

STATE OF THE ART REVIEW

New opportunities for nuclear cardiology with total-body positron emission tomography/computed tomography

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Abstract

Total-body positron emission tomography (PET) systems with a long axial field of view (LAFOV) are now commercially available and represent the state of the art in PET imaging. These systems provide wide anatomical coverage and markedly increased detection sensitivity. Clinical studies have demonstrated enhanced image quality, superior quantification, and benefits for tracer kinetic modeling through dynamic imaging. LAFOV PET/CT allows for substantial reductions in acquisition time and radiation dose while maintaining diagnostic image quality. Full-body coverage enables dynamic whole-body imaging, which enables tracer kinetic modeling across multiple organs and the large vascular structures, offering new opportunities for studying their interactions in cardiovascular and systemic diseases. Furthermore, these systems facilitate the development of new PET methods including pharmacokinetics of new tracers. This review discusses the emerging opportunities and challenges associated with the application of LAFOV PET/CT systems in cardiovascular diseases.

Keywords: Long axial field-of-view PET/CT, Total-body PET/CT, Atherosclerosis, Heart failure, Coronary artery disease, Perfusion imaging, Molecular imaging

INTRODUCTION

Long axial field of view (LAFOV), or total-body, positron emission tomography/computed tomography (PET/CT) systems have become commercially available and are emerging as the state-of-the-art clinical platforms [1–3]. These systems offer large axial detector coverage, which enables dynamic imaging of most or all of the entire human body (106–194 cm axial field of view) simultaneously, which was not possible with conventional scanners. Furthermore, the LAFOV PET/CT systems offer markedly increased detection sensitivity, owing to the extended axial-detector length and volume [1–3]. Clinical studies have shown superior image quality and enhanced lesion quantification in terms of signal-to-noise ratio [4–6]. These studies have also

demonstrated that acquisition times can be substantially shortened or the injected radiotracer dose reduced without compromising image quality [4–6]. Furthermore, high temporal resolution and sensitivity of dynamic imaging provides advantages for evaluating tracer kinetics and facilitate modeling of physiological parameters [7–10].

These systems offer several new opportunities for nuclear cardiology (Table 1), although there is currently limited published data. The extended anatomical coverage of LAFOV PET/CT allows for the simultaneous assessment of the heart, large vessels, and multiple organs using dynamic imaging and tracer kinetic modeling. The cardiovascular system is involved in several systemic diseases, and cardiovascular diseases are linked

ABBREVIATIONS

CAD	Coronary artery disease
LAFOV	Long-axial field of view
PET/CT	Positron emission tomography/computed tomography
¹⁸ F-FDG	¹⁸ F-fluorodeoxyglucose
SUV	Standardized uptake value
MFR	Myocardial flow reserve

to systemic factors—including immune, neuro-humoral, and endocrine pathways—and may potentially benefit from a comprehensive multi-organ evaluation [7–9]. This may improve risk assessment and uncover novel disease mechanisms relevant to therapy. Furthermore, LAFOV PET/CT systems are well suited to support the development of new PET tracers.

Table 1. Opportunities for nuclear cardiology with LAFOV PET

Feature	Opportunities
Low-dose imaging	Enables repeated studies for therapy monitoring and disease progression with reduced radiation exposure
Short acquisition time	Increases patient throughput and improves workflow
High signal-to-noise ratio	Enhances image quality and lesion detectability
Late time-point imaging	Improves visualization of focal uptake in inflammation, infection, and atherosclerosis; supports tracer development
Advanced kinetic modeling	Allows detailed analysis of perfusion and metabolic parameters through dynamic imaging
High-resolution gated imaging	Enables precise assessment of cardiac volumes and function
Large axial coverage	Facilitates multiorgan analysis of systemic mechanisms and risk markers
Systemic disease assessment	Improves detection and characterization of cardiovascular involvement in amyloidosis, sarcoidosis, infection, systemic inflammatory disease, and vasculitis
Pharmacologic studies	Supports evaluation of investigational therapies, drug distribution, and tracer pharmacokinetics
New tracer development	Enables low-dose, high-sensitivity studies for early-phase tracer testing

LAFOV, long axial field of view; PET, positron emission tomography.

