Standardization of the heart-to-mediastinum ratio of 123I- labelled-metaiodobenzylguanidine uptake using the dual energy window method: Feasibility of correction with different camera-collimator combinations

Standardization of the heart-to-mediastinum ratio of iodine-123-labeled-meta-iodobenzylguanidine uptake using dual energy window method: Feasibility of correction from different camera-collimator combinations

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ABSTRACT

Background. Although heart-to-mediastinum (H/M) ratio in a planner image has been used for practical quantification for ^{123}I-metaiodobenzylguanidine (MIBG) imaging, standardization of the parameter is not yet established. We hypothesized that the value of H/M can be standardized to the various types of camera-collimator combinations.

Methods and Results. Standard phantoms consisting of the heart, mediastinum were made. A low-energy high-resolution (LEHR) collimator, and medium-energy (ME) collimator were used. We examined multi-window correction methods with ^{123}I- dual-window (IDW) acquisition and planar images were obtained with IDW with LEHR. The images were obtained by using GCA-9300A (Toshiba Co., Ltd.), E.CAM Signature (Toshiba Co., Ltd, Tokyo) and Varicam (GE, Tokyo). Cardiac phantom studies demonstrated contamination of the H/M count ratio was greater with LEHR collimator and least with the ME collimator. The H/M ratio with collected LEHR collimator was similar to that with ME collimators. The uncorrected H/M ratio in ME collimator had a linear relationship with the corrected H/M ratio by IDW method in LEHR collimator. The relationship between uncorrected LEHR (Toshiba GCA9300A) and ME collimator is y= 0.56 x + 0.49: y=H/M in e.cam, x=H/M in ME collimator. The averages of the normal values for the low-energy type collimator (n=18) was 2.2 $\pm$ 0.2 (initial H/M), 2.42 $\pm$ 0.2 (delayed H/M), and 2.63 $\pm$ 0.25 (initial H/M), 2.87 $\pm$ 0.19 delayed H/M) for low-medium-energy (LME) collimator (n=14). H/M value in previous clinical studies using LEHR was comparable to that of ME collimators.

Conclusions. The H/M ratio with corrected LEHR, after application of the IDW method, was similar to that of ME collimator. This finding could make it possible to standardize planar imaging of the H/M ratio among various collimators in clinical setting.

Abbreviations: MIBG:metaiodobenzylguanidine, collimator, iodine-dual-energy window method

TEXT

^{123}I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy has been widely used to evaluate the cardiac sympathetic system [1-21]. Because sympathetic activity is enhanced with increasing severity of congestive heart failure, the severity and prognosis of congestive heart failure can be evaluated based on parameters determined by ^{123}I-MIBG scintigraphy [2,3,7]. The evaluation of severity or prognosis of heart failure is considered as class I evidence in Japanese Circulation Society guidelines for nuclear cardiology use [1]. Parameters obtained with late MIBG scintigraphy images such as heart/mediastinum (H/M) ratio and washout rate can be used as indicators for sympathetic activity. Patients with the lowest uptake of MIBG have the poorest prognosis [10, 17]. Normal value of H/M differs in each institution [3]. Although ^{123}I-MIBG studies have been accepted for clinical routine use in many countries, standardization of MIBG parameter is not yet fully performed. Without proper validation and standardization, the use of ^{123}I-MIBG might be limited to a single center research tool for understanding the physiology of myocardial sympathetic nerve activities under different conditions [3]. A standardized method for measuring MIBG uptake in various gamma camera systems is required in clinical setting [3]. The effect of collimator choice substantially influences the estimation of H/M ratio. Low-energy collimators are often applied to cardiac ^{123}I-MIBG imaging. However, Inoue et al reported that the medium-energy (ME) collimators provided high quantitative accuracy and may enhance reliability in the MIBG study [4]. The H/M ratio with the ME collimator, after application of multi-window methods, was close to the theoretical value in the phantom study [5].

We hypothesized that the value of H/M can be standardized in various camera-collimator combinations. The improvements in quantification can be better achieved by a multiple-window approach [5]. In this study we performed phantom experiments to assess quantitative value in ^{123}I-MIBG H/M ratio with low energy high resolution (LEHR) collimator and ME collimator using various types of gamma camera to make correction among collimators. Moreover, we aimed to validate the phantom studies and previous clinical studies in order to achieve proper standardization.

