

A New Horizon in Nuclear Cardiology in Brazil: Impact and Barriers of F-18 Flurpiridaz

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Introduction

Advances have been made in positron emission tomography (PET) myocardial perfusion since the Food and Drug Administration (FDA) approved the use of flurpiridaz, which was shown effective in the detection of coronary artery disease (CAD) in two phase III trials, with a high diagnostic precision as compared with Single Photon Emission Computed Tomography (SPECT) scintigraphy.¹⁻⁴ Flurpiridaz is an injectable radiotracer, labeled with fluorine-18 (F-18), developed by GE HealthCare, that will be sold as “Flyrcado” in the United States from 2025 onwards.⁴

With a half-life of 110 minutes, F-18-flurpiridaz requires neither a generator nor a local production of tracers, allowing a more efficient distribution among hospitals and imaging centers,⁵ similarly to Fluorodeoxyglucose labeled with Fluorine-18 (F-18 FDG).⁶ This feature may favor the adoption of myocardial perfusion PET, benefiting more patients with cardiovascular diseases.⁷ Besides, the longer half-life of F-18-flurpiridaz allows the combination of a physical stress test, optimizing the evaluation of ischemia and improving patients' experience.^{7,8}

Flurpiridaz approval, announced on September 27, 2024,³ marks the beginning of a new era in nuclear cardiology, with the expectation to expand the use of myocardial perfusion PET in the United States and in the world.⁷ In Brazil, this technology brings opportunities and challenges, that will be discussed in this paper, focusing on advantages, regulatory and access barriers to the implementation of myocardial perfusion PET.

The role of PET with F-18 flurpiridaz in the new CAD phenotype

CAD was the main cause of death in Brazil in the last decade.⁹ Projections of cardiovascular health by 2050 are alarming, highlighting the need for significant

interventions. The prevalence of risk factors is expected to increase, with more than 50% of the general population and 80% of specific groups suffering from hypertension and obesity.^{10,11} Demographic changes and population aging may exacerbate the impact of cardiovascular diseases globally, aggravated by diabetes and obesity, despite promising reductions in smoking and hypercholesterolemia.⁹⁻¹¹

In 2019, data from the Brazilian national health report showed that 57.5% of men and 62.6% of women were overweight, and 21.8% of men and 29.5% of women were obese.⁹ The increase in cardiometabolic disorders, like diabetes and chronic renal disease, is associated with factors that increase the risk of cardiovascular diseases and death. Conditions affecting the coronary circulation, like atherosclerosis and microvascular dysfunction, are critical for cardiovascular morbidity.^{12,13}

Myocardial perfusion scintigraphy using SPECT or PET has been crucial in the measurement of ischemia. The clinical efficacy of these tests should consider all variables that influence patient management.¹⁴ Studies have suggested that coronary revascularization in patients with chronic chest pain does not necessarily improve long term outcomes, due to the diffuse nature of CAD. The insufficient role of imaging techniques in guiding this therapy raises questions about the accuracy of these tests, often obsolete and ineffective in detecting subendocardial ischemia.⁸

Structural and functional abnormalities of coronary circulation, including diffuse non-obstructive atherosclerosis and coronary microvascular dysfunction, are important mediators of cardiovascular morbidity and mortality in individuals with cardiometabolic diseases. Over the last years, the use of PET in the assessment of myocardial perfusion and coronary flow has increased in the United States, and an even greater increase is expected with the introduction of F-18 flurpiridaz.^{3,4,7,8} A recent, large-scale study showed that PET with myocardial flow reserve detects nonobstructive CAD and microvascular dysfunction more precisely than SPECT, especially in high cardiovascular risk patients.¹⁵ Therefore, PET should be preferably considered for individuals with cardiometabolic diseases, aiming at more effective preventive therapies.^{14,15}

In Brazil, despite investments made by some centers in SPECT with dedicated gamma cameras, the accuracy of this technique remains lower than that of PET.^{1,3,8} These cameras are specific for cardiac tests, limiting its applicability and elevating the costs of investments. On the other hand, myocardial perfusion PET stands out for its high diagnostic accuracy and for the existing

Keywords

Positron Emission Tomography Computed Tomography; Coronary Artery Disease; Radiopharmaceuticals.

