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Nuclear myocardial perfusion imaging using thallium-201 with a novel multifocal collimators SPECT/CT device: IQ-SPECT versus conventional protocols in normal subjects

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Key words: Diagnosis; IQ-SPECT; Nuclear imaging

Abstract

Objective: A novel multifocal collimator, IQ-SPECT (Siemens) consists of cardio-centric and 3D iterative SPECT reconstruction and makes it possible to perform MPI scans in a short time. The aims are to delineate the normal uptake in thallium-201 (^{201}Tl) SPECT in each acquisition method and to compare the distribution between new and conventional protocol, especially in patients with normal imaging.

Methods: Forty patients (eight women, mean age of seventy-five years) who underwent myocardial perfusion imaging were included in the study. All patients underwent one-day protocol perfusion scan after an adenosine-stress test and at rest after administrating ^{201}Tl and showed normal results. Acquisition was performed on a Symbia T6 equipped with a conventional dual-headed gamma camera system (Siemens ECAM) and with a multifocal collimator called IQ-SPECT. Imaging was performed with a conventional system followed by IQ-SPECT/computed tomography (CT). Reconstruction was performed with or without X-ray CT-derived attenuation correction (AC). Two nuclear physicians blinded to clinical information interpreted all MPI studies. A semi-quantitative myocardial perfusion was analyzed by a 17-segment model with a 5-point visual scoring. The uptake of each segment was measured and left ventricular functions were analyzed by QPS software.

Results: IQ-SPECT provided good or excellent image quality. IQ-SPECT images without AC were similar to those of conventional LEHR study. Mid-inferior defect score (0.3±0.5) in conventional LEHR study was increased significantly in IQ-SPECT with AC (0±0). IQ-SPECT (AC) improved the mid-inferior decreased perfusion shown in conventional images. The apex in IQ-SPECT (AC) was decreased compared to that in LEHR (0.1±0.3 vs. 0.5±0.7, $p<0.05$). The left ventricular ejection fraction from IQ-SPECT was significantly higher than that from the LEHR collimator ($p=0.0009$).

Conclusion: The images of IQ-SPECT acquired in a short time are equivalent with that of conventional LEHR. The results indicated that the IQ-SPECT system with attenuation correction is capable of correcting inferior artifacts with high image quality.

(Ann Nucl Med)

Key words: multifocal collimator, CTAC, LEHR, artifact, ^{201}Tl

Introduction

The evaluation for known or suspected coronary artery disease using electrocardiogram (ECG)-gated myocardial perfusion single photon emission computed tomography (SPECT) imaging has been established in the diagnosis and the risk assessment [1]. As a gatekeeper, precise determination of normal images is critically important for the risk stratification of the patients with coronary artery disease. Normal stress myocardial perfusion imaging (MPI) was associated with an average annual cardiovascular event rate of 0.6-0.9% [2-3]. Normal SPECT provides important information for clinicians, indicating the excellent prognosis of patients who do not require further invasive therapy [2-3]. Therefore the delineation of the normal image is indispensable to avoid misguiding the strategy.

Multifocal collimators with dedicated reconstruction software have been introduced [4-5]. This IQ-SPECT system with ^{99m}Tc agents reportedly shortens scan times and considered to be clinically applicable in diagnosing patients with coronary artery disease [4]. With IQ-SPECT, it is possible to perform MPI scans in one-fourth the time or using one-fourth the administered dose as compared to a standard protocol using parallel-hole collimators [6-7]. In Japan, thallium-201 (^{201}Tl) myocardial perfusion study is conducted in more than 50% of stress examinations [8]. It was reported that there was a significant difference between Japanese and Western populations and that the best diagnostic accuracy was obtained by using the population- and orbit-specific normal database [9]. The normal values of a novel IQ-SPECT machine need to be determined in each population.

Furthermore, ^{201}Tl scan is known to have imaging artifacts that mimic either reversible or fixed perfusion abnormality [10]. However there are few studies on using Tl-201 to test the clinical value by IQ-SPECT/computed tomography (CT) protocol. Therefore the purposes of this study are to delineate the normal uptake in Tl-201 SPECT in each acquisition method and to compare this new protocol to already validated standard ones by using ^{201}Tl, especially in patients with normal perfusion imaging who are known to have low risk of cardiac event.