Methods

Preparation of Phantoms The phantom was designed for measuring the planar H/M ratio [5]. Because the purpose of this study was to standardize the H/M ratio among different collimator types and manufacturers by eliminating septal penetration and scatter, we tried to simplify the structure as much as possible, as previously reported [5]. In short, each organ part was designed so that the radioactivity was distributed uniformly in the organ region of interest (ROI). The size of the phantom was 380 mm in width and length, and the thickness of the each organ was flat and constant. The thickness of each organ part was adjusted by changing the number of slices. Four types of acrylic slice parts, with a thickness of 5 mm per slice, were combined and arranged into various numbers and orders. In the phantom studies, true H/M ratios were mathematically calculated in these models, assuming the linear attenuation coefficient (μ) of ^{123}I for water as 0.147/cm. The standard equation for attenuation, that is $e^{-\mu x}$, where x was thickness of attenuation, was used. A slice was divided into 0.05 mm of thin slices, and the summation of the count was calculated using Mathematica software (version 5.2, Wolfram Research, Inc., Champaign, I11, USA). The phantom measurement was repeated with and without three acrylic plates (9.7 mm/plate) over the phantom as scatter media. The H/M could be calculated, with anterior and posterior views from the two phantoms (Table 1).

Data Acquisition and Correction Methods Planar images were simultaneously obtained with five energy windows, and were combined to make three correction methods, i.e., windows 1 to 5 were 132-142, 143-175, 176-186, 187-208, and 209-294 keV. The ^{123}I dual-window (IDW) method used an energy window on the high-energy side to estimate the number of scattered 529-keV photons, in which an original upper window (176-208 keV, IDW_0) by Motomura et al [18] and a wide upper window (176-294 keV, IDW_1) were examined. The energy window setting is shown in Figure 1. The IDW method subtracted mainly septal penetration counts by rectangular approximation. The original IDW methods used Butterworth filtering for subwindow images, and subtracted the filtered image from the main-window image. However, in this study, no image subtraction was performed, to avoid a decrease in count and an increase in noise even after filtering. Subwindow images were used only for calculating the counts on the same ROIs as the main window.

Collimators For the phantom study, low-energy high-resolution (LEHR) and medium-energy (ME) collimators were used. The special resolution was 7.4, 10.1, and 7.6 mm for LEHR, ME, and low-medium-energy high resolution (LMEHR) collimators at a collimator-to-source distance of 10 cm, respectively. The sensitivity of the collimators was 5.5, 6.1, and 5.4 cpm/kBq, respectively. The LEHR of three manufactured companies were used to measure H/M. E.CAM signature in Kanazawa University Hospital (Toshiba Co. Limit, Tokyo, Japan), GSA 9300A in Kanazawa University Hospital (Toshiba, Tochigi, Japan) and Varicam in Kanazawa Cardiovascular Center (GE Medical Systems, Tokyo, Japan).

For clinical studies, data from working group of Japanese Society of Nuclear Medicine for myocardial SPECT standardization (chief investigator: Kenichi Nakajima) were used [22]. A low-medium-energy general purpose (LMEGP) collimator (in Shizuoka Cancer Center: E.CAM), specifically designed for ^{123}I high-energy photons, was also used to calculate H/M. And low-energy general purpose (LEGP) collimators (in Toho University Hospital) were also used to determine H/M. These two collimators were used to examine H/M in 28 patients without heart disease as a clinical study.

Method of clinical study Twenty-eight patients without heart disease were enrolled in this study [15 females and 18 males, aged 52±22]. The ^{123}I-MIBG (111 MBq) was injected intravenously, and the planar images were obtained using gamma cameras (Toshiba, Tochigi, Japan) with LEHR collimators in 14 patients, and with LME collimator in 14 patients. For this study, anterior images were obtained again 3 hours after injection with both LEGP and LME collimators.

Data Processing for H/M Ratios The ROIs were set over the heart and the upper third of the mediastinum on the main-window image. The same ROIs were used to measure the count on the five subwindow images. The H/M ratios were calculated by average heart count divided by average mediastinal count.

