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Left Ventricular Global Longitudinal Strain Calculated from Manually Traced Endocardial Border Lengths Utilizing the Images for Routine Ejection Fraction Measurement by Biplane Method of Disks

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ABSTRACT

Purpose: The purpose of this study was to test whether the fractional change in the endocardial border length between end-diastolic and end-systole as manually traced in left ventricular ejection fraction (LVEF) measurement using the biplane method of discs (MOD) consistent with the global longitudinal strain derived from speckle-tracking echocardiography.

Methods: For 105 patients who underwent echocardiography, two- and four-chamber images with manually traced endocardial lines for LVEF measurement by MOD were stored. LV endocardial lengths at end-diastole and at end-systole were measured on both images to calculate the fractional length changes, which were averaged (GLS_{MOD}). Speckle-tracking analysis was performed to measure global longitudinal strains in the apical two- and four-chamber and long-axis images, and the three values were averaged (GLS_{STE}) according to the ASE and EACVI guidelines.

Results: There was no significant difference between GLS_{MOD} and GLS_{STE}. GLS_{MOD} correlated well with GLS_{STE} ($r=0.81$, $p<0.001$), and there was no fixed bias in the Bland-Altman analysis. The intraclass correlations for the intra- and inter-observer comparisons for GLS_{STE} were excellent and those for GLS_{MOD} were adequate.

Conclusion: The fractional LV endocardial border length change, GLS_{MOD}, showed sufficient agreement with GLS_{STE} to justify its use as a substitute for the STE-derived global longitudinal strain.

Key words: global longitudinal strain; speckle-tracking echocardiography; biplane method of disks; ejection fraction; left ventricular systolic function

INTRODUCTION

The development of speckle-tracking echocardiography (STE) in the past two decades has enabled assessment of regional and global myocardial deformation in various directions [1-4]. Among the STE parameters, global longitudinal strain, which represents the relative length change of the global left ventricular (LV) myocardium in the longitudinal direction between end-diastole and end-systole, is recognized as the most important marker of decreased myocardial function and prognosis of patients with various cardiac diseases [4-6]. To measure global longitudinal strain in routine echocardiographic examinations will contribute to more accurate assessment of LV myocardial function in patients with a wide variety of cardiac diseases. However, at present, the STE software is not installed in all the echocardiographic machines, and the analysis algorithm to calculate myocardial strain was not unified among vendors until recently [7]. Thus, the measurement of global longitudinal strain is not widely performed in routine examinations.

On the other hand, the measurement of the LV ejection fraction (LVEF) using the biplane method of discs (MOD) is routinely performed in almost all echocardiographic laboratories. When measuring LVEF, an examiner manually traces the LV endocardial borders at end-diastole and at end-systole. The fractional change in the endocardial border length between end-diastolic and end-systole should theoretically be consistent with the global longitudinal strain. However, this hypothesis has not been sufficiently validated. If global longitudinal strain can be accurately measured in a similar process such as the LVEF measurement using MOD, examiners could obtain global longitudinal strain information using any available ultrasound machine. The purpose of the present study was to test whether the fractional change of manually traced endocardial border length between end-diastole and end-systole can serve as a substitute for the global longitudinal strain derived from STE.

SUBJECTS AND METHODS

Study Subjects

We studied 105 patients who underwent echocardiographic examination with good image quality. The underlying diseases of the study patients were hypertensive heart disease in 17, primary or secondary cardiomyopathy in 10, ischemic heart disease in 8, valvular heart disease in 6, cor pulmonale in 1, and pericarditis in 1; the remaining 62 patients did not have any prominent abnormality in the echocardiographic examination. Among them were 9 patients with atrial fibrillation and 1 with artificial ventricular pacing.

Echocardiographic Measurements and Biplane Method of Disks

The standard echocardiographic examination was performed in accord with the guidelines of the ASE and EACVI in all patients using an ACUSON SC2000 echocardiographic system (Siemens AG, Healthcare Sector, Erlangen, Germany) equipped with a 4V1c transducer (1.25 to 4.5 MHz) [5]. The biplane MOD was performed to measure LVEF in each patient during routine examination, and two-dimensional images with manually traced lines were stored (**Figure 1**). After the examination, the stored image was analyzed off-line using Image-J software (National Institutes of Health, Bethesda, Maryland, USA). LV endocardial myocardial lengths at end-diastole (MLdia) and at end-systole (MLsys) were measured in the stored two-chamber and four-chamber images, and the fractional LV endocardial length change in each view was calculated as follows:

$$\text{Fractional LV endocardial length change (\%)} = (\text{MLsys} - \text{MLdia})/\text{MLdia} \times 100$$

The global longitudinal strain based on the manual endocardial border tracing of the images for

LVEF measurement by MOD (GLS_{MOD}) was obtained by averaging the absolute values of the fractional LV endocardial length changes in the two-chamber and four-chamber views. In patients with atrial fibrillation, the MOD measurement was done for a single beat for which the preceding and prepreceding R-R intervals were almost equal [8].

