Nuclear cardiac imaging for the assessment of myocardial viability

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An important aspect of the diagnostic and prognostic work-up of patients with ischaemic cardiomyopathy is the assessment of myocardial viability. Patients with left ventricular dysfunction who have viable myocardium are the patients at highest risk because of the potential for ischaemia but at the same time benefit most from revascularisation. It is important to identify viable myocardium in these patients, and radionuclide myocardial scintigraphy is an excellent tool for this. Single-photon emission computed tomography perfusion scintigraphy (SPECT), whether using ^{201}thallium, ^{99m}Tc-sestamibi, or ^{99m}Tc- tetrofosmin, in stress and/or rest protocols, has consistently been shown to be an effective modality for identifying myocardial viability and guiding appropriate management.

Metabolic and perfusion imaging with positron emission tomography radiotracers frequently adds additional information and is a powerful tool for predicting which patients will have an improved outcome from revascularisation. New techniques in the nuclear cardiology field, such as attenuation corrected SPECT, dual isotope simultaneous acquisition (DISA) SPECT and gated FDG PET are promising and will further improve the detection of myocardial viability. Also the combination of multislice computed tomography scanners with PET opens possibilities of adding coronary calcium scoring and noninvasive coronary angiography to myocardial perfusion imaging and quantification. (*Neth Heart J* 2005;13:408-15.)

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Assessment of myocardial viability in patients with coronary artery disease (CAD) and left ventricle (LV) dysfunction is of major importance for prognosis.[1,2] It is well known that LV dysfunction is not necessarily an irreversible process. Dysfunctional but viable myocardium has the potential to recover after restoration of myocardial blood flow by either coronary arterial bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA), whereas scarred tissue will not recover.[2-4] Patients with CAD and severe dysfunction but viable LV have a poor prognosis when treated with medical therapy alone.[5] In selected patients with sufficient viable myocardium, coronary revascularisation appears to afford a long-term survival benefit.[6] Nuclear imaging techniques such as positron emission tomography (PET) or single positron emission computed tomography (SPECT) play a major role in the assessment of myocardial viability.[2,4,7,8] Further improvement in the detection of myocardial viability is expected, because new techniques are being developed in the field of nuclear cardiology, such as attenuation corrected SPECT, dual isotope simultaneous acquisition (DISA) SPECT and gated FDG PET. Also the combination of multislice computed tomography scanners with PET opens possibilities of adding coronary calcium scoring and noninvasive coronary angiography to myocardial perfusion imaging and quantification.

In the next paragraphs we describe several conventional and new nuclear techniques, and give a radiopharmaceutical overview and pathophysiogical backgrounds of myocardial viability.

Pathophysiology of myocardial contractile dysfunction

LV dysfunction may be caused by (repetitive) stunning, widespread hibernation or by infarcted necrotic myocardium. Myocardial stunning is a condition of prolonged, postischaemic dysfunction of viable tissue that can be salvaged by reperfusion.[9] Stunning may occur after acute coronary occlusion followed by thrombolysis, but also after a period of unstable angina or exercise-induced ischaemia. Repetitive stunning is a phenomenon defined as repeated episodes of ischaemia inducing reduction in contractility. It appears that one of the mechanisms responsible for myocardial stunning ischaemia is an alteration of contractile proteins resulting in decreased responsiveness of the contractile machinery to Ca^{2+}, so that the myocardium generates less force.[10] In this sense, myocardial stunning could be viewed as a disturbance of myofilament function.

