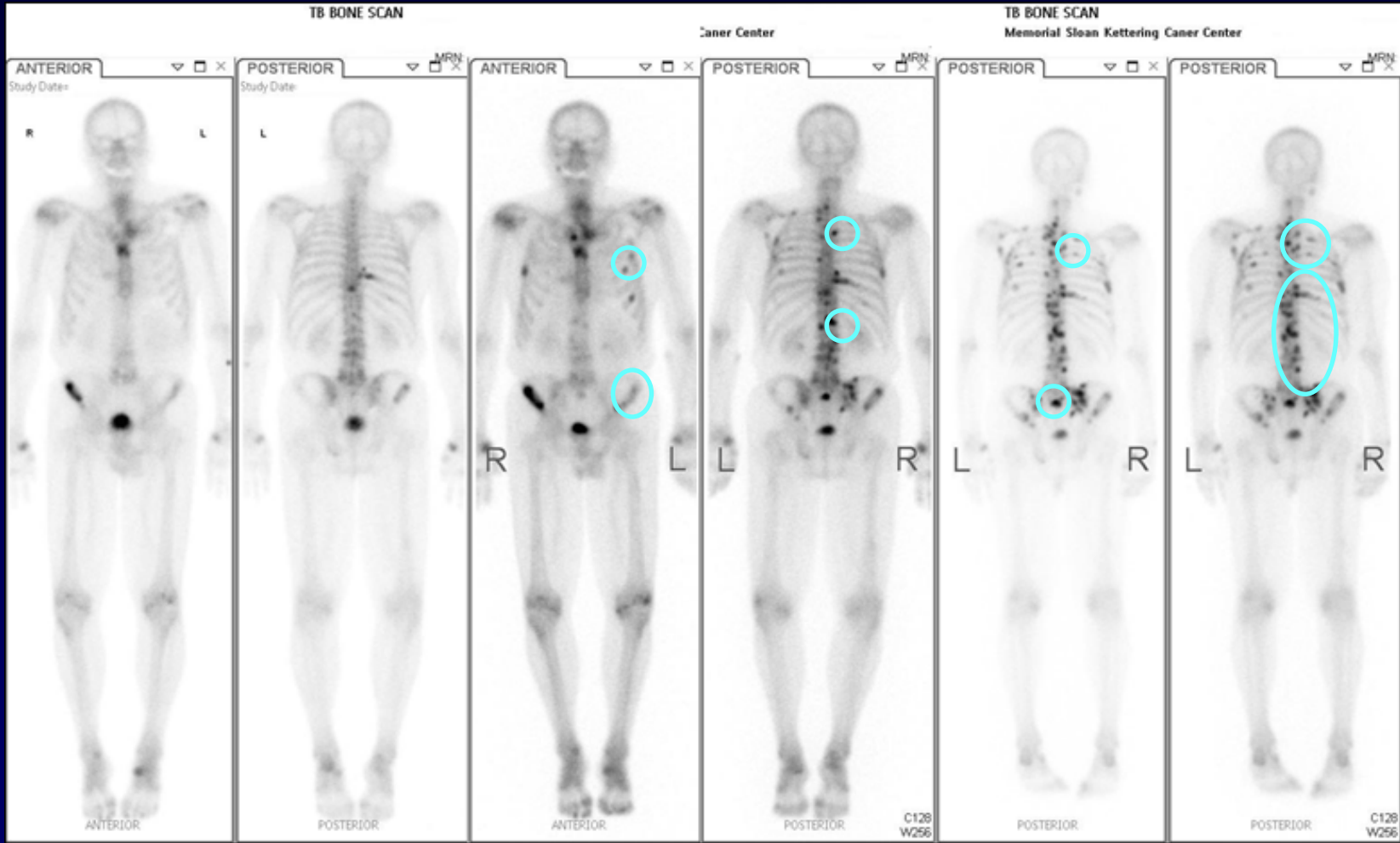
- Progression of disease
- Progression is generally defined by scans now
- Progression should not be confused with response and flare
  - CAN WE DISTINGUISH THE TWO? yes

