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Research paper

Regional myocardial strain measurements from 4DCT in patients with normal LV function

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ABSTRACT

Background: CT SQUEEZ is a new automated technique to evaluate regional endocardial strain by tracking features on the endocardium from 4D cine CT data. The objective of this study was to measure the range of endocardial regional strain (RS_{CT}) values obtained with CT SQUEEZ in the normal human left ventricle (LV) from standard clinical 4D coronary CTA exams.

Methods: RS_{CT} was measured over the heart cycle in 25 humans with normal LV function using cine CT from three vendors. Mean and standard deviation of RS_{CT} values were computed in 16 AHA LV segments to estimate the range of values expected in the normal LV.

Results: Curves describing RS_{CT} vs. time were consistent between subjects. There was a slight gradient of decreasing minimum RS_{CT} value (increased shortening) from the base to the apex of the heart. Mean RS_{CT} values at end-systole were: base = −32% ± 1%, mid = −33% ± 1%, apex = −36% ± 1%. The standard deviation of the minimum systolic RS_{CT} in each segment over all subjects was 5%. The average time to reach maximum shortening was 34% of the RR interval.

Conclusions: Regional strain (RS_{CT}) can be rapidly obtained from standard gated coronary CCTA protocols using 4DCT SQUEEZ processing. We estimate that 95% of normal LV end-systolic RS_{CT} values will fall between −23% and −43%; therefore, we hypothesize that an RS_{CT} value higher than −23% will indicate a hypokinetic segment in the human heart.

1. Introduction

Assessment of regional myocardial function is critical to the evaluation of both ischemic and nonischemic cardiomyopathy. For quantitative strain analysis, MR tagging is considered a standard of reference1,21,21,2 and feature tracking with MRI has emerged as a simpler alternative[3] but conflicting reports exist on the reproducibility of tissue tracking.[4,5] Data acquisition for both tagging and tissue tracking requires multiple heartbeats and multiple breath-holds; image analysis is not trivial and usually requires human assisted segmentation.[6] Hence, MR tagging and tissue tracking have only seen use in research settings where highly accurate myocardial strain is required – either are rarely used in clinical cardiology.

Recently a new method, SQUEEZ,[7] was introduced to measure regional strain from cine CT by tracking features on the endocardium. SQUEEZ has been shown to distinguish normal from infarcted regions in animals,[7] and has been validated in animal models using MRI tagging[8]; however, the use of CT SQUEEZ to measure LV function in humans remained undocumented.

The overarching purpose of this research is to establish a method for measuring regional ventricular strain in human subjects using standard cine CT images obtained with CT coronary angiography protocols currently in use on scanners from different vendors. In order to move toward this goal, in this paper we: 1) establish that CT SQUEEZ can be

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used to derive regional endocardial strain (RS_{CT}) robustly in humans with standard coronary imaging protocols on scanners from different vendors, and, 2) obtain the preliminary estimates of the range of SQUEEZ derived regional endocardial strain values in the normal human LV.

2. Methods

2.1. Subjects

Subjects were scanned under IRB approved protocols at three centers (NIH Radiology, NHLBI Cardiology, UCSD); cine CT was performed in conjunction with coronary CT angiography. Thirty-two subjects from 2012 through 2015 who had the necessary full R-wave to R-wave (RR) coverage were selected retrospectively as potential subjects. It was important to ensure that the LV function of each subject was considered normal; therefore, four necessary criteria for inclusion were tested in each subject: 1) the ejection fraction was > 55%, 2) Global Longitudinal Strain (GLS) as measured on reformatted long axis CT images between end-diastole and end-systole was in a normal range[9] (between −0.18 and −0.24), 3) end diastolic LV wall thickness was in the normal range[10] (> 5.5 mm), and 4) the CT cine study did not show a wall motion abnormality on review by four experienced readers. Visual evaluation of cine CT for identifying abnormal LV function has been previously validated.[11,12] Using these four criteria 25 subjects were included in the normal group and used in this study.

The average characteristics of these subjects were (mean ± SD): age 54 ± 12, heart-rate 56 ± 7, ejection fraction (from CT thresholding) 73% ± 4%, global longitudinal strain (from CT) −0.21 ± 0.02. There were 17 males in the group.

2.2. CCTA imaging protocols

Cine CCTA protocols were optimized according to recommended protocols by each CT manufacturer. Scans were performed on either: Toshiba Aquillion One, Siemens Force, or GE HD 750 scanners. The gantry rotation for the acquisitions were between 275 ms and 350 ms. Electrocardiogram (ECG) gated imaging was performed during an inspiratory breath-hold. Beta blockers were administered if no contraindications were present in order to reduce the heart-rate to below 60 beats per minute if possible; however, some patients were scanned at higher heart-rates. Localization and coronary calcium scans were performed before the CCTA acquisition. In some cases a test bolus of 20 ml of iodinated contrast (Iopamidol, Isovue 370, Bracco) was administered at a rate of 4.5–5.0 ml/s to obtain the time of optimal opacification of the coronary arteries; in other cases (Toshiba scans) the bolus tracking option was used to trigger image acquisition based on a threshold HU setting in the ascending aorta. For the CCTA acquisition 60–80 ml of contrast was injected followed by a 50 ml saline flush. Some studies were dose modulated, prospectively gated protocols while other studies were retrospective helical scans. For the scans on the Toshiba Aquilion scanner, a single wide area detector volume was used and single heartbeat scans were reconstructed using “half-scan”. On the GE and Siemens scanners, either a prospective axial step and shoot or retrospective helical ECG-triggered acquisition was used.

