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Right Ventricular Mechanics using a Novel Comprehensive Three-View Echocardiographic Strain Analysis in a Normal Population

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Abstract

Background—While quantitative RV strain analysis may be useful in congenital and acquired heart disease populations with RV failure, a comprehensive, standardized approach is lacking. An 18 segment RV strain analysis obtained from 3 standardized RV apical echo images was used to determine the feasibility, normal values and reproducibility of the method in normal adults.

Methods—Forty healthy, prospectively-enrolled volunteers with no cardiac history and normal QRS duration received an echo optimized for strain analysis including 3 RV apical views. 2D speckle tracking longitudinal strain analysis was performed on EchoPAC software. Eleven retrospectively-identified subjects with RV disease were included as a pilot population. All had been imaged using the same protocol including the 3 RV apical views.

Results—All control subjects had normal anatomic morphology and function by echo. Feasibility of the RV strain analysis was good (adequate tracking in 696/720 (97%) of segments). RV global peak systolic strain was $-23 \pm 2\%$. Peak strain was highest in the RV free wall and lowest in the septum. Dyssynchrony indices demonstrated no dyssynchrony using LV criteria. Reproducibility of most strain measures was acceptable. This methodology identified important disease not seen in the 4-chamber apical view alone in the pilot population of 11 patients with RV disease. Strain pattern and values were different from the control population indicating differences do exist from normal.

Conclusions—The 18 segment RV strain analysis is feasible with strain measures falling into discrete ranges in this normal population. Those with RV disease illustrate the potential utility of

this approach. These data indicate that this model can be utilized for more detailed studies evaluating abnormal RV populations where its full potential can be assessed.

Introduction

Two-dimensional speckle tracking echocardiography is often utilized for assessment of quantitative indices of global and regional left ventricular (LV) function by means of three standardized views¹⁻⁴ but no such multiple-view model is yet available for the right ventricle (RV). The lack of a comprehensive RV model may be due to multiple factors common in the RV. These include limited target access induced by chest wall configuration in combination with the anterior retrosternal position of the RV, a lack of standardized multiple RV views and the lack of readily available RV strain analysis software.

LV strain analysis has enjoyed clinical success, in part because global and regional LV longitudinal strain is assessed in 18 segments (18S) from three standardized LV apical views.⁵ RV strain analysis, on the other hand, has only been performed in a few studies using 6 segments (6S) from one view (apical 4-chamber).⁶⁻⁸ To our knowledge, there are no studies using an 18S three-view RV strain analysis model. Early work during the development of this approach to RV strain analysis was performed in a systemic RV population (D-transposition of the great arteries post atrial switch) in our institution, and suggested the potential need for comprehensive image acquisition due to important findings seen outside of the 4-chamber RV apical view (unpublished data).

Clinical RV functional assessment may be aided by a more detailed RV strain analysis that would be useful for clinical management of patients with forms of congenital heart disease, pulmonary hypertension, RV infarction, and even LV assist devices. Furthermore, a comprehensive 18S RV model may also be useful for determination of regional strain abnormalities resulting from activation delays (dyssynchrony) of the RV as is found in the LV.^{3,9-12} This includes those with congenital heart disease and heart failure in a systemic or single RV who might benefit from cardiac resynchronization therapy (CRT).¹³⁻¹⁶

This study evaluates the feasibility, reproducibility, RV regional variability, and proposes normal ranges for an RV 18S longitudinal strain acquisition and analysis model for evaluation of global and regional RV mechanics in a healthy young adult population using currently available software. Such validation in a normal population is an important precursor to the application of this comprehensive RV model to patients with heart disease. Three cases (two congenital and one with pulmonary hypertension) from a pilot group of eleven patients with abnormal right ventricles are provided to demonstrate the potential for such a model and possibilities for further investigation.

Methods

Study Subjects

Complete transthoracic echocardiograms were obtained on 40 young, healthy, prospectively-enrolled, volunteer subjects, with the addition of three apical RV views optimized for strain analysis. All subjects had normal cardiac physical examinations. Inclusion criteria were a

minimum age of 18 years at the time of the study, no history of cardiac abnormalities, normal echo findings including anatomy, LV ejection fraction (LVEF) 50%, fractional area change (FAC) 35% and tricuspid annular plane systolic excursion (TAPSE) 16 mm. Exclusion criteria included any abnormal echo findings or prolonged QRS duration. Studies were obtained at Duke from March to July, 2012. This study was approved by the Duke Institutional Review Board, and all control subjects gave informed consent.

This study in the normal population was performed after noticing some regional abnormalities in patients with RV disease during routine clinical studies that prompted development of the scanning methodology. The normal subjects were the main focus of this study.

Pilot study patients

An additional small pilot test population of 11 adult patients with abnormal right ventricular function consequent to congenital or acquired disease was to determine if any gross differences could be found in preliminary comparison to the normal population. These subjects were chosen from populations with RV pathology to illustrate the potential utility of the 18S model and cardiac resynchronization therapy in diseased states, but not to characterize abnormal populations in a comprehensive or quantitative manner. The pilot subjects were retrospectively identified for this study, but had complete echocardiograms with the 3 RV apical views.

