# Multimodality imaging in chronic coronary artery disease

Henneman, M.M.

# Chapter 5

# Comparison of multi-slice computed tomography to gated single photon emission computed tomography for imaging of healed myocardial infarcts

Maureen M. Henneman[1], Joanne D. Schuijf[1], Petra Dibbets-Schneider[2], Marcel P.M. Stokkel[2], Rob J. van der Geest[3], Ernst E. van der Wall[1], Jeroen J. Bax[1]

[1]Department of Cardiology, [2]Department of Nuclear Medicine, and the [3]Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands

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## Abstract

**Introduction:** Recently, multi-slice computed tomography (MSCT) has been demonstrated to allow detection of myocardial infarct by the presence of hypo-enhanced areas. However, direct comparisons with other imaging modalities for infarct imaging are scarce. The aim of the present study was to evaluate the performance of MSCT for detection and semiquantitative analysis of healed myocardial infarct in comparison with single photon emission computed tomography (SPECT).

**Methods:** In 69 patients with healed myocardial infarct (>3 months) the presence of myocardial infarct and infarct score was assessed on SPECT and MSCT. In addition, regional and global left ventricular (LV) function were assessed on MSCT.

**Results:** In 62 of the 69 (90%) patients a perfusion defect was detected on resting gated SPECT. On MSCT, in all these 62 (100%) patients hypo-enhanced areas reflecting infarct could be demonstrated. In 3 of the 7 (43%) patients without perfusion defects on gated SPECT, MSCT identified regions of infarct. Infarct score on MSCT related well with SPECT infarct score (12±10% vs. 16±13%, r=0.93, P <0.0001). In addition, good (inverse) correlations were shown for infarct score on MSCT and parameters of LV function.

**Conclusions:** Healed myocardial infarct can accurately be detected by MSCT, with a good correlation with SPECT.

# Introduction

Recently, several studies have suggested that myocardial infarct can be identified by hypo-enhanced areas on MSCT during contrast administration,[1-3] thus obviating the need for an additional examination. Ko et al.[1] investigated myocardial enhancement patterns with 2-phase MSCT in 16 patients with acute myocardial infarct. The authors demonstrated that hypo-enhanced areas could be detected on the early scans in 15 of 16 patients (94%). No comparison was performed with other imaging modalities for infarct imaging. The current study evaluates the performance of MSCT for the detection of healed myocardial infarcts in direct comparison with gated SPECT. Furthermore, semiquantitative analysis of infarct score was performed and compared between MSCT and gated SPECT. In addition, the relations between infarct score assessed with MSCT versus end-diastolic wall thickness (EDWT) in the infarct zone, wall motion score index (mean segmental wall motion score per patient, WMSI) and the left ventricular ejection fraction (LVEF) were determined.

# Methods

**Patients and study protocol**

Sixty-nine patients with previous myocardial infarct (>3 months before the study) who underwent 64-slice MSCT imaging and gated myocardial perfusion SPECT imaging to assess coronary artery disease, were included in the study protocol. Myocardial infarct was documented by typical chest pain lasting >30 minutes, elevated creatine kinase-MB protein and/or troponin-T and typical electrocardiographic changes. Contra-indications to MSCT included (supra-) ventricular arrhythmias, renal insufficiency (serum creatinine >120 mmol/l) and known allergy to iodine contrast media. In all patients the performance of MSCT for the detection of healed myocardial infarct was assessed. Furthermore, semi-quantitative assessment of the infarct score was performed and regional as well as global LV function was evaluated. In the center of the infarct region, the EDWT was measured. In addition, the performance of MSCT for the detection of infarct and the semiquantitative analysis of infarct score was compared with gated SPECT imaging. Also, the relations between infarct score on MSCT and EDWT, WMSI and LVEF were evaluated. All patients gave informed consent to the study protocol, which was approved by the local ethics committee.