Only scans with full RR data acquisition were used in this study. Fifteen of the scans had dose modulation with the x-ray tube current (mA) reduced from the maximum during the non-diastolic time frames of the RR interval, while ten scans had purely retrospective acquisition with constant mA. This led to differences in the contrast to noise ratio (CNR) between LV blood and myocardium in of some timeframes in the resultant movies; while the dependence of the precision and accuracy of SQUEEZ as a function of CNR has been measured,[13] it was not the purpose of this study. The range of CNR values at end-diastole was 5.1 through 21.7, with a mean value of 13.9 (median = 14.6) and a standard deviation of 4.1 around the mean. All studies were treated equally in the SQUEEZ analysis.

All images were reconstructed on a 512 × 512 pixel matrix in the axial plane with 1–1.5 mm slice thickness. The images were reconstructed into 10 or 20 evenly spaced timeframes across the RR

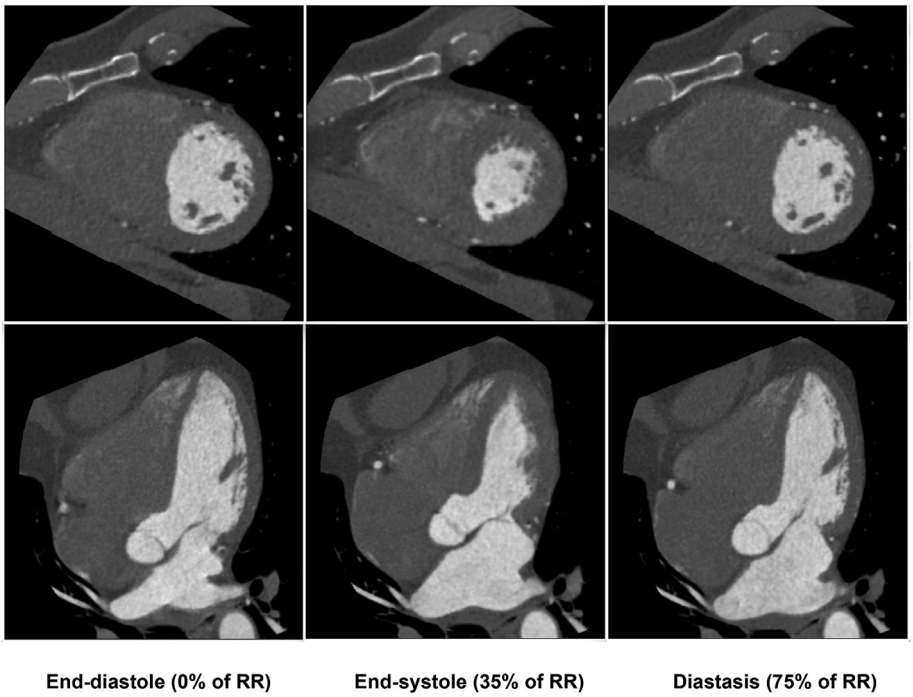

Fig. 1. (a): Three time frames from the 20 timeframes representing the full RR interval shown in two traditional views: short axis (top row), and four-chamber view (bottom row). For this subject, there was no mA modulation during the single heartbeat acquisition providing high CNR data throughout the entire RR interval. **(b):** Three time frames from the 20 timeframes representing the full RR interval shown in two traditional views: short axis (top row), and four-chamber view (bottom row). For this subject there was an mAs modulation during the single heartbeat acquisition; in most time frames the mAs was reduced to 50% of the mAs used during diastasis. High CNR data is available during diastasis, and lower CNR data is available throughout the remainder of the RR interval.

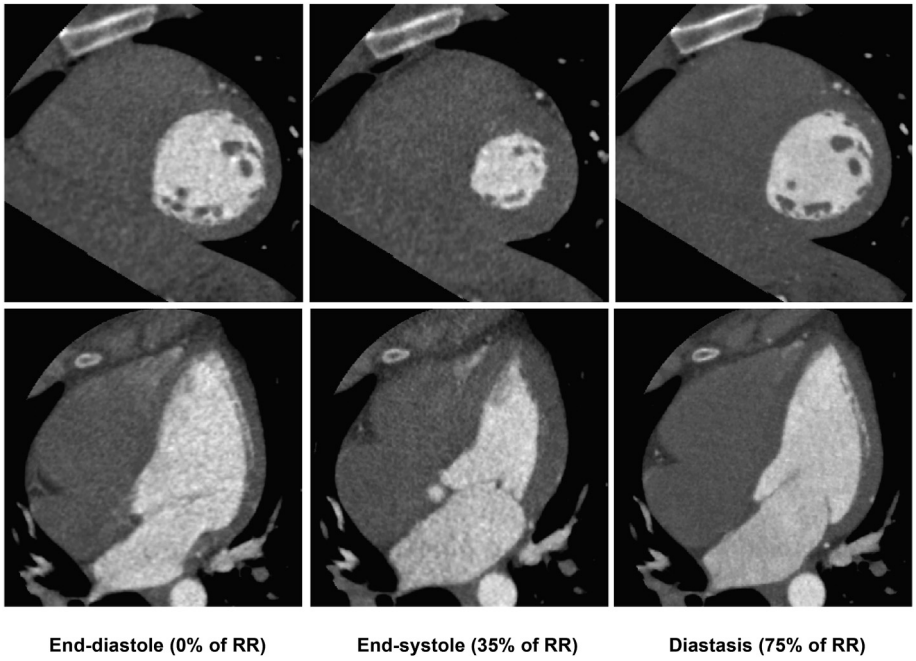

Fig. 1. (*continued*)

interval using the vendor provided reconstruction method chosen by each site for their default cardiac function image reconstruction. We did not impose any change to their reconstruction process.