# Bone Scan Progression

Baseline

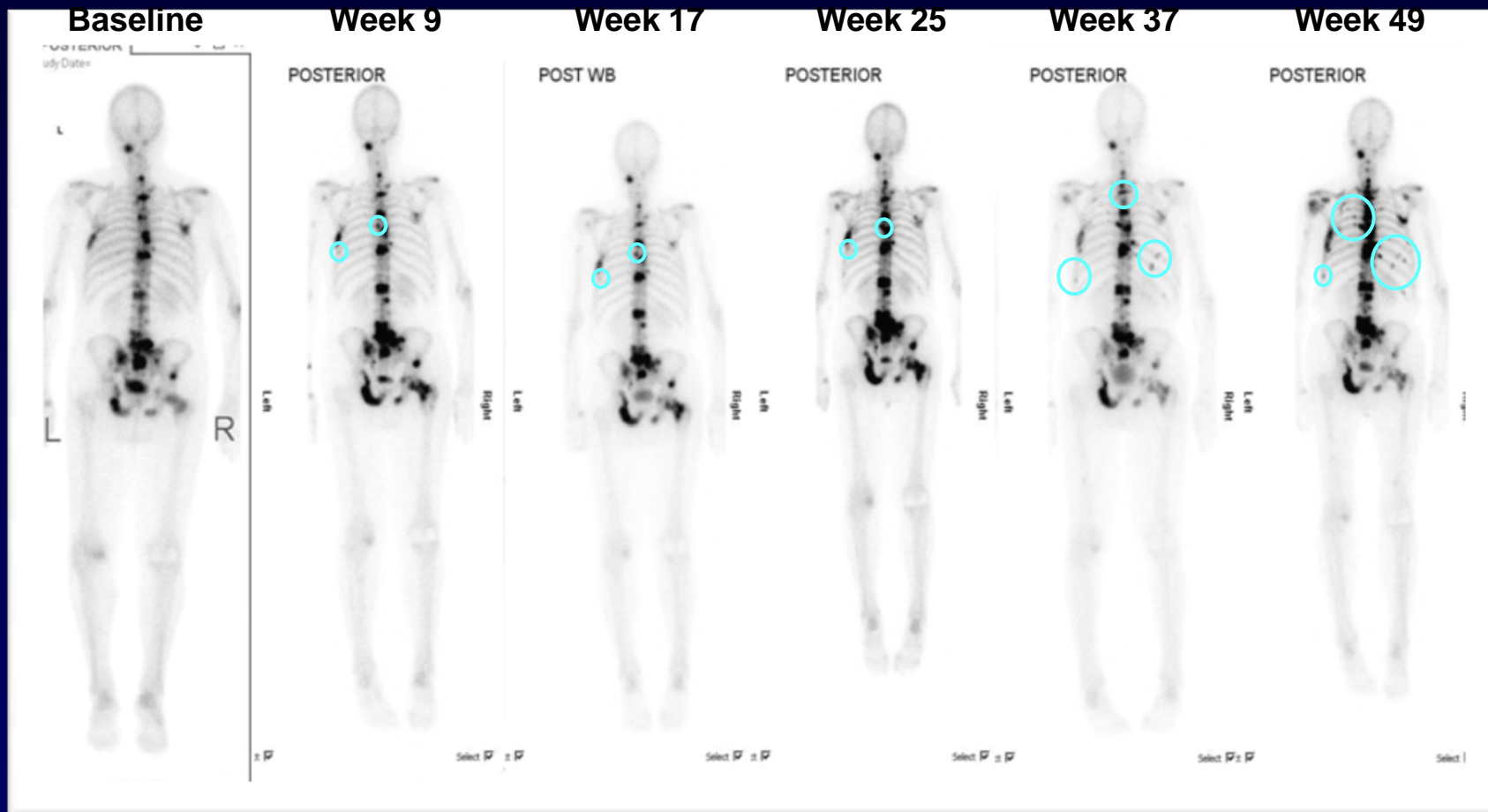
Week 9

Week 17

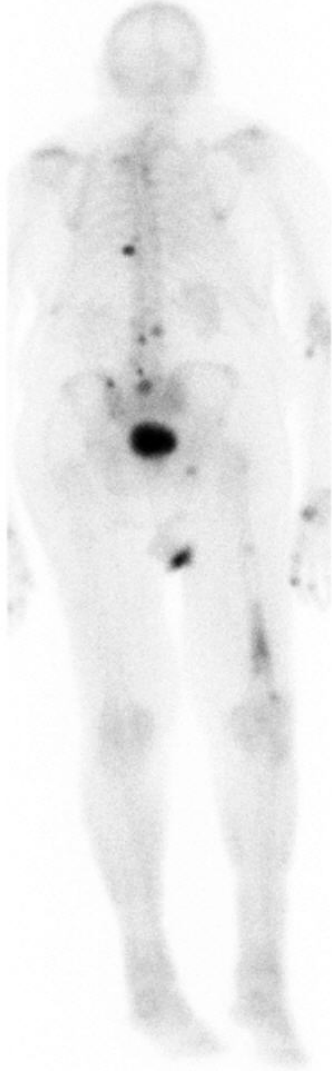
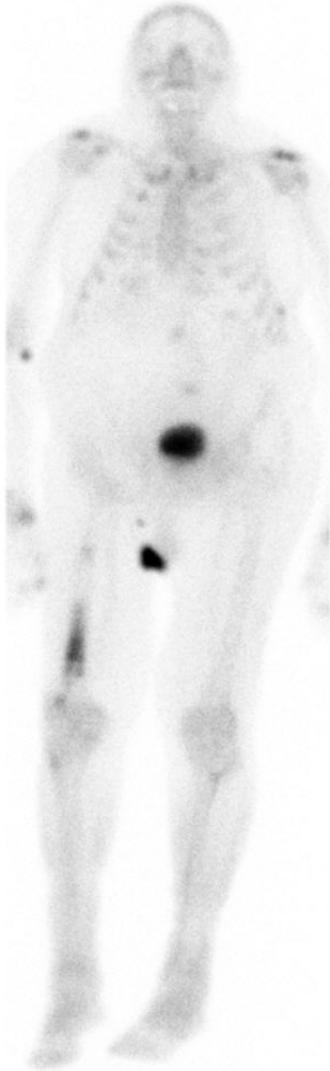


