First clinical experience with the bicyclic peptide radiotracer [^{68}Ga]Ga-BCY25286 for PET/CT imaging of MT1-MMP in lung, urothelial and head and neck cancer

Abstract #

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INTRODUCTION

- Membrane type 1 matrix metalloproteinase (MT1-MMP) is overexpressed in various solid tumors and associated with poor prognosis. Despite its established role in tumor progression and its potential as a theranostic target [1], clinical translation of MT1-MMP-targeted radiopharmaceuticals has not been previously reported. This study presents the first clinical experience with [^{68}Ga]Ga-BCY25286, a bicyclic peptide-based PET radiotracer, for imaging of MT1-MMP expression in patients with lung, urothelial, and head and neck cancer.

METHODS

- Seven patients (lung cancer: n=3; urothelial carcinoma: n=3, head and neck CUP: n=1) underwent [^{68}Ga]Ga-BCY25286 PET/CT imaging (MT1-PET/CT). Four patients had prior [^{18}F]FDG-PET/CT within a maximum interval of 16 days. MT1-PET/CT scans were performed 15, 30, 45 and 60 min after intravenous injection of [^{68}Ga]Ga-BCY25286 (mean activity: 203 MBq). Standardized uptake value (SUVs) was determined for all lesions and organs of interest (liver, blood pool, kidneys). In selected patients histopathological confirmation and MT1-MMP immunohistochemistry were performed and correlated with imaging findings (ethical approval #25-1019-S1).

RESULTS

- In 6 out of 7 patients, tumors and/or metastatic lesions demonstrated increased [^{68}Ga]Ga-BCY25286 uptake compared to the local background. Mean (± SD) SUVmax values at 60 minutes after injection was 7.4 ± 3.8 g/mL for primary tumors, 4.6 ± 1.7 g/mL for lymph node metastases, and 5.5 ± 2.4 g/mL for organ metastases. Kinetic analysis revealed rapid tracer accumulation in tumors, with optimal tumor-to-background ratios achieved within 60 minutes after injection. Physiological tracer distribution was characterized by persistent vascular activity (SUVmean: 1.9 ± 0.3 g/mL at 60 min), high renal uptake reflecting renal excretion (SUVmean: 9.4 ± 2.0 g/mL) and low hepatic uptake (SUVmean: 1.5 ± 0.2 g/mL). Compared to [^{18}F]FDG-PET/CT, [^{68}Ga]Ga-BCY25286-PET/CT yielded a comparable lesion visualization in two patients, although [^{18}F]FDG-PET/CT showed higher SUVmax (13.9 g/mL vs. 6.7 g/mL). In one patient, lymph nodes that were false-positive on [^{18}F]FDG-PET/CT exhibited markedly lower SUVmax on [^{68}Ga]Ga-BCY25286-PET/CT (8.4 ± 1.9 g/mL vs. 3.2 ± 0.3 g/mL). In one patient with histologically confirmed lung cancer, [^{68}Ga]Ga-BCY25286-PET/CT showed no relevant tracer uptake, despite high uptake on [^{18}F]FDG-PET/CT. In cases with histological validation, PET-positive lesions demonstrated membranous and/or stromal MT1-MMP expression.

Figure 1: Comparison of Maximum intensity projections (MIP) of [^{68}Ga]Ga-BCY25286-PET/CT and [^{18}F]FDG-PET/CT.

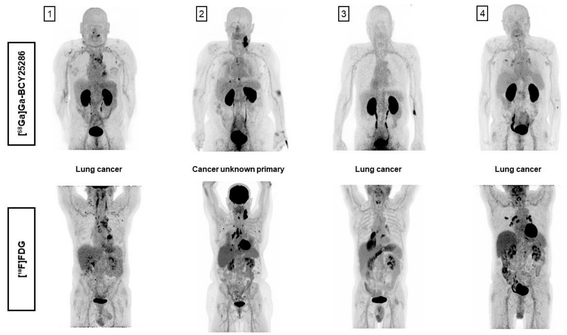


Figure 2: MT-1-MMP-PET/CT imaging in breast and urothelial cancer. Maximum intensity projection of [^{68}Ga]Ga-BCY25286 PET imaging (A) with representative axial PET/CT fusion slices (B-D) and corresponding immunohistochemistry staining (Hematoxylin&Eosin, MT1-MMP-specific) showing the primary breast cancer (B) and bladder cancer (C) with both lymph node and bone metastases in the left sacral bone (D).

