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LETTER TO THE EDITOR

Letter to the Editor Regarding Paper "Automatic Computation of Left Ventricular Volume Changes over a Cardiac Cycle from Echocardiography Images by Nonlinear Dimensionality Reduction"

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Question: 1—Echocardiography images

Images were acquired from end of diastole to end of systole at different phases (7 phases) within a cardiac cycle by a Vivid 3 GE Health echocardiography machine. To obtain worthy images at denoted phases, it would be dependent to operator (for the best clinical examination). Of course, having assumed images not only were acquired from A4C and A2C but also from short-axis views. Short axis views have not been used at your papers, so some radial, circumferential and sample rotatory data would be missed.

Response: It is simply possible for us to record and analyze images of short-axis views. However, according to American Society of Echocardiography (ASE) [1, 2], in the modified Simpson's rule which is a method for LV volume computation from 2-D echocardiography images, it suffices to acquire apical two and four chamber views (A4C, A2C) for left ventricular (LV) volume computation.

Question: 2—Observed data y_i's

Echocardiography images paly role of observed data and they are symbolized by y_i's. there is a sequence of observed data $y_1, y_2,\ldots,y_N$. N is the number of obtained images. In fact we have made a chain of displacement, rotation and pure strain or nonrigid transformation (deformation) by these observed data that is started from y_1 and is ended up to y_N.

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This chain has some conceptual interpretations of the elasticity of the global left ventricular motion/function and the regional LV fiber arrangement/movement.

Response: Yes, it is correct.

Question: 3—Embed observed data to a high dimensional space

Response: Yes, it is correct.

Question: 4—Image processing on y_i's and geodesic distance between y_i's

Observed data $y_1, y_2,\ldots,y_N$ are embed to a meshed surface sized number of pixels of an image. Translation, rotation and pure deformation of $y_1, y_2,\ldots,y_N$ are occurred/and studied at this surface utilizing the mathematical elasticity theory. A distance metric is defined that computes distances between observed points. Medical interpretations of observed points over the time should be checked/and stated clearly at your manuscripts. Images are not usual images but also are images from the left ventricle. Motion (displacement and velocity), deformation (strain and strain rate) and torsion of each myocardial sample have to be extracted during a cardiac cycle in the mentioned surface. These are used on the creation of graph G referred to their papers.

Response: In this stage, we have just computed the distance between the two images in a cardiac cycle using non-rigid image registration regardless of relationship between images over the time. Therefore by this method, the motion and longitudinal deformation (short-axis views are needed to get for radial and circumferential deformations) of LV myocardium between all of two images in a cardiac cycle are extracted (for example, between end systole image and end diastole image, etc.). Then, in other stage of our method (calculation of the matrix of pairwise geodesic distance and apply multidimensional scaling on the resulting geodesic distance matrix to construct the low dimensional data points x_i), motion and longitudinal deformation of LV myocardium during a cardiac cycle are extracted.

Question: 5—An Isomap f

The main tool at this method is the function "f" which is an isometric map [2, 3]. I will be interested to know the structure/formula or relationship of this isometric function which has most probably a lot of practical information of the left ventricular function and structure. I mean, how we can get a good representation of such a this function "f" for heart science study? Is it "f" known as an algebraic function? What information has been coded to fibers (f^{-1}) of this isometric function "f"?

Response: Isomap algorithm is one of the most popular sets of nonlinear dimensionality reduction (NLDR) algorithms. This algorithm attempts to extract low-dimensional data points from input points in a high-dimensional space in such a way that pairwise geodesic distances (the distance between two points measured over the manifold) are preserved. So that nearby and far points in high-dimensional space map to nearby and far points in low-dimensional space. This method is frequently used for visualization of medial image set. Detail of this method is described in Tenenbaum et al. and Borg et al. [3, 4]. It should be noted that we do not change the structure or formula of isomap algorithm. We only define a new image distance function based on image registration in calculation of geodesic distance between $y_i^{\prime}$s in isomap algorithm. With this modification, Isomap algorithm is specified for assessment of the left ventricular function and structure. However, precise mathematical descriptions of f and (f^{-1}) applied to echocardiography images and using the other NLDR algorithms need further researches in the following of this article.

Question: 6—A reconstructed curve on a 2D manifold space & hidden data $x_i^{\prime}$s; $f(y_i) = x_i$

Isometric function results in a reconstructive curve crossing from hidden data ($x_i^{\prime}$s) in a surface. It's natural that some information (maybe clinical information) would betransferred to these hidden points like the curve of LV volume changes and so on and so on. A main question is: what are these new points $x_i^{\prime}$s exactly (medically point of view)? What the other data has been come out from these hidden points? I think all of these questions back to gain a good understanding of isometric function "f".

Response: These points $x_i^{\prime}$s will probably enable physicians to diagnose and follow up many cardiac structures and functions that also open doors to much more research at imaging cardiology in the future.

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