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Chapter 4

Impact of a predefined mediastinal ROI on inter-observer variability of planar $^{123}$I-$m$IBG heart-to-mediastinum ratio

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ABSTRACT

Aim
Purpose of this study was to assess the impact of mediastinal region of interest (ROI) definition on intra- and inter-observer variability in relation to collimator type.

Materials and methods
Thirty-five subjects with CHF (80% men, mean age 66 ± 9 years, NYHA 2.4 ± 0.5, LVEF 29 ± 8.4%) were enrolled. 15 minutes and 4 hours post-injection (p.i.) of \textsuperscript{123}I-mIBG, planar images were sequentially acquired with low energy high energy (LEHR) and medium energy (ME) collimators. In the first analysis, observer-defined mediastinal ROI was used. In the second analysis, a predefined mediastinal ROI was used. Intra- and inter-observer variability of late H/M ratio was assessed using Lin’s concordance coefficient (LCC).

Results
There was substantial agreement between all three observers using predefined mediastinum ROI. LCCs for LEHR were 0.98, 0.96, and 0.95, for ME 0.98, 0.97, and 0.97. However, observer-defined mediastinal ROI resulted in poor-moderate agreement. LCCs for LEHR were 0.82, 0.94, and 0.70, for ME 0.77, 0.91, and 0.80. Intra-observer analysis using predefined mediastinal ROI showed substantial agreement. LCC was 0.97 for LEHR and 0.96 for ME.

Conclusion
Predefined mediastinal ROI results in low intra- and inter-observer variability of late H/M ratio and is, therefore, to be preferred over observer-defined mediastinal ROI. Intra- and inter-observer variability of late H/M ratio is not influenced by collimator choice.
INTRODUCTION

In patients with chronic heart failure (CHF) compensation mechanisms like the sympathetic nervous system and the renin-aldosterone-angiotensin system (RAAS) are activated. Initially, increased sympathetic stimulation compensates for impaired myocardial function, but long-term stimulation has detrimental effects on myocardial structure and function causing remodeling of the left ventricle. Increased myocardial sympathetic activity increases exocytosis of norepinephrine (NE) from in the presynaptic vesicles. In addition, the NE re-uptake via NE transporter (also called uptake-1) in the sympathetic terminal nerve axons is decreased. This results in increased NE concentration in the synaptic cleft.

Meta-iodobenzylguanine (mIBG) is a NE analog that shares the same presynaptic uptake, storage, and release mechanism as NE. Radiolabeling of mIBG with $^{123}$I allows assessment of the sympathetic system. In 1981, the potential use of $^{123}$I-mIBG for cardiac imaging was suggested. Especially since $^{123}$I-mIBG became available, myocardial $^{123}$I-mIBG scintigraphy has been increasingly used, mainly in Europe and Japan. And just recently, the Food and Drugs Administration has given the approval for myocardial $^{123}$I-mIBG scintigraphy in the United States of America.

The most commonly used semi-quantitative measurements of myocardial $^{123}$I-mIBG uptake are the calculated heart-to-mediastinum (H/M) ratio and $^{123}$I-mIBG washout (WO), determined from planar $^{123}$I-mIBG images. The early H/M ratio reflects the integrity of sympathetic nerve terminals. The late H/M ratio offers information about neuronal function resulting from uptake, storage, and release. The WO reflects neuronal integrity of sympathetic tone/drive. In patients with CHF, a low late H/M ratio has been shown to be an independent predictor for ventricular arrhythmia, appropriated ICD therapy, sudden cardiac death, and mortality. Additionally, an increased WO has been associated with an adverse prognosis.

