False dyssynchrony: Problem with image-based cardiac functional analysis using x-ray computed tomography

Masafumi Kidoh*1, Zeyang Shen1,2, Yuki Suzuki1,3,4, Luisa Ciuffo1, Hiroshi Ashikaga1, George S. K. Fung1, Yoshito Otake4, Stefan L. Zimmerman1, Joao A. C. Lima1, Takahiro Higuchi5, Okkyun Lee1, Yoshinobu Sato4, Lewis C. Becker1, Elliot K. Fishman1, and Katsuyuki Taguchi1

1Johns Hopkins University School of Medicine (Baltimore, MD, U.S.A.)
2Southeast University (Nanjing, China)
3Osaka University (Osaka, Japan)
4Nara Advanced Institute of Science and Technology (Nara, Japan)
5University of Würzburg (Würzburg, Germany)

ABSTRACT

We have developed a digitally synthesized patient which we call “Zach” (Zero millisecond Adjustable Clinical Heart) phantom, which allows for an access to the ground truth and assessment of image-based cardiac functional analysis (CFA) using CT images with clinically realistic settings. The study using Zach phantom revealed a major problem with image-based CFA: “False dyssynchrony.” Even though the true motion of wall segments is in synchrony, it may appear to be dyssynchrony with the reconstructed cardiac CT images. It is attributed to how cardiac images are reconstructed and how wall locations are updated over cardiac phases. The presence and the degree of false dyssynchrony may vary from scan-to-scan, which could degrade the accuracy and the repeatability (or precision) of image-based CT-CFA exams.

Keywords: Computed tomography, cardiac function analysis, dyssynchrony

1. INTRODUCTION

Cardiovascular diseases remain the leading cause of death in the western world, placing an ever-increasing burden on health services. Assessment of regional cardiac functions (CFA)—which refers to regional wall motion and “dyssynchrony”—has shown great promise to improve the identification of patients at high risk and the standard of care for cardiovascular disease. The regional wall motion refers to how much each region of ventricular and atrial walls are moving, and dyssynchrony refers to how much the rhythm or timing of the wall motion is not synchronized among different regions (Fig. 1, bottom). In the following, we show the clinical value of the assessment of regional CFA. First, the assessment of regional left ventricular (LV) functions improves the accuracy of a stress test in combination with myocardial perfusion imaging and coronary computed tomography angiography. Recent studies showed that the degree of regional LA and LV dyssynchrony during sinus rhythm are proportional to the extent of underlying fibrosis and scarring [1-3]. Thus, performing regional CFA conjunction with coronary computed tomography angiography or myocardial perfusion imaging could improve the accuracy of the detection and characterization of focal or diffuse myocardial infarctions and ischemia. Second, the LV dyssynchrony during sinus rhythm could be a good predictor of future cardiac events including myocardial infarction, heart failure, and stroke and death [4]. Third, the assessment of regional left atrial (LA) and LA appendage functions during sinus rhythm show promises for the prediction of the outcome
(recurrence) of pulmonary vein isolation procedures and the risk-stratification of stroke or transient ischaemic attack in patients with atrial fibrillation, respectively [5]. Fourth, ventricular dyssynchrony is found frequently in patients with heart failure and cardiac resynchronization therapy improves mortality and decreases the need for hospitalization. In summary, there are critical clinical needs for robust and comprehensive regional CFA for more accurate diagnosis, risk stratification, and patient care management for patients with various conditions. It is thus highly desirable to make regional CFA more accessible, robust, and easier to perform.

Fig. 1. Cardiac cycle. (Top) Systole and diastole of ventricles and atria are offset. The ventricular systole consists of (1) an isovolumetric contraction phase and (2) an ejection phase. The ventricular systole is followed by relaxation and refill of both ventricles and atria, which consists of (3) isovolumetric relaxation, (4) rapid inflow, and (5) diastasis phases. The last one (6) is atrial systole (or “atrial kick”), which forces the final 25% of blood volume into the near-full ventricle. (Bottom) Typical dyssynchrony assessment. (a) Index values measured at two regions have no difference in time-to-peak duration, indicating that the two regions are in synchrony, while (b) there is a delay in timing, indicating dyssynchrony. The delay in timing (in ms) is interpreted as a severity of dyssynchrony and those studied in the literature ranged 10–40 ms. Top figures modified from https://my.bpc.edu/content/blgy224/CardiacSystem/CardiacSystem_print.html.