All abnormal patients had chronic elevation of right ventricular pressure. The right ventricle was systemic in five D-transposition of the great artery subjects (subaortic RV consequent to atrial switch operations in infancy), and 6 had normal anatomy (subpulmonic RV with acquired chronic pulmonary hypertension due to primary lung disease). All patients had NYHA class II-IV symptoms requiring multiple heart failure medications. RV studies in the abnormal pilot group were obtained in the same fashion as the normal population between June 2010 and July 2012.

Functional echocardiography with three apical RV views

All echo studies were acquired with a GE Vivid E9 imaging system using a 3.5-MHz ultrasound probe (GE, Vingmed Ultrasound, Horten, Norway). Echo RV systolic function was assessed with the traditional markers of FAC and TAPSE measured according to the standard methodology on the 4-chamber apical view in RV end-systole and end-diastole.¹⁷ LV systolic function was assessed by left ventricular ejection fraction (LVEF) using biplane Simpson's method.¹⁸

The gray scale echocardiogram was performed with images optimized for longitudinal 2D speckle tracking strain analysis (50–90 frames per second) from three apical RV views with the subjects in the standard left lateral recumbent position. The three apical RV views were equivalent to the imaging planes of the 2-, 3-, and 4-chamber LV apical views but with the transducer angled rightward (Figure 1). In the early phase of this investigation, equivalent LV and RV imaging planes were ensured by starting from the LV view and simply angling rightward without changing transducer position to obtain the RV view. However, view optimization of the “inflow” view often required repositioning of the transducer towards the

left anterior axillary line, especially to image the anterior RV wall segments. Once RV landmarks were established, proper RV views were confirmed through a combination of starting with LV views and angling rightward, and RV landmarks. Prior to performing study exams, sonographers attended an echo strain mechanics course to learn the new RV views and to determine when an image was of adequate quality for strain analysis. The training included a more experienced observer with hand held over the examining sonographer's hand during an instructional examination to ensure proper transducer orientation at 60° rotational intervals. Sonographers performed on-line strain analyses at the time of study to verify adequacy of the images.

The volumetric probe was used as an aid in development and training for 60° rotation examinations. After initial learning, this probe was no longer necessary, particularly due to its inability to supply adequate acquisition frame rates.

The views were initially termed "equivalent" in reference to: (1) preserved LV transducer plane orientations, and (2) as a reminder where the image data should be entered into the analysis software for planar spatial reconstruction in the resulting target diagram that was designed for the LV. The resulting 4-chamber equivalent view has four chambers (RA-RV-LV-LA), the 2-chamber equivalent view, alternately called the "Outflow" view, has three (RA-RV-RVOT) and the 3-chamber equivalent view, alternately termed the RV "Inflow" view, has two chambers (RA-RV) (Figure 1).

Right ventricular 2D speckle tracking longitudinal strain analysis

Longitudinal strain was analyzed in all 40 subjects by two experienced investigators. Off-line strain analysis was performed using EchoPAC PC version BT11 (GE- Vingmed Ultrasound, Horten, Norway) using conventional LV software with the RV views substituted for the standard LV views. The reference point was placed at the beginning of the QRS. Pulmonary valve closure (PVC) relative to the QRS was defined on spectral Doppler tracing of pulmonary outflow.

The EchoPAC speckle tracking software was then applied to each properly obtained RV view to produce six segmental peak strain curves and time-to-peak intervals. This software has been previously validated for determination of global peak strain in the LV from the 2-, 3-, and 4-chamber apical LV views.^{1,18} The planes of those views were maintained in the equivalent apical RV views with 60° counter-clockwise rotations between each view (Figure 1). The RV endocardial border was manually traced in end-systole using the medial and lateral tricuspid valve annulus as the beginning and endpoints in the 4-chamber and inflow views. In the outflow view, the myocardium was traced from the tricuspid valve annulus on the posterior wall to the most basal region of the anterior septal wall visible in this view prior to its transition to the proximal RVOT (Figure 2). The region of interest (ROI) was adjusted to include myocardial thickness but exclude the pericardium. The integrity of RV speckle tracking was automatically detected by the software and visually confirmed. In case of poor tracking, the tracing was readjusted or the ROI thickness changed. Segments with persistent inadequate tracking were excluded from analysis.

Global peak strain was calculated by averaging the peak strain values of all RV segments for that subject. Regional averages (septal, apical, and free wall) of global peak strain or time-to-peak strain were calculated by averaging the segmental values of the six segments in each of those regions. Two measures of RV mechanical dyssynchrony using time-to-peak methods were analyzed: (1) the standard deviation of the time-to-peak intervals (SDttp) in all segments, and (2) the maximum opposing wall delay (MOW), which was measured as the maximal delay in time-to-peak between the opposing walls in the mid or basal segments. Regional pattern analysis³ was also applied.

