Left ventricular function assessment by free-breathing magnetic resonance sequence with multiple excitations*

Avaliação da função ventricular esquerda pela sequência de ressonância magnética sem apneia e com múltiplas excitações

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Abstract **OBJECTIVE: To evaluate the efficacy of free-breathing magnetic resonance sequence with three excitations in the determination of ventricular volumes and masses in individuals without breath-holding. MATERIALS AND METHODS: Left ventricular volumes and masses determined in 32 healthy volunteers through two cine magnetic resonance imaging sequences were compared: the first sequence, traditionally utilized and considered as a standard, performed under apnea, with a single excitation, and the second one, with free-breathing and three excitations. Three observers at different levels of experience evaluated the agreement and reproducibility. Intraclass correlation coefficient, paired *t*-test, Bland-Altman plots and sign test were utilized for statistical analysis. RESULTS: According to the two most experienced observers, intraclass correlation coefficients were > 0.913, the paired *t*-test demonstrated *P* values > 0.05, Bland-Altman plots had differences randomly distributed around zero and the sign test descriptive levels were > 0.05. CONCLUSION: The sequence evaluated presents an excellent agreement and reproducibility as compared with the standard sequence, and can be utilized in patients with respiratory limitations.**
Keywords: Heart; Ventricular function; Magnetic resonance imaging.

Resumo **OBJETIVO: Avaliar a eficácia da sequência de ressonância magnética com três excitações, para obtenção de volumes e massas ventriculares, em indivíduos com respiração livre, sem apneia. MATERIAIS E MÉTODOS: Em 32 voluntários sadios, foram comparados os volumes e massas do ventrículo esquerdo, obtidos por meio de duas sequências de ressonância magnética em modo cine. A primeira, tradicionalmente utilizada e considerada padrão, em apneia e com excitação única, e a segunda, em respiração livre e com três excitações. Três leitores, com diferentes níveis de experiência, testaram a concordância e a reprodutibilidade. Para a análise estatística foram utilizados o coeficiente de correlação intraclasse, o teste *t*-pareado, os gráficos de Bland-Altman e o teste do sinal. RESULTADOS: Para os dois observadores mais experientes, os coeficientes de correlação intraclasse foram superiores a 0,913, assim como os níveis descritivos do teste *t*-pareado acima de 0,05, os gráficos de Bland-Altman com as diferenças distribuídas aleatoriamente em torno do zero e o teste do sinal com seu nível descritivo superior a 0,05. CONCLUSÃO: A sequência testada apresenta ótima concordância e reprodutibilidade em relação à sequência padrão, podendo ser aplicada em indivíduos com limitações respiratórias.**
Unitermos: Coração; Função ventricular; Imagem por ressonância magnética.

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INTRODUCTION

An accurate evaluation of left ventricular systolic function (LVSF) is essential for the diagnosis, management and follow-up of several cardiac and extracardiac diseases[1,2].

This evaluation can be performed by means of an invasive technique such as cineventriculography[3] and other less invasive techniques such as echocardiography[4], radionuclide ventriculography, single photon emission computed tomography (SPECT) and positron emission tomography (PET)[5], magnetic resonance imaging (MRI)[6] and, most recently, by computed tomography (CT)[7].

Currently, MRI is considered as the reference method in the study of LVSF for its accuracy in the ventricular volume evaluation and high reproducibility. However, the MRI reliability in the LVSF calculation depends on the acquisition of images free of motion artifacts that degrade images and

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impair the delimitation between the myocardium and the ventricular cavity. Among the most common motion artifacts, one can mention the respiratory artifacts that can be eliminated by means of apnea during images acquisition.

In some situations, with the current MRI parameters optimized for LVSF evaluation, the sequence duration exceeds the breath-hold capability of the patient. In these cases, the required breath-hold time may be shortened, decreasing the spatial and/or temporal resolution of the images. The disadvantage of such practice is that the definition of the ventricular end-systole is based on non-reliable functional data[8,9]. Another hypothesis is the free-breathing acquisition with real-time sequences[10,11]. However, these are recent innovations still to be made widely available.

One of the ways of minimizing motion artifacts on a MRI study is to increase the number of excitations or the number of signal average. Thus, motion-corrected free-breathing images acquisition without the utilization of real-time sequences can be achieved by increasing the number of excitations (generally to three). The disadvantage of this technique is the lower quality of the images as compared with those of the standard breath-hold sequences.