Methods

Patient characteristics

All patients underwent adenosine pharmacological stress myocardial perfusion imaging with ^{201}Tl in accordance with the guideline for stress MPI proposed by the Japanese Circulation Society [11]. The stress/rest myocardial perfusion SPECT as performed using ^{201}Tl, and quantitative gated SPECT (QGS) analysis were made. The inclusion criteria for the patients were subjects with normal myocardial perfusion imaging (MPI). The subjects included patients of more than 20 years of age, and patients scheduled to undergo stress/rest ECG-gated SPECT due to suspected or extant ischemic heart disease. The subjects were considered to be normal if summed stress score (SSS) was less than 3, and if QGS functional data was normal. Normal limits for gated SPECT and QGS software were determined based on the J-ACCESS database [2]. Excluded from the study were patients with idiopathic cardiomyopathy, severe arrhythmia, or heart failure with class III or higher New York Heart Association (NYHA) functional classification, or severe liver or renal disorders. Subjects were also excluded from the study if there was ECG abnormality or suspicion of ischemia. Hypertension could be included if it was mild and well managed. No significant coronary stenosis was documented, if coronary angiography (CAG) was conducted. CAG was not needed when there was no indication of CAG. Absence of respiratory and body movements was needed.

The study was approved by the institutional ethics committee, and written informed consent was obtained from all patients to participate in the study.

^{201}Tl Single Photon Emission Computed Tomography (SPECT).

Stress ^{201}Tl imaging was performed using stress/rest 1-day protocol [12]. Stress myocardial perfusion study was performed using 74 MBq of ^{201}Tl. Myocardial perfusion study was performed at rest using 37 MBq of ^{201}Tl. The study protocol is illustrated in Figure 1. Acquisition was performed using large-field measurements on Symbia T6 dual-head hybrid SPECT/CT cameras (Siemens Medical Solutions, Munich, Germany) equipped with a conventional gamma camera system (Siemens ECAM) or with a multifocal collimator called IQ-SPECT [13]. ECG-gated SPECT images were acquired with a 64x64 matrix, 6˚ step, and 360˚ rotation. QGS (Cedars Sinai Medical Center, LA, USA) analysis was also performed at stress and at rest. Eight electrocardiographic gated frames per cardiac cycle were acquired. Scan time per view was 14 s in the imaging protocols. The matrix size was 128x128. Projections were acquired through a 20% window centered on the 70 keV peak. All images were reconstructed by using 3-D ordered subset conjugate gradient modified (3D-OSCGM) with an iteration of 10, subset of 3, and Gaussian filter of 13.0 mm.

All CT was obtained on the 6-slice CT scanner of the integrated SPECT/CT apparatus (Symbia T6) during breath-hold with slight expiration after IQ-SPECT imaging. CT attenuation correction (AC) and scatter correction were used on IQ-SPECT data. Images not corrected for attenuation and scatter correction were also reconstructed. When necessary, images were motion-corrected manually.

Patient background data

Age, gender, height, weight, subjective symptoms, renal function, arrhythmia, and coronary risk factors were surveyed.

Data analysis

Visual Analysis

Image quality was assessed by evaluating resting images with IQ-SPECT and the conventional LEHR collimator. The scoring was made by mutual consent of two nuclear medicine physicians (1, poor; 2, fair; 3, good; 4, excellent) [14].

Segmental uptake of ^{201}Tl was quantified using semi-quantitative scores by quantitative perfusion SPECT (QPS) software and was confirmed by two experienced nuclear cardiologists. A 17-segment model of the left ventricle was used with a 5-point scale (0=normal uptake, 1=mildly-reduced uptake, 2=moderately-reduced uptake, 3=severely-reduced uptake, and 4=no uptake) (Fig. 2). The total defect score was defined as a sum of 17 segments [15]. Intra-observer discrepancy was resolved by consensus. Finally, a clinical diagnosis was determined from perfusion image as normal, probably abnormal, or abnormal.

For data analysis, the QGS program was applied to process short-axis tomograms to determine end-diastolic volume (EDV), end-systolic volume (ESV), and left ventricular ejection fraction (LVEF).

% Uptake Analysis

A two-dimensional polar map was created and % uptake of the left ventricle was determined by using QPS software.

Statistical analysis

Statistical analysis was performed using JMP software (version 9.02 for Windows). All values are presented as mean values ± standard deviation. To examine differences between groups, a t-test and non-parametric analysis using Wilcoxon/Kruskal-Wallis test were used to compare the data. To assess the difference in LV functions between LEHR and IQ-SPECT, a paired t-test was used. A *p*-value of less than 0.05 was considered to be significant.

Results

Clinical characteristics

The study group consisted of 40 patients (32 males/ 8 women, mean age 75±7 years). The subject height was 162±10cm, and the weight was 61±11kg. There was no subject whose estimated glomerular filtration rate was less than 45mL/min. No subjects had ECG abnormality. All examinations were conducted with informed consent in 40 subjects. A representative case of a normal SPECT patient is shown in Figure 3. Mean acquisition time was 16 minutes with conventional SPECT and 6 minutes with IQ-SPECT.