- Early flare at Week 9, patient rapidly progressed at Week 17

# Controlling for Progression with 2+2, per PCWG3

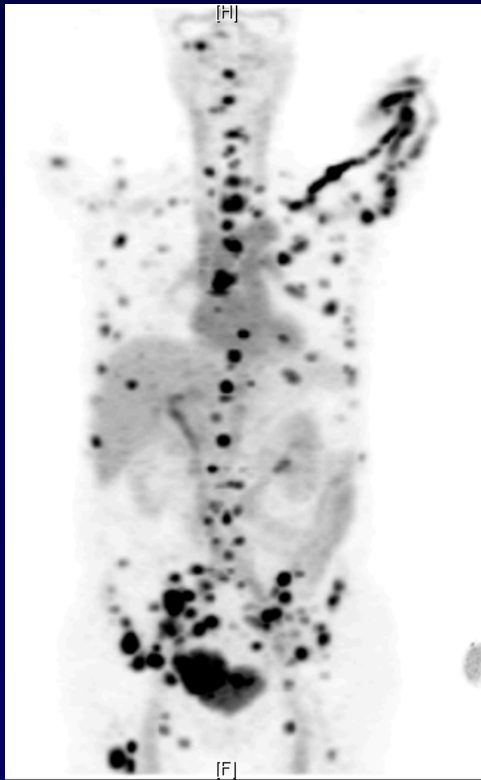


# Fluoride Bone PET/CT Imaging vs. Traditional Bone Imaging

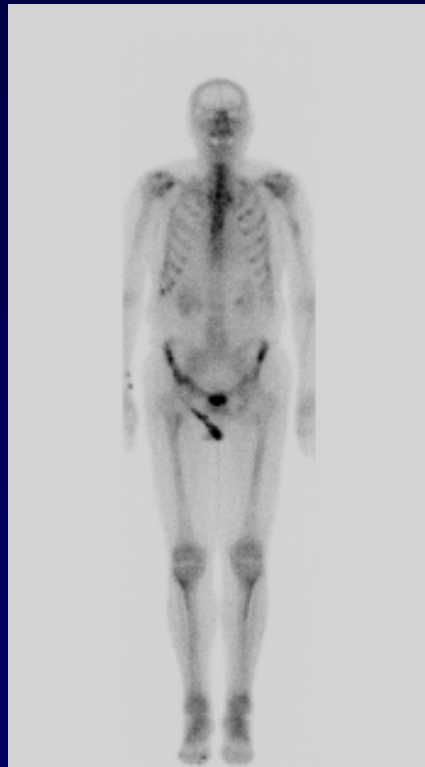


New Imaging Modalities: Image  
the tumor and not the bone

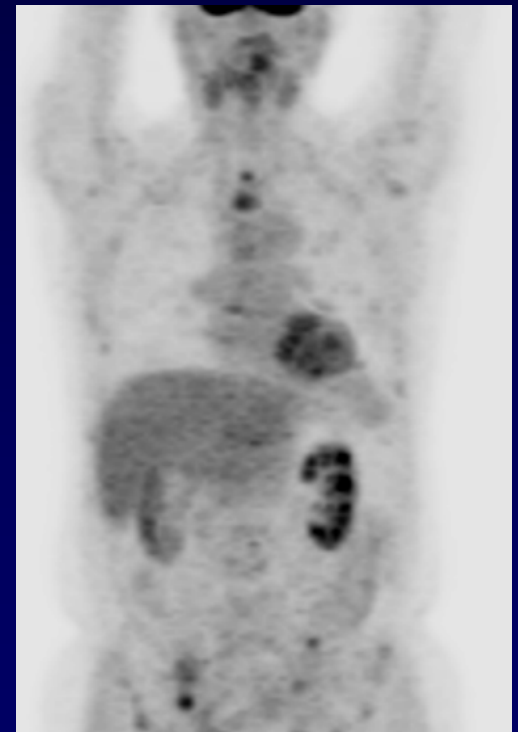
# Visualizing Prostate Cancer Using the Androgen Receptor



**Androgen Receptor**



**Bone scan**



**Standard PET**

# Using the androgen receptor PET to develop drugs: Enzalutamide



$^{18}\text{F}$ -FDHT PET/CT  
Baseline



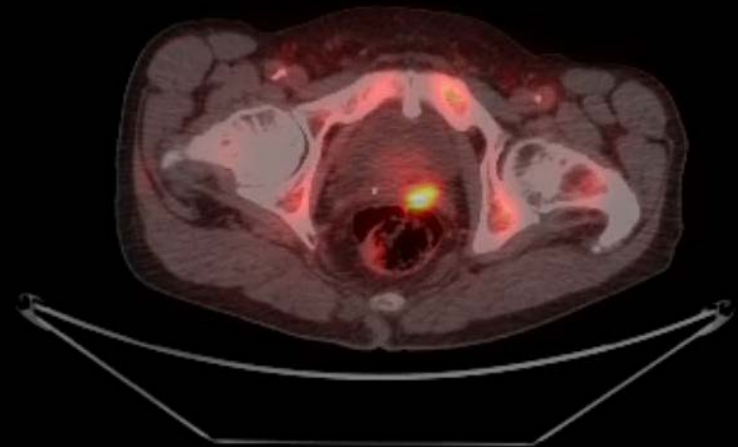
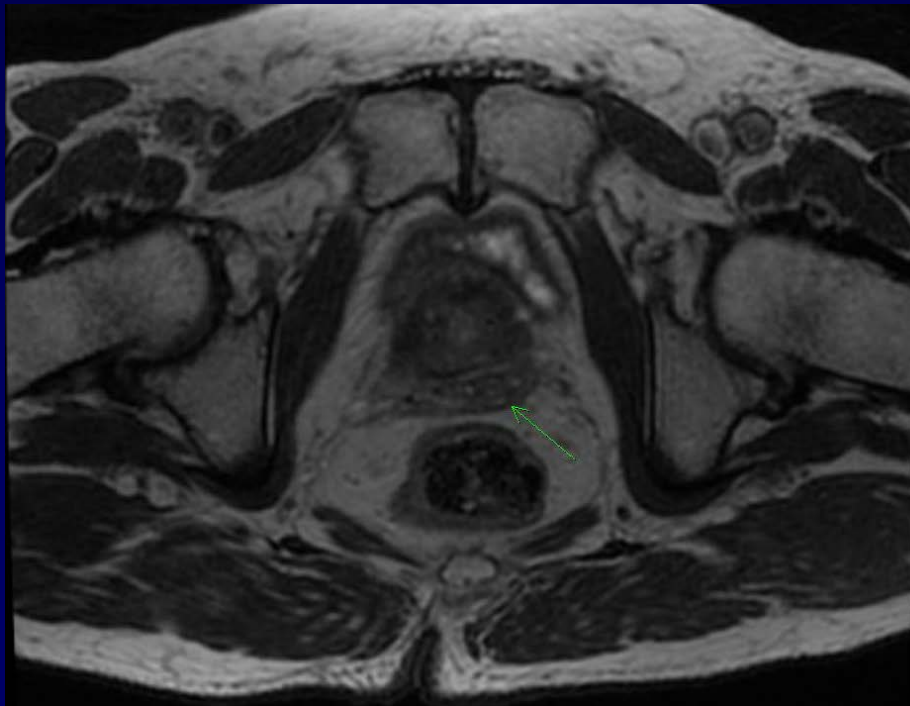
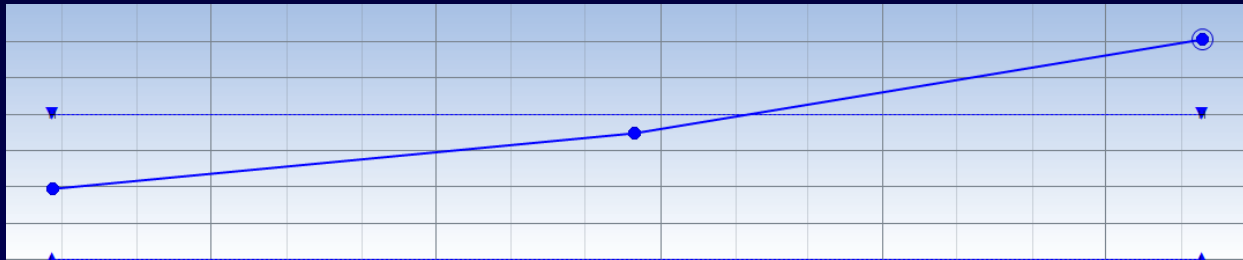
$^{18}\text{F}$ -FDHT PET/CT  
4 wks after MDV3100