Almost all reports about $^{123}$I-mIBG images include the late H/M ratio. However, the methods used to obtain these parameters show substantial variation and have not been standardized yet. This variation can be caused by acquisition parameters: collimator choice, acquisition time and duration, and post-processing analysis: size, shape, and location of the cardiac and mediastinal region of interest (ROI). Somsen et al. has demonstrated that the inter- and intra-individual variability is low using myocardial ROI including left ventricle cavity. Veltman et al. demonstrated a low intra- and inter-observer variability of H/M ratio on planar $^{123}$I-mIBG images using a fixed rectangular mediastinal ROI. In both studies, $^{123}$I-mIBG images were assessed with low energy high resolution (LEHR) collimators. However, there are studies that indicate better results with respect to variability and accuracy of myocardial parameters using medium energy (ME) collimators. To our best knowledge, there are no studies that
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have compared the use of LEHR and ME collimators on the intra- and inter-observer variability. Therefore, the objective of this present study was to assess the impact of mediastinal ROI definition on intra- and inter-observer variability in relation to collimator type used for $^{123}$I-mIBG image acquisition.

Study Population
The study population consisted of patients with CHF with New York Heart Association (NYHA) functional class II-III/IV and an impaired left ventricle ejection fraction (LVEF) of < 35% who were referred for $^{123}$I-mIBG myocardial scintigraphy to the Department of Nuclear Medicine of the Diakonessenhuis, Utrecht, The Netherlands. The Diakonessenhuis is a larger teaching hospital with a large regional adherence area. All patients were individually optimally treated according to the ESC guidelines for acute and chronic heart failure.

Data acquisition
All subjects were pre-treated with 250 mg oral sodium perchlorate to block uptake of free $^{123}$I by the thyroid gland 30 minutes before intravenous (IV) injection of 185 MBq $^{123}$I-mIBG (AdreView™, GE Healthcare, Eindhoven, The Netherlands). $^{123}$I-mIBG planar images were acquired with the subject in supine position. 15 minutes (early images) and 4 hours (late images) after IV injection of $^{123}$I-mIBG 10-minute planar images were acquired from an anterior thoracic view (256 x 256 matrix). All images were acquired with a 15% energy window centered at the 159 keV photopeak of $^{123}$I. Images were acquired using a dual-headed gamma camera (Philips skylight, Eindhoven, The Netherlands). Per time-point (i.e., early and late) an acquisition with a LEHR collimator was made directly followed by an acquisition with a ME collimator (Figure 1). By mounting a LEHR on one head of the gamma camera and the ME collimator on the second gamma camera head, it was possible to quickly switch between two different acquisitions. After the LEHR acquisition, the camera rotated so that the ME collimator was in the same anterior position as the earlier made LEHR acquisition while the subject was lying in the same supine position.

Planar $^{123}$I-mIBG images analysis
One experienced (V.B.) and one inexperienced (P.J.H.) nuclear medicine physicians from the same centre (Diakonessenhuis) and one experienced nuclear medicine researcher from the Academic Medical Center (D.O.V.) were asked to analyse the planar $^{123}$I-mIBG images using post-processing software on a workstation. All observers were blinded from patient data. The H/M ratios were calculated from the planar $^{123}$I-mIBG images using a ROI over the heart and the upper part of the mediastinum. The cardiac ROI was manually drawn over the myocardium including the left ventricular cavity. The mediastinal ROI with a rectangular shape was placed on the upper part of the mediastinum. The H/M ratio was calculated by dividing the mean count density in the cardiac ROI by the mean count density in the mediastinal ROI.
\[^{123}\text{I}-\text{mIBG} \text{ scintigraphy and influence of ROI definition}\]

**Statistical analysis**

All continuous variables are expressed as mean ± standard deviation. The intra- and inter-observer variability of the early and late H/M ratio were assessed using Lin’s concordance coefficient (LCC) and the Bland-Altman analysis (expressed as mean difference between observers and 95% limits of agreement). First, the result for the LEHR and ME collimator were analysed separately based on absolute numbers. It was expected that the mean early and late H/M ratio using ME collimator would most likely be higher compared to the LEHR collimator obtained ratios. This would make a direct comparison between the collimator types difficult. Therefore, to allow for a better comparison between the LEHR and ME Bland-Altman analysis obtained results a relative mean difference was calculated, i.e., the mean difference between two observers was divided by the mean H/M ratio of two observers. This enables a better comparison between the ME and LEHR collimator obtained results. For clinically relevant agreement, the following criteria were used: LCC values < 0.90, 0.90 - 0.95, 0.95 - 0.99, and > 0.99 were considered poor, moderate, substantial, and almost perfect, respectively. All statistical analyses were performed using SPSS software package, version 20.0 (SPSS, Chicago, IL).

