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Quantitative Assessment of Atrial Regional Function Using Motion Estimation CT

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Abstract

Objectives—We validated a novel image-based motion estimation CT technique (iME) to quantify atrial regional function in swine *in vivo*.

Methods—Domestic swine (n=8) underwent CT scan with intravenous contrast before and after median sternotomy where 15–30 glass beads were sutured to the atria to calculate the motion estimation error. Four-dimensional motion vector field (MVF) was estimated using iME. Area change ratio (%AC) was calculated over the atrial endocardium to assess the surface deformation.

Results—The error between the measured and the calculated coordinates based on MVF was 0.76 ± 0.43 mm. %AC was regionally heterogeneous. %AC time course was significantly different between the right and the left atrium ($P < 0.001$), and between the right atrial appendage and the right atrial chamber ($P = 0.004$).

Conclusions—Quantitative assessment of atrial regional function using iME is highly accurate. iME can quantify subtle regional dysfunction that is not apparent in global functional indices such as ejection fraction.

Keywords

Cardiac CT; Image processing; Regional function; Atrial function

Introduction

Three-dimensional (3-D) quantitative assessment of atrial regional function is challenging due to the complex anatomy of the atria. The most commonly used clinical imaging

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technique to assess atrial regional function is echocardiography. In particular, 3-D echocardiography combined with speckle-tracking imaging is a promising technique that allows quantification of heart surface deformation(1). However, it is still limited by factors inherent to echocardiography, including operator-dependence and inability to view the whole heart. Cardiac MRI with tissue tagging is another technique that could be used for quantitative assessment of atrial regional function. Despite its accuracy, tagged MRI is limited by poor spatiotemporal resolution and labor intensive post-processing. Importantly, MRI is still generally contraindicated in patients with cardiac implantable electrical devices. Given the growing prevalence of implantable cardioverter-defibrillators in patients with cardiac dysfunction, clinical utility of cardiac MRI to assess regional function is limited.

Image-based motion estimation CT (iME) is a novel image processing technique similar in concept to 3-D speckle-tracking imaging to estimate regional function of the whole heart while taking advantage of high spatial resolution of cardiac CT(2) (Figure 1). The objective of this study was to validate the performance of iME to assess atrial regional function quantitatively. To attain the objective of this study, we tested the hypothesis that iME could be used to quantify atrial regional function. We tested our hypothesis by quantifying the error between the measured and the calculated motion of glass beads surgically sutured to the atria in normal swine *in vivo*.

Materials and Methods

All studies were performed according to the position of the American Heart Association on research animal use.(3) The protocol was approved by the animal care and use committee of the Johns Hopkins University School of Medicine.

Experimental Protocol

Under general anesthesia, domestic swine (female sex, 20–30kg, n=8) underwent a baseline CT scan during sinus rhythm using either a dual-source 128-slice CT scanner (Siemens SOMATOM Definition Flash, n=5) or a single-source 320-slice CT scanner (Toshiba Aquilion ONE, n=3). Multi-cycle reconstruction was used to maximize the essential temporal resolution (up to 37 ms and 58 ms in the dual-source and single-source scanner, respectively). IV contrast iodixanol was infused at a rate of 2–5 ml/sec for a total of 60–100 ml. Ventilation was suspended at the end of expiration and imaging performed using a retrospective ECG gating with no tube-current modulation. After the animal was allowed to recover for at least 36–48 hours to clear IV contrast from the system, the animal was brought to the surgical suite and underwent median sternotomy under general anesthesia (n=6). Fifteen to thirty radiopaque glass beads (3-mm diameter) were sutured to both the atria such that they were evenly spread over the atrial surface (Figure 2A). The chest cavity was approximated to maintain the normal geometry of the thorax. Post-operatively, the animal received another CT scan during sinus rhythm with the same imaging protocol as the baseline CT scan as described above. After the scan was completed, the animal was euthanized with IV barbiturate overdose followed by KCl injection.

Estimation of MVF

The volumetric image data were reconstructed from the raw projection data at each cardiac phase (0–99% R-R interval by 1% increment, a total of 100 cardiac phases per R-R interval). The reconstructed spatial and temporal resolution was $0.21\text{--}0.31 \times 0.21\text{--}0.31 \times 0.25\text{--}0.40$ mm³ and 5–10 msec, respectively. The detailed method of image-based motion estimation (ME) was described previously(2) (Figure 1). Briefly, the iME algorithm estimated the motion vector field (MVF) using four-dimensional (4-D) (3-D + time) nonrigid registration with cubic B-splines between the reference phase and all the other phases. The technique is similar in concept to 3-D speckle-tracking imaging. The cost function consisted of a sum of squared weighted differences, and spatial and temporal regularization terms. A nested conjugate gradient optimization algorithm was applied to minimize the cost function. The computation was performed in a GPU-based parallel computing platform (2.0GHz Intel Xeon, 48GB RAM, 6.5TB hard drive, 3GB NVIDIA Tesla C2050).