Hibernation means chronically reduced myocardial perfusion at rest associated with impairment in contractile function, which can be reversed after revascularisation. The reduction of contractile function associated with hibernation may be a protective response of the myocardium in order to meet the reduced supply of oxygen and substrates, leading to a new situation of perfusion-contraction matching, which prevents apoptosis and cell death.[11] In hibernating myocardium, myocytes are in a stable noncontractile state. Cell membrane and cellular metabolism remain intact and little or no evidence of apoptosis is present.[12] The time course of functional recovery of hibernating myocardium may vary considerably, and depends on several factors including the duration and severity of myocardial ischaemia, the time and completeness of myocardial revascularisation, and the extent of ultrastructural alterations within the dysfunctional myocardium.[13]

The induction of apoptosis and necrosis is regulated by many of the same biochemical intermediates, including alterations in high-energy phosphates, intracellular calcium accumulation, and reactive oxygen species. Apoptosis, first described by Kerr and coworkers, is characterised by morphological changes, including cell shrinkage and formation of membrane-bound apoptotic bodies.[14] In contrast, necrosis is characterised by cell swelling, depletion of high energy stores, disruption of the cellular membrane involving fluid and electrolyte alterations and fragmentation of DNA, due to mechanisms such as ischaemia and thrombosis.[15] Several imaging techniques are based on the detection of viable myocardium in order to select those patients who will benefit from revascularisation.

Methods for the detection of myocardial viability

What is the gold standard for viability studies? The choice of gold standard or reference technique for viability is still unclear. There have been many endpoints proposed for viability studies, including preserved cellular metabolism,[1] histological examination of biopsied tissue,[16] preserved regional wall contraction by low-dose dobutamine echocardiography, gated SPECT or magnetic resonance imaging (MRI),[17] regional or global functional recovery,[2] symptom improvement[18] and improved survival (table 1).[18]

Table 1. Outline of the different methods for the assessment of myocardial viability.

Assessment viability	Technique
Cellular function	Biopsy
	^{99m}Tc-annexin V
	FDG
	^{11}C-acetate
	^{11}C-palmitate
	^{99m}Tc-sestamibi/
	^{99m}Tc-tetrofosmin
	^{201}Tl
Regional LV contractility	Dobutamine stress MRI
	Dobutamine stress echocardiography
	Dobutamine stress gated SPECT
Clinical	Cardiac events
	Symptoms
	LV recovery postrevascularisation

Tc=technetium, FDG=^{18}F-fluorodeoxyglucose, Ti=thallium, MRI=magnetic resonance imaging, SPECT=single-photon emission computed tomography perfusion scintigraphy, LV=left ventricular.

From a pathophysiological point of view, biological signals as generated from PET and SPECT or histological examination provide important insights into viability at the cellular or molecular level. ^{18}F-fluorodeoxyglucose (FDG) uptake in myocardial tissue indicates preserved viability.[1] High ^{99m}Tc-annexin affinity to the cellular wall, due to phosphatidyl-serine overexpression, indicates apoptosis, associated with programmed cell death.[19] Regional dysfunctional contractility of the left ventricle can be transiently reversed by positive inotropic stimulation. During stimulation with dobutamine infusion (used in MRI, gated SPECT or echocardiography), systolic wall thickness will increase in viable, but not in scarred myocardium, because only viable cells will respond to the inotropic stimulus. From a clinical point of view, the improved survival and symptoms following revascularisation are the optimal endpoint of viability studies, because these are considered the main goals of revascularisation procedures, but this requires a long follow-up period. The global improvement of LV function and reduction in end-systolic and end-diastolic volume (reverse remodelling) after revascular-

isation is probably an acceptable alternative, because this is easy to measure and is likely to be associated with improved prognosis.[18] PET is an attractive technique for the assessment of myocardial viability. This will be outlined in the next paragraph.

PET

PET imaging differs from conventional radionuclide imaging because it uses radionuclides that decay with positron emission. A positron has the same mass as an electron but has a positive charge. The positron travels a short distance, up to a few millimeters, interacts with an electron, and the two undergo a mutual annihilation, resulting in the production of two 511-kev gamma photons, 180° apart from each other. PET imaging consists of detection of these photons in coincidence in a ring detector system. Imaging by PET leads to high acquisition efficiency, resulting in high-quality images.