Speckle-Tracking Echocardiography

Also after the examination, speckle-tracking analysis was performed in three apical views by the standard software (SC2000 Workplace R5.0 eSieVVI; Siemens AG, Healthcare Sector, Erlangen, Germany) (**Figure 2**), which complied with the ASE/EACVI statement in 2015 [7]. The highest-quality single-beat image was selected for the analysis in each view. The global longitudinal strain at the inner myocardial layer was measured as a change of the endocardial line length in each apical long-axis view, two-chamber view and four-chamber view, and the average of the three values (GLS_{STE}) was calculated. For the GLS_{STE} measurements in patients with atrial fibrillation, we used a single beat for which the preceding two R-R intervals were nearly equal [8].

Statistical Analysis

The statistical analysis was performed with standard statistical software (IBM SPSS ver. 25 for Windows, IBM Co., Armonk, NY, USA). Pearson’s linear correlation and Bland-Altman analysis were used to assess the relationship between GLS_{MOD} and GLS_{STE}. A paired t-test was used to compare GLS_{MOD} and GLS_{STE} values. The reproducibilities of GLS_{MOD} and GLS_{STE} were examined in 20 patients randomly selected from the subject population, and intraclass correlation analysis was performed for the intra-observer comparison (K.O.) and for the inter-observer comparison (K.O. and M.A.). For all statistical tests, p-values <0.05 were considered to indicate significance.

RESULTS

Patient Characteristics and Echocardiographic Measurements

The patient characteristics and standard echocardiographic parameters of the study subjects are summarized in **Table 1**. Among the patients, LV hypertrophy (LV mass index >115 g/m^2 for male and >95 g/m^2 for female) was seen in 34 patients, decreased LVEF (<50%) was seen in 11, and LV asynergy was in 6.

Relationship between GLS_{MOD} and GLS_{STE}

There was no significant difference between GLS_{MOD} and GLS_{STE} (19.3±4.2 vs 18.9±3.8%, p=0.08). GLS_{MOD} correlated well with GLS_{STE} (r=0.81, p<0.001), and there was no fixed bias between GLS_{MOD} and GLS_{STE} in the Bland-Altman analysis (the difference between the means was 0.42% [95% confidence interval (CI): −0.06 to 0.90] (**Figure 3**). The difference between GLS_{MOD} and GLS_{STE} was out of mean±2SD range in 5 subjects, who did not have any heart disease and their GLS value was relatively high (GLS_{STE}: 20.4±2.9% and GLS_{MOD}: 19.7±3.5%). In addition, the difference between GLS_{STE} and GLS_{MOD} did not significantly correlate with any echocardiographic parameter of LV geometry or function.

Reproducibility

As shown in **Table 2**, the intraclass correlation coefficients for the intra- and inter-observer comparisons for GLS_{STE} were excellent (0.96 and 0.95, respectively) and those for GLS_{MOD} were adequate (0.86 and 0.78, respectively).

DISCUSSION

The present study demonstrated that GLS_{MOD}, which is the global longitudinal strain derived from the manual tracing of endocardial borders in the images for the biplane MOD procedure, was well correlated with GLS_{STE} without any fixed bias in the Bland-Altman analysis. In addition, we also confirmed that the intra- and inter-observer reproducibilities of the GLS_{MOD} were adequate.

Many investigators reported that the global longitudinal strain can detect myocardial abnormalities before LVEF decline and is useful for estimating the prognosis of patients with heart failure, valvular heart disease, cardiomyopathy, and ischemic heart disease [9-14]. Therefore, the measurement of the global longitudinal strain may become increasingly important in routine echocardiographic examinations. However, global longitudinal strain measurement using STE is far less common than LVEF measurements because the former is available only in some parts of machines used in the world. In the present study, we showed that GLS_{MOD}, which is available on almost all echocardiographic machines, can be a substitute for GLS_{STE}. Moreover, the addition of a GLS_{MOD} calculation program to the MOD software may not be difficult. If the GLS_{MOD} calculation function was added to all echocardiographic machines including low-end ones, GLS_{MOD} could be very easily measured simultaneously with LVEF, and both LV chamber function and myocardial function could be evaluated without any additional time or labor.

