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# Function and anatomy: SPECT-MPI and MSCT coronary angiography

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**KEYWORDS**

*SPECT, CT, coronary artery disease, myocardial perfusion imaging*

## Abstract

For the diagnosis of coronary artery disease (CAD), non-invasive cardiac imaging is indispensable. Myocardial perfusion imaging (MPI) by single photon emission computed tomography (SPECT) investigates the pathophysiological consequences of luminal obstructive CAD, while multislice computed tomography coronary angiography (CTA) indicates the presence, extent and location of coronary atherosclerosis. The integration of CTA and SPECT data may provide important information which may be useful for patient management. In this manuscript the value of both techniques will be described. In addition, the feasibility and potential value of combined anatomic and functional imaging will be discussed.

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## Introduction

Coronary artery disease (CAD) is still one the most prevalent healthcare problems in the industrialised world. Cardiovascular imaging plays an important role in the diagnosis of CAD. In the last decades several non-invasive functional imaging techniques such as single photon emission computed tomography (SPECT), magnetic resonance imaging and contrast echocardiography have become readily available. SPECT myocardial perfusion imaging (MPI) in particular is generally widely used and a well established non-invasive tool for the diagnosis of ischaemic coronary disease. Reflecting the pathophysiological consequences of luminal obstructive CAD, this technique has been used for more than 30 years and has proven to be highly accurate.[1,2]

In recent years, non-invasive assessment of cardiac anatomy has also become possible with the introduction of multislice computed tomography coronary angiography (CTA), which allows for detection of significant CAD with a high diagnostic accuracy compared to conventional invasive coronary angiography.[3,4] Comparative studies between SPECT and CTA have shown that a significant stenosis detected on CTA, results in a perfusion abnormality on SPECT in only approximately 50% of patients, conversely a normal SPECT was unable to rule out the presence of significant CAD or atherosclerosis in general.[5,6] CTA and SPECT thus provide complementary information regarding the presence and haemodynamic effects of CAD. As a result the focus of non-invasive imaging has shifted towards combined assessment of both anatomy and function. In this review we will briefly describe the technique and clinical applications of SPECT and CTA, and we will describe the usefulness and the advances in combined anatomic and functional imaging.

## Myocardial perfusion imaging by SPECT

### The technique

The underlying principle of this technique is that under conditions of stress, territories supplied by diseased coronary arteries receive less blood flow than normal myocardium. A cardiac specific radiopharmaceutical (Technetium-99 m or Thallium-201) is administered, while the heart rate is raised (exercise or dobutamine) to induce myocardial stress or during maximal vasodilatation by adenosine or dipyridamole infusion. SPECT is a nuclear tomographic imaging technique using gamma rays, which are emitted by the injected radiopharmaceutical. SPECT imaging is performed by using a gamma camera to acquire 2-dimensional images from multiple angles. A computer is used to apply a tomographic reconstruction algorithm to the multiple projections, yielding a 3-dimensional dataset. This dataset may then be manipulated to show thin slices along any chosen axis of the body. To acquire SPECT images, the gamma camera is rotated around the patient. Projections are acquired at defined points during the rotation, typically every 3–6 degrees. In most cases, a full 360 degree rotation is used to obtain an optimal reconstruction. The time taken to obtain each projection is also variable, but 15–20 seconds is typical. This results in a total scan time of 15–20 minutes. SPECT imaging performed after stress reveals the distribution of the radiopharmaceutical, and therefore the relative blood flow to the different regions of the myocardium. Diagnosis is made by comparing stress images to a set of images obtained at rest. The site, extent and depth of these abnormalities are assessed. Homogeneous myocardial uptake of the tracer indicates normal myocardium and perfusion. Absence of the tracer means clinically significant infarction or coronary stenosis. A defect at stress images that normalises in the rest images indicates an inducible perfusion abnormality, and generally corresponds to a significant coronary stenosis. A defect both at stress and rest images (a fixed defect) indicates an area with loss of viable myocardium, for instance myocardial infarction. With SPECT, it is possible to obtain cardiac gated acquisitions. Triggered by the electrocardiogram (ECG) to obtain differential information about the heart in various parts of its cycle, gated myocardial SPECT can be used to obtain quantitative information about myocardial perfusion, thickness, and contractility of the myocardium during various parts of the cardiac cycle. It also allows calculation of left ventricular ejection fraction, stroke volume, and cardiac output. In addition, distinction between true perfusion abnormalities and true artefacts is possible. Regions with true perfusion defects that are non-reversible will contract abnormally, while those associated with attenuation artefacts would demonstrate normal motion and thickening.