Validation of MVF

The glass beads on the atrial surface (15–30 beads per animal) were identified on the reconstructed images at each cardiac phase (Figure 2B). The measured 3-D coordinates of the glass beads were defined as the center of mass of each bead calculated by thresholding based on signal intensity. Separately, the 3-D coordinates of the glass beads were also calculated based on estimated MVF. More specifically, the 3-D coordinates of the glass beads in the reference phase were measured as described above. Then the 3-D coordinates of the glass beads in the target phase were calculated by the MVF. This process was repeated for all the cardiac phases. The error was defined as the 3-D Euclidean distance (in mm) between the measured and the calculated 3-D coordinates based on MVF.

Estimation of Atrial Regional Function

The endocardial surface of both the right and the left atria was segmented based on signal intensity using a DICOM viewer (OsiriX 64-bit) (Figure 3A). Surface rendering was performed with triangular mesh (Figure 3B, 3C). The relative change in the area from the atrial end diastole to the other phases of interest, called area change ratio (%AC), was calculated for each mesh triangle at each cardiac phase to assess the surface deformation over time (Figure 3C and 3D). Atrial end diastole was defined as the cardiac phase when the atrial volume was the maximum, which roughly corresponded to 40–50% R-R interval. %AC is also called 3-D area strain, and is clinically used to measure regional myocardial function in 3-D speckle tracking echocardiogram(1). Compared to traditional indices of myocardial deformation, %AC is more sensitive, has a higher signal-to-noise ratio (SNR), and is highly reproducible(4).

Statistical Analysis

Descriptive statistics were shown in means $\pm$ SD. Two-factor repeated-measures ANOVA was used for three separate %AC time course analyses. The first analysis was to assess the effect of atrial chambers (right vs. left atrium) and cardiac phase on %AC. The two remaining analyses were to assess the effect of atrial segments (right atrial appendage vs. right atrial chamber and left atrial appendage vs. left atrial chamber) and cardiac phase on

%AC. Statistics were performed using MATLAB R2013b with Statistics Toolbox (Mathworks, Inc.). A two-sided value of $P < 0.05$ was considered statistically significant.

Results

The animal weighed 28 ± 4 kg. There was no significant difference between the heart rate at the baseline scan and the post-operative scan (84 ± 18 vs. 86 ± 28 bpm, $P = 0.657$). The reconstructed spatial and temporal resolution was $0.24 \pm 0.03 \times 0.24 \pm 0.03 \times 0.34 \pm 0.08$ mm³ and 7.4 ± 1.6 msec, respectively.

Motion Estimation Error

A total of 19.8 ± 8.6 glass beads per animal were implanted to the atrial surface to quantify 3-D motion estimation errors. The errors were calculated at every 10 cardiac phases (= 10% R-R interval), with intervals of ~70 msec between phases. Representative errors over a cardiac cycle are shown in Figure 4. The mean errors plateaued at 30–40% R-R where the displacement is maximum at ventricular end systole, and stayed between 0.6 and 0.8 mm. The overall 3-D error throughout the cardiac cycle for all the animals was 0.76 ± 0.43 mm (95% confidence interval: 0.68 to 0.84 mm).

Atrial Regional Function

The anatomy of swine atria is similar to that of human atria, but two distinct features are noted. First, the atrial appendages occupy the bulk of the atrial volume. Second, the atrial septum is part of the right superior pulmonary vein (RSPV) (Figure 5).

%AC was calculated for every triangle on the atrial endocardial surface at each cardiac phase. Global functional indices of the atria are shown in Table 1. Figure 6 shows the atrial configuration for 5 consecutive phases from atrial end diastole to the atrial end systole (Video 1). Atrial regional function was color-coded by % change in area change ratio from the atrial end diastole. The maximum regional contraction is shown in Figure 7. Atrial function was regionally heterogeneous; the maximum regional contraction was greater in the posterior region of the left atrium and the edges of the atrial appendages.