Fig. 1 shows the image quality in a reformatted long axis and short axis view for two of the subjects; Fig. 1(a) shows images from a subject with a full retrospective data acquisition and Fig. 1(b) shows image from a subject with 50% mA reduction outside diastasis.

2.3. Image analysis

Image processing was performed using custom software in MATLAB and Osirix plugins. The basic steps were[7]:

1) A region of interest around the LV cavity was defined from the mitral valve plane to the apex for each time frame.
2) An LV cavity threshold level was measured by obtaining the average HU intensity in a single slice of the LV cavity.
3) The LV cavity was segmented by retaining all connected voxels above the measured threshold.
4) The LV volume vs. time was computed by counting the voxels above the threshold and LV Ejection Fraction was calculated.
4) The temporal sequence of 3D LV cavity volumes was submitted to SQUEEZ analysis[7] with the "template" volume being the earliest timeframe after the QRS (representing maximum LV filling), and the "target" volumes being the later time points.

An overview of the result of this processing is shown in Fig. 2.

The temporal evolution of SQUEEZ was then plotted in 16 standard regions of the LV. In each of the 16 regions, the average SQUEEZ value was computed. From the average SQUEEZ values we computed Regional Strain from CT SQUEEZ (RS_{CT}) as

$$RS_{CT} = (\text{SQUEEZ-1}) \quad (1)$$

We computed average RS_{CT} over different longitudinal regions of the heart (base, mid and apex). Using the slopes of the average curves we computed the average rate of change of RS_{CT} with time during systolic contraction (0% through 35% of RR interval), and diastolic filling (40% through 50% RR interval). We calculated the average time of end-systole (minimum RS_{CT}) over all segments, and the average increase in RS_{CT} between diastasis and the end of atrial kick.

In addition, LV volume was computed by counting the pixels above a HU threshold in the LV cavity below the mitral valve plane. This method may underestimate total LV volume normally used for ejection fraction from hand drawn contours because the LV outflow tract is not included and the papillary muscles and much of the trabecular tissue is not included.

3. Results

Fig. 3 shows the SQUEEZ values computed for all 25 subjects in this study in all segments of the LV. For visualization, the curves were interpolated onto 96 points across the RR window from 0% through 95% using linear interpolation followed by a ± 5% temporal smoothing window. The typical characteristics of myocardial strain vs. time are seen in each region. Systolic contraction occurs over the first 30–40% of the RR interval, with a sustained contraction occurring around end-systole at 35%. LV relaxation is shown as a rapid increase in SQUEEZ values during rapid filling between 40 and 50% of the RR interval. During diastasis (60–80% of the RR) the SQUEEZ values stay relatively constant at a value just above 0.9, until atrial contraction occurs causing a further stretch in the LV to return the SQUEEZ values to close to 1.0. These local regional measurements look very similar in different regions of the LV in these hearts. When the minimum SQUEEZ value is found for each subject, the mean of those values is 0.66 +- 0.05 yielding a mean value of RS_{CT} of −0.34 +- 0.05.

Fig. 4 shows the result of averaging all of the SQUEEZ curves from the 25 subjects; the average value at each time is shown as a bold solid line. The standard deviation above and below the mean at each time point is given by the thinner black lines. This shows that SQUEEZ values are highly consistent in normal hearts. The time of minimum average SQUEEZ value occurs at 34% ± 5% of the RR interval when averaged over all segments. There is a slight increase in strain from base to apex with the mean values:

base = −32% ± 1%, mid = −33% ± 1%, apex = −36% ± 1%.

The estimates of selected physiological parameters found in the normal heart using CT SQUEEZ are given in Table 1. The parameters