A few recently released Japanese echocardiographic machines (Aplio i- and a-series, Canon Medical Systems, Otawara, Japan; and ALOKA LISENDO 880, Hitachi, Ltd., Tokyo, Japan) automatically calculate GLS_{MOD} simultaneously with LVEF calculation. However, to our knowledge, no other machines are equipped with such software. Because our institution does not have any of the above recent machines, we had to rely on off-line analysis of the stored stop-frame image (re-tracing the stored tracing line). So far, only one study has tried to investigate the clinical usefulness of the endocardial shortening derived from manually traced endocardial border lengths [15]. Kobayashi et al. reported that the manually derived endocardial shortening in the apical four-chamber view had an excellent correlation with STE-derived longitudinal strain in the four-chamber view (R^2=0.84, $p<0.001$) and that the bias between them was 0.4% (95% confidence interval (CI): −2.8 to 3.6%) in 250 patients (50 normal, 100 dilated cardiomyopathy and 100 hypertrophic cardiomyopathy). However, they did not measure the GLS_{STE}, namely, the averaged value of the three apical views recommended in the guidelines [5]. In the present study performed on unselected patients visiting a small cardiovascular clinic, we showed that our GLS_{MOD} correctly reflected the GLS_{STE} measured according to guidelines. At present, measuring the GLS_{MOD} on most echocardiographic machines in the world would require the somewhat inconvenient process that we performed in the present study. We think an addition of the automatic GLS_{MOD} calculation program would not be difficult for ultrasound instrument makers, while the practical usefulness would be considerably high for both users and patients.

There have been several reports indicating the good reproducibility of global longitudinal strain compared to that of EF [14-16]. The reproducibility of the GLS_{STE} was also excellent in the present study. The reproducibility of GLS_{MOD} was slightly inferior to that of GLS_{STE} but can be considered adequate for clinical use. In many echocardiographic machines used in the real world, STE is not available or has several limitations including machine dependency due to differences in analysis algorithms [17]. We would argue that GLS_{MOD}, which is based on a far simpler theoretical ground than $GLS_{STE,}$ can provide a practical parameter of LV myocardial function independent of differences in vendors, release years and other features.

Limitations

There are several limitations to the present study. First, the data collection was performed at a single center and the study population was relatively small. Second, GLS_{MOD} and GLS_{STE} were not measured in a blind fashion. Third, because GLS_{MOD} was measured using a manually traced endocardial borderline, the accuracy of our method may have been affected by the image quality. In addition, our GLS_{MOD} did not include information of the apical long-axis view because this view is not used in the MOD procedure. This might have contributed to the difference between GLS_{MOD} and GLS_{STE} values. Finally, a good correlation between GLS_{STE} and GLS_{MOD} might not necessarily guarantee the clinical usefulness of GLS_{MOD} [18]. Further study will be needed to establish the practical usefulness of GLS_{MOD}, and the use of GLS_{STE} may be recommended in the situation associated with serious clinical decision.

CONCLUSION

The fractional LV endocardial border length change between end-diastole and end-systole, GLS_{MOD}, was in good agreement with GLS_{STE}, suggesting that GLS_{MOD} derived from routine echocardiographic imaging can be used as a substitute for the STE-derived global longitudinal strain.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest

This study was financially supported by grant-in-aid for scientific research from the Japanese Society of Sonographers (No. 2017-1). The authors declare no other conflicts of interest.

Ethical approval

This study was approved as a retrospective observational study by the Research Ethics Committee of the Faculty of Health Sciences at Hokkaido University. Instead of obtaining informed consent, the objectives and methods of the present study were shared with the public through our institution’s home page and a physical bulletin board; patients who did not wish to participate could request their data to be deleted from the study.

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Figure Legends

Figure 1. Left ventricular endocardial border length measurement

The biplane method of disks was performed in each patient to measure the left ventricular (LV) ejection fraction, and two-dimensional images with manually traced lines were stored. After the examination, the stored image was analyzed off-line and LV endocardial myocardial lengths at end-diastole and at end-systole were measured from the stored two-chamber and four-chamber views.