Multiple non-invasive imaging modalities can be used to perform CFA such as x-ray computed tomography, magnetic resonance imaging (MRI), speckle-tracking transthoracic echocardiogram, and single photon emission computed tomography. We believe, however, that no CFA methods currently available have a sufficient ability to detect and characterize regional CFA abnormality robustly in terms of the temporal/spatial resolution, repeatability, and the volume coverage. (1) The differences in time-to-peak strain and strain rate caused by dyssynchrony observed with MRI are 10–35 ms [6], while regions at risk have smaller differences (<10 ms). Thus, the temporal resolution needs to be at least better than 10 ms to detect early onset of dyssynchrony. (2) It is critical to have highly repeatable CFA index values to detect dyssynchrony robustly: For example, if time-to-peak strain and strain rate values measured at the
same region change from scan to scan, it decreases the ability to detect and characterize dyssynchrony reliably. If the CFA is performed on a two-dimensional (2D) plane, it does not capture through plane motion; and since the plane is manually selected, the CFA index value may vary depending on the choice of the plane. (3) It is critical to assess the regional CFA over the entire heart comprehensively because abnormalities may be focal.

Potential problems with various CFA methods are that these CFA methods rely on the accuracy and repeatability of images on which CFA is performed; however, to our knowledge neither the cardiac images nor CFA methods have been assessed using clinical images with an access to the ground truth. Therefore, the purposes of this study are to develop a digitally synthesized cardiac patient based on clinical data that serves as the ground truth and to assess the accuracy of CFA that uses cardiac x-ray CT images.

2. METHODS

We describe the synthesized patient development in Sec. 2.1 and the CFA assessment in Sec. 2.2.

2.1 “Zach phantom”

Clinical patient data allow neither for accessing the ground truth nor for repeating scans with different conditions. We have therefore developed an innovative scheme to conduct realistic patient studies on computers, which we call a synthesized patient study. The key ingredient is a digitally synthesized patient which we call “Zach” (Zero millisecond Adjustable Clinical Heart) phantom. We started with clinical patient images reconstructed over 20 phases over one heart beat. We then estimated the cardiac motion (or time-dependent non-rigid cardiac motion vector fields, MVFs) using image-based motion estimation method [7]. The motion estimation method models MVFs using cubic B-splines, which decreases the dimension of the problem from an unrealistically large size (i.e., $512^3 	imes 20 	imes 3$ for volume $\times$ time $\times$ 3 directions) to a manageable size (i.e., $32^3\times50\times3$).

The estimated MVFs were expected to be inaccurate due to (a) the limited temporal resolution of CT images, (b) “false dyssynchrony” we study in this work, and (c) the decreased magnitude of motion due to the image reconstruction process [8]. Thus the estimated MVFs were modified substantially and systematically as follows in order to agree with typical cardiac motion observed by echocardiogram. The systolic and diastolic motion were made synchronized intra-ventricularly, the magnitudes and speeds of motion were increased, and the time duration for systole was made shorter while that for diastole was made longer.

Two cardiologists (L.C. and H.A.) and three radiologists (S.L.Z., T.H., and E.K.F.) confirmed that the motion of LV and LA was very realistic and similar to that observed in echocardiography. To our knowledge, Zach phantom is the first realistic phantom specifically designed to assess the accuracy of CFA methods.

2.2 CT image-based CFA

We “scanned” the Zach phantom during a sinus rhythm. The heart beat was 60 beats per minute and the heart was warped using cubic B-spline interpolation for the time at which a cone-beam CT projection was calculated by forward projection. The simulated CT system had a gantry rotation speed of 280 ms per rotation, 1,000 projections per rotation, the full fan angle of 49.2 degrees, and 512 detector rows. The scan was repeated 4 times, with the scans started from 0°, 30°, 60°, and 90°. Most of the program was...
coded using compute unified device architecture (CUDA) language and performed on a graphics processing unit (GPU).

Fifty images over one heart beat were reconstructed using halfscan [9] cone-beam filtered backprojection [10] algorithm [11], which is essentially the same as cardiac algorithms implemented in commercial CT systems. The effective temporal resolution of images was 140 ms and the temporal increment of images was 20 ms.

Both the true and reconstructed Zach phantom images were converted to the short axis images at the middle of the LV for CFA. The wall thickness were measured at the following four segments—the anterior wall, the inter-ventricular septa, the inferior wall, and the lateral wall—with these images. The time-to-peak wall thickness was measured at each wall.