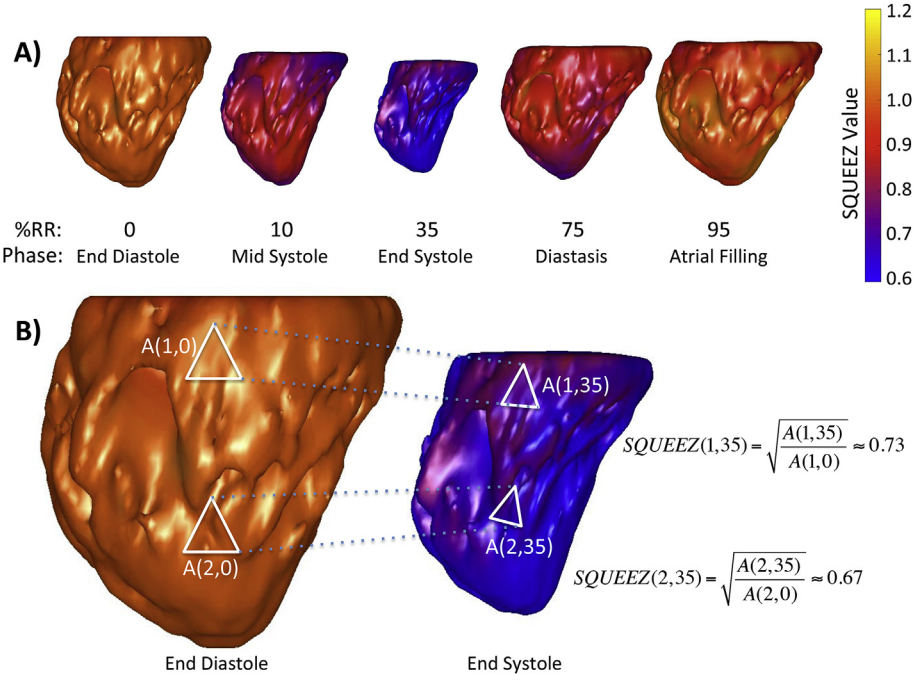

Fig. 2. Overview of the SQUEEZ algorithm. A) The lateral wall endocardial surface at 5 key time points in the RR interval; the "template" surface is end-diastole. The surfaces were extracted by simple thresholding of the LV blood signal. The colormap shows values of SQUEEZ at each location on the surface. B) The calculation of SQUEEZ at two example locations on the lateral wall shown by the triangles A(1) and A(2). These triangles are larger than the actual mesh; they are magnified to demonstrate the computation of SQUEEZ at two distinct points on the heart wall at the 35% time frame.

RS_{CT} and pre-stretch are unitless fractional length changes in the myocardium. The rate of change of RS_{CT} is reported as change in fractional length per RR interval.

Fig. 5 shows the SQUEEZ values (red line) from a subject who had relatively subtle local wall motion abnormality in the basal region of the LV. This abnormality was observed both on cine display of the CT data and in the SQUEEZ plots shown in Fig. 5. Clear regions of hypokinesis exist in 5 of the 6 segments in the base of the LV when compared with the average normal LV values show as a solid line. Due to the observation of hypokinesia on the cine CT, this subject was not included in the normal cohort.

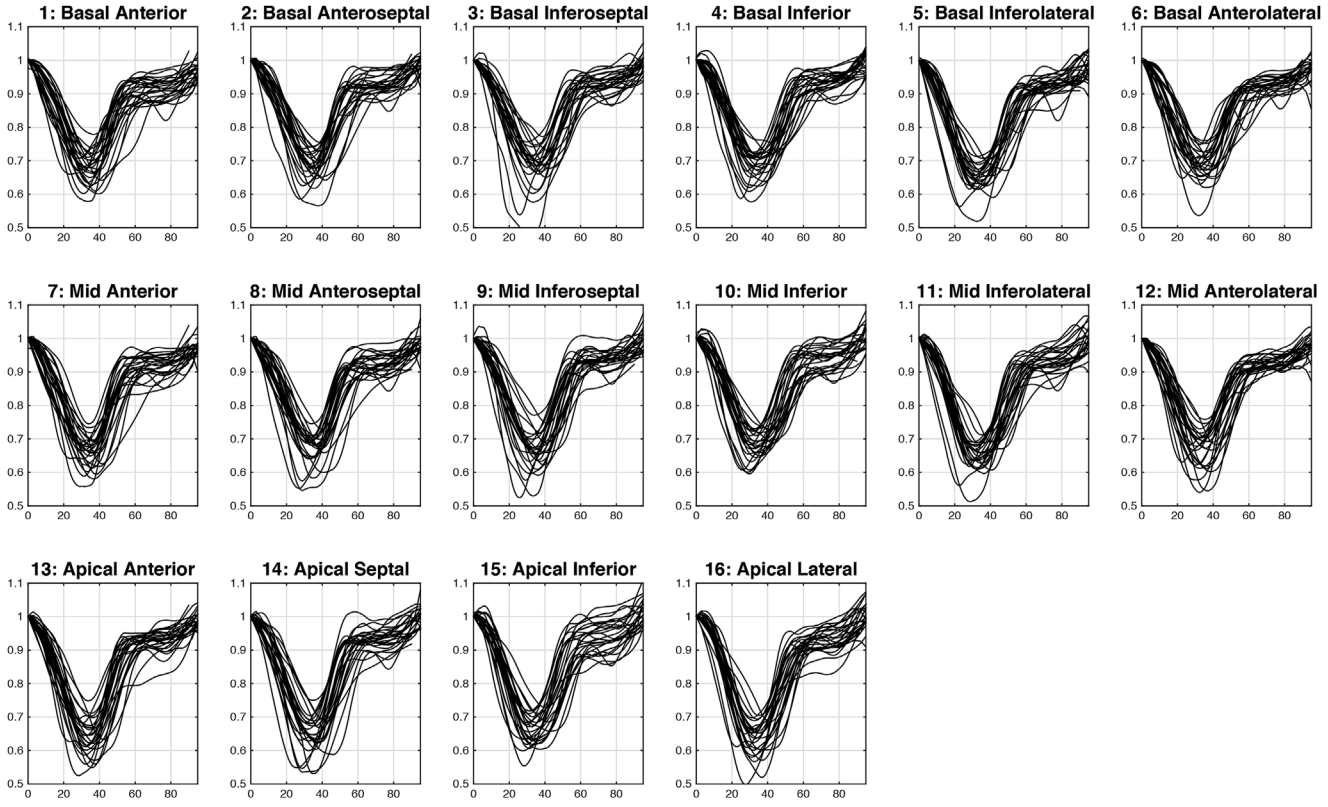

Fig. 3. SQUEEZ vs. %RR in the 16 standard AHA segments for the 25 subjects included in the study. The SQUEEZ values start at 1.0 at 0%RR (no contraction), decrease to ~0.66 (strain RSct = −0.34) at end systole (35% RR), increase to ~0.9 during diastasis (60–80% RR), and increase to 1.0 after atrial kick.

