The Difference Among Stress and Rest Normal Reference Databases Using Non-Corrected, Scatter Corrected, and Scatter with Attenuation Corrected Bull's Eye Myocardial Perfusion Scintigraphy in Both Genders

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Objectives: *To compare 3 types of Bull's eye normal reference maps; non-corrected, scatter corrected, and scatter with attenuation corrected Bull's eye in both genders.*
Material and Method: *Sixty-seven normal healthy males and females volunteered for the present study. After screening tests to identify low post-test (exercise EKG) likelihood of coronary artery disease, 41 subjects (20 males and 21 females) had stress and rest myocardial perfusion scintigraphy (^{99m}Tc-sestamibi). The data were reconstructed by filtered back projection reconstruction in three ways as follows; 1) non-correction (NoC), 2) scatter elimination only (SC), 3) scatter elimination and attenuation correction (SC+AC). Three sets of reconstructed data of both stress and resting studies were added into 6 sets of Bull's eye. The data of each Bull's eye were normalized to 100% of the maximum count. Percentage of uptake in each area was compared by t-test statistics.*
Results: *Stress and rest count distribution of NoC and SC sets were lowest at the inferior wall, followed by the septal wall, anterior wall, and lateral wall in both genders. In the SC+AC sets, septum and lateral walls showed more uptake than anterior and inferior walls. A significant difference of percentage uptake between stress and rest images at septum in NoC and SC images in male and in SC image in female was observed. No difference was seen in the SC+AC groups.*
Conclusion: *There was similarity of count distribution between NoC and SC images. SC+AC caused more uniform image. However, some non-uniformity was observed. The use of sex-independent SC+AC bull's eye is possible. Stress study can be omitted for bull's eye collection of normal files.*

Keywords: *Myocardial perfusion imaging, Normal database, Bull's eye, Scatter elimination, Attenutation correction*

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Attenuation correction and scatter elimination are methods to improve error of myocardial perfusion scintigraphy interpretation and are increasingly used nowadays. Both methods had demonstrated improved diagnostic accuracy and quality of myocardial perfusion SPECT images(1). The two widely used commercially available normal reference databases, CEqual and Cedar-Sinai Bull's eye reference files, obtained data by acquisition without corrections of the aforementioned artifacts. The authors developed 3 types of Bull's eye normal reference maps, which are non-corrected, scatter corrected, and scatter with attenuation corrected Bull's eye in both genders, and compared each Bull's eye files to investigate the effect of these artifacts.

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Material and Method

The volunteers who participated in the present study had to be healthy without a history or family history of heart disease, had no other major medical diseases, non-cigarette smokers, absence of abnormalities on physical examination and no ischemic pattern changes on resting EKG (right bundle branch block was not an exclusion criteria but left bundle branch block was), blood pressure not more than 160/95 mmHg), serum cholesterol not more than 200 mg/dl and no medical therapy, fasting plasma glucose not more than 126 mg/dl.

Sixty-seven males and females volunteered. Some had hypertension, excess level of cholesterol, fasting glucose, and some had abnormalities on resting EKG. Fifty-six volunteers passed the screening tests and had the exercise treadmill test. Individual post-test (exercise EKG) likelihood of coronary artery disease (CAD) was calculated from Diamond and Forrester's pooled data on asymptomatic subjects[2]. After the exercise treadmill test, forty-six volunteers achieved at least stage 3 of Bruce's protocol and had at least 85% of maximal predicted heart rate. All had less than 5% likelihood of CAD. To further minimize the risk of including subjects, all subjects were studied by multigated cardiac blood pool study (MUGA) to exclude wall motion abnormalities and decreased global left ventricular ejection fraction at rest. Among this group, 5 patients were further excluded due to some error in scintigraphic acquisition and data storage. The final reference group thus consisted of 41 subjects, 20 males and 21 females. All volunteers gave informed consent. The present study was approved by the ethics committee of the faculty. Table 1 reveals age, sex, body mass index (BMI), blood pressure, percentage of heart rate achieved in the exercise test, and global left ventricular ejection fraction (%).

