

The Inverse Radius for Detection of Patients with Cardiac Dyssynchrony

Martin S Andersen¹, Cooper Moore², Olaf T von Ramm², Peter Sogaard³, Johannes J Struijk¹, Samuel E Schmidt¹

¹ Aalborg University, Aalborg, Denmark

² Duke University, Durham, USA

³ Aalborg University Hospital, Aalborg, Denmark

Abstract

Cardiac dyssynchrony, particularly in patients with Left Bundle Branch Block (LBBB), poses significant challenges in clinical diagnostics. This study investigates the curvature of the interventricular septum (IVS) throughout the cardiac cycle, as a potential biomarker for detecting cardiac dyssynchrony in patients. Data from 28 subjects into three groups of which 14 subjects with no diagnosed cardiac abnormalities (Normal), and 14 dyssynchrony patients undergoing CRT treatment, with active external pacing (On), and without active pacing (Off). At all temporal points the IVS contour was fitted to a circle using the Levenberg-Marquardt algorithm, and the radius extracted and inverted. The inverse radius decreased significantly depending on cardiac health with the Normal, On, and Off groups being 0.43 ± 0.16 , 0.49 ± 0.10 , and 0.53 ± 0.15 respectively. Findings suggest that the inverse radius could serve as a biomarker for identifying cardiac dyssynchrony in LBBB patients, potentially guiding therapeutic decisions and improving patient outcomes.

1. Introduction

Cardiac dyssynchrony is a significant contributor to heart failure (HF), particularly in patients with Left Bundle Branch Block (LBBB) [1, 2]. LBBB disrupts the normal sequence of electrical activation, leading to left ventricular dyssynchrony and exacerbating HF symptoms [1, 3, 4]. Effective management of cardiac dyssynchrony remains challenging, with Cardiac Resynchronization Therapy (CRT) being a primary intervention to restore synchronized contraction and improve cardiac function [3]. However, CRT's efficacy varies, and identifying reliable biomarkers for dyssynchrony is crucial for optimizing treatment outcomes.

This study explores the curvature of the interventricular septum (IVS) from ultrasound images as a novel marker for detecting cardiac dyssynchrony. By analyzing the in-

verse radius of a fitted circle at 100 temporal points during the cardiac cycle, we aim to differentiate dyssynchrony in subjects with no diagnosed cardiac abnormalities and those with diagnosed left ventricular dyssynchrony, both with and without CRT pacing. Previous research has indicated that septal deformation can reflect underlying mechanical dysfunction and may serve as a valuable diagnostic tool [5]. This investigation seeks to enhance our understanding of dyssynchrony and improve clinical management strategies for affected patients.

2. Methods

2.1. Data

Table 1. Demographic characteristics of subjects.

	Male	Female	Total
Gender	16	12	28
Conduction Disorders	9	5	14
Age	47 ± 21	54 ± 22	50 ± 22

Data was acquired using the experimental ultrasound system T5, developed and located at Duke University Hospital in Durham, USA. Data was acquired at 360 fps to 1000 fps, and down sampled to 100 frames per cardiac cycle. Data was reanalyzed from a previously published study, comprising a total of 28 subjects, ages 47 ± 21 , where 16 subjects being male, divided into groups: 14 subjects with no diagnosed cardiac abnormalities, and 14 patients with cardiac dyssynchrony who underwent CRT [2, 6]. Subjects were categorized into three groups based on cardiac status and therapy condition: those with no diagnosed cardiac abnormalities (Normal), those with LBBB with active CRT pacing (On), and those with LBBB without active pacing (Off).

