Stroke, also known as cerebro-vascular accident (CVA), is the third leading cause of death and disability in the world. Treating the morbidity and mortality arising from stroke is estimated to consume up to 7% of total healthcare spending [1].

40% to 50% of these CVA hemispheric events are related to embolic debris and thrombi originating from atherosclerotic plaque involving the carotid bifurcation. For patients with established disease, diagnostic efforts concentrate on the prediction of those patients at high risk, with possible treatment by surgery or other intervention.

In the case of carotid stenosis, the traditional approach of assessing the severity of a lesion and the resultant risk of CVA is based on its dimensions (e.g. percent of area stenosis) and the lesion composition (visual assessment of plaque morphology). The selection criteria are based on the estimation of the arterial lumen reduction, using anatomical visualization and blood velocity measurements. Images of lumen diameter on angiograms provide information regarding comparative degrees of lumen narrowing, but do not provide an accurate appraisal of lesion cross-sectional area, volume or composition. Flow velocity profiles characteristics of stenoses can be detected using duplex Doppler ultrasound. However, evaluation of the chemical composition of highly stenotic lesions, performed after endarterectomy, has failed to reveal any significant differences between symptomatic and asymptomatic plaques [2, 3].

It is believed that plaque rupture is due to a structural failure of the diseased vessel, and that mechanical features of the atherosclerotic lesion significantly influence its probability of rupture [4, 5]. Recognition of specific features that increase vulnerability to disruption would allow prediction of plaques that are most likely to cause acute events.

The principle behind the ultrasound techniques presented in this article is that plaque fracture probability is determined both by the cyclic stress imposed by the arterial pulse pressure, and by the strength of the heterogeneous plaque material. In fact, atherosclerotic lesions are made up of stiff fibrous materials, focal calcifications and very soft necrotic lipid pools. These complex structures cause heterogeneous stress-strain states, which may ultimately lead to rupture.

The Arterial Wall Motion (AWM) technique has the potential to reveal these mechanical interactions [6]. It permits non-invasive investigation of tissue motion and arterial wall motion, for the assessment of the biomechanical behavior of the artery wall. It also provides completely new functional information, currently unavailable by other diagnostic means. By examination of such features as the intraparietal strain (i.e. strain within the thickness of the arterial wall) and local differential motions along an arterial segment it is possible to both quantify and image the biomechanical function of the arterial walls. