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Analytical and Clinical Validation of Automated Bone Scan Index (BSI) as a Biomarker Indicative of Treatment Efficacy

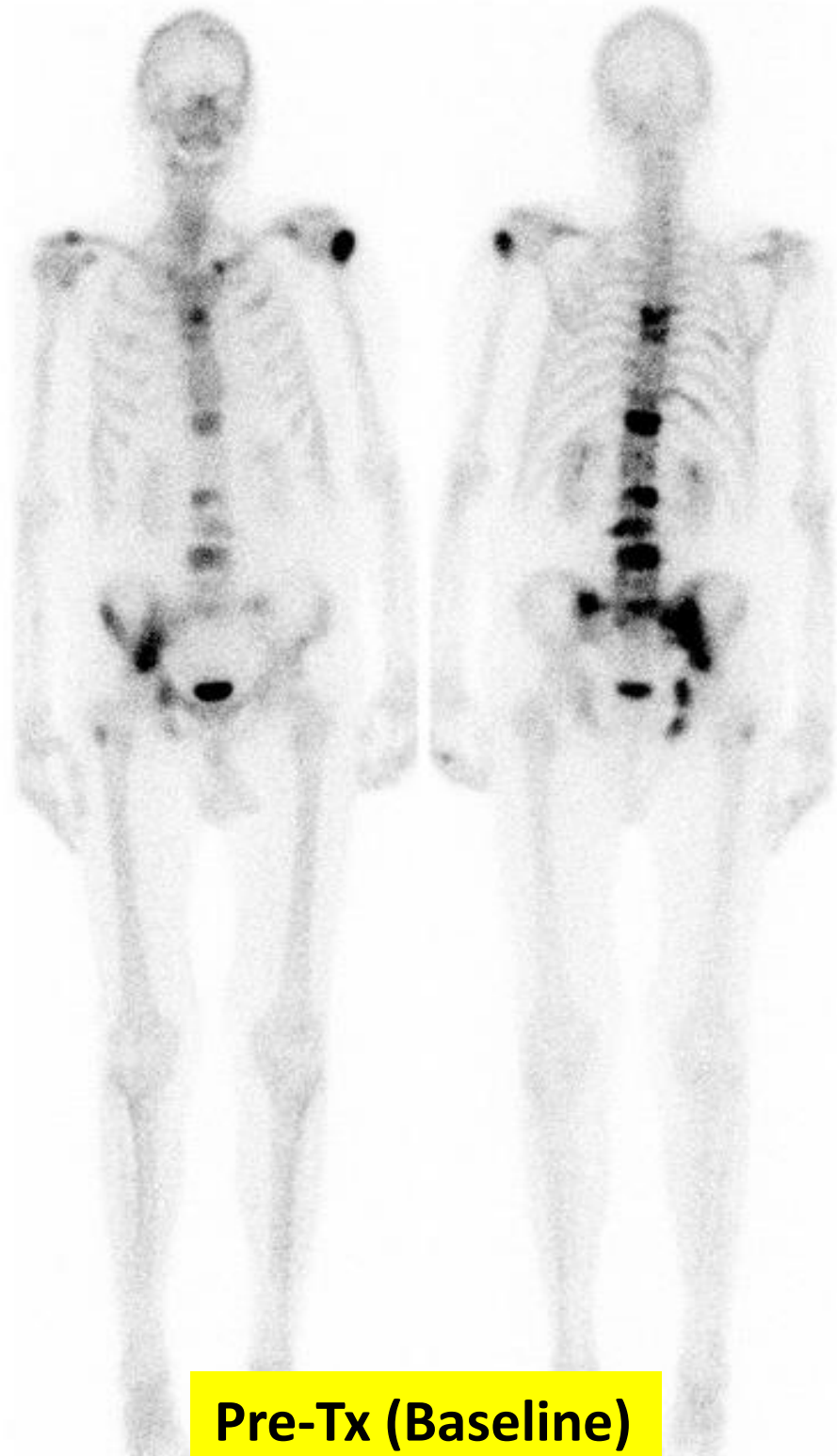
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The issue – Qualitative and Subjective interpretation