**Figure 1.** Example of planar \[^{123}\text{I}-\text{mIBG} \] images. Panel A shows the planar \[^{123}\text{I}-\text{mIBG} \] image derived with a LEHR collimator. Panel B shows the planar \[^{123}\text{I}-\text{mIBG} \] image from the same patient derived with a ME collimator. Panel C shows an example of post processing planar \[^{123}\text{I}-\text{mIBG} \] images. The positioning of the mediastinum ROI (M) is determined in relation to the lung apex, the lower boundary of the upper mediastinum, and the midline between the lungs. The manually drawn cardiac ROI (H) is placed over the myocardium including the left ventricular cavity.
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RESULTS

Patient population
A total of 35 patients (80% men, mean age 65 ± 7.8 years) were included in the study. The baseline characteristics of the patient population are shown in Table 1. The mean NYHA functional class was 2.4 ± 0.5 and the mean LVEF was 29 ± 8.4%. Of the 35 patients, 83% had ischaemic cardiomyopathy. Medication used consisted of beta-blockers (87% of patients), angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin II receptor blockers (ARB) (94% of patients), lipid-lowering agents (77% of patients), and loop diuretics (69% of patients).

Inter-observer variability of planar $^{123}$I-mIBG imaging
The mean early and late H/M ratio of all three readers using observer-dependent mediastinal ROI and predefined fixed mediastinal ROI are shown in Table 2. In general, these values are in line with the population of CHF patients studied.

LCC for inter-observer variability of early and late H/M ratio determined on planar $^{123}$I-mIBG images using LEHR and ME collimators with observer-defined (non-fixed) and fixed mediastinal ROI are shown in Table 3. An observer-defined mediastinal ROI resulted in a high inter-observer variability between all three readers, with a poor agreement for both early and late H/M ratio, independent of collimator choice. A predefined fixed mediastinal ROI improved the inter-observer agreement between all three observers. The inter-observer agreement for the early H/M ratio was poor to moderate when using a LEHR collimator. The observer agreement increased to moderate/substantial when using a ME collimator. The inter-observer agreement for the late H/M ratio was substantial for both the LEHR and the ME collimator.

The Bland-Altman analysis showed that the absolute mean difference (95% limits of agreement) in late H/M ratio with a fixed mediastinal ROI using LEHR collimator between all three observers was small, -0.02 (-0.06 to 0.02), -0.04 (-0.13 to 0.05), and -0.05 (-0.14 to 0.04), OBS1 vs OBS2, OBS1 vs OBS3, and OBS2 vs OBS3, respectively (Table 4). The Bland-Altman analysis for the ME collimator showed a small absolute mean difference (95% limits of agreement) of -0.01 (-0.20 to 0.18), 0.06 (-0.12 to 0.24), and 0.05 (-0.15 to 0.25), OBS1 vs OBS2, OBS1 vs OBS3, and OBS2 vs OBS3, respectively (Table 4).

