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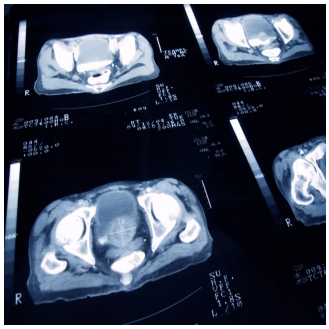
Advancing Prostate Cancer Imaging: The Role of [68Ga]Ga-PSMA-R2



Prostate cancer remains one of the most prevalent malignancies in men, with early and accurate detection playing a crucial role in determining patient outcomes. Conventional imaging techniques such as MRI, CT and bone scans often struggle to identify small or early-stage metastatic lesions, particularly in cases of biochemical recurrence (BCR). Given the limitations of standard imaging methods, there has been a growing interest in positron emission tomography (PET) imaging using prostate-specific membrane antigen (PSMA)-targeted radiotracers. These advanced imaging agents offer enhanced sensitivity in detecting prostate cancer lesions. Among them, [68Ga]Ga-PSMA-R2 has emerged as a promising PET/CT agent for prostate cancer imaging. A phase 1/2 study, PROfind, evaluated its safety, dosimetry and efficacy in identifying prostate cancer lesions in patients with BCR or metastatic prostate cancer (mPC). The study provided valuable insights into the performance of [68Ga]Ga-PSMA-R2 compared with conventional imaging methods.

Safety and Dosimetry of [68Ga]Ga-PSMA-R2

The PROfind study assessed the safety and tolerability of [68Ga]Ga-PSMA-R2 in patients diagnosed with BCR or mPC. The radiotracer was generally well tolerated, with no treatment-emergent adverse events directly linked to its administration. The adverse events reported were mild or moderate, with fatigue and rash being the most common. One participant experienced a serious adverse event, ileus, which was unrelated to the administration of [68Ga]Ga-PSMA-R2. Importantly, no deaths or treatment-related serious adverse events were observed, supporting the favourable safety profile of this radiotracer.

Dosimetry analysis provided critical data regarding radiation exposure. The highest absorbed radiation doses were observed in the urinary bladder and kidneys, reflecting the urinary excretion of the radiotracer. However, a key finding of the study was the low absorbed radiation doses in at-risk organs such as the salivary and lacrimal glands. This is a notable advantage, as previous PSMA-targeted imaging agents have exhibited higher uptake in these glands, leading to undesirable side effects such as xerostomia (dry mouth). The mean effective whole-body radiation dose of [68Ga]Ga-PSMA-R2 was also found to be within acceptable ranges, comparable to other PSMA PET imaging agents. These findings suggest that [68Ga]Ga-PSMA-R2 may provide a safer alternative for prostate cancer imaging, particularly for patients undergoing repeated imaging or those being considered for PSMA-targeted radiopharmaceutical therapy.

Imaging Performance and Clinical Implications

The PROfind study compared [68Ga]Ga-PSMA-R2 PET/CT imaging with conventional imaging methods such as CT, MRI and bone scans to determine its efficacy in identifying prostate cancer lesions. The results demonstrated that PET/CT with [68Ga]Ga-PSMA-R2 was significantly more effective in detecting lesions, particularly in patients with BCR. Conventional imaging failed to identify any lesions in these patients, whereas [68Ga]Ga-PSMA-R2 PET/CT successfully detected multiple lesions. This highlights the superior sensitivity of [68Ga]Ga-PSMA-R2 in identifying local, regional and metastatic prostate cancer lesions.

Optimal imaging times were also evaluated, with data indicating that the best results were obtained between one and two hours post-injection. Imaging at these time points provided a clear distinction between tumour lesions and surrounding tissues, aiding in precise detection and assessment. The ability to detect PSMA-positive lesions with greater accuracy has significant clinical implications, as it can assist in more effective staging, restaging and treatment planning. Improved lesion detection may also enhance patient stratification for targeted therapies, ensuring that only those who will benefit from PSMA-targeted treatment are selected.

Potential for Theranostic Applications

Beyond its role as a diagnostic agent, [68Ga]Ga-PSMA-R2 also shows promise for theranostic applications when combined with therapeutic radionuclides such as 177Lu or 225Ac. The biodistribution data from the study suggest that the radiotracer's relatively low radiation exposure to non-target tissues could make it a viable candidate for PSMA-targeted radiopharmaceutical therapy. Given the increasing interest in PSMA-

directed treatments following the success of therapies such as [177Lu]Lu-PSMA-617, further investigation into the therapeutic potential of [68Ga]Ga-PSMA-R2 is warranted.

The lower radiation uptake in critical organs, such as the salivary and lacrimal glands, could reduce the risk of common side effects associated with PSMA-targeted treatments. Patients undergoing radiopharmaceutical therapy often experience dry mouth and glandular toxicity due to high radiation doses in these areas. The biodistribution profile of [68Ga]Ga-PSMA-R2 suggests that it may offer a safer alternative with reduced adverse effects. If confirmed in further studies, this could make [68Ga]Ga-PSMA-R2 a strong candidate for use in selecting patients for targeted PSMA therapy.

The findings from the PROfind study provide compelling evidence that [68Ga]Ga-PSMA-R2 is a safe and effective PET/CT imaging agent for detecting prostate cancer lesions. With its superior lesion detection capabilities and favourable safety profile, it has the potential to improve diagnostic accuracy in patients with BCR and metastatic disease. The lower absorbed radiation doses in non-target tissues further support its use, particularly for repeated imaging and potential therapeutic applications. Additionally, its suitability for theranostic applications offers promising opportunities for precision medicine in prostate cancer treatment.

Further clinical trials will be essential to establish its role in routine oncology practice and its potential impact on patient outcomes. If subsequent studies confirm its efficacy and safety, [68Ga]Ga-PSMA-R2 could represent a significant advancement in prostate cancer imaging, aiding in earlier detection and more precise treatment planning. Its potential for therapeutic applications also positions it as a promising tool in the evolving landscape of prostate cancer management, where personalised treatment strategies are becoming increasingly important.

Source: **Journal of Nuclear Medicine**

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