### Clinical application

In clinical practice MPI-SPECT is commonly used for the following indications:

1: diagnosis of suspected CAD in patients with an intermediate risk of CAD
2: risk stratification in patients with suspected and proven CAD
3: risk assessment before non-cardiac surgery
3: detection and quantification of viability/hibernating myocardium
4: assessment of functional significance in patients with proven multivessel CAD
5: assessment of intervention effect

For the diagnosis of CAD the extent and severity of an abnormal study is commonly used for the separation of patients into high and low risk for subsequent cardiac events. Patients with a low risk scan can be treated with medical therapy and unnecessary further testing and medical costs can be avoided.[7] On the other hand, patients with extensive and severe myocardial ischaemia have worse prognosis and are referred for invasive coronary angiography and may benefit from intervention.[8,9]

## Computed tomography coronary angiography

### The technique

Currently CTA scans are typically performed using a 64-detector row computed tomography scanner. After infusion of an iodinated contrast agent, patients are scanned during an inspiratory breath hold to counter acquisition problems arising from cardiac motion during breathing. To avoid coronary motion artefacts, acquired images are linked to the ECG in order to retrospectively select good quality images from a “motion free” phase of the cardiac cycle, typically end diastolic. Because of the need for end diastolic images of every level of the heart, and because of the limited coverage of the 64-detector row CTA scanner in the craniocaudal direction, acquisition of data is performed during multiple heartbeats. After acquisition, a dataset of the full heart is reconstructed with information obtained during the end diastolic phases of several heartbeats. Before the CTA scan patient's heart rate and blood pressure are generally monitored to determine the need for heart rate reduction. In the absence of contraindications patients with heart rate's exceeding 65 beats per minute are typically administered oral or intravenous beta blocking medication in order to reduce heart rate and improve image quality.

Several developments have occurred since the introduction of 64-detector row scanners. Dual-source scanners employing two X-ray tubes have been developed to increase temporal resolution resulting in improved image quality and less dependency on heart rate control.[10] A further improvement has been the introduction of prospective ECG gating which allows for acquisition of images during a small predetermined "motion free" part of the cardiac phase, which substantially lowers radiation dose to approximately 1.1-3.0 mSv.[11] Finally, entire cardiac coverage in one heart beat can be obtained by the recently introduced 320-slice detector row CTA system.[12] This decreases artefacts from the merging of data from different heartbeats and decreases radiation dose when used in combination with prospective ECG triggering.

CTA allows for non-invasive assessment of the coronary artery tree and is used for the detection of coronary artery stenosis. In contrast to invasive coronary angiography which only visualises contrast in the lumen, CTA is able to image the vessel wall thereby directly detecting coronary atherosclerosis. A differentiation can be made between normal coronary arteries showing no signs of atherosclerosis, non-significant CAD with <50% luminal narrowing and significant CAD with ≥50% luminal narrowing.

## Clinical application

Although CTA is still a relatively new cardiovascular imaging modality, its value in the assessment of patients presenting with suspected CAD is beginning to emerge. The diagnostic accuracy of CTA has been studied extensively. In early single centre studies an average weighted sensitivity of 97.5 (95% confidence interval 96-99) and specificity of 91 (95% confidence interval 87.5-95) have been observed for the detection of significant CAD compared to invasive coronary angiography.[13] More recently several prospective multicentre studies have been published showing similar sensitivities and specificities.[3,4] Importantly, CTA has an especially high negative predictive value, and as a result the technique is increasingly used as a gatekeeper for further diagnostic testing. In addition, data are emerging that early identification of CAD with CTA may be useful for risk stratification. Since the first publications on the prognostic value of CTA in 2007, a number of studies have been published providing further insight into the potential value of non-invasive anatomic imaging for risk stratification.[14,15] These studies have shown that patients with a significant stenosis on CTA have worse outcome as compared to patients without significant CAD. An annualised event rate for the occurrence of all cause mortality and myocardial infarction ranging between approximately 1% and 5% has been observed in patients with significant CAD compared to approximately 0% to 2% in patients without significant CAD.