Averaged or calculated strain values were performed in the 18S model. When the 18S model was compared to the 6S model (traditional four-chamber apical view only), a subscript 18 or 6 denotes which model was used.

Statistical Analysis

Continuous variables (mean $\pm$ standard deviation) were compared using paired and unpaired T-tests after visualizing the data to confirm normality. Categorical variables (reported as percentages) were tested for differences using Fisher's exact tests. A p-value <0.05 was considered statistically significant. Averaged strain indices were compared between the 18S and 6S models using absolute mean difference and coefficient of variation (CV), which were calculated in the standard fashion. Statistical analyses were performed using STATA 12 (College Station, TX).

Inter- & intra-observer variability of averaged and segmental strain measures was reported as absolute mean difference and CV. For inter-observer variability, strain analysis was performed on a randomly selected subpopulation of 25 of these subjects using the same cardiac cycle by a second experienced reader blinded to the results of the primary reader. For intra-observer variability, the primary reader also repeated measurements in a blinded fashion no sooner than one month after the first assessment on the 25 subjects.

Results

Normal Population

In the normal population, there were 40 young healthy adult patients with normal cardiac function and anatomy. Baseline population characteristics and traditional echo functional characteristics are listed in Table 1. Adequate tracking for strain analysis was obtained in 696/720 (97%) of all segments. The anterior free wall segments (RV 3-chamber equivalent view) had the lowest strain tracking rate (86%). Averaged strain measures assessing global and regional averaged peak strain are reported for the 18S model (Table 2). Regional peak strain comparing free wall, apical, and septal regions was highest in the free wall and lowest in the septum. Individual segmental peak strain is reported in Table 3.

Time-to-peak dyssynchrony indices (SDttp, MOW) and regional contraction times averaged across all normal subjects are reported in Table 2. The sequence of the contraction for each patient was determined by the averaged time-to-peak intervals for the three ventricular wall regions (free wall, septal, and apical). The majority of subjects demonstrated a septal-apical-free wall contraction sequence (42.5%) or a septal-free wall-apical sequence (30.0%). There

was a significant minority of subjects whose contraction started in the apex including apical-septal-free wall (17.5%) and apical-free wall-septum (7.5%). There was one subject with a free wall-septal-apical sequence. Using regional strain pattern analysis, no subject had a pattern consistent with activation delayed RV dyssynchrony. Segmental time-to-peak intervals for all eighteen individual segments were also reported (Table 3).

Global peak strain did not vary appreciably in the normal subjects between the 18S and 6S models with a peak strain₁₈ of $-23 \pm 2\%$ and a peak strain₆ of $-23 \pm 3\%$ ($p=0.95$). The mean difference was 0.1% and CV 7%. Assessing mechanical dyssynchrony, a small but statistically significant difference emerged between the models (SDt₁₈ = 25 ± 8 ms; SDt₆ = 22 ± 9 ms; $p=0.01$). The mean difference was 2.8 ms and CV 31%.

Intra- and inter-observer variability (IOV) was good for averaged strain measures (reported as absolute mean difference, CV). There was strong reproducibility for global peak strain₁₈ with both intra-observer variability (1,6%) and inter-observer variability (0,9%). For the SDt₁₈ dyssynchrony analysis, intra-observer variability (1 ms,10%) and inter-observer variability (0 ms,11%) demonstrated good reproducibility. The reproducibility of peak strain and timing measurements for the individual segments are reported in Table 3.

Abnormal RV Subjects

All patients in the pilot group had abnormal right ventricles that were at least moderately dilated, hypocontractile and were variably symptomatic of heart failure with NYHA symptoms of class II-IV. The age range of the five adults with D-transposition is 31–47 years (3/5 male), and the age range of the 6 adults with pulmonary hypertension is 45–77 years (2/6 male). Adequate images for analysis could be obtained in all. The results of regional strain analysis showed variations from the normal population in all and demonstrated the potential of the comprehensive 18 segment model. Three cases are used for illustration.

Case 1 is a 32 year old female with D-transposition of the great arteries post atrial switch procedure in infancy. She was followed with a moderately dilated systemic right ventricle with moderately decreased systolic function and NYHA III symptoms on multiple heart failure medications. She was ventricularly paced due to sinus node dysfunction and chronic atrial fibrillation with accompanying RBBB (QRS duration 172 ms). Non strain indices were a TAPSE of 8 mm and a FAC of 25%. RV global peak strain was -7.8% with more severely diminished regional function noted in the septum. There was dyssynchrony by all indices in all three views with SDt₁₈ 139 ms, MOW 232 ms and a regional pattern analysis that demonstrated the “Classic” pattern of opposing wall movements³ characteristic of subjects who respond to the CRT when these abnormalities are found in the left ventricle³. The “Classic” pattern utilizes multiple criteria to identify early septal contraction opposed by early freewall stretch with late contraction consistent with underlying electrical activation delays causing mechanical dyssynchrony.³ She underwent CRT with the additional epicardial RV lead placed in the basal segment of the lateral free wall. Figure 3 shows the 4-chamber apical view with the “Classic” pattern and global peak strain of -7.8% pre-CRT. Five months later, she showed evidence of response to CRT with reduction in symptoms to

NYHA class I-II and improvements in TAPSE to 13 mm, FAC to 33% and global peak strain to -10.4%.