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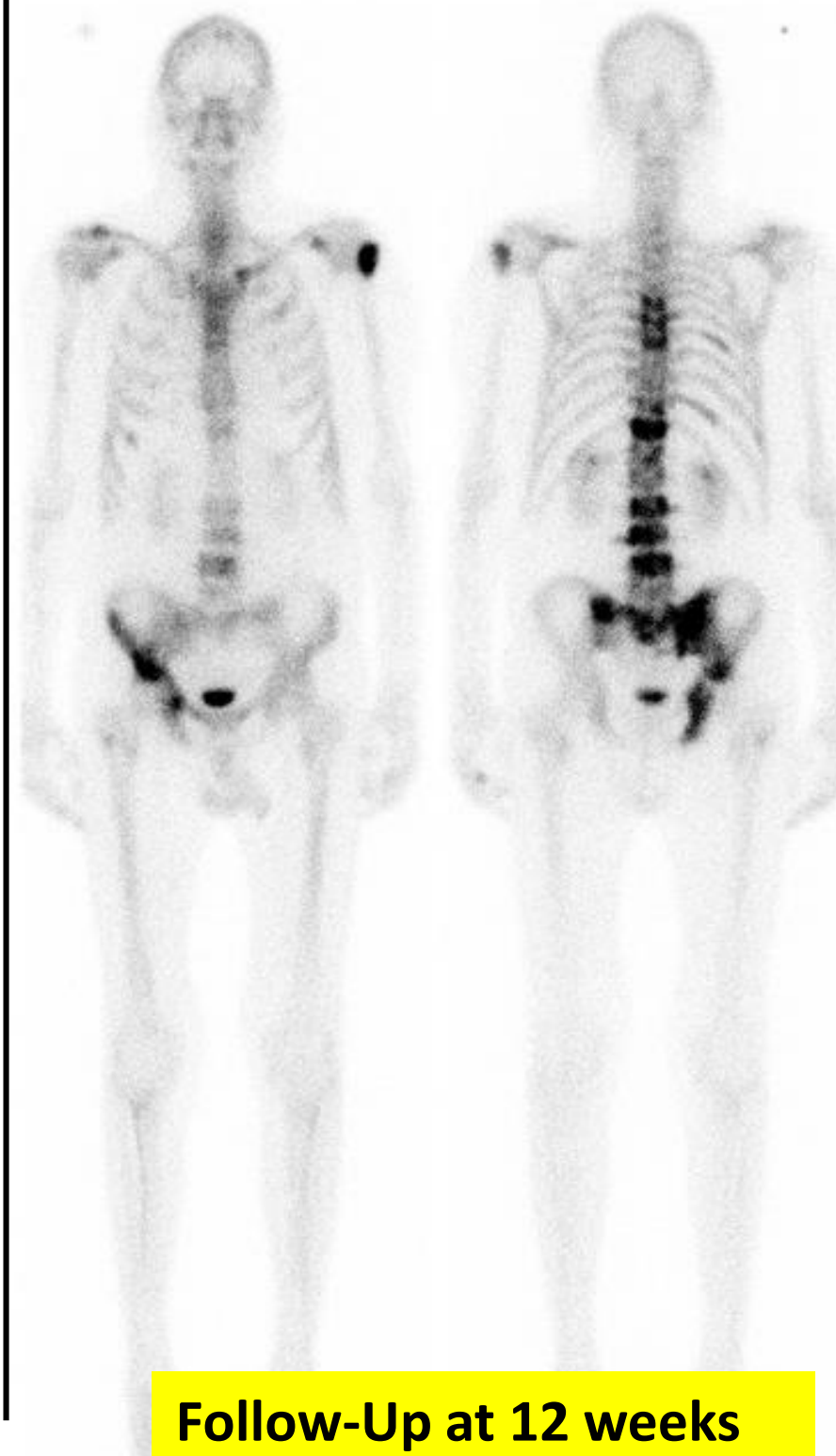
POST



Pre-Tx (Baseline)

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POST



Follow-Up at 12 weeks

Case

metastatic prostate cancer Patient, who received Abiraterone.