Statistics Dara analysis was done using a computer-based programme, 'The statistical Discovery Software', JMP IN (version 5.0.1, SAS institute, Cary, USA). Average counts in ROIs were used for image data analysis. Statistics of the average and standard deviation (SD) were calculated. An analysis of variance for the mean was performed, based on groups with collimator types and correction methods. A paired *t* test was also used for the comparison of correction methods. A linear regression line for two variables was calculated by standard linear regression analysis. $P < .05$ was considered significant.

Results

Phantom Study: LEHR vs.ME

Mathematically calculated H/M was listed in Table 1. There was a clear difference in image quality between LEHR and ME collimators. Planar data were higher for ME than LEHR collimators among three cameras (Table 2).

Table 3 shows the calculated H/M ratios divided by uncorrected H/M ratio with ME collimator. The no corrected H/M ratio with a LEHR collimator was from 0.85 ± 0.08. On the other hand, the result from corrected H/M ratio with IDW0 was 1.01 ± 0.05, and the corrected H/M ratio with IDW1 was 1.0 ± 0.02.

Phantom Study: corrected LEHR vs. ME

The relationship between the uncorrected H/M ratio with the ME collimator, and the H/M ratios with the LEHR collimator are shown in figure 2. The uncorrected H/M ratio in ME collimator had a linear relationship with the corrected H/M ratio by IDW method in LEHR collimator.

*Uncorrected LEHR (Toshiba, E.CAM) vs. ME collimato*r

y= 0.56 x + 0.49 (y=H/M in E.CAM, x=H/M in ME collimator)

Uncorrected LEHR (Toshiba, GCA9300A) vs. ME collimator

y = 0.59 x + 0.49 (y=H/M in Toshiba, GCA9300, x=H/M in ME collimator)

Uncorrected LEHR (GE Varicam) vs. ME collimator

y = 0.61 x + 0.52 (y=H/M in GE, Varicam, x=H/M in ME collimator)

Table 4 shows the coefficient of correlation and p value for the correlation between the uncorrected H/M of the ME collimator and the IDW-collected H/M of LEHR collimator.

Clinical Studies

The averages of the normal values for the low energy type collimator (LEGP and LEHR) (n=18) was 2.2±0.2 (initial H/M), 2.3±0.2 (delayed H/M), and corrected normal values using the correction reference of the methods above (GE, Varicam) were 2.7±0.3 (initial H/M), 3.0±0.3 (delayed H/M).

The averages of the normal values for LMEGP collimator (n=14) were 2.6 ± 0.3 (initial H/M) and 2.9 ± 0.2 (delayed H/M).

To analyze the distribution of H/M with each collimator, box plats were generated for LE type, LME, corrected LE type (Figure 2). There was a significant difference in initial H/M and delayed H/M between LE type and LME (initial, 2.2 ± 0.2 vs. 2.6 ± 0.3, $p<0.05$; delayed, 2.3 ± 0.2 vs. 2.9 ± 0.2, $p<0.05$). After using correction reference of IDW method, there was no significant difference in initial H/M and delayed H/M between corrected LE type and LME (initial, 2.7 $\pm$ 0.3 vs 2.6 $\pm$ 0.3; delayed 3.0 $\pm$ 0.4 vs 2.9 $\pm$ 0.2, not significant).

Discussion

This study showed that the application of IDW correction methods provided comparable values to the uncorrected data from ME collimator, and that this was applicable to various types of gamma camera, including manufactures such as GE, Siemens and Toshiba. The application of IDW correction methods with the LEHR collimators of these companies yielded values comparables to those with the ME collimator. Therefore the value of H/M can be standardized in various camera-collimator combinations with IDW correction. Moreover in clinical situation, the IDW correction method could be used and enhance the acquisition of comparable results in different institutions.

Collimator Choice

As we have previously reported that the H/M ratio with the ME collimators, or after application of the TEW or IDW methods, was close to theoretical value in the phantom study [5,23]. Because H/M ratio is computed from count in relatively large regions, it may be inferred from that septal penetration that takes precedence over high resolution. Former clinical studies could divide into two groups of collimators, one is ^{123}I-specific collimators, including ME collimator and LME collimator [5]. These collimators have characteristics that septal penetration is low, providing high quantitative accuracy. Another group of collimator is designed mainly for ^{99m}Tc, not ^{123}I-specific like LEHR, LEGP collimator. Comparatively large amount of septal penetration tend to make H/M value smaller.