Case 2 is a 36 year old male also with D-transposition of the great arteries post atrial switch procedure in infancy. He also was followed with a moderately dilated systemic right ventricle with moderately decreased systolic function and NYHA III symptoms on multiple heart failure medications. He was ventricularly paced due to post-operative complete heart block with accompanying RBBB (QRS duration 194 ms). RV systolic function was moderately diminished with a global peak RV strain of -10.6%. Non strain indices at the time of study were TAPSE 9 mm, and FAC 26%. Figure 4 shows the 3 RV apical views with the “Classic” pattern seen only in the RV Outflow view. Dyssynchrony, as indicated by the presence of the “Classic” pattern or measured by SDtp₁₈ 78 ms, and MOW 196 ms was only noted in the RV Outflow view, but not seen the 4-chamber view.

Case 3 is a 71 year old female with long standing idiopathic pulmonary hypertension with a pulmonary vascular resistance of 9.6 Wood units. She had a severely dilated sub-pulmonic RV with mild-moderately diminished systolic function and NYHA III symptoms on multiple heart failure medications. Non strain indices at the time of study were TAPSE = 9mm and RV FAC = 23%. Figure 5 shows the 3 RV apical views with the Inflow and Outflow views demonstrating significantly lower RV peak strain values (-12.3%, -12.1% respectively) in comparison to the 4-chamber view (-18.0%) alone. The 4-chamber view derived global peak strain was in the normal range, whereas the global peak strain derived from the 18S model was mildly decreased at -14.1%.

In the other D-transposition subjects in the pilot group, there was an additional subject that mirrored Case 1 with CRT response seen in the presence of the RV “Classic” pattern. There are also two other subjects that mirrored Case 2 with the RV “Classic” pattern seen only outside of 4-chamber view (1 Inflow view; 1 Outflow view). In the pulmonary hypertension subjects, the other 5 subjects mirrored Case 3 with significantly different 18S global PS than 6S global PS (average mean global PS difference -3%).

Discussion

These data indicate that the 18S regional RV strain analysis was feasible and the values of global peak strain and time-to-peak dyssynchrony measures fell into consistent ranges for normal subjects. There was a functional peak strain gradient among regions that was highest in the free wall, then apical, and lowest in the septum. Reproducibility of functional and timing measures in averaged global indices and individual RV segments was moderate to good except for the peak strain measures in the apical and basal posterior RV free wall segments. While differences between the time-to-peak measure of the 18S and 6S models were small in this homogeneous, normal population, agreement was poor between the two measures demonstrating that additional data is present in the 18S measure, and future studies assessing abnormal RV populations may show more exaggerated differences between the models imaging is possible, practical and likely necessary to properly diagnose regional functional heterogeneities and electrical activation delays in this abnormal population. The

results of the current study provide a compendium of normal indices for eventual systematic comparison to abnormal populations.

Feasibility

The feasibility of this strain analysis was good with 97% of all segments tracking adequately. All RV walls except for the anterior free wall were obtained with a very high level of consistency. The anterior free wall, located just behind the chest wall, was the most difficult to image from an apical approach. Despite this relative difficulty, the anterior free wall segments still had an acceptable tracking rate (86%). With adequate training of imaging personnel, these new RV apical views were consistently adequate for strain analysis using existing software and could be practically incorporated into an echo examination. Compared to the LV, the thinner RV wall diameter and different geometry did not negatively affect the feasibility in the subjects studied.

Reproducibility

The reproducibility of averaged/calculated strain measures such as the global peak strain₁₈ and SDtp₁₈ was good (CV 11%) for both intra-and inter-observer variability. This was identical to the reported CV 11% for RV global longitudinal peak strain₆ in pediatric patients using 2D speckle tracking strain analysis.¹⁹ The present study also evaluated the reproducibility of 18 individual segmental strains. The reproducibility of the segmental time-to-peak intervals was excellent (CV 2–8%) with insignificant absolute mean differences. However, the segmental peak strain had a wider range of reproducibility. All of the mid and basal segments demonstrated moderate-good reproducibility (CV 7–22%) except for the basal segment of the posterior free wall (CV 28%). Tracking difficulties encountered in this basal segment may exist due to the relatively hyperdynamic movement in this region. Also, care was taken to trace the ROI adjacent to the tricuspid valve annulus, but not into the atrial tissue.

The apical segments demonstrated the poorest peak strain reproducibility (CV 15–40%). This was likely due to the sharp curvature and the difficulty in obtaining high quality near field 2D images in some individuals using the GE Vivid E9. Another concern about utilizing longitudinal strain to track apical segments is that apical shortening movement is lateral (across the azimuth angle of the sector arc) likely confounding speckle tracking in this dimension due to variable beam width and convergence of scan lines in the near field. Overall, the reproducibility of individual segmental peak strain for all basal and mid segments (except the basal posterior free wall) was acceptable; apical segmental peak strain was less reproducible.