The clinical utility of PET imaging to identify viable myocardial tissue was first described by Tillisch et al. in the mid-1980s.[2] The accuracy of fluorine-18 fluorodeoxyglucose (FDG) (with or without an additional perfusion tracer) imaging for predicting improvement in LV function after revascularisation, as reported in several previous studies, is high, with a negative predicting value ranging from 76 to 90% and a positive predicting value ranging from 82 to 100%.[17,20-24] Therefore, PET is recognised as an accurate technique for the quantification of metabolism and perfusion of the myocardium, resulting in high diagnostic accuracy for the detection of myocardial viability.

Metabolic imaging: FDG

Fatty acids play a major role in the metabolism of the nonischaemic heart, whereas glucose becomes the major substrate for the myocardium during ischaemic conditions.[25] FDG closely resembles glucose and is therefore a suitable tracer to visualise glucose metabolism.

A prerequisite for FDG imaging of the heart is high myocardial uptake. For most studies using FDG, glucose loading either by oral glucose administration or by insulin clamp is essential. Euglycaemic-hyperinsulinaemic clamping is an approach that mimics the postabsortive steady state and leads to an enhancement of glucose utilisation. Insulin clamping stimulates uptake of both glucose and FDG in the myocardium and yields images of consistently high diagnostic quality, even in patients with diabetes. Acipimox, a nicotinic acid derivate, may be an alternative to clamping. Acipimox inhibits peripheral lipolysis and therefore reduces plasma free-fatty acid levels, and, indirectly stimulates cardiac FDG uptake in this way.[26] Previous data have shown that good image quality can be obtained using acipimox (comparable with clamping and superior to oral glucose load).[27]

The clinical applicability of FDG is based on the effective intracellular trapping after phosphorylation of FDG into FDG-6-phosphate. In contrast to glucose-6-phosphate, FDG-6-phosphate is not a substrate for further metabolism. Therefore, FDG enables detection of metabolic changes at the cellular level during ischaemia. The preserved or increased glucose utilisation, and subsequent FDG uptake in hypoperfused and dysfunctional myocardium (flow-metabolism mismatch) is regarded as a metabolic marker of cell survival and viability, whereas concordant reduction in both blood flow and FDG uptake (matched defect) is indicative of scar (figure 1).

Images are mainly interpreted semiquantitatively, based on the relatively regional uptake of FDG.[28] Absolute quantification of regional myocardial glucose utilisation by dynamic imaging and compartment modelling does

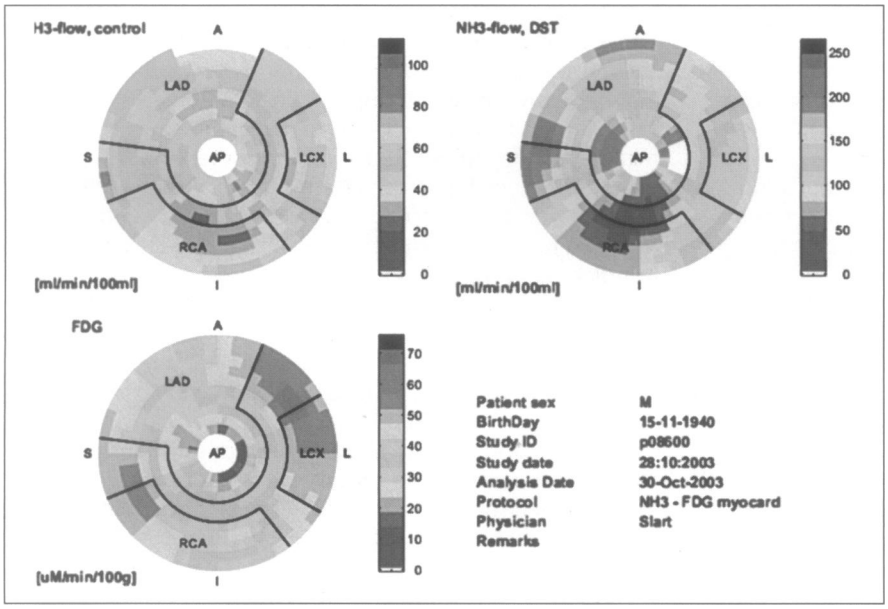

Figure 1. PET polar maps display. The first polar map illustrates rest ^{13}N-ammonia perfusion of the left ventricle. In the mid-inferior wall a relatively small defect is visible and becomes larger on the second, dypiridamole (DST) stress ^{13}N-ammonia perfusion polar map, indicating insufficient flow reserve. ^{18}F-fluorodeoxyglucose (FDG) in the inferior wall is largely preserved on the lowermost polar map, indicating ischaemia and viability. A minor FDG defect persists in the mid-inferior region, indicating a small infarcted area.