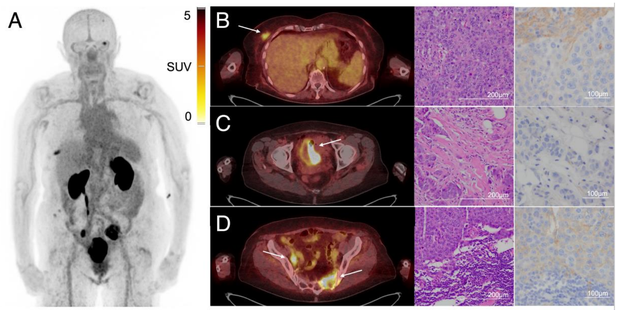


Figure 3: Uptake comparison between [^{68}Ga]Ga-BCY25286 and [^{18}F]FDG. SUVmean in tumor lesions and physiological reference tissues.

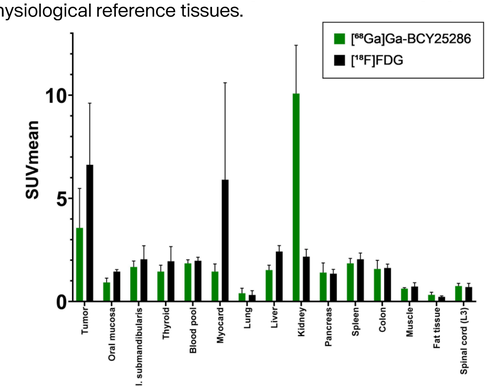
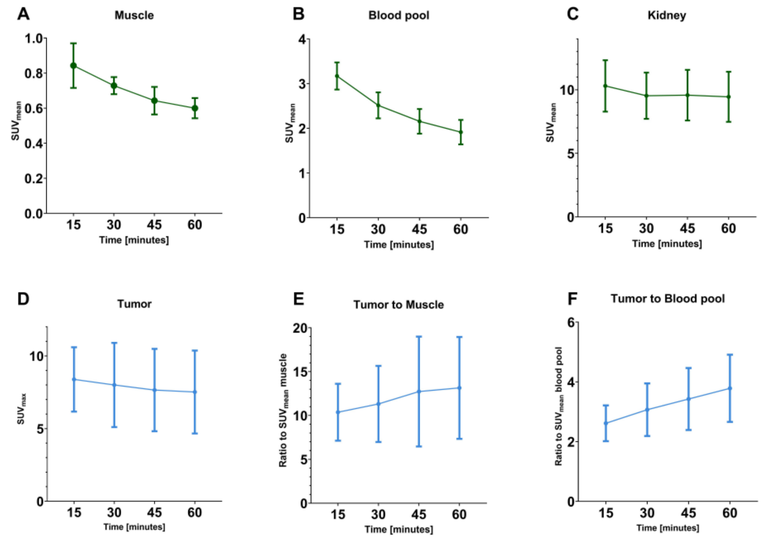


Figure 4: Uptake kinetics in normal tissues and tumor-to-background ratios of [^{68}Ga]Ga-BCY25286.



CONCLUSIONS

- This first clinical series of [^{68}Ga]Ga-BCY25286 imaging in cancer patients demonstrates the feasibility of visualizing MT1-MMP-expressing primary tumors and metastatic lesions. These initial results support further investigation of this radiotracer as a diagnostic tool for tumor characterization in MT1-MMP-positive cancers, potentially facilitating personalized treatment strategies and improved patient management.

REFERENCES

1. Eder et al., Cancer Res. 2019 Feb 15;79(4):841-852.