This review aims to discuss the emerging opportunities and practical challenges of LAFOV PET/CT in the evaluation and management of cardiovascular diseases, with examples across multiple domains of application.

MYOCARDIAL AND WHOLE-BODY PERFUSION IMAGING

Myocardial perfusion imaging is the main application of cardiac PET [7–9]. Noninvasive quantification of myocardial blood flow (MBF) and myocardial flow reserve (MFR) through dynamic imaging and kinetic modeling using flow tracers such as ¹⁵O-water, ⁸²Rb, ¹³N-ammonia, and ¹⁸F-flurpiridaz is established in clinical practice. In addition to obstructive coronary artery disease (CAD), quantitative myocardial perfusion imaging can identify microvascular dysfunction, which often coexists and mimics CAD, and may also be present in other organs besides than the heart. LAFOV PET systems offer potential advantages over conventional scanners that are relevant to imaging myocardial perfusion including improved image quality, the possibility for lower injected activity, and shorter imaging protocols (Figure 1). Additionally, cardiac function and volume assessment may benefit from the high spatial and temporal resolution of these scanners when using tracers that accumulate in the myocardium. A recent feasibility study evaluated gated ¹³N-ammonia myocardial perfusion images obtained with LAFOV PET/CT system [10]. Quantitative perfusion and function metrics (eg, total perfusion deficit, MBF, and ejection fraction) and visual image quality remained diagnostically reliable down to 3 minutes, and images reconstructed with 5-minute data were rated equivalent to those with 10-minute data [10]. Shortened scan protocols in retention-based studies using retention images would offer improvements in patient comfort, motion reduction, and scanner efficiency. However, given the diagnostic and prognostic importance of quantitative MBF, scan time reductions in myocardial perfusion imaging may be limited due to the requirements for kinetic modeling of MBF.

An interesting opportunity provided by LAFOV PET is the ability to perform dynamic whole-body imaging, which enables kinetic modeling of perfusion across multiple organs, which is not possible with standard PET systems. Each LAFOV scan includes high quality visualization of the blood pool (eg, ventricles or aorta), enabling estimation of the image-derived input function to inform about radiotracer delivery. Early experiences in whole-body perfusion imaging using high-extraction tracers including ¹⁵O-water [7,11]