Visual Analysis

IQ-SPECT (AC) provided good or excellent image quality (3.5±0.5), and IQ-SPECT without AC was 3.7±0.5. The quality scores of the images acquired with IQ-SPECT (AC) were lower than those of LEHR (3.5±0.5 vs. 3.8±0.4, p=0.006). The quality score obtained by IQ-SPECT without CTAC was identical to that of LEHR (3.8±0.4 vs. 3.7±0.5, NS) (Table 1). Rest scores of visual analysis are listed in Table 2. Conventional Tl-201 study had a decrease in the mid-inferior segment (#10) of the left ventricle. IQ-SPECT images without CTAC were similar to those of conventional LEHR study. IQ-SPECT (AC) improved inferior decreased perfusion shown in conventional images in mid-inferior segments (#10). There was a tendency toward slight apical (#17) or apical anterior (#13) decrease by IQ-SPECT (AC) (table 1).

Final diagnosis of the subjects

A clinical diagnosis was determined by each image. From SPECT image obtained from a LEHR collimator, 40 subjects were determined as normal MPI. Forty out of forty subjects (100%) were also determined as normal from the SPECT image obtained by IQ-SPECT (AC). SPECT image obtained from IQ-SPECT without AC had diagnosed all the 40 subjects as normal. There was no subject with neither probably abnormal nor with abnormal SPECT. Clinical diagnosis obtained in the LEHR collimator was 100% concordant with that of IQ-SPECT collimator.

% uptake analysis in LEHR and IQ-SPECT

Figure 4 shows % uptake of the anterior and apex and inferior segments of the left ventricle. There was a significant difference between the mid anterior and mid inferior segment of the left ventricle (p<0.01). The uptake of the apical inferior was smaller than that of apical anterior segment (p<0.01). IQ-SPECT (AC) shows there was no difference in the uptake between anterior and inferior (NS). There was a decrease in uptake of apical or apical anterior in IQ-SPECT (AC).

LV functional analysis

Table 3 shows a comparison of EDV, ESV and LVEF at rest obtained from QGS using data of LEHR acquisition and IQ-SPECT acquisition. EDV obtained from IQ-SPECT (AC) was significantly lower than that from LEHR collimator ($p=0.003$). In addition, LVEF from IQ-SPECT was significantly higher than that from the LEHR collimator ($p=0.0009$). There was no statistical difference in ESV between the two ($p=0.12$).

Discussion

Our study showed that IQ-SPECT provided improved imaging especially in the inferior segments, which tended to have an inferior attenuation artifact of conventional ^{201}Tl study [16]. There was a tendency towards a slight decrease in apex or apical anterior by the AC image of IQ-SPECT. All the images of IQ-SPECT were good or excellent in image quality. We also observed that no significant difference in the quality of the images was registered between IQ-SPECT and conventional SPECT.

IQ-SPECT/CT system

Several types of gamma cameras have recently been introduced with semiconductor material instead of the conventional sodium iodine crystals [5]. This improvement is achieved by means of a multifocal collimator that rotates around the patient in a cardio-centric orbit resulting in a four-fold magnification of the heart while keeping the entire torso in the field of view. The IQ-SPECT system with SMARTZOOM collimator was introduced by Siemens in 2010. It was reported to have significantly improved the efficiency of myocardial perfusion imaging (MPI) using conventional, large field-of-view SPECT and SPECT/CT systems [4]. Flash 3D is a statistically based iterative reconstruction method based on ordered subset expectation maximization (OSEM). SPECT/CT allowed acquisition of MPI imaging and a CT scan, and fusion and registration of the two images. Complementary information such as calcium scoring could be obtained with SPECT/CT [13], although Symbia T6 cannot perform CT coronary angiography for fusion imaging between CT and MPI [14]. Attenuation correction could be successfully achieved with a CT attenuation map, and this method is more patient-specific to compensate for attenuation [17].

Technical and diagnostic characteristics with IQ-SPECT

^{201}Tl study might be prone to have inferior attenuation in some populations, which made it difficult to distinguish from inferior infarction [18]. Gender, obesity and difference between ^{201}Tl and ^{99m}Tc tracers are also to be taken into consideration. Apical anterior uptake might be lower in women. Patient body attenuation can be a factor to degrade image quality, when a patient has high body mass index. The location of soft tissue attenuation depends heavily on the position of the tissue in relation to the left ventricle. The severity of the attenuation artifact can be influenced by the energy of the incident photon [19]. Therefore attenuation of ^{201}Tl is more marked than for ^{99m}Tc [8, 20]. Experienced nuclear cardiologists can recognize the artifacts of the inferior wall with information of regional wall motion, differentiating attenuation artifact from myocardial scarring. However less experienced cardiologists or internists may misdiagnose it as an inferior infarction, which may lead the patient to further invasive study. IQ-SPECT with CT attenuation correction successfully improved inferior attenuation, in accordance with previous studies [21]. Recent studies showed that attenuation correction made diagnostic accuracy increase [22]. Attenuation and scatter correction using IQ-SPECT/CT would improve diagnostic confidence levels, especially in the right coronary artery. There are conflicting results of attenuation correction of ^{201}Tl studies that conclude it cannot have a beneficial effect on the prognosis [23].

