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Myocardial perfusion analysis in cardiac computed tomography angiographic images at rest

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ABSTRACT

Cardiac computed tomography angiography (CTA) is a non-invasive method for anatomic evaluation of coronary artery stenoses. However, CTA is prone to artifacts that reduce the diagnostic accuracy to identify stenoses. Further, CTA does not allow for determination of the physiologic significance of the visualized stenoses. In this paper, we propose a new system to determine the physiologic manifestation of coronary stenoses by assessment of myocardial perfusion from typically acquired CTA images at rest. As a first step, we develop an automated segmentation method to delineate the left ventricle. Both endocardium and epicardium are compactly modeled with subdivision surfaces and coupled by explicit thickness representation. After initialization with five anatomical landmarks, the model is adapted to a target image by deformation increments including control vertex displacements and thickness variations guided by trained AdaBoost classifiers, and regularized by a prior of deformation increments from principal component analysis (PCA). The evaluation using a 5-fold cross-validation demonstrates the overall segmentation error to be 1.00 ± 0.39 mm for endocardium and 1.06 ± 0.43 mm for epicardium, with a boundary contour alignment error of 2.79 ± 0.52. Based on our LV model, two types of myocardial perfusion analyzes have been performed. One is a perfusion network analysis, which explores the correlation (as network edges) pattern of perfusion between all pairs of myocardial segments (as network nodes) defined in AHA 17-segment model. We find perfusion network display different patterns in the normal and disease groups, as divided by whether significant coronary stenosis is present in quantitative coronary angiography (QCA). The other analysis is a clinical validation assessment of the ability of the developed algorithm to predict whether a patient has significant coronary stenosis when referenced to an invasive QCA ground truth standard. By training three machine learning techniques using three features of normalized perfusion intensity, transmural perfusion ratio, and myocardial wall thickness, we demonstrate AdaBoost to be slightly better than Naive Bayes and Random Forest by the area under receiver operating characteristics (ROC) curve. For the AdaBoost algorithm, an optimal cut-point reveals an accuracy of 0.70, with sensitivity and specificity of 0.79 and 0.64, respectively. Our study shows perfusion analysis from CTA images acquired at rest is useful for providing physiologic information in diagnosis of obstructive coronary artery stenoses.

1. Introduction

Despite improvements in therapies targeted at reducing disease burden, coronary artery disease (CAD) continues to afflict >16 million US adults, accounting for more than 1/3 of all deaths and responsible for ~1.2 million hospitalizations annually (Lloyd-Jones et al., 2010). Numerous non-invasive physiologic imaging tests exist for assessment of CAD, including echocardiography, magnetic resonance imaging (MRI) and myocardial perfusion scintigraphy by either single photon emission computed tomography (SPECT) or positron emission tomography (PET) (Berman et al., 2006; Gershlick et al., 2007). These modalities identify stress-induced wall motion abnormalities or regional myocardial perfusion defects to determine individuals who may have severe coronary stenoses. Recently, computed tomography (CT) of >64-detector rows has become a promising non-invasive option for coronary angiography, now allowing for acquiring virtually motion-free images at isotropic spatial resolution of 0.5 mm in a few seconds (Min et al., 2010).

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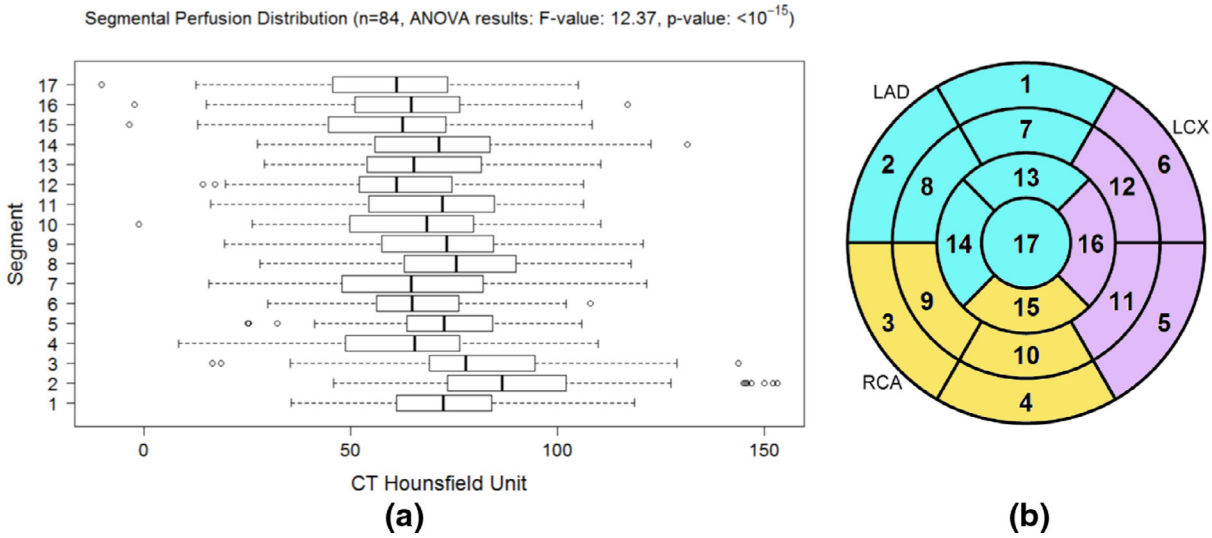