Scatter-corrected H/M

^{123}I gamma photon radiation included a 529 keV component in 1.39% of the total number of photons [20]. Therefore, the number of scattered photons from 529 keV component depends on the physical characteristics of the collimators. Moreover, the high-energy photon causes a significant amount of septal penetration, and the high background activity was the results of multiple complex scatters. The scatter distribution and septal penetration comes with a broad distribution all over the field of view, that was also shown in the image of the 187 to 209-keV and 210 to 294-keV windows [20]. The distribution of septal penetration did not seem to reflect the real structure of tracer distribution. Scatter correction method, IDW is one of the commercially available methods. IDW is effective to eliminate this septal penetration from the high-energy photon [3-5]. In the present phantom study, the three different camera systems with corrected LEHR collimators produced similar semi-quantitative planar H/M ratios, which is comparable to that of ME collimators (Table 3). Apparently, ME collimator or LME collimators, which are specific to ^{123}I, plays an important role in reducing variability in the results. In order to make it feasible to make comparison between institutions or to compare previous clinical data, the results in this study might be useful. The understanding of collimator choice may help to achieve the standardization in MIBG values. H/M ratio with ME collimator or corrected LEGP collimator may be a simple method which allows comparison of inter-individual and inter-institutional results, by correcting for differences in body geometry and attenuation between individual subjects.

Clinical significance

The acquisition of MIBG imaging with IDW method is simple and has a high reproducibility. This method is applicable to almost all institution, since this is not complicated as before and does not need special facility. We can not only understand numerous studies of past MIBG imaging by the correction, but also use the IDW methods in acquiring MIBG imaging from now on. Actually we recommend all institution should use the IDW methods as a gold standard in calculating MIBG H/M.

In published ^{123}I-MIBG studies, we could divide into two groups of values of H/M, although the precise collimator information was not available from all studies. In one group, the delayed H/M ratio ranged from 2.1 to 2.4, using LEHR or LEGP collimators [7,14,24,25]. Another group showed a comparatively higher delayed H/M ratio, from 2.8 to 3.0. using ME collimator or LME collimator [9,11]. The results of this study confirmed this hypothesis that corrected value of H/M with ^{123}I-nonspecific collimator comes near to that of ^{123}I-specific collimators and that the H/M ratio with collected LEHR, after application of the IDW method, was similar to that of ME collimator [3,5]. By examining human ^{123}I-MIBG data in various collimators in this study, it turned out that we can apply phantom results to clinical data. Technical improvement with IDW method can facilitate the acquisition of comparable results of various collimators, which is of clinical importance for investigations in multicenter collaborations.

^{123}I-MIBG values have been demonstrated by numerous studies to have prognostic values in congestive heart failure patients [7,10,17]. Although some study were conducted by ME collimator, many hospitals now continue to use low-energy collimators, and most of the previous data were accumulated by using low-energy collimators. Therefore, the result of this study makes it possible to compare these results among previous studies. The results of this phantom will help to calibrate inter-institutional differences in H/M ratio. Furthermore this study showed the possibility of using LEHR collimators were used with the scatter correction of IDW method as a standardization of MIBG H/M ratio. The corrected value of H/M can be used in different camera-collimator combinations.

Limitation

As a factor that influences MIBG H/M, the difference of setting region of interest (ROI) is one of the big factors. We used same ROI in evaluating the planar imaging. A method to set the shape of the ROI has to be standardized, and this could be a limitation. Automatic selection would improve reproducibility among institutions.

In conclusions, The H/M ratio with collected LEHR, after application of the IDW method, was similar to that of ME collimator. The scatter-corrected method with IDW method could make it possible to standardize planar imaging of the H/M ratio among various collimators in clinical setting.

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tables and figures

Table 1 Phantom types and mathematically calculated H/M ratios

	Ratio of thickness		Mathematically calculated H/M	
	Heart	Mediastinum	Ant.	Post.
Type B	6	2	2.6	3.50
Type D	5	3	1.55	1.80

H/M, heart-to-mediastinum count ratio; Ant, anterior; Post, posterior

Table 2 Planar H/M ratios obtained from phantom study: LEHR vs. ME vs. LMEHR (Anterior phantom B)

	IDW0	IDW1	No Correction	Mathematically caculated H/M
LEHR	2.13	2.27	1.76	2.60
MEGP	2.46	2.53	2.26	2.60
LMEHR	2.36	2.41	2.12	2.60

LEHR, low-energy high resolution; MEGP, medium-energy general purpose; LMEHR, low medium-energy high resolution; H/M, heart-to-mediastinum count ratio; IDW, ^{123}I dual-window.

