# Bilateral asymmetry in ultrasound-image-based mechanical and textural features in subjects with asymptomatic carotid artery disease

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*Abstract*— **Carotid atherosclerosis is a principal cause of stroke and transient ischaemic attack. It has recently been postulated that potential asymmetries between the left and right carotids may be important in terms of disease progression. In this work, we sought to investigate differences between the two carotid arteries using ultrasound-image-based mechanical and textural features. Sixteen arterial segments (8 from the left and 8 from the corresponding right side) of elderly subjects with bilateral asymptomatic carotid atherosclerosis were interrogated. Left and right sides had similar stenosis degrees. Mechanical features were estimated via motion analysis using adaptive block matching. They included motion amplitudes, velocities and diastole-to-systole displacements of selected regions around and adjacent to the plaque. Textural features included first- and second-order statistical as well as multiresolution measures. One texture and eleven mechanical features were significantly different between the two arterial sides, indicating that bilateral asymmetry is characterised better in terms of mechanical properties, rather than via tissue composition, which is expressed through texture analysis. These findings suggest that not only systemic, but also focal, factors are probably responsible for atherosclerosis development. The identification and definition of the role of these factors may help to clarify the pathogenesis of this disease and to improve the clinical and therapeutic approaches.**

## I. Introduction

Although atherosclerosis is generally considered as a systemic disease, caused or favoured by specific risk factors, including high blood pressure, high blood cholesterol levels, diabetes and smoking, it is well known that it occurs at a few particular arterial sites; the carotid artery is one of them. Carotid atherosclerosis (CA) is a principal cause of stroke and transient ischaemic attack. One additional important aspect of atherosclerosis involving symmetrical beds, e.g. the carotid, is the asymmetry of lesions between the left and right sides. Such asymmetry may hold valuable information about the pathogenesis of atherosclerosis and may be useful for disease monitoring and treatment. A relatively limited number of studies have addressed this issue of bilateral asymmetry in normal and diseased symmetrical districts.

In regards to anatomy, it was recently reported that the left common carotid artery is significantly longer and slightly more curved than the right one; also its diameter is smaller [1]. The measurements were based on 3D contrast-enhanced magnetic resonance angiograms. By imaging pairs of carotid arteries from cadaveric donors using MRI and electron-beam CT, it was found that total wall volume and plaque calcification were substantially similar between the two sides [2]. This finding suggests that individuals with atherosclerosis in one carotid artery are likely to have disease in the contralateral side. Along the same line, a recent study demonstrated that ultrasound-image-based estimations of CA echogenicity and texture were bilaterally similar when the ipsilateral plaque causes high-degree stenosis [3]. In another study, symptomatic plaques were found stiffer than their contralateral asymptomatic sides [4]. Stiffness was estimated from MRI-based arterial cross-sections and tonometry-based pulse pressure. Bilateral asymptomatic plaques, however, were less stiff than asymptomatic ones with contralateral symptomatic plaques [4]. On the other hand, Gnasso et al showed that wall shear stress was lower in arteries with plaque than in plaque-free arteries [5]. In that study, stress measurements for atheromatous cases were performed at plaque-free locations, upstream from the plaque.

In addition, it was recently shown that the intima-media thickness (IMT), an established indicator of CA, is bilaterally similar in both normal and diseased subjects [6]. However, a study on subjects with CA reported significant bilateral variation in the IMT, which was also found to be associated with vascular alteration better than IMT [7]. Furthermore, it is not only the characteristics of the atheromatous plaque itself, but also the combination of those with the characteristics of the arterial wall adjacent to it or even the wall of the contralateral artery. In particular, it was shown that, although the common carotid artery is not prone to plaques, its morphological characteristics are positively correlated with a number of risk scores [7].

Ultrasound imaging, which is widely used in the diagnosis of CA, allows investigating the potential asymmetrical nature of arterial disease. Ultrasound imaging holds a prominent position in the diagnosis of vascular disease due to its advantages, including non-invasiveness, widespread availability, short examination times, lack of radiation exposure, and low cost [8]. Furthermore, recent advances in computerised methods for ultrasound image analysis have allowed the extraction of features for describing tissue echogenicity/texture, motion/elasticity and morphology, thus providing additional information on plaque composition and stability [9]. These measures allow

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quantitative descriptions of various localised physiological phenomena taking place within and adjacent to the atheromatous plaque.

