Original Investigation

Measurement Accuracy of Atherosclerotic Plaque Structure on CT Using Phantoms to Establish Ground Truth

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Rationale and Objectives: The purpose of this study was to characterize analytic performance of software-aided arterial vessel structure measurements across a range of scanner settings for computed tomography angiography where ground truth is known. We characterized performance for measurands that may be efficiently measured for clinical cases without use of software, as well as those that may be done manually but which is generally not done due to the effort level required unless software is employed.

Materials and Methods: Four measurands (lumen area, stenosis, wall area, wall thickness) were evaluated using tissue-mimicking phantoms to estimate bias, heteroscedasticity, and limits of quantitation both pooled across scanner settings and individually for eight different settings. Reproducibility across scanner settings was also estimated.

Results: Measurements of lumen area have a near constant bias of +1.3 mm for measurements ranging from 3 mm^2 to 40 mm^2; stenosis bias is +7% across a 30%–70% range; wall area bias is +14% across a 50–450 mm^2 range; and wall thickness bias is +1.2 mm across a 3–9 mm range. All measurements possess properties that make them suitable for measuring longitudinal change. Lumen area demonstrates the most sensitivity to scanner settings (bias from as low as +.1 mm to as high as +2.7 mm); wall thickness demonstrates negligible sensitivity.

Conclusions: Variability across scanner settings for lumen measurands was generally higher than bias for a given setting. The converse was true for the wall measurands, where variability due to scanner settings was very low. Both bias and variability due to scanner settings of vessel structure were within clinically useful levels.

Key Words: CTA; atherosclerosis; plaque imaging; stenosis.

INTRODUCTION

Assessment of atherosclerotic plaque is an essential diagnostic and treatment-planning tool. Extensive efforts have begun to provide quantitative information to the physician in assessing an individual patient's immediate cardiovascular risk. Sophisticated and powerful, post-processing of computed tomography (CT) and magnetic resonance imaging has been proposed (1–5), and this technology offers noninvasive alternatives to invasive catheterization procedures.

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To evaluate an image-based analysis, performance should be compared to ground truth evaluated across a spectrum of disease and imaging protocols routinely used in clinical practice. In this work, we use synthetic vessel phantoms with readily measured ground truth values. The phantoms are fabricated using vessel tissue-mimicking material, as the true vessel wall thickness value in excised tissue would be difficult to ascertain, and bias is not expected to differ with clinical data. Our group has also conducted reader variability studies using clinical data to study precision based on the assumption that patient anatomy variability contributes significantly to the variability in the measurements. Our use of phantoms to estimate bias, and clinical data to estimate variability, is based on this rationale.

MATERIALS AND METHODS

The bias and precision of CT angiography (CTA)-derived arterial vessel structure measurements were estimated using a set of precision-machined phantoms where ground truth measurements are assessed by a handheld micrometer. The phantoms were fabricated to specifications to mimic appropriate

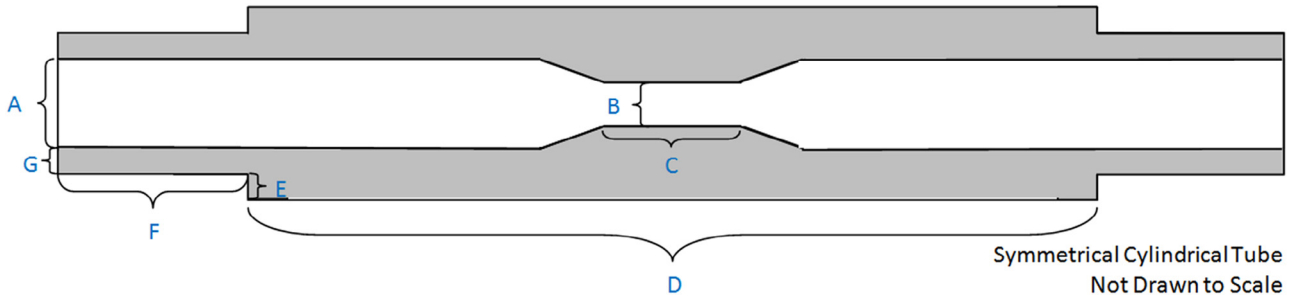

Figure 1. Physical geometry of vascular phantoms. Dimensions designated by the letters A–G are used in calculations of specific ground truth values, as indicated in the Results section, where A is the reference lumen, B is the stenotic lumen, C is the length of the stenosis, D is the length over which the wall is thickest, E is the difference between where the wall is thickest and where it is thinnest, F is the length over which the wall is thinnest, and G is the thinnest wall. Each phantom has different dimensions so as to coincide with typical arterial presentations.