Imaging protocol A separate day protocol was used. For the stress study, 700 MBq (20 mCi) of Tc-99m sestamibi was injected at peak exercise treadmill (at least 85% of maximal predicted heart rate). Exercise was continued for 1 minute after injection. Patients were advised to have a fatty meal 30 minutes thereafter. Imaging was acquired 30 minutes after the fatty meal. Rest study was usually performed 1 day prior to or after the stress study. A triple headed SPECT (Triad; Trionix Lab, Twinsburg, OH, USA) equipped with a low-energy, ultra-high resolution parallel hole collimator with a 20% symmetric window around 140 keV and 360-degree elliptical rotation was used for acquisition. Matrix size was 128x128. Acquisition time of emission tomography was 30 second/projection, 120 views for both stress and resting studies in the supine position. Non-uniform attenuation correction (transmission scan) was performed using Gadolinium-153 scanning line source after the emission scan. Transmission acquisition time was 30 second/projection, 30 views in 180 degree from 0 degree to 180 degree and 128x128 matrix size. Scatter elimination was performed by using a pixel-by-pixel spectrum analysis (SESAME software). Reconstruction

The emission images were pre-filtered using a Butterworth filter with cutoff frequency of 0.45 and order 5. The transmission images were filtered using Hamming filter with cut off frequency 0.55. The data were reconstructed by filtered back-projection reconstruction in three ways as followed; 1) non-correction, 2) scatter elimination only, 3) scatter elimination and attenuation correction.

Bull's eye reconstruction and display The transverse reconstructed images were re-oriented in short axis, horizontal long axis, and vertical long axis slices. The method for three-dimentional quantification of tomographic study was similar to that previously described[3]. Briefly, the analysis consisted of the following steps. The base (and apex slices were defined from the horizontal and vertical long axis views. The base and apex in the same patient was defined using the same limit among each set of images (non-corrected, scatter corrected, scatter with attenuation corrected). The basal to apex rings of the Bull's eye were constructed from maximum-count circumferential profiles of short axis slices. The apex and base slices were defined from horizontal and vertical long axis slices.

Table 1. Age, sex, body mass index (BMI), BP, %MPHR, and LVEF in 41 healthy subjects

Age (yrs)	No.	BMI (mean±SD)	BP ranges (systolic/diastolic)	%MPHR (range)	LVEF(%) (mean ± SD)
Males					
47.9±10.3	20	23.5±2.7	(100-160) / (42-95)	104 (85-132)	62.1±7.8
Females					
51.8±9.8	21	23.4±2.7	(100-160) / (60-90)	99 (85-108)	62.1±6.7

BMI, body mass index; BP, blood pressure; %MPHR, % maximal predicted heart rate;
LVEF, left ventricular ejection fraction

The number of rings was fixed at 12. The number of slices of patients having more than 12 slices was automatically decreased, and patients having less than 12 slices were automatically increased to meet 12 rings. This was accomplished through an interpolation algorithm. Pixels counts inside all rings were normalized to a constant normalization value (100). The Bull's eye was divided into apex, anterior wall, inferior wall, septum, and lateral wall.

Analysis after reconstruction : the three sets of data of both stress and resting studies were added into 6 sets of Bull's eye. Mean±SD of the percentage of uptake in each area was reported. Paired t-test was used to compare difference between uptake in each wall. The paired t-test was applied to compare the difference between male and female. A value of p lesser than 0.05 was considered statistical significant.

Results

The Bull's eye images of non-correction, scatter elimination, scatter elimination with attenuation correction in both genders are shown in Fig. 1. The greatest difference was only 3% between stress and rest in some distributions of some sets. Count distribution of non-correction sets was lowest at the inferior wall, followed by septal wall, anterior wall, and lateral wall in both genders. The difference of inferior wall low uptake was more prominent in males than females. In the scatter elimination sets, the pattern of count distribution was similar to the non-correction sets. There was equal uptake at septum and lateral walls, which showed more uptake than anterior and inferior walls in the scatter elimination with attenuation correction sets. The uptake difference of inferior and anterior walls from septum and lateral walls is less prominent in female than male. Uptake defect at apex in these sets of images is noted. The comparisons of the percentage uptake (mean±SD) at each distribution between stress and rest studies in both sexes are shown in Table 2. There was a significant difference of percentage uptake between stress and rest images at septum in a non-corrected and scatter eliminated images in male and in scatter eliminated image in female. When compare between walls by using a ratio of inferior to anterior and septum to lateral wall in non-correction, scatter elimination, and scatter with attenuation correction images, the values were as followed: in male stress studies 0.83, and 0.90, 0.80 and 0.87, 0.96 and 1.0; in male rest studies 0.83 and 0.88, 0.80 and 0.86, 0.95 and 0.97; in female stress studies 0.89 and 0.88, 0.87 and 0.85, 0.99 and 0.97; in female rest studies 0.91 and 0.87, 0.88 and 0.85, 1.0 and 0.94, respectively. Table 3 compares the percentage uptake of stress study between males and females by using unpaired t-test. There was no difference of activity distribution except at inferior wall in both non-corrected and scatter corrected images (p=0.03). No statistical difference throughout the myocardial walls is seen in the scatter with attenuation correction images.