## Combined anatomic and functional imaging

The combination of anatomic and functional imaging has the potential to improve patient management by providing complementary information for diagnosis of CAD. Assessment of the presence of coronary stenosis on CTA and its haemodynamic consequences as assessed by SPECT may improve decision making regarding referral to invasive coronary angiography and potentially revascularisation. In addition, it has been shown that CTA and SPECT provide complementary prognostic information; thus combined assessment may potentially improve risk stratification.[16]

Combination of CTA and SPECT data can be acquired using different approaches. Besides separate or side-by-side analysis of datasets (Figures 1 and 2), CTA and SPECT scan data can be retrospectively fused using image integration software.[17] By integration of the datasets, perfusion defects may be more accurately allocated to the corresponding arteries and lesions. In a study by Gaemperli et al, the accuracy of cardiac image fusion was determined.[18] An example of this is shown in Figures 3 and 4. The authors concluded that in almost one third of patients, fusion of CTA and SPECT provided additional diagnostic information compared to side-by-side analysis of SPECT and CTA, especially in functionally relevant lesions in distal segments and diagonal branches and in vessels with extensive disease or calcifications. In addition to retrospective fusion of datasets, CTA and SPECT data can also be integrated by use of dedicated hybrid SPECT/CTA scanners.[19] Hybrid SPECT-CT imaging first application was for the apparent reduction in tracer uptake in the anterior wall of the heart due to breast attenuation or in the inferior wall of the heart due to "diaphragmatic" attenuation, which

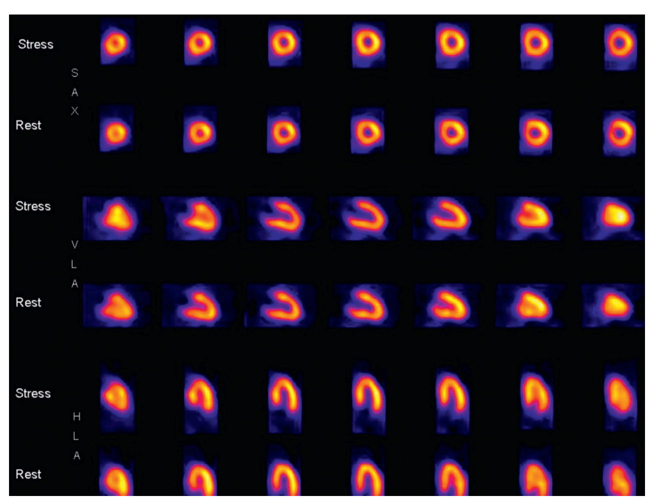


*Figure 1. SPECT-MPI of a 59 year old south-Asian male with diabetes, hypertension and hypercholesterolaemia referred for screening of silent myocardial ischaemia. There is normal uptake of the tracer in the entire myocardium, without reversibility or persistent defect. ECG-gated images showed no wall motion abnormalities and good global left ventricular function at rest and post-stress. SAX: short axis; VLA: vertical long-axis; HLA: horizontal long-axis*


*Figure 2. CTA in the same patient as Figure 1, shows diffuse coronary atherosclerosis. Panel A shows a 3D image of the heart. Panel B: Right coronary artery (RCA), proximal in the RCA - There is a non-calcified plaque (black arrow) and the mid RCA shows a mixed plaque (white arrow). Panel C: Left descending artery (LAD), with a non-calcified plaque in the left main (black arrow) with significant stenosis. Furthermore, there is a long mixed plaque from the proximal LAD till mid LAD (white arrows) with significant stenosis. Finally, there is a non-calcified plaque (black arrow) in the mid LAD. Panel D: Left circumflex artery (LCx) and the marginal obtusus (MO) branch, showing again the significant stenosis of the LM (black arrow). The patient was referred for invasive angiography, confirming the suspicion of significant three-vessel disease and significant left main stenosis. The patient underwent uneventful coronary artery bypass grafting.*