Echogenicity/texture as well as motion analysis have gained attention as determinants of plaque vulnerability. In carotid artery ultrasound images, texture quantifies the spatial distribution of gray levels in the imaged tissue, which, in turn, determines the pattern of allocation of echogenic (fibrous and calcified tissue) and anechoic (blood, lipids) materials. A number of studies have compared symptomatic and asymptomatic cases in terms of their texture characteristics. Moreover, it has been stated that more advanced texture analysis methods, based on multiresolution and multiscale analyses, which provide information at different image resolutions, can be more efficient than statistical measures in discriminating different plaque types [10], [11].

The analysis of motion of the carotid artery plaque from ultrasound image sequences is a powerful tool for investigating mechanical phenomena, which may be more sensitive to early vascular alterations due to disease. Radial and longitudinal arterial wall motion has been associated with risk for cerebrovascular symptoms [12]. Furthermore, a number of sophisticated methods are emerging ([12]-[14]), which aim at improving the motion analysis procedures of challenging scenarios, such as tracking the fuzzy arterial borders.

It is with these findings in mind that we sought to determine potential differences between left and right atheromatous carotid arteries of asymptomatic subjects, in terms of ultrasound-image-based mechanical and textural features. A large number of features, derived from advanced methods for ultrasound image analysis, were used to investigate such differences in a small, yet carefully designed, dataset.

## II. Material and Methods

### A. Ultrasound Image Acquisition and Pre-processing

A total of 16 arterial segments (8 from the left and 8 from the corresponding right side) of elderly subjects (aged 50-86 years) with bilateral carotid atherosclerosis were interrogated. All subjects were asymptomatic, i.e. they presented no neurological symptoms within a 6-month time period prior to the time of the examination. No statistically significant differences were found in the degrees of stenosis between the left and the right arterial sides.

The local institutional review board approved ultrasound image examinations and all subjects gave their informed consent to the scientific use of the data. For each subject, the carotid artery was scanned in the longitudinal direction according to a standardized protocol (dynamic range, 60 dB; persistence, low) and a B-mode ultrasound image sequence was recorded at a rate higher than 25 frames/s for at least 3 s (2-3 consecutive cardiac cycles). Dynamic B-mode ultrasound imaging of longitudinal sections of the arterial wall allows the estimation of tissue motion in two dimensions, namely longitudinal, i.e. along the vessel axis, and radial, i.e. along the vessel radius, and perpendicular to the longitudinal one. Figure 1 (a, b) shows examples of B-mode ultrasound image recordings for the left and right carotid artery of a subject with bilateral atherosclerotic plaque.

For each artery, an experienced vascular physician traced four regions of interest (ROIs), namely the posterior (PWL) and anterior wall-lumen (AWL) interfaces and the plaque top (PTS) and bottom surfaces (PBS) (Fig. 1 (c, d)). PWL and AWL correspond to the arterial wall adjacent to the plaques and they were included in motion analysis due to recent findings proposing ultrasound image-based features of healthy parts of the arterial wall close to the plaque as potential risk markers for CA [5], [12].

