A Novel Analysis Algorithm for Potential Quantitative Assessment of Myocardial Computed Tomography Perfusion

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Rationale and Objectives: Cardiac computed tomography (CT) has emerged as a robust modality for imaging coronary stenosis and has recently been used to evaluate myocardial abnormalities such as ischemic perfusion defects and infarction. We developed a new image analysis algorithm for the semiautomatic and quantitative assessment of myocardial perfusion by CT.

Materials and Methods: The algorithm semiautomatically segments two-dimensional short-axis reformatted DICOM images of the left ventricle into regions of interest (ROIs) in accordance with American Heart Association (AHA) standards and is capable of creating nine further ROI subsegments. This includes separate endocardial, mid-ventricle, and epicardial layers. Image intensity values (Hounsfield unit) and relative myocardial thickness are quantitatively reported for each ROI and segment.

Results: The algorithm allows comparison of the HU values at the same ROI locations between rest and stress. The reproducibility is very good; ICC 0.89 for rest images, 0.83 for stress images. The mean time for generating ROIs for the entire heart was 11 minutes versus 22 minutes for manual tracing.

Conclusion: The algorithm reports parameters relevant for evaluation of stress perfusion CT studies and will allow more accurate and reproducible analysis in cardiac CT research.

Key Words: Computed tomography; image analysis; cardiac imaging; algorithm; myocardial perfusion.

Coronary artery disease (CAD) remains the leading cause of death in the developed world (1). Coronary atherosclerotic plaque progressively narrows the coronary arteries, potentially leading to impaired myocardial perfusion, myocardial dysfunction, and subsequent myocardial infarction. The investigation of CAD often involves the functional assessment of stenosis severity by means of noninvasive imaging stress tests using nuclear scintigraphy, echocardiography, or cardiac magnetic resonance imaging (MRI). A flow-limiting stenosis in a coronary artery usually results in a relative deficit in myocardial perfusion (via first-pass imaging nuclear radiotracers or intravenous contrast boluses) or systolic function (wall motion) in the supplied myocardial territory between the stress and rest imaging. Myocardial stress computed tomography (CT) perfusion (CTP) is a recently described technique that uses cardiac CT to perform stress and rest first-pass perfusion imaging, simultaneously allowing imaging of anatomical coronary stenosis as well as resultant perfusion abnormalities (2,3).

The evaluation of left ventricular function and myocardial perfusion defects by noninvasive imaging modalities has largely followed the American Heart Association (AHA) 17 segment model of the heart (4). Determination of myocardial perfusion defects on most imaging modalities including CT are usually performed by visual comparison of the relative intensity of the myocardium between rest and stress phases. Automatic quantitative processes that compare the rest and stress phases on a segmental basis could potentially be more efficient, accurate, and reproducible in determining areas of ischemia. Such software has been reported in nuclear myocardial perfusion imaging, cardiac MRI, and, in a proprietary algorithm, in CTP (3,5–7).

A methodology to automate and quantify the analysis of CTP images is clearly needed. A widely available, automated software would allow the medical community to define what CT intensity values (Hounsfield units [HU]) constitute areas

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of myocardial infarction on rest scans and myocardial ischemia (via relative difference in HU values between rest and stress scans). Currently, one must manually draw regions of interest (ROI) in the exact corresponding locations of both rest and stress scans (Fig 1). This highly operator-dependent method is not uniform, is time-consuming, and is not reproducible. We therefore sought to develop a semiautomated algorithm to quantitate myocardial density and relative thickness in the standard AHA segments as well as nine further subsegments that allow for transmural perfusion ratio and subsegmental analyses.

MATERIALS AND METHODS

Cardiac imaging was conducted using a dual-source clinical CT system (Definition, Siemens Medical System, Forchheim, Germany) at rest and during pharmacologic stress. Double-oblique standard short-axis DICOM images of the heart were generated using a standard three-dimensional multiplanar reformatting workstation (Syngo Leonardo, Siemens Medical System). Three short-axis slices corresponding to the level of the base, mid-ventricle, and apical segments of each heart were selected for analysis.