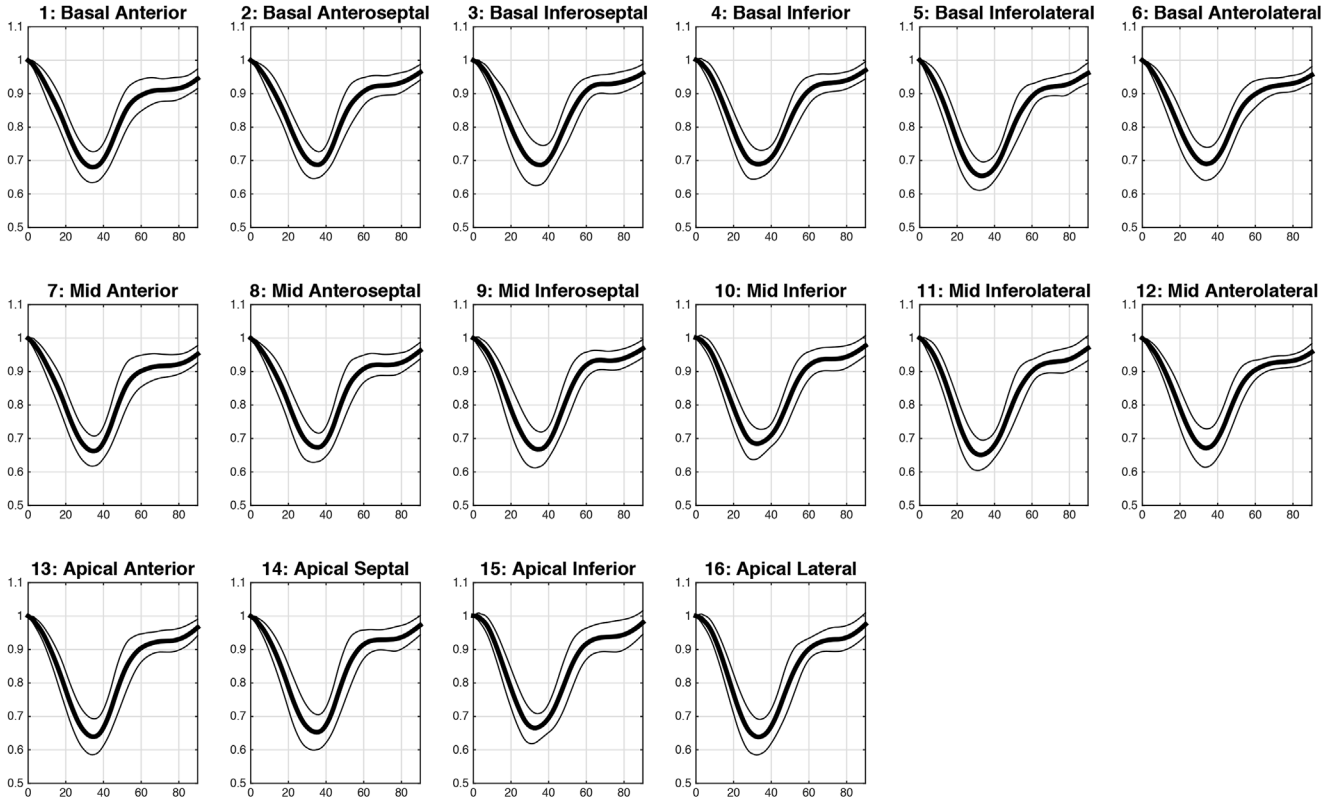

Fig. 4. The SQUEEZ vs %RR graph averaged over the 25 subjects analyzed. The bold central line give the mean value at each time point; the thin black lines give + and – one standard deviation of the 25 values used to calculate the mean. The average of the minimum SQUEEZ value is 0.66 +- 0.05 over all segments, yielding an average strain of RSCT of −0.34 +- 0.05. The average time through systole at which the minimum occurs is 34% +- 5%.

Table 1
The mean values and one standard deviation for five LV function parameters. Minimum systolic regional strain RS_{CT}, and pre-stretch from atrial kick are given in fractional changes in length. Systolic and diastolic rate of change of RS_{CT} are given as fractional change of length per R-wave to R-wave (RR) interval. The average time of end-systole is given as a percentage of the RR interval. RS_{CT} = (SQUEEZ-1).

Parameter	Measured Value ± SD over 25 subjects
Min systolic RS_{CT}	−0.34 ± 0.05
Normal pre-stretch from atrial kick	0.08 ± 0.04
Normal systolic RS_{CT} rate (0 through 30%)	−1.17 ± 0.15
Normal diastolic RS_{CT} relaxation rate (40–50%)	1.50 ± 0.15
Mean %RR to max systolic RS_{CT} (end-systole)	34% ± 5%