We observed decreased perfusion in the apex with IQ-SPECT attenuation-corrected images. We have previously reported that the correlation in attenuation corrected myocardial perfusion count and myocardial thickness in normal myocardial perfusion patients. Both low myocardial uptake with attenuation correction and myocardial thinning were recognized at the apex. Therefore, apical thinning on the attenuation-corrected images was caused by anatomical thinning of the myocardium as previously reported [24]. Attenuation-corrected images would provide an accurate relationship between myocardial count and thickness because of the apical volume effect. The results of this study would help to standardize the image database. In IQ-SPECT, reducing acquisition time may reduce the likelihood of patient of motion artifacts, may increase camera efficiency, and may lead to improved patient throughput, although it may increase the image noise [25, 26].

SPECT images were acquired first with LEHR, followed by IQ-SPECT acquisition. Because of redistribution of ^{201}Tl, slight washout might have occurred in 30 minutes after stress when IQ-SPECT was performed. However, higher washout localized only in the apical region may not be explained by the higher statistical noise in the delayed image. Although shorter time acquisition of IQ-SPECT imaging might have a lower count, IQ-SPECT succeeded in achieving good image quality [22].

LV functional analysis

It is well known that ESV is underestimated in subjects with small hearts in QGS software [27]. Our study showed that there was a difference in EDV and LVEF between LEHR and IQ-SPECT. LV delineation in diastole using IQ-SPECT underestimates EDV and resulted in decreased LVEF. The relatively higher frequency of small hearts in this study population might be one of the factors [28]. The finding of this study suggested that this technical problem requires further investigation [28-29].

Study limitations

The present study had several limitations. First, this was a single-center, retrospective, observational study. Therefore, a multicenter study is needed to make a normal database in a Japanese population. Second, the small number of patients investigated requires further intensive studies to confirm clinical results in determining the prognosis in coronary artery disease. Third, the reduction of radiation doses in myocardial scintigraphy is an important issue. Finally, we did not attempt dose reduction.

Conclusion

The multifocal collimators SPECT/CT device provides reliable, high quality imaging by using ^{201}Tl. IQ-SPECT/CT in short time acquisition can be used appropriately in clinical study and is a feasible apparatus in finding, characterizing, and monitoring the disease.

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Legends for illustrations

Figure 1 The study protocol of pharmacological stress test. Conventional SPECT images were obtained with a low-energy high-resolution (LEHR) collimator, followed by IQ-SPECT acquisition and CT image for attenuation correction.

Figure 2 Left ventricular segmentation. Diagrammatic presentation of a circumferential polar plot of a 17 segment model of left ventricle: 1, basal anterior; 2, basal anteroseptal; 3, basal inferoseptal; 4, basal inferior; 5, basal inferolateral; 6, basal anterolateral; 7, mid-anterior; 8, mid-anteroseptal; 9, mid-inferoseptal; 10, mid-inferior; 11, mid-inferolateral; 12, mid-anterolateral; 13, apical anterior; 14, apical septal; 15, apical inferior; 16, apical lateral; 17, apex.

Figure 3 A case of normal myocardial perfusion imaging is shown. SPECT images in the left side (A) were obtained from Tl-201 conventional study with a low-energy high-resolution collimator. There was a decrease in the inferior segment of the left ventricle. On right side (B), the image of IQ-SPECT is shown, obtained in 6 minutes with CT attenuation correction. IQ-SPECT using AC provides improved imaging especially in the inferior segments.

Figure 4 The uptake of 5 segments of left ventricular myocardium calculated by QPS software was calculated. Mid-anterior, apical anterior, apex and apical inferior, mid-inferior segments are shown in the graph.

Table 1 Comparison of image quality scores between LEHR and IQ-SPECT

LEHR	IQ-SPECT (AC)	IQ-SPECT
3.8±0.4	3.5±0.5*	3.7±0.5

* P <0.05 vs. conventional LEHR without AC

Table 2 Visual SPECT analysis of each method

	LEHR	IQ-SPECT (AC)	IQ-SPECT (without AC)
1	0±0	0±0	0±0
2	0±0	0±0	0±0
3	0.1±0.3	0±0	0±0
4	0.4±0.6	0.3±0.2	0.4±0.7
5	0±0	0.03±0.2	0.1±0.3
6	0±0	0±0	0±0
7	0±0	0.1±0.4	0.1±0.5
8	0±0	0±0	0±0
9	0±0	0±0	0±0
10	0.3±0.5	0±0*	0.4±0.6
11	0.3±0.5	0±0	0.03±0.2
12	0.03±0.2	0±0	0±0
13	0.03±0.2	0.5±0.7*	0.1±0.4
14	0±0	0.1±0.2	0±0
15	0.2±0.4	0.1±0.3	0.2±0.4
16	0.1±0.2	0.1±0.3	0.1±0.2
17	0.1±0.3	0.5±0.7*	0.1±0.4

AC, attenuation correction;

The number from 1 to 17 indicates the segment number of the left ventricle.