The present study is aimed at evaluating the efficacy of sequences with a higher number of excitations (number of signal average) in the calculation of the LVSF and left ventricular mass in patients with free-breathing, without apnea.

MATERIALS AND METHODS

The present study included 32 (17 male and 15 female) healthy individuals in the age range between 23 and 48 years (mean, 32.4 years) with no previous history of cardiac or pulmonary disease.

The examinations were performed in Siemens (Siemens Medical Systems; Erlangen, Germany) high-field 1.5 tesla MRI units Magnetom Symphony (n = 22) and Magnetom Avanto (n = 10) models. The maximum gradient amplitude was 30 mT/m (Symphony) and 45 mT/m (Avanto) and the slew rate, 75 T/m/s (Symphony) and 200 T/m/s (Avanto). The body coil was utilized as transmitter, and the posterior spinal coil as well as the anterior two-element surface phased-array coil (Symphony) and the six-element surface phased-array coil as receivers.

The calculation of ventricular volume and mass was based on 9 to 11 slices (sections) perpendicular to the interventricular septum in the short axis plane, from the left ventricle base to the apex. Segmented fast imaging with steady-state precession (TRUE-FISP) sequence was utilized with ECG-gating in cine mode. Each section was acquired during 6- to 11-second expiratory apnea and presented a temporal resolution around 30 ms and spatial resolution on the imaging plane of 2.1 × 1.4 mm. Slice thickness was 8 mm at 2 mm interval (Figure 1).

After the acquisition of this set of left ventricular short axis images considered as a standard in the ventricular function calculation, a new sequence was performed with the same parameters, except for the higher number of excitations (n = 3 excitations [3NEX]) and without breath-holding. Neither type of respiratory belt/synchronizer nor paramagnetic contrast agent was utilized.

Left ventricular short axis images were analyzed on a workstation with a dedicated software for ventricular mass and volume calculations (Leonardo – Argus and Viewer; Siemens Medical Solutions, Erlangen, Germany), by three radiologists with different experience levels. The observer 1 had four-year experience, the observer 2, two-month experience, and the observer 3, five-year experience in cardiac MRI.

The observer 1 classified the sequences quality into three categories: excellent, good and poor. Excellent corresponded to demonstration of well defined myocardial edges and blood in the ventricular cavity on all of the imaging sections; good corresponded to distorted and ill-defined endocardial limits on up to three imaging sections; and poor corresponded to ill-defined images on more than four sections.

Initially, a semi-automatic algorithm for myocardial edges definition was utilized in the left ventricular delineation. In cases where correction was required, the endocardial and epicardial limits would be manually adjusted and delineated. In this process, the papillary muscles were considered as part of the ventricular cavity. The intermethod agreement (standard sequence *versus* 3 NEX sequences) was evaluated by means of a second reading randomly performed by the same observer 30 days after the first reading.

The statistical analysis was performed with the intraclass correlation coefficient, the paired t-test, Bland-Altman plots and the sign test. The significance level adopted was 5% (α = 0.05).

The research project was submitted, analyzed and approved by the Committee for Ethics in Research of Universidade Federal de São Paulo/Hospital São Paulo, São Paulo, Brazil.

RESULTS

Among the 32 individuals evaluated with the standard sequence, 29 presented images with excellent quality and three with good quality. In the evaluation with the 3 NEX sequence, 10 individuals had images with excellent quality, 14 with good quality, and eight with poor quality.

The analysis of intermethod agreement in the measurements performed with standard sequence and 3 NEX sequence demonstrated optimum agreement for the observers 1 and 3. For all the parameters evaluated, the intraclass correlation coefficient was > 0.900 and the descriptive level (P) of the paired t-test, was > 0.05 (Tables 1 and 2). Additionally, in a random evaluation of the Bland-Altman plots and sign test, the authors observed that the differences between the standard sequence and the 3 NEX sequence were distributed around the zero value with a descriptive level < 0.05 (Figures 2 and 3). Although with a high intraclass correlation coefficient, a full agreement was found for the observer 2 in relation to ventricular mass (Table 3). Statistically significant difference was observed in relation to mean ejection fraction, with higher values found in the measurement with 3 NEX sequence. Values for ventricular volumes were lower in the 3 NEX sequence, with descriptive level (P) < 0.05 for mean ventricular volumes and sign test values (Figure 4).

