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Foreword

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Total-Body PET/CT in Theranostics: Advancing Molecular Imaging in Precision Oncology

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Abstract

Total-body PET/CT is emerging as a transformative technology in theranostics—the integration of diagnostic imaging with targeted radionuclide therapy. By employing long axial fields-of-view (FOV) PET/CT and increased sensitivity, these scanners are reshaping oncology imaging and patient management. This article introduces theranostics and total-body PET/CT, reviews recent advances, and discusses their clinical impact through real-world experience. The unprecedented sensitivity and speed of total-body imaging enhance lesion detection, therapy planning, and treatment monitoring, while enabling more precise and personalized cancer care. Key challenges, including cost and data management, are addressed alongside future directions in dosimetry and novel radiopharmaceutical development.

" *Whole-body PET/CT technology isn't just about pixels or counts; it's about giving patients a fighting chance where cancer has nowhere to hide*."

Theranostics

Over the past two decades, this "see what you treat" strategy has been firmly established as a pillar of precision oncology (1). Foundational clinical work in neuroendocrine tumors (NETs) demonstrated the feasibility and efficacy of peptide receptor radionuclide therapy (PRRT), and early experience with prostate-specific membrane antigen (PSMA)–directed radioligand therapy broadened the scope of theranostics in prostate cancer (2,3). The advent of PSMA PET imaging provided the crucial diagnostic backbone, enabling reliable target visualization, patient selection, and therapy monitoring (4). Together, these foundational efforts laid the basis for routine adoption of PET-guided therapy selection and monitoring in oncology (5,6).

Building on this foundation, landmark phase 3 trials have confirmed the clinical value of theranostics. In NET, the NETTER-1 trial showed that [177Lu] Lu-DOTA-TATE (177Lu-Dotatate) significantly improved progression-free survival (PFS), leading to regulatory approval, and the recent NETTER-2 trial demonstrated benefit in higher-grade gastroenteropancreatic NETs (7,8). In prostate cancer, the pivotal VISION trial showed that [177Lu]Lu-PSMA-617 (177Lu-PSMA-617) improved overall survival (OS) in patients with advanced castration-resistant disease, while the PSMAfore trial moved PSMA radioligand therapy earlier into the taxane-naive metastatic castration-resistant prostate cancer (mCRPC) setting with radiographic PFS benefit (9,10). Looking ahead, the multicenter WARMTH Act study underscored the promise of 225Ac-PSMA as an alpha-emitter option after progressing on 177Lu-PSMA (11). Across these studies, PET serves as a gatekeeper for target expression and as a tool for serial response assessment, cementing its role in theranostics workflows.

Total-Body PET/CT

The concept of an extended axial FOV PET arose to the need to maximize sensitivity and enabling comprehensive kinetic imaging across distributed diseases. In 2018, Cherry and colleagues reported the first prototype and early human studies, demonstrating that with total-body PET/CT entire body could be scanned in one bed position and it could improve the detection of avid tracer uptake while shortening acquisition time (12). Traditional PET/CT systems cover ~20–30 cm per bed, requiring multiple passes for whole-body coverage. In contrast, total-body PET/CT systems extend to ~1–2 meters, enabling true head-to-toe imaging in a single acquisition. Depending on AFOV length, detector technology, and reconstruction, effective sensitivity gains on the order of ~10–40× have been reported, permitting high-quality scans in minutes (12).

One immediate benefit is enhanced lesion detectability. Long axial FOV PET improves the detection of small lesions and low-contrast lesions compared with conventional scanners (13). The ability to lower administered activity while maintaining non-inferior diagnostic performance has been validated in selected settings, supporting dose reduction and

patient-centric protocols (14). Furthermore, advanced imaging protocols on total-body PET/CT—dynamic acquisition and delayed imaging –improving contrast-to-noise and quantitative accuracy beyond static imaging alone (15).

These advantages are now being demonstrated in prospective clinical settings. Early studies have shown that total-body PET can achieve diagnostic-quality images in a fraction of the time traditionally required, underscoring the potential for dramatically faster workflows and greater patient comfort (16). Simultaneously, total-body PET/CT systems facilitate first-in-human evaluations of novel radiopharmaceuticals by tracking whole-body distribution and pharmacokinetics in unprecedented detail (17). Together, these applications refine established protocols that illustrate and accelerate the development and translation of new theranostic agents—bridging discovery and clinical care with speed, sensitivity, and scalability.

