Cardiovascular computed tomography for diagnosis and risk stratification of coronary artery disease

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Part 3

Future perspectives

Chapter 17

Myocardial perfusion imaging to assess ischemia using multislice computed tomography

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Abstract

Multi-slice computed tomography (MSCT) coronary angiography is an accurate non-invasive imaging technique, but cannot determine the functional relevance of the lesions it detects. However, MSCT perfusion imaging can detect the presence of myocardial infarction during rest and can assess viability using delayed enhancement. With recent developments in MSCT scanner technology it has become possible to image myocardial perfusion and the capability of MSCT to determine the presence of ischemia through perfusion imaging during stress is currently investigated. Although only limited data are available, non-invasive imaging with MSCT has the potential to assess both coronary anatomy and myocardial perfusion in one procedure. This review describes the feasibility of myocardial perfusion imaging using MSCT and its potential use in clinical practice.

Introduction

Imaging plays an important role in the diagnosis of coronary artery disease (CAD). In the last decades several non-invasive techniques such as single photon emission computed tomography (SPECT), MRI and contrast echocardiography have become readily available to assess myocardial perfusion in order to demonstrate the presence of ischemia. In recent years, non-invasive assessment of cardiac anatomy has also become possible with the introduction of multi-slice computed tomography (MSCT). MSCT coronary angiography (MSCTA) has emerged as an accurate and robust imaging technique, [1-4] which is able to detect the presence of atherosclerosis at an early stage and can accurately rule out the presence of significant CAD.[5] However, when significant CAD is detected, MSCTA is unable to assess the hemodynamic consequences, i.e. the effect on myocardial perfusion.[6-9] Accordingly, treatment decisions remain uncertain in case of a positive MSCTA as information on the presence of ischemia is needed.

The combination of this important limitation and recent progress in scan technology has renewed interest in the innovation of MSCT perfusion imaging. This review describes the feasibility and technical aspects of myocardial perfusion imaging using state of the art MSCT. In addition, the currently available evidence and its potential use in clinical practice will be discussed.

Feasibility of myocardial perfusion imaging using MSCT

CT perfusion imaging is based on myocardial tissue attenuation changes during the infusion of contrast medium. The ability to assess myocardial perfusion using CT technology was first studied around 1980.[10, 11] Following this breakthrough, others have studied CT perfusion imaging using electron beam computed tomography (EBCT) scanners first in animal models, [12-14] and later in humans.[15,16] The introduction of MSCT scanning technology resulted in a higher spatial resolution and enabled increasingly larger volume coverage in shortened acquisition times. With each new generation MSCT scanner the number of detectors increased, from 4 to 16 to 64, and up to 320 with the current state of the art systems. These advancements have enabled fast acquisition of coronary anatomy, and may also allow reliable visualization of myocardial perfusion. Moreover, because of its high spatial resolution MSCT perfusion imaging may even allow assessment of transmural perfusion.

MSCT acquisition techniques for perfusion imaging

Depending on the scanner system, different protocols can be applied to assess myocardial perfusion. Early studies have used a dynamic imaging protocol for absolute quantification of myocardial perfusion. With dynamic imaging the table is fixed and image data are acquired during the entire infusion of contrast. By measuring the changes in tissue attenuation over time, attenuation curves of the myocardium can be calculated.(Figure 1, panel A) In a recent study by George et al. myocardial perfusion was quantified in 6 mongrel dogs using dynamic 64-slice MSCT.[17] The authors employed two methods to quantify myocardial perfusion. The first approach was a semi-quantitative method based on the upslope of the time attenuation