Table 3. Phantom MIBG study

Divided by uncorrected H/M ratio with ME collimator

	Type D		Type B	
	Ant.	Post.	Ant.	Post.
IDW0 LEHR				
Toshiba/Siemens:ECAM	0.98	0.99	0.94	0.96
GE;Varicom	1.10	1.02	1.04	1.08
Toshiba:GSA9300	1.02	1.01	1.02	1.04
IDW1 LEHR				
Toshiba/Siemens:EC AM	1.00	1.02	1.00	1.02
GE:Varicom	1.05	1.01	0.97	1.00
Toshiba:GSA9300	1.02	1.01	0.98	0.97

Ant.,anterior, Post.,posterior

IDW, ^{123}I dual-window; LEHR, low-energy high resolution; ME, medium-energy; MIBG, metaiodobenzylguanidine.

Table 4

The coefficient of correlation and p value for the correlation between the uncorrected H/M of the ME collimator and the IDW-collected H/M of LEHR collimator

	R	p-value
IDW0-collected LEHR		
Toshiba/Siemens:ECAM	0.998	0.0012
GE:Varicom	0.994	0.0031
Toshiba:GSA9300	0.994	0.0031
IDW1-collected LEHR		
Toshiba/Siemens:ECAM	0.999	0.0005
GE:Varicom	0.995	0.0035
Toshiba:GSA9300	0.999	0.0003

IDW, ^{123}I dual-window; H/M, heart-to-mediastinum count ratio; ME, medium-energy; LEHR, low-energy high resolution.

Figure 1

Schematic representation of the ^{123}I dual-window (IDW) methods. Sub energy windows are shown with the energy spectrum of ^{123}I obtained with the low-energy high-resolution (LEHR) collimator. The thick lines in the main windows indicate subtracted counts.

Figure 2

Relationship between the uncorrected heart-to-mediastinum (H/M) ratio with the mediam-energy (ME) collomator, and the H/M ratios with the low-energy-high-resolution (LEHR) collimator. Green lines shows the relationship between uncorrected H/M in LEGP and H/M with ME collmators. Red lines shows corrected H/M with IDW methods were comparable to uncorrected H/M with ME collimators. IDW, ^{123}I dual-window