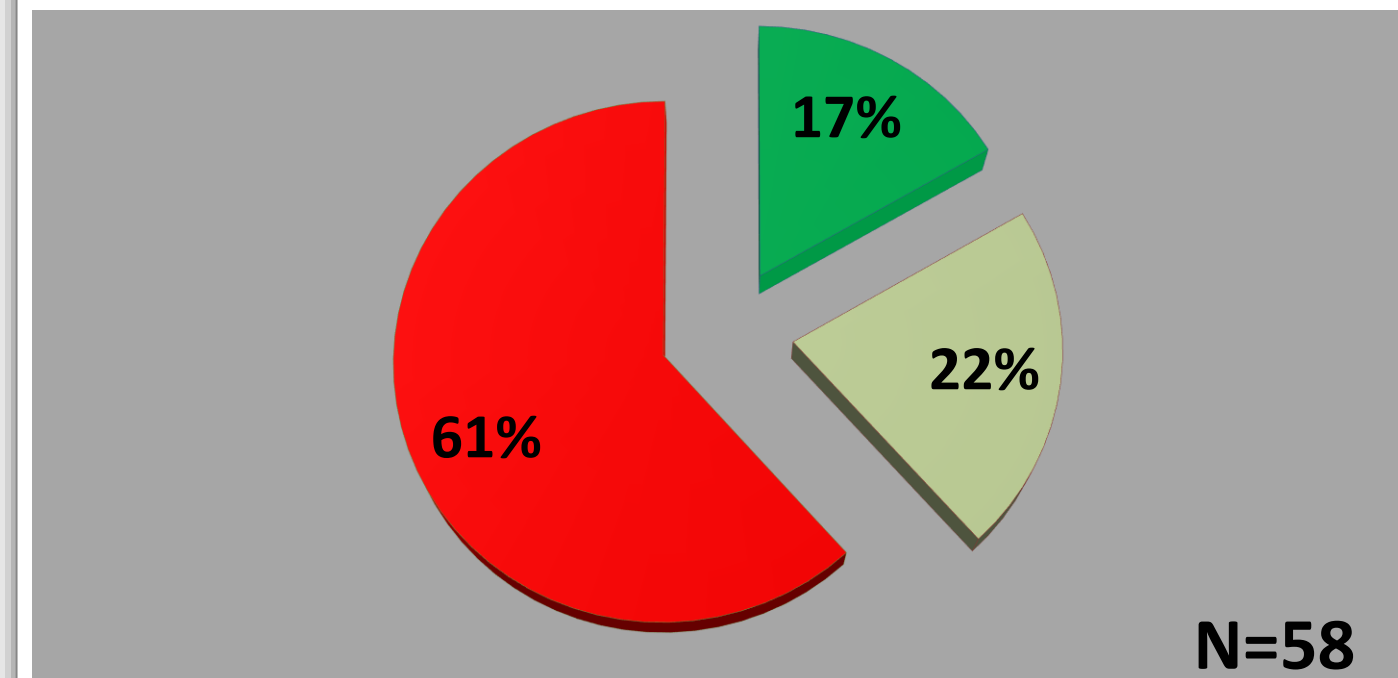
Impression

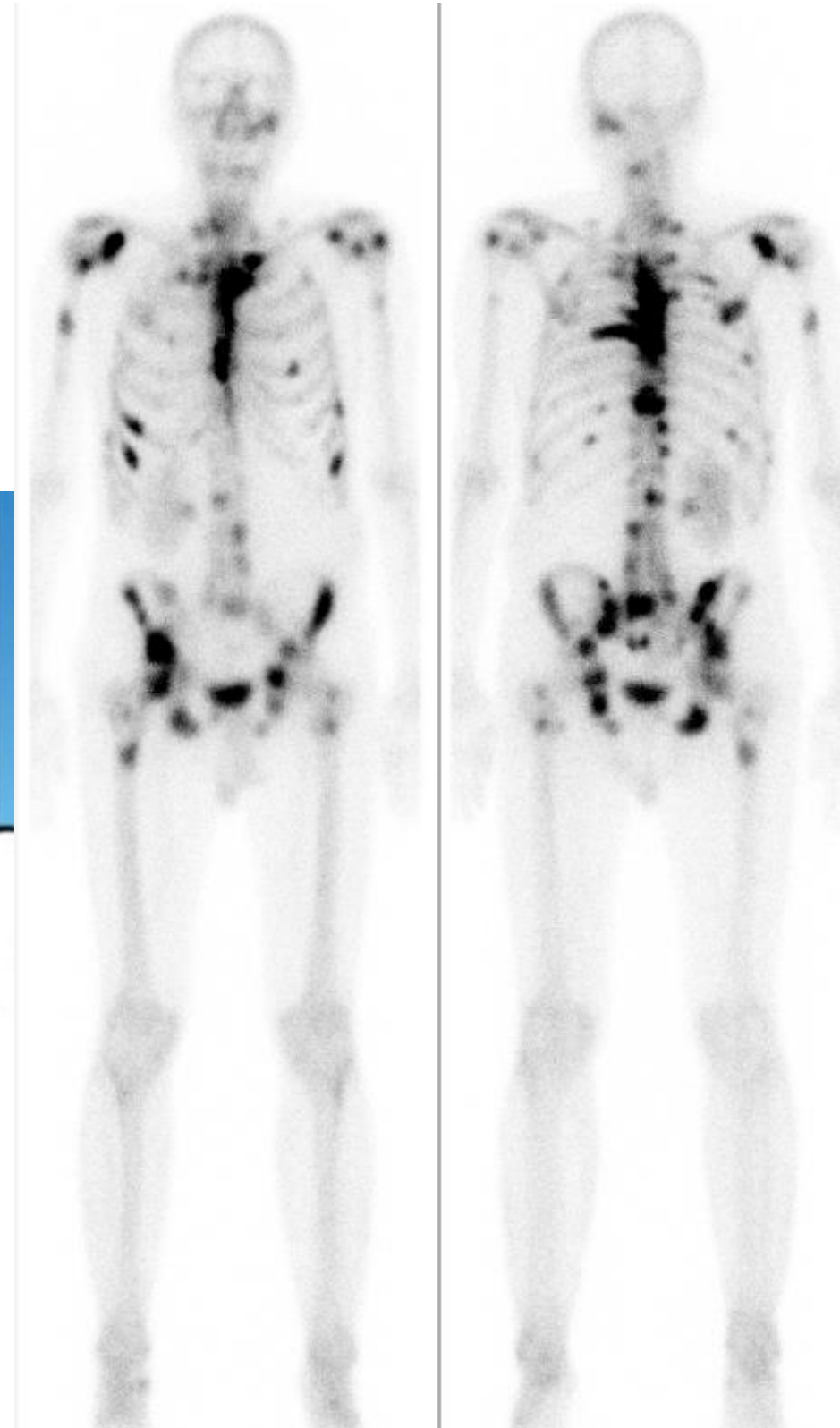
A Improvement

B Stable disease

C Progression