2.2. Algorithm

For each subject, the curvature of the IVS was evaluated at 100 time points throughout the cardiac cycle. At

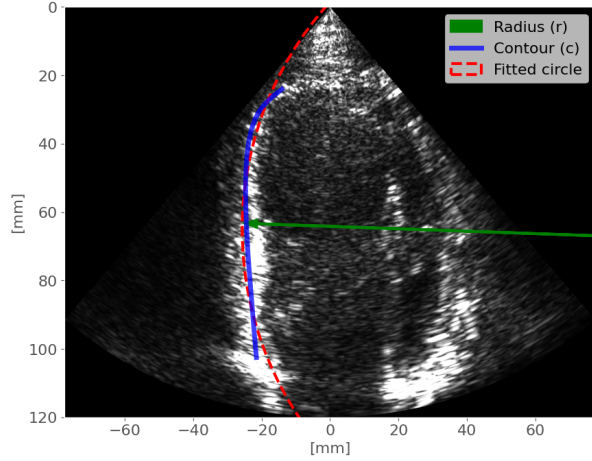


Figure 1. Apical 4 chamber view of a subject, with the tracked contour (c) in blue, fitted circle in red, and the circle radius (r) marked with a green arrow. $r = 99\text{mm}$ and $c = 82\text{mm}$.

Dunn's Post-hoc Test (Pairwise Group Comparisons)

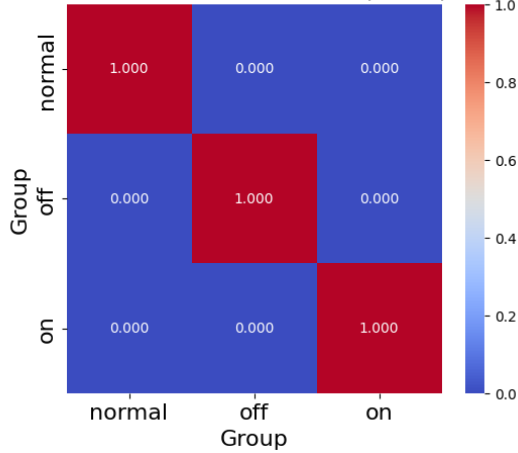


Figure 2. Dunn's Post-hoc test for pairwise group comparisons, with Bonferroni correction.

each time point, the IVS contour was fitted to a circle using the Levenberg-Marquardt least squares algorithm for robust fitting of the contour to a circle, with residuals ε calculated using Equation 1. A fitted circle is illustrated by the red dotted line in Figure 1, where the tracked IVS contour length (c) is marked in blue, and the radius (r) of the circle by the green arrow, which for Figure 1 was $r = 99\text{mm}$ and $c = 82\text{mm}$.

$$\varepsilon = (x - \bar{x})^2 + (y - \bar{y})^2 - r^2 \quad (1)$$

The inverse of the fitted radius (r^{-1}) was calculated, see Equation 2.

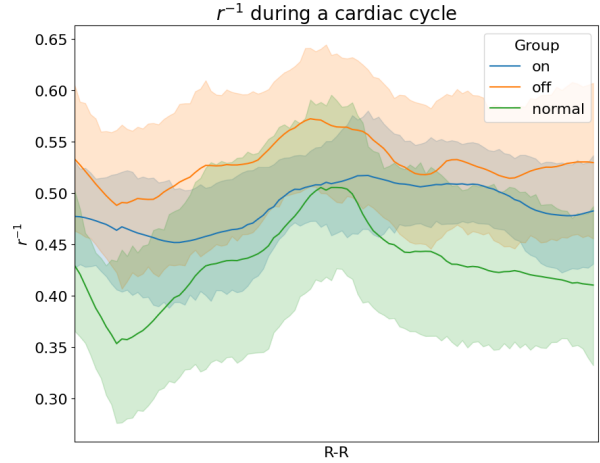


Figure 3. Inverse radius (r^{-1}) during the cardiac cycle, for the groups Off, On, and Normal.

$$r^{-1} = \frac{c}{r + c} \quad (2)$$

where the contour length c was used as a normalization factor. r^{-1} was calculated for 100 frames equally distributed through 1 cardiac cycle, providing a time-resolved measure of septal curvature.

2.3. Statistical Analysis

To assess group-level differences in septal curvature, statistical analysis was performed on the inverse radius of curvature over the cardiac cycle for each subject. A non-parametric Kruskal-Wallis test was used to evaluate overall differences across the three groups. When significant differences were detected, pairwise comparisons were conducted using Dunn's post hoc test with Bonferroni correction to adjust for multiple comparisons. All statistical analyses were conducted with a significance threshold set prior to analysis.

Table 2. Summary of the inverse radius results from the three groups Off, On, and Normal.