**MSCT**

***Data acquisition***

MSCT examination was performed with a 64-slice Toshiba Multi-slice Aquilion 64 system (Toshiba Medical Systems, Otawara, Japan). Scan parameters were: a collimation of 64x0.5 mm and a rotation time of 400 or 450 ms, depending on heart rate. Tube current and voltage were 300 mA (range 250-400 mA) and 120 kV, respectively. A total amount of 80 ml contrast (Iomeron 400, Altana, Konstanz, Germany) was administered, followed by a saline flush of 40 ml. After a predefined threshold of +100 HU was reached in the region of interest placed in the aorta, the helical scan started automatically. All images were acquired during an inspiratory breath hold, while the electrocardiogram was recorded simultaneously for retrospective gating of the data. For evaluation, 5.0-mm slices were reconstructed in the short-axis orientation at 20 time points, starting at early systole (0% of cardiac cycle) to end-diastole (95% of cardiac cycle) in steps of 5%.

***Image analysis***

Reconstructed images were transferred to a remote workstation with dedicated cardiac function analysis software (MR Analytical Software System, Medis, Leiden, The Netherlands).[4] Two observers blinded to all other data, assessed by consensus the presence of healed myocardial infarct, which was defined as the observation of hypo-enhanced areas, on the short-axis slices using a 17-segment model.[5] The transmural extent of these hypo-enhanced areas was then evaluated using the same 17-segment model, with a 5-point score: 0=no hypo-enhancement, 1=a hypo-enhanced area involving 1%-25% of the LV wall, 2=a hypo-enhanced area involving 26%-50% of the LV wall, 3=a hypo-enhanced area involving 51%-75% of the LV wall, and 4=a hypo-enhanced area involving >75% of the LV wall.[6] To assess the performance of MSCT in the estimation of infarct score, all 17 scores were summed per infarct. The resulting summed score on MSCT ranged in theory from 0 to 68, and infarct score on MSCT was expressed as the percentage of the maximum possible score of 68.[7] Furthermore, the EDWT was measured quantitatively in the center of infarct. In addition, regional wall motion was evaluated by consensus on the short-axis slices using the same 17-segment model[5] and a 3-point scoring system was used to assign to each segment a wall motion score: 1=normokinesia, 2=hypokinesia, 3=a- or dyskinesia.[8] Subsequently, the WMSI was calculated on a per-patient basis. To determine LV function, endocardial borders were manually outlined on the short-axis images. The papillary muscles were regarded as being part of the LV cavity. The LV end-systolic and end-diastolic volumes were calculated and the LVEF was derived. Five patients had a history of 2 myocardial infarcts (all >3 months before entrance in the study). In these patients infarct score of both infarcts were assessed separately.

**Gated SPECT imaging**

***Data acquisition***

Resting myocardial SPECT imaging with technetium-99m tetrofosmin (500 MBq, injected at rest) was performed using a triple head SPECT camera system (GCA 9300/HG, Toshiba Corp.) equipped with low energy-high resolution collimators. Around the 140-KeV energy peak of technetium-99m tetrofosmin, a 20% window was used. A total of 90 projections (step and shoot mode, 35 seconds per projection, imaging time 23 minutes) was obtained over a 360-degree circular orbit. Data were stored in a 64x64 matrix.

***Data analysis***

Additional reconstruction yielded standard long- and short-axis projections perpendicular to the heart-axis. The short-axis slices were displayed in polar map format, adjusted for peak myocardial activity (100%). The myocardium was divided into 17 segments, as previously proposed.[5] Myocardial perfusion was analyzed quantitatively with previously validated and commercially available automated software (quantitative gated SPECT, QGS, Cedars-Sinai Medical Center, Los Angeles, California)[9] and segmental tracer activity was categorized on a 4-point scale: 0= >75% of maximum tracer activity; 1=51%–75% of maximum tracer activity; 2=25%–50% of maximum tracer activity; 3= < 25% of maximum tracer activity.[10] Images were evaluated for the presence of perfusion defects which were defined as regions containing <75% of maximum tracer activity.

