

Nuclear Cardiology: From Consolidation to Integration

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Introduction

Over the past decade, nuclear cardiology has undergone a profound transformation.^{1–5} What was once primarily a diagnostic tool focused on ischemia detection has evolved into a comprehensive platform for physiological understanding, risk stratification, and precision cardiovascular care.^{2,6–12} In this context, the field has shifted from simply identifying disease to elucidating its underlying mechanisms, echoing Marie Curie's insight that “nothing in life is to be feared, it is only to be understood.”

The year 2025 did not stand out for isolated disruptive discoveries, but rather for something equally important: clinical consolidation.^{1,2,13} During this period, previously emerging concepts matured into actionable clinical paradigms, allowing the field to move from promise to practice.^{1,13}

Positron emission tomography (PET) has become a central modality for the quantitative assessment of myocardial blood flow, microvascular dysfunction, and integrated myocardial pathophysiology.^{1,7,10,12–14} Advances in radiotracers, scanner technology, and analytic frameworks have moved from proof-of-concept to structured clinical implementation, reinforcing the role of PET in contemporary cardiovascular imaging.^{1,2,13}

In this context, 2025 represented a pivotal transition year for nuclear cardiology, defined by maturation, integration, and growing clinical relevance. This editorial reflects on key areas where consolidated evidence is available, highlights emerging applications that have gained momentum, and outlines ongoing and future directions, with PET positioned at the core of precision cardiovascular imaging.

From Ischemia Detection to Physiologic Phenotyping: Consolidation in 2025

One of the most defining developments in nuclear cardiology over recent years has been the shift from ischemia detection toward physiological phenotyping,

a transition that reshaped clinical practice.^{1,14} Central to this evolution is the recognition of coronary microvascular dysfunction (CMD) as a clinically meaningful phenotype rather than an incidental or secondary finding.¹⁵ CMD is now increasingly understood as a key biological substrate underlying persistent symptoms, cardiometabolic disease, diffuse coronary atherosclerosis, and heart failure syndromes, even in the absence of obstructive epicardial disease.^{1,7,10,13}

In this context, PET has emerged as the reference standard for the quantitative assessment of myocardial blood flow and myocardial flow reserve.¹³ The ability to noninvasively quantify coronary physiology across the entire myocardium has reshaped clinical evaluation, enabling more accurate diagnosis, risk stratification, and therapeutic decision-making in patients with complex or diffuse disease patterns. By 2025, these quantitative PET-derived metrics have moved beyond research applications and are increasingly incorporated into routine clinical workflows at experienced centers.¹

The clinical maturation of flurpiridaz further exemplifies this paradigm shift.^{3,14,16,17} Once viewed primarily as a promising investigational tracer, flurpiridaz entered a phase of structured clinical implementation, supported by its favorable imaging characteristics, logistical advantages, and robust physiologic performance.^{14,16} Its potential to expand access to PET myocardial perfusion imaging (i.e., improved image quality, flexible stress protocols, and streamlined workflows) represents a critical step toward broader adoption of physiologic imaging.^{3,16} Together, these developments underscore a fundamental change in nuclear cardiology.

Expansion Beyond Obstructive Coronary Disease

In 2025, nuclear cardiology continued to expand beyond the traditional framework of obstructive coronary artery disease, reflecting a broader understanding of cardiovascular disease as a complex, dynamic biological system.^{4,6} Cardiovascular pathology is recognized as the result of interacting metabolic, inflammatory, neurohormonal, and fibrotic processes that evolve over time,^{10,11} with growing recognition of the tight interplay between myocardial metabolism and immune activation as fundamental drivers of disease expression.¹⁸ No single metric can fully capture this complexity, helping explain the wide variability in clinical presentation, therapeutic response, and outcomes observed across patients.

Keywords

Positron Emission Tomography; Inflammation; Precision Medicine.