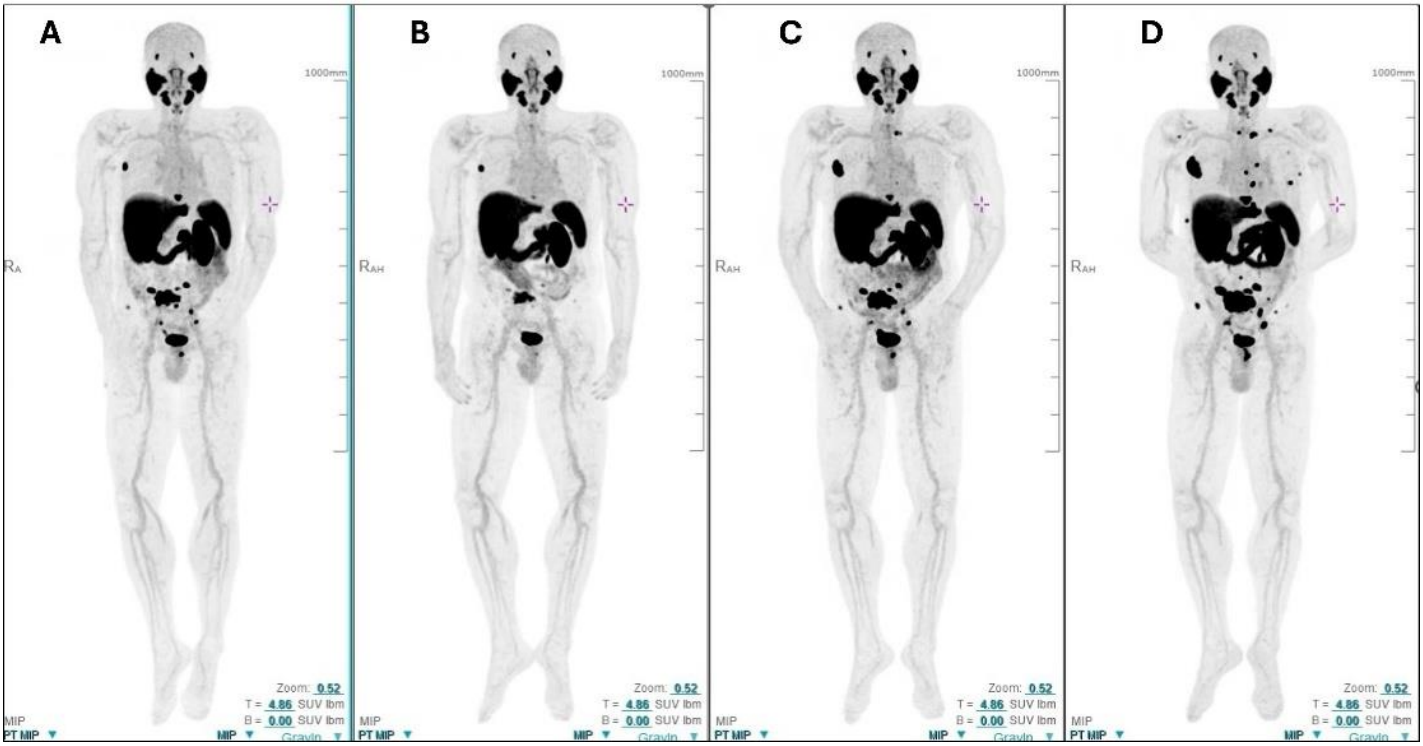

Fig. 1 A 65-year-old man with Gleason 4+5 metastatic prostate cancer previously treated with nine cycles of 177Lu-PSMA radioligand therapy at an outside center. He initially demonstrated a good response, followed by continued disease progression documented on serial ^{68}Ga-PSMA-11 total-body PET/CT (A–D, sequential MIP images).

In theranostics, sensitive detection, serial monitoring, and pharmacokinetics /dosimetry are crucial—these advances are transformative. Total-body PET/CT enhances patient care through earlier detection and individualized monitoring, and also opens pathways for innovation in tracer development, dosimetry, and adaptive therapy strategies.

Scaling Theranostics with Total-Body PET/CT: Impact, Challenges, and Future Potential

Speed, sensitivity, and quantitation

Total-body PET/CT has reshaped theranostic practice by bringing speed, sensitivity, and quantitation into daily practice. Exams that once required 30–40 minutes can often be completed within 5 minutes, mitigating patient burden, motion artifacts, and scheduling bottlenecks, thereby enabling a significantly higher patient throughput.

