

# Histopathologic Features that Influence the Detection of Occult Lymph Node Metastasis Using PET/CT Imaging with Anti-PSMA <sup>89</sup>Zr-Df-IAB2M in Newly Diagnosed High Risk Prostate Cancer Patients.

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## Background

Accurate detection of nodal disease in High Risk Prostate Cancer (HRPC) is critical for proper patient management when undergoing radical prostatectomy (RP). However, conventional imaging (CI) with CT/MRI and bone scan fails to detect metastatic disease in up to 50% of HRPC patients. <sup>111</sup>In-Capromab Pendetide (CP; ProstaScint®), an approved imaging agent for detecting prostate cancer, offers some improvement over CI but still lacks adequate sensitivity and specificity. Thus better tools are needed to improve the detection of nodal disease in patients undergoing RP. IAB2M is a novel anti-PSMA minibody (Mb) based on the humanized J591 antibody that targets the extracellular domain of PSMA. <sup>89</sup>Zr labeled IAB2M is a promising PET agent for the detection of metastatic deposits<sup>1</sup>. A recently completed phase II, single center trial comparing <sup>89</sup>Zr-Df-IAB2M PET to <sup>111</sup>In Capromab Pendetide (CP) SPECT imaging in HRPC patients with negative CI revealed superiority of <sup>89</sup>Zr-Df-IAB2M over CP and CI for detecting LN metastasis using histopathology as the truth standard. However, the biologic and cellular properties of PC deposits influencing the visualization of LN on <sup>89</sup>Zr-Df-IAB2M PET/CT is not completely understood. We report here the histologic properties of LN disease and other measures that may account for <sup>89</sup>Zr-Df-IAB2M uptake on PET/CT scans in 19 enrolled subjects.

## Objectives

- To determine histopathologic features that influence the detection of occult lymph node metastasis using PET/CT imaging with anti-PSMA <sup>89</sup>Zr-Df-IAB2M in newly diagnosed high risk prostate cancer patients

## Material and Methods

- The study protocol and informed consent were approved by a central IRB
- 19 Subjects with histologically confirmed PC scheduled to undergo RP with  $\geq 15\%$  associated risk of extracapsular disease by Briganti nomogram or Gleason score  $\geq 9$  were enrolled
- All subjects underwent sequential <sup>111</sup>In-CP SPECT/CT (5mCi <sup>111</sup>In, whole body scans obtained 3 days p.i.) and <sup>89</sup>Zr-Df-IAB2M (2.5mCi, whole body scans obtained 2 days p.i.) up to 28 days prior to planned RP with standard lymph node dissection (SLND).
- A central laboratory evaluated PSMA expression using IHC and assigned a combined H Score based on staining intensity (0-3) and the % of positive tumor cells present at each staining intensity.

## <sup>89</sup>Zr-IAB2M Imaging Parameters

- <sup>89</sup>Zr-Df-IAB2M (manufactured and shipped from IBA, Somerset, NJ) was administered intravenously at 2.5mCi (+/- 10%) co-infused to yield a 10 mg total protein dose
- Whole Body PET/CT were obtained at 48h ( $\pm 24$ h) on GE Discovery LS, 2D mode, 3-5min/bed position, set for <sup>89</sup>Zr positron ( $t_{1/2} = 78.4$ h, 897 keV, branching fraction = 0.227), iterative reconstruction, 6mm Gaussian, CT 40mA.