# Laboratory values and novel tracers associate with survival in univariate analyses

Variable	HR	95% CI	p-value
PSA	1.14	(1.01, 1.30)	0.03
Hgb	0.15	(0.04, 0.66)	0.01
LDH	4.28	(2.64, 6.94)	<0.0001
Alk Phos	1.67	(1.31, 2.13)	<0.0001
Albumin	0.38	(0.20, 0.70)	0.002
Gleason score	1.06	(0.88, 1.28)	0.53
KPS 90 vs other	0.75	(0.51, 1.10)	0.14
FDGmax	1.32	(0.95, 1.85)	0.10
FDGmaxavg	2.25	(1.58, 3.20)	<0.001
FDHTmax	1.33	(0.79, 2.25)	0.29
FDHTmaxavg	1.91	(1.22, 3.00)	0.005

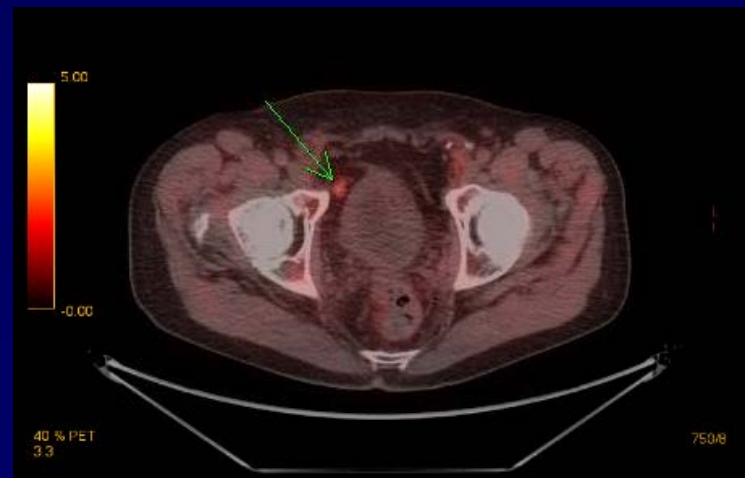
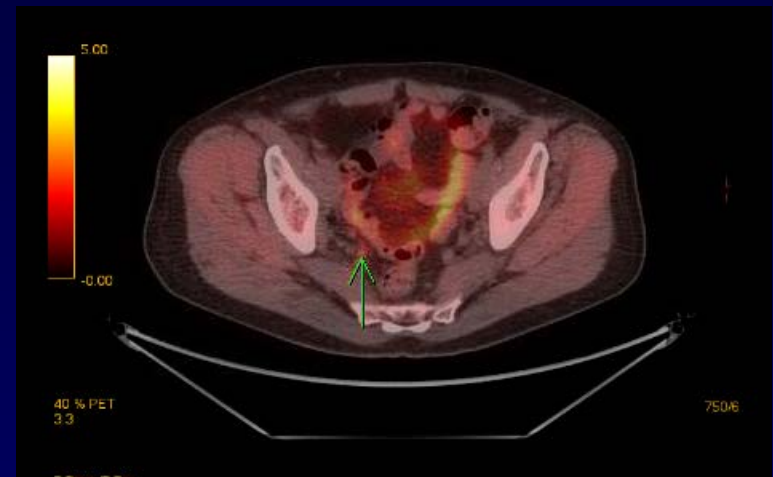
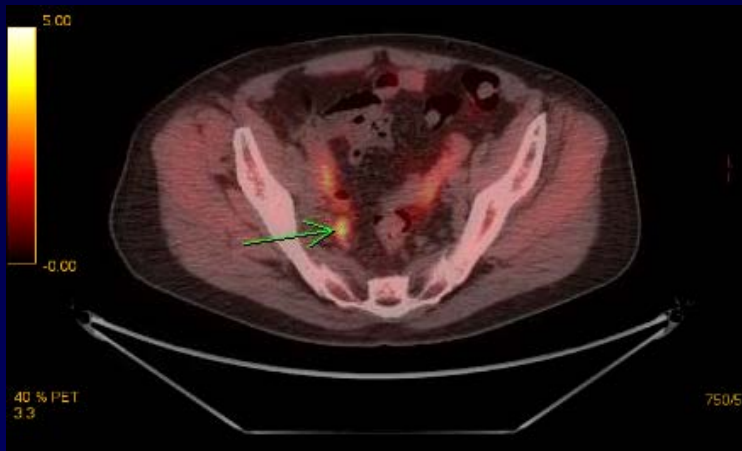
# C-11 Choline: Fatty Acids (FDA Approved)