Fig. 1. (a) The difference of segmental myocardial perfusion distribution in normal patients (without 50% coronary stenosis defined by QCA). With correction for multiple comparison, the pairs with significant differences (p-value$<$0.005) are 2–17, 2–15, 2–12, 2–4, 2–16, 2–7, 2–13, 2–10, 2–6, 3–17, 3–15, 2–11, 2–14, 2–9, 3–12, 2–5, 8–17, 8–15, 2–1, 3–4, 3–16, 8–12, 3–7, 1–17, 1–15, 2–8, 5–17, 3–13, 5–15, 3–10, 3–6, 8–4, 8–16, 9–17, 9–15, 14–17, 14–15, 1–12, 5–12. (b) AHA 17-segment model with territory assigned to left anterior descending (LAD), left circumflex (LCX), and right coronary (RCA) arteries.

Compared to an invasive reference standard, coronary CT angiography (CTA) demonstrates excellent diagnostic performance in stenosis detection (Budoff et al., 2008). Yet CTA is prone to artifacts—including those from motion, beam hardening and mis-registration—which reduce the diagnostic accuracy of CTA. Further, CTA is prone to overestimation of stenosis severity and more recent data has suggested that an anatomic stenosis visualized on CTA is not necessarily associated with interruption of coronary blood flow. Quantitative coronary angiography (QCA) is the most common clinical reference standard to determine the diameter percentage of luminal stenosis, which is performed by computer-assisted calculation of the ratio of the minimal lumen diameter of a stenosis to the reference vessel diameter on conventional X-ray angiographic images (Reiber et al., 1984). Fractional flow reserve (FFR) is an emerging reference standard to determine if a stenosis significantly limits the blood flow, which is defined by the ratio of maximal blood flow distal to a stenosis to normal maximal flow in the same vessel (Pijls et al., 1996). However, both tests require invasive insertion of a catheter in the artery and thus should only be used when necessary. To identify functionally significant stenoses non-invasively, new computational and imaging methods have been developed. For example, a technique to compute FFR by computational fluid dynamics has been shown to improve diagnostic performance over using CTA alone (Taylor et al., 2013), yet it requires lengthy processing times and is unable to reveal abnormal myocardial perfusion caused by microvascular diseases. Stress CT perfusion imaging shows great promise in this area but requires additional imaging sessions thus leads to increased radiation exposure (George et al., 2006).

No previous work has been performed to determine the diagnostic value of myocardial perfusion quantified using CTA alone acquired at rest. This is desirable if myocardial perfusion noninvasively evaluated at rest provides useful information about the severity of coronary artery lesions while requiring no additional imaging. In this regard, automated and quantitative analysis of myocardial perfusion is ideal to maximize diagnostic accuracy, reduce burden of manual interpretations and enhance objectivity and reproducibility of such analyses. Previous CT perfusion analyses have been primarily carried out manually (Mehra et al., 2011), while sometimes assisted by semi-automated tools (George et al., 2006, 2009; Kachenoura et al., 2009). Automatic and fast methods to quantify perfusion abnormalities have been lacking. Precise delineation of endocardium and epicardium of the left ventricle (LV) is mandatory for accurate perfusion analysis because false detection may occur in intraventricular or pericardial regions with low or high attenuation densities. In contrast, all previous studies followed straightforward approaches to define presence and severity of a perfusion deficit, either by visual inspection with the help of a chosen window level or quantification using a defined threshold. However, the distribution of CT perfusion intensity varies significantly in different regions of the myocardium within a group of normal subjects (shown in Fig. 1). Because of low contrast, it is generally difficult to reliably distinguish a hypoattenuated area from neighboring normal regions. In addition, several confounding factors—including noise or other artifacts—can resemble or hide perfusion abnormalities. Beam hardening is one of the most common ones, and causes hypoattenuated shadowing effects within the myocardium. Therefore, the use of a global window level or threshold is indeed questionable. Furthermore, no consensus has been presently established as the optimal variable to characterize perfusion defects, which leads to multiple possibilities.

In this study, we propose a new system to analyze myocardial perfusion using CTA alone acquired at a rest state and assess its diagnostic value to identify severe coronary lesions that cause myocardial perfusion deficits. Our myocardial perfusion analysis is based on the contrast enhancement information in CTA images, instead of absolute myocardial perfusion (in ml/min/g), which is not available in a single resting scan. From CTA images, we develop a compact representation of LV by subdivision surfaces, which ensure the smoothness even with small number of vertices. The thickness of the myocardium is explicitly modeled in this representation, enabling the coupling between endocardial and epicardial layers. We then divide the myocardium automatically into American Heart Association (AHA) 17-segment model (Cerqueira, 2002) using mesh parameterization. We perform two independent studies to assess the usefulness of quantifying myocardial perfusion from different perspectives. Using a new concept of perfusion network analysis, we measure the degree of correlations of perfusion among different segments in order to assess the heterogeneous perfusion network structure exhibiting in normal subjects, as well as the disturbed perfusion network in the diseased subjects. Finally, normalized perfusion intensity, transmural perfusion ratio, and myocardial wall thickness are calculated in all segments as features, and the ability to predict the existence or