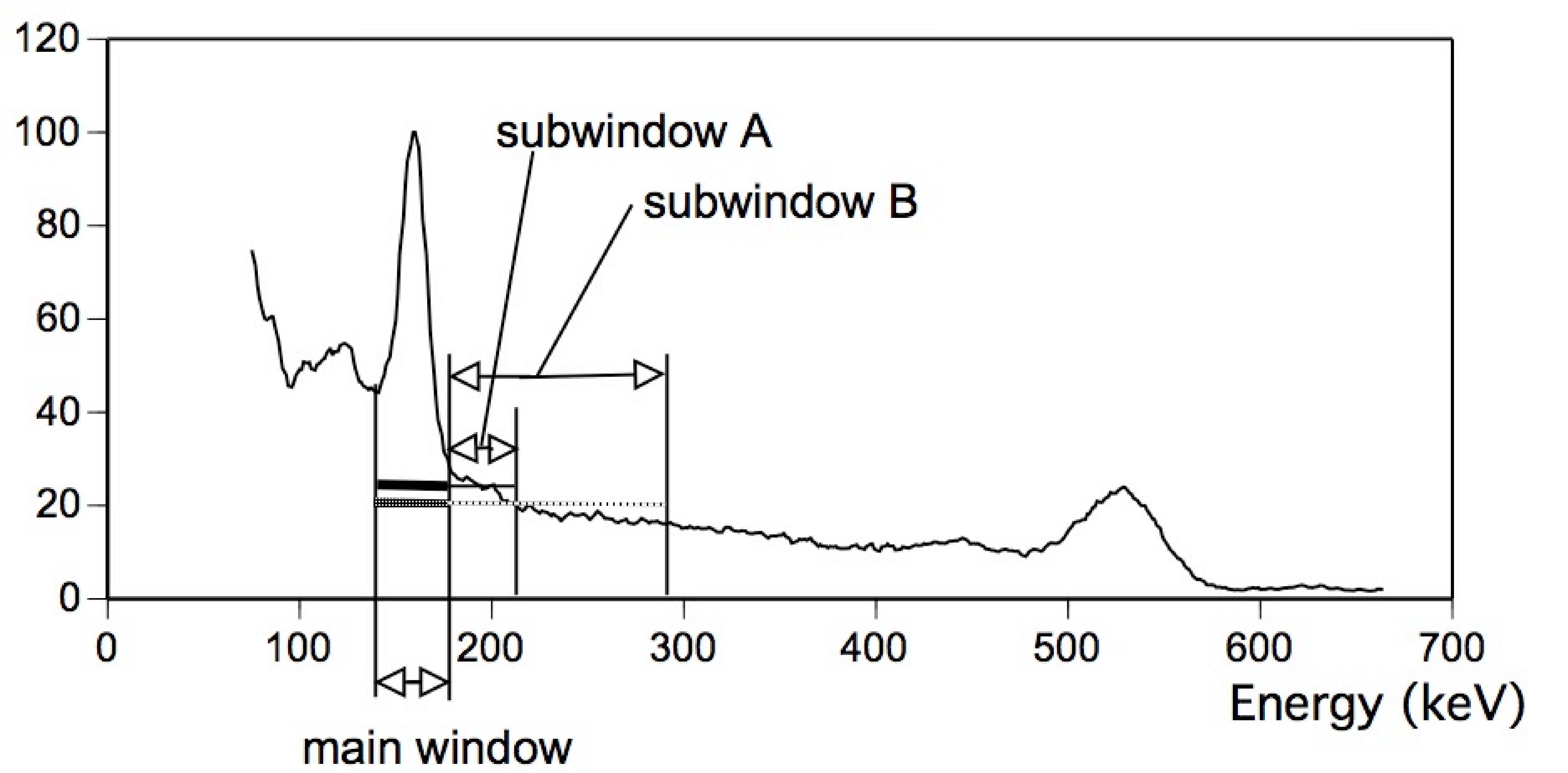
Figure 3

Images of five energy windows with the medium-energy (ME) and low-energy high resolution (LEHR) collimators. The maximum count is shown in the image and normalized to 100% for each image. The left panel of the 143 to 175-keV image was obtained in the main window.