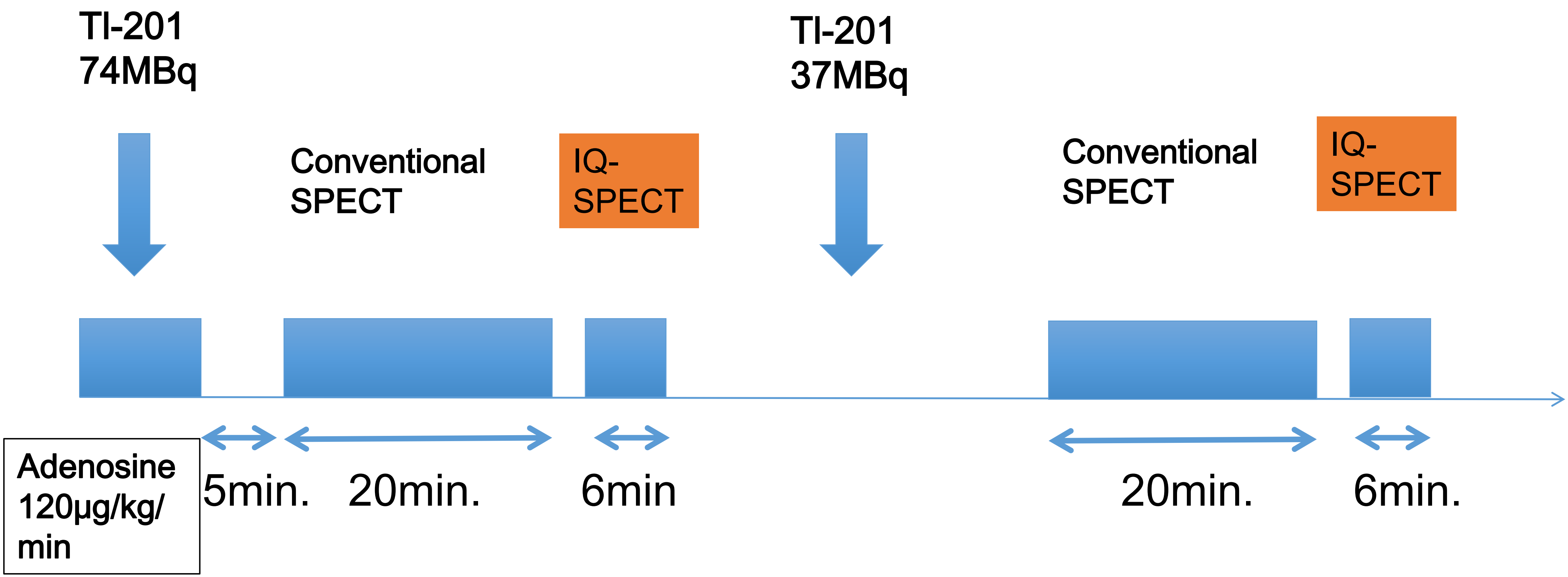
LEHR, low-energy high-resolution; AC, attenuation correction.

* P <0.05 vs. conventional LEHR without AC

Table 3 Paired comparisons between parameters determined using LEHR and IQ-SPECT

Parameter	LEHR	IQ-SPECT	p value
EDV (ml)	57.5±19.8	53.4±18.5	0.003
ESV (ml)	20.5±12.8	22.3±13.0	0.12
LVEF (%)	66.9 ±10.7	62.0± 13.8	0.0009

EDV, end diastolic volume; ESV, end systolic volume; LVEF, left ventricular ejection fraction.


