Advances in Radiopharmaceuticals for Myocardial Perfusion Imaging

J. Ballinger (London)

Myocardial perfusion imaging (MPI) is one of the greatest success stories of nuclear medicine, growing continuously since the late 1970s to now constitute more than 50% of imaging procedures in some countries. This success resulted from the development of improved imaging agents, the direct impact of the test results on patient prognosis, and the technique being embraced by cardiologists. With SPECT myocardial imaging now being firmly entrenched, we may see a similar growth in cardiac PET. There are three main localisation mechanisms for MPI tracers: active transport, passive diffusion, and mitochondrial targeting.

Active transport. 201Tl thallous chloride is taken up primarily by the sodium-potassium ATPase pump as a potassium analogue. 201Tl has a number of limitations as a radionuclide and has largely been replaced by newer agents, but still has some uses. The generator produced positron emitter 82Rb also accumulates by active transport [1]. It is infused directly from the generator into the patient and a rest, stress, and attenuation correction sequence can be acquired within 30 minutes. However, 82Rb requires high throughput to be cost effective due to the cost of the generator which must be replaced on a monthly basis.

Passive diffusion. 15O-water and 13N-ammonia are cyclotron produced MPI tracers for use with PET imaging. 15O-water is not retained, complicating the analysis of images, while 13N-ammonia is trapped by enzymatic conversion to glutamine. Their use is limited to centres with a cyclotron.

Mitochondrial targeting. The two most widely used MPI tracers for SPECT are 99mTc-sestamibi and 99mTc-tetrofosmin, both of which enter cardiac cells by passive diffusion followed by trapping in mitochondria due to their positive charge. 18F-flurpiridaz, which also targets the mitochondria, is under development as an MPI tracer for PET [2].

Tracers under development. It is unlikely that any new SPECT tracers will become available in the near future as the market is felt to be mature. However, there is active interest in PET tracers. BFPET, an 18F labelled phosphonium ion, is currently in Phase II studies [3]. A variety of 62Cu and 68Ga complexes have been evaluated; these could be extremely useful due to the availability of the radionuclide from a generator rather than requiring a cyclotron, but an agent with ideal properties has not yet been developed [4,5]. MPI faces competition from other modalities (CT, MR, echo) but remains a widely used and clinically important technique.

References:

1. Machac J. Cardiac positron emission tomography imaging. Semin Nucl Med 2005;35:17-36.
2. Yu M, Nekolla SG, Schwaiger M, Robinson SP. The next generation of cardiac positron emission tomography imaging agents: discovery of flurpiridaz F-18 for detection of coronary disease. Semin Nucl Med 2011;41:305-13.
3. Gurm GS, Danik SB, Shoup TM, et al. 4-[18F]-tetraphenylphosphonium as a PET tracer for myocardial mitochondrial membrane potential. J Am Coll Cardiol Imaging 2012;5:285-92.
4. Herrero P, Hartman JJ, Green MA, et al. Regional myocardial perfusion assessed with generator-produced copper-62-PTSM and PET. J Nucl Med 1996;37:1294-300.
5. Tarkia M, Saraste A, Saanijoki T, et al. Evaluation of 68Ga-labeled tracers for PET imaging of myocardial perfusion in pigs. Nucl Med Biol 2012;39:715-23.