4. Discussion

The primary observation from this work is that standard clinical protocols, with standard image reconstruction can be used successfully to obtain very stable values of LV function from SQUEEZ. Also, we establish preliminary baseline values for regional strain in the LV as measured by CT SQUEEZ; similar work has been carried out to determine the range of normal LV strain values measured by 3D echocardiography,[14] and MR tagging,[15] and MR tissue tracking[4] and our results compare well. This encourages us to continue to acquire a larger data set to fully characterize SQUEEZ in the normal human, and to study the optimization of image reconstruction for SQUEEZ. It has been demonstrated strain values obtained by 3D echocardiography speckle tracking are dependent on the software used[16] demonstrating a need for an alternative method with more reproducible values. These preliminary results from SQUEEZ show that there is a very tight distribution of normal values for LV function (Table 1) even though we used images from different vendors and protocols; this is very encouraging because this tight distribution should hold up when studies are included from different sites with CT scanners from different vendors. The values we report for RS_{CT} are biased toward a greater amount of strain through systole than those measured at the midwall with MRI tagging or with speckle tracking. This is not surprising, as the SQUEEZ technique tracks the area change of a complex endocardial surface obtained by thresholding, while 3D echo techniques rely on smooth contours. As the complex endocardial surface collapses in the cine CT data, the amount of area change will be greater than that obtained for a smooth surface. Similarly, when our results are compared with the midwall strains reported in normal human hearts from MRI tagging through systole, our strains are larger.[15] Again, this bias is from the complex surface, and the fact that our data is on the inner boundary of the endocardium; it is well reported that strain increases from the epicardium

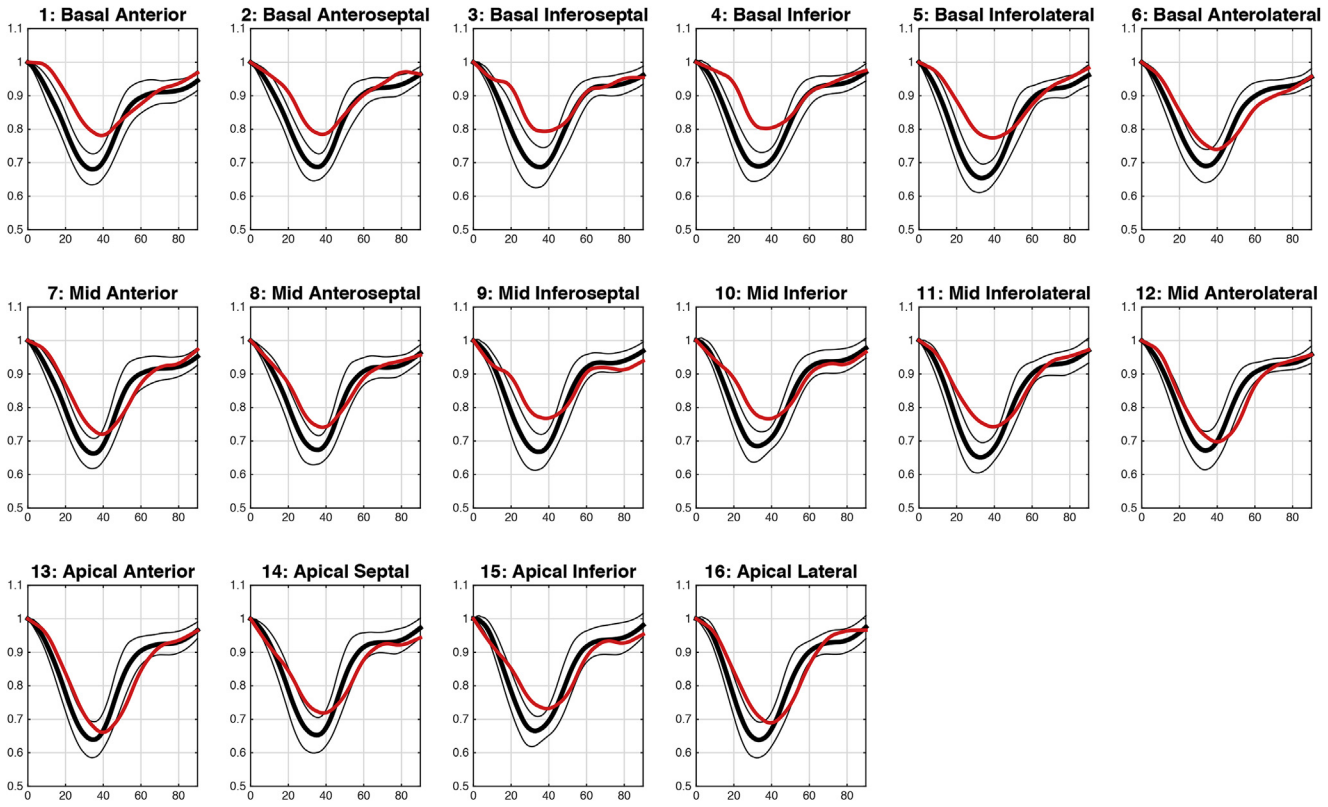

Fig. 5. A comparison of a regional SQUEEZ values in a subject with subtle hypokinesia in the basal slices of the heart vs. the average normal SQUEEZ values found in the normal subjects.

to endocardium in the human LV.[15] SQUEEZ does not measure mid-wall myocardial strain; however, it does yield an estimate of strain that correlates well with mid-wall strain measured with MRI tagging[8] ($r = 0.71$).

A number of significant disease states change regional LV regional function including myocardial ischemia, cardiomyopathies, electromechanical dyssynchrony and structural heart disease. The mechanical consequences of these conditions have been characterized with both echocardiography[17] and MRI tagging.[18] We believe SQUEEZ will also yield useful estimates of changes in local myocardial function from these disease states.[19] and the current results encourage us to optimize SQUEEZ for these applications.