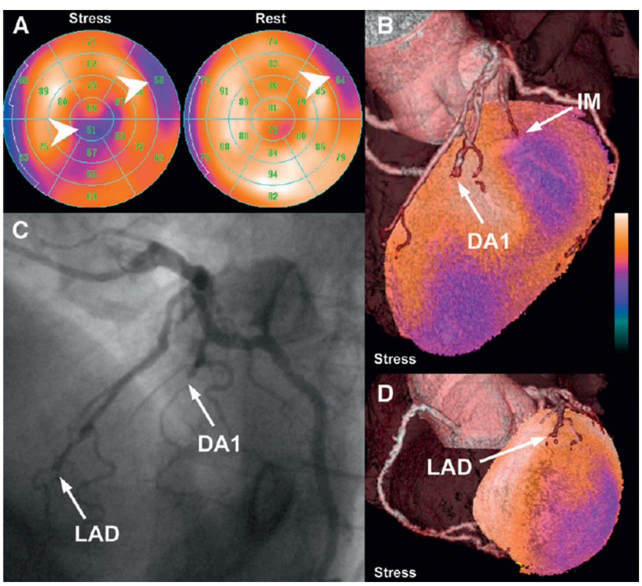


*Figure 3. (A) Stress and rest perfusion polar maps of SPECT-MPI study show mixed basal anterolateral defect and reversible inferoapical perfusion defect (arrowheads). (B and D) Fused SPECT/CT images reveal total occlusion of ramus descending artery (LAD) and subtotal occlusion of first diagonal branch (DA1), which are confirmed by conventional coronary angiography (C). Anterolateral perfusion defect is caused by lesion of partially calcified small intermediary branch (IM); however, this vessel is not well visualised by conventional angiography. (Reprinted by permission of the Society of Nuclear Medicine from: Gaemperli O, Schepis T, Valenta I, et al. Cardiac Image Fusion from Stand-Alone SPECT and CT: Clinical Experience. J Nucl Med. 2007;48:696-703. Figure 2.)*

can lead to diagnostic challenges. An example of this application is shown in Figures 5 and 6. Since the enormous progression of image quality of the coronary arteries from the CT scanners, hybrid SPECT-CT imaging can nowadays not only be used for attenuation correction but for “real” image fusion of the coronary arteries and

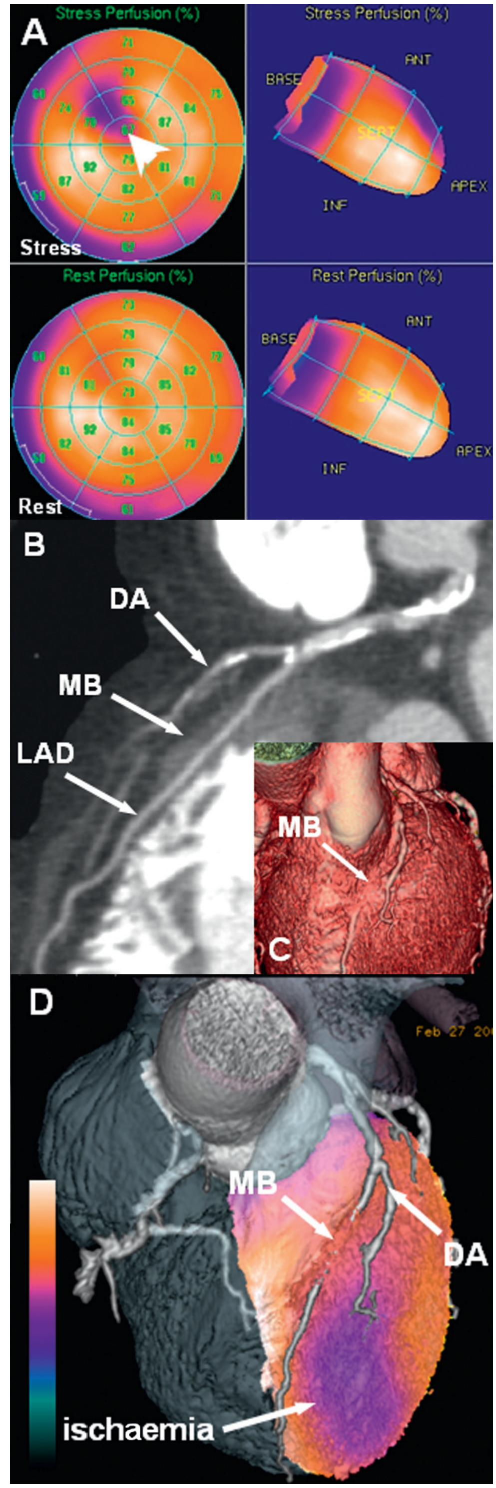


*Figure 4. (A) Perfusion polar maps at stress (dobutamine stress) and rest show reversible anteroseptal perfusion defect. (B and C) 64-slice MSCT-angiography revealed myocardial bridging (MB) of mid LAD of 0.2-cm length and calcified plaque at origin of first diagonal branch (DA). (D) Fused 3D SPECT/CT images could allocate reversible perfusion defect to DA, whereas MB seemed to be haemodynamically insignificant. (Reprinted by permission of the Society of Nuclear Medicine from: Gaemperli O, Schepis T, Valenta I, et al. Cardiac Image Fusion from Stand-Alone SPECT and CT: Clinical Experience. J Nucl Med. 2007;48:696-703. Figure 3.)*