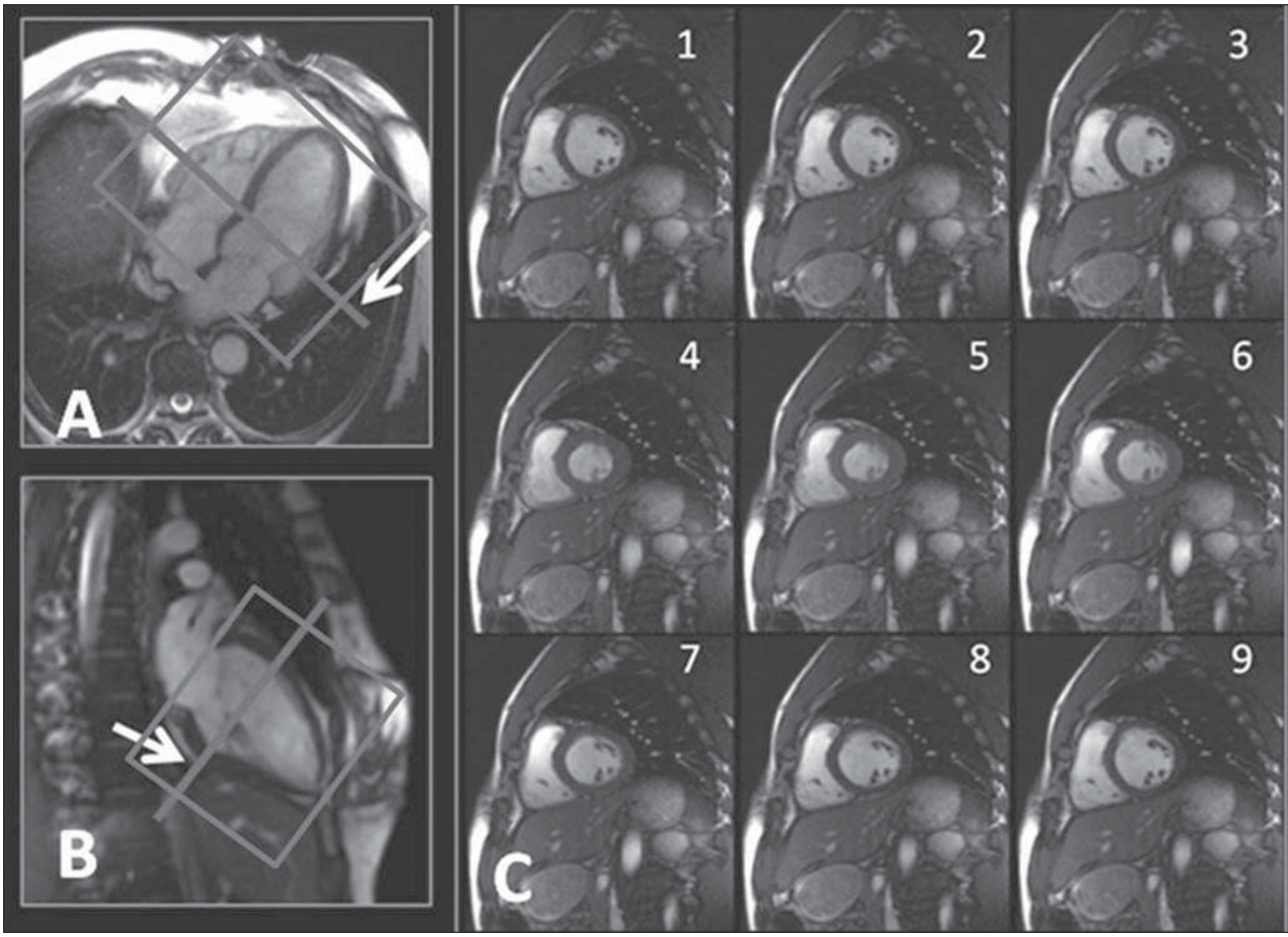


Figure 1. A,B: Scheduling of sections on left ventricle short axis orthogonal to the interventricular septum. **C:** Some of the images included in the series of standard cine MRI sequences in the slice positioning indicated by the arrows on **A** and **B**.