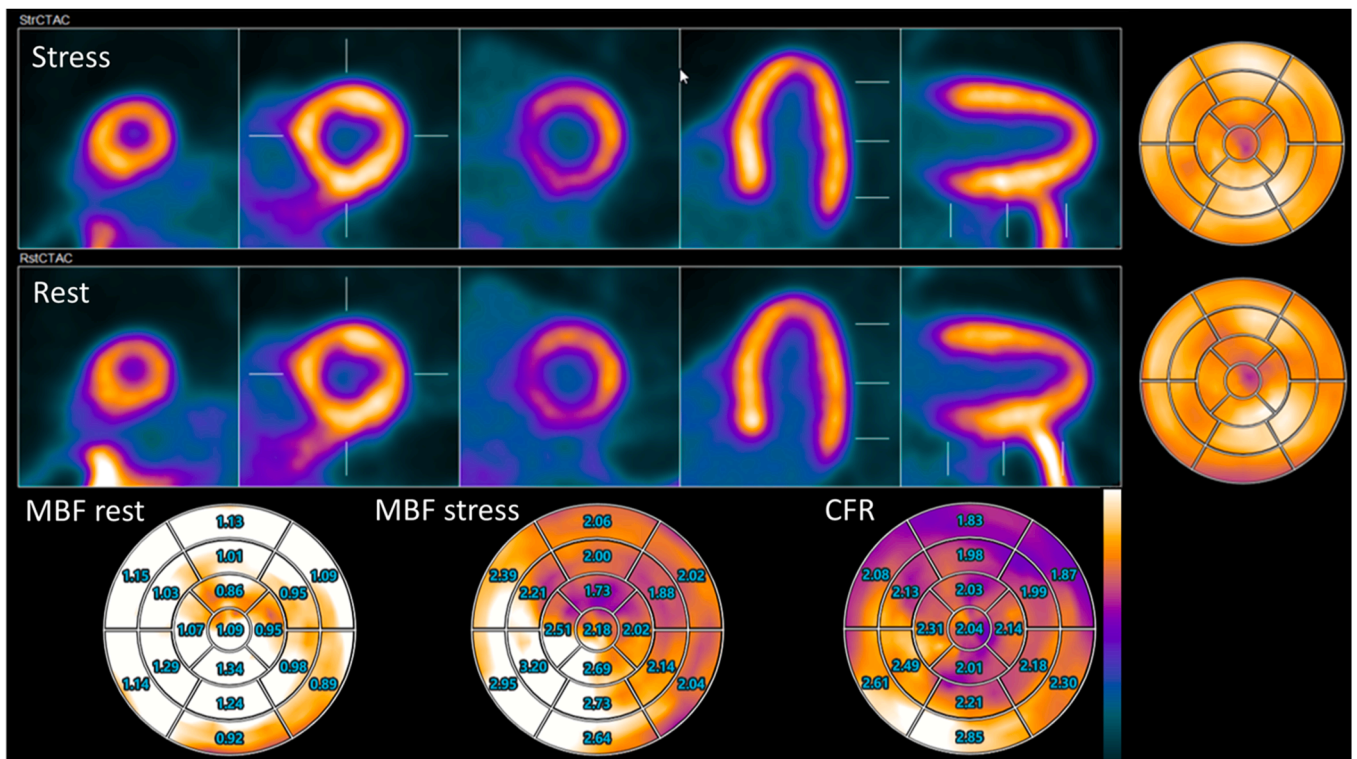


Figure 1. Myocardial perfusion images with ^{82}Rb and long-axial field of view PET/CT. Images were acquired using the Biograph Vision Quadra long-axial field of view PET/CT system (Siemens Healthineers) after injection of 370 MBq ^{82}Rb in a patient with chronic chest pain. Upper and middle panels show retention images and polar maps at stress and rest, respectively. Lower panels show MBF at rest and stress and myocardial flow reserve (MFR, scale bar 0-1 mL/g/min for rest, 0-2.7 mL/g/min for stress and 0-3.0 for CFR). Tracer uptake is normal and quantified MBF and CFR are within normal range. Image courtesy of Federico Caobelli, Inselspital Bern, Bern, Switzerland. MBF, myocardial blood flow; PET/CT, positron emission tomography/computed tomography.

and ^{11}C -butanol [12] demonstrate the feasibility of this approach. Studies with ^{15}O -water have shown that parametric images of flow, perfusable tissue fraction and arterial blood volume can be generated using a single image-derived input function from the aorta and the same one-tissue compartment model applied voxel-wise across the body (Figure 2) [7,11]. Furthermore, a study introduced a novel method for quantitative blood flow imaging using the first two minutes of dynamic ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET combined with high-temporal-resolution kinetic modeling (1-2 second frames) [13]. In contrast to existing methods that use blood-to-tissue transport rate as a surrogate of blood flow, the method directly estimated blood flow using a distributed kinetic model. Validated against ^{11}C -butanol in the same subjects, the technique enabled accurate estimation of whole-body perfusion, with regional blood flow values aligning well with literature references across diverse organs. This approach could enable single-tracer flow-metabolism imaging using widely available ^{18}F -FDG.

Registry data show substantial overlap between coronary and peripheral artery disease, with a marked increase in adverse cardiovascular events

when multiple vascular territories are affected [14]. Perfusion assessment across different vascular beds using LAFOV PET systems provides relevant prognostic information on the extent of atherosclerotic disease, on comorbidities [14–16], and may incidentally reveal clinically significant extracardiac findings such as cerebral perfusion defects, during routine cardiac imaging (Figure 3). A recent study using ^{13}N -ammonia PET demonstrated the feasibility of simultaneous myocardial and renal perfusion imaging [16]. Renal perfusion correlated with myocardial flow reserve, estimated glomerular filtration rate, and histological renal fibrosis.

