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Heterogeneous PSMA expression in prostate cancer: reason for negative ⁶⁸Ga-PSMA PET/CT scan? Immunohistochemical validation of 40 surgical specimens

W. Cytawa¹, S. Kircher², A. K. Seitz², S. Weber², P. Hartrampf², T. Bandurski¹, P. Lass¹, W. Polom¹, C. Lapa³, A. K. Buck²; ¹Medical University of Gdansk, Gdansk, POLAND, ²University Hospital Würzburg, Würzburg, GERMANY, ³University of Augsburg, Augsburg, GERMANY.

Aim/Introduction: The aim of this study was to immunohistochemically validate the primary tumor PSMA expression in prostate cancer (PCa) patients imaged with ⁶⁸Ga-PSMA PET/CT prior to surgery, with special consideration to PET negative cases. Materials and Methods: The study included 40 men with newly diagnosed, treatment-naïve PCa who were imaged with ⁶⁸Ga-PSMA I&T PET/CT before radical prostatectomy. All the primary tumors were routinely stained with H&E for diagnosis, with immunohistochemical validation of PSMA expression of the specimens, expressed as immunoreactive score (IRS) classification. Imaging findings were correlated with histopathologic data. Results: 83% (33/40) of patients presented focal uptake of ⁶⁸Ga-PSMA I&T in the primary tumor in at least one prostate lobe. Among PSMA PET positive patients one third had lymph node metastases (LNMs) detected in post-operative histopathology, while in PET negative patients only 1 out of 7 suffered from regional LN involvement; PSMA-avid distant lesions, predominantly in bones, were observed in 15% and 0% of patients, respectively. The median IRS classification of PSMA expression in tumor tissue was 2 (range 1-3) both in PSMA positive and negative prostate lobes, with significantly different interguartile range: 2-3 vs. 2-2, respectively (p=0.03). The median volume of PSMA-PET positive tumors was 6.0 ml (0.2-32.9) as compared to 1.6 ml (0.3-24.4) of PET negative tumors (p<0.001). Conclusion: Heterogeneity of PSMA expression justifies the presence or absence of focal uptake in PSMA PET imaging only to a

certain extent, other factors, including tumor volume, also influence this. Focal accumulation in the primary tumor may correlate positively with aggressiveness of PCa, harboring higher risk of regional lymph node involvement and distant metastatic spread. **References:** None