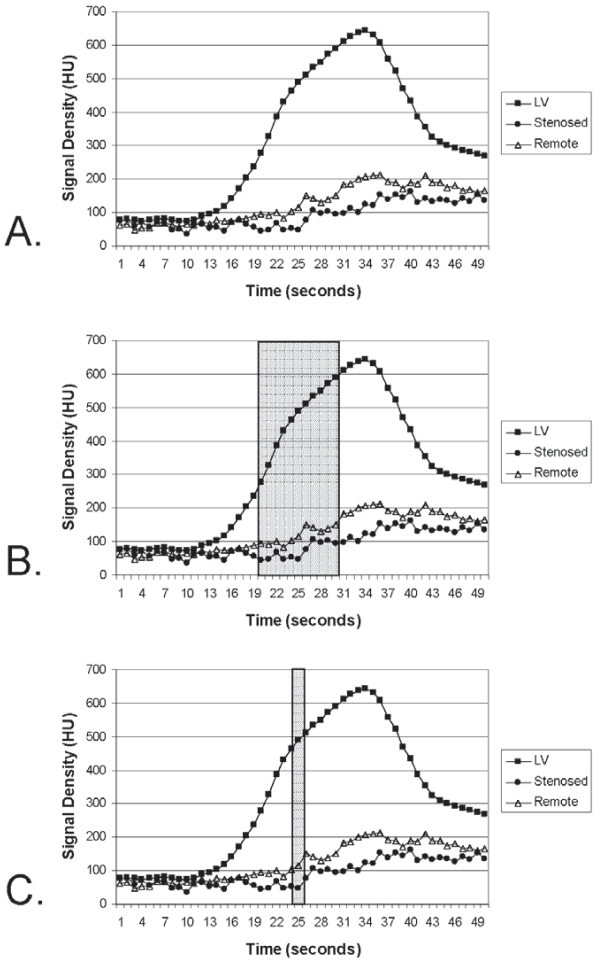

Figure 1. MSCT signal density time curves during infusion of adenosine and iodinated contrast agent using a dynamic imaging approach (panel A). The highlighted regions in panels A and B illustrate the acquisition window of retrospective ECG gated 64-slice helical scanning mode (panel B) and the acquisition window for prospective ECG gated 320-slice volumetric scanning mode (panel C). Adapted and reprinted with permission from reference 17.

curves of ischemic myocardium, normalized for the arterial/input function by dividing myocardial upslope by the left ventricular blood flow upslope or the upslope in a remote myocardial region. With the second approach the authors aimed to perform absolute quantification of myocardial blood flow by combining the time attenuation curves in a model representing the blood tissue exchange in the myocardium. Both methods resulted in an excellent correlation with microsphere derived myocardial blood flow. Although dynamic MSCT allows quantification of myocardial blood flow it is dependant on a prolonged acquisition time which is associated with a high radiation dose. Furthermore dynamic imaging with the current industry standard 64-slice MSCT only provides limited coverage; selected slices are acquired rather than the entire heart which limits its clinical utility.

A second approach to myocardial perfusion imaging with MSCT is ECG gated helical scanning or spiral imaging. This approach is currently used in 64-slice MSCTA protocols and can be used to cover a large area by moving the table slowly through the MSCT tube during acquisition of several heart beats. By gating the images to the ECG, it is possible to create reconstructions of the entire heart during different phases of the R-R interval. By selecting a phase with the least motion the heart can essentially be 'frozen' allowing motion free assessment of the coronary arteries but also of myocardial perfusion. With helical scanning data acquisition is started when a sufficiently high concentration of contrast agent has reached the coronary arteries. As a result, myocardial perfusion can be assessed with this approach only during the upslope of the contrast infusion and at the peak of contrast enhancement.(Figure 1, panel B) The cardiac reconstructions that are derived in this manner combine the information obtained from different heart beats, therefore absolute quantification is not possible. However myocardial perfusion may be assessed semi-quantitatively by measuring myocardial signal density in hypoenhanced regions of the myocardium and normalizing it to the signal density in remote myocardial segments or the left ventricular cavity.[18] This approach results in a signal density ratio which has been shown to correlate very well with microsphere derived blood flow measurements in animal models. Helical scanning enables larger coverage and reduces the scan time and therefore the radiation dose as compared to dynamic imaging. Nevertheless, imaging is still performed during several heart beats resulting in attenuation variations between base and apex. Furthermore helical scanning employs a considerable overlap; accordingly, radiation exposure remains substantial with this technique.