Higher sensitivity captures subtle disease—tiny nodes, early marrow/bone lesions, or faint visceral deposits—that directly influence eligibility and treatment planning. Total-body dynamic acquisitions add another dimension: pharmacokinetics and dosimetry may be measured in a

single visit, shifting the paradigm from “image and infer” to “measure and personalize”. In routine operations, where full research dosimetry is not yet standard or reimbursed, protocolized quantitative PET and safety labs care are increasingly evaluated in trials and select clinical pathways.

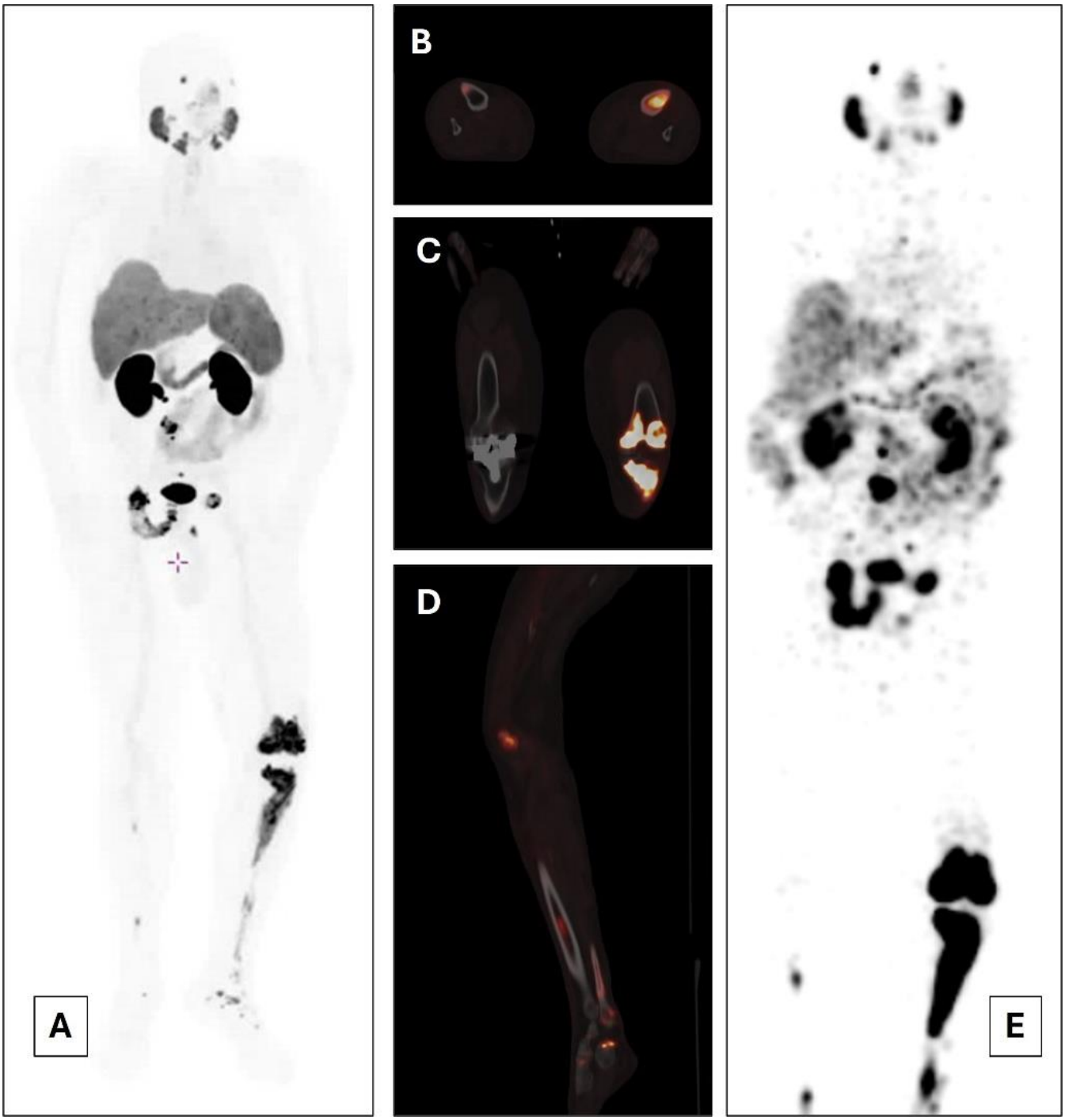

Fig. 2 An 81-year-old man with stage IVB (cTXN0M1b, Gleason 4+4=8, Grade Group 4) prostate adenocarcinoma (pre-treatment PSA 56 ng/mL). He received androgen deprivation therapy followed by apalutamide, pelvic external beam radiation, and 5 cycles of docetaxel chemotherapy (nadir PSA 1.9 ng/mL), complicated by congestive heart failure and peripheral neuropathy. (A–D) Pre-therapy ^{68}Ga-PSMA-11 PET/CT demonstrates extensive PSMA-avid osseous metastases, predominantly in the left femur, tibia, and tarsal bones, as well as additional lesions in the right lower limb and pelvis.

A scalable care model

At BAMF Health, these capabilities are embedded in an end-to-end pathway: standardized referral and triage, on-site GMP radio-pharmacy support, target-specific PET for eligibility, multidisciplinary review, therapy delivery, and post-therapy molecular response assessment. High-throughput imaging supports high-throughput, data-informed care. Robust molecular responders may be de-escalated or paused to limit exposure, and treatment continuation is guided by standardized imaging and clinical criteria. Throughout, standardized acquisition, reconstruction, and calibration and quality assurance (QA) maintain quantitative rigor as volumes grow.

PET/CT plus PET/MR

Co-location with PET/MR adds complementary strengths. PET/CT offers speed, sensitivity, and throughput; PET/MR provides superior soft-tissue contrast, diffusion metrics, and motion-robust sequences. Hybrid strategies include rapid total-body PET/CT for eligibility and quantity followed by targeted PET/MR for problem regions, and PET/MR for organ-specific monitoring when minimizing radiation is desirable. Together, the modalities support precise target confirmation, confident lesion detection, and cleaner longitudinal response curves.