Group	μ	σ	Median	Min	Max
Off	0.53	0.15	0.52	0.17	0.78
On	0.49	0.10	0.48	0.14	0.78
Normal	0.43	0.17	0.39	0.05	0.79

3. Results

The r^{-1} measurements were analyzed for three groups: Off, On, and Normal. The mean values for each group were as follows: Off (0.53 ± 0.15), On (0.49 ± 0.10), and Normal (0.43 ± 0.17). The Off group had the highest mean

value of 0.53 with a median of 0.52. The On group had a mean value of 0.49 with a median of 0.48. The Normal group had the lowest mean value of 0.43 with a median of 0.39, see Table 2.

These results indicated that measurements of r^{-1} vary across different groups, with the Off group showing the highest values and the Normal group showing the lowest values. A Kruskal-Wallis H-test for independent samples was conducted to determine statistically significant differences in the measurements of r^{-1} between the three groups Off, On, and Normal ($H = 302.2$ and $p\text{-value} < 0.0001$). A pairwise post-hoc Dunn's test was performed showing statistically significant differences between all groups ($p\text{-values} < 0.0001$), see Figure 2. A temporal representation of differences in r^{-1} measurements through the cardiac cycle between groups is illustrated in Figure 3.

4. Discussion

The Off group had the highest r^{-1} value of 0.53 ± 0.15 , followed by the On group at 0.49 ± 0.10 , and the Normal group had the lowest value at 0.43 ± 0.17 . These findings highlight the potential influence of different cardiovascular conditions on r^{-1} measurements.

The r^{-1} measure shows promise as a potential biomarker for optimizing cardiac resynchronization therapy (CRT), as it provides beat-to-beat information on myocardial contraction dynamics. This capability could enable clinicians to tailor CRT settings to individual patient needs, ultimately improving therapeutic outcomes.

In conclusion, the significant differences observed between the groups highlight the importance of considering specific clinical and physiological conditions when interpreting r^{-1} measurements. Future studies should investigate the underlying mechanisms driving these differences and evaluate how r^{-1} can be integrated into patient se-

lection, therapy optimization, and real-time monitoring in CRT.

References

- [1] Sillanmäki S, Lipponen JA, Tarvainen MP, Laitinen T, Hedman M, Hedman A, Kivelä A, Hämäläinen H, Laitinen T. Relationships between electrical and mechanical dyssynchrony in patients with left bundle branch block and healthy controls. *Journal of Nuclear Cardiology* 2019;26(4):1228–1239.
- [2] Andersen MS, Moore C, LeFevre M, Arges K, Friedman DJ, Atwater BD, Kisslo J, Sogaard P, Struijk JJ, von Ramm OT, et al. Contractile fronts in the interventricular septum: a case for high frame rate echocardiographic imaging. *Ultrasound in Medicine Biology* 2020;46(9):2181–2192.
- [3] Kirk JA, Kass DA. Electromechanical dyssynchrony and resynchronization of the failing heart. *Circulation research* 2013;113(6):765–776.
- [4] Seo Y, Ishizu T, Sakamaki F, Yamamoto M, Aonuma K. Left bundle branch block and echocardiography in the era of crt. *Journal of Echocardiography* 2015;13(1):6–14.
- [5] Haddad F, Guihaire J, Skhiri M, Denault AY, Mercier O, Al-Halabi S, Vrtovec B, Fadel E, Zamanian RT, Schnittger I. Septal curvature is marker of hemodynamic, anatomical, and electromechanical ventricular interdependence in patients with pulmonary arterial hypertension. *Echocardiography* 2014;31(6):699–707.
- [6] Andersen MV, Moore C, Sogaard P, Friedman D, Atwater BD, Arges K, LeFevre M, Struijk JJ, Kisslo J, Schmidt SE, et al. Quantitative parameters of high-frame-rate strain in patients with echocardiographically normal function. *Ultrasound in Medicine Biology* 2019;45(5):1197–1207.

Address for correspondence:

Martin Siemienski Andersen
Selma Lagerlöfs Vej 249, 9260 Gistrup, Denmark.
mvan@hst.aau.dk