Discussion

From the result of the present study, there is

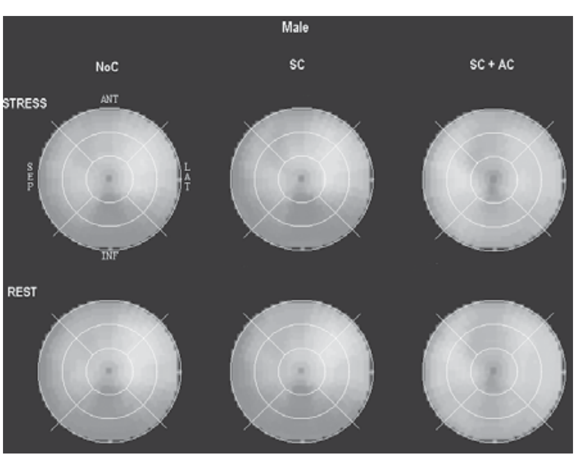

Fig. 1a Bull's eye plot in male of non-correction (NoC), scatter elimination (SC), and scatter elimination with attenuation correction (SC+AC). Top row=stress study, Bottom row=rest study

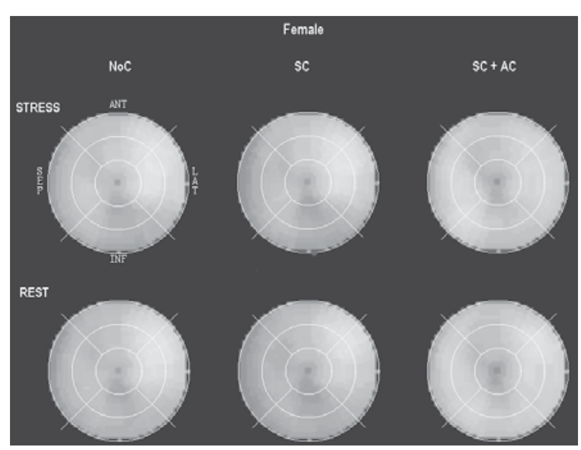

Fig. 1b Bull's eye plot in female of non-correction (NoC), scatter elimination (SC), and scatter elimination with attenuation correction (SC+AC). Top row=stress study, Bottom row=rest study

Table 2. Comparison of percentage uptake (mean±SD) at each distribution between stress and rest studies in both sexes

	Male			Female		
	stress	rest	p-value	stress	rest	p-value
Non-correction						
Anterior wall	79.3±4.0	80.0±4.6	0.18	82.7±1.5	80.7±1.5	0.07
Inferior wall	66.0±3.0	66.3±2.1	0.67	73.7±1.5	73.3±1.5	0.74
Septal wall	75.7±6.8	74.0±7.2	0.04*	76.7±4	75.3±2.1	0.38
Lateral wall	84.0±4.6	84.3±5.0	0.40	87.3±2.1	86.3±2.1	0.59
Ratio of Interior to Anterior	0.83	0.83		0.89	0.91	
Ratio of Septal to Lateral	0.90	0.88		0.88	0.87	
Scatter correction						
Anterior wall	80.0±5.0	80.3±4.0	0.67	83.0±1.7	79.7±1.2	0.06
Inferior wall	64.0±3.0	64.3±3.1	0.42	72.0±1.0	70.3±1.5	0.13
Septal wall	73.7±4.9	72.0±6.6	0.04*	73.7±4.9	70.7±4.0	0.03*
Lateral wall	84.0±3.0	83.3±4.0	0.42	86.3±2.9	83.3±1.5	0.12
Ratio of Interior to Anterior	0.80	0.80		0.87	0.88	
Ratio of Septal to Lateral	0.87	0.86		0.85	0.85	
Scatter+attenuation correction						
Anterior wall	78.3±1.5	79.0±1.0	0.42	81.0±1.0	80.7±1.5	0.40
Inferior wall	75.3±1.5	74.7±1.2	0.18	80.3±2.5	80.3±3.1	1.00
Septal wall	83.0±5.3	82.0±3.6	0.42	82.7±3.1	81.0±2.6	0.20
Lateral wall	83.3±2.1	84.3±1.1	0.22	85.0±1.0	86.0±2.0	0.42
Ratio of Interior to Anterior	0.96	0.95		0.99	1.00	
Ratio of Septal to Lateral	1.0	0.97		0.97	0.94	

