Abstract:
The relevance of prostate-specific membrane antigen (PSMA) targeting in the clinical management of prostate cancer (PCa) is continually increasing, entailing the development of PSMA-targeted molecular probes. Recently, a first PSMA-targeted theranostic concept has been successfully implemented by [(68)Ga/(177)Lu]PSMA-I&T.; To further exploit the excellent PSMA-targeting characteristics and in vivo performance of the PSMA-I&T; platform, [(111)In]PSMA-I&T; was evaluated as a complementary probe for radioguided surgery and SPECT imaging. Compared to [(68)Ga/(177)Lu]PSMA-I&T;, [(111)In]PSMA-I&T; showed unchangedly high PSMA-affinity and enhanced internalization into PSMA-expressing LNCaP PCa cells. Biodistribution studies in LNCaP xenograft-bearing mice (1 h p.i.) revealed slightly reduced background accumulation of [(111)In]PSMA-I&T; compared to [(177)Lu]PSMA-I&T; and identical tumor uptake of both compounds, leading to increased tumor/background ratios for [(111)In]PSMA-I&T.; An exemplary patient with metastatic PCa underwent preoperative [(68)Ga]HBED-CC-PSMA PET/CT (1 h p.i.) and [(111)In]PSMA-I&T; SPECT/CT (4 h p.i.), followed by prostatectomy and radioguided extended pelvic lymphadenectomy (24 h p.i.). In [(111)In]PSMA-I&T;
SPECT/CT, the previously identified PCa lesions ([(68)Ga]HBED-CC-PSMA PET/CT) showed high tracer accumulation and were also detectable using planar scintigraphy. The intraoperative use of a hand-held gamma probe allowed detection and resection of all [(111)In]PSMA-I&T-accumulating lesions. The presence of PSMA-positive tumor tissue in the resected specimens was confirmed histopathologically and via [(111)In]PSMA-I&T autoradiography. [(111)In]PSMA-I&T shows efficient PSMA targeting in vitro and in vivo, combined with low background accumulation. In an exemplary PCa patient, [(111)In]PSMA-I&T was successfully applied for preoperative SPECT/CT visualization and radioguided resection of PSMA-positive lesions, hinting towards a high value of [(111)In]PSMA-I&T; as a complementary tool to [(68)Ga/(177)Lu]PSMA-I&T; in the clinical management of prostate cancer.

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