Table 1 Correlation between standard sequence and 3 NEX sequence for observer 1.

	Mean ± standard deviation				
Parameters	Standard	3 NEX	*t* Test (*p*)	ICC	CI 95%
Ejection fraction	65.59 ± 5.06	64.95 ± 5.31	0.224	0.914	(0.824; 0.958)
End-diastolic volume	136.22 ± 29.98	137.54 ± 30.47	0.388	0.979	(0.958; 0.990)
End-systolic volume	47.32 ± 14.36	48.48 ± 14.03	0.207	0.966	(0.931; 0.984)
Ejection volume	88.89 ± 18.68	89.07 ± 19.92	0.887	0.966	(0.930; 0.983)
Mass	111.19 ± 29.35	110.09 ± 31.04	0.615	0.957	(0.912; 0.979)

ICC, intraclass correlation coefficient; IC, confidence interval.

Table 2 Correlation between standard sequence and 3 NEX sequence for observer 3.

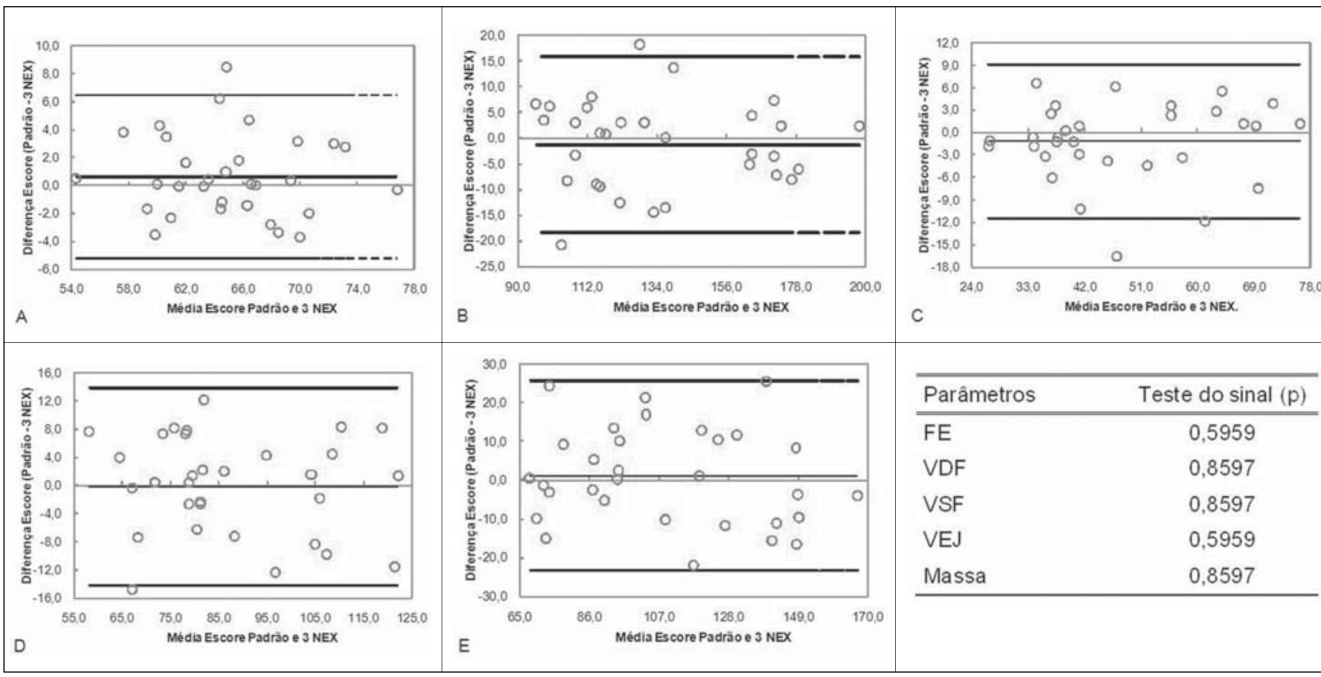
	Mean ± standard deviation				
Parameters	Standard	3 NEX	*t* Test (*p*)	ICC	CI 95%
Ejection fraction	65.03 ± 4.71	64.35 ± 5.53	0.192	0.913	(0.822; 0.958)
End-diastolic volume	128.25 ± 28.95	126.86 ± 28.07	0.444	0.967	(0.933; 0.984)
End-systolic volume	45.37 ± 14.14	45.71 ± 14.37	0.658	0.977	(0.952; 0.989)
Ejection volume	82.88 ± 17.23	81.15 ± 17.11	0.225	0.936	(0.868; 0.969)
Mass	103.98 ± 26.20	103.06 ± 26.05	0.710	0.924	(0.844; 0.963)

ICC, intraclass correlation coefficient; IC, confidence interval.