CT characteristics, in sizes that represented a wide clinical spectrum of vessel sizes. The phantoms used in this study were designed for the validation of CTA images of peripheral and central vessels.

The vascular phantom set consists of hollow Noryl tubes with a stenotic region in the center of the length. The density of Noryl is 1.06 g/mL, which was selected to mimic the density of vessel wall in CT analysis, and dimensions were chosen to represent a range of human arteries (see Fig 1). The phantoms used in this study were manufactured at Trans Form Plastics Inc. (Danvers, MA), one to represent the aorta, two to represent femoral arteries, three to represent carotid arteries, and one to represent vertebral arteries.

The phantoms were filled with contrast media used in routine CTA and scanned in a range of scanner settings representative of current clinical practice. Statistical measures of bias were estimated from these data.

Imaging

For the scans, the phantoms were filled with diluted contrast agent (Omnipaque, GE Healthcare, Chicago, IL) between 10 and 12 mg iodine/mL to achieve the same contrast between vessel wall and lumen found in patient CTA scans at 100–120 kVp (based on published relationship of iodine concentration vs Hounsfield units for 80–120 kVp) (6). The phantoms were suspended in a plastic cage, submerged in a box of vegetable oil (to emulate surrounding fat), and scanned simultaneously.

Imaging was performed across image acquisition protocols representative of clinical practice using a Siemens SOMATOM Definition Flash at the Brigham and Women's Hospital (Boston, MA), and 120 and 100 kVp, radiation exposure levels of 5–15 mGy, and various reconstruction kernels were used. Apart from parameters that were varied in Tables 1–4, the scans also had a slice thickness of 0.75 mm, single collimation width of 0.6 mm, total collimation width of 38.4 mm, spiral pitch factor of 0.8, and pixel spacing of 0.64 mm.

Target Definition and Analysis

The eight image series described in Tables 1–4 were loaded into dedicated software (vascuCAP, Elucid Bioimaging Inc., Wenham, MA) for analysis. Based on user initialization by clicking on relevant points on the image, the software generates the path lines and initial lumen and vessel segmentations. Editing, using built-in CTA-derived tools of the segmentations generated by the software, was used to remove or mitigate artifacts (eg, bubbles) in the phantom.

Target Initialization

For each vessel, a sequence of points along each vessel centerline was manually created by clicking on a volume rendering of the CTA. Three-dimensional (3D) coordinates and an initial lumen radius were estimated at each point by ray-casting.

Lumen Segmentation

To avoid false-positive inclusion of calcified regions of plaque as lumen, after the software attenuates detected regions of calcium, the segmentation of the lumen is performed by an algorithm that uses a numerical analysis of surfaces and shapes referred to as a level set model, which allows numerical computations involving curves and surfaces on a fixed Cartesian grid and using a threshold determined as the Otsu threshold of the region surrounding the target initialization variable radius tube (7,8).

Wall Segmentation

The outer wall of the vessel (serosa/adventitia) is segmented using a geodesic active contour level set evolution, initialized with the union of lumen segmentation after min/max curvature evolution and the target initialization centerline expanded by 1.2 mm to account for the wall at areas of complete stenosis (9,10). The level set edge potential function captures outer wall image edges using distance to Canny edge detections transformed through a logistic sigmoid function (11).

Segmentation Editing

Readers are provided tools to manually edit the lumen or the wall segmentation. For each mode, the results are visualized in real time in both 2D and 3D views. In "Draw Mode," the mouse cursor becomes a variable radius 3D sphere "paintbrush" that can either add or subtract regions.

Figure 2 depicts examples of phantoms from our study.