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Within this context, molecular imaging has assumed a strategic role. Its value lies not only in detecting disease, but in visualizing and quantifying underlying biological processes *in vivo*; many of which represent potentially modifiable therapeutic targets. By interrogating inflammation, fibroblast activation, autonomic dysfunction, and microvascular physiology, nuclear cardiology provides a window into disease mechanisms that extend beyond luminal anatomy,^{5,6} including metabolic stress–driven immune activation.¹⁹

Several clinical domains illustrate this expansion. In heart failure, PET imaging has enabled more refined phenotyping through the assessment of CMD, providing insights into myocardial remodeling and functional decline. In conduction diseases, particularly left bundle branch block, nuclear imaging has moved beyond descriptive findings to characterize mechanical dyssynchrony, regional perfusion patterns, and their association with adverse remodeling.⁸ In cardio-oncology, cardiac FDG PET has emerged as a powerful tool for probing early metabolic and inflammatory myocardial responses to cancer therapy,^{9,20} capturing biologic vulnerability that may precede, and is not reliably mirrored by, early functional deterioration.²¹ These metabolic changes do not consistently correlate with early reductions in left ventricular ejection fraction or global longitudinal strain, indicating that FDG PET captures a distinct, biologically meaningful signal rather than serving as a surrogate for functional impairment alone.⁹

Collectively, these applications reflect a broader conceptual shift. Nuclear cardiology is transitioning from a predominantly diagnostic and prognostic discipline toward a driver of mechanism-based therapy. Imaging is increasingly used to guide patient selection, define optimal intervention windows, and monitor biological response to treatment.^{6,22} In this evolving paradigm, the true value of nuclear cardiology lies in its ability to quantify biological processes that can be acted upon for the benefit of the patient.²

Technology and Tracers: From Innovation to Clinical Implementation

Advances in technology and radiotracers in nuclear cardiology were defined less by novelty and more by clinical readiness in 2025.^{2,7,14,16,22,23} Improvements in the reproducibility of quantitative metrics, shorter workflows, and tighter integration between hardware and software platforms marked a transition from proof-of-concept to structured clinical implementation. Together, these developments strengthened confidence in quantitative PET and facilitated its broader adoption in routine clinical practice.^{5,16}

Cardiac amyloidosis exemplifies this maturation. While bone-avid SPECT tracers remain foundational for diagnosis, recent advances extend beyond traditional approaches.² PET tracers, such as 124I-*evuzamitide* (AT-01) and emerging SPECT agents, including 99mTc-p5+14, highlight the potential for more specific

tissue characterization.^{22,23} These tools may enhance differentiation between light chain and transthyretin amyloidosis, support earlier disease detection, and improve integration of diagnosis, prognostication, and therapeutic decision-making.

Physiologic assessment has also advanced through refined flow quantification.^{12,17} PET remains the reference standard for quantitative assessment of myocardial blood flow,¹³ enabling evaluation of transmural and subendocardial perfusion and uncovering regional vulnerability not captured by global metrics alone.¹² Parallel validation studies using cadmium zinc telluride SPECT cameras demonstrate strong correlation with PET, signaling a future in which precision physiology may become accessible beyond specialized centers.²⁴

Last, artificial intelligence and large-scale datasets are reshaping image interpretation and risk assessment.²⁵ Automated quantification, integration with biobanks, and sex- and age-specific reference values are improving robustness and reproducibility.⁷ Registries (e.g., REFINE PET) now exceeding 35,000 patients, illustrate how data-driven approaches can connect imaging, physiology, and personalized cardiovascular care.^{4,25}

Nuclear Cardiology in 2026: The Integration Era

Nuclear cardiology has clearly entered a new phase. The year 2025 represented more than incremental progress, it marked the consolidation of a discipline that now plays a decisive role in understanding cardiovascular physiology, refining diagnosis, and guiding patient management. Quantitative PET, supported by validated radiotracers, advanced hardware, and robust clinical evidence, has become central to this transformation.¹ At the same time, continued advances in quantitative methodologies and the development of increasingly sensitive and specific PET and SPECT tracers are expanding the biological and clinical insights accessible by nuclear cardiology.^{3,22,23}