The variability between the measurements by the two sequences, i.e., the percentage of the absolute value of the difference in relation to the averages between the two measurements for the three observers is demonstrated on Table 4.

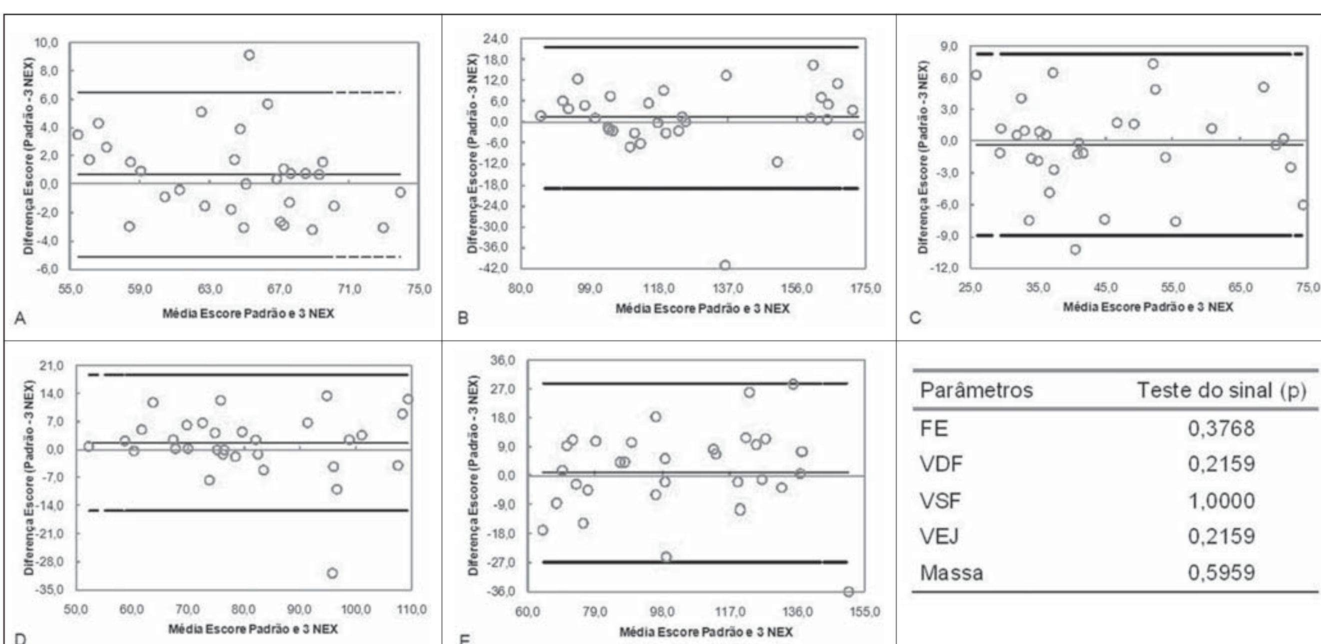
DISCUSSION

Magnetic resonance imaging is considered as the most refined method for evaluating the left ventricular systolic performance[12]. This method allows an extremely effective calculation of ventricular mass and volume, and serial studies with high reproducibility and low variability because of a better contrast between the myocardium and the ventricular cavity, the absence of acoustic window limitations, the lower