Table 2. Tracer properties.

Tracer	Assessment	*Uptake mechanism*
^{201}Tl	Perfusion/viability	Na^+/K^+-ATPase cell membrane pump
^{99m}Tc-sestamibi	Perfusion (viability)	Mitochondrial K^+-ATP channel
^{99m}Tc-tetrofosmin	Perfusion (viability)	Mitochondrial K^+-ATP channel
^{15}O-water*	Perfusion	Diffuses freely across cell membrane
^{13}N-ammonia*	Perfusion	Diffuses freely across cell membrane. The ammonium form is intracellularly trapped in glutamine via the enzyme glutamine synthase
^{82}Rb*	Perfusion/viability	Na^+/K^+-ATPase
^{18}FDG	Glucose consumption	Intracellular trapping after phosphorylation of FDG to FDG-6-phosphate
^{11}C-acetate*	Oxidative metabolism/perfusion	Converted intracellular to acetyl-CoA and further metabolised in the Krebs cycle of the mitochondrion to $^{11}CO_2$
^{11}C-palmitate*	Free fatty acid metabolism	FFA intracellularly converted to FFA-CoA, cleavage of carbon fragments of FFA-CoA during β-oxidation and further metabolised in the Krebs cycle of the mitochondrion to $^{11}CO_2$

Ti=thallium, Tc=technetium, Rb=rubidium, FDG=^{18}F-fluorodeoxyglucose, FFA=free fatty acids. *Short-living PET tracers.

not appear to enhance the diagnostic accuracy of FDG PET to detect viable myocardium, probably because of high variability in glucose utilisation rates in individual patients, even in comparison with a normal database.[29]

Metabolic imaging: fatty acids

Under aerobic conditions, the heart uses predominantly fatty acids, but after carbohydrate loading, the inhibitory effect of insulin on release of fatty acids from adipocytes diminishes circulating fatty acids and upregulates glucose use by the heart. During myocardial ischaemia, fatty acid metabolism is diminished and glucose uptake is enhanced.[30] Normal (relative to flow) or enhanced glucose metabolism serves as the metabolic signature of ischaemic myocardium. Stunned or hibernating myocardium also demonstrates preserved oxygen use relative to perfusion and function.[31]

Because the diminished use of fatty acids is a key metabolic feature of myocardial ischaemia, early interest with PET focused on the use of fatty acids such as ^{11}C-palmitate (table 2).[32]

However, because of its relatively complicated synthesis, the need for an on-site cyclotron, and the complex tracer kinetics, this tracer is not currently used for identification of viable myocardium.

^{11}C-acetate is also a PET tracer for studying myocardial oxidative metabolism and a marker of regional myocardial blood flow, because of its relatively high first-pass extraction in myocardial tissue. However, this tracer also requires a cyclotron in addition to the assessment of washout kinetics, thereby making this tracer somewhat less useful for most centres.

Flow tracers

The ideal tracer for the assessment of myocardial perfusion would possess the following properties: distribution in the myocardium in linear proportion to blood flow (without plateau effect at high flow rates) over the full range of values experienced in health and disease, efficient myocardial extraction from the blood on the first passage through the myocardium, stable retention within the myocardium during data acquisition, rapid elimination allowing rapid repeat studies, good availability, competitive pricing and good imaging characteristics (short half-life, high photon flux, adequate energy, low radiation burden to the patient). No current tracer possesses all of these properties and compromises have to be made.