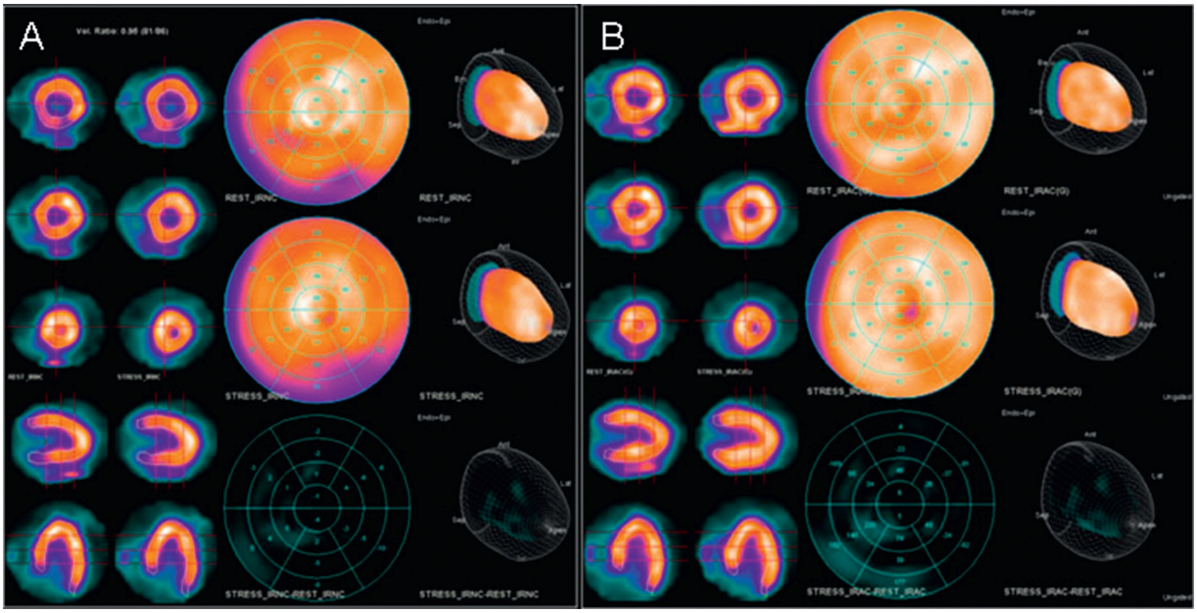


*Figure 5. SPECT-MPI imaging of a 57-year old male with hypertension, hypercholesterolaemia and atypical chest pain. Panel A: Short-axis, vertical long-axis and horizontal long-axis view and polar map, without attenuation correction. Left rest, right stress images, showing a persistent defect of the inferior wall. Panel B: same patient and views with attenuation correction, showing no defect of the inferior wall.*