As we move through 2026, the emphasis is expected to shift from consolidation to integration. Phenotype-driven and prognosis-oriented imaging⁸ supported by artificial intelligence, large-scale datasets,²⁵ and standardized quantitative metrics,⁷ will increasingly inform clinical decision-making. In this evolving landscape, nuclear cardiology is no longer positioned as a complementary diagnostic modality but as a core component of precision cardiovascular medicine; thus, transforming complex biological signals into clinically actionable knowledge.⁶ In this sense, the field continues to embody Marie Curie's insight: moving from what is feared to what is understood. While 2025 marked consolidation, 2026 marks the phase of integration and impact (Figure 1).

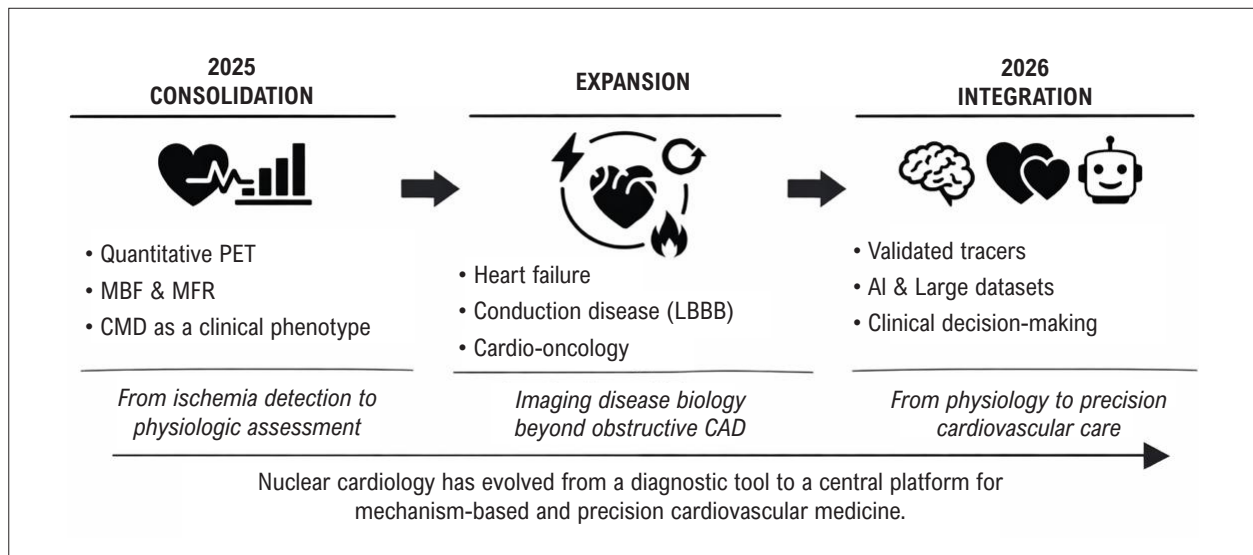


Figure 1 – Evolution of nuclear cardiology from consolidation to integration (2025–2026). In 2025 (Consolidation), quantitative positron emission tomography (PET) with routine assessment of myocardial blood flow (MBF) and myocardial flow reserve (MFR) consolidated the shift from ischemia detection to physiologic assessment, establishing coronary microvascular dysfunction (CMD) as a clinical phenotype. The Expansion phase reflects the extension of nuclear cardiology beyond obstructive coronary artery disease (CAD) to imaging disease biology in heart failure, conduction disease, particularly left bundle branch block (LBBB), and cardio-oncology. In 2026 (Integration), validated tracers, artificial intelligence (AI)-driven analysis of large datasets, and imaging-guided clinical decision-making converge to enable precision cardiovascular care.

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