With the introduction of the novel 256- and 320-slice MSCT scanners, allowing true volumetric imaging, the difficulties associated with dynamic and helical scanning using current 64-slice scanners may be eliminated.[19-22] These state-of-the-art scanners have sufficient coverage to scan the entire heart within a single rotation. Through scanning in a dynamic mode, myocardial perfusion of the entire ventricle can be quantified. Furthermore, a full volume scan of the heart can be performed within a single heart beat, thereby reducing scan

time and radiation dose compared to helical scanning. The implementation of prospective ECG-triggering allows further reduction in radiation dose by scanning only during a small part of the R-R interval. The short scan time also results in more homogenous attenuation of the myocardium. With this new technique myocardial perfusion can be assessed during the upslope of contrast infusion by comparing uptake in stenosed and remote regions either visually, or semi-quantitatively using signal density ratios (Figure 1, panel C).[23, 24]

Rest and stress imaging

Assessment of myocardial perfusion at rest has been performed in animals and humans in several studies using first pass perfusion to determine the presence of resting perfusion defects indicating myocardial infarction.[25-30] Hypodense areas during arterial phase CT imaging may represent viable as well as necrotic myocardium. A distinction between viable and necrotic myocardium may however be made using delayed enhancement imaging.[31-34] In a study by Henneman et al. MSCT perfusion imaging was compared to SPECT imaging in 69 patients with previous infarction, of which 62 (90%) displayed a perfusion defect on SPECT.[25] The presence of hypoenhanced regions was identified on MSCT in all 62 patients. Nieman et al. showed that MSCT can also accurately detect late enhanced regions in a comparative study with MRI.[34]

Only few studies have evaluated stress imaging protocols for detection of inducible perfusion defects. In the previously mentioned studies by George et al. in dogs, [17,18] MSCT was able to assess ischemia during hyperemia in comparison to microsphere derived myocardial blood flow both quantitatively in dynamic mode as well as semi-quantitatively in helical scan mode. When using the semi-quantitative approach, mean myocardial signal density was significantly lower in stenosed (92.3±39.5 HU) versus remote myocardium (180.04±41.9), and a significant linear relationship was observed between the signal density ratio on MSCT and microsphere derived myocardial blood flow in both stenosed and remote territories within the clinically important range of flows (<8ml/g/min). Importantly, further research is needed to assess the accuracy of flow measurements also at lower ranges. An example of a myocardial perfusion abnormality observed on MSCT is shown in Figure 2. Recently, reports have been published on the feasibility of stress/rest myocardial perfusion imaging with MSCT in humans.[23, 35, 36] Kurata et al. performed a study in 12 patients undergoing both stress and rest perfusion imaging using 16-slice MSCT.[36] Myocardial perfusion was visually assessed and compared to SPECT. The authors observed an agreement of 83% between the MSCT and SPECT perfusion scans. In preliminary work by George et al. myocardial perfusion was assessed during rest and stress using a prototype 256-slice MSCT scanner.[24] Myocardial perfusion was quantified by comparing the attenuation values between sub-endocardial and subepicardial regions. This resulted in a transmural perfusion ratio which accurately detected the presence of significant CAD as compared to SPECT.

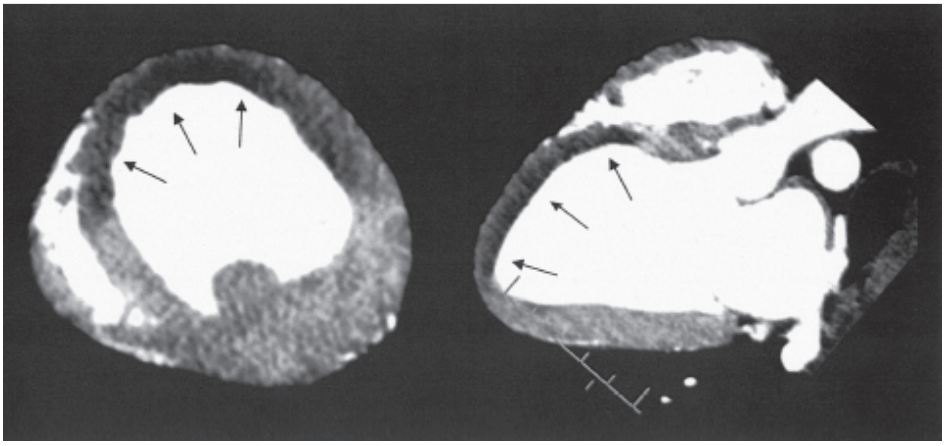

Figure 2. An example of a perfusion defect observed on MSCT using a helical acquisition mode. The stenosis in the left anterior descending coronary artery results in a perfusion defect of the anteroseptal, anterior, and anterolateral wall of the myocardium (arrows) as observed in the axial slice in panel A. In the long axis multi-planar reconstruction in panel B, the perfusion defect extends from the anteroseptal wall to the apex. Reprinted with permission from reference 17.