To evaluate the total infarct score as percentage of the LV on gated SPECT, all 17 scores were summed per infarct. The resulting summed score ranged in theory from 0 to 51 and was thereafter expressed as the percentage of the highest possible score of 51.[7]

**Statistical analysis**

Categorical data are expressed as number (%) and continuous variables as mean±SD. The overall agreement for detection of infarct between gated SPECT and MSCT was calculated on a per-patient basis as well as on a per-segment basis, and κ values were determined (<0.4, poor agreement; 0.4-0.75, fair to good; >0.75, excellent).[11] The comparison between gated SPECT and MSCT for the semiquantitative analysis of infarct score was performed with Pearson's regression analysis. To calculate the limits of agreement and systematic error between the 2 modalities for each pair of values of infarct score, Bland-Altman analysis was performed.[12] Infarct score on MSCT in relation to EDWT was compared with unpaired Student *t* test. The relations between infarct score on MSCT and WMSI or LVEF were calculated with the Pearson's regression analysis. A P-value <0.05 was considered statistically significant.

# Results

The 69 patients included in the study had a history of 74 healed myocardial infarcts; 5 patients had 2 previous infarcts. Clinical characteristics of the study population are summarized in **Table 1**.

**Table 1.** Clinical characteristics of the study population (n=69).

| Characteristic | |
|---|---|
| Age (years) | 60±12 |
| Men | 57 (83%) |
| Previous myocardial infarct* | 69 (100%) |
| Location of the infarct | |
| Anterior wall | 41 (60%) |
| Inferior wall | 23 (33%) |
| Both | 5 (7%) |
| Q wave on electrocardiogram | 39 (57%) |
| Multi-vessel coronary artery disease | 43 (62%) |
| Percutaneous coronary intervention/Coronary artery bypass graft surgery | 57 (83%)/10 (14%) |
| Left ventricular ejection fraction (%) | 48±13 |
| Angina pectoris | |
| Canadian Cardiovascular Society class I/II | 57 (83%) |
| Canadian Cardiovascular Society class III/IV | 12 (17%) |
| Heart failure | |
| New York Heart Association class I/II | 59 (86%) |
| New York Heart Association class III/IV | 10 (14%) |

**69 patients had in total 74 infarctions*

**Diagnostic accuracy of infarct detection with MSCT as compared to SPECT**

In 62 of 69 (90%) patients, a perfusion defect was identified on resting gated SPECT. On MSCT, in all these 62 (100%) patients hypo-enhanced areas could be demonstrated. Of the 7 patients without a perfusion defect on gated SPECT, 3 (43%) had evidence of healed myocardial infarct on MSCT. In **Table 2**, the agreement between gated SPECT and MSCT for infarct detection is shown on a per-patient basis, whereas in **Table 3** the agreement for infarct detection is provided on a per-segment basis. An example of a patient with an anteroseptal infarct on SPECT and the corresponding MSCT image is provided in **Figure 1**.

**Table 2.** Agreement between gated single photon emission computed tomography and multi-slice computed tomography for the detection of hypoenhancement representing myocardial infarct on a per-patient basis (overall agreement 96%, κ=0.71).

| SPECT | | Normal | Infarct | Total |
|---|---|---|---|---|
| **MSCT** | **Normal** | **4** | 0 | 4 |
| | **Infarct** | 3 | **62** | 65 |
| **Total** | | 7 | 62 | 69 |

**Table 3.** Agreement between gated single photon emission computed tomography and multi-slice computed tomography for the detection of hypo-enhancement representing myocardial infarct on a per-segment basis (overall agreement 93%, κ=0.83).

| SPECT | | Normal | Infarct | Total |
|---|---|---|---|---|
| **MSCT** | **Normal** | **825** | 38 | 863 |
| | **Infarct** | 41 | **269** | 310 |
| | **Total** | 866 | 307 | 1173 |