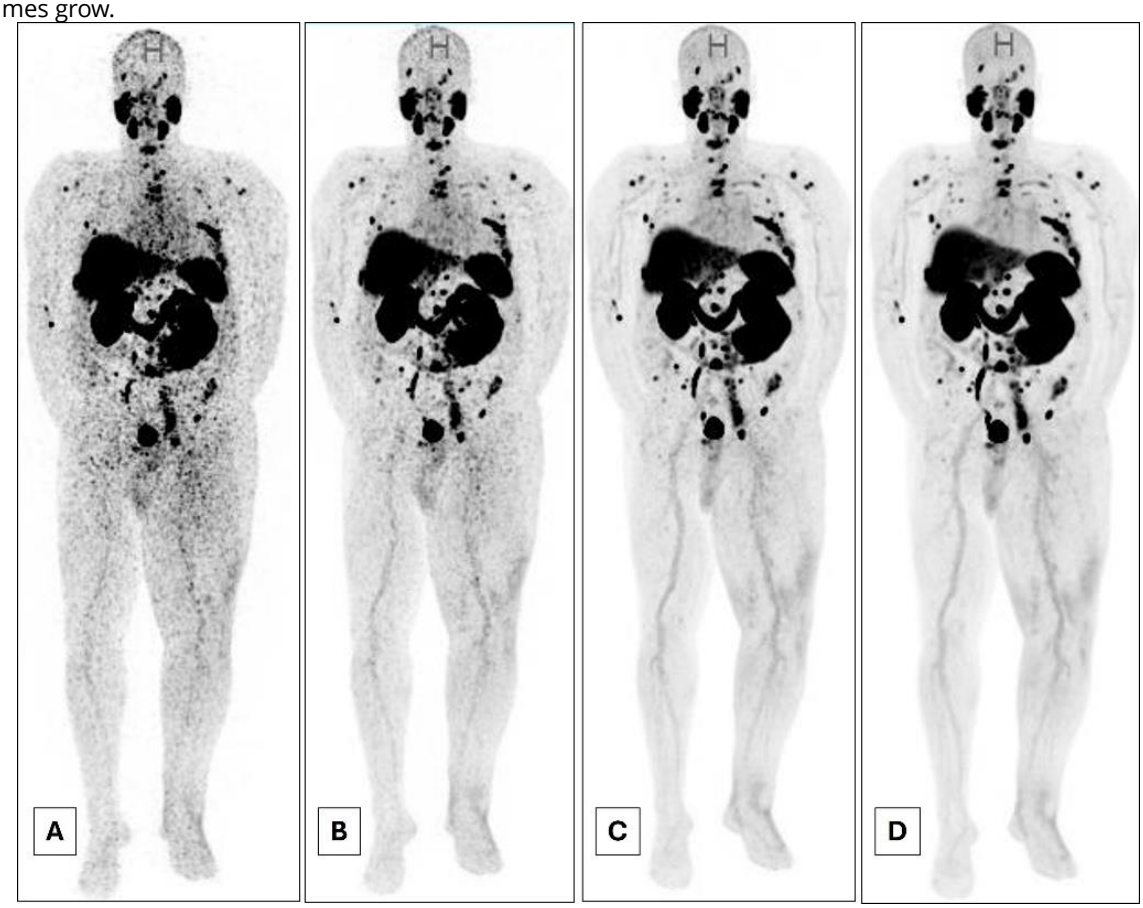

Fig. 3 A patient with Gleason 4+3=7 prostate adenocarcinoma after androgen deprivation therapy, novel androgen-axis therapy, and docetaxel. ^{68}Ga-PSMA-11 PET/CT demonstrates widespread PSMA-positive lymph node and osseous metastases. The patient was deemed eligible for177Lu-PSMA radioligand therapy. (A–D) MIP images with varying acquisition times: (A) 10 seconds, (B) 30 seconds, (C) 2 minutes, (D) 5 minutes. Even the 30-second acquisition clearly delineates the PSMA-positive disease burden.

Refining therapy response

Total-body PET/CT enables more consistent quantification of whole-body tumor burden by combining complete coverage with high sensitivity. With complete body coverage and superior sensitivity, cumulative uptake metrics can be quantified more reliably, enabling consistent tracking of global tumor burden. In NETs, reductions in somatostatin receptor-positive tumor volume (SSTR-TV) have been shown

to align with clinical improvement after PRRT. In prostate cancer, accurate quantification on PSMA PET enables whole-body tumor burden measurement and offers prognostic insights that can help guide decision-making. Beyond static measures, dynamic and longitudinal imaging provides access to biomarkers that may predict treatment efficacy early in the course of therapy. Faster, lower-dose acquisitions also open the door to more frequent monitoring, enabling nimble, evidence-driven adjustments.

Remaining challenges

Capital expenditure and facility build-out limit the access of LAFOV systems. Dynamic acquisitions generate vast data volumes, demanding robust PACS/VNA infrastructure and GPU-enabled analytics. Multicenter harmonization requires phantom experiment, cross-calibration, and locked or standardized reconstructions to preserve SUV fidelity. Workforce readiness—from physicians and physicists to technologists and nursing—must keep pace via standardized training. Supply-chain fragility for isotopes and reimbursement gaps for dosimetry and dynamic studies also constrain scalability. Finally, interpretation requires discipline, as physiological uptake variants are more conspicuous on highly sensitive images.