■ regression ■ stable ■ progression





Clinical Trial Recommendations:

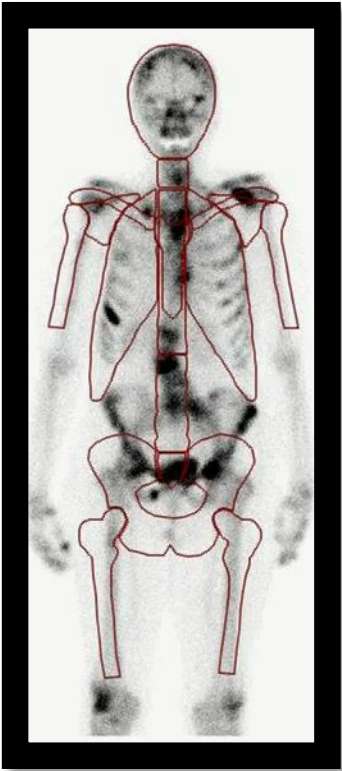
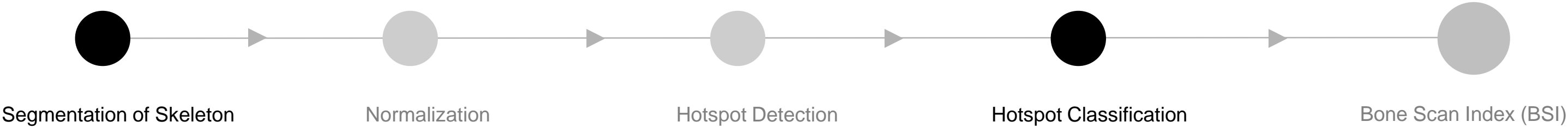
- **PCWG2**