Alternative approaches

In preliminary studies with dual source CT myocardial tissue iodine content could be evaluated by using two detectors with different X ray spectra. Ruzsics et al showed in 35 patients with suspected or known CAD a good correlation between observations on MSCT and SPECT data.[37] A limitation of dual source CT technology however is the lack of cardiac coverage which may result in longer scan time with increased risk of contrast variations from base to apex. Another approach to perfusion imaging is the use of perfusion weighted color maps. Although they do not represent true perfusion imaging, they provide a surrogate of perfusion and enhance the ability to detect perfusion deficits.[38] Future research is however needed to further develop these techniques and establish their feasibility in clinical practice.

Potential clinical implications

Although only limited data are available, the studies that have been performed illustrate the potential of MSCT perfusion imaging. Because of its high spatial resolution and fast acquisition time MSCT may potentially have an advantage over conventional perfusion imaging using SPECT. Furthermore the ability to investigate patients with metal implants provides an advantage over MR perfusion imaging. Potentially, MSCT may serve as an alternative myocardial perfusion imaging technique in patients with contraindications to MRI. However, the major advantage of MSCT perfusion imaging may be the ability to combine perfusion with anatomy. This could allow comprehensive assessment of coronary anatomy and perfusion

during a single imaging procedure. With the use of new generation wide coverage scanners and prospectively triggered scan protocols, myocardial perfusion can potentially be assessed semi-quantitatively in combination with MSCTA with an acceptable radiation dose.[39] Such an integrated imaging approach has several advantages for the diagnosis and potentially the prognosis of CAD.

Complementary value for diagnosis of CAD

Anatomic and functional imaging modalities provide complementary information as has been demonstrated by previous studies comparing MSCTA to conventional perfusion imaging using SPECT.[6-9] In the study by Schuijf et al., only 50% of patients with a significant (>50%) lesion on MSCTA had an abnormal perfusion on SPECT.[9] Conversely, normal perfusion on SPECT was unable to rule out the presence of significant CAD or atherosclerosis in general. (Figure 3) The combination of anatomic and functional imaging in a single procedure may facilitate patient management. Patients with normal coronary anatomy without perfusion abnormalities can be discharged, while patients with significant CAD and abnormal perfusion may be directly referred for conventional coronary angiography followed by revascularization. Finally, those with (significant) atherosclerosis but without evidence of perfusion abnormalities will most likely benefit from risk factor modification and strict control at the

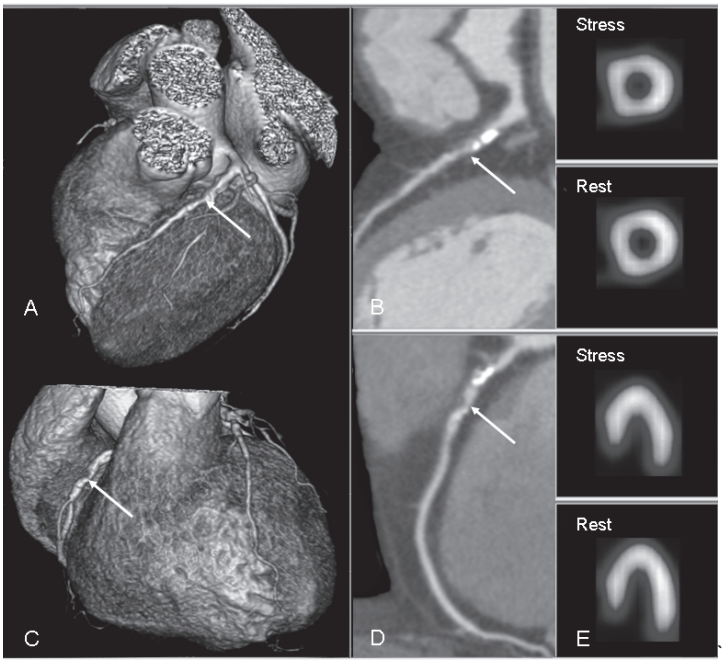

Figure 3. Case example of a patient with significant atherosclerotic lesions in both the left anterior descending coronary artery (arrows panels A, and B) as well as in the right coronary artery (arrows panels C, and D), while normal myocardial perfusion was observed (panel E).