* significant difference by paired t-test

Table 3. Comparison of stress percentage distribution between male and female in the 3 sets of images

	Non-correction				Scatter elimination				Scatter+Attenuation correction			
	anterior	inferior	septum	lateral	anterior	inferior	septum	lateral	anterior	inferior	septum	lateral
Male	79.3±4.0	66.0±3.0	75.7±6.8	84.0±4.6	80.0±5.0	64.0±3.0	73.7±4.9	84.0±3.0	78.3±1.5	75.3±1.5	83.0±5.3	83.3±2.1
Female	82.7±1.5	73.7±1.5	76.7±4	87.3±2.1	83.0±1.7	72.0±1.0	73.7±4.9	86.3±2.9	81.0±1.0	80.3±2.5	82.7±3.1	85.0±1.0
p -value	0.29	0.03*	0.84	0.34	0.41	0.03	1.00	0.39	0.07	0.05	0.93	0.30

*significant difference by unpaired t-test

a noticeable point that in Thai normal volunteers (which may imply to other Asian females) with a less than 5% likelihood of coronary artery disease, the count distribution in females was less at the inferior wall instead of anterior wall as is usually described[4,5]. This finding is seen in the non-corrected and scatter corrected images, but resolves in the scatter with attenuation corrected images (Fig 1, Table 3). However, the low-uptake at the inferior wall in female is less prominent than in males. This might be because of the smaller breast size in Asian people, which causes lesser attenuation of counts at the anterior wall. The uptake distribution in the scatter-eliminated studies is similar to the non-corrected images except for the difference of septum and lateral wall, and inferior and anterior wall are slightly more pronounced. This might be the effect of the software elimination of scatter counts from extra-cardiac region (liver and bowel) in the inferior wall and septal region (see Table 2). This is showing that the scatter-eliminated method may cause only minor effect on the count distribution and thus might be abandoned from the routine image processing. However, a study by Almquist et al[6] which used Tc-99m based radiopharmaceutical one-day protocol (rest 350 MBq, stress 900 Mbq) pointed out that the inferior to anterior wall ratio was greatly reduced at rest. They indicated that the results were due to under correction of down-scatter at exercise. Another study by Chouraqui et al[7] found similar result but in the setting of Thallium stress-redistribution without scatter correction. So, it can be noticed that both studies have common factors that were in the resting images there were low counts with attenuation correction. Thus, the effect of enhanced inferior wall to anterior wall ratio might not be caused by the effect of scatter itself but might be because of the low count factor. As the authors have already proved in the present study of high count images of stress and rest and found no difference between sets of images. The count distribution in the scatter with attenuation corrected images is more uniform than the other 2 sets of images as seen by the ratio of inferior to anterior and septum to lateral walls which approach 1. This means that attenuation correction is concentrated at the septal wall and inferior wall. This finding agrees with other studies[8-10]. From our study, the count distribution in the stress and rest studies are similar except at the septal wall (stress>rest) in the non-corrected (male) and scatter corrected (male&female) studies. For the scatter corrected images, the explanation could be due to the over correction of scatter activity from the liver, which is more prominent in the resting study. But for the non-corrected studies, there is still no explanation. Attenuation correction causes more homogeneity of count distribution as discussed above, but some inhomogeneity is still seen as a streak defect from anterior passing apex to inferior wall in both sexes. The defect is more prominent at the apex, which was also observed in other studies[11,12]. In the study by Pretorius et al[11] which compared the effect of attenuation correction with attenuation and scatter correction showed that the low uptake at apex was seen in the latter set. This implies that this effect might be caused by scatter elimination rather than attenuation correction itself. This makes nuclear medicine physician reluctant of reading the defect at this region. Due to the imperfection of scatter with attenuation correction as described above, normal Bull's eye reference databases are still needed for comparison with patients' studies. From the present study, there is a close similarity of the male and female polar maps of the scatter with attenuation correction images, which can implement that there is no need to collect a sex different normal file. This is concordant with the study by Araujo et al[13]. However, their study compared only the effect of attenuation correction and compared only the resting study between genders, not between stress and rest. In our study we perform the comparison between stress and rest image sets as well and found that there was no difference between these sets of images. Thus, the authors suggest not performing stress for the collection of normal reference databases if this kind of correction is used.