- Does not measure response only confirms progression
- Sclerotic diffused disease
- Complete manual labor intensive

- **FDA – Central Reads**

- Local sites know the patient better
- Complete Manual Process

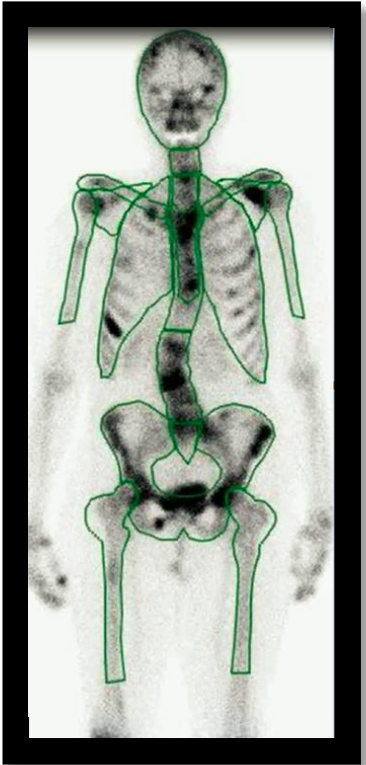
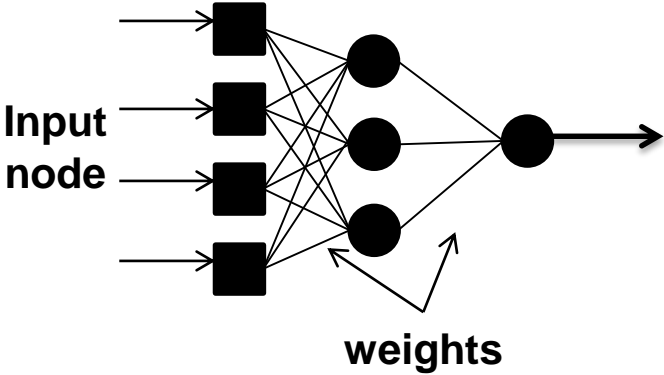
Automated BSI Combines the recommendation of FDA and PCWG2 - Lesion Classification and Lesion Count



Video 1

Segmentation of Skeleton is based on 2D image registration of an Atlas over the patient's Bone Scan

Artificial Neural Network (ANN)



Video 2

Hotspot classification is based on Artificial Neural Network (ANN) which is a complex computer algorithm making non-linear decisions based on given data parameters.

Automated BSI a quantitative biomarker

BSC001 (M) BSC001 6/14/07

FINDINGS:

HISTORY: The patient is a 55 year-old male with history of prostate cancer, status post prostatectomy. Evaluate for osseous metastases.

PROCEDURE: Anterior and posterior whole body images were obtained 3 hours following IV administration of 27.5 mCi of Tc99m-MDP.

FINDINGS: The bone scan shows asymmetric uptake in the superior pubic rami with increased uptake on the left relative to the right. Irregular uptake is seen in the lumbar and cervical spine, the bilateral knees and the bilateral feet likely representing degenerative change. Irregular uptake in the right shoulder may represent degenerative change and/or inflammatory process. Focal uptake in the right ankle is of uncertain etiology and may be traumatic in nature. Correlate with plain radiographs as clinically indicated. Both kidneys are seen. A defect along the inferior surface of the bladder is seen from the midline to the left the midline. Correlation with CT is recommended.

IMPRESSION:

Abnormal Radionuclide Bone Scan

1. Asymmetric uptake in the inferior pubic rami with increased uptake on the left relative to the right is suspicious for osseous metastatic disease. Correlation with CT or MRI is recommended.
2. Degenerative change in the cervical spine, lumbar spine and several joints.
3. Large defect in the inferior aspect of the bladder from the midline to the left the midline. Correlation with CT is recommended as this is the site of prior surgery; a pelvic mass cannot be excluded.