An algorithm for automatic segmentation of DICOM images of the heart was written using commercially available software (Matlab v7.12 [R2011a], MathWorks, Natick, MA). The algorithm is intended to be operated by a physician with appropriate training in cardiac imaging (i.e., radiologist or cardiologist). The algorithm requires three user inputs to generate ROIs within the myocardium: tracing the endocardial and epicardial borders as well as marking the right ventricle insertion points. These essentially define the boundaries of myocardial tissue, whereas the RV insertion points are referenced in the AHA 17-segment model to demarcate the septal wall from the anterior and inferior walls. The myocardial borders are traced by selecting points on the short-axis image via an interactive user interface. User-defined points establish a polygonal representation of the myocardium, and the accuracy of this geometry is positively correlated with the number of points selected by the user. A smoothing function is applied to the geometry to lessen rigidity and returns a natural cubic spline curve passing through the initially selected points. Once inner and outer myocardial boundaries are computed, the algorithm computes the centroid of the inner myocardial boundary, shown in Figure 2.

The short-axis DICOM images produced by CT workstation software can often be "rotated" clockwise with respect to the horizontal orientation of the heart. To achieve a standardized horizontal orientation, a line should be defined that is perpendicular to the interventricular septum. By using the line that joins the right ventricle insertion points as a fixed reference, a perpendicular line that defines the horizon can be established (4). This horizontal line divides the lateral and septal walls into anterolateral/septal and inferolateral/septal, respectively, as defined by the AHA model (4). The user defines right ventricle insertion points

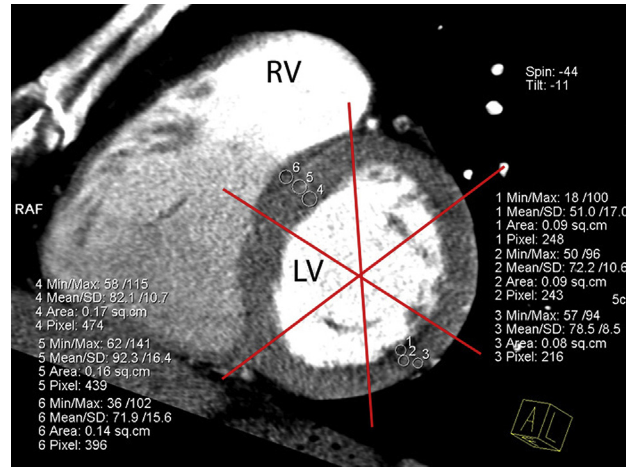

Figure 1. Basal short-axis slice of the heart showing the standard American Heart Association (AHA) segmentation (*red lines*). Manually drawn regions of interest (ROIs, numbered 1–6) are positioned carefully with the results displayed. There is a perfusion defect of the endocardial inferolateral wall (ROI #1) with a Hounsfield unit (HU) of 51. The epicardium is relatively normal (ROI #3) with an HU of 78. However, there is potential for error because the ROI may not be drawn in the same position between rest and stress phases. Similarly, another user will probably place ROIs in slightly different positions within the same AHA segment, which may yield a vastly different HU. LV, left ventricle; RV, right ventricle. (Color version of figure is available online).

by selecting two points on the short-axis image, shown in Figure 2. The algorithm computes the line that connects the right ventricle insertion points (the interventricular septum). The horizontal orientation line, shown in Figure 2, is then computed as the line that passes through the centroid and has a slope perpendicular to that of the interventricular septum. The horizontal orientation line acts as the virtual zero-degree starting point for subsequent algorithm operations and allows for the establishment of ROIs in the standard AHA myocardial segments.

From the centroid, lines are projected radially at 1° increments (k), beginning at the previously established "horizontal orientation" line ($k = 1$). Image resolution has no effect on the incremental step (1°) of radial projections to ensure consistency of ROI generation. For every 1° increment, the points at which the line intersects the two concentric user-defined polygons are computed, represented as a_k and b_k for the k-th line in Figure 2. The distance (D_k) between these two points $(\overrightarrow{a_k}, \overrightarrow{b_k})$, the myocardial thickness, is then calculated as:

$$D_k = \left|\overrightarrow{b_k} - \overrightarrow{a_k}\right|, \quad for\ k = 1, \ldots, n \tag{1}$$

where n is the number of angles. To establish the endocardial, mid-ventricular, and epicardial layers, the myocardial thickness is divided into three equal layers having thickness of $D_k/3$. Points establishing the boundary of these layers along the k-th line is calculated as:

$$\overrightarrow{L}_{i,k} = \hat{a}_k\left[|\overrightarrow{a}_k| + \frac{i}{3}D_k\right], \quad for\ i = 0, 1, 2, 3 \tag{2}$$