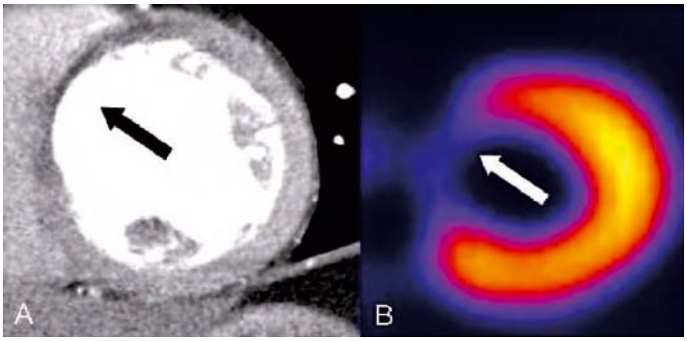


**Figure 1.** Example of a patient with anteroseptal myocardial infarct. Panel A: MSCT short-axis image with hypo-enhanced area anteroseptal (black arrow). Panel B: SPECT short-axis image with perfusion defect anteroseptal (white arrow).

### Semiquantitative analysis of infarct score: MSCT vs. gated SPECT

The mean infarct score on MSCT was 12±10% of the LV compared to 16±13% of the LV as measured with gated SPECT. A good correlation was observed between the infarct score assessed by both techniques, with a correlation coefficient of 0.93 (**Figure 2A**). Bland-Altman analysis displayed a small but statistically significant underestimation of infarct score with MSCT compared with gated SPECT (mean difference of 4%, 95% limits of agreement ranging from -6% to 15%) (**Figure 2B**). The average number of segments with hypo-enhancement on MSCT and perfusion defects on SPECT was 4±3 and 4±3 per infarct, respectively.

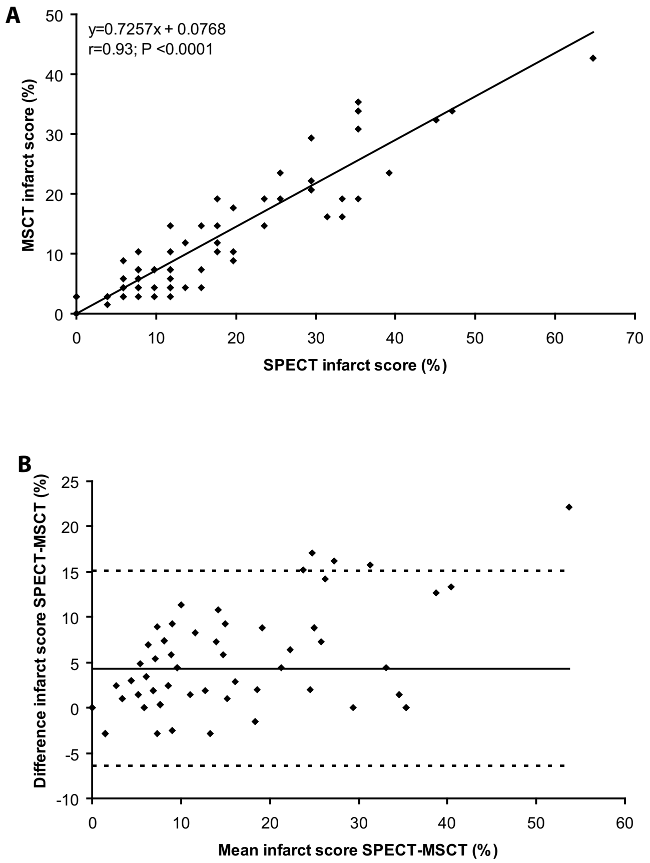


**Figure 2.** Pearson's correlation coefficient (A) and Bland-Altman analysis (B) for MSCT compared with gated SPECT regarding infarct score. (A) Linear regression plot illustrating the correlation between infarct score as measured by SPECT and MSCT. (B) Bland-Altman plot of infarct score showing the difference between each pair plotted against the average value of the same pair, i.e. the mean value of differences (solid line) and the mean value of differences±2 SDs (dotted lines).