Absolute quantification of myocardial blood flow is feasible using PET and tracer kinetic models.[33] In clinical practice, FDG PET is often combined with a flow tracer to assess myocardial perfusion. Although FDG PET imaging without a flow tracer has sufficient sensitivity and specificity for detecting viable tissue,[34] a combination of flow and metabolism provides more comprehensive information on viability and thus the differentiation between hibernation and stunning.[35]

^{13}N-ammonia

^{13}N-ammonia allows quantification of perfusion both at rest and after application of vasodilatating agents to assess myocardial perfusion reserve, such as dipyridamole or adenosine.[33] With the use of a two- or three-compartmental model, satisfactory reproducibility and accuracy can be obtained.[33]

The suitability of ^{13}N-ammonia as a myocardial flow tracer has been established in numerous studies.[33,36,37] Kitsiou et al. demonstrated that ^{13}N-ammonia retention rather than absolute myocardial blood flow was a good marker of cellular viability.[38] The use of ^{13}N-ammonia is restricted to sites with a cyclotron.

^{15}O-water

Unlike ^{13}N-ammonia, ^{15}O-water diffuses freely across plasma membranes and makes this tracer a favourite for quantification of myocardial blood flow. In theory, ^{15}O-water is considered to be an ideal tracer for measurement of myocardial blood flow without plateau effect at high flow rates.[39] However, poor contrast between the myocardium and cardiac blood pool, due to the properties of ^{15}O-water (necessity for subtraction of blood pool activity), and a very short physical half-life time may cause heterogeneity of flow measurements, as demonstrated by Nitzsche et al.[40]

The use of ^{15}O-water is restricted to sites with a cyclotron.

Rubidium-82 (^{82}Rb)

^{82}Rb is produced in a commercially available generator by decay from strontium-82 attached to an elution column. ^{82}Rb decays by positron emission with a short half-life of 75 s. Therefore it facilitates the rapid completion of a series of resting and stress myocardial perfusion studies. ^{82}Rb, just as thallium-201, is a cation and an analogue of potassium. Uptake of ^{82}Rb is a function of both blood flow and of myocardial cell integrity. Unlike ^{201}Tl, there are minimal problems with liver or bowel uptake. PET imaging with ^{82}Rb has proven to be highly accurate in the detection and functional assessment of coronary artery stenoses and infarct size imaging.[41]

Gated FDG PET

Compared with echocardiography, MRI, CT, gated SPECT, gated blood pool SPECT, and PET systems also offer the capability to perform an electrocardiograph (ECG)-gated acquisition and to generate systolic and diastolic images of the heart.[42,43] In combination with myocardial perfusion, gated FDG PET permits a complete LV evaluation, using a single modality for evaluation of major myocardial parameters, including glucose metabolism, flow reserve and LV function. Assessment of cardiac function by gated FDG PET without the need for other clinical modalities will significantly reduce the time and costs of pre-revascularisation work-up. Other PET techniques including gated blood pool PET after red blood cell labelling with C^{15}O[44] or gated ^{13}N-ammonia[45] also provide information about LV volumes and function, but give no information about metabolism.

SPECT

Myocardial perfusion scintigraphy (MPS) SPECT is an established imaging technique that is already an integral part of the managing of coronary artery disease and is included in a number of professional guidelines. Many studies have assessed the diagnostic accuracy of MPS for the detection of coronary artery disease.[46-48] In a study of 2560 patients randomised to each of the three tracers (^{99m}Tc-sestamibi, ^{99m}Tc-tetrofosmin and ^{201}thallium) and using mainly adenosine stress (the ROBUST study, UK based), overall sensitivity in the subset of patients undergoing angiography was 91% and specificity 87%, with no significant difference between the three tracers.[46] For many patients with coronary artery disease, the assessment of prognosis, or likelihood of future cardiac events is an essential step in choosing between medical management and revascularisation. MPS is perhaps the area of nuclear cardiology where the evidence is most strong.[49-51] The most important variables that predict the likelihood of future events are the extent and severity of induced ischaemia[52] but other predictors are increased lung uptake of ^{201}thallium[53] and stress-induced ventricular dilatation.[54] MPS has incremental prognostic value even after clinical assessment, exercise electrocardiography, and coronary angiography.[55] In contrast, a normal MPS indicates good clinical outcome with <0.6% event rate of major cardiac events yearly as reported in a multicentre registry of 4728 patients.[56] Further, ^{99m}Tc-labelled myocardial perfusion tracers reflect not only flow, but also myocardial viability.[22]