Gleason 7, rec'd brachytherapy, now with a rising PSA

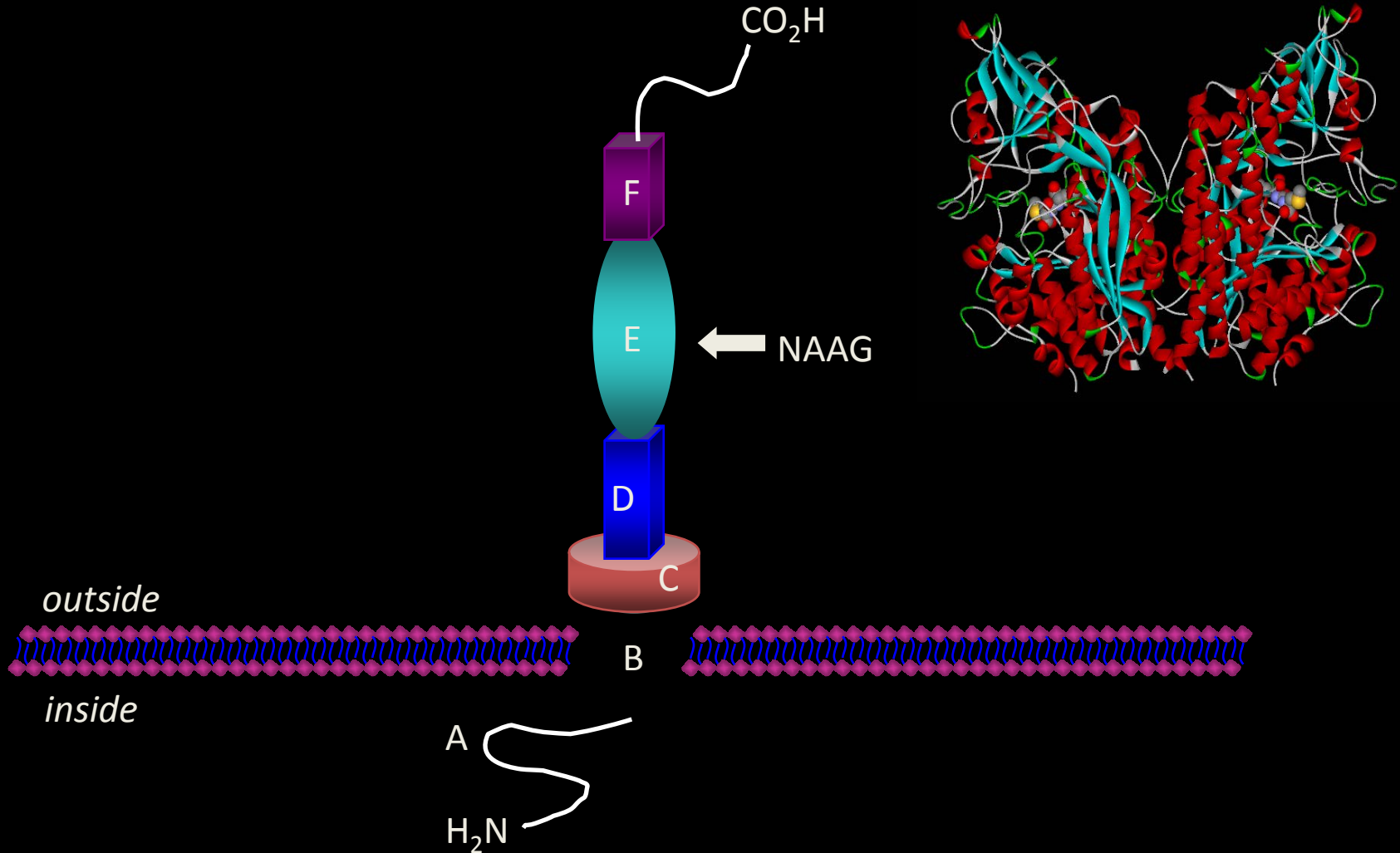


# C-11 Choline, Relapse in Nodes

Gleason 8, rec'd surgery, 1/19 nodes positive, now with a rising PSA

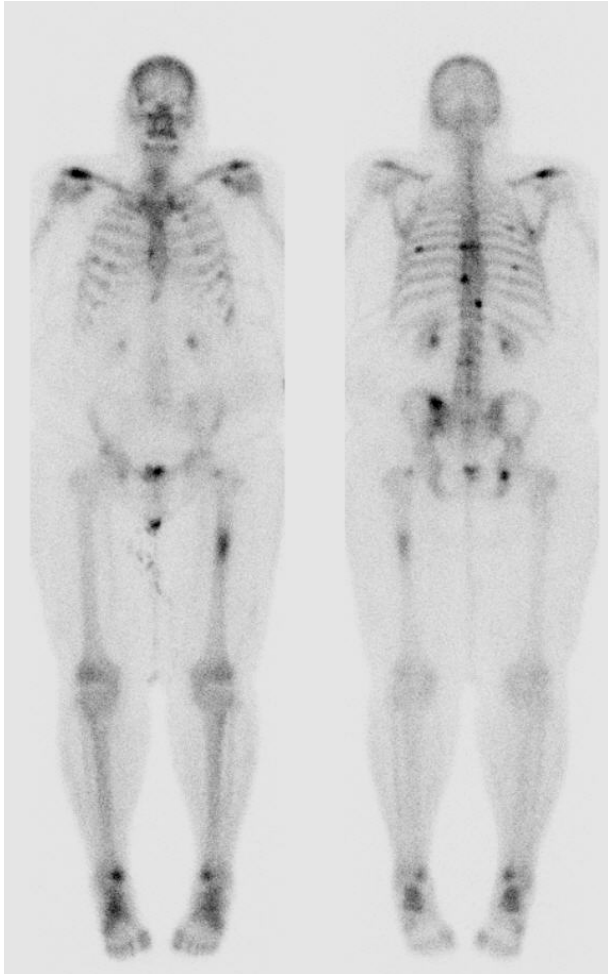


# Prostate-specific membrane antigen (PSMA): a marker for prostate cancer and tumor neovasculature



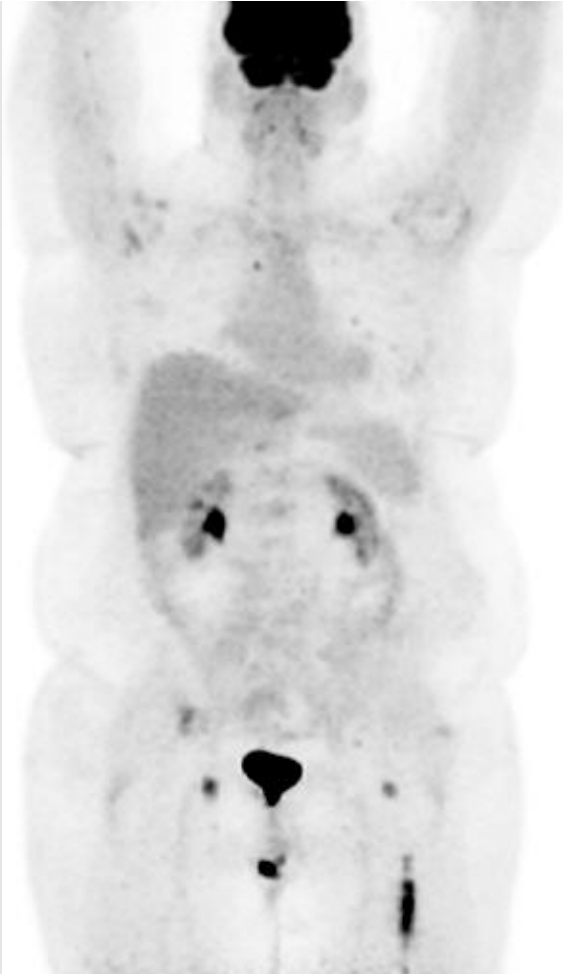