**Infarct score with MSCT, relation with end-diastolic wall thickness**

EDWT was measured quantitatively at the center of the infarct region. A cutoff value of 6 mm was proposed; transmural infarct was defined in the presence of EDWT <6 mm, whereas non-transmural infarct was defined as EDWT ≥6 mm.[13] An EDWT ≥6 mm was observed in 41 myocardial infarcts, whereas in the remaining 33 infarcts the EDWT was <6 mm. The infarct score differed significantly between the 2 groups (EDWT <6 mm: 20 ± 10% vs. EDWT ≥6 mm: 5±3%, P <0.0001; **Figure 3**).

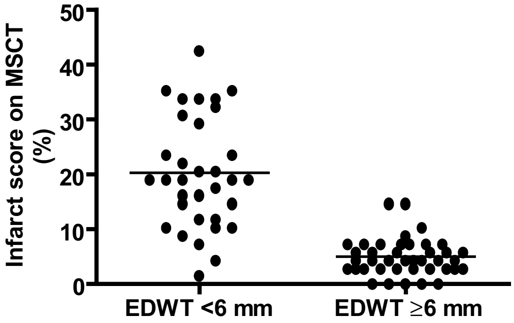


**Figure 3.** Relation between infarct score and EDWT, both assessed on MSCT. The mean infarct score was significantly higher in the EDWT <6 mm group compared with the EDWT ≥6 mm group (20±10% vs. 5±3%, P <0.0001).

**Infarct score with MSCT: relation with WMSI**

In all patients regional wall motion was assessed with MSCT on a segmental basis, according to the 17-segment model. Accordingly, the WMSI was calculated per patient. Correlation on per-patient basis between WMSI and infarct score was good (r=0.80, P <0.0001; **Figure 4A)**.

**Infarct score with MSCT, relation with LVEF**

Mean LVEF evaluated with MSCT was 48±13%. A significant correlation between the LVEF and the infarct score was demonstrated (r=-0.61, P <0.0001) (**Figure 4B**).

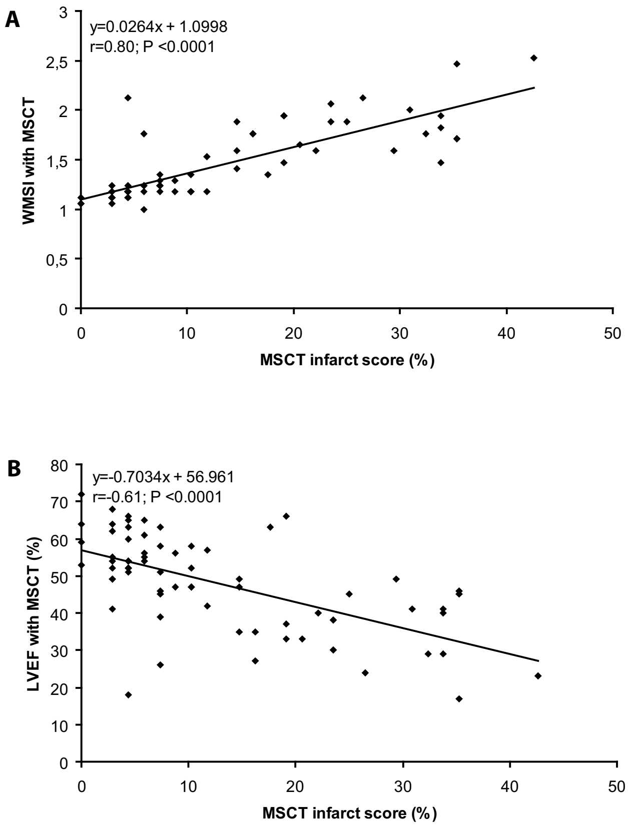


**Figure 4.** Pearson's correlation coefficient for (A) infarct score and WMSI, both assessed with MSCT and (B) for infarct score and LVEF, both assessed with MSCT. (A) Linear regression plot showing the correlation between infarct score and WSMI, both assessed with MSCT and (B) linear regression plot showing the correlation between infarct score and LVEF, both assessed with MSCT.