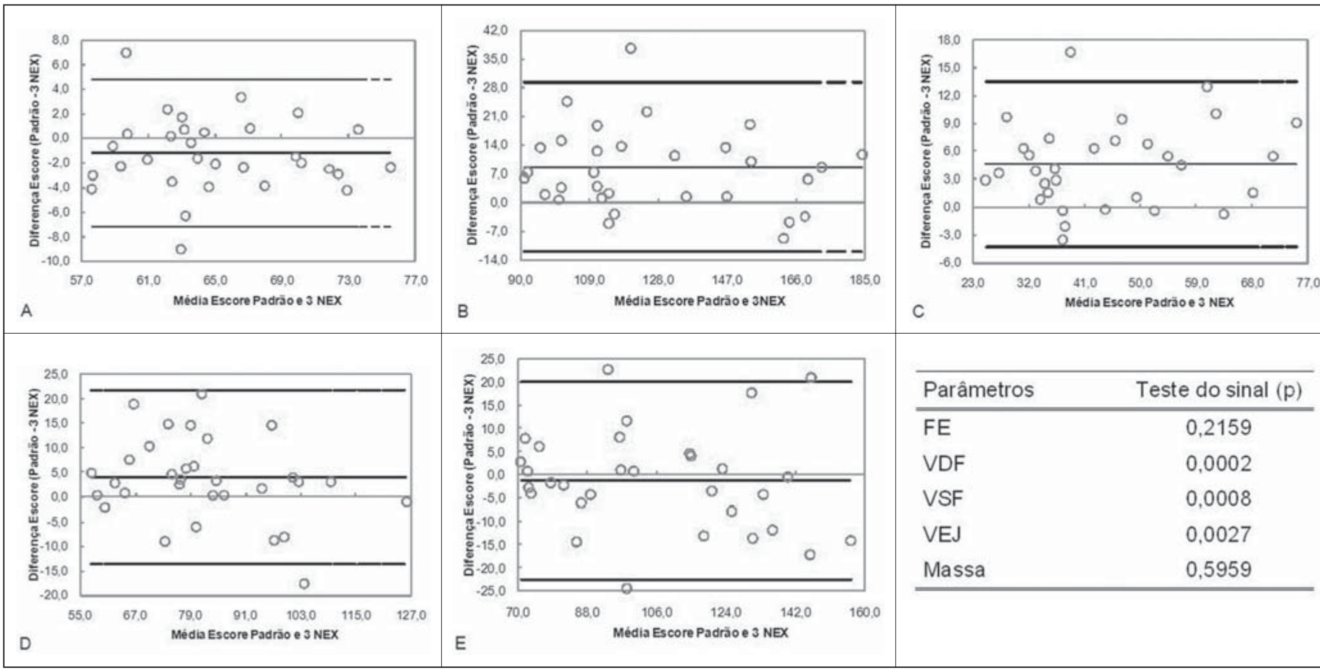
Parâmetros	Teste do sinal (p)
FE	0,5959
VDF	0,8597
VSF	0,8597
VEJ	0,5959
Massa	0,8597

Figure 2. Sign test and Bland-Altman plot for ejection fraction (**A**), end-diastolic volume (**B**), end-systolic volume (**C**), ejection volume (**D**) and left ventricle mass (**E**), found by the observer 1 by means of standard sequence and 3 NEX sequence.



Parâmetros	Teste do sinal (p)
FE	0,3768
VDF	0,2159
VSF	1,0000
VEJ	0,2159
Massa	0,5959

Figure 3. Sign test and Bland-Altman plot for ejection fraction (**A**), end-diastolic volume (**B**), end-systolic volume (**C**), ejection volume (**D**) and left ventricle mass (**E**), found by the observer 3 by means of standard sequence and 3 NEX sequence.



Parâmetros	Teste do sinal (p)
FE	0,2159
VDF	0,0002
VSF	0,0008
VEJ	0,0027
Massa	0,5959

Figure 4. Sign test and Bland-Altman plot for ejection fraction (**A**), end-diastolic volume (**B**), end-systolic volume (**C**), ejection volume (**D**) and left ventricle mass (**E**), found by the observer 2 by means of standard sequence and 3 NEX sequence.

Table 3 Correlation between standard sequence and 3 NEX sequence for observer 2.

Parameters	Mean ± standard deviation		*t* Test (*p*)	ICC	CI 95%
	Standard	3 NEX			
Ejection fraction	64.74 ± 5.13	65.97 ± 5.26	0.029	0.908	(0.811; 0.955)
End-diastolic volume	132.12 ± 27.57	123.52 ± 28.50	< 0.001	0.965	(0.929; 0.983)
End-systolic volume	47.01 ± 13.95	42.42 ± 13.26	< 0.001	0.973	(0.944; 0.987)
Ejection volume	85.13 ± 16.89	81.10 ± 18.10	0.015	0.931	(0.859; 0.966)
Mass	106.12 ± 25.90	107.24 ± 27.46	0.556	0.958	(0.914; 0.980)

ICC, Intraclass correlation coefficient; CI, confidence interval.