Tl-201
74MBq
Conventional
SPECT
IQ-
SPECT
Tl-201
37MBq
Conventional
SPECT
IQ-
SPECT
Adenosine
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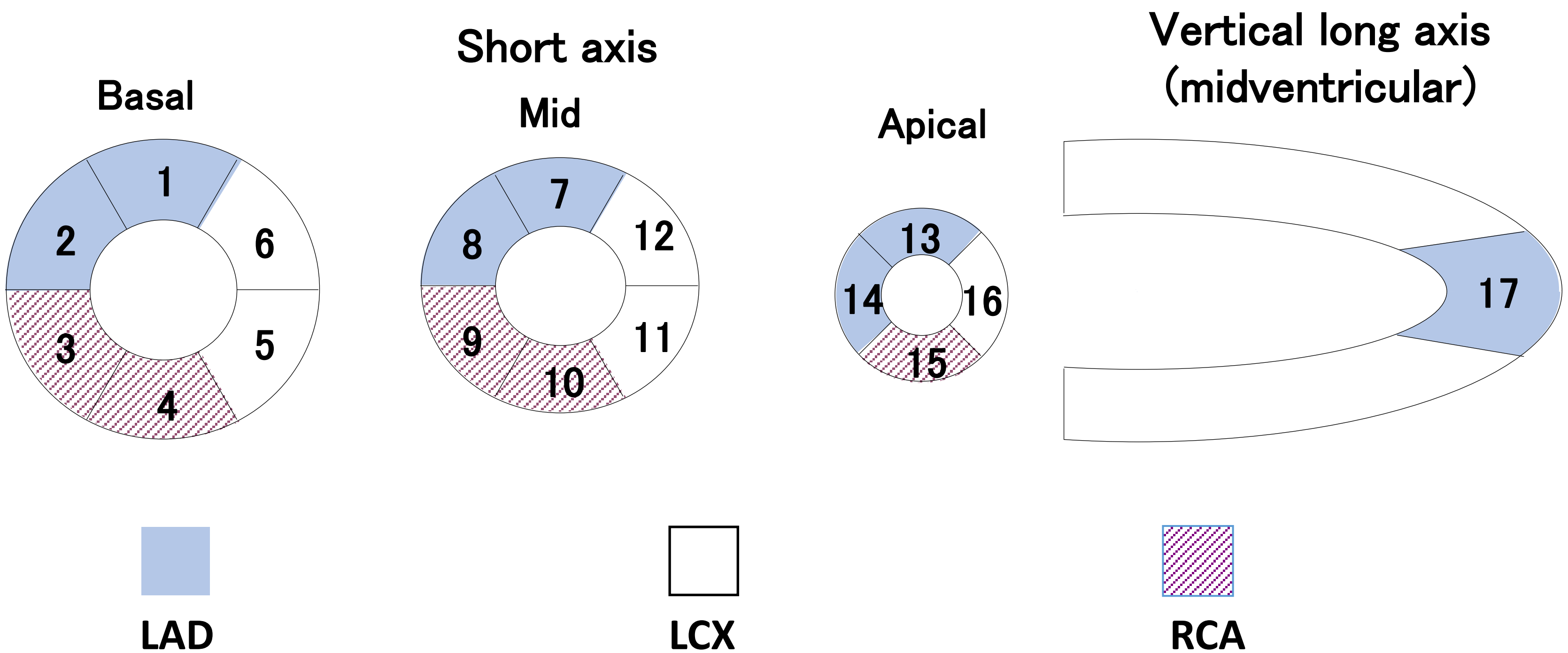
min
5min.
20min.
6min
20min.