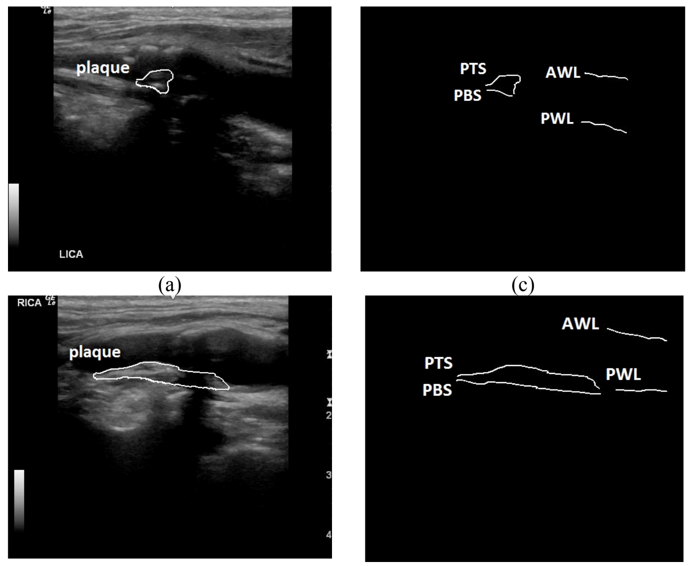


Fig. 1. Examples of (a, b) B-mode ultrasound images of the (a) left and (b) right carotid artery of a patient with carotid atherosclerosis and (c, d) the selected ROIs.

Subsequently, image intensities ([0: black, 255: white]) were linearly adjusted so that the median grey level value of the blood was 0, and the median grey level value of the adventitia was 190 [15]. This pre-processing step was necessary to ensure comparable measurements among different image recordings.

### B. Motion Analysis of Image Sequences

All pixels composing the four ROIs, as well as the whole plaque region, i.e. the region contoured by PTS and PBS, were selected as motion targets. The radial and longitudinal positions of the targets across time were estimated using $ABM_{KF-K2}$, a recently proposed motion estimator with enhanced accuracy in motion tracking of the arterial wall [12], [14].

From the produced waveforms, a wide variety of kinematic and strain indices were estimated. Specifically, kinematic indices were derived by estimating target-wise indices representing (a) median and standard deviation in velocities during the cardiac cycle, (b) motion amplitudes, defined as the absolute difference between the corresponding maximum and minimum positions of the target, and (c) diastole-to-systole displacements, for each cardiac cycle. Strain indices were estimated, using motion waveforms for pairs of pixels, to express relative movements between ROIs or local deformations in a ROI during the cardiac cycle [12], [14]. In all cases, descriptive statistical measures (minimum, maximum, mean, median, standard deviation, skewness, kurtosis, entropy) of the mean (over the cardiac cycles) values of the target- or pair-wise indices were calculated.

### *C. Texture Analysis of Isolated Images*

Plaque texture was measured using first- and second-order statistical properties [15], as well as multiresolution features [10] of image intensities corresponding to the manually selected plaque region (Fig. 1 (a, b)). A total of 17 statistical features were assessed.

Multiresolution texture features were extracted from subimages derived after the application of a wavelet-packet-based decomposition scheme using the coiflet function, and three levels of decomposition [10]. Higher (lower) decomposition levels correspond to coarser (finer) texture. At the first level of decomposition, four subimages are derived, namely an approximation (A) and three detail images, including horizontal (Dh), vertical (Dv) and diagonal (Dd) subimages. At each subsequent level, each subimage is further decomposed into new four subimages. The extracted texture features consist in the mean and standard deviation values of the resulting subimages. A total of 126 multiresolution features were estimated.

All textural features were estimated for specific instants of the cardiac cycle, namely, systole and diastole, which were identified as the time points corresponding to the maximal and minimal radial distances, respectively, between PWL and AWL.

The exact Wilcoxon test was used to evaluate differences between left and right sides. Because the sample size was small, the exact Wilcoxon test was used to avoid the computation of invalid p-values. Exact statistical methods do not use assumptions in contrast to traditional methods, such as the t-test. A p-value of 0.05 or less was considered significant.

## III. Results

Table I shows average ± standard deviation values of the 12 biomechanical and textural features which were found significantly different between the left and the right carotid sides. As we can see, the majority of the features are of a mechanical nature, suggesting that the two sides may differ in terms of their mechanical properties. For three features, namely 'Entropy (over targets) of median (over time) radial velocity', 'Skewness of LSI in PTS' and 'Skewness of longitudinal diastole-to-systole', the standard deviations were considerably large.

It is worth noting that, in a subset of 5 subjects with bilateral stenosis of 40%, a total of 20 features were significantly different between left and right sides. Four of these were common with those of the entire group; these included ‘energy ($45^0$) of total motion amplitude’, ‘energy ($90^0$) of total motion amplitude’, and ‘energy ($135^0$) of total motion amplitude’ in the entire plaque, and ‘skewness of total diastole-to-systole displacement’ in PTS. These features were lower in the right arterial side.

