Semi-automated segmentation of carotid artery total plaque volume from three dimensional ultrasound carotid imaging

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ABSTRACT

Carotid artery total plaque volume (TPV) is a three-dimensional (3D) ultrasound (US) imaging measurement of carotid atherosclerosis, providing a direct non-invasive and regional estimation of atherosclerotic plaque volume – the direct determinant of carotid stenosis and ischemic stroke. While 3DUS measurements of TPV provide the potential to monitor plaque in individual patients and in populations enrolled in clinical trials, until now, such measurements have been performed manually which is laborious, time-consuming and prone to intra-observer and inter-observer variability. To address this critical translational limitation, here we describe the development and application of a semi-automated 3DUS plaque volume measurement. This semi-automated TPV measurement incorporates three user-selected boundaries in two views of the 3DUS volume to generate a geometric approximation of TPV for each plaque measured. We compared semi-automated repeated measurements to manual segmentation of 22 individual plaques ranging in volume from 2mm^3 to 151mm^3. Mean plaque volume was 43±40mm^3 for semi-automated and 48±46mm^3 for manual measurements and these were not significantly different (p=0.60). Mean coefficient of variation (CV) was 12.0±5.1% for the semi-automated measurements.

Keywords: 3D ultrasound, carotid atherosclerosis, Total Plaque Volume, segmentation, semi-automated, validation

1. DESCRIPTION OF PURPOSE

Carotid atherosclerosis progresses from an initial thickening of the intima and media layers of the arterial wall and manifests as complex plaque lesions within the arterial wall and eventual stenosis that can potentially result in ischemic stroke[1]. In order to monitor plaque development in patients at risk and to track the effects of new therapies direct, non-invasive and local measurements of plaque are required[2-4]. Ultrasound (US) imaging of the carotid arteries provides a noninvasive way to monitor the progression and regression of atherosclerosis[5,6]. Although several 3DUS imaging phenotypes have been developed[7], there is currently no way to generate reproducible, direct measurements of plaque in real time at the bedside and this is critical for translation of these measurements to clinical use and clinical trials. Total Plaque Area (TPA) is a 2D estimation of plaque in the longitudinal plane[8]. While this cross-sectional area provides a rapid estimation of plaque area, measurement variability is inherently high because image acquisition depends on repeatedly selecting the same representative longitudinal view for each new measurement. In contrast, Total Plaque Volume (TPV) provides a plaque estimation that encompasses the complex geometries and morphologies associated with plaque[9,10] but manual segmentation is laborious, time-intensive and has high intra- and inter-observer variability. Accordingly, our objective was to generate a semi-automated method that can be used in real time for quantifying plaque volume with precision similar to manual methods. While TPA (measured in the longitudinal view) and manual TPV (measured in the axial view) are measured in a single plane only, our aim was to generate a method that incorporated information from both the longitudinal and axial views, maximizing the use of the 3DUS information to approximate TPV. In other words, we aimed to incorporate the longitudinal view - ideal for rapidly identifying the ends of a plaque and the cross-sectional axial view measurements – ideal for providing information on plaque morphology in our semi-automated approach.

2. METHODS

2.1 Imaging

3DUS images of the carotid arteries of ten subjects with carotid stenosis greater than 60% (defined by carotid Doppler flow velocities) were evaluated for the measurement of 22 individual plaques in the common and internal carotid arteries. Subjects recruited from The Premature Atherosclerosis Clinic (London Health Sciences Centre, London,

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Ontario, Canada) provided written informed consent to the protocol approved by the local ethics review board. Ultrasound images were acquired using a Philips ATL HDI 5000 machine by translating an 8.5MHz ultrasound transducer (L12-5, 50mm, Philips, Bothell, WA, USA) along the lateral side of the neck. Parallel 2D images separated by 0.15mm were acquired at a uniform speed of 3mm/s for 4.0cm along the neck without cardiac gating. After completing acquisition, all 2D images were reconstructed into a 3D volume. Since the position and orientation of each 2D image was known, voxel based reconstruction allowed for each 2D image to be transformed within the 3D volume as previously described[11].

2.2 Manual segmentation

We used methods previously described for the manual measurement of TPV (Fenster et al. 2006). Briefly, the user identified the bifurcation of the common carotid artery and selected a parallel axis for segmentation in the 3DUS volume. An Intuos3 professional pen tablet (Wacom Technology Corporation, Vancouver, WA, USA) was used to manually segment plaque boundaries. Initialization of the measurement occurred in the axial plane whereby the end of the plaque was identified and a boundary was segmented to generate a cross-sectional area. Plaque segmentation along the parallel axis at 1mm inter-slice distances was performed until the entire plaque was measured. Cross-sectional areas were multiplied by the inter-slice distance to generate volumes for individual plaques. For each subject, TPV was generated as the sum of all plaques measured on the left and right carotid artery. Manual measurements were timed with a stopwatch initiated after setting the bifurcation point.