The Bland-Altman analysis of the relative mean difference (95% limits of agreement) in late H/M ratio with a fixed mediastinal ROI using LEHR collimator was slightly smaller compared with ME collimator use, but not clinical relevant. The Bland-Altman plots of the inter-observer relative mean difference for both LEHR and ME collimators are shown in Figure 2. It shows neither bias nor trend between differences in late H/M ratio.
**Table 1.** Patient characteristics of study population (n=35)

| Characteristic                                      | Value                  |
|-----------------------------------------------------|------------------------|
| Gender (male), n (%)                                | 28 (80)                |
| Age, mean ± SD (year)                               | 65 ± 7.8               |
| **Heart failure characteristics, n (%)**           |                        |
| Ischaemic cardiomyopathy                            | 29 (83)                |
| Non-ischaemic cardiomyopathy                        | 6 (17)                 |
| NYHA functional class, mean±SD                      | 2.4 ± 0.5              |
| LVEF, mean ± SD (%)                                 | 29 ± 8.4               |
| **Heart rhythm, n (%)**                             |                        |
| Sinus rhythm                                        | 29 (83)                |
| Atrial fibrillation                                 | 6 (17)                 |
| **Clinical cardiovascular risk factors, n (%)**     |                        |
| Family history                                      | 18 (54)                |
| Diabetes Mellitus                                   | 8 (23)                 |
| Hypercholesterolemia                                | 20 (57)                |
| Hypertension                                        | 19 (54)                |
| **Medication, n (%)**                               |                        |
| Beta-blocker                                        | 31 (87)                |
| ACE-I or ARB                                        | 33 (94)                |
| Calciumchannel blocker                              | 3 (9)                  |
| Lanoxin                                             | 4 (11)                 |
| Loop diuretic                                       | 24 (69)                |
| Lipid-lowering agent                                | 27 (77)                |
Table 2. Mean early and late H/M ratios determined on planar $^{123}$I-mIBG images of all observers using LEHR and ME collimators with observer defined (non-fixed) and fixed mediastinal region of interest (ROI).

|                      | OBS1          | OBS2          | OBS3          |
|----------------------|---------------|---------------|---------------|
| **Mean early H/M ratio** |               |               |               |
| LEHR collimator      |               |               |               |
| Non-fixed mediastinal ROI | 1.40 ± 0.19  | 1.51 ± 0.21  | 1.60 ± 0.25  |
| Fixed mediastinal ROI | 1.50 ± 0.20  | 1.53 ± 0.22  | 1.58 ± 0.21  |
| ME collimator        |               |               |               |
| Non-fixed mediastinal ROI | 1.87 ± 0.42  | 2.11 ± 0.47  | 2.09 ± 0.47  |
| Fixed mediastinal ROI | 2.09 ± 0.45  | 2.09 ± 0.43  | 2.08 ± 0.42  |
| **Mean late H/M ratio** |               |               |               |
| LEHR collimator      |               |               |               |
| Non-fixed mediastinal ROI | 1.30 ± 0.18  | 1.40 ± 0.21  | 1.43 ± 0.22  |
| Fixed mediastinal ROI | 1.39 ± 0.22  | 1.40 ± 0.21  | 1.44 ± 0.21  |
| ME collimator        |               |               |               |
| Non-fixed mediastinal ROI | 1.65 ± 0.39  | 1.87 ± 0.48  | 1.79 ± 0.48  |
| Fixed mediastinal ROI | 1.86 ± 0.48  | 1.87 ± 0.46  | 1.81 ± 0.46  |

OBS 1 = P.J.H., OBS 2 = V.B., OBS 3 = D.O.V.
Table 3. Lin’s Concordance Coefficient (LCC) for inter-observer variability of early and late H/M ratio determined on planar $^{123}$I-mIBG images using LEHR and ME collimatorws with observer defined (non-fixed) fixed and mediastinal ROI.

