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Titel des Beitrags:
68Ga- and 177Lu-Labeled PSMA I&T: Optimization of a PSMA-Targeted Theranostic Concept and First Proof-of-Concept Human Studies.

Abstract:
On the basis of the high and consistent expression of prostate-specific membrane antigen (PSMA) in metastatic prostate cancer (PC), the goal of this study was the development, preclinical evaluation, and first proof-of-concept investigation of a PSMA inhibitor for imaging and therapy (PSMA I&T) for (68)Ga-based PET and (177)Lu-based endoradiotherapeutic treatment in patients with metastatic and castration-resistant disease. PSMA I&T; was synthesized in a combined solid phase and solution chemistry strategy. The PSMA affinity of (nat)Ga/(nat)Lu-PSMA I&T; was determined in a competitive binding assay using LNCaP cells. Internalization kinetics of (68)Ga- and (177)Lu-PSMA I&T; were investigated using the same cell line, and biodistribution studies were performed in LNCaP tumor-bearing CD-1 nu/nu mice. Initial human PET imaging studies using (68)Ga-PSMA I&T; as well as endoradiotherapeutic treatment of 2 patients with metastatic PC using (177)Lu-PSMA I&T; were performed. PSMA I&T; and its cold gallium and lutetium analog revealed nanomolar affinity toward PSMA. The DOTAGA (1,4,7,10-tetraazacyclododecane-1-(glutamic acid)-4,7,10-triacetic acid) conjugate PSMA I&T; allowed
fast and high-yield labeling with (68)Ga(III) and (177)Lu(III). Uptake of (68)Ga-(177)Lu-PSMA I&T; in LNCaP tumor cells is highly efficient and PSMA-specific, as demonstrated by competition studies both in vitro and in vivo. Tumor targeting and tracer kinetics in vivo were fast, with the highest uptake in tumor xenografts and kidneys (both PSMA-specific). First-in-human (68)Ga-PSMA I&T; PET imaging allowed high-contrast detection of bone lesions, lymph node, and liver metastases. Endoradiotherapy with (177)Lu-PSMA I&T; in 2 patients was found to be effective and safe with no detectable side effects. (68)Ga-PSMA I&T; shows potential for high-contrast PET imaging of metastatic PC, whereas its (177)Lu-labeled counterpart exhibits suitable targeting and retention characteristics for successful endoradiotherapeutic treatment. Prospective studies on larger cohorts of patients are warranted and planned.