

Tumor Sink Effect: Myth or Reality?

TO THE EDITOR: We thank Prive et al. for their correspondence. As acknowledged in our publication (1), the main limitation of the study is the use of a single-time-point SUV measurement as a surrogate for radiation dose. Differential prostate-specific membrane antigen (PSMA) uptake patterns and tumor-to-background ratios are observed when PSMA PET image acquisition is performed at late time points in comparison to images acquired at 1 h after injection (2–5). Thus, it is clear that images acquired 1 h after injection cannot reflect the biologic effects of ^{177}Lu -PSMA that occur over more than 3 wk (biologic half-life). However, even if not perfectly accurate, PSMA PET imaging performed at 1 h still provides a fair estimate of the patient target expression and of the biodistribution of a PSMA-targeted radiopharmaceutical, and prior studies have reported that pretherapeutic PSMA PET measurements may be correlated with radiation dose to tumor and normal organs from ^{177}Lu -PSMA therapy (6–8).

Regarding the definition of low- and high-volume disease, it is important to note that CHARTED and LATTITUDE criteria were based on conventional imaging (9). Applying these criteria for an analysis of PSMA PET can lead to major discordance in patient stratification, as described previously (10). Therefore, we recommend explicit use of the term *PSMA-VOL* in reference to the whole-body PSMA PET volumetric assessment and not just *low-volume* or *high-volume* metastatic, as follows: very low PSMA-VOL (<25 cm³), low PSMA-VOL (25–188 cm³), moderate PSMA-VOL (189–531 cm³), high PSMA-VOL (532–1,354 cm³), and very high PSMA-VOL ($\geq 1,355$ cm³).

As the authors mention, we agree that patients with low-volume metastatic disease or oligometastases can safely benefit from PSMA-based radionuclide therapy without decreasing the commonly applied dose-activity level of 7.4 GBq per cycle currently in use in the ongoing trial NCT04443062 and as supported by preliminary data (11). On the other hand, our results suggest that the dose-activity level of ^{177}Lu -PSMA could be increased safely in patients with very high PSMA-VOL ($\geq 1,355$ cm³). Nevertheless, these findings warrant further validation by dosimetry studies and safety assessments in prospective clinical trials.

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Thoughts on “Tumor Sink Effect in ^{68}Ga -PSMA-11 PET: Myth or Reality?”

TO THE EDITOR: We read with great interest the recent article by Gafita et al. published in *The Journal of Nuclear Medicine* (1). They observed that patients with a very high tumor load showed a significantly lower SUV in healthy organs on a ^{68}Ga -prostate-specific membrane antigen (PSMA) PET scan, suggesting a tumor sink effect. A comparable observation was also described by Gaertner et al. (2). These authors postulated that a similar effect might occur with PSMA-targeted radioligand therapy. However, dissimilar results regarding the tumor sink effect have also been reported (3).

Although the results of Gafita et al. may support higher treatment activities of ^{177}Lu -PSMA for those with a very high volume of disease ($\geq 1,355$ mL), there were actually no significant differences in the SUV_{mean} of healthy organs between a very low volume of disease (<25 mL) and a high volume (<1,355 mL). These results are in line with what we recently observed in a therapeutic ^{177}Lu -PSMA study on patients with low-volume metastatic hormone-sensitive prostate cancer (4,5). We saw that the dosimetry results based on posttherapeutic SPECT imaging in patients with a maximum of 10 prostate cancer metastases—or a very low volume of metastasis following the definition of Gafita et al.—were comparable to previously reported results on patients with high-volume metastatic prostate cancer (6–8). This result suggests that the sink effect in the setting of low-volume metastatic disease may be of less concern than is commonly anticipated.

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