The clinical impact of LAFOV PET on myocardial perfusion imaging studies remains to be demonstrated. There is a need for studies evaluating robustness of diagnostic accuracy and kinetic modeling of MBF in comparison with conventional PET systems, and the potential for a faster clinical workflow. Such LAFOV PET data are expected to be soon available from institutional databases using these systems in clinical routine and for research. Furthermore, several challenges must be addressed, including processing of large-amount of data, time-consuming segmentation

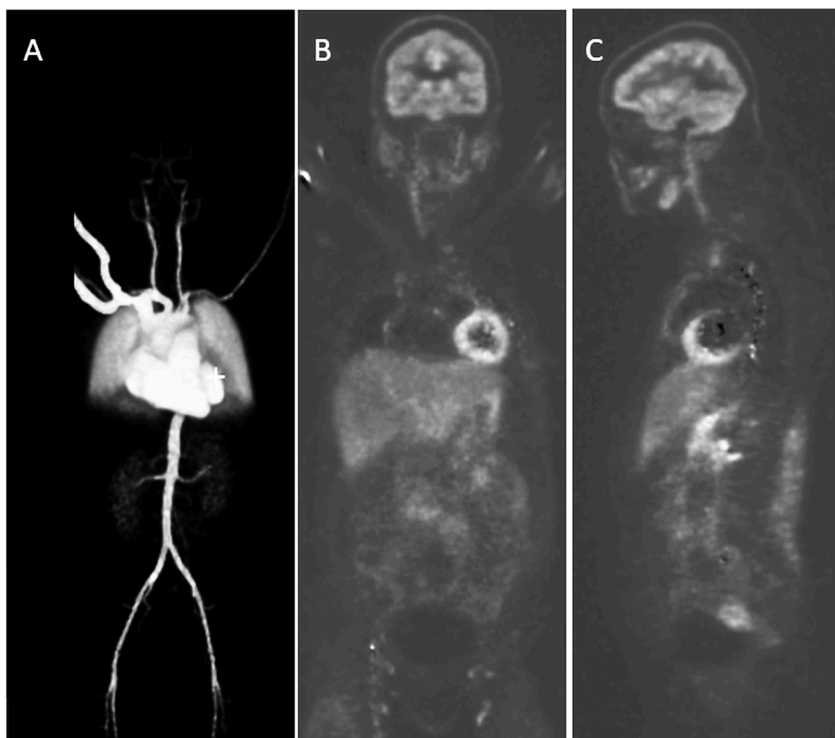


Figure 2. Whole-body dynamic perfusion PET imaging using ^{15}O -water. Dynamic perfusion imaging with ^{15}O -water acquired using the Biograph Vision Quadra large axial field of view PET/CT system (Siemens Healthineers). (A) Three-dimensional parametric image of arterial blood volume (V_a). (B and C) Parametric images of organ-specific blood flow (k_1 , mL/min/mL) in horizontal (B) and sagittal (C) planes, respectively. High perfusion is visible in the myocardium and kidneys in images centered on the heart. PET/CT, positron emission tomography/computed tomography.

of multiple organs, a wide range of perfusion rates within and between tissues, differences in tracer extraction, and the presence of dual blood supplies in certain organs such as the liver, the lungs, and the kidneys [7]. Current image analysis software is compatible for standard analysis of LAFOV PET data, but there is a need for approaches tailored to facilitate kinetic analysis of dynamic whole-body studies. For example, an automated pipeline (TurBO, Turku total-Body, <https://turbo.utu.fi>) has been developed for pre-processing and kinetic modeling of LAFOV data with ^{15}O -water and ^{18}F -FDG PET data [7,11]. This pipeline incorporates coregistration of motion-corrected images, automated CT-based segmentation of major organs, image-derived input function determination, principal component analysis of time–activity curves, and region-specific kinetic modeling with correction for tracer delay. Processing of tissue-specific outcome values and parametric maps at both regional and voxel levels can be accomplished typically in less than two hours Figure 2 [11]. The framework allows for organ-specific kinetic models and is adaptable to different tracers, but further optimization and validation are required to ensure physiologically accurate and disease-relevant perfusion quantification.