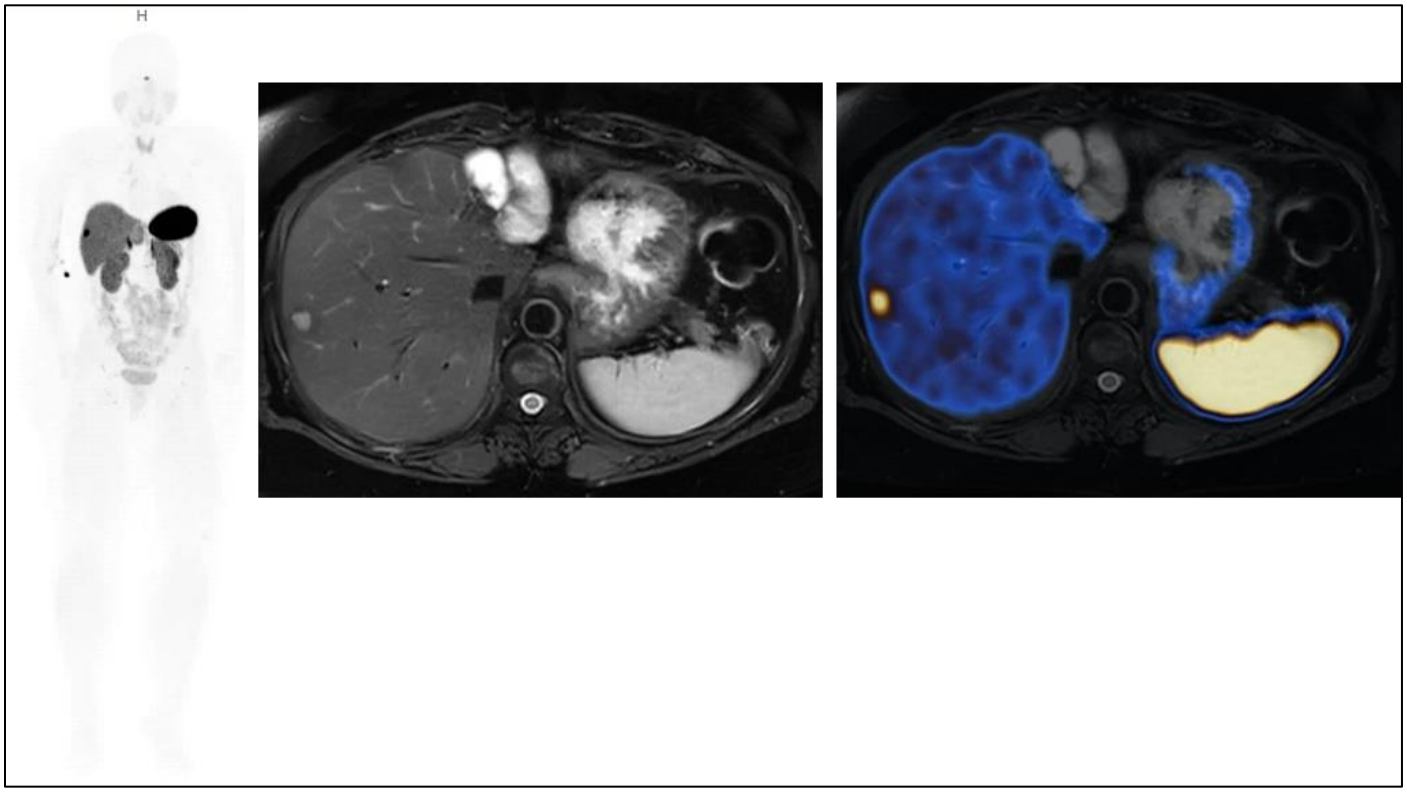

Fig. 4 ^{68}Ga-DOTATATE total-body PET/CT (A, MIP) in a patient with resected, well-differentiated ileal neuroendocrine tumor (NET) revealed a solitary liver lesion in segment VIII. Subsequent PET/MR performed with the same injection confirmed the lesion as a somatostatin receptor–positive metastasis (B, MRI; C, fused PET/MR).

The near future

Looking ahead, several trajectories are within reach. Routine prospective dosimetry with short multi-time-point scans is likely to become standard for PRRT and PSMA radiopharmaceutical therapies, improving dose–response correlations. Pre-therapeutic dosimetry using longer-lived positron emitters (e.g., 64Cu- or 89Zr-labeled analogues/antibodies) allows imaging over extended periods to model tumor and organ kinetics before therapy. This provides a pathway toward true individualized therapy planning in precision oncology.

AI-assisted quantitation could reduce reporting time and

inter-reader variability by automating lesion detection, whole-body tumor burden metrics, and kinetic mapping. Fast acquisitions further support the concept of a "one-stop" therapy day: eligibility PET in the morning, therapy midday, and a short post-therapy verification scan in the afternoon.

Expanding tracer portfolios, including FAP, GRPR, CXCR4, HER2, and antibody-based agents—can be evaluated rapidly in early-phase studies, accelerating drug development and translation. Finally, networked theranostics built on harmonized imaging standards will allow patients to be imaged and treated closer to home. In this vision, high-sensitivity long axial FOV PET/CT systems serve as the enabling technology, linking advanced quantitation with scalable, patient-centered care.

Why does this matter?

For patients, these advances translate into shorter and less stressful scans, earlier detection of actionable disease, and faster therapy adjustments when treatments underperform. For health systems, throughput and quantitation expand capacity while raising the bar for precision. And for innovators, total-body PET/CT provides the measurement engine that turns theranostics from promise into reproducible, scalable care—the very model BAMF is designed to deliver.

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