2.3 Semi-automated segmentation: Development and application

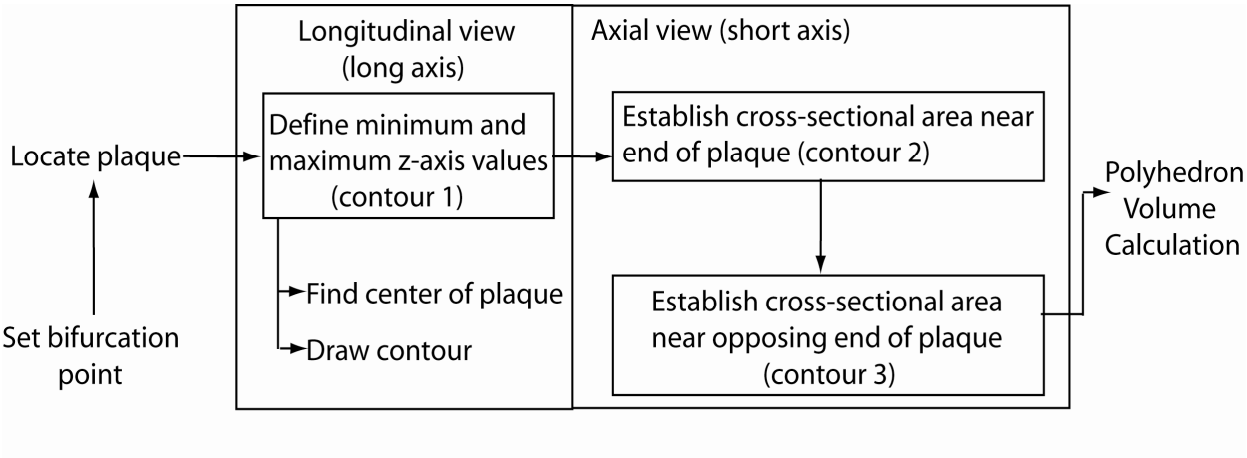

Figure 1. 3DUS TPV measurement algorithm pipeline.

The algorithm that we developed to measure TPV semi-automatically takes advantage of the fact that in a 3DUS volume, both the longitudinal and axial views provide a way to estimate the ends of each plaque and the morphology across each individual plaque. The algorithm pipeline is summarized in Figure 1. The first step involved the observer using the 3DUS volume in the longitudinal and axial planes to identify the estimated ends of a single plaque visibly obvious as echogenic plaque. The second step involved identification of the estimated midpoint of the plaque in the longitudinal plane and a contour generated from this midpoint (Contour 1, C1). From C1, the minimum and maximum values along the z-axis were identified by the algorithm as the end points of the plaque. To assist with geometric approximation of the entire plaque volume, two additional boundaries in the longitudinal view were generated by the user (Contour 2, C2 and Contour 3, C3). Finally, the maximum and minimum z values (end points) were automatically joined to 20 points along C2 and C3.