3. RESULTS

The true Zach phantom images at the end-diastole and end-systole were shown in Fig. 2. It can be seen, although it would have been much more clearly and convincingly seen with movies, that the cardiac motion of Zach phantom was much more dynamic and similar to those appeared in echocardiogram than the motion observed in reconstructed CT images.

![Fig. 2. Images of the true Zach phantom at the end-diastole at 0% R-R interval (top panel) and the end-systole at 30% R-R interval (bottom panel).](image-url)
Figure 3 presents the true and reconstructed images and the corresponding time-normalized wall thickness-curves of four segments. The reconstructed images (Fig. 3b) present motion artifacts and stiff motion of LV that is often observed in clinical cases [7, 12]. It can be seen that the true time-normalized wall thickness-curves measured at the four segments were in synchrony (Fig. 3c), while the measured curves appeared to be dyssynchrony (Fig. 3d). The conventional, image-based CT-CFA was applied and the standard deviation of time-to-peak thickness over 4 segments was found to be 62.2 ms while the true value was 19.1 ms. If the threshold of dyssynchrony detection were set at 25–35 ms, the test outcome of the image-based CT-CFA would be “dyssynchrony present” and a false positive. This is called false dyssynchrony and a major problem with image-based CT-CFA methods. It was also found that the time-to-peak thickness values were fluctuated over 4 scans by as much as 30.7 ms on average. When the fluctuation of time-to-peak values is as large as dyssynchrony we wish to detect, both the dyssynchrony detection performance and the repeatability of the CFA test is degraded significantly.

Fig. 3. (a,b) the short axis images at the middle of LV of the true Zach phantom (a) and reconstructed by ECG-gated method with the scan started from 0° (b). The wall thicknesses in the reconstructed images were deviated from the true thicknesses (arrows). (c,d) Normalized time-wall thickness-curves measured at 4 segments of the short axis image: the anterior wall (black), the inter-ventricular septa (magenta), the inferior wall (blue), and the lateral wall (red). Circles indicate the peak of the curve. The four segments were in synchrony with the true images (c) while they appeared to be dyssynchrony with the reconstructed images (d). The standard deviation of time-to-peak thickness measured by image-based CT-CFA was as large as 62.2 ms, indicating dyssynchrony, while the true value was 19.1 ms and in the normal range.

We have performed a simple simulation to demonstrate that the cause of the false dyssynchrony is indeed the cardiac image reconstruction method. A double-circle phantom (Fig. 4) is created where the inner circle changed the size during the scan while the outer circle was stationary. The phantom was then scanned and images were reconstructed using the halfscan algorithm. It can be seen that the boundary of the inner-circle had a spiral motion artifact because the location of the object boundaries was updated only when they were seen with cone-beam projections as the tangent (or parallel) to x-ray beams. Thus, the wall location is updated only every 180 degrees (or every 140 ms). Therefore, even though the motion of the all segments of the inner-circle were in synchrony, the update of segments is delayed by
\[ \theta \frac{180}{\pi} \times T_{\text{rot}}, \text{ where } \theta \text{ is the tangential angle for the segment and } T_{\text{rot}} \text{ denotes time per gantry rotation, and consequently, regional wall motions might appear to be dyssynchrony. Note also that, since the gantry angle and cardiac phase cannot be controlled, there will be a significant scan-to-scan variation in the level of false dyssynchrony. It would degrade the repeatability of the image-based CT-CFA exams.} \]

**Fig. 4.** The true (a) and reconstructed (b) images of the double-circle phantom.

### 4. DISCUSSION AND CONCLUSIONS

We have developed Zach phantom, which is a digitally synthesized cardiac patient, for the assessment of cardiac functional analyses. The study using Zach phantom revealed a major problem of image-based CT-CFA: false dyssynchrony. It is attributed to how cardiac images are reconstructed and how images are updated over cardiac phase. Thus, it is possible that image-based MR-CFA would suffer from the same problem. Nonetheless, this study demonstrated the value of Zach phantom which provides the access to the ground truth and clinically relevant images and motions. By the time of the conference, we will introduce regional abnormalities with different levels to Zach phantom and assess the detectability and repeatability of CFA exams.

### ACKNOWLEDGEMENT

This work was supported in part by NIH research grant No. R56 HL 125680 and Japan Government Grant MEXT/JSPS KAKENHI #26108004.

### REFERENCES