## IV. Discussion

In this study, associations between left and right carotid arteries were investigated with the aid of ultrasound-image-based estimates of motion and texture. To the best of our knowledge, this is the first time bilateral motion differences are reported in the carotid artery. One textural and 11 motion features were found significantly different between the two sides.

TABLE I. Average ± Std of biomechanical and textural features which were found significantly different between left and right carotid sides. PBS: plaque bottom surface, PTS: plaque top surface. LSI: longitudinal strain index, RSI: radial strain index.

| Feature | Left side | Right side |
|---|---|---|
| *Biomechanical - Entire plaque* | | |
| Entropy (over targets) of median (over time) radial velocity | 0.753±0.736 | 1.929±1.277 |
| Energy ($0^0$) of total motion amplitude | 0.676±0.105 | 0.552±0.118 |
| Energy ($45^0$) of total motion amplitude | 0.646±0.112 | 0.513±0.120 |
| Energy ($90^0$) of total motion amplitude | 0.651±0.112 | 0.519±0.120 |
| Energy ($135^0$) of total motion amplitude | 0.644±0.114 | 0.512±0.121 |
| *Biomechanical - PBS/PTS* | | |
| Skewness of LSI in PTS | 1.330±0.846 | 2.568±1.276 |
| Skewness of RSI between PBS/PTS | 2.552±0.968 | 1.265±0.806 |
| Skewness of longitudinal diastole-to-systole displacement in PTS | -0.068±0.259 | 0.580±0.527 |
| Skewness of radial diastole-to-systole displacement in PTS | 3.139±0.719 | 2.400±0.262 |
| Skewness of total diastole-to-systole displacement in PTS | 3.435±0.933 | 2.350±0.218 |
| Kurtosis of total motion amplitude in PTS | 2.683±0.427 | 2.248±0.355 |
| *Textural* | | |
| Std of $Dh_3Dh_2Dh_1$ at systole | 0.060±0.014 | 0.075±0.010 |

The fact that motion features outnumbered textural ones may be an indication that bilateral asymmetry is characterised better in terms of mechanical properties, rather than tissue composition, which is expressed through texture analysis. This finding agrees with previously reported results demonstrating similar texture properties in bilateral carotid plaques [3]. It is also in agreement with a previous study, which showed asymmetry in plaque-free areas between normal and diseased carotid segments, in terms of mechanical factors, namely wall shear stress [5].

Histogram-based metrics of mechanical parameters, namely kurtosis and, even more so, skewness, identified differences between sides. It is concluded that such metrics should be used more often in addition to commonly used ones, eg. mean, standard deviation and median, when studying spatial distributions of pixel-based measurements.

The sole texture feature that was significantly different between left and right sides, namely the standard deviation of $Dh_3Dh_2Dh_1$, is a feature derived from multiresolution analysis. Specifically, it corresponds to a horizontal detail subimage. Horizontal detail subimages have been shown to outperform other multiresolution and statistical features in discriminating between symptomatic and asymptomatic carotid plaques [10]. Consequently, multiresolution analysis, and, in particular, horizontal detail images, seem to be promising tools toward efficient characterisation of arterial wall tissue.

A number of reasons may be responsible for the observed asymmetry between left and right carotid sides. As an example, different geometries ([1]) may cause different flow patterns and therefore different stresses and corresponding strains on the arterial wall.

Our findings suggest that CA may be the result not only of systemic factors but also of focal parameters. Additional studies involving larger samples with various stenosis degrees are required to corroborate these results. These studies will outline the importance of potential bilateral asymmetries toward improving clinical and therapeutic approaches.

## V. Conclusion

In a small population sample, we showed for the first time that asymmetries between left and right carotid artery may be quantified through motion analysis from ultrasound imaging; texture analysis is less efficient in characterising such asymmetries. These findings suggest that not only systemic, but also focal, factors are probably responsible for atherosclerosis development. The identification and definition of the role of these factors may help to clarify the pathogenesis of this disease and to improve the clinical and therapeutic approaches.


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