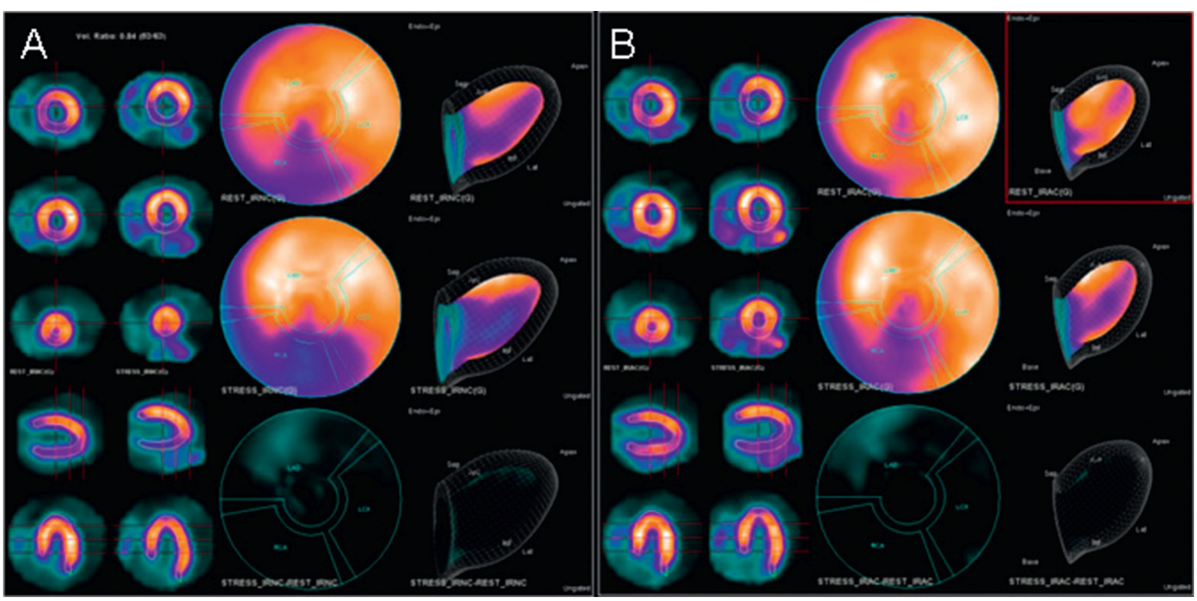


*Figure 6. SPECT-MPI imaging of a 66-year old female with obesity, diabetes and chest pain one week before presentation. Panel A: Short-axis, vertical long-axis and horizontal long-axis view and polar map, without attenuation correction. Left rest, right stress images, showing a partial reversible defect of the inferior wall. Panel B: same patient and views with attenuation correction, showing the same reversible defect as Panel A.*

myocardial perfusion of the left ventricle. It is unclear if the integration of CTA and SPECT using a hybrid SPECT-CTA scanner provides improved diagnostic imaging compared to retrospective fusion of separately obtained SPECT and CTA datasets. The use of a SPECT-CTA scanner may however be advantageous from a logistic point of view as patients can be scanned during a single session in a single room.

Although, the combination of SPECT and CTA using stand alone SPECT and CTA, or by use of a hybrid scanner may provide complementary information for diagnosis and risk stratification, it is questionable if information regarding anatomy and function is necessary in all patients referred for diagnostic imaging. In patients with a normal CTA (no evidence of coronary atherosclerosis) the likelihood of a perfusion abnormality is very low, and the survival rate is very high, suggesting that no further imaging is necessary in this subgroup. Furthermore as both CTA and SPECT are associated with ionising radiation and as most centres do not have access to a hybrid scanner, combined imaging may result in increased radiation burden and logistical problems. As a result, sequential imaging may be a more viable alternative approach. A flow chart advocating such a strategy has been recently published.[20] Using CTA as an initial imaging technique to rule out the presence of CAD, patients with a normal CTA can be safely discharged and do not require further testing. In patients with non-obstructive CAD (<50%) medical therapy and aggressive risk factor modification may be indicated. Patients with a significant or borderline lesion or patients with an unequivocal CTA may be referred for SPECT imaging to determine the haemodynamic effects on myocardial perfusion and to determine if revascularisation is indicated. Finally, patients with severe CAD detected on CTA may be directly referred to invasive coronary angiography. Such an approach may result in an overall reduction in mean radiation dose as was shown recently by Pazhenkottil et al[21]. Compared to combined CTA and SPECT imaging in all patients, an individualised three tiered approach of CTA followed by stress only SPECT followed by rest SPECT only, if the preceding scan was abnormal, resulted in an approximately 40% reduction in average radiation dose.

## Conclusion

Although, the first results of hybrid imaging using SPECT and CTA seems to provide additional clinical value compared to either technique alone or side-by-side analysis, more data are necessary to answer the following issues: What is the impact on treatment strategy and outcome? What is the radiation exposure to the patient? Is hybrid SPECT-CTA imaging cost-effective? Can the rapid changes in CTA technology and ultrafast MPI-SPECT be integrated in SPECT-CT machines? Although new low-dose CTA acquisition protocols with prospective ECG triggering and stress only SPECT MPI seems promising, more data are necessary to validate the clinical role of SPECT-CT.

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