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***In vivo* imaging of CD8⁺ T cells in metastatic cancer patients: first clinical experience with simultaneous [⁸⁹Zr]Zr-Df-IAB22M2C PET/MRI**

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Abstract

Aim/Introduction: Despite the spectacular success of immune checkpoint inhibitor therapy (ICT) in patients with metastatic cancer, only a limited proportion of patients benefit from ICT. CD8⁺ cytotoxic T cells are important gatekeepers for the therapeutic response to ICT and are able to recognize MHC class I-dependent tumor antigens and destroy tumor cells. The radiolabeled minibody [⁸⁹Zr]Zr-Df-IAB22M2C has a high affinity for human CD8⁺ T cells and was successfully tested in a phase I study. Here, we aimed to gain the first clinical PET/MRI experience with the noninvasive assessment of the CD8⁺ T-cell distribution in cancer patients by *in vivo* [⁸⁹Zr]Zr-Df-IAB22M2C with a distinct focus of identifying potential signatures of successful ICT. **Material and Methods:** We investigated 8 patients with metastasized cancers undergoing ICT. Radiolabeling of Df-IAB22M2C with Zr-89 was performed according to Good Manufacturing Practice. Multiparametric PET/MRI was acquired 24 h after injection of 74.2±17.9 MBq [⁸⁹Zr]Zr-Df-IAB22M2C. We analyzed [⁸⁹Zr]Zr-Df-IAB22M2C uptake within the metastases and within primary and secondary lymphatic organs. **Results:** [⁸⁹Zr]Zr-Df-IAB22M2C injection was tolerated well without noticeable side effects. The CD8 PET/MRI data acquisitions 24 hours post-administration of [⁸⁹Zr]Zr-Df-IAB22M2C revealed good image quality with a relatively low background signal due to only low unspecific tissue uptake and marginal blood pool retention. Only two metastatic lesions showed markedly increased tracer uptake in our cohort of patients. Furthermore, we observed high interpatient variability in [⁸⁹Zr]Zr-Df-IAB22M2C uptake within the primary and secondary lymphoid organs. Four out of five ICT patients exhibited rather high [⁸⁹Zr]Zr-Df-IAB22M2C uptake in the bone marrow. Two of these four patients as well as two other patients yielded pronounced [⁸⁹Zr]Zr-Df-IAB22M2C uptake within nonmetastatic lymph nodes. Interestingly, cancer progression in ICT patients was associated with a relatively low [⁸⁹Zr]Zr-Df-IAB22M2C uptake in the spleen compared to the liver in 4 out of the 6 patients. Lymph nodes with enhanced [⁸⁹Zr]Zr-Df-IAB22M2C uptake revealed significantly reduced apparent diffusion coefficient (ADC) values in diffusion weighted MRI. **Conclusion:** Our first clinical experiences revealed the feasibility of [⁸⁹Zr]Zr-Df-IAB22M2C PET/MRI in assessing potential immune-related changes in metastases and primary and secondary lymphatic organs. According to our results, we hypothesize that alterations in [⁸⁹Zr]Zr-Df-IAB22M2C uptake in primary and secondary lymphoid organs might be associated with the response to ICT.

Figures

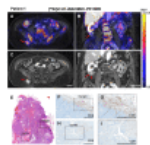


Figure 1 A/C: Axial fused
[⁸⁹...

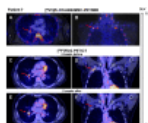


Figure 2 A/B: Axial (A)
and coronal...

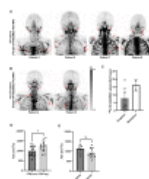


Figure 3 A: In Patients 3,
6,...

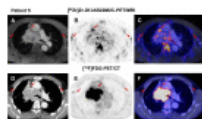


Figure 4 A-C: Patient 5
presented with...

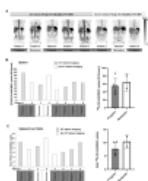


Figure 5 A: High [⁸⁹
Zr]Zr-Df-IAB22M2C...

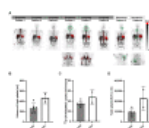


Figure 6 A: The areas
with the...

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