EXINI DIAGNOSTICS

Graph: Index (%) vs. Scan 3: 2.56

06	6/14/07
02	-
04	-
08	0.48
57	0.56
-	-
34	0.78
-	0.15
22	0.58

21/06 6/14/07

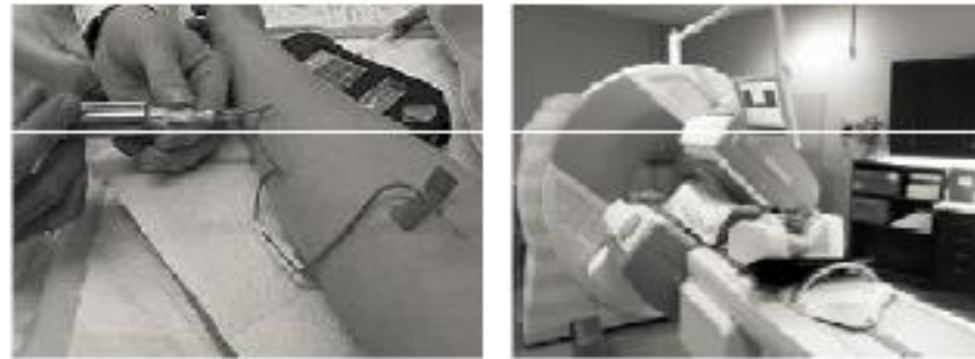
73 / 1.81	1.53 / 1.48
15 / 1.28	1.04 / 1.08

Thorax 0 0 5
Pelvis 1 3 3

- Automatic **lesion detection** and classification
- Automatic tracking of old and **new lesion** and **its location**
- Automatic calculation of **BSI**
- Electronic Reports

1. Analytically validation

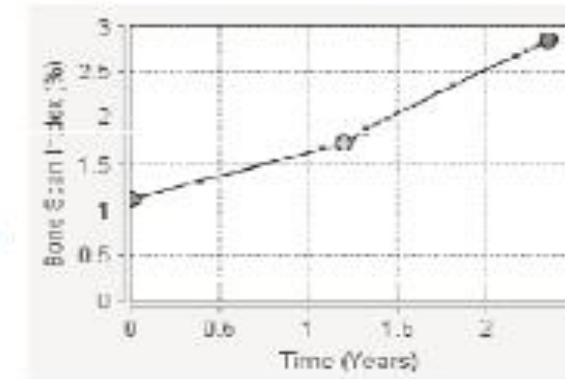
Bone Scan



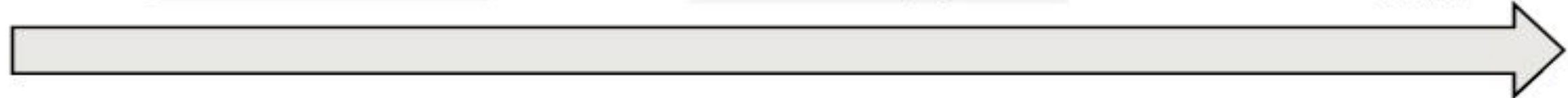
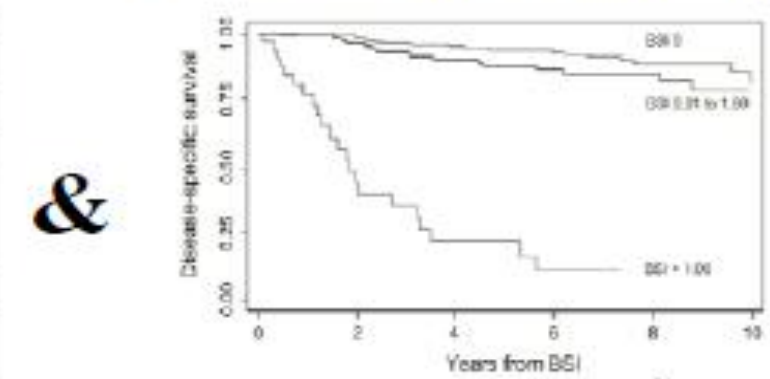
Bone Scan Data



Bone Scan Index (BSI)



BSI W/ Clinical Outcome



- **Reproducibility**
- **Accuracy**
- **Linearity**
- **Specificity**
- **Sensitivity**