6min.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Basal
Mid
Apical
Vertical long axis
(midventricular)
1
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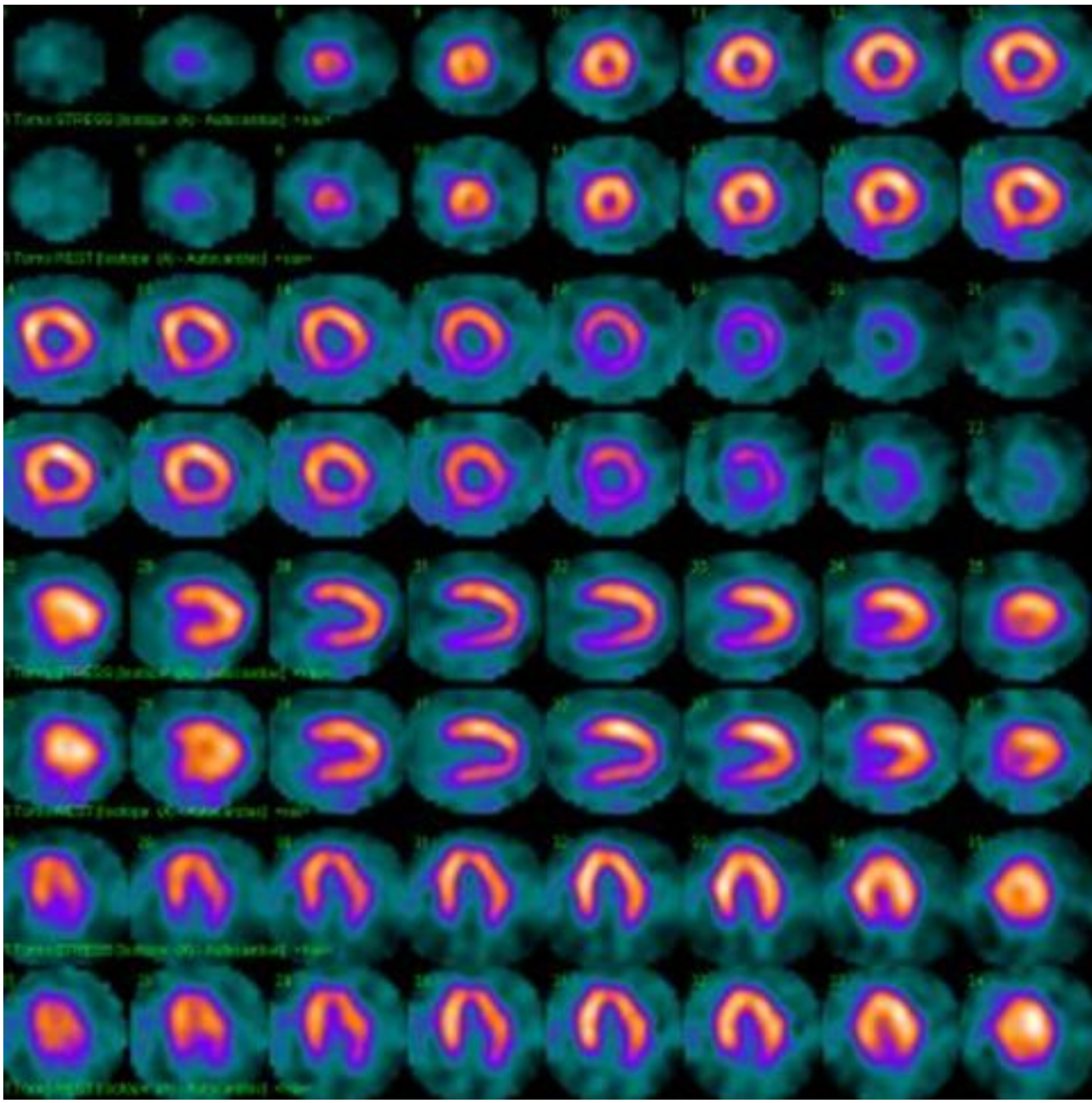
