In prostate cancer (PC) patients, the differentiation between lung metastases and lesions of different origin, for example, primary lung cancer, is a common clinical question. Herein, we investigated the use of Glu-NH-CO-NH-Lys(Ahx)-HBED-CC ((68)Ga-PSMA-HBED-CC) for this purpose. PC patients ($n = 1,889$) undergoing (68)Ga-PSMA PET/CT or PET/MR scans were evaluated retrospectively for suggestive lung lesions. For up to 5 lesions per patient, location, CT diameter, CT morphology, and SUVmax were determined. The standard for classification was either histopathologic evaluation or, in the case of PC metastases, responsivity to antihormone therapy. A comparison of the different classes was executed by Student $t$ test. Prostate-specific antigen and prostate-specific membrane antigen (PSMA) immunohistochemistry were performed if histologic samples were available; (68)Ga-PSMA autoradiography was performed on an exemplary case of PET-positive lung cancer. Eighty-nine lesions in 45 patients were identified, of which 76 were classified as PC (39 proven, 37 highly probable), 7 as primary lung cancer, and 2 as activated tuberculosis; 4 lesions remained unclear. The mean SUVmax was $4.4 \pm 3.9$ for PC metastases and $5.6 \pm 1.6$.
for primary lung cancer (P = 0.408). Additionally, substantial differences in SUVmax intraindividually were detected. The 2 tuberculous lesions showed an SUVmax of 7.8 and 2.5. Using immunohistochemistry, we could demonstrate PSMA expression in the neovasculature of several PSMA PET-positive lung cancers as well as in tuberculous lesions from our histologic database. Quantitative (SUV) analysis of (68)Ga-PSMA PET was not able to discriminate reliably between pulmonary metastases and primary lung cancer in PC patients. The reason for the unexpectedly high tracer uptake in non-PC lesions is not completely clear. PSMA expression in neovasculature provides a possible explanation for this finding; however, other contributing factors, such as tracer binding to proteins other than PSMA, cannot be excluded at present.

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