Functional assessment

Averaged RV peak strain (global or free wall) is a reproducible measure of RV function that agrees with MRI ejection fraction and other traditional markers of function in both adults and children.^{20–21} In certain studies, RV global peak strain actually better predicts outcomes than traditional markers.^{8,22} Within this current healthy population with normal traditional markers of function, the RV global peak strain ranged from –18 to –27% (mean –23%). This was approximately 5% greater than the global peak strain mean (–18%) reported in the

LV.²³ Higher RV strain values were likely to due to the different geometry of RV longitudinal contraction. Differences in loading conditions and fiber orientation may have also played a role. The RV global peak strain in the systemic RV cases fell well outside of this range, which agrees with their moderately diminished function by traditional functional markers.

As expected, in the normal population, RV segmental peak strain demonstrated wider ranges than the averaged index of global peak strain (Table 3). The lower limit for individual segments ranged from -4 to -17%, with only two segments less negative than -10% (moderately-severely diminished). As none of these subjects had any suggestion of regional wall motion abnormalities, these two lower values may be due to sub-optimal tracking of the strain software. Looking at averaged regional values of peak strain, a functional strain gradient appeared to exist in these normal subjects. Free wall peak strains were greatest, followed by the apical and then septal. The RV free wall in normal subjects is a relatively thin, hypermobile region with excellent potential for larger deformation. The deformation of the thicker septal myocardium may also be influenced by requirements of the septum to both ventricles.

Contraction timing and implications for mechanical dyssynchrony

Time-to-peak intervals assessing the RV contraction sequence demonstrated that most subject's contraction sequence began in the septum with a relatively equal split between the apex and free wall being next in sequence. There was a significant minority whose earliest contraction was in the apical segments. These findings may be, in part, explained by the fact that the right bundle remains insulated from surrounding myocardium until it nears the transition point from the septal to apical region.²⁴ Identifying variations in normal RV contraction is important because many congenital and acquired heart disorders can result in abnormal RV electrical conduction that may produce mechanical dyssynchrony and concomitant RV dysfunction. However, at present, there are no validated measures of mechanical dyssynchrony in the RV to explore a causal relationship between dyssynchrony and dysfunction.

SDttp is a frequently used LV strain index that quantifies the variability in the time-to-peak intervals for a subject.^{1,25} In the LV, mechanical dyssynchrony with response to CRT is reported to correlate with longitudinal SDttp >60 ms¹, although the specificity is inadequate. The SDttp in the RV of our normal population were all well below this LV cut-off (maximum 42 ms). Another method of determining mechanical dyssynchrony is maximum opposing wall delays in time-to-peak intervals (MOW). When analyzing MOW in our population, the values were well below the cut-off of 130 ms cited in LV strain guidelines to define mechanical dyssynchrony predictive of CRT response.¹ These findings suggest that normal RV variability of time-to-peak strain may fall into normal previously defined LV ranges in this population, although further study is necessary.

Unfortunately, most of the LV dyssynchrony indices have a relatively high CRT non-response rate (30–40%), including SDttp and MOW. With this limitation, a novel approach to LV dyssynchrony recently identified a “Classic” pattern of dyssynchrony in patients whose mechanical dyssynchrony was caused by electrical activation delay in viable

myocardium. Pattern analysis has improved test characteristics for predicting response to LV CRT.³ As expected, using regional pattern analysis in the RV of our normal population, no subject met the criteria for “Classic” pattern of dyssynchrony. This methodology may have implications in RV dyssynchrony as the underlying principles for predicting CRT response in failing RVs with activation delays should be similar to the LV. The systemic RV subjects demonstrated dyssynchrony both by time-to-peak indices and the “Classic” pattern using those criteria developed in the LV. In the two transposition cases post atrial switch that underwent CRT, the subjects with the “Classic” pattern responded well to CRT both by echocardiographic function and clinical symptoms. None of the pilot population with pulmonary hypertension demonstrated dyssynchrony. Future studies evaluating the predictive indices of RV CRT response are required.

Model comparison and implications for congenital heart disease

There have been few published attempts to develop a comprehensive image acquisition model for evaluation of RV strain. There is reasonable acceptance of the 3 apical views (18S model) for LV regional strain examination. In comparison to the LV, the RV asymmetry and variable wall thickness calls for at least as detailed a model for examination. The challenges of obtaining the Inflow and Outflow RV apical views have likely discouraged such investigation in the past. To our knowledge, only one other study assessed RV global peak strain in any view other than the four chamber apical view. Roche *et al* assessed an 8 segment (8S) RV tissue Doppler velocity model by adding an opposing wall pair from the RV outflow tract to the standard four chamber apical view.²⁶ That study demonstrated that children with tetralogy of Fallot developed a statistically significant level of RV dyssynchrony with exercise compared to controls when measured by the 8S model, but not when measured with just the standard four chamber view (6S).