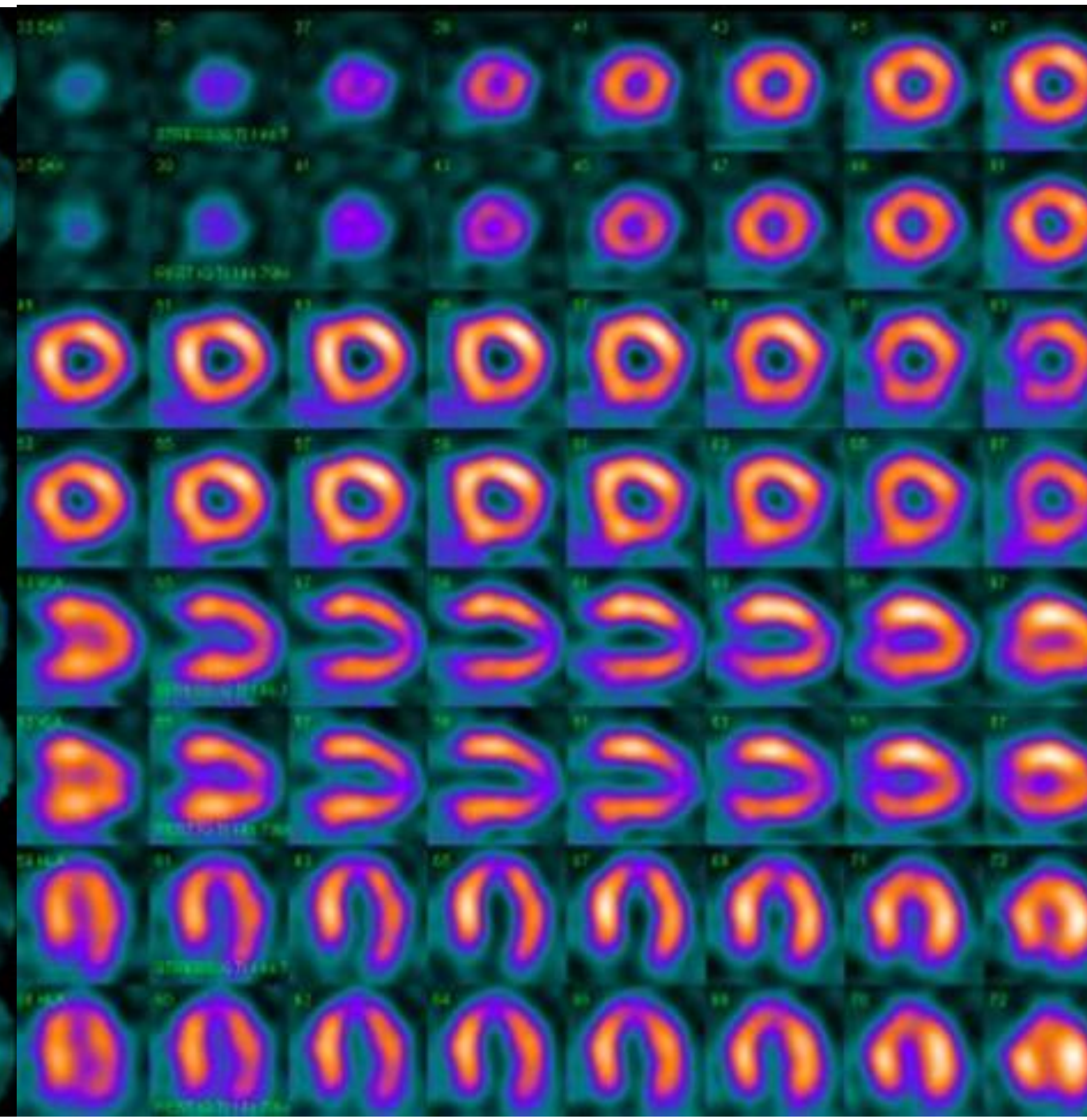
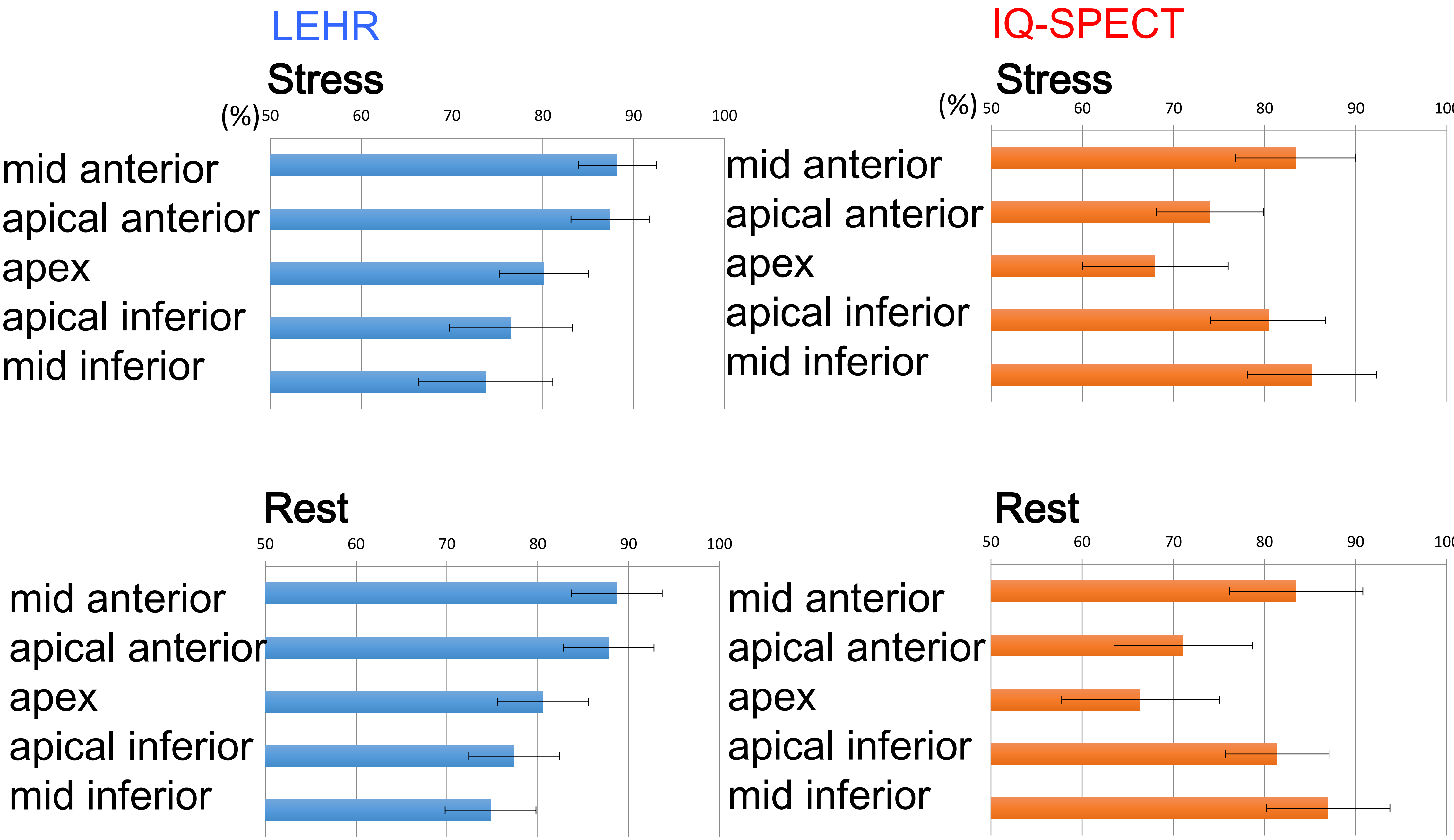
LAD
LCX
RCA

A LEHR



B IQ-SPECT





LEHR
IQ-SPECT
Stress
(%)
50
60
70
80
90
100
mid anterior
apical anterior
apex
apical inferior
mid inferior
Rest