|                      | OBS 1 vs. OBS 2 | OBS 2 vs. OBS 3 | OBS 1 vs. OBS 3 |
|----------------------|-----------------|-----------------|-----------------|
| **LEHR collimator**  |                 |                 |                 |
| Analysis with non-fixed mediastinal ROI |                 |                 |                 |
| LCC Early H/M ratio  | 0.689 (0.506 – 0.811) | 0.760 (0.597 – 0.0863) | 0.484 (0.289 – 0.641) |
| (95% CI)             |                 |                 |                 |
| LCC Late H/M ratio   | 0.818 (0.703 – 0.891) | 0.940 (0.886 – 0.968) | 0.703 (0.544 – 0.813) |
| (95% CI)             |                 |                 |                 |
| Analysis with fixed mediastinal ROI |                 |                 |                 |
| LCC Early H/M ratio  | 0.915 (0.843 – 0.955) | 0.918 (0.849 – 0.957) | 0.850 (0.742 – 0.915) |
| (95% CI)             |                 |                 |                 |
| LCC Late H/M ratio   | 0.977 (0.956 – 0.988) | 0.962 (0.930 – 0.980) | 0.946 (0.903 – 0.970) |
| (95% CI)             |                 |                 |                 |
| **ME collimator**    |                 |                 |                 |
| Analysis with non-fixed mediastinal ROI |                 |                 |                 |
| LCC Early H/M ratio  | 0.694 (0.513 – 0.816) | 0.854 (0.730 – 0.923) | 0.581 (0.347 – 0.747) |
| (95% CI)             |                 |                 |                 |
| LCC Late H/M ratio   | 0.766 (0.629 – 0.858) | 0.907 (0.831 – 0.949) | 0.796 (0.646 – 0.886) |
| (95% CI)             |                 |                 |                 |
| Analysis with fixed mediastinal ROI |                 |                 |                 |
| LCC Early H/M ratio  | 0.955 (0.915 – 0.977) | 0.931 (0.869 – 0.965) | 0.899 (0.811 – 0.948) |
| (95% CI)             |                 |                 |                 |
| LCC Late H/M ratio   | 0.980 (0.961 – 0.989) | 0.973 (0.949 – 0.986) | 0.971 (0.945 – 0.985) |
| (95% CI)             |                 |                 |                 |

OBS 1 = P.J.H., OBS 2 = V.B., OBS 3 = D.O.V.
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Figure 2. Inter-observer variability of the late H/M ratio with fixed mediastinal ROI determined on planar \textsuperscript{123}I-MIBG images using LEHR collimator (left panel) and ME collimator (right panel). (OBS 1 = P.J.H., OBS 2 = V.B., OBS 3 = D.O.V.)
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**Figure 3.** Intra-observer variability (first vs. second measurement) of the late H/M ratio with fixed mediastinal ROI determined on planar 123\textit{I}-\textit{m}IBG images using LEHR collimator (left panel) and ME collimator (right panel). Use.

**Table 4.** The inter-observer variability of late H/M ratios determined on planar 123\textit{I}-\textit{m}IBG images using LEHR (left panel) and ME (right panel) collimators.

|                      | LEHR collimator       | ME collimator       |
|----------------------|-----------------------|---------------------|
| **Non-fixed mediastinal ROI** |                       |                     |
| OBS1 vs OBS2         | -0.10 (-0.26 – 0.06)  | OBS1 vs OBS2 -0.23 (-0.77 – 0.21) |
| OBS2 vs OBS3         | -0.03 (-0.26 – 0.10)  | OBS2 vs OBS3 -0.10 (-0.24 – 0.44) |
| **Fixed mediastinal ROI** |                       |                     |
| OBS1 vs OBS2         | -0.13 (-0.35 – 0.09)  | OBS1 vs OBS3 -0.13 (-0.60 – 0.34) |
| OBS2 vs OBS3         | -0.02 (-0.06 – 0.02)  | OBS1 vs OBS2 -0.01 (-0.20 – 0.18) |
| **OBS1 vs OBS3**     | -0.05 (-0.14 – 0.04)  | OBS1 vs OBS3 0.05 (-0.15 – 0.25) |

The absolute mean differences (95 % limits of agreement) in the inter-observer analysis using non-fixed and fixed mediastinal ROI. OBS 1 = P.J.H., OBS 2 = V.B., OBS 3 = D.O.V.