# Discussion

The purpose of the current study was to evaluate the performance of MSCT in the detection and semiquantitative analysis of healed myocardial infarct in comparison with gated SPECT. Furthermore the relations were evaluated between infarct score on MSCT and other parameters derived from MSCT (EDWT, WMSI and LVEF) that also (indirectly) reflect infarct expansion. In 62 (90%) of the patients, regions of infarct were detected on resting gated SPECT. On MSCT, in all these 62 (100%) patients hypo-enhanced areas could be demonstrated. Importantly, in 3 of 7 (43%) patients without perfusion defects on SPECT, MSCT images revealed areas with hypo-enhancement, suggesting that MSCT may potentially be more accurate for the detection of myocardial infarct. In addition, semiquantitative analysis of infarct score was performed both with SPECT and MSCT. Planimetry has been suggested to be a reliable technique for assessment of infarct score, however this procedure is time consuming and therefore a less practical tool for clinical routine use. Comte et al.[7] have investigated the feasibility of semiquantitative assessment of infarct score using a 17-segment model. Summing of all segmental scores and subsequent dividing of the results by the maximum possible score, yielded the infarct score as a percentage of the total LV. The authors demonstrated excellent agreement (r=0.91) between this approach and planimetry of the infarcted area.[7] In the present study, an excellent correlation was demonstrated between SPECT and MSCT for assessment of infarct score as percentage of the total LV (r=0.93, P <0.0001). The infarct score on MSCT was slightly smaller as compared to SPECT (12±10% vs. 16±13%), with a systematic underestimation of 4% of the infarct score with MSCT. Sanz et al.[14] reported similar findings for the comparison of infarct score between contrast-enhanced MRI and MSCT. A possible explanation for this finding could be that hypo-enhancement on MSCT reflects diminished or delayed delivery of the contrast agent. During infarct healing, capillary infiltration occurs from the periphery. This infiltration may not fully extend to the center of the infarct, resulting in a hypovascularized area, which could hamper contrast delivery to this area and may partially explain the underestimation of infarct score with MSCT. The clinical significance of this systematical, slight underestimation remains to be established. Moreover, in the current study, other parameters reflecting infarct correlated well with infarct score on MSCT. For example, the EDWT was measured quantitatively at the center of the infarct on MSCT, and infarcts with thinned walls (EDWT <6 mm) had a significantly larger infarct score as compared to infarcts with relatively preserved wall thickness. Similarly, good (inverse) correlations were shown for infarct score on MSCT and parameters of LV function (WMSI or LVEF).

Several limitations of the study need attention. First, only patients with known healed myocardial infarcts were included in the current study, and results cannot be extrapolated to patients with acute infarct. At present, MSCT is mainly used in patients with suspected coronary artery disease, and less frequently in patients with previous infarct. The current study demonstrates the feasibility of MSCT for infarct imaging, which could be useful in patients with subclinical infarct. Second, patients with severely depressed LVEF were not included and need to be evaluated in future studies. Third, planimetric quantification of infarct regions on MSCT was not performed and therefore absolute quantification of infarcted tissue was not feasible. Finally, the cutoff value of 6 mm for EDWT has only been validated for MRI and it is currently not known if this cutoff value can be extrapolated to MSCT. A general limitation of MSCT imaging is the use of potential nephrotoxic contrast and the need for the patient to be able to perform a single inspiratory breath hold. However, with the current generation of 64-slice MSCT scanners, acquisition of high-resolution 3 dimensional images of the entire heart can be performed in less than 10 seconds.

# References


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