MULTIORGAN APPROACH IN CARDIOVASCULAR DISEASES

It is increasingly appreciated that diseases of the cardiovascular system are connected with dysregulation of other organ systems, including the immune, nervous, endocrine and renal systems [16–19]. This has been highlighted by recent therapeutic advances in obesity and diabetes associated with improved cardiovascular outcomes [20]. In patients with preexisting atherosclerotic cardiovascular disease and overweight or obesity but without diabetes, semaglutide, a glucagon-like peptide-1 receptor agonist, was superior to placebo in reducing the incidence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke [20]. The mechanisms of cardiovascular protection with semaglutide remain partially unclear, but these agents affect a broad range of metabolic pathways associated with glucose metabolism, energy homeostasis, and inflammation that might be hypothesized to also improve cardiovascular outcomes. In heart failure, alterations of myocardial substrate metabolism may be both a consequence and a contributor to disease progression [19,21]. These changes are often related to systemic metabolic disturbances such as those

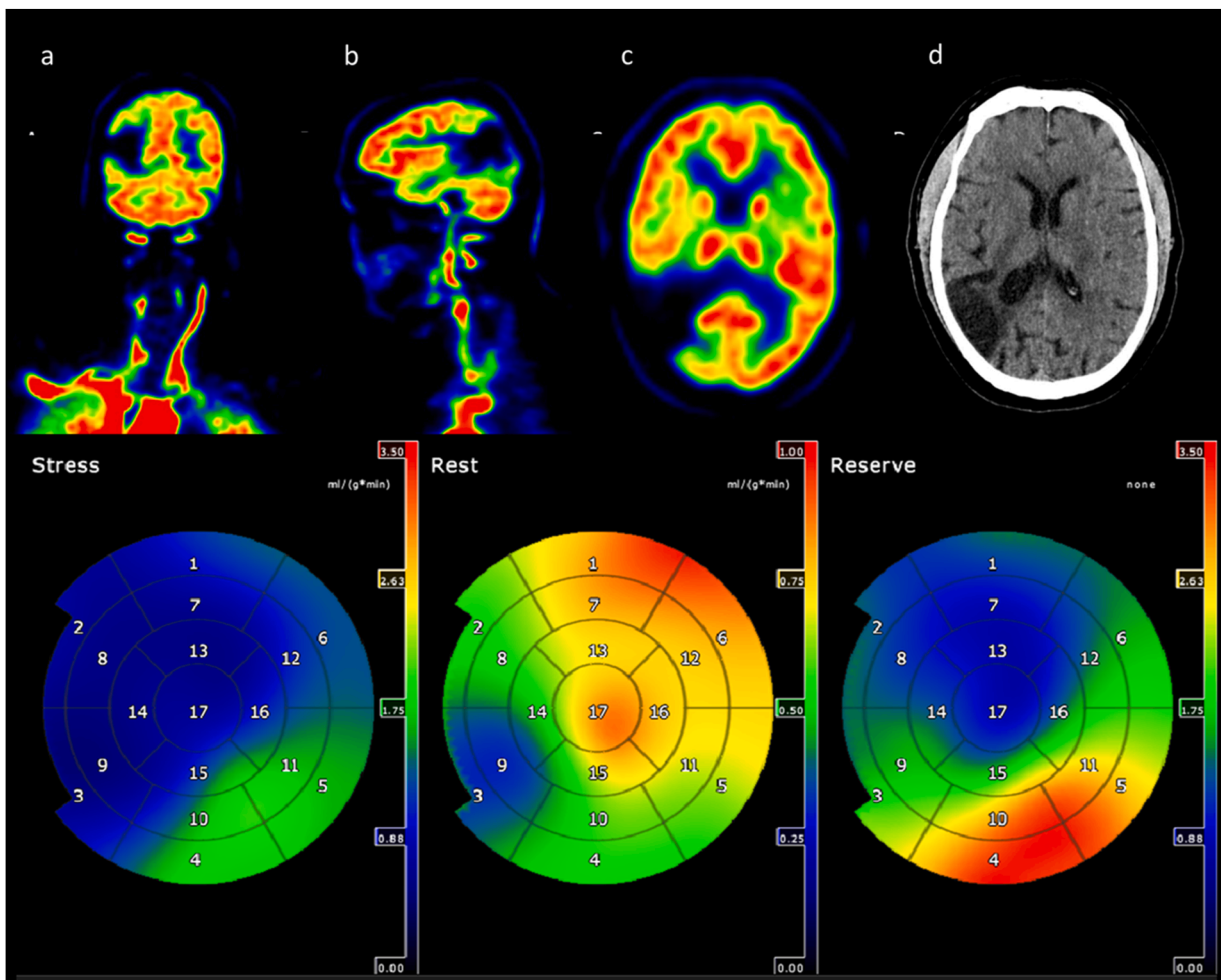


Figure 3. Brain infarction and myocardial ischemia detected by whole-body perfusion PET imaging using ^{15}O -water. Whole-body perfusion PET reveals a brain infarction in the parieto-occipital area in a patient undergoing myocardial perfusion imaging due to suspected CAD. Coronal (A), sagittal (B), and transaxial (C) PET slices from dynamic summed images, and corresponding CT image confirming cerebral infarction (D). The patient had recovered from stroke and was referred to myocardial perfusion imaging due to angina. Polar maps show reduced stress myocardial blood flow (MBF, lower left panel) throughout the left ventricular myocardium, whereas rest MBF (lower middle panel) is reduced in the inferior part of the interventricular septum. Myocardial flow reserve (MFR, lower right panel) is severely reduced in the left anterior descending coronary artery territory. Coronary angiography showed chronic total occlusion of the LAD, diffuse CAD in the right coronary artery, and intermediate stenosis in the left circumflex coronary artery. This example demonstrates the feasibility of whole-body perfusion imaging in detecting clinically relevant extra-cardiac findings in combination with myocardial perfusion imaging. CAD, coronary artery disease; CT, computed tomography; PET, positron emission tomography.