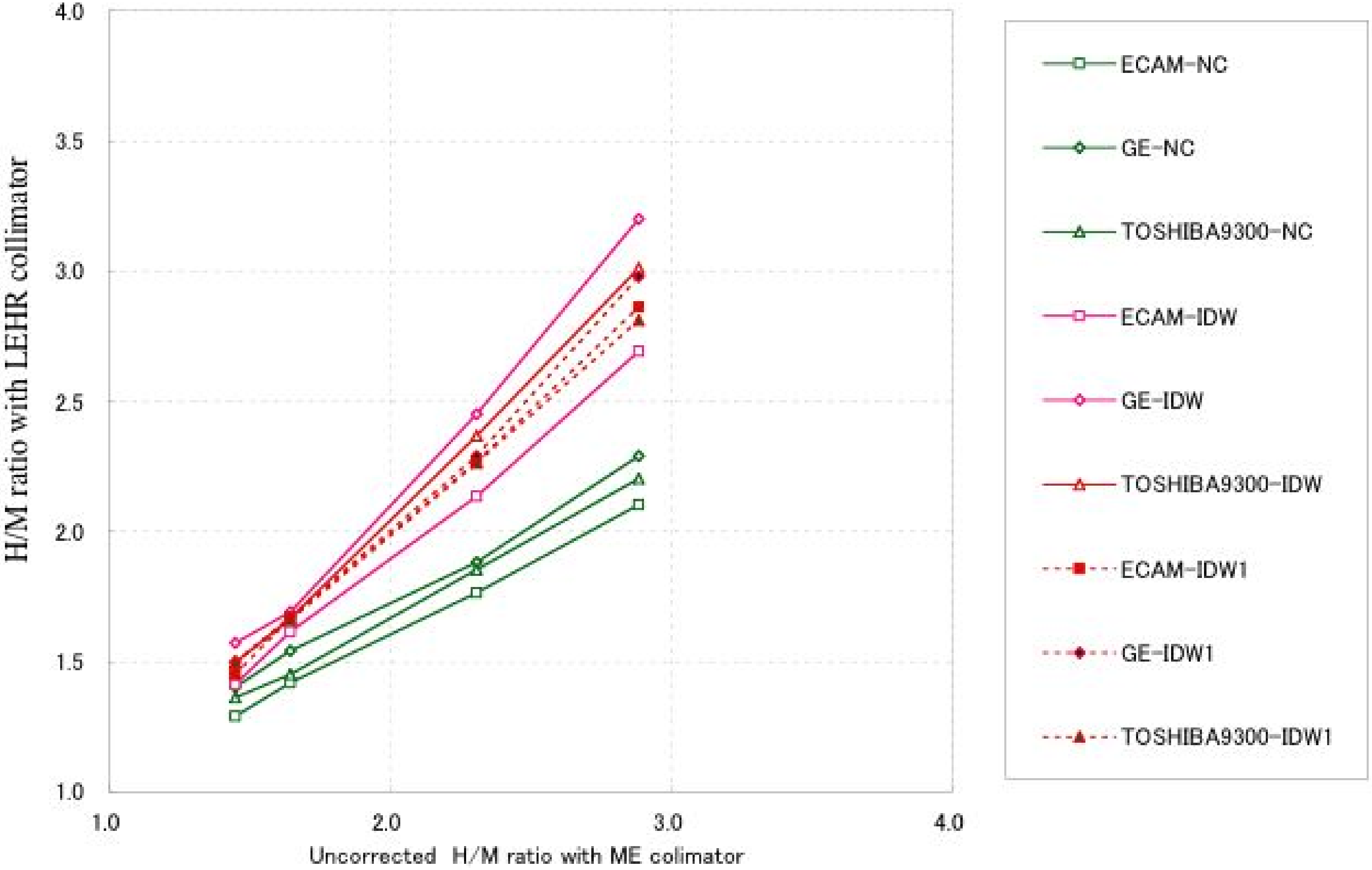
Figure 4

Box plots of the variability of H/M. The box indicates a median with upper and lower quartiles (defined as 75^{th} and 25^{th} percentiles) and upper and lower bars indicate 90^{th} and 10^{th} percentiles, respectively.

LE-i, initial low-energy type; LME-I, low medium-energy high resolution; c-LE-i, initial corrected low-energy type; d, delayed. NS, not significant



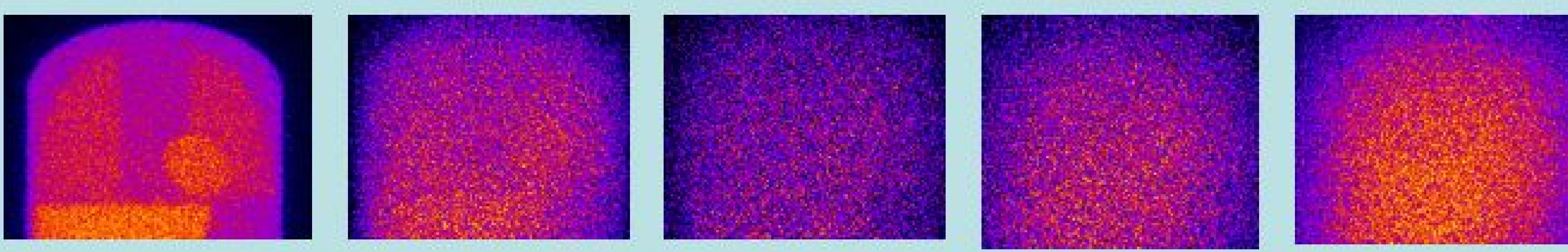
120
100
80
60
40
20
0
subwindow A
subwindow B
0
100
200
300
400
500
600
700
Energy (keV)
main window


H/M ratio with LEHR collimator
Uncorrected H/M ratio with ME colimator
1.0
1.5
2.0
2.5
3.0
3.5
4.0
ECAM-NC
GE-NC
TOSHIBA9300-NC
ECAM-IDW
GE-IDW
TOSHIBA9300-IDW
ECAM-IDW1
GE-IDW1
TOSHIBA9300-IDW1

Phantom-Type D (Theoretical H/M=1.55)