Figure 2. Speckle-tracking analysis

Speckle-tracking analysis was performed in the apical long-axis view (**a**), two-chamber view (**b**), and four-chamber view (**c**). The global longitudinal strain was obtained in each view and the averaged value was calculated as GLS_{STE}.

Figure 3. Relationship between global longitudinal strain derived from manual endocardial border tracing (GLS_{MOD}) and that from speckle-tracking echocardiography (GLS_{STE}).

Results of the correlation and regression analysis (**a**) and Bland-Altman analysis (**b**) are shown.

Table 1. Patient characteristics and standard echocardiographic parameters

Parameters	mean±SD	Range
Clinical characteristics		
Age (years)	71.7±12.3	36 – 98
Male/female	57/48	
Body surface area (m^2)	1.60±0.21	1.11 – 2.10
Systolic blood pressure (mmHg)	123±19	80 – 190
Diastolic blood pressure (mmHg)	68±13	48 – 106
Heart rate (bpm)	64±16	46 – 155
Hypertension (n, [%])	77 [73%]	
Diabetes (n, [%])	14 [13%]	
Dyslipidemia (n, [%])	60 [57%]	
Echocardiographic parameters		
LV end-diastolic diameter (mm)	47.9±5.2	36 – 72
LV end-systolic diameter (mm)	31.3±6.2	23 – 65
LV ejection fraction (%)	62.5±10.0	22 – 77
Interventricular septal thickness (mm)	9.8±1.7	6 – 18
LV posterior wall thickness (mm)	8.7±1.3	6 – 12
LV mass index (g/m^2)	97±22	41 – 160
Left atrial volume index (mL/m^2)	42.1±17.5	17 – 119
E (cm/s)	71.8±19.5	38 – 140
E/A	0.94±0.36	0.43 – 2.27
DT (ms)	230±50	93 – 390
e′ (cm/s)	7.1±2.1	3.4 – 13.2
E/e′	10.4±3.4	5.5 – 29.0

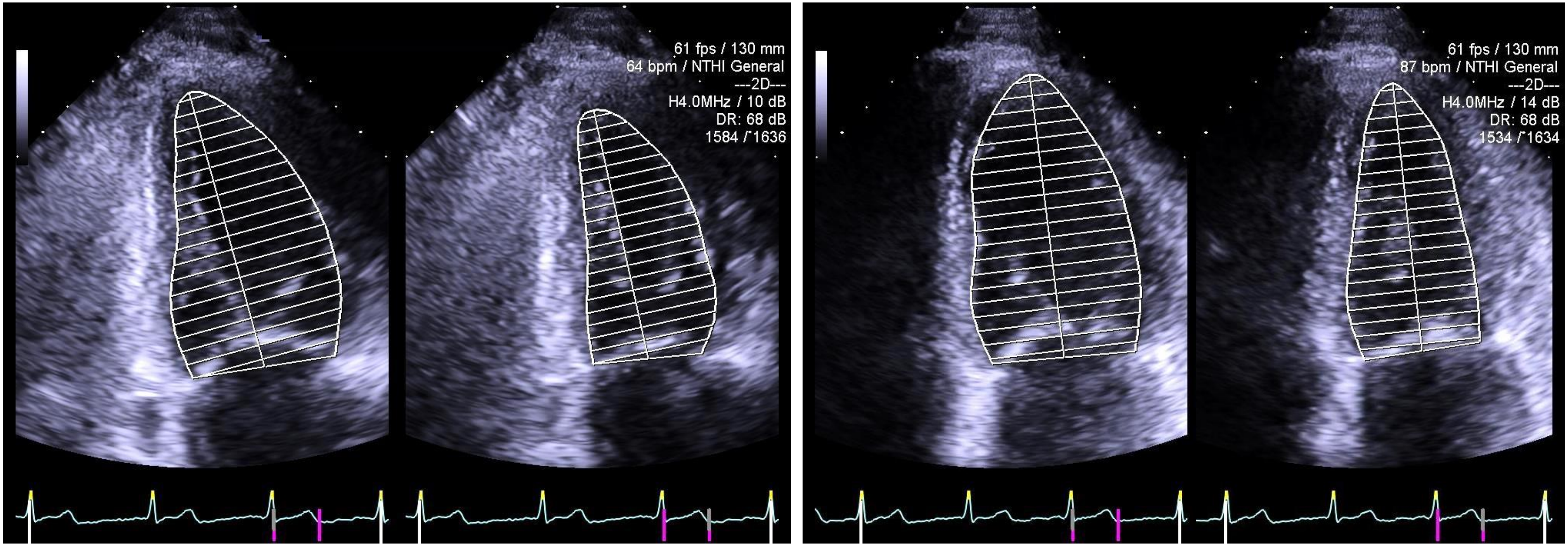
LV, left ventricle; E, peak early-diastolic transmitral flow velocity; E/A, the ratio of the E to peak atrial-systolic transmitral flow velocity; DT, deceleration time of the E; e′, peak early-diastolic mitral annular velocity at septal annulus.