It can be argued that this 18S model does not evaluate all walls pertinent to RV function in congenital heart disease, although it does improve upon the traditional 6S model. It can further be argued that given wall segments may shift as the RV dilates or hypertrophies in diseased states. This 18 segment model is only a beginning to comprehensive RV strain analysis. Other intermediate or alternate views are possible and the true benefit of any comprehensive model/combination of views will be determined over time.

In the current study, global peak strain was not significantly different between the 18S and 6S models in this healthy population, with agreement between models approximating the IOV agreement. However, this finding in a normal population should not discount its potential use in abnormal populations as uniformity amongst neighboring segments was anticipated in the healthy myocardium. The true value of the 18S model was illustrated in those with an abnormal RV where regional differences may be expected due to fibrosis, surgical scar, and other regional processes.

When assessing timing of regional contraction in the controls, the SDtp₁₈ was elevated compared to the SDtp₆, although it well within the normal range. While clinically insignificant in this homogeneous, normal population, these differences may become exaggerated in an abnormal population. In addition, there was poor agreement between the models for SDtp (CV 31%) potentially demonstrating additional information is present in

the 18S model. The CV for this comparison was substantially higher than the IOV comparisons. The 18S model in the LV is clearly useful for the detection of the abnormal physiology associated with LBBB by regional pattern analysis as the “Classic” pattern was noted only in the LV 2-chamber view in patients who responded to CRT.³ In systemic RV Case 2, a “Classic” pattern is present in the Outflow view that is not present in the RV 4-chamber equivalent view. None of the dyssynchrony indices would have identified mechanical dyssynchrony in only the 4-chamber view. Dyssynchrony outside of the traditional 4-chamber view was seen in a significant minority of systemic RV subjects with the “Classic” pattern. Overall, further studies of abnormal RV populations using the 18S model are warranted.

The pilot study

These patients were included for simply demonstrating whether gross differences in regional function could be found in patients with disordered RV function. No attempt was made to derive detailed statistical analysis for the pilot study population. It is of interest that differences could be readily demonstrated. Case 1 illustrated the possibility that regional abnormalities of strain may occur and the associated mechanical dyssynchrony can be correctable. It also shows the possibility that the presence of the “Classic” pattern (or other abnormal indices) of mechanical delay can exist in the right ventricle, just like the left, and that opposing wall delays may have similar predictive value in the RV as in the LV. Case 2 demonstrated that mechanical dyssynchrony may be found only in views outside of the apical 4-chamber in some subjects. Case 3 and others in the adult pulmonary hypertension sub-group showed that global RV strain derived from multiple views may differ from that derived from the apical 4-chamber view alone. The other subjects in the pilot group provide further examples of the findings demonstrated in the three cases. The fact that differences were seen should not be taken as a declaration of recommended use of this model regarding diagnosis or therapeutic intervention in patients with congenital or acquired heart disease and it is improper to portray them as such. Such detailed studies based on the 18S strain model are ongoing in these patients and await analysis, detailed presentation and critical review.

Limitations

There are multiple limitations to this study in addition to those previously mentioned: (1) Outside of the pilot population, abnormal populations were not evaluated as part of this study and normal values cannot be compared to abnormal values or assessed for overlap between these ranges as yet. This is one focus of continued investigation. (2) The current population was a relatively young and healthy population and may only represent a limited spectrum compared to the full “normal” spectrum of patients, limiting the generalizability of these results. (3) There was no view that could fully assess the distal portion of the RV outflow tract except for modifications of angulation that varied from this rotational examination. Data from this angulation is not included in this study. (4) The relatively low sampling rate used in speckle tracking strain analysis (17 ms for frame rates of 60 frames per second) may limit its ability to discern small differences in regional contraction timing in this normal population. (5) Additional personnel training was necessary to obtain proper views and perform strain analysis and interpretation. (6) High quality parasternal short axis

RV imaging for radial and circumferential strain was not feasible despite multiple attempts and therefore was not available for analysis. This study is limited only to longitudinal strain and no attempts were made, or data available, for transverse, radial or circumferential strain. (7) The abnormal RV cases were provided only to demonstrate the utility and need for more comprehensive RV image acquisition and not to provide any conclusions about myocardial mechanics in this population. Systemic study of pathologic RV populations will follow. (8) The computer analytic model used was developed and marketed for LV strain analysis. The thin diameter of the RV wall with fewer speckle targets, could theoretically lead to poor speckle tracking or underestimation of strain due to an inability to exclude the pericardium from the thin-walled RVs of the normal population. Otherwise, there was no reason to suspect that RV longitudinal speckle tracking strain measurements are inherently different than an LV wall given appropriate orientation of moving speckle target information in the transducer field of view. The thinner RV wall and the asymmetric geometry of the RV did not appear to negatively affect the feasibility except potentially in the apex. Further study into the utility of RV apical strain is required.

Finally, (9) the lack of universal standardized nomenclature for these newer RV views was a limitation and may be controversial. The term “equivalent” was a necessary learning tool which initially helped to describe the RV planes, however, the use of “Inflow” and “Outflow” view is less confusing and more accurate. More appropriate nomenclature may be possible, particularly if the software could be relabeled for the RV. Detailed discussion of the multiple possible variations in view nomenclature is not within the intent of this report.