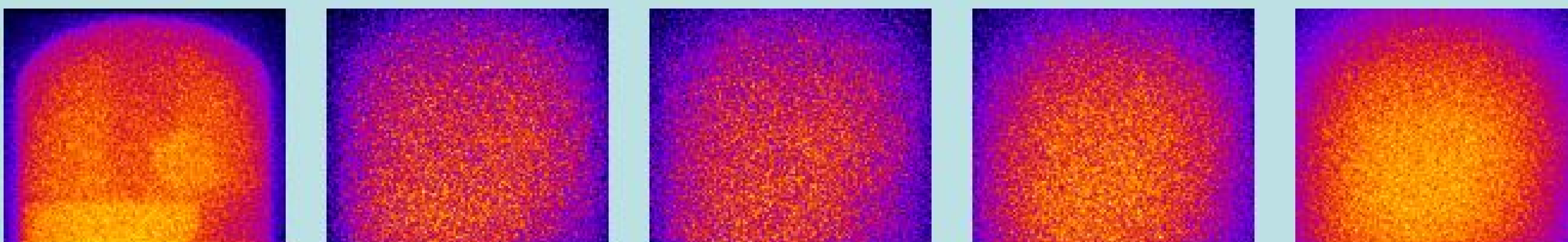
Medium Energy Collimator

Max 89 | 21 | 13 | 15 | 28 count/pixel

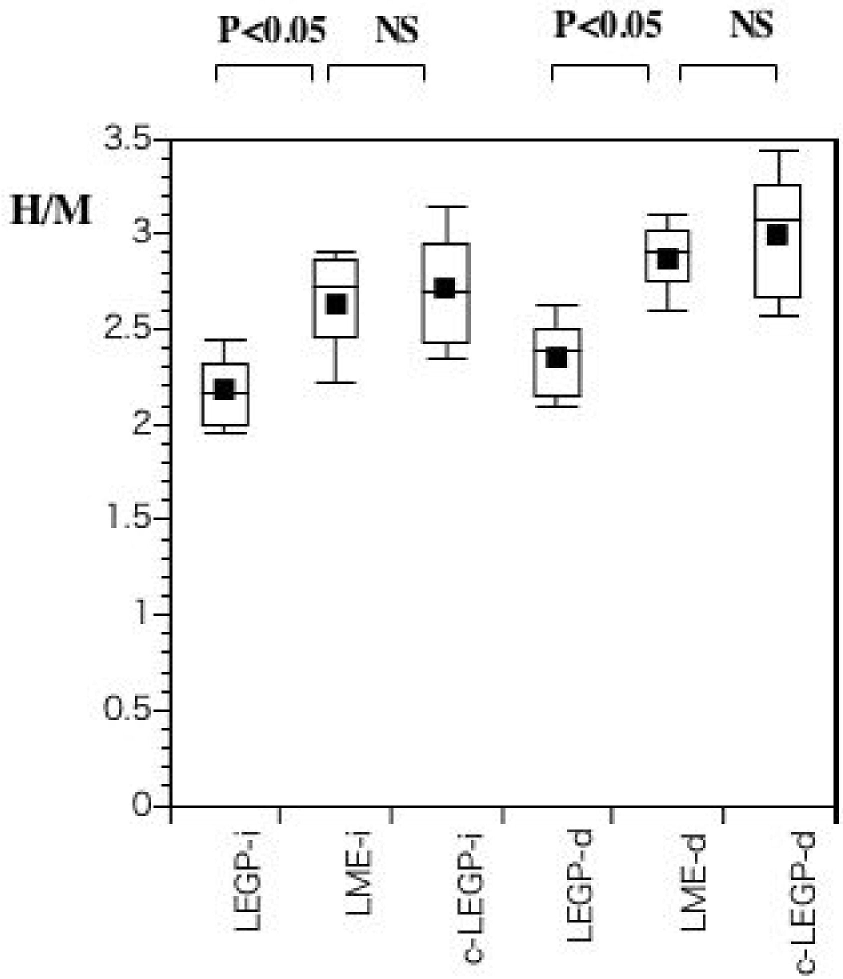


Low Energy High Resolution Collimator

Max 113 | 28 | 28 | 40 | 100 count/pixel



143-175 | *132-142* | *176-186* | *187-208* | *209-294 keV*


P<0.05
NS
P<0.05
NS
H/M
3.5
3
2.5
2
1.5
1
0.5
0
LEGP-i
LME-i
c-LEGP-i
LEGP-d
LME-d
c-LEGP-d