observed in obesity and diabetes. Cardiac and systemic insulin resistance are typical in heart failure and are associated with reduced functional capacity and worse prognosis [21]. However, the mechanisms underlying insulin resistance differ between cardiac and skeletal muscle, suggesting the need for a systems-level metabolic approach. Accordingly, imaging modalities capable of capturing multiorgan interactions and systemic effects of interventions may provide added value for investigating the effects of therapies, disease mechanisms, and risk markers in cardiovascular diseases.

PET imaging has played an important role in advancing the understanding of atherosclerosis

by enabling noninvasive, molecular-level assessment of vascular inflammation and plaque biology [18]. Tracers such as ^{18}F -FDG and ^{18}F -NaF have been extensively used to detect arterial wall inflammation and microcalcification, respectively, offering insights into plaque activity beyond luminal narrowing [18]. Importantly, PET has also illuminated the systemic nature of atherosclerosis, revealing increased metabolic activity in hematopoietic organs such as the bone marrow and spleen, which correlates with vascular inflammation and cardiovascular risk [18]. For example, ^{18}F -FDG PET imaging has demonstrated that arterial wall inflammation increases after myocardial infarction and

correlates with psychological stress (amygdala activation) and bone marrow activity [22]. Retrospective cohort studies have further linked amygdala activation with future cardiovascular events [17,18].

Dynamic whole-body ^{18}F -FDG imaging has demonstrated a high vessel wall signal and target-to-background ratio, even after several half-life times of radiotracer decay, allowing parametric imaging of metabolic rate of ^{18}F -FDG [23,24]. Extending imaging to as late as 12 hours post-injection of a standard ^{18}F -FDG dose revealed a pronounced washout of tracer from the circulating blood pool, concomitant with heightened uptake in the vessel wall. On parametric images, arterial wall signal showed better correlation with hematopoietic and lymphoid organ activity as well as atherosclerotic risk factors than signal from standardized uptake value (SUV) images. These findings support the utility of total-body PET in mapping cardiovascular disease within a broader systemic immunologic framework.

Studies using LAFOV PET have also demonstrated the feasibility of advanced modeling of multiple compartments in dynamic datasets to derive new insights into metabolic pathways. Dynamic total-body ^{18}F -FDG PET was applied to model influx rates, distribution volumes, and fractional blood volumes, in both oncology and infectious disease recovery contexts [25,26]. Such quantitative whole-body data may open opportunities for systems-level analysis, including artificial intelligence-driven approaches to map individual metabolic networks and organ crosstalk.