The average regional contraction over time was calculated for each chamber (Figure 8). Overall, it showed a classic two-step contraction pattern, showing ventricular suction as the first step and atrial contraction as the second step (Figure 3D). Following the ventricular suction, the right atrium appeared to relax and return to near the baseline before atrial contraction, suggesting continuous venous return to the right atrial chamber. In contrast, the left atrium showed minimal relaxation between ventricular suction and atrial contraction (Figure 8A).

%AC time course analyses showed significant interaction between atrial chamber (right vs. left atrium) and cardiac phase ($P < 0.001$), indicating that the %AC time course was significantly different between the right and the left atrium. There was also significant interaction between the right atrial segments (right atrial appendage vs. right atrial chamber) and cardiac phase ($P = 0.004$), indicating that the %AC time course was significantly different between the right atrial appendage and the right atrial chamber. There was no significant

interaction between the left atrial segments (left atrial appendage vs. left atrial chamber) and cardiac phase ($P=0.11$), indicating that the %AC time course was not different between the left atrial appendage and the left atrial chamber.

Discussion

The present study validated the accuracy of a novel image-based cardiac motion estimation technique called iME to quantify 3-D atrial regional function. Our results indicate that quantitative assessment of atrial regional function using iME is highly accurate with an error of 0.76 ± 0.43 mm. This finding provides assurance that iME will allow accurate assessment of complex 3-D regional atrial function *in vivo* with high spatiotemporal resolution. This finding is important, because it will put iME on a unique position to overcome the limitations of other clinically available imaging techniques such as echocardiogram and MRI to assess atrial regional function. Our results also indicate that atrial function is regionally heterogeneous. This finding underscores the advantage of iME that can quantify subtle regional dysfunction that is not apparent in global functional indices such as ejection fraction (Table 1).

Advantages of iME over other imaging techniques

There are several major advantages of iME over other imaging techniques. First, iME takes advantage of the high spatial resolution of cardiac CT. iME estimates MVF voxel-by-voxel for each cardiac phase for the entire volumetric data. Therefore, iME can estimate the regional function of essentially any region of the heart. A recently developed CT-based technique (SQUEEZE) that tracks morphological features of the endocardium showed excellent accuracy in quantitative assessment of regional function of the ventricular endocardium(5). However, the assessment is limited to the endocardial surface, and its performance with the atria with complex endocardial structures is unknown. Second, iME can quantify 3-D regional function. In this study we limited our regional function analysis to %AC, which is essentially a surface deformation index. However, since iME provides 4-D MVF, any 3-D indices of myocardial deformation can be calculated (e.g. circumferential, longitudinal or radial strains). Third, since this imaging technique is based on CT, the acquisition time is short, requiring a breathhold for only a few seconds. This is a great advantage over tagged MRI, which would require multiple cycles of breathhold of at least 15–20 seconds. This level of breathhold would be challenging for the patients with heart failure who would most benefit from regional function analysis. Fourth, post-processing for iME is simple and requires little user input. In particular, since iME is based on cardiac CT, segmentation of each heart chamber is substantially easier than that of cardiac MRI because of the higher spatial resolution and the higher contrast-to-noise ratio. For these advantages, iME can easily be incorporated into routine clinical practice.

Radiation dose

Ionizing radiation exposure is one of the major disadvantages of any CT-based techniques over other clinical imaging modalities. Because this study required accurate validation of the technique, we used retrospective ECG gating with no tube-current modulation technique to image all the cardiac phases during the entire cardiac cycle with minimal noise. However,

iME can be combined with motion-compensated iterative reconstruction (MCR) algorithms to achieve a higher image quality and a lower radiation dose at the same time. For example, the motion estimation and motion-compensated iterative reconstruction (ME-MCR) algorithm(2) requires no more radiation dose than that of the standard prospective gating CT. Due to the improved image quality, overall radiation could be lowered further by lowering the tube current in the tube-current modulation technique.

Clinical implications

Atrial fibrillation (AF) accounts for one in four strokes in those aged 80 years or older(6). Recent evidence suggests that AF may not be the cause but a manifestation of underlying fibrotic atrial cardiomyopathy (FACM)(7). In fact, atrial fibrosis is independently associated with the risk of stroke(8). Although quantitative assessment of atrial fibrosis using MRI *in vivo* is technically challenging, the presence and extent of fibrosis could potentially be estimated by quantifying atrial regional dysfunction(9). Quantitative, noninvasive assessment of regional atrial function using iME would provide objective criteria to justify more effective prophylactic interventions in older adults at a higher risk, such as anticoagulation, catheter ablation of AF, or left atrial appendage closure, while avoiding the complications and the cost of interventions in lower-risk individuals.