# Standard Imaging vs. PSMA

**Anterior and posterior**



**BONE SCAN**

**MIP**



**Standard  
PET scan**

**MIP**

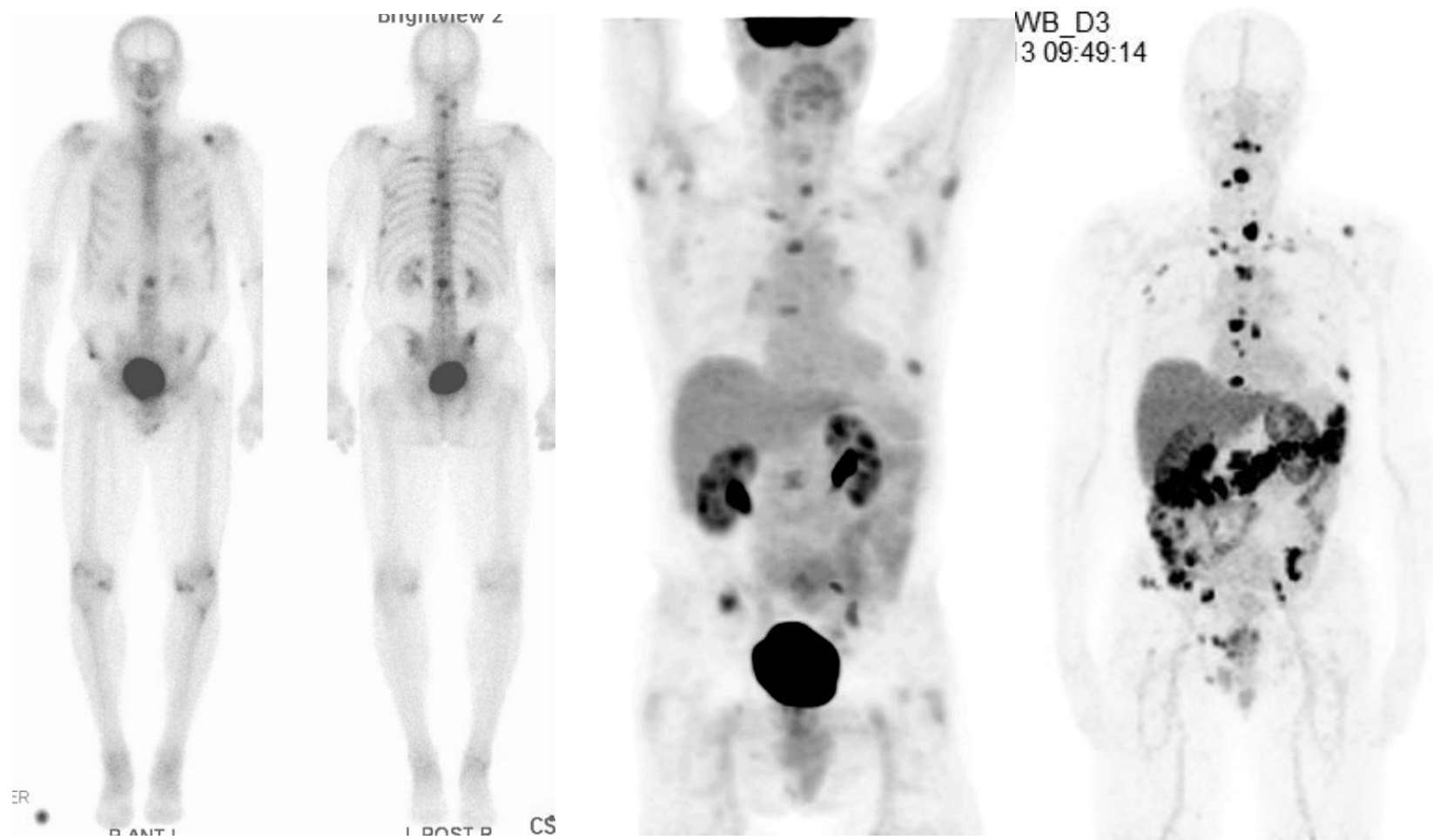


**PSMA scan Day 3**



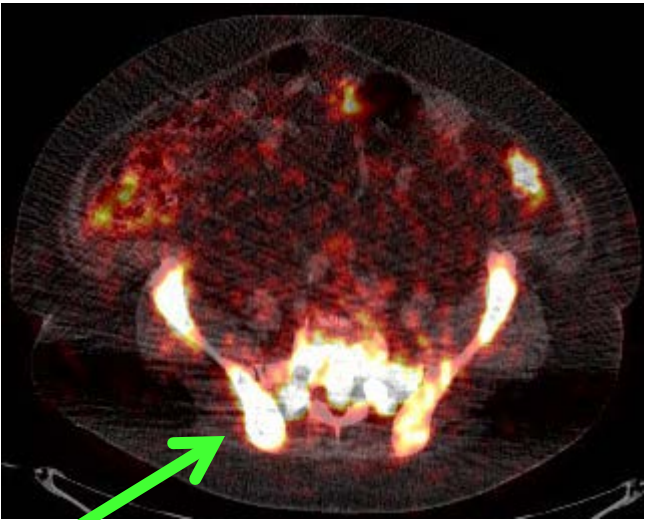
# PSMA imaging

## Comparison with Bone scan and FDG PET

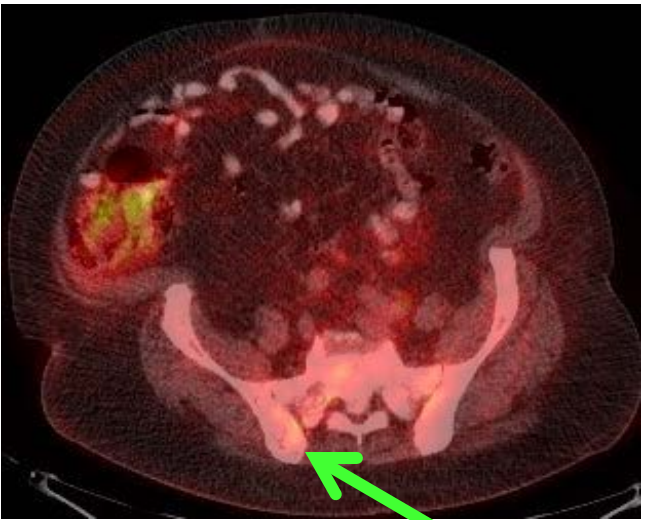