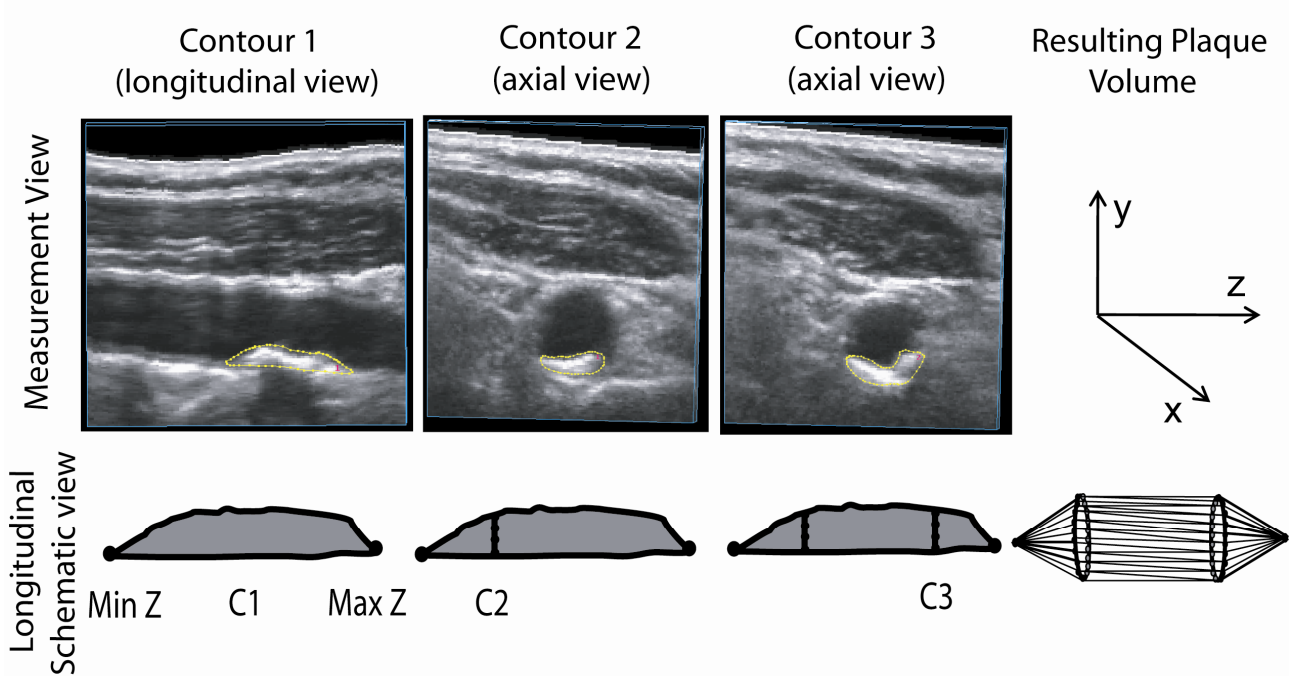

Figure 2. User input for semi-automated TPV measurement. In the longitudinal view (and with assistance from the axial view, not shown) the user identifies the maximum and minimum z-values representing the end points of the plaque (Min Z and Max Z). The user identifies the mid-point of the plaque (C1) and finally C2 and C3 are identified and generated in the axial view. Uniform plaque geometry between C2 and C3 is assumed and a final volume is generated.

The points along C2 and C3 were used as representative vertices (P_{Fj}) and linearly interpolated to generate surface areas. The resulting geometric approximation was a polyhedron with several surface areas (A_i) where m faces (F_j) labeled $F_0,\ldots F_{m-1}$ were used to compute a volume[12] as shown in equation 1 below. The time to perform measurements was measured automatically using a timer that was built into the measurement software. The user activated the timer prior to beginning the measurement and stopped timing after the algorithm generated a plaque volume.

$$V = \frac{1}{3}\sum_{j=0}^{m-1} P_{Fj} \bullet A_j = \frac{1}{6}\sum_{j=0}^{m-1} P_{Fj} \bullet (2A_j) \qquad (1)$$

2.4 Evaluation

As previously described, we defined TPV as the sum of all plaque volumes within a single subject including both common and internal carotid arteries. Typically, left and right sides were summed to generate a cumulative TPV for each subject. However, for the analysis presented here, each individual plaque was evaluated independently for comparison of manual and semi-automated methods. Semi-automated measurements for all plaques were repeated five times by a single observer who was blinded to study subject identity and for each segmentation round, the order of subjects and plaques was randomized. Semi-automated measurements were compared to manual segmentations using linear regression and Bland Altman Analysis. For an estimation of intra-observer variability, the coefficient of variation (CV) for each plaque was generated (standard deviation of five independent measurements divided by the mean) based on five repeated semi-automated measurements.

3. RESULTS

A single observer identified and measured 22 atherosclerotic plaques within 1.5cm of the carotid bifurcation (1.0cm distal to bifurcation in common carotid artery and 0.5cm proximal to bifurcation in internal carotid artery) in 10 different subject images (4 left carotid artery and 6 right carotid artery). Figure 3 provides images of representative segmentation contours generated for manual (red) and semi-automated (yellow) measurement methods in the axial (A) and longitudinal (B) views. The mean TPV measured using the semi-automated measurement 43±40mm^3 was not significantly different than the mean TPV obtained using manual measurements 48±46mm^3 ($p = 0.60$). Table 1 shows manual and semi-automated mean plaque volume and repeated measures CV for the semi-automated measurements.

