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Treatment Response Evaluation in Prostate Cancer Using PSMA PET/CT

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Definition of RECIP 1.0

Definition	Criterion
New lesion	
Any new focal uptake of PSMA ligand	
Higher than surrounding background	
With tumor SUV_{max} > blood-pool SUV_{max}	
Not present on baseline scan (tumor SUV_{max} < blood-pool SUV_{max})	
With tumor uptake not attributable to physiologic uptake or pitfalls	
Any new malignant lesion detected on follow-up CT images independent of PSMA ligand uptake	
RECIP 1.0 classification	
RECIP CR	Absence of any PSMA ligand uptake on follow-up PET scan
RECIP PR	≥30% decrease in TTV without appearance of new lesion(s)
RECIP PD	≥20% increase in TTV with appearance of new lesion(s)
RECIP SD	Does not meet the criteria for CR, PR, or PD

Abstract

The demand for PET tracers that target prostate-specific membrane antigen (PSMA) continues to increase. Meeting this demand with approved 68Ga- and 18F-labeled PSMA tracers is challenging outside of major urban centers. This is because the short physical half-life of these radionuclides makes it necessary to produce them near their sites of usage. To overcome this challenge, we propose cyclotron-produced 61Cu for labeling PSMA PET tracers. 61Cu can be produced on a large scale, and its 3.33-h half-life allows shipping over considerably longer distances than possible for 68Ga and 18F. Production of true theranostic twins using 61Cu and the β–-emitter 67Cu is also feasible.

Methods:

PSMA-I&T (DOTAGA-(l-y)fk(sub-KuE)) and its derivative in which the DOTAGA chelator was replaced by NODAGA (NODAGA-(l-y)fk(sub-KuE)), herein reported as DOTAGA-PSMA-I&T and NODAGA-PSMA-I&T, respectively, were labeled with 61Cu and compared with [68Ga]Ga-DOTAGA-PSMA-I&T, [68Ga]Ga-NODAGA-PSMA-I&T, [68Ga]Ga-PSMA-11, and [18F]PSMA-1007. In vitro (lipophilicity, affinity, cellular uptake, and distribution) and in vivo (PET/CT, biodistribution, and stability) studies were performed in LNCaP cells and xenografts. Human dosimetry estimates were calculated for [61Cu]Cu-NODAGA-PSMA-I&T. First-in-human imaging with [61Cu]Cu-NODAGA-PSMA-I&T was performed in a patient with metastatic prostate cancer.

Results:

[61Cu]Cu-DOTAGA-PSMA-I&T and [61Cu]Cu-NODAGA-PSMA-I&T were synthesized with radiochemical purity of more than 97%, at an apparent molar activity of 24 MBq/nmol, without purification after labeling. In vitro, natural Cu (natCu)-DOTAGA-PSMA-I&T and natCu-NODAGA-PSMA-I&T showed high affinity for PSMA (inhibitory concentration of 50%, 11.2 ± 2.3 and 9.3 ± 1.8 nM, respectively), although lower than the reference natGa-PSMA-11 (inhibitory concentration of 50%, 2.4 ± 0.4 nM). Their cellular uptake and distribution were comparable to those of [68Ga]Ga-PSMA-11. In vivo, [61Cu]Cu-NODAGA-PSMA-I&T showed significantly lower uptake in nontargeted tissues than [61Cu]Cu-DOTAGA-PSMA-I&T and higher tumor uptake (14.0 ± 5.0 percentage injected activity per gram of tissue [%IA/g]) than [61Cu]Cu-DOTAGA-PSMA-I&T (6.06 ± 0.25 %IA/g, P = 0.0059), [68Ga]Ga-PSMA-11 (10.2 ± 1.5 %IA/g, P = 0.0972), and [18F]PSMA-1007 (9.70 ± 2.57 %IA/g, P = 0.080) at 1 h after injection. Tumor uptake was also higher for [61Cu]Cu-NODAGA-PSMA-I&T at 4 h after injection (10.7 ± 3.3 %IA/g) than for [61Cu]Cu-DOTAGA-PSMA-I&T (4.88 ± 0.63 %IA/g, P = 0.0014) and [18F]PSMA-1007 (6.28 ± 2.19 %IA/g, P = 0.0145). Tumor-to-nontumor ratios of [61Cu]Cu-NODAGA-PSMA-I&T were superior to those of [61Cu]Cu-DOTAGA-PSMA-I&T and comparable to those of [68Ga]Ga-PSMA-11 and [18F]PSMA-1007 at 1 h after injection and increased significantly between 1 and 4 h after injection in most cases. Human dosimetry estimates for [61Cu]Cu-NODAGA-PSMA-I&T were similar to the ones reported for 18F-PSMA ligands. First-in-human imaging demonstrated multifocal osseous and hepatic metastases.

Conclusion:

[61Cu]Cu-NODAGA-PSMA-I&T is a promising PSMA radiotracer that compares favorably with [68Ga]Ga-PSMA-11 and [18F]PSMA-1007, while allowing delayed imaging.

要旨

- PSMA PETは、診断と治療計画における臨床的ユーティリティの証拠に基づき、複数の前立腺がん（PCa）適応症で承認されている

- しかしながら、治療反応評価におけるPSMA PETの使用については、臨床的有用性を確立するためのデータは限定的である。

- 本稿では、PCaにおける治療反応評価にPSMA PETを使用する最新の知見を概説する。

- 具体的には、放射線療法、アンドロゲン受容体経路阻害薬（ARPI）、および放射性リガンド療法などの主要な治療法に対するPSMA PETの反応性の特徴を記述する。

- さらに、PSMA　PET専用の反応評価基準として提案されたPSMA　PET　Progression（PPP）とResponse Evaluation Criteria in PSMA PET/CT（RECIP 1.0）の特徴とエビデンスについても取り上げる。

- 最後に、今後の標準化および規制的受容のための将来的な方向性について考察する。

セラヨコ・トーク

・RECIPは重要なクライテリアになりそうだね

・SUVmeanはマストですね