Error evaluation of ventricular mechanics measurement in patients with discoordinate ventricular contraction [version 1; peer review: 1 approved with reservations]

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Abstract
In patients with discoordinate ventricular contraction, accurate identification of local mechanics from all heart regions is essential. Current measurement techniques are imperfect because a large part of the ventricular wall may be excluded, resulting in non-physiological average strain. In order to evaluate this error, we propose to compare the measured average strain to a reference strain obtained by averaging through a series of measurements. We assessed magnetic resonance (MR)-tagged images and determined circumferential strain in 160 regions of the ventricular wall in 10 patients with idiopathic dilated cardiomyopathy and left bundle branch block and 9 healthy volunteers. For each subject a global strain was calculated as the average of all measured strains. Then a reference strain was determined as the average of global strains for both experimental groups.

The reference strains of a patient group and healthy controls both had a physiological pattern, with a peak shortening of -0.034 and -0.15, respectively.

A large difference between the measured global strain and the reference strain indicates measurements which have large regions of ventricular wall which are excluded in the measurements.

Keywords
error evaluation, ventricular contraction

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Introduction

A cardiac strain pattern explains how a part of the ventricular wall is shortening or lengthening during the cardiac cycle. In ventricles of healthy subjects, all parts of the ventricular wall shorten fairly uniformly during systole\textsuperscript{1,2}. This is different in patients whose patterns of myocardial electrical activation and/or regional distribution of myocardial contractility are irregular\textsuperscript{3,4}.

In these patients, the contraction is discoordinate and the uniformity of strain shortening is replaced by a complex interplay of simultaneous shortening and stretching in different regions. The regions that are activated earlier shorten, and those that are activated later and have not developed enough tension, stretch.

In studies evaluating ventricular mechanics, the accurate identification of local mechanics from all regions is essential. The existing measurement techniques such as magnetic resonance (MR)-tagging and ultrasound speckle tracking only measure a limited number of regions within the left ventricular wall\textsuperscript{5–7}. Some parts of the ventricular wall that are important in determining the global ventricular mechanics may be excluded from the regions measured\textsuperscript{8–10}. Therefore, the resulting average strain may appear non-physiological, for example, as lengthening during systole, which indicates cardiac filling. But we know that ventricle is contracting during ejection and therefore the average strain must always have negative slope during this period. We suggest that this characteristic could be used to evaluate the quality of the measurements.

In this study, a reference strain was determined from a series of measurements by averaging. Separate reference strains were determined for patients with discoordinate contraction and healthy controls.

Methods

The study included 10 patients (age 67±8) with idiopathic dilated cardiomyopathy (DCM) and left bundle branch block (LBBB) who were selected for cardiac resynchronization therapy (DCM+LBBB group) and 9 healthy volunteers (control group). The ethics committee of the Catharina Hospital approved the study protocol, and all subjects gave informed consent.

The methods for acquiring the MR-tagged images, the measurement parameters, the technique of strain extraction from the recorded MR-tagged images and the partial data analyses of the measured data have been described previously\textsuperscript{11,12}. Briefly, images were acquired using a conventional 1.5-T scanner (Philips Gyroscan T5-II, Philips Medical Systems, Best, The Netherlands). A 500-ms acquisition period was started 20 ms after the electrocardiogram trigger, and the time interval between two consecutive images was 20 ms. MR-tagged images were recorded in five parallel short-axis cross-sections, each slice was further divided into 32 sectors. For each of 160 sectors, we determined the pattern of circumferential mid-wall strain ($\varepsilon_{cc}$).

A global strain was obtained as an average of 160 strain measurements. A reference strain was obtained as an average of global strains separately for patients and controls. The ejection phase based on the reference strain was determined as described previously\textsuperscript{11}. Briefly, we located the peak negative slope during systole on the strain curve and fitted a linear curve to it. The beginning and the end of the ejection phase were determined where the linear curve crossed the zero strain and maximum strain points, respectively.

Results

Figures 1A and 1B show the measured strain patterns from 160 regions of a patient with DCM+LBBB and a healthy control.
respectively. The patient with DCM+LBBB showed an exchange of negative and positive slopes during the initial systole phase in the average strain pattern. In contrast, the control subject showed an increasingly negative slope during the same period. The strain patterns in the patient with DCM+LBBB were highly heterogeneous compared to the control subject, and the curve band patterns were similar. The peak shortening for the average strain was -0.06 and -0.17 for the patient and control, respectively.

The shortcomings of this measurement technique are reflected in patient individual average strains. The first measured point in the strain pattern is during systole, that is, 20 ms after the electrocardiogram QRS trigger has started the measurements. In five of the patients assessed, the average strain pattern (Figure 2A) had a positive slope during the first half of systole. A positive slope on the curve indicates ventricular filling, but ventricular filling does not occur after the onset of tension generation in the ventricular wall. This measurement technique does not assess the mechanics of the entire ventricular wall, just a part of it. It relies on the coincidence of individual cardiac mechanics and selection of regions, which are measured irrespective of whether this artifact is pronounced. Because of the stochastic nature of this event, the averaging of cardiac strains throughout the group yields a better estimate of the actual cardiac strain than individual measurements.