Conclusions

This prospective study evaluated a comprehensive methodology for RV strain analysis that demonstrated good feasibility and defined normal ranges for functional and timing measures in a small, young, healthy population. Strain measures had adequate reproducibility for all averaged measures and individual segmental values other than individual apical and basal posterior free wall peak strain. A functional peak strain gradient was seen regionally with the highest peak strain in the RV free wall, then apex, and lowest in the septum. Global peak strain in the RV was increased from the previously reported LV measures likely due to a thinner, more dynamic RV free wall with different loading conditions and myocardial fiber orientation. The observed contraction sequences to time-to-peak strain observed are explained by the underlying anatomy of the right bundle. None of the normal patients had dyssynchrony by either time-to-peak indices or pattern analysis. Example cases of subjects with an abnormal RV demonstrate the utility and likely need for this comprehensive imaging model in pathologic RV populations.

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Abbreviations

2D	2 dimensional
6S, 8S, 18S	6, 8, or 18 segment model
ant	Anterior
AVC	Aortic valve closure
CRT	Cardiac resynchronization therapy
CV	Coefficient of variation
FAC	Fractional area change (right ventricle)
FW	Free wall
GE	General Electric
IOV	Inter/intra-observer variability
LV	Left ventricle
LVEF	Left ventricular ejection fraction
mm	Millimeter
MOW	Maximal opposing wall delay
ms	Millisecond
NYHA	New York Heart Association
post	Posterior
PVC	Pulmonary valve closure
ROI	Region of interest
RA	Right atrium
RV	Right ventricle
RVOT	Right ventricular outflow tract
SDttp	Standard deviation of the time-to-peak
TAPSE	Tricuspid annular plane systolic excursion
TTP	Time-to-peak

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Figure 1. Comprehensive RV 18S image acquisition image planes

Center: a gross anatomic image of a short axis of the normal heart through the ventricles and the RV outflow tract (RVOT) looking from apex towards the cardiac base. The three RV apical echo imaging planes are represented by the white lines (arrow head = transducer notch). The infundibulum is identified by the yellow dotted line. The counterclockwise wall numbering system is maintained through the figure (1=septum, 2=anterior septum, 3=anterior free wall, 4=lateral free wall, 5=posterior free wall, 6=posterior septum). Anatomic photo courtesy of Robert H. Anderson, MD.

Figure 2. Comprehensive RV 18S strain analysis

Strain curves obtained from one of the normal subjects showing normal peak strain and synchronous contraction timing in the 18 segments of all three views. Insets of the strain analysis tracking region of interest overlying the 2D images for each view are included. Compare to scan planes found in Figure 1.

Figure 3. Case 1. CRT response in a systemic RV subject with a “Classic” pattern

Strain curves from the apical 4 chamber view in an adult with D-Transposition of the Great Arteries post atrial switch procedure with progressive RV dysfunction and NYHA class III heart failure symptoms. The pre-CRT panel shows a “Classic” pattern with earliest contraction in the septum and apex and the early stretch/late contraction in the free wall. Evidence for mechanical dyssynchrony was found in all three views. The post-CRT panel shows a resynchronization of the strain curves with improved function and heart failure symptoms. Blue arrow – stretching segments; yellow arrow – earliest contracting segments; red arrow – latest contracting segments. For details, see text.

Figure 4. Case 2: The “Classic” pattern in only the RV outflow view of a systemic RV subject Strain curves from the 18S model from an adult patient, post atrial switch operation. The “Classic” pattern of mechanical dyssynchrony is found only in the Outflow view between the anterior septum and posterior free wall. There is no dyssynchrony present in the other views in this RV with moderately diminished function. Blue arrow – stretching segments; yellow arrow – earliest contracting segment. For details, see text.

Figure 5. Case 3. Varying global strain curves from a patient with pulmonary hypertension
Strain curves from the 18S model from an adult patient, with pulmonary hypertension. Global peak strain derived from only the 4-chamber view is -18% . In comparison, 18S global peak strain is -14.1% when calculated from all three views. For details, see text.

Table 1
Subject Characteristics and Echo Indices

Baseline & functional characteristics: Baseline characteristics are reported as mean (range) or n (%). Functional echo measures all fall within the normal range and are reported as mean $\pm$ standard deviation (lower limit, upper limit). TAPSE (tricuspid annular plane systolic excursion); FAC (fractional area change); LVEF (left ventricular ejection fraction).

(n=40)	
Age, yr	29 (18,52)
Gender, male	16 (40%)
QRS duration 120ms	0
TAPSE, mm	22 $\pm$ 3 (15,30)
FAC, %	43 $\pm$ 5 (35,57)
LVEF, %	59 $\pm$ 4 (50,65)

Table 2
Averaged Strain Measures and Significance

Averaged strain measurements using the RV 18S strain model: Global and regional peak strains and regional time-to-peak intervals are averages of the six segments in each region. All continuous variables reported as mean $\pm$ standard deviation (lower limit, upper limit).