Table 4 Variability (%) between standard sequence and 3 NEX sequence.

Parameters	Mean ± standard deviation		
	Observer 1	Observer 2	Observer 3
Ejection fraction	3.42 ± 3.06	3.93 ± 3.24	3.56 ± 2.97
End-diastolic volume	5.40 ± 4.41	8.21 ± 7.28	5.13 ± 5.63
End-systolic volume	8.01 ± 7.70	11.87 ± 9.47	7.65 ± 7.13
Ejection volume	6.66 ± 4.98	8.94 ± 7.64	6.82 ± 6.75
Mass	9.34 ± 7.40	7.49 ± 6.32	10.41 ± 7.65

operator dependency, and the utilization of the Simpson's method that does not rely on geometric approximations to calculate volumes. Thus, it has advantages over traditionally used methods such as echocardiography and SPECT. Additionally, MRI is a practically noninvasive method that, differently from cineventriculography, does not utilize ionizing radiation for images acquisition.

However, the MRI reliability in the LVSF calculation depends on the acquisition of images free of motion (generally respiratory) artifacts that degrade images and impair the delimitation between the myocardium and the ventricular cavity.

Usually, depending on cardiac frequency, equipment utilized and optimized parameters a 7-13-second breath-hold is required to achieve artifacts suppression. In children and individuals with reduced capacity because of the underlying disease, the breath-holding duration may represent a limiting factor in the acquisition of quality images. In these cases, alternative techniques can be adopted, with reduction of the acquisition time and, consequently, of the breath-holding duration, by means of manipulation of temporal and spatial resolution parameters. The disadvantage of this method is the influence on the left ventricle functional parameters, particularly with manipulation of the temporal resolution[9].

Another alternative would be the utilization of real-time sequences that do not require breath-holding[13]. However, this is a new technique, requiring technologically advanced equipment and software that are still unavailable.

Thus, the authors evaluated the effectiveness of respiratory artifacts reduction on the sequence traditionally utilized (segmented, ECG-gated TRUE-FISP) in an individual with free-breathing, and increasing the number of excitations (number of signal average). In the present study, the number of excitations of a sequence considered as the current standard (TRUE-FISP) was triplicated, and the other parameters remained unchanged.

The agreement between data regarding sequences, ventricular volumes (end-diastolic volume and end-systolic volume), their ratios (ejection fraction and ejection volume) and myocardial mass obtained by each observer with the 3 NEX sequence were compared with those obtained by the same observer with the standard sequence.

Optimum intermethod (standard sequence *versus* 3 NEX sequence) agreement was found for the two most experienced observers (1 and 3) in relation to all the evaluated parameters. For the observer 2 (less experienced), in spite of the excellent correlation for all the evaluated parameters, a full agreement was observed only in the calculation of the ventricular mass.

As the standard sequences were repeated twice, the variability observed between the measurements performed with these two sequences for the observers 1 and 3 was similar to the variability described in the literature[14,15]. The arithmetic mean of this variability for the two mentioned observers was 3.49% for ejection fraction, 5.27% for end-diastolic volume, 7.83% for end-systolic volume, 6.74% for ejection volume and 9.87% for ventricular mass. For the observer 2, the variability in the values for volumes was higher, justifying the absence of agreement for these parameters. The higher variability and the absence of intermethod agreement reported by the observer 2 can be explained by the lower quality of images acquired with the 3 NEX sequence and the lower experience of this observer.

The 3 NEX sequence adds difficulties in the myocardial limits delineation because of the lower image quality, although reproducible and agreeing results can be achieved by experienced and appropriately trained observers with the current standard sequences.

The present study has not been completed yet, considering that its results were based on a population of healthy volunteers, with an assumed and limited variability. Further studies involving patients with heart diseases are necessary to validate the actual effectiveness of the 3 NEX sequence.

CONCLUSION

The 3 NEX sequence presents optimum reproducibility and agreement as compared with the standard sequence, and can be used in patients with respiratory limitations.

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