Table 2. Intra- and inter-observer reproducibility

	Intra-observer			**Inter-observer**		
	ICC	**95% CI**	**p**	**ICC**	**95% CI**	**p**
GLS_{STE}	0.96	0.91–0.98	<0.001	0.95	0.89–0.98	<0.001
GLS_{MOD}	0.86	0.68–0.94	<0.001	0.78	0.54–0.91	<0.001

ICC, intraclass correlation coefficient; GLS_{STE}, global longitudinal strain derived from speckle tracking echocardiography; GLS_{MOD}, global longitudinal strain measured as a fractional change of manually traced endocardial border length between end-diastole and end-systole

Figure 1


61 fps / 130 mm
64 bpm / NTHI General
---2D---
H4.0MHz / 10 dB
DR: 68 dB
1584 /ˉ1636
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87 bpm / NTHI General
---2D---
H4.0MHz / 14 dB
DR: 68 dB
1534 /ˉ1634

Figure 2

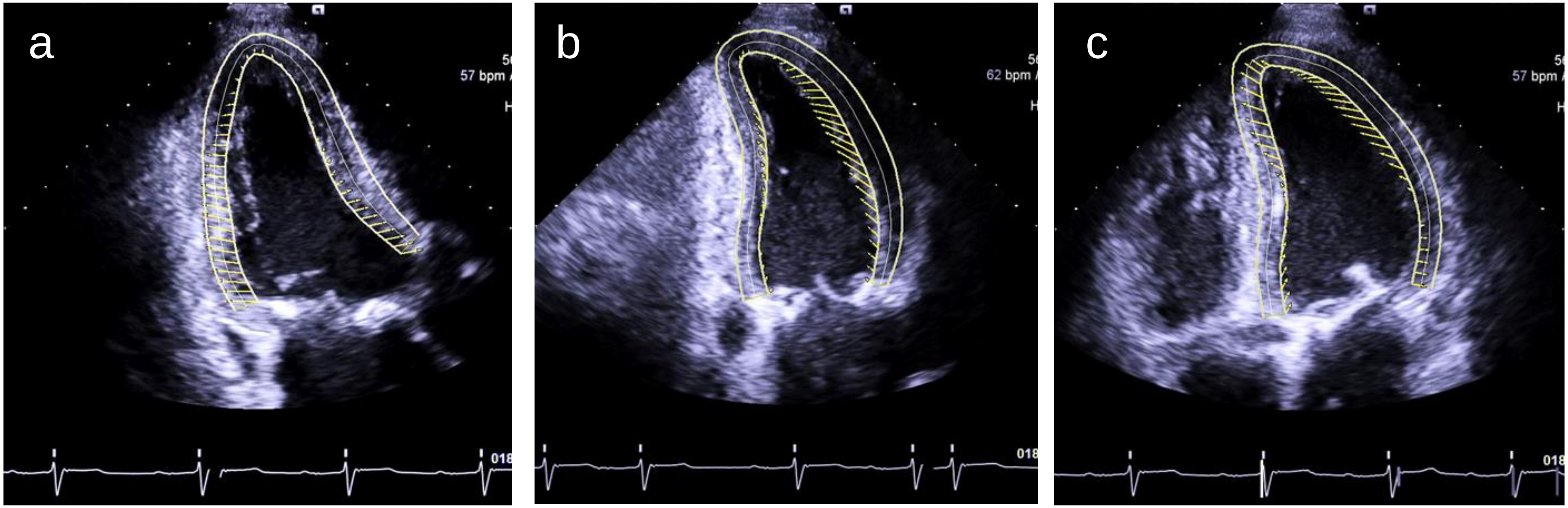
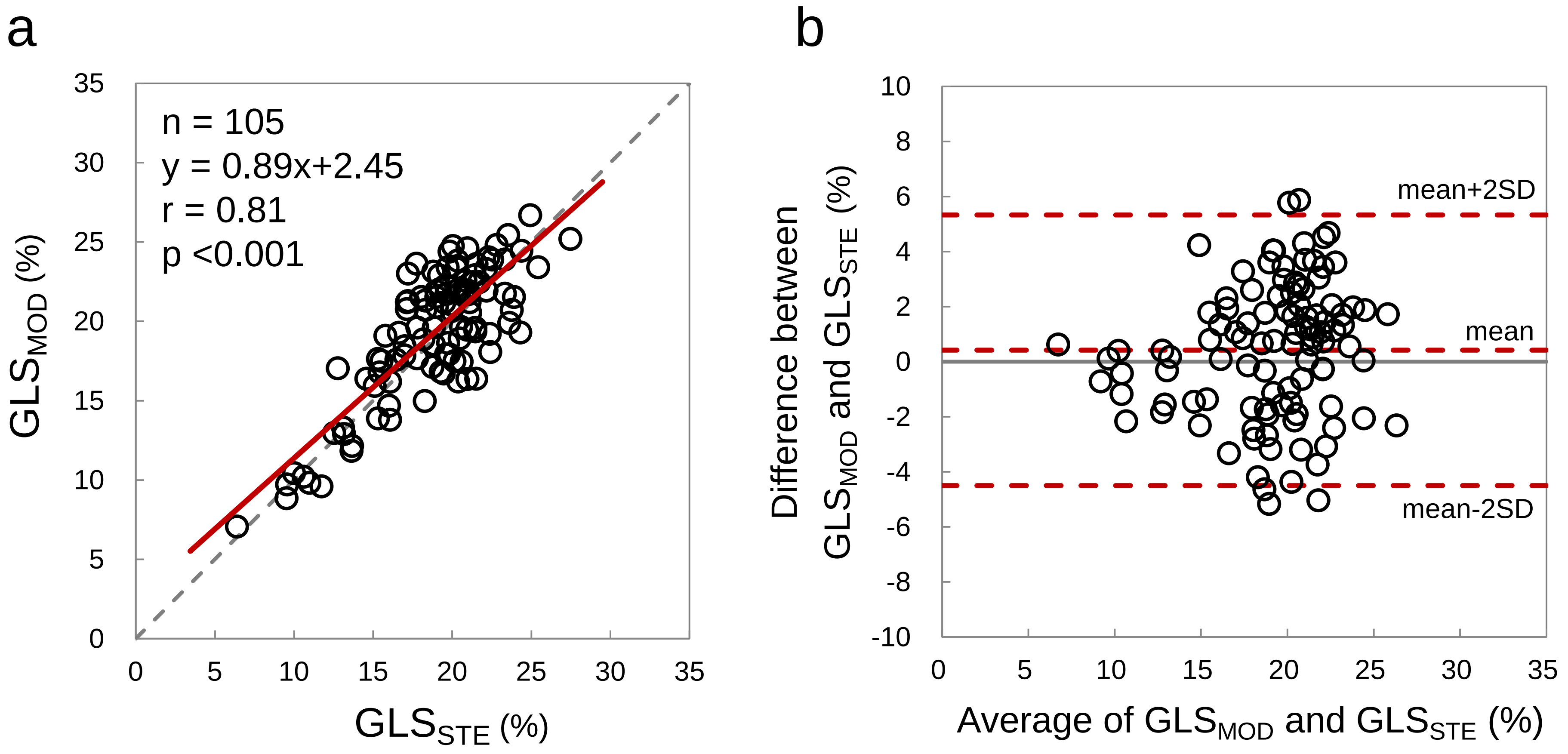


Figure 3


a
n = 105
y = 0.89x+2.45
r = 0.81
p <0.001
35
30
25
20
15
10
5
0
0
5
10
15
20
25
30
35
GLS$_{MOD}$ (%)
GLS$_{STE}$ (%)
b
10
8
6
4
2
0
-2
-4
-6
-8
-10
mean+2SD
mean
mean-2SD
0
5
10
15
20
25
30
35
Difference between GLS$_{MOD}$ and GLS$_{STE}$ (%)
Average of GLS$_{MOD}$ and GLS$_{STE}$ (%)