Limitations

There are several limitations that should be considered before our results are translated to human patients. First, the sample size was relatively small. However, with this sample size we believe that we still achieved the objective of the study because the 95% confidence interval of the error was less than 1 mm. Second, there is substantial difference in atrial anatomy between human and swine (Figure 5). Because the atrial appendages in human are smaller relative to the size of the atrial chamber, it is possible that atrial chambers may make a greater contribution to the global atrial function than atrial appendages. Third, atrial regional function was examined in anesthetized swine. Therefore, our results may not precisely reflect the regional function in awake individuals. Fourth, the 3-D motion may be underestimated due to the essential temporal resolution of reconstructed images (40–60ms). The essential temporal resolution is limited by the gantry rotation speed. However, this limitation can be circumvented by the use of multi-cycle reconstruction, faster gantry speed of the newer generation CT scanners, and the ME-MCR algorithm.

Conclusion

Quantitative assessment of atrial regional function using iME is highly accurate. iME can quantify subtle regional dysfunction that is not apparent in global functional indices such as ejection fraction. iME is a noninvasive imaging tool that can be incorporated into routine clinical assessment of atrial regional function despite the complex anatomy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Motion vector field (MVF) derived from iME algorithm

A. iME algorithm estimates MVF between the reference phase and each cardiac phase ("Phase n " in the figure) over the cardiac cycle, using four-dimensional (4-D) (3-D + time), nonrigid registration with cubic B-splines. B. MVF estimated from ME-MCR is shown on an axial CT image. Each vector (red arrow) is shown on every 16 voxels. Note an unequal aspect ratio in the Z direction (unit in XYZ axes = voxel).

Figure 2. Validation of 3-D MVF

Glass beads (white arrows) were surgically implanted on the atrial surface (A), and the XYZ coordinates of the beads (red arrows) were determined in each image (B). The Euclidean distance (error, in mm) was measured between the measured and the calculated coordinates based on MVF.

Figure 3. Regional wall motion described by %AC

A. Axial CT image of a swine heart including the atria. B. 3-D surface rendering of the swine atria. C. Enlarged atrial mesh with individual triangles, and calculation of %AC. D. %AC over time during sinus rhythm in one representative triangle. Positive and negative values represent atrial stretch and contraction, respectively. SVC, superior vena cava; RAA, right atrial appendage; RIPV, right inferior pulmonary vein; IVC, inferior vena cava; LAA, left atrial appendage; LIPV, left inferior pulmonary vein.

Figure 4. Error of atrial motion estimation from 3-D MVF

Values indicate means $\pm$ SD. The Euclidean distance (error, in mm) between the measured coordinates and the calculated coordinates based on MVF was 0.76 ± 0.43 mm.

Figure 5. Anatomy of swine atria

All images are in a posterior view. *A. Thorax. B. Heart. C. Atria connected to the pulmonary veins and the vena cavae. D. Right (blue) and left atrium (red).* LSPV, left superior pulmonary vein; RSPV, right superior pulmonary vein. See Figure 3 for the rest of abbreviations.

Figure 6. Atrial regional function from atrial end diastole to atrial end systole

Atrial regional function is color-coded by area change ratio (%). Atrial end diastole and atrial end systole were defined as the cardiac phase when the atrial volume was the maximum and the minimum, respectively.

Figure 7. Maximum regional contraction, shown in area change ratio (%)

A. Posterior view, B. Left lateral view, C. Anterior view, D. Right lateral view. LA, left atrium; RA, right atrium; TV, tricuspid valve; MV, mitral valve.

Figure 8. Time plot of average area change ratio (%)

Values indicate means $\pm$ SD. A. *Right (RA) vs. Left atrium (LA)*, B. *Right atrial appendage (RAA) vs. Right atrial chamber*, C. *Left atrial appendage (LAA) vs. Left atrial chamber*.

Table 1

Global functional indices of the atria.

Variable	Right Atrium	Left Atrium	P value
End-diastolic Volume	29.0±6.0	52.3±13.2	0.002
End-systolic Volume	23.0±4.7	39.8±11.3	0.002
Ejection Fraction (%)	20.1±7.5	23.7±13.7	0.33
Maximum Contraction (%)	-20.4±6.9	-18.9±7.0	0.48

Values indicate means±SD. Maximum contraction is represented by the mean minimum %AC.