

Expanding the Horizons of Theranostics Beyond Oncology - Lessons from PSMA

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Introduction

The term "theranostics" has transcended its status as a mere buzzword in the realm of nuclear medicine, thanks largely to the groundbreaking advancements in prostate-specific membrane antigen (PSMA)-targeted radioligands. These radioligands, which can be labeled with either positron- or γ -emitting isotopes for imaging or with β - or α -emitting isotopes for therapy, have revolutionized prostate cancer management over the past decade. Their success has not only led to the rapid adoption of PSMA-targeted imaging and therapy as a new clinical standard but also inspired exploration into other diseases. This development begs the question: What makes PSMA theranostics so successful, and how can these principles be applied to other areas in nuclear medicine?

The Success of PSMA Theranostics

PSMA theranostics' success hinges on its ability to provide actionable information leading to new or more effective therapies. Unlike traditional oncologic imaging, which often merely shifts patients between prognostic groups without improving outcomes, PSMA PET/CT has guided new therapeutic options. For instance, in metastatic castration-resistant prostate cancer, high PSMA radioligand uptake suggests the viability of PSMA radioligand therapy. Furthermore, PSMA PET's high specificity in detecting lymph node metastases has enabled targeted treatments like stereotactic radiotherapy and salvage lymph node dissection, previously unfeasible due to the limitations of CT and MRI.

Broadening the Scope of Theranostics

The success of PSMA theranostics offers a blueprint for expanding the concept beyond oncology. For example, in neurology, the combination of β -amyloid imaging and antibody therapy illustrates this broader application. The recent FDA approval of the amyloid antibody lecanemab, contingent on amyloid PET scan results, exemplifies theranostics providing actionable information leading to novel therapy.

Similarly, emerging radiopharmaceuticals in immunology and fibrosis, novel disease-modifying therapies in amyloidosis, dopamine transporter imaging in Parkinsonian syndromes, and bacteria-selective radioligands for differentiating inflammation from infections, all represent the expanding scope of theranostics. In each case, the imaging component offers specific and actionable information that guides clinical decision-making for various therapies, including external-beam radiotherapy, surgery, medical therapy, or cellular therapy.

Regulatory and Clinical Implications

This expanded definition of theranostics provides a clear path to regulatory approval as a companion diagnostic, facilitating clinical trials and broader clinical application. For instance, imaging with 18F-fluoroestradiol for estrogen receptor–targeted therapies, or imaging of human epidermal growth factor receptor 2 for selecting appropriate therapies, shows the potential of theranostics beyond traditional radioligand therapies.

Conclusion

Theranostics, as exemplified by the success of PSMA-targeted treatments, offers a promising paradigm shift in nuclear medicine and beyond. Its principles, when applied across various medical disciplines, can lead to more precise, effective, and personalized patient care. By focusing on the actionable information provided by molecular imaging and aligning it with specific therapies, theranostics paves the way for innovative treatments and enhanced patient outcomes, extending its benefits far beyond the confines of oncology.

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