In conclusion, there is similarity of non-corrected and scatter – corrected tracer distribution Tc-99m sestamibi polar maps in the population with a lesser than 5% likelihood of coronary artery disease. Attenuation correction causes more uniform images but still some streak artifacts and apical defect. The use of sex-independent scatter with attenuation correction Bull's eye is possible. Furthermore, there is no need to perform stress for the collection of normal reference databases. Finally, in Asian people, the effect of breast attenuation in females is less prominent.

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ความแตกต่างของการตรวจเลือดมาเลี้ยงหัวใจชนิด scintigraphy แบบบูลส์อาย ในภาวะออกกำลังและภาวะพักโดยการใช้วิธี ไม่แก้ไข (non-correct), การแก้ไขรังสีกระเจิง (scatter correct), และการแก้ไขรังสีกระเจิงร่วมกับการแก้ไขการเบาบางของรังสี (scatter ร่วมกับ attenuation correct) ในทั้ง 2 เพศ

สุภัทรพร เทพมงคล, ปัญญา ภาสว่าง, อัญชลี กฤษณจินดา, สุพจน์ ศรีมหาโชติ

วัตถุประสงค์: *เพื่อเปรียบเทียบระหว่าง 3 วิธีของบูลส์อาย ในคนปกติ คือ non-correct, scatter correct, และ scatter ร่วมกับ attenuation correct ในทั้ง 2 เพศ*

วัสดุและวิธีการ: *อาสาสมัครชายและหญิงปกติ 67 คนได้เข้าร่วมการศึกษานี้ หลังจากทำการตรวจคัดกรองเพื่อหาผู้ที่มีความน่าจะเป็นของโรคหลอดเลือดหัวใจโคโรนารีย์ต่ำหลังจากทำ exercise EKG แล้ว มีผู้ที่เข้าเกณฑ์ทั้งสิ้น 41 คน (ชาย 20 คน หญิง 21 คน) จึงทำการตรวจเลือดมาเลี้ยงหัวใจโดยใช้วิธี scintigraphy สารที่ใช้คือ ^{99m}Tc-sestamibi ในภาวะออกกำลังและภาวะพัก ข้อมูลที่ได้ถูกนำมาสร้างเป็นภาพโดยวิธี filtered back projection ร่วมกับ 3 วิธีย่อยคือ 1) non-correction (NoC), 2) scatter elimination (SC), 3) scatter elimination ร่วมกับ attenuation correction (SC+AC) เมื่อได้ภาพแล้วจึงทำการใส่ข้อมูลลงใน Bulls eye ซึ่งจะได้ภาพทั้งหมด 6 ชุด ข้อมูลที่อยู่ใน บูลส์อายจะถูกทำให้เป็น 100% ที่บริเวณที่มีค่านับวัดสูงสุด ค่าร้อยละของค่านับวัดในแต่ละบริเวณจะถูกเปรียบเทียบกันระหว่างชุดโดยใช้ t-test*

ผลการศึกษา: *ค่านับวัดของ No C และ SC ต่ำสุดที่ inferior wall ตามด้วย septal wall, anterior wall และ lateral wall ในทั้ง 2 เพศ ส่วนใน SC+AC มีค่านับวัดที่ septum และ lateral wall มากกว่า anterior และ inferior wall มีความแตกต่างอย่างมีนัยสำคัญของร้อยละของค่านับวัดระหว่างภาวะออกกำลังและภาวะพักที่ septum ใน NoC และ SC ในผู้ชายและ SC ในผู้หญิง แต่ไม่พบความแตกต่างนี้ใน SC+AC*

สรุป: *การกระจายของค่านับวัดระหว่าง NoC และ SC มีความคล้ายคลึงกัน และพบว่า SC+AC ค่อนข้างที่จะให้ภาพที่สม่ำเสมอกันมากกว่าชุดอื่นๆ การใช้ SC+AC บูลส์อายโดยไม่แยกเพศมีความเป็นไปได้ และไม่มีความจำเป็นที่จะต้องเก็บภาพบูลส์อายของคนปกติโดยใช้การออกกำลัง*