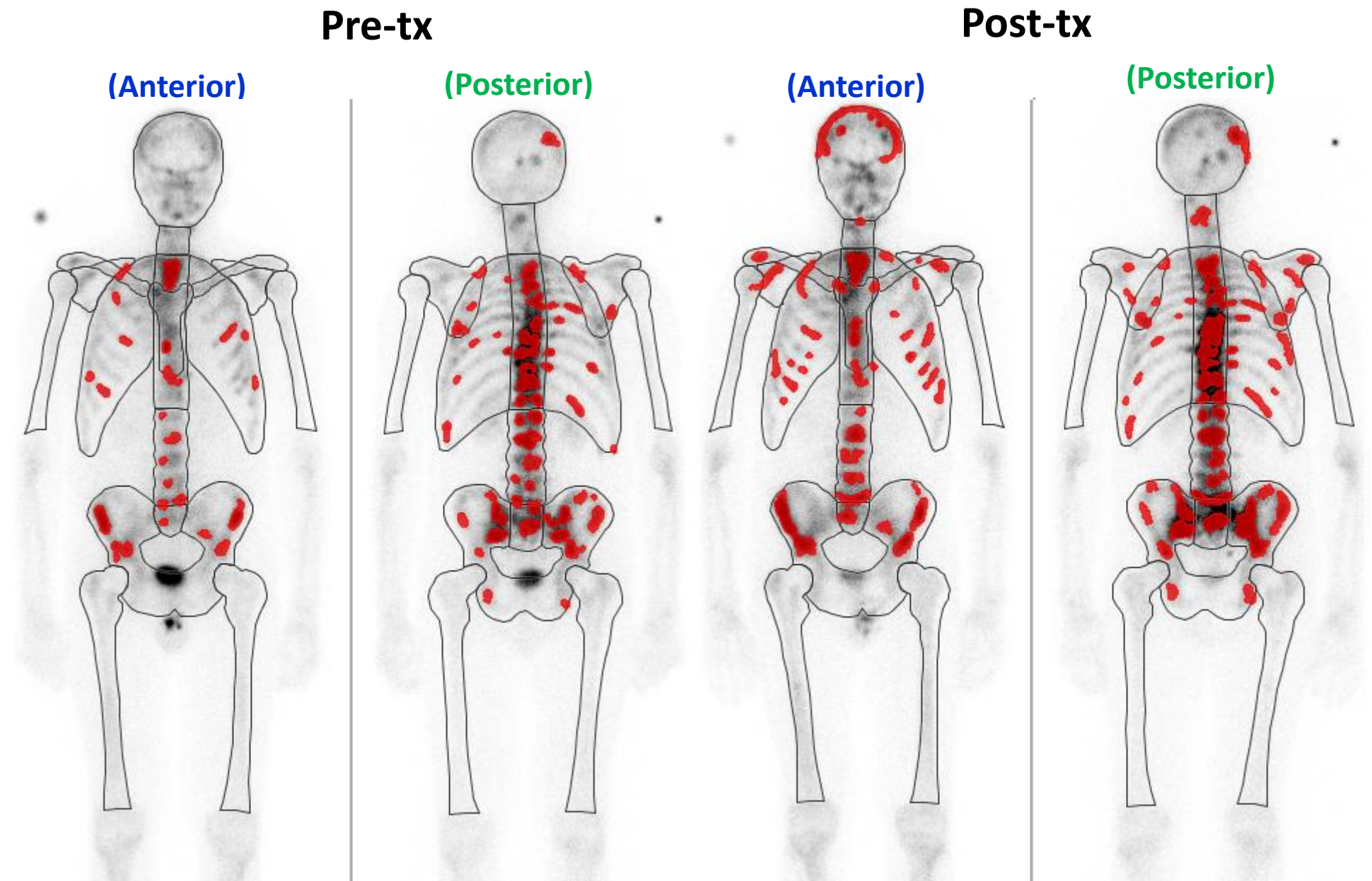
**Biomarker
Qualification**

**Clinical Validation
(Context of Use)**

**Analytical Validation
(Performance Characteristics)**

1. Clinical Validation

**Automated BSI as an analytically
validated AND quantitative
CLINICAL TOOL**



	12/5/13	3/10/14
Bone Scan Index (%)	5.62	9.95
Number of high probability hotspots	59	73

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