	Echo Strain (n=40)	P-value
Function		
Global peak strain, %	$-23 \pm 2\%$ (-18,-27)	
Septal peak strain, %	$-20 \pm 2\%$ (-16,-24)	$<0.001^1$
Apical peak strain, %	$-22 \pm 4\%$ (-15,-30)	$<0.001^2$
Free wall peak strain, %	$-27 \pm 4\%$ (-20,-36)	$<0.001^3$
Timing of Contraction		
Septal time-to-peak, ms	408 ± 25 (357,487)	$<0.0011^1$
Apical time-to-peak, ms	421 ± 24 (382,474)	0.0032^2
Free wall time-to-peak, ms	430 ± 25 (385,491)	$<0.0013^3$
Dyssynchrony Indices		
Basal MOW, ms	38 ± 14 (0,93)	
Mid MOW, ms	29 ± 15 (0,112)	
SDttp, ms	25 ± 7 ms (10,42)	
“Classic” Pattern, n	0	

SDttp (standard deviation of the time-to-peak intervals); MOW (maximum opposing wall delay between time-to-peak intervals). The reported p-values are obtained from paired t-tests comparing septal-apical¹, apical-free wall², free wall-septal³.

Table 3

Individual Segment Strain Measures

Individual segment strain measures: Peak strain and time-to-peak intervals in the individual segments with the wall naming convention established in figure 1 in parentheses in column one. Continuous variables reported as mean $\pm$ standard deviation (lower limit, upper limit). IOV reported as absolute mean difference (same units as the measured variable), coefficient of variation with columns for both intra-observer variability and inter-observer variability. Post (posterior); ant (anterior); FW (free wall); IOV (intra/inter-observer variability); ms (milliseconds).

Segment	Peak strain (%)	IOV (%), %	Time-to-peak (ms)	IOV (ms, %)
Basal (wall #)		Intra- Inter-		Intra- Inter-
Septum(1)	-19 $\pm$ 3 (-13, -25)	0, 8 1, 12	398 $\pm$ 35 (351,519)	2, 5 -5, 7
Ant Septum(2)	-17 $\pm$ 3 (-13, -36)	0, 15 0, 18	415 $\pm$ 31 (351,488)	-8, 6 -2, 5
Ant FW(3)	-31 $\pm$ 8 (-17, -44)	1, 12 0, 15	433 $\pm$ 39 (305,514)	-6, 6 -12, 8
Lateral FW(4)	-27 $\pm$ 5 (-13, -36)	0, 15 1, 22	435 $\pm$ 33 (386,502)	3, 3 1, 4
Post FW(5)	-24 $\pm$ 5 (-16, -42)	1, 16 0, 28	435 $\pm$ 32 (372,520)	2, 6 5, 8
Post septum(6)	-23 $\pm$ 3 (-17, -30)	1, 9 1, 15	407 $\pm$ 35 (342,496)	10, 4 8, 5
Mid (wall #)				
Septum(1)	-19 $\pm$ 3 (-12, -24)	0, 7 1, 13	404 $\pm$ 27 (351,505)	-1, 3 -11, 5
Ant septum(2)	-19 $\pm$ 3 (-13, -27)	1, 15 0, 20	426 $\pm$ 35 (368,520)	2, 4 8, 6
Ant FW(3)	-29 $\pm$ 5 (-13, -36)	1, 15 2, 18	433 $\pm$ 34 (379,514)	1, 3 -5, 5
Lateral FW(4)	-28 $\pm$ 4 (-13, -38)	1, 10 1, 11	420 $\pm$ 27 (380,489)	4, 4 0, 8
Post FW(5)	-26 $\pm$ 5 (-16, -37)	0, 12 1, 13	423 $\pm$ 31 (372,520)	5, 4 1, 8
Post septum(6)	-22 $\pm$ 3 (-17, -31)	1, 10 0, 14	400 $\pm$ 26 (342,465)	3, 3 1, 4
Apical (wall #)				
Septum(1)	-20 $\pm$ 5 (-8, -33)	0, 22 1, 25	420 $\pm$ 31 (351,478)	0, 4 -9, 7
Ant septum(2)	-22 $\pm$ 5 (-14, -33)	1, 19 0, 35	427 $\pm$ 38 (369,520)	4, 4 0, 6
Ant FW(3)	-20 $\pm$ 7 (-4, -33)	-1, 21 -1, 40	428 $\pm$ 35 (379,505)	-19, 5 -19, 8
Lateral FW(4)	-26 $\pm$ 6 (-11, -37)	1, 16 0, 17	414 $\pm$ 30 (351,477)	2, 3 -4, 8
Post FW(5)	-26 $\pm$ 5 (-15, -37)	1, 15 1, 21	417 $\pm$ 34 (369,504)	-5, 4 -9, 6
Post septum(6)	-19 $\pm$ 6 (-17, -31)	0, 28 0, 29	423 $\pm$ 29 (379,491)	13, 7 13, 7