Patient positive on PSMA, Bone Scan positive, standard

PSMA

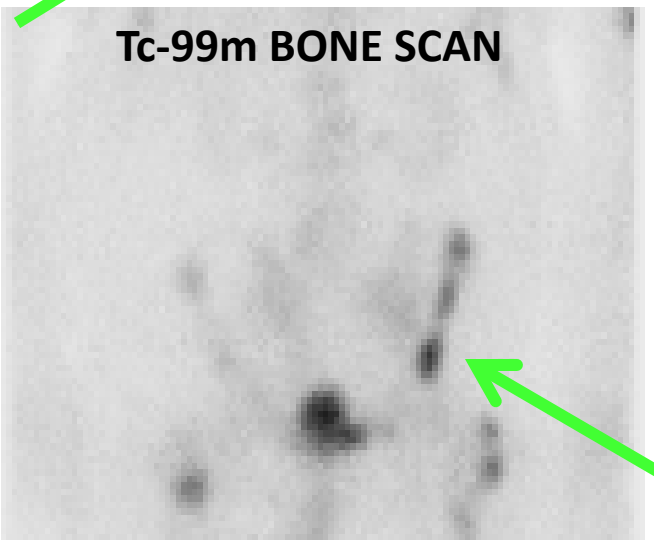


PET negative

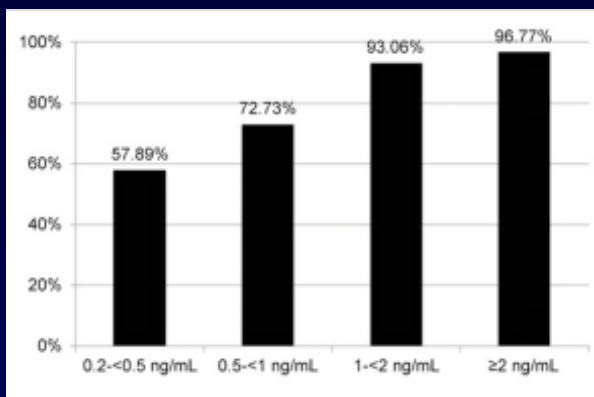


FDG

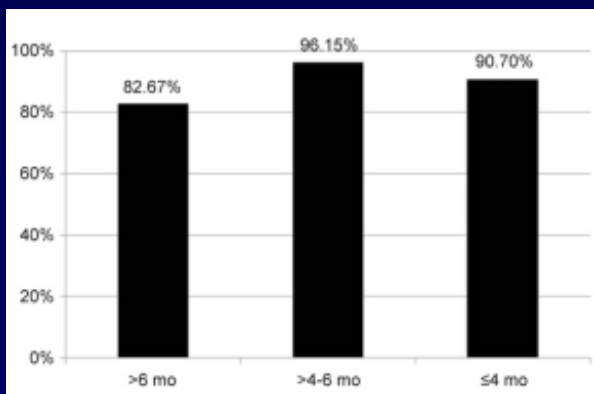
Tc-99m BONE SCAN



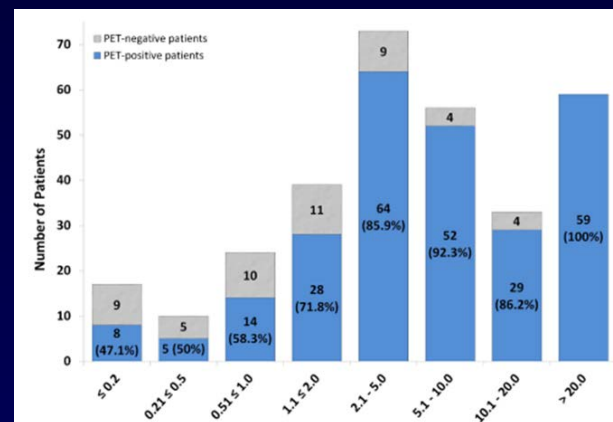
# PSMA PET in biochemical recurrence: Pt positivity rates in relation to PSA levels and PSA doubling times



