

Tc-99m Labeled Small Molecule Inhibitors of Prostate Specific Membrane Antigen (PSMA): New Molecular Imaging Probes to detect Metastatic Prostate Adenocarcinoma (PCa).

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Background: PSMA is a well established target for developing radiopharmaceuticals for imaging and therapy of PCa. We have recently developed novel ^{99m}Tc-labeled small molecule inhibitors of the enzymatic domain of PSMA. Preclinical studies with PSMA positive LNCaP cells and xenografts demonstrate that ^{99m}Tc-MIP-1404 and ^{99m}Tc-MIP-1405 bind to PSMA with high affinity and localize in tumors rapidly. This study reports the first human data in men with metastatic PCa and in healthy male subjects.

Methods: Under an exploratory IND, using a cross-over design, the pharmacokinetics, biodistribution, and tumor uptake of ^{99m}Tc-MIP-1404 and ^{99m}Tc-MIP-1405 were compared in 6 healthy men and 6 men with radiographic evidence of metastatic PCa. Whole body images were obtained at 10 min, 1, 2, 4 and 24 hr. Single photon emission computed tomography (SPECT) was performed between 3-4 hours post injection.

Results: Both agents cleared the blood rapidly with MIP-1404 demonstrating significantly lower urinary activity (7%) compared to MIP-1405 (26%). Both agents showed persistent uptake in the salivary, lacrimal and parotid glands. Uptake in liver and kidney was minimal (<5%). In men with PCa, both agents rapidly localized in bone and lymph node lesions as early as 1 hr post injection. SPECT demonstrated excellent lesion contrast. Good correlation was seen with bone scans, however, more lesions were demonstrated with ^{99m}Tc-MIP-1404 and ^{99m}Tc-MIP-1405. The high contrast images exhibited signal:noise ratios from 3:1 to 28:1 at 4 and 24 hr.

Conclusion: ^{99m}Tc-MIP-1404 and ^{99m}Tc-MIP-1405 identified a greater number of lesions than bone scans and rapidly detected soft tissue PCa lesions including sub-cm lymph nodes. Since ^{99m}Tc-MIP-1404 has minimal activity in the bladder, further work is planned to correlate imaging findings with histopathology in patients with high risk metastatic PCa.