**Intra-observer variability of planar 123\textit{I}-\textit{m}IBG imaging**

The intra-observer analysis using a predefined fixed mediastinal ROI showed a substantial agreement. The LCCs for the late H/M ratio using LEHR collimator was 0.97 and for the ME collimator 0.96, respectively. The intra-observer analysis showed a small absolute mean difference (95% limits of agreement) of -0.01 (-0.12 to 0.10) using LEHR collimator and -0.04 (-0.27 to 0.19) using medium collimator. The Bland-Altman plots of the intra-observer relative mean difference for both LEHR and ME collimators are shown in Figure 3.
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DISCUSSION

This study showed that inter-observer variability of both early and late H/M ratios on planar $^{123}$I-mIBG images is largely influenced by definition of the mediastinal ROI. There was a substantial inter- and intra-observer reproducibility of late H/M ratio on planar $^{123}$I-mIBG images using a predefined fixed mediastinal ROI. However, an observer-defined mediastinal ROI negatively influenced the inter-observer reproducibility resulting in a poor inter-observer agreement. The choice of collimator had no influence on inter-observer agreement of the late H/M ratio. However, the inter-observer agreement of the early H/M ratio improved when using a ME collimator.

In general, our findings are comparable with the publication of Veltman et al. They reported a low variability of early and late H/M ratio determined on planar $^{123}$I-mIBG myocardial scintigraphy in CHF patients (age 64.5 ± 8.7 years, LVEF 26 ± 7.4, ischaemic CMP 63%) using a fixed mediastinal ROI. The inter-observer analysis showed an intraclass correlation coefficients (ICC) for late H/M ratio of 0.98 (0.97 - 0.99). However, this study was performed with only a LEHR collimator. The current study demonstrates that measurement of the late H/M ratio on planar $^{123}$I-mIBG myocardial scintigraphy is reliable and independent of collimator choice.

It has been demonstrated that late H/M ratio is a good prognostic indicator independent of other clinical used parameters such as left ventricular ejection fraction (LVEF). Therefore, $^{123}$I-mIBG myocardial scintigraphy could assist in a more individualized medical therapy in patients with CHF. Although the prognostic value of $^{123}$I-mIBG myocardial scintigraphy has been demonstrated, the technique has not been fully implemented in the clinical arena. This might be explained by the fact that there is considerable variation in the methods to obtain H/M ratios. This variation can be caused by acquisition parameters such as collimator choice, acquisition time, and duration. Inter-observer variation may also depend on the size and location of the cardiac and mediastinal ROI. Therefore, standardization of acquisition and post-processing analysis as proposed by Flotats et al. is essential. Improved standardization of cardiac $^{123}$I-mIBG imaging protocols would contribute to increased clinical applicability of $^{123}$I-mIBG scintigraphy.

The mediastinal ROI on planar cardiac $^{123}$I-mIBG scintigraphy reflects non-specific mediastinal activity. This region is regarded as a good reference for the qualification of cardiac sympathetic activity because it has less scatter from other organs and the low sympathetic activity in the mediastinum. Our study shows that the size and location of cardiac and mediastinal ROI can contribute to the variation of H/M ratio significantly. A rectangular mediastinal ROI is recommended. The size of the mediastinal ROI depends on the matrix size (128 × 128 or 256 × 256) and varies in the literature. A smaller mediastinal ROI leads to a more precise estimation of non-specific mediastinal uptake and is less influenced by non-specific scatter from uptake in the...
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lungs. Therefore, in theory a relatively small ROI would lead to a more appropriate estimation of the non-specific mediastinal uptake (i.e., lower mediastinal count density). However, the disadvantage of a smaller ROI is that it is more susceptible to sample variability in low-count regions such as the mediastinum. The use of a smaller ROI requires, therefore, a more precise and preferably predefined placement, based on “anatomical” landmarks. Our study showed that the size and positioning of the mediastinal ROI varies when observer dependent and that these differences resulted in variation of H/M ratios between the observers. Using a predefined fixed rectangular mediastinal ROI minimized this variation and resulted in an increased reproducibility and decreased variation between observers.