^{201}Thallium

The active uptake of ^{201}Thallium (^{201}Tl) by myocardial cells is dependent on myocardial blood flow and active transport.[57] ^{201}Tl is a potassium analogue that is actively transported into myocytes by a Na^+/K^+-ATPase-dependent mechanism. Its uptake thus requires an intact, functional cell membrane. Therefore, myocardial ^{201}Tl uptake represents both myocardial perfusion and cellular viability. Modified ^{201}Tl protocols such as reinjection technique[4] have enhanced the detection of viable myocardium, although viability in myocardium may still be underestimated by ^{201}Tl as compared with FDG PET. Kitsiou et al. showed that stress induced reversible defects are highly predictive of functional recovery after revascularisation.[58] Therefore, the use of stress and redistribution imaging protocol is preferred.

^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin

Technetium-99m labelled flow tracers such as ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin are lipophilic and positively charged, and now widely available as alternatives to ^{201}Tl. Compared with ^{201}Tl, these ^{99m}Tc-labelled agents emit higher energy photons yielding better image quality, and the shorter half-life time of ^{99m}Tc allows the administration of higher doses. Experimental studies have demonstrated that myocardial retention of both ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin requires cellular viability.[59] Uptake and retention of ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin is dependent on cell membrane integrity and mitochondrial function.[60]

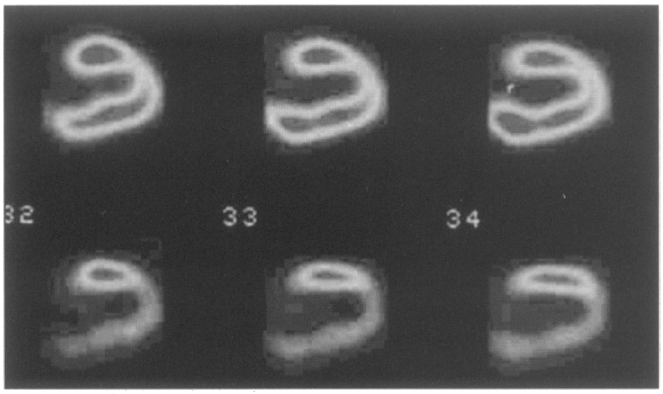

Figure 2. Improvement generated by attenuation correction (AC). Lower row shows vertical long-axis slices of myocardial perfusion rest SPECT without correction, showing a marked inferior defect originally judged to be an infarction. Upper row shows corresponding images after AC, now correctly normal.

Udelson et al.[61] described the utility of ^{99m}Tc-sestamibi for the prediction of functional recovery after revascularisation, which was comparable with that of ^{201}Tl in patients with severe CAD. Similar results have been reported for ^{99m}Tc-tetrofosmin, a relatively newer ^{99m}Tc-labelled flow tracer.[62]

Methods to enhance the detection of viability: nitrates

Nitrates improve collateral blood flow to hypoperfused myocardial regions as demonstrated in previous studies using ^{201}Tl imaging.[63] Bisi et al.[64] proposed that nitrates might have a role in improving the ability of ^{99m}Tc-sestamibi imaging to predict myocardial viability. Several more recent studies have demonstrated that the use of nitrates further improves the diagnostic accuracy of viability tests with flow tracers.[63,65]

Attenuation correction

It is well known that attenuation artefacts may unfavourably affect the diagnostic accuracy of myocardial perfusion SPECT imaging. The nonuniform attenuation of the emitted radiation may produce severe artefacts which may result in fixed defects on SPECT images that could easily be mistaken for myocardial infarction. Common causes of attenuation artefacts are associated with breast attenuation in women, and diaphragmatic attenuation in men.