The use of CCTA is rapidly gaining international acceptance in cardiology as numerous clinical trials show its effectiveness at ruling out coronary syndromes in patients with chest pain,[20] and it has superior sensitivity to the existence of coronary disease as seen on xray-angiography.[21] For these patients, a concomitant accurate measurement of regional LV function over the entire left ventricle may provide important clinical information – and we have shown in this study that this information can be obtained easily *during the same data acquisition,* in fact, during the same heartbeat. The existence of resting wall motion abnormalities observed with CT in these subjects has been shown to increase the likelihood of ACS significantly.[22,23] It is possible that the acquisition of LV function during CCTA could eliminate the need for immediate diagnostic echocardiography or SPECT in these patients if a resting wall motion abnormality is found which is concomitant with a moderate to severe coronary lesion; however, this hypothesis would need to be tested in a multi-center trial. Because LV function can be measured during the same heartbeat as the CCTA acquisition, we believe it may be easily included as part of the CCTA exam in selected patients with appropriate tube current modulation and temporally dependent averaging[24] during the RR interval to minimize the additional dose. Initial results from qualitative analysis of low dose CT are very encouraging; it is likely that very low dose (< 1 mSv additional dose above CCTA dose) SQUEEZ analysis will be possible.[25,26] Recent results[13] show that SQUEEZ estimates are stable and accurate for LV blood - myocardium CNR levels above 4.

Comparisons of echocardiography and CMR with functional CT using 2D techniques show good correlations.[27,28] However, 4D analysis with SQUEEZ has an advantage over 2D techniques (echocardiography, MRI or CT) because it does not suffer confounding artifacts from tissue entering the 2D slice over time. In addition, we have demonstrated in this study that SQUEEZ can use 4D data obtained from a *single heartbeat*; this dramatically improves the robustness of the imaging study to variable heart rate, problematic ECG triggering, and artifacts from measuring mechanical parameters from selected 2D slices fixed in space. Techniques such as 3D echo based Global Area Strain (which requires 6 beats)[29] and MRI tagging require a highly skilled imaging technologist, and numerous consecutive heartbeats which are very similar.

Fig. 5 gives a single example of a subtle reduction in LV function detected with SQUEEZ. Given the relatively tight distribution of values of RS_{CT} small changes in function will be detected with high sensitivity. For example, if we attempt to detect an increase in average maximum strain from -0.34 in normal subjects to more than -0.24 in hypokinetic subjects, at a power of 0.9 and $\alpha = 0.05$, we would need a cohort of only ~ 12 subjects, assuming that the variance in the abnormal subjects is the same as that measured in the normal subjects. The fact that we can analyze different vendors and different reconstructions with SQUEEZ gives us the opportunity to compute SQUEEZ in databases of *previously* acquired CTA studies to discover the relationship of SQUEEZ to patient outcomes.

There were several limitations of this study. First, only 25 subjects were included which is a relatively small sample size; however, the standard deviation measured over the 25 subjects for the parameters in Table 1 is quite small, therefore these estimates are valuable. As is

common in CT analysis, we scaled the RR interval to 0–95%; this allowed pooling of subjects with different heart rates. While radiation dose and LV blood – myocardium CNR varied widely in the subjects, adequate image quality was present in all cases for SQUEEZ analysis; the SNR dependence on SQUEEZ was not tested. While two different time resolutions were used (10 frames per RR vs. 20 frames per RR) we did not study any bias due to this difference; the effect of time resolution on SQUEEZ accuracy will require carefully executed studies that isolate this effect. This study did not characterize SQUEEZ in pathological hearts – these studies remain to be performed.

5. Conclusion

CT SQUEEZ is a simple, robust, operator independent method for measuring 4D regional wall function over the entire human left ventricle. We have demonstrated that SQUEEZ can be obtained rapidly from standard ECG gated CT protocols on scanners from three different vendors. A normal range of values of regional strain derived from SQUEEZ (RS_{CT}) can be used to characterize normal local LV function: we estimate that 95% of normal LV end-systolic RS_{CT} values will fall between −23% and −43%. Therefore, we hypothesize that RS_{CT} values higher than −23% indicate hypokinetic segments in the human heart.

Disclosures

Drs. McVeigh and Pourmorteza are inventors on intellectual property for SQUEEZ licensed to Cardiowise Inc. by Johns Hopkins University.