Recent studies have demonstrated the prognostic value of extracting quantitative body composition biomarkers from PET/CT attenuation data. In a multicenter cohort ($n = 10,085$) undergoing PET myocardial perfusion imaging, deep learning automatically quantified skeletal muscle, bone, and multiple adipose depots (subcutaneous, visceral, intermuscular, and epicardial) from low-dose CT attenuation images [27]. Abnormal volumes and densities of these tissues were independently associated with death or myocardial infarction over a median of 4.2 years, beyond established PET markers such as MFR and coronary calcium. High visceral adipose tissue density and low skeletal muscle volume were particularly prognostic, and combinations of tissue metrics improved risk stratification. In another cohort ($n = 669$) of patients with ischemia and no obstructive CAD, higher intermuscular adipose tissue and lower skeletal muscle volumes were independently associated with lower MFR and increased major adverse

cardiovascular events over 6 years, even after adjusting for body mass index and other adiposity measures [28]. The combination of high intermuscular adipose tissue and coronary microvascular dysfunction identified a novel high-risk cardiometabolic phenotype. Total-body PET could enhance such analyses by providing higher-quality, multiregional body composition assessment in the same scan, enabling integrated cardiac function, perfusion, and systemic phenotype evaluation.

SYSTEMIC DISEASES INVOLVING THE CARDIOVASCULAR SYSTEM

LAFOV PET offers opportunities for investigating the cardiovascular manifestations of systemic diseases such as amyloidosis, sarcoidosis, vasculitis, systemic inflammatory disorders, and infections. It also enables better characterization of the interplay between the heart, vasculature, and other organs.

In cardiac amyloidosis, LAFOV PET imaging may improve early and accurate diagnosis of cardiac involvement, while simultaneously quantifying total systemic disease burden including dynamic and parametric data [9]. This is particularly relevant in light-chain amyloidosis, which frequently affects multiple organs (eg, heart, gastrointestinal tract, liver, kidneys). LAFOV PET may also enhance evaluation of cardiac sarcoidosis by identifying extracardiac involvement (eg, in the brain, lungs, skin, and lymph nodes), thereby improving diagnostic accuracy. Given the low sensitivity of myocardial biopsy, histologic proof of extra-cardiac sarcoidosis guided by PET can serve as a valuable diagnostic approach [9].

In large vessel vasculitis, LAFOV PET may enhance the detection of vascular inflammation, particularly in challenging cases such as steroid-treated or smoldering disease [9]. Similar to atherosclerosis [23,24], improved resolution and kinetic modeling may provide superior target-to-background ratios compared to conventional PET. In addition to primary vasculitis, chronic systemic inflammatory diseases are associated with a significantly increased risk of cardiovascular disease, driven by chronic immune activation, endothelial dysfunction, and accelerated atherosclerosis [17]. Molecular imaging with ^{18}F -FDG PET/CT has provided direct evidence of increased arterial wall inflammation in rheumatoid arthritis patients [17]. LAFOV PET/CT may enhance comprehensive cardiovascular phenotyping in these conditions. In systemic sclerosis, LAFOV PET/CT using ^{68}Ga -FAPI-46 to non-invasively assess fibroblast activation found

abnormally elevated FAPI uptake in the lungs, heart, kidneys, and skeletal muscles, aligning with clinical findings and standard diagnostic methods [29].

In cardiovascular infections, ^{18}F -FDG PET/CT facilitates early diagnosis—prior to overt morphologic damage—and allows for detection of remote septic emboli or extracardiac infection sites [9]. LAFOV PET holds the potential to improve differentiation of infection and nonspecific inflammation by leveraging dynamic imaging. Distinct kinetics of ^{18}F -FDG uptake in infection vs inflammation may become apparent with this approach [30]. High sensitivity and late-timepoint imaging, enhancing lesion-to-background ratios, may improve detection accuracy, particularly in detecting smaller, mobile intracardiac structures such as vegetations in infective endocarditis—lesions that may be missed by conventional PET/CT. Furthermore, multiple organ systems relevant to infection and immune activation—including bone marrow, spleen, and lymph nodes—can be simultaneously assessed for signs of immune activation.