Attenuation correction using transmission scans may help in distinguishing attenuation artefacts from myocardial infarction patterns, especially in the posterior, posterolateral and posteroseptal wall, where misinterpretation is most common. Several methods for transmission scan based attenuation correction have now become available.[66] Commercialised SPECT attenuation correction systems measure the non-homogeneous attenuation distribution utilising external collimated radionuclide sources[67] or X-ray CT with hibrid systems.[68] Attenuation correction may considerably change the appearance of images that readers have long been used to (figure 2).

Gated SPECT

The widespread application of ^{99m}Tc-labelled myocardial perfusion tracers and data processing capacity have made ECG-gated SPECT imaging part of the clinical routine in nuclear imaging laboratories.[69] The automatic quantification of LV volumes, ejection fraction (EF), regional myocardial wall motion and thickening from gated SPECT is rapid and accurate, with minimal operator interaction, and is therefore widely used. Gated SPECT is also valuable in its ability to enhance artefact identification by differentiating scarred tissue from attenuation artefacts, because these artefacts reveal normal wall motion and thickening. The combination of gating and attenuation correction provide the highest diagnostic accuracy and should be considered complementary.[70] Gated SPECT imaging also showed an important role in the risk assessment of patients with known or suspected CAD.[71] Travin et al. demonstrated in a group of 3207 patients that abnormal gated SPECT wall motion score was associated with an annual event rate of 6.1% compared with 1.6% for a normal score, and an abnormal left ventricular ejection fraction was associated with an event rate of 7.4% compared with 1.8% for normal patients.[72]

FDG SPECT and DISA SPECT

Substantial effort has been invested in the development of SPECT using extra-high energy collimators, which may permit larger scale clinical use of FDG imaging.[73-75] Several clinical studies have shown that FDG SPECT offers diagnostic information similar to PET. Despite the difference in resolution of both systems, FDG SPECT shows a good agreement (94%) with ^{18}FDG PET.[76] As with PET studies, metabolic activity measured by FDG SPECT is generally interpreted in combination with a flow tracer. For this purpose, a dual-isotope simultaneous acquisition (DISA) SPECT protocol with FDG and ^{99m}Tc-perfusion tracer is attractive because it enables assessment of myocardial glucose utilisation and perfusion in a single study (figure 3).[75,77]

DISA SPECT shortens the duration of the procedure, with the advantage of an identical geometric registration of the different isotope images. Matsunari et al. published a small study about the concordance and discordance of ^{99m}Tc-sestamibi/FDG DISA SPECT and ^{13}N-ammonia/FDG PET in ten patients with CAD, by using the difference between the perfusion tracer and ^{18}FDG of both techniques.[77] They found a good overall concordance between the activity distribution of FDG and flow tracers of both techniques.

Different FDG-perfusion patterns can be observed in the left ventricle with contractile dysfunction