On the basis of the reference strain, the ejection phase was from 1 to 16 of the MR-tagged images in patients with DCM+LBBB and from frames 1 to 14 in controls.

Data of ventricular mechanistic measurements evaluation

4 Data Files

http://dx.doi.org/10.6084/m9.figshare.940973

Discussion

We constructed a reference strain for patients with cardiac activation disorder and healthy controls. As expected, the resulting reference strain presented a negative slope during the entire early systole phase. A large difference between the measured global strain of each subject and the reference strain is indicative of insufficient measurements.

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A standard procedure to determine the ejection phase on the basis of the average cardiac strain is based on identifying the peak negative slope during systole, fitting a linear curve to it, and identifying the time points where the linear curve crosses the zero strain and maximum strain points, which represent the beginning and end of the ejection phases, respectively. Without considering if the patients had positive slopes during systole, this procedure would be associated with several errors in case of our measured strains. The reference strain averages out the measurement errors in patients and thus facilitates more accurate detection of cardiac phases.

Currently, ventricular function is frequently evaluated on the basis of patterns of a regional strain. A simple test of global ventricular strain could additionally verify whether the measurements included all the relevant regions of the ventricle.

Figure 2. The global strain from 10 patients with idiopathic dilated cardiomyopathy (DCM) and left bundle branch block (LBBB) (A) and from 9 healthy controls (B). The group average, that is, the reference average strain, is identified by a red line.
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Data availability
figshare: Data of ventricular mechanistic measurements evaluation. http://dx.doi.org/10.6084/m9.figshare.940973

Consent
Written informed consent for publication of clinical details and clinical images was obtained from all the participants involved.

Competing interests
There are no conflicts of interest to declare.

References
1. Strain is a novel method for objective quantification of systolic function using 2-D echocardiography, 3D-Echocardiography or MRI. Cardiac MRI (cMRI) is usually considered the reference standard for measurement of myocardial strain. The most common cMRI method, termed tagged cMRI, allows full 3D assessment of regional strain. However, due to its complexity and lengthy times for analysis, tagged cMRI is not usually used outside of academic centers. Tagged cMRI is also primarily used only in research studies.

Strain echocardiography (StE) promises to be a new tool for quantitative assessment of cardiac function. Clinical application in daily routine has begun at the moment. Analysis of intra- and interobserver reliability is an important aspect in the process of developing these novel techniques from theory to the implementation into daily routine diagnostics. This is also true for MRI. A reproducibility study should be done in this study/report. I miss the definition of a concrete aim of the study and clinical conclusions. I miss a statistical analysis. Does the study have a descriptive character?

All findings can be open discussed, but they should be discussed and so I am missing an open, positive-negative, hypothetical and critical discussion about MRI-strain.

This study is in principle well conducted and promising, but can be “indexed” only after some changes.

It is an interesting idea that the segmental split/deviation of the strain values discredit this method for clinical use. Otherwise medicine works with “deviations” (e.g. colour doppler findings). Is this what the author wants to tell us?

Generally there is a need for critical discussion regarding the decision-making process in individual patient and specific diagnosis or the diagnostic consequences. I believe that it is important issue to discuss controversial findings and to analyze the clinical relevance of novel methods. I am sure,
regarding the strain measurements, that there are a lot of open questions. We have to be aware of all possible pitfalls and ambiguities concerning strain-technology with the knowledge of asynchronicity, poor echo-window pitfalls (echocardiography), and reproducibility problems.

2. The author has to increase the number of patients (a minimum of 30 participants with DCM and 20 healthy participants) and there is a need for statistical comparison. 20 Patients with preserved function and without left bundle branch block would be very important too.

3. The author should compare the research tool MRI with 2D Strain- or 3D Strain-echocardiography. We have to learn more about the comparability of MRI-Strain values and echocardiography values.

4. In the results section the times of the investigation of the single patients and the time for the analysis must be specified (for MRI and for Echocardiography). The number of non-examined segments in both techniques should be examined/ counted.

5. There is a need for a comparison of strain values measured by MRI and echocardiography.

6. Author have to improve the discussion of the clinical importance of strain measured by MRI, in comparison to echocardiography (when MRI and when echocardiography?) and should discuss advantages and disadvantages.

7. The error/problems of MRI and the applicability in daily routine and the costs have to be discussed.

8. An inter-observer reproducibility of the analysis should be carried out (if possible, in comparison to echocardiography).

9. The impact of left bundle branch block on the results of strain values in comparison to normal synchronisation should be discussed (for example Sonne et al., 2009).13

10. The final message should be emphasized. Is MRI-Strain not ready for use in clinical routine? Is the error/deviation of the values so big, that a diagnosis is not possible? The “split” or width range of segmental strain-values are known (the relevance of these mechanism for human health is still unclear), otherwise the clinical use of global strain and “averaged values” is accepted.

References


**Competing Interests:** No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
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