## Results

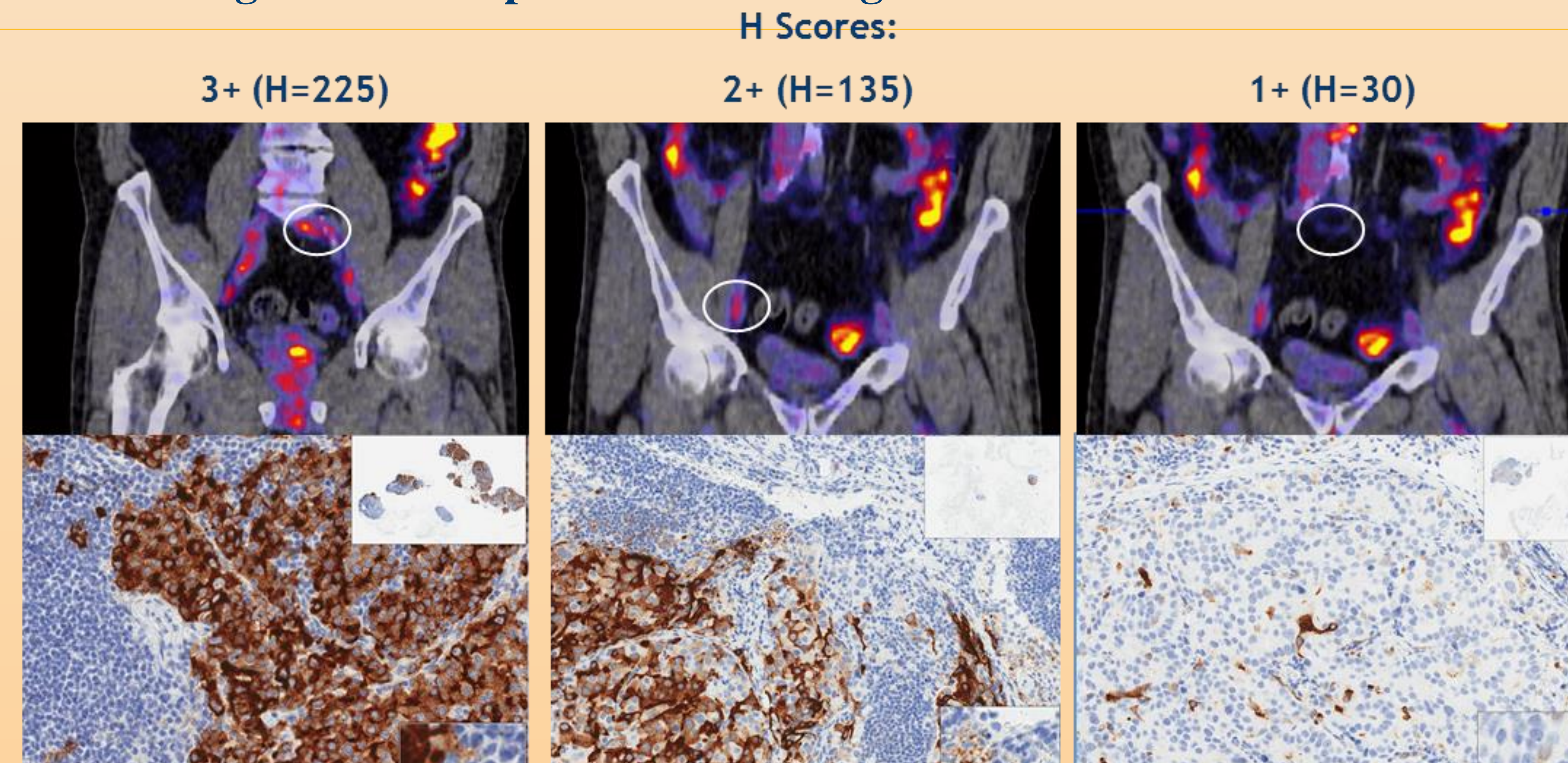
**Table 1: Demographics and Results**

Characteristics	No. (%) or Median (range)
Number of Scanned Subjects (n)	19
Age (y.o.)	65 (51-75)
PSA (ng/ml)	9.8 (3.3-110.5)
Gleason Score	8 (7-9)
Subjects with Regional LN Involvement	53% (10/19)
<sup>89</sup> Zr-Df-IAB2M Positive Scans (n)	50% (5/10)
<sup>111</sup> In-CP Positive Scans (n)	0% (0/10)
Lymph Node Positive Pathology Samples	22% (27/121)

**Table 2: Correlation of PSMA Staining with Lesion Detection by <sup>89</sup>Zr-Df-IAB2M PET**

Parameter	Pathology Confirmed Nodal Disease		P value (Student's t-test)
	<sup>89</sup> Zr-Df-IAB2M Positive PET (mean $\pm$ SD)	<sup>89</sup> Zr-Df-IAB2M Negative PET (mean $\pm$ SD)	
PSA	17.4 ( $\pm 4.7$ )	20.9 ( $\pm 10.4$ )	NS
% Tumor Cellularity	32.0 ( $\pm 27.0$ )	35.1 ( $\pm 33.3$ )	NS
PSMA 3+	43.1 ( $\pm 21.3$ )	39.6 ( $\pm 36.5$ )	NS
PSMA 2+	24.6 ( $\pm 13.3$ )	14.5 ( $\pm 15.1$ )	0.040
PSMA 1+	28.7 ( $\pm 10.4$ )	16.6 ( $\pm 14.8$ )	0.005
PSMA 0+	3.6 ( $\pm 7.5$ )	29.3 ( $\pm 37.0$ )	0.001
H-Score	207.2 ( $\pm 40.0$ )	164.4 ( $\pm 105.2$ )	0.060

**Figure 1: Example PSMA Staining and <sup>89</sup>Zr-Df-IAB2M PET**



Anti PSMA staining of nodal disease and corresponding regions of <sup>89</sup>Zr-Df-IAB2M PET/CT uptake. Note the correlation between <sup>89</sup>Zr-Df-IAB2M signal in nodal stations (white circles) and H-score values. The H-score method is a semi-quantitative approach often used to indicate the extent of IHC staining based upon the following formula: 3 x percentage of strongly staining cells + 2 x percentage of moderately staining cells + percentage of weakly staining cells, giving a range of 0 to 300. H Scores  $\geq 200$  (3+) represent high expression, 100-199 (2+) moderate expression, 1-99 (1+) low expression and 0 (0+) no expression of PSMA.

## Conclusions

- As expected, the lack of PSMA staining cells (PSMA 0+) was significantly higher in scan negative than in scan positive nodal stations
- PSMA 2+ and PSMA 1+ containing lesions are significantly higher for scan positive than for scan negative nodal stations
- H scores tended to be higher in scan positive than in scan negative nodal stations approaching statistical significance
- Neither tumor cellularity nor subject PSA levels contributed to scan positive or negative nodal stations
- Additional factors such lesion size, probe penetration and/or vascularity may contribute to PSMA lesion detection
- <sup>89</sup>Zr-Df-IAB2M remains a promising imaging agent for the detection of occult PSMA positive nodal disease

## References

Gburek B, Woodruff A, Wyman B, Keppler J, Wu A, Masci P and Korn R. Head-to-Head Comparison of <sup>89</sup>Zr-Df-IAB2M PET/CT to <sup>111</sup>In Capromab Pendetide SPECT/CT Scans in the Detection of Occult Prostate Cancer in Patients Undergoing Radical Prostatectomy (RP) with Negative Conventional Imaging (CI) Studies. *World Mol Imaging Congress 2015; Honolulu, Hawaii*

## Funding

ImaginAb Inc.

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