CHALLENGES AND FUTURE PERSPECTIVES

LAFOV or total-body PET/CT systems represent a transformative development in imaging, offering new possibilities in cardiovascular imaging (**Graphical abstract**). These scanners offer exceptional sensitivity, wide anatomical coverage, and high temporal resolution, enabling multiorgan, dynamic imaging and advanced tracer kinetic analysis. However, realizing the full potential of this technology in research and clinical applications requires validation in specific clinical conditions and addressing several challenges (Table 2 [7–9]).

From an implementation standpoint, the high cost and limited availability of LAFOV systems

may pose barriers to widespread clinical adoption. Additionally, computational demands for image reconstruction and modeling remain high. The substantial data volume generated by LAFOV PET/CT scans necessitates robust data management infrastructure including high-performance computing, storage capacity, and automated processing pipelines. In clinical settings, the availability of user-friendly and reliable software for analysis and kinetic modeling remains limited, especially for dynamic whole-body applications that involve multiple organ systems. Manual postprocessing of dynamic datasets across numerous target regions significantly increases workload and complexity. One technical limitation is the continued reliance on CT for attenuation correction, which challenges efforts to minimize radiation exposure. However, new developments—such as ultra-low-dose CT, deep learning-based reconstruction, and CT-free attenuation correction methods—offer solutions to this, once validated. Motion correction is also critical, especially for dynamic whole-body imaging protocols, where even small patient movements can compromise image quality.

While it is clear that total-body PET has a number of research applications, which might inform future clinical practice, it remains to be seen whether the higher sensitivity offered by such scanners translates into either to improved scan performance or being more cost-effective compared to standard systems. In addition to data demonstrating added diagnostic and clinical value, there is a need for standardized protocols harmonized across centers to demonstrate the potential of LAFOV PET in clinical practice. From a cardiovascular perspective, this innovative imaging methodology has the potential to enhance our understanding of the systemic effects and interactions of various cardiovascular disorders, which may have implications in risk assessment and the development of therapy. LAFOV PET/CT makes serial imaging and therapy monitoring more feasible, which may be particularly relevant in clinical trials and systemic diseases such as sarcoidosis, amyloidosis, vasculitis, and atherosclerosis. Furthermore, whole-body dynamic imaging capabilities at high sensitivity will be valuable in assessing the effects of investigational therapies and the development of new tracers. Imaging at late time points, very low injected activities, and whole-body kinetic modeling can support characterization of tracer biology including dosimetry, and address regulatory issues related to radiation exposure and toxicology of new tracers [31,32].

In summary, LAFOV PET/CT not only enhances image acquisition and quantification but also

Table 2. Challenges of LAFOV PET

<p>Large datasets causing major demands for reconstruction, data transfer, storage, and advanced analysis</p> <p>Validation and clinical translation of tracer- and organ-specific whole-body kinetic models</p> <p>Limited availability and high cost requiring documentation of added clinical value and cost-effectiveness</p> <p>Radiation exposure related to whole-body CT for attenuation correction</p> <p>Multiscale patient motion (cardiac, respiratory, whole-body) and need for robust correction strategies</p> <p>Biological and interpretive complexity of multiorgan signals</p> <p>Need for standardization and multicenter harmonization</p>

CT, computed tomography; LAFOV, long axial field of view; PET, positron emission tomography.

facilitates comprehensive, systems-level evaluation of cardiovascular and systemic diseases. The clinical superiority of LAFOV PET/CT over standard PET systems remains largely to be demonstrated, and future research should focus on validating clinical utility, optimizing protocols, and integrating this technology into routine workflows through automation and cost-efficient solutions.

CONCLUSIONS

Total-body PET/CT with long axial field-of-view technology offers several opportunities in nuclear cardiology. Its ability to capture high-resolution dynamic images of the entire body allows for simultaneous assessment of cardiovascular function and systemic processes. This integrated approach supports an improved understanding of disease mechanisms, enhances diagnostic accuracy, and facilitates therapy monitoring across a range of cardiovascular and systemic conditions. Ongoing technical development, validation studies, and cost-effectiveness assessments will be crucial in determining its place in future nuclear cardiology.

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