EDITORIAL POINT OF VIEW

Positron Emission Tomography Myocardial Perfusion Imaging Tracer Choice for Assessment of Myocardial Blood Flow

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Abstract

Myocardial perfusion imaging (MPI) using positron emission tomography (PET) has high diagnostic accuracy and prognostic value in patients with known or suspected coronary artery disease (CAD). In addition, PET MPI can be used to quantify global left ventricle (LV) and regional LV myocardial blood flow (MBF) and myocardial flow reserve (MFR). Currently, there are four major PET perfusion tracers: ^{82}rubidium, ^{13}N-ammonia, ^{15}O-water, and ^{18}F-flurpiridaz. The characteristics of each tracer have been described and fully compared. Given increasing clinical needs for accurate MBF and MFR measurements, the use of PET MPI should be expanded in clinical settings in the near future.

Keywords: Myocardial blood flow, Positron emission tomography, Quantification
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Stress myocardial perfusion imaging (MPI) has been considered a valuable imaging approach for diagnosis of coronary artery disease (CAD) as well as part of a treatment strategy that includes percutaneous coronary intervention (PCI). While single-photon emission computed tomography (SPECT) MPI has been used in clinical settings, positron emission tomography (PET) MPI has several advantages over SPECT MPI. PET MPI has been shown to have more accurate diagnostic value than does SPECT MPI, and high incremental prognostic value in patients with CAD (1–5). Another big advantage of PET over SPECT is better quantification of tracer kinetics. PET permits quantitative analysis of myocardial blood flow (MBF) in millilitres per gram per minute and of myocardial flow reserve (MFR: hyperemic MBF/resting MBF) using a suitable radiotracer kinetics model. This technique affords comprehensive identification and delineation of subclinical and clinically manifest coronary atherosclerosis and various other cardiovascular disorders (6–9). On the basis of Japanese Circulation Society guidelines and ACC/AHA/ASNC guidelines, PET MPI is considered to be a class 1 indicator in the diagnosis of CAD (10, 11).

PET myocardial perfusion tracers

There are four major PET MPI tracers (11–14). ^{82}Rubidium (^{82}Rb) and ^{13}N-ammonia (^{13}N-NH_3) are widely available in the US and Canada (12, 13). In Japan, the Japanese Ministry of Health, Labor and Welfare approved reimbursement for ^{13}N-NH_3 perfusion PET in 2012 with higher reimbursement in 2018 (14, 15). We have performed clinical trials of ^{82}Rb at Hokkaido University (16, 17). In addition, ^{15}O-water (^{15}O-H_2O) has been used for clinical investigation in several PET centers that have an in-house cyclotron (18). ^{18}F-flurpiridaz has been used for phase III clinical trials and its clinical use is expected in the near future (19, 20).

Comparison of PET tracers

Characteristics of each PET tracer are summarized in Table 1. PET perfusion study permits visual or semi-quantitative assessment of the relative distribution of perfusion tracer uptake in stress and rest images of the left ventricular myocardium, similar to the case with SPECT MPI study. For this purpose, the best quality of perfusion images are achieved using ^{18}F-flurpiridaz. Next in quality are ^{13}N-NH_3 and then ^{82}Rb, based on differences in extraction fraction and positron range. ^{15}O-H_2O does not provide myocardial perfusion images

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Table 1 Characteristics of PET Myocardial Perfusion Imaging Tracers

Tracer	Half-life	Time for stress-rest study	Tracer Production	EF* at high flow	Advantages	Disadvantages
^{82}Rubidium	76 sec	30 min	Generator	65%	・High patient throughput ・No need for in-house cyclotron ・Low radiation dose	・Inferior image quality ・Less accurate for MBF analysis due to low EF
^{15}O-water	110 sec	30 min	On-site Cyclotron	100%	・Most suitable for MBF analysis due to 100% EF ・Low radiation dose	・No perfusion images ・Repetitive need for cyclotron ・Low patient throughput
^{13}N-ammonia	10 min	90 min	On-site Cyclotron	80–90%	・High quality MPI ・Suitable for MBF analysis due to high EF	・Repetitive need for cyclotron ・Low patient throughput
^{18}F-flurpiridaz	110 min	3–4 hrs or 2 days	Delivery	>90%	・Excellent quality MPI ・Suitable for MBF analysis due to high EF ・Exercise perfusion study available	・Not clinically available ・Long waiting for the second test due to long physical half-life

*EF=extraction fraction

since it is a diffusible tracer.

MBF analysis has been conducted using various PET tracers. Among them, ^{15}O-H_2O PET permits the most accurate estimate of MBF and MFR due to its 100% extraction fraction even in the high-flow range (4). ^{18}F-flurpiridaz also has a great potential for estimating MBF due to its high extraction, followed by ^{13}N-NH_3 (20).

Given their ultrashort physical half-lives, ^{82}Rb and ^{15}O-H_2O are suitable for rapid acquisition rest-stress studies, within 30 minutes (18, 21). Such short physical half-life PET perfusion tracers may be advantageous in reducing the radiation burden on each patient. A ^{13}N-NH_3 PET study may require approximately 90 minutes for rest-stress perfusion study due to its long (10 min) physical half-life (12). For the same reason, an ^{18}F-flurpiridaz rest-stress PET study may take at least 3–4 hours at one time or over two separate days due to its longer (110 min) physical half-life. On the contrary, this tracer may be suitable for performing an exercise perfusion study, similar to SPECT perfusion imaging. In addition, because of the excellent image quality of ^{18}F-flurpiridaz MPI, a stress-only study may be possible in clinical settings in the near future.

^{15}O-H_2O and ^{13}N-NH_3 have inherent limitations with regard to wide clinical use since they must be produced using an in-house cyclotron. On the other hand, ^{82}Rb has the potential for wide clinical since it does not require a cyclotron for production. Actually, the number of PET perfusion studies in the US has risen, mainly due to the use of ^{82}Rb generators (5, 13).

^{82}Rb is useful for centers that perform many patient studies since it has a shelf-life of 1–2 months and can be produced using one generator system without a cyclotron. Though an individual ^{82}Rb generator is expensive, the cost of each PET study may be significantly lowered when many PET studies can be performed with one generator within 1 to 2 months. ^{82}Rb is considered the best choice for high-volume centers that do not have a cyclotron (13). ^{82}Rb generators are widely available in North America, and wide clinical use throughout the world is expected in the near future.

Future perspectives for PET tracers

Of the four PET perfusion tracers, only ^{18}F-flurpiridaz is not available for clinical use. Once this tracer is approved for clinical use, it will be commercially distributed from a major cyclotron center and wide clinical application may be expected, similar to the case with ^{18}F-fluorodeoxyglucose (FDG). ^{18}F-flurpiridaz may prove advantageous over the other tracers since it does not have several disadvantages that they do.

The need for accurate measurement of MBF and MFR in clinical settings is increasing. PET perfusion study should therefore be expected to play more important roles in the near future in various circumstances, not only in CAD diagnosis, but also in risk analysis, treatment planning, and assessment of treatment effects, etc. In this respect, clinical evidence of the usefulness or clinical role of PET-perfusion MPI assessment using suitable PET tracers will be required in the near future.

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Conflicts of interest

I declare that there is no conflict of interest in this

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