outpatient clinic. Although improved management has not yet been proven, initial data support the notion that combined assessment of anatomy and perfusion may result in a higher diagnostic accuracy for the detection of hemodynamically significant coronary artery lesions.[40] By fusing both anatomic and perfusion datasets into a single, three-dimensional anatomic representation of the heart with overlying coronary anatomy, diagnostic accuracy may also improve on a vessel basis. This approach may enable accurate allocation of perfusion defects to the corresponding arteries. Gaemperli et al. assessed the accuracy of cardiac image fusion by combining MSCTA and SPECT.[41] The authors concluded that in almost one third of patients, fusion of MSCTA and SPECT provided additional diagnostic information, especially in functionally relevant lesions in distal segments and diagonal branches and in vessels with extensive disease or calcifications. Fusion of MSCTA and MSCT perfusion datasets may provide similar information with higher accuracy as misalignment between datasets will occurs less frequently.

Complementary value for prognosis

MSCT is a relatively new imaging technique. So far only limited studies are available assessing the prognostic value of MSCTA. Preliminary work by Pundziute et al. and by Min et al. has shown promising results.[42, 43] The presence of significant CAD is associated with an increased risk for cardiac events, while a completely normal MSCTA confers a very low risk. Conversely, perfusion imaging using SPECT has been well validated for risk stratification, and can accurately distinguish between patients at low and high risk for future cardiac events.[44-46] As MSCT and SPECT provide complementary information about the presence and extent of CAD, it is intuitively expected that their combined use may further improve risk stratification.[47] Although no prognostic data are available, combined assessment of myocardial perfusion imaging and coronary anatomy with MSCT may also provide increased risk stratification compared to the use of MSCTA or MSCT perfusion imaging alone.

Limitations

Several issues need to be resolved before MSCT perfusion imaging can be added to MSCTA in clinical practice. An important issue is radiation dose. Dynamic mode scanning is attractive since it allows quantification of myocardial blood flow, but is associated with a high radiation dose. Therefore imaging during first pass infusion of contrast using a semi-quantitative approach will probably be more feasible as exposure time and resulting radiation dose is less. Further developments in wide coverage scanners and prospective ECG-triggering, can potentially reduce the radiation dose to 7-11 mSv for combined perfusion and coronary angiography imaging.[39]

Secondly, when combining MSCTA with perfusion imaging, the combination of beta blockade - which is frequently required for MSCTA - and pharmacological stress needed for stress imaging may pose a problem. The use of beta blockers may alter the resting and hyperemic myocardial blood flow resulting in increased myocardial flow reserve, which may decrease the sensitivity for the detection of myocardial ischemia.[48, 49] Furthermore MSCTA will be less reliable during stress imaging as image quality decreases with increasing heart rates.

Finally a general limitation of MSCT is its limited temporal resolution, which can result in motion artefacts in the myocardium that can be mistaken for perfusion deficits. Other artefacts that may be observed are those caused by beam hardening. To circumvent this problem, extensive effort is currently invested to develop and validate beam hardening correction algorithms.[50] Furthermore temporal resolution has increased with dual source CT technology.[51, 52]

Conclusion

With the introduction of wide volume scanners enabling prospective ECG-triggering, MSCT perfusion imaging has become increasingly feasible. MSCT has the potential to visualize myocardial perfusion during rest and stress in combination with anatomic assessment of the coronary arteries. This may enable use of MSCT as a “one stop shop” for the diagnosis and potentially the prognosis of CAD. However, before MSCT perfusion imaging can be implemented in clinical practice, more clinical data are needed.

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