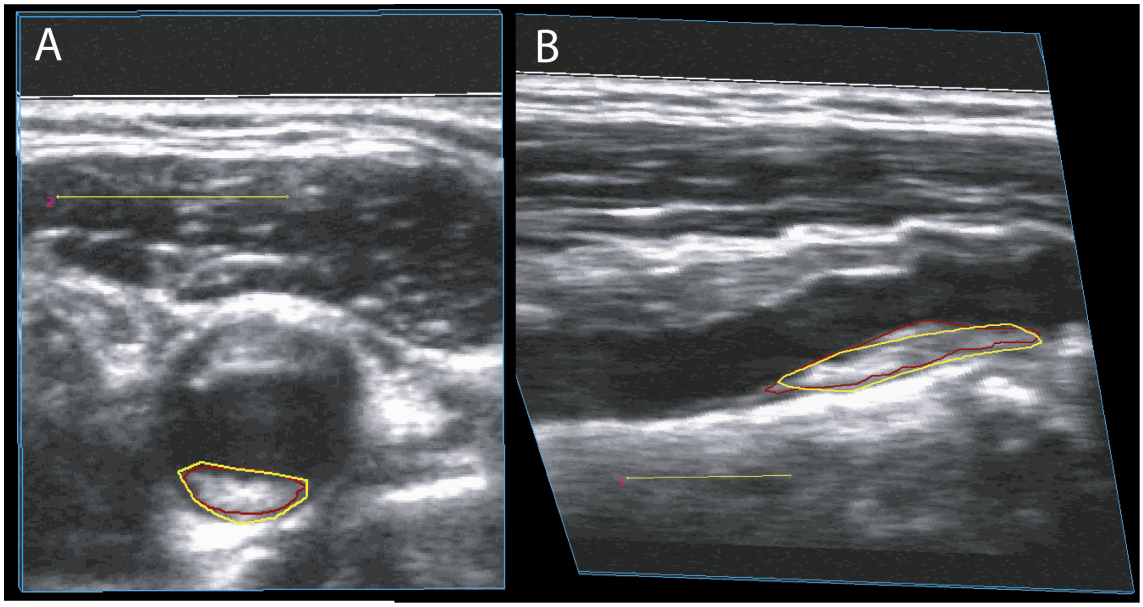

Figure 3. Representative manual and semi-automated segmentation boundaries. (A) axial view, (B) longitudinal view. Manual (red) algorithm contours (yellow). Yellow bar = 10mm.

Table 1. Semi-automated and manual measurements for 22 carotid plaques.

Plaque	Semi-automated Plaque Volume mm^3 (±SD)	Mean Semi-automated Plaque Volume Segmentation Time (min)	Manual Plaque Volume (mm^3)	Manual Plaque Volume Segmentation Time (min)	CV Semi-automated (%)
1	18.7±3.7	2.1±0.8	23.2	4.1	19.6
2	43.6±4.6	3.9±2.5	44.8	4.8	10.6
3	7.9±1.2	2.5±1.3	7.5	2.9	14.6
4	4.9±0.7	2.8±2.2	4.9	2.8	14.7
5	77.7±10.2	3.4±1.6	87.3	6.0	13.1
6	30.6±2.0	3.5±1.2	37.4	6.3	6.5
7	2.5±0.4	1.6±0.6	4.5	3.9	17.6
8	119.5±11.4	3.4±1.7	137.5	4.5	9.6
9	139.5±11.1	4.6±3.1	145.4	4.3	8.0
10	67.5±3.8	2.4±0.5	78.5	3.9	5.6
11	34.6±3.0	1.8±0.4	41.6	3.2	8.7
12	72.3±4.5	3.1±2.1	72.4	4.1	6.3
13	15.4±2.2	2.7±1.0	20.5	3.0	14.5
14	20.9±2.9	2.2±1.0	24.9	3.1	13.7
15	12.2±1.9	1.4±0.2	10.8	3.0	15.2

16	2.0±0.5	2.2±0.6	2.0	2.3	26.6
17	42.6±1.8	2.3±0.6	34.6	2.9	4.3
18	35.4±3.4	2.3±0.4	35.0	3.0	9.7
19	26.7±2.8	2.7±1.4	26.8	3.2	10.4
20	21.6±2.3	2.6±0.8	34.5	4.4	10.7
21	121.4±11.6	3.6±1.5	151.4	5.7	9.6
22	21.3±3.1	2.0±0.7	26.0	5.0	14.5
Mean	42.7±40.4	2.7±0.8	47.8±45.6	3.9±1.1	12.0±5.1

Figure 4 shows the relationship between variability (using CV of each plaque measurement) and mean plaque volume (left) and the relationship between manual and semi-automated measurements (right). The mean coefficient of variation for all plaques measured with the semi-automated method was 12±5%. Manual TPV segmentations were significantly correlated with semi-automated measurements ($r = 0.99$, $p < 0.0001$). Semi-automated TPV segmentation was 2.7±0.8 minutes compared to 3.9±1.1 minutes for manual TPV measurements.