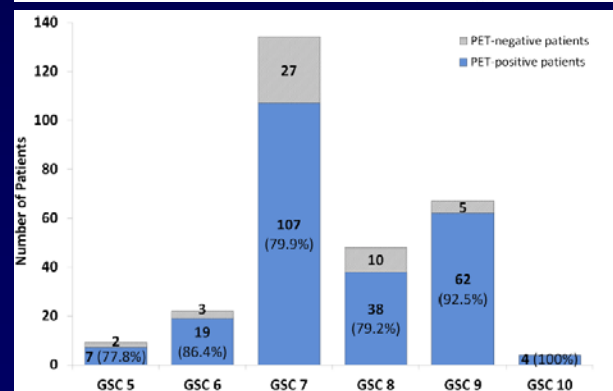
PSA level, n=222



PSA doubling time



PSA level, n=311

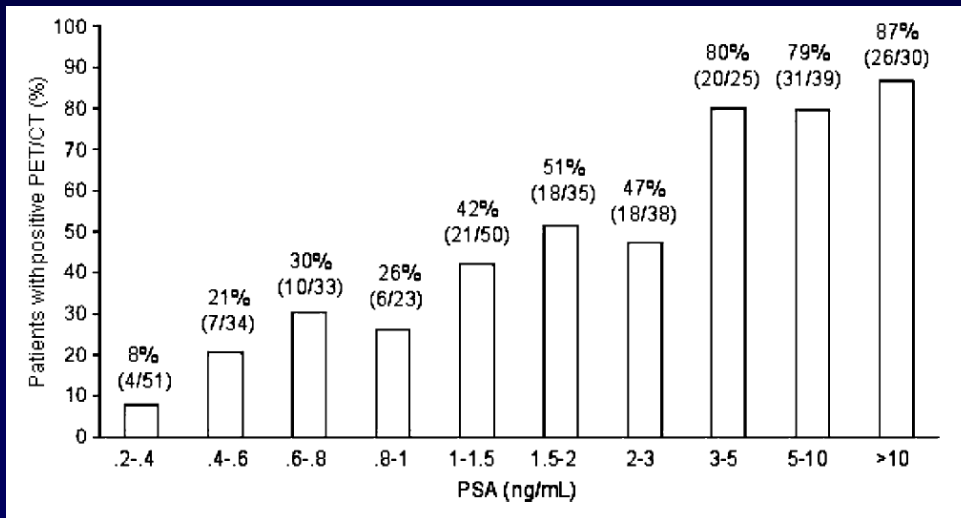


Gleason

Eiber et al JNM (2015)  
Afshar-Oromieh et al EJNMMI (2015)

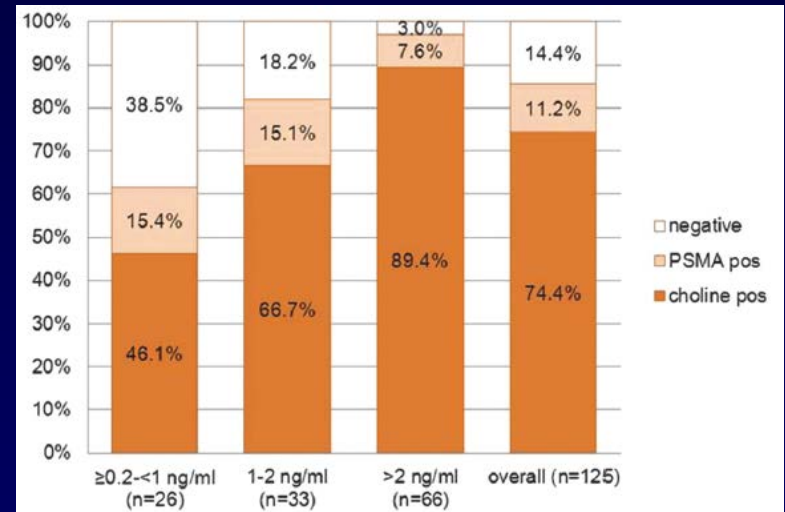
# Choline, and choline vs. PSMA

N= 161 positive scans/358 scans performed, C-11 Choline



Giovacchini et al. Eur J Nucl Med Mol Imag (2010)

N=125  
F-18 Choline vs. PSMA



Bluemel Clin Nuc Med 2016

# So the future is....

- We can now see more disease than we could
- We need to *study* new ways to treat disease we could not otherwise perceive, and ensure that this treatments benefit patients
- Better means to personalize our views of patient's disease
- Better means to predict outcomes

# The Will Roger's Phenomenon

- “When the Okies left Oklahoma and moved to California, they raised the average intelligence level in both states”
- The disease will likely be *upstaged*... this could be very confusing.
  - Some local disease will be staged as metastatic
  - Some Rising PSA patients will be found to be metastatic
  - Susceptibility to the Will Roger's effect
- We take high risk patients out of one category and they become the low risk patients of another, making both seem more favorable.
  - High risk local and Rising PSA patients will become early/favorable metastatic patients

# Studies at MSK

- FDG vs. FDHT for men with castration resistant metastatic disease
- PSMA imaging for men with metastatic disease or who are to undergo surgery (high risk)
- C-11 choline for men with any prostate cancer stage

# Thank you

## Medical oncology

Michael Morris

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Karen Autio

Daniel Danila

Lewis Kampel

Dana Rathkopf

Susan Slovin

Howard Scher

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Steven Larson

Josef Fox

Heiko Schoder

Somali Gavane

Neeta Pandit-Taskar



## Biostatistics

Mithat Gonen

Glenn Heller

## Medical physics

John Humm