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References

1. Jeung M-Y, Germain P, Croisille P, et al. Myocardial tagging with MR imaging: overview of normal and pathologic findings. *Radiographics* Radiological Society of North America. 2012;32:1381–1398.
2. McVeigh E, Ozturk C. Imaging myocardial strain. *IEEE Signal Process Mag.* 2001;18:44–56.
3. Hor KN, Baumann R, Pedrizzetti G, et al. Magnetic resonance derived myocardial strain assessment using feature tracking. *JJ Vis Exp.* 2011;48:2356.
4. Hor KN, Gottliebson WM, Carson C, et al. Comparison of magnetic resonance feature tracking for strain calculation with harmonic phase imaging analysis. *JACC Cardiovasc Imaging United States.* 2010;3:144–151.
5. Augustine D, Lewandowski AJ, Lazdam M, et al. Global and regional left ventricular myocardial deformation measures by magnetic resonance feature tracking in healthy volunteers: comparison with tagging and relevance of gender. *J Cardiovasc Magn Reson.* 2013:15.
6. Ibrahim E-SH. Myocardial tagging by cardiovascular magnetic resonance: evolution of techniques–pulse sequences, analysis algorithms, and applications. *J Cardiovasc Magn Reson England.* 2011;13:36.
7. Pourmorteza A, Schuleri KH, Herzka DA, et al. A new method for cardiac computed tomography regional function assessment: stretch quantifier for endocardial engraved zones (SQUEEZ). *Circ Cardiovasc Imaging.* 2012;5:243–250.
8. Pourmorteza A, Chen MY, van der Pals J, et al. Correlation of CT-based regional cardiac function (SQUEEZ) with myocardial strain calculated from tagged MRI: an experimental study. *Int J Cardiovasc Imaging United States.* 2016;32:817–823.
9. Yingchoncharoen T, Agarwal S, Popovic ZB, et al. Normal ranges of left ventricular strain: a meta-analysis. *J Am Soc Echocardiogr United States.* 2013;26:185–191.
10. Shah DJ, Kim HW, James O, et al. Prevalence of regional myocardial thinning and relationship with myocardial scarring in patients with coronary artery disease. *JAMA United States.* 2013;309:909–918.
11. Sarwar A, Shapiro MD, Nasir K, et al. Evaluating global and regional left ventricular function in patients with reperfused acute myocardial infarction by 64-slice multidetector CT: a comparison to magnetic resonance imaging. *J Cardiovasc Comput Tomogr.* 2009;3:170–177.
12. Rizvi A, Deano RC, Bachman DP, et al. Analysis of ventricular function by CT. *J Cardiovasc Comput Tomogr.* 2015;9:1–12.
13. Pourmorteza A, Keller N, Chen R, et al. Precision of regional wall motion estimates from ultra-low-dose cardiac CT using SQUEEZ. *Int J Cardiovasc Imaging Springer Netherlands.* 2018;0:1–10.
14. Kleijn SA, Pandian NG, Thomas JD, et al. Normal reference values of left ventricular strain using three-dimensional speckle tracking echocardiography: results from a multicentre study. *Eur Heart J Cardiovasc Imaging England.* 2015;16:410–416.
15. Moore CC, Lugo-Olivieri CH, McVeigh ER, et al. Three-dimensional systolic strain patterns in the normal human left ventricle: characterization with tagged MR imaging. *Radiology.* 2000;214:453–466.
16. Muraru D, Cucchini U, Mihaila S, et al. Left ventricular myocardial strain by three-dimensional speckle-tracking echocardiography in healthy subjects: reference values and analysis of their physiologic and technical determinants. *J Am Soc Echocardiogr United States.* 2014;27:858–871 e1.
17. Biswas M, Sudhakar S, Nanda NC, et al. Two-and three-dimensional speckle tracking echocardiography: clinical applications and future directions. *Echocardiography* Wiley Online Library. 2013;30:88–105.
18. Shehata ML, Cheng S, Osman NF, et al. Myocardial tissue tagging with cardiovascular magnetic resonance. *J Cardiovasc Magn Reson BioMed Central.* 2009;11:1.
19. Behar JM, Rajani R, Pourmorteza A, et al. Comprehensive use of cardiac computed tomography to guide left ventricular lead placement in cardiac resynchronization therapy. *Hear Rhythm United States.* 2017;14:1364–1372.
20. Shaw LJ, Hausleiter J, Achenbach S, et al. Coronary computed tomographic angiography as a gatekeeper to invasive diagnostic and surgical procedures: results from the multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: an International Multicenter) registry. *J Am Coll Cardiol.* 2012;60:2103–2114.
21. Douglas PS, Hoffmann U, Patel MR, et al. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med United States.* 2015;372:1291–1300.
22. Seneviratne SK, Truong QA, Bamberg F, et al. Incremental diagnostic value of regional left ventricular function over coronary assessment by cardiac computed tomography for the detection of acute coronary syndrome in patients with acute chest pain: from the ROMICAT trial. *Circ Cardiovasc Imaging.* 2010;3:375–383.
23. Schlett CL, Banerji D, Siegel E, et al. Prognostic value of CT angiography for major adverse cardiac events in patients with acute chest pain from the emergency department: 2-year outcomes of the ROMICAT trial. *JACC Cardiovasc Imaging.* 2011;4:481–491.
24. Wai B, Thai W, Brown H, et al. Novel phase-based noise reduction strategy for quantification of left ventricular function and mass assessment by cardiac CT: comparison with cardiac magnetic resonance. *Eur J Radiol Elsevier Ireland Ltd.* 2013;82:e337–e341.
25. Groves DW, Olivieri LJ, Shanbhag SM, et al. Feasibility of low radiation dose retrospectively-gated cardiac CT for functional analysis in adult congenital heart disease. *Int J Cardiol Netherlands.* 2017;228:180–183.
26. Contijoch FJ, Groves DW, Chen Z, et al. A novel method for evaluating regional RV function in the adult congenital heart with low-dose CT and SQUEEZ processing. *Int J Cardiol Elsevier B.V.* 2017;249:461–466.
27. Buss SJ, Schulz F, Mereles D, et al. Quantitative analysis of left ventricular strain using cardiac computed tomography. *Eur J Radiol Ireland.* 2014;83:e123–e130.
28. Takx RAP, Moscariello A, Schoepf UJ, et al. Quantification of left and right ventricular function and myocardial mass: comparison of low-radiation dose 2nd generation dual-source CT and cardiac MRI. *Eur J Radiol Ireland.* 2012;81:e598–604.
29. Reant P, Barbot L, Touche C, et al. Evaluation of global left ventricular systolic function using three-dimensional echocardiography speckle-tracking strain parameters. *J Am Soc Echocardiogr United States.* 2012;25:68–79.