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infrastructure of PET/CT in Brazil (thanks to the oncology field), which, with the emergence of F-18 flurpiridaz, will potentially be used in nuclear cardiology.¹⁶ The adoption of F-18 flurpiridaz provides a new perspective for cardiac perfusion tests, with meaningful benefits to the centers where PET is already available.

Will F-18 flurpiridaz really coming to Brazil?

We still don't know. As far as we know, F-18 flurpiridaz (Flycado, GE HealthCare) will become available in the United States only. Unfortunately in Brazil, the entry of novel radiopharmaceuticals usually faces great challenges, as we have seen with MIBG-I123 (for assessment of cardiac sympathetic activity), technetium-99m-pyrophosphate (for scanning for transthyretin cardiac amyloidosis), markers of cerebral amyloid plaques in PET (PiB-C11, F-18 flutemetamol, F-18 florbetaben, F-18 florbetapir), PSMA-Ga68 (primarily for prostate cancer), I-123 Ioflupane (for Parkinson disease), among others. The truth is that few centers have access to these technologies in Brazil, especially in the national Unified Health System (SUS). The access, when exists, is usually limited to private services or to a very restricted number of public or philanthropic research institutions.

However, despite this unfavorable background, we cannot give up. In spite of these challenges, significant progress has been made. In Brazil, overcoming obstacles to provide the population with cutting-edge resources requires immense resilience, perseverance and focus. In addition to difficulties commonly seen in first world countries, like staff training and technical excellence, we must face additional barriers. Nevertheless, each step given is a victory, and the advances, despite gradual, pave the way to a more accessible and promising future for nuclear medicine in our country.

Barriers to F-18 flurpiridaz implementation in Brazil

The entry of F-18 flurpiridaz in Brazil will probably face several challenges to the implementation of this technology in country.¹⁶⁻¹⁸

- **Regulatory barriers:** the approval of F-18 flurpiridaz by the Brazilian Health Regulatory Agency is one of the main obstacles. The regulatory process may be complex and take a long time, and the lack of a viable business model for GE HealthCare and nuclear medicine centers in Brazil may delay the introduction of the product nationwide.

- **Limited infrastructure:** despite the presence of a solid infrastructure for PET/CT exams, most equipment distributed across several regions in Brazil was acquired for oncology studies. Therefore, these services must be adapted to nuclear cardiology purposes and costs must be optimized to make the use of F-18 flurpiridaz feasible.

- **Health coverage:** the inclusion of PET with F-18 flurpiridaz into the list of procedures covered by the Brazilian National Health Agency and by the SUS is crucial. Without an appropriate coverage, the access to the exam will be limited to private services or to a very low number of public institutions.

- **Access challenges:** the truth is that many Brazilian centers have limited access to new imaging technologies, especially public ones. This results in disparities in the access to advanced diagnosis, which may negatively impact the treatment of patients with cardiovascular diseases.

- **Professional qualification:** F-18 flurpiridaz implementation will require training and qualification of healthcare professionals for the correct utilization of the new technology and interpretation of results.

Final considerations

The introduction of F-18 flurpiridaz in Brazil can revolutionize the detection of CAD and improve the prognosis of patients with cardiovascular diseases. However, in this regard, it is fundamental to overcome regulatory barriers, guarantee an adequate infrastructure, add PET with F-18 flurpiridaz to the coverage list of Brazilian health systems, and qualify healthcare professionals. In addition, the collaboration between medical societies, government agencies and industry will be crucial to make the implementation of this emerging technology viable in Brazil.

Although geography is not the main limiting factor in this case, cultural, political barriers and inefficient management have hampered access to this important diagnostic technology. As Timothy Marshall highlights in his work "Prisoners of Geography", it is not always geographical constraints that determine the fate of a nation, but rather the choices, priorities, and will of its leaders and citizens.

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Conception and design of the research, acquisition of data, analysis and interpretation of the data, writing of the manuscript and critical revision of the manuscript for intellectual content: Brandão SCS.

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This article does not contain any studies with human participants or animals performed by any of the authors.

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