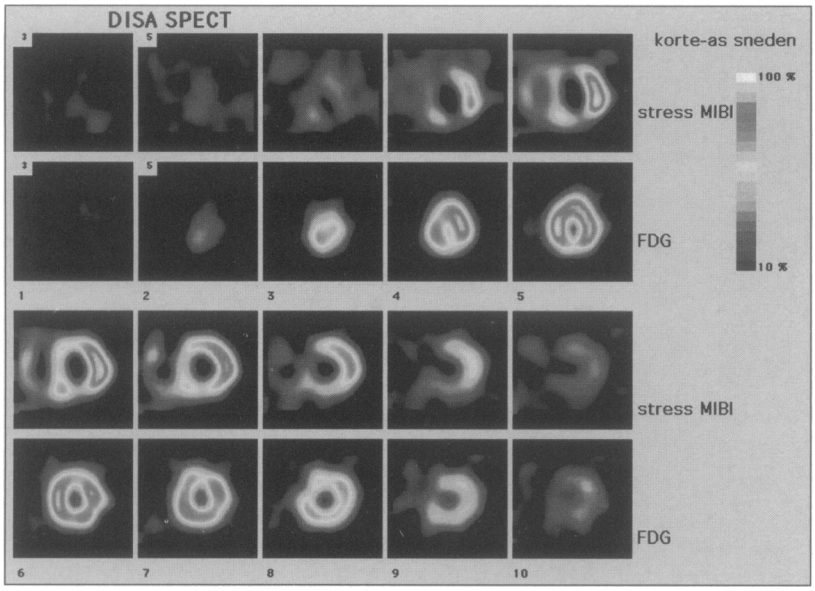

Figure 3. Short-axis view of a dual isotope simultaneous acquisition (DISA) SPECT image. The first row demonstrates a large perfusion defect in the apex, mid-anterior, septal and inferior wall after (dypiridamole) stress ^{99m}Tc-sestamibi. The simultaneously performed FDG study on the second row shows adequate uptake in these regions, indicating ischaemia or preserved viability.

(table 3). ECG-gated FDG SPECT or DISA SPECT is an additional technique to assess LV function.[78] DISA SPECT has the potential to assess myocardial glucose utilisation, perfusion, and LV function in a single study.

SPECT/CT and PET/CT

The introduction of the combination of CT scans into SPECT and PET systems is a recent development. For cardiological purposes CT could be used for attenuation correction, calcium score, functional LV assessment and visualisation of coronary arteries and accompanying stenoses.

A potential application of the single combined unit is the possibility of obtaining coronary calcium scores at the same imaging session as the SPECT or PET scan, which is feasible with an 8- or 16-slice multi-detector CT scanner. The clinical value of coronary calcium scoring is currently still an open question in clinical practice and its interaction and significance needs to be explored.[79]

An intriguing possibility is the potential value of CT coronary angiography performed together with PET rest and stress for viability imaging. Multislice (16 slices or greater) CT (MSCT) scans have been found to have sufficient temporal resolution to image, with intravenous contrast, coronary arteries with a diameter or 1.5 mm or greater.

There are limitations in visualising lesions in the smallest distal vessels, and in the presence of heavy calcifications. The latter limitation can be overcome with the aid of the PET perfusion results.

It is conceivable that patients with known or suspected disease could be studied with sequential stress-rest perfusion imaging and CT angiography and ventriculography, allowing acquisitions of superimposed images of both coronary anatomy, perfusion, wall motion, and viability. This complete set of spatially mapped information could add precision and ease to decision-making for interventions in multivessel disease intervention planning, or in patients with physiologically abnormal perfusion but anatomically normal coronary arteries. This proposition still needs to be evaluated in clinical studies, because the experience of PET/CT is scarce at present.

Conclusion

Imaging techniques in nuclear cardiology play an important role for the noninvasive evaluation of myocardial viability in patients with coronary artery

Table 3. Different FDG-perfusion patterns in left ventricle with contractile dysfunction.

	Contraction	Perfusion	FDG uptake	Recovery after revasularisation
Normal myocardium	N	N	N	
Repetitive stunning	↓	N	N to ↑	+
Hibernation	↓	↓	N to ↑	+
Transmural scar	↓	↓↓	↓↓	–
Nontransmural scar	↓	↓	↓	–/+

N=normal, ↓=decreased, ↓↓=severely decreased, ↑=increased. FDG=^{18}F-fluorodeoxyglucose.

disease. It becomes clear that FDG is a very accurate tracer for the assessment of myocardial viability. With the new developments in attenuation correction, DISA SPECT, gated FDG PET and combined cameras (PET/CT or SPECT/CT), addition of nitrates, accuracy for the detection of myocardial ischaemia and viability will be further improved. The increasing infrastructure of PET(/CT) scanners, and availability of FDG have set the stage for more widespread use of PET(/CT) for indications shown to be of benefit. The question to be addressed is whether the additional costs imposed by the different techniques are offset by the improved diagnostic accuracy. Addition of a combined SPECT/CT camera system to DISA SPECT will further improve the accuracy for the assessment of myocardial viability, especially the added value of CT for attenuation correction, calcium score and functional LV measurement. ■

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