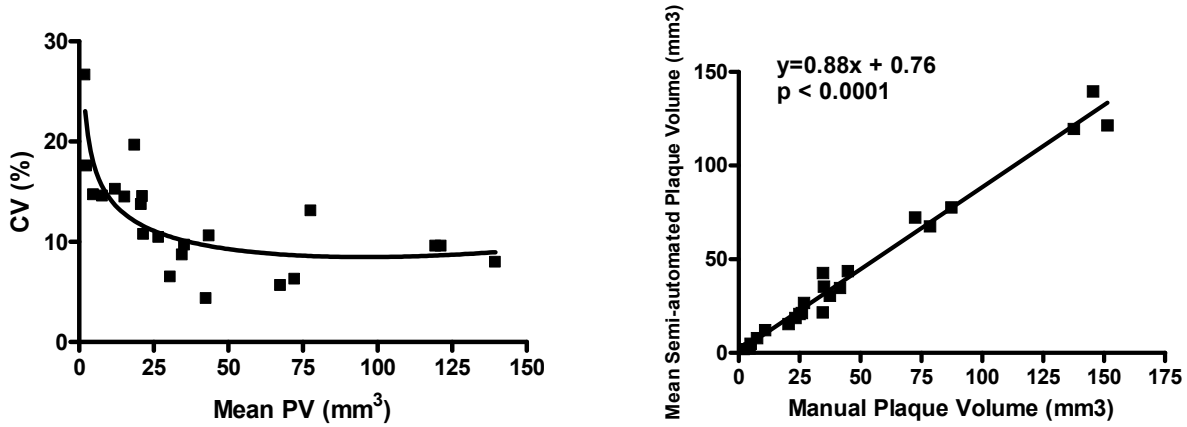

Figure 4. Relationship of semi-automated plaque volume and variability of measurement (CV) (left). Relationship between manual and Semi-automated measurements (right).

Figure 5 shows Bland Altman analysis of manual compared to semi-automated TPV measurements. The mean difference between semi-automated and manual measurements was represented as a bias of -11.8 %.

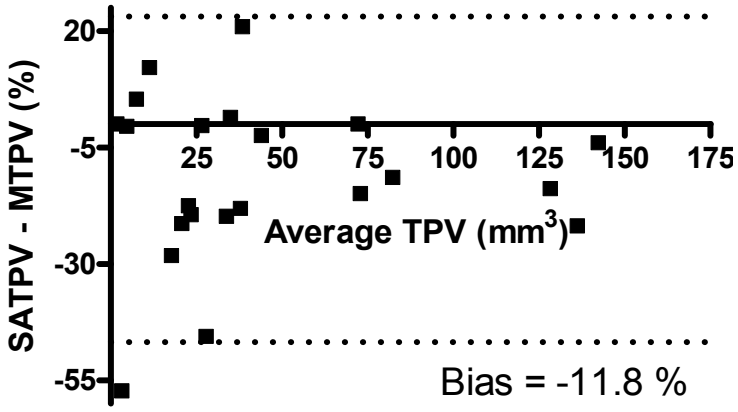

Figure 5. Bland-Altman Analysis of Agreement between manual and semi-automated TPV. Percent difference between mean semi-automated TPV measurement (SATPV) and manual total plaque volume measurement (MTPV) plotted against the average of both measurements. Limits of agreement within two standard deviations are shown with dotted lines.

4. NEW OR BREAKTHROUGH WORK TO BE PRESENTED

We developed a semi-automated measurement of carotid atherosclerotic plaque volume for real-time measurements at the bedside. Variability of the semi-automated measurement was similar to manual segmentation methods reported by Landry even for plaques in the 50-100mm^3 range, more common in moderate disease without stenosis[13]. Bland Altman and linear regression analysis indicated a bias in semi-automated measurements underestimating manual total plaque volumes. On average, plaque volume was underestimated by approximately 12%.

5. CONCLUSIONS

We developed a semi-automated segmentation tool to measure 3DUS TPV. The geometric volume approximation this tool provides may provide a more accurate estimate compared to edge detection methods because signal void and artifacts, common in 3DUS carotid images would not influence contour shape and plaque morphology using a geometric method. Although the semi-automated measurement of TPV provided an underestimated measurement in comparison with manual TPV, this bias may not be clinically significant in longitudinal comparisons. The measurement tool we developed provided a way to estimate plaque burden in real time at the bedside. Next steps include the evaluation of inter-observer variability enabling multiple observers to perform measurements in real-time to monitor carotid atherosclerosis.

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