In this study, all three reviewers scored a lower early and late H/M ratio derived for the planar *123*I-mIBG images assessed with the LEHR collimator compared to the ME collimator (Table 2). A collimator is a pivotal part of a gamma camera and constitutes of a leaden slate with holes and septa. These septa allow only those photons traveling parallel to the septa to pass through and be recorded by the crystal. Photons not traveling parallel to the septa are filtered out by the septa and therefore the thickness of the collimator septa is a major determinant of photon-penetration and image quality. In general, LEHR collimators are widely available and frequently used for *123*I-mIBG imaging. However, in addition to the main photopeak of 159 keV *123*I has a low-abundance of high-energy photons (approximately 3% with a photon energy of 529 keV). These high-energy photons penetrate the LEHR septa, resulting in a decreased image quality, especially in the presence of high count sources in the direct vicinity such as the liver and lungs. It has been described that this scatter affects the H/M ratios substantially.\textsuperscript{19,20} The scatter issue can be solved by using a ME collimator. In general, these collimators have thicker septa and are therefore better equipped to stop the high-energy *123*I photons. Indeed, the decrease in scatter provides higher values of the H/M ratios for ME compared to LEHR collimators. However, the question whether these ME collimator obtained higher H/M ratios are a better reflection of true myocardial sympathetic activity remains to be answered. In addition, ME collimators are not as widely available as LEHR collimators, hampering standardized implementation of this solution.

The inter-observer variability of the early and late H/M ratio is largely affected by size and place of mediastinal ROI and less by the choice of collimator type. Compared to the LEHR collimator, the ME collimator slightly increased the inter-observer agreement for late H/M ratio from moderate to substantial (Table 3). An explanation would be the lack of scattering of high-energy photons from liver and lungs using the ME collimator resulting in better contrast between mediastinal/myocardium and liver/lung. In turn this increased contrast could improve the accuracy and reduce variation in drawing and placing of mediastinal and cardiac ROI and thereby reduce the variation in the late H/M ratio.
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To allow for a direct comparison between the LEHR and ME collimator derived results the
mean difference between the observers was divided by the mean difference between
of two observers by the mean H/M ratio of two observers. Interestingly, the Bland-
Altman plots of this “corrected” relative mean difference between all three observers
showed a greater variation using ME collimator compared to LEHR collimator (Figure
2). This is probably explained by the fact that the mediastinal and myocardial ROI
when using a LEHR collimator has higher total counts as a result of scattering of high-
energy photons from liver and lungs compared to ME collimator use. ROI’s with lower
total counts will have more variability compared with ROI’s with high total counts. This
effect would result in a regression to the mean on the LEHR obtained images and could
explain the difference in variation between LEHR and ME collimator use.

LIMITATION

The primary limitation of the present study is the relatively small number of subjects
included. However, as already stated our results are in line with the publication of
Veltman et al. It seems therefore that our conclusions with regard to the mediastinal
ROI definition are valid. Second, in this study only the intra and inter-observer variability
on planar 123I-mIBG images was assessed. The intra- and inter-observer variability
analyses on myocardial 123I-mIBG SPECT were not performed in this current study.
The SPECT images give information on the regional sympathetic innervation/activity.
This regional information appears to be of additional clinical value to the planar-derived
parameters. For a proper understanding of these SPECT images, the variability of
myocardial 123I-mIBG SPECT imaging needs to be assessed in future studies.

CONCLUSION

Inter-observer variability of both early and late H/M ratios on planar myocardial 123I-mIBG
images is largely dependent on the definition of the mediastinal ROI. A predefined fixed
mediastinal ROI showed a substantial agreement between observers, independent
of collimator choice. In addition, compared to LEHR collimated acquisitions the ME
collimated acquisitions resulted in higher H/M ratios. However, the choice of collimator
type did not have a large impact on intra- and inter-observer variability.
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