Background
Nuclear cardiology investigations are some of the most commonly utilised in the diagnosis of patients with heart disease. However, it is easy to overlook advances that have occurred in recent years given the attention paid to cardiovascular computed tomography (CT) and magnetic resonance (CMR). With this in mind, this brief review is intended to update the reader on a number of key innovations.

New cameras: Hardware and software
Conventionally, single photon emission CT (SPECT) myocardial perfusion scintigraphy (MPS) has been undertaken with Anger-type cameras, based on photomultiplier tube technology. In the last decade, solid state gamma cameras that use smaller zinc telluride crystals to convert and digitalise gamma radiation have been introduced. Combined with new reconstruction techniques (iterative reconstruction rather than filtered back projection) and resolution recovery software, the result is improved count sensitivity, spatial and energy resolution. Machines are smaller (figure 1) and associated with lower radiation exposure, better image quality and faster acquisition times (from 15-20 minutes down to 2-3 minutes).

An alternative to SPECT
SPECT provides both perfusion and functional data on the left ventricle (LV) including end-diastolic and end-systolic volumes, ejection fraction and regional wall motion. However, to detect areas of abnormal perfusion, it relies on a relative differential in count density between hypo-perfused and normal myocardium. This drawback is underlined by patients with three vessel disease where so called balanced ischaemia can occur, resulting in a “normal” perfusion scan. While three-vessel disease can be inferred from ancillary findings (ie transient ischaemic dilatation and diminishment of ejection fraction with stress), this remains an unsettling feature for scan referrers and readers alike.

Positron emitting technology (PET) permits quantification of absolute, rather than relative, flow and therefore avoids the problem described for SPECT. In addition, coronary flow reserve can be calculated by determining flow for the entire LV at both rest and stress. This carries important information on the state of the coronary microcirculation as well as the epicardial coronary arteries and, as such, has attracted greater interest.

From a practical perspective, generator-created Rubidium tracers (figure 2) is keenly awaited as initial trials have been promising. While cost remains an important consideration, cardiac PET is likely to grow from the small number of centres currently practising it in the UK.

A novel stressor and protocol
Being the most physiological form of stress, exercise is recognised to be the optimal means of unmasking cardiac ischaemia. However, not all patients can perform exertion adequately and for these, vasodilator and isotropic pharmacological stressors are available.

Unfortunately, vasodilatation is often associated with side effects related to the non-selective action of adenosine and dipyridamole, ie heart block, bronchoconstriction, flushing and hypotension. A selective adenosine blocker, regadenoson, whose site of action is limited to the A2a receptor, has been developed to counteract these effects. It has taken up quickly in North America, reflecting the fact that it increases the number of patients eligible for vasodilator stress, is simple to administer and has a fast onset and offset of action.

The basis for another innovation, which has shortened protocols, is the demonstration that patients with a normal stress scan have an identical prognosis to those who have a normal stress and rest scan. Based on this data, when a stress scan is normal in patients with low to intermediate risk, a rest scan is justifiably unnecessary. Dose and camera time savings can therefore improve cost and throughput.

Indications: From ischaemia to heart failure
In parallel with these developments, clinical practice is being encouraged to evolve in ways that are particularly important for modalities imaging ischaemia, including SPECT MPS.

In the COURAGE trial, that had involved more than 2,000 patients with stable angina randomised to optimal medical therapy with or without PCI, a nuclear sub study found that in patients with >10% LV ischaemia undergoing intervention, a significant reduction in ischaemia was noted in the interventional arm compared to the group taking optimal medical therapy. In exploratory unadjusted analysis, improved survival was related to the degree to which a reduction in inducible ischaemia had occurred with treatment.

Although it remains uncertain whether stratifying patients with >10% ischaemia to angioplasty results in improved outcomes, these findings emphasise the importance of quantifying ischaemia. More recently, NICE recent onset of chest pain guidelines (CG95) recommended non-invasive functional imaging in several patient groups (detailed in table 1).

Consequent to the release of appropriateness criteria, increasing efforts are being made to ensure inappropriate testing is kept to a minimum. A new initiative led by the American College of Cardiology is designed to support centres in achieving this aim by making a number of resources available for audit and education among referring physicians.

The management of patients with heart failure has progressed with the re-emergence of meta-iobenzylguanidine (mIBG), a long used tracer in nuclear medicine. Building on the principle that sympathetic overactivity occurs in heart failure due to increased release and reduced uptake of noradrenaline in cardiac neurons, mIBG imaging allows cardiac sympathetic activity to be non-invasively assessed (figure 3). In the ADMIRE-HF study, involving 961 patients, a heart:mediastinal (H/M ratio) >1.6 predicted heart failure progression and sudden cardiac death.
**Hybrid imaging**

Hybrid imaging represents an important advance allowing complementary information concerning a patient’s coronary artery disease to be displayed and interpreted as a whole. Anatomical data (normally defined by cardiac CT) is superimposed with functional, perfusion-based data. In this way, one can immediately determine the relevance of a coronary artery lesion and, conversely, see whether a perfusion defect is subtended by a stenosed artery. The combination of CT coronary angiography with SPECT and PET/CT can be captured in a single examination or created by importing separately acquired data into dedicated software.

**TABLE 1**

<table>
<thead>
<tr>
<th>NICE recommended indications for non-invasive functional imaging (including SPECT MPS). Adapted from NICE CG95.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with confirmed coronary disease when it is uncertain whether the pain is caused by coronary disease.</td>
</tr>
<tr>
<td>Patients with 10-29% likelihood of coronary artery disease and a CT calcium score of 1-400 with uncertainties over whether significant coronary disease is present on CT angiography.</td>
</tr>
<tr>
<td>Patients with 30-60% likelihood of coronary artery disease when:</td>
</tr>
<tr>
<td>- Coronary angiography is not appropriate or acceptable/ coronary revascularisation is not being considered;</td>
</tr>
<tr>
<td>- Uncertain if significant coronary disease is present following coronary angiography.</td>
</tr>
</tbody>
</table>

**Future perspectives**

Finishing where we started, one cannot talk about nuclear cardiology without considering its place among other imaging modalities. One recently published study found that SPECT MPS had a similar specificity but a poorer sensitivity for the identification of significant coronary disease compared to CMR (featuring adenosine perfusion, cines and late Gadolinium enhancement for the detection of prior myocardial infarction). Given the costs and expertise associated with CMR, it remains to be seen how this will alter the shape of imaging services and their protocols in the future.

**Conclusion**

MPS has been the standard for many years, but has recently been challenged by other modalities. The nuclear cardiology community has responded with a number of technological developments for use in existing and new applications. The current economic climate will have an impact on technology upgrades, however the wealth of data and ease of use of most nuclear cardiology techniques will stand them in good stead for the future.

**References**


**FIGURE 1**

Solid state dedicated cardiac gamma camera installed at Leeds General Infirmary. Photo courtesy of Dr Fahmid Chowdhury.

**FIGURE 2**

Cardiac PET perfusion with new 18F flurpiridaz tracer compared to Tc MPS. The patient has normal coronaries with a reversible inferior perfusion defect on MPS. The PET images have improved signal to noise ratio and show no evidence of inducible ischaemia. Image courtesy of Dr Jamshid Maddahi, UCLA, Los Angeles, USA.
FIGURE 3
Cardiac mIBG scanning in heart failure. This patient has a very poor cardiac uptake with a reduced heart:mediastinal ratio indicating a high likelihood of cardiac events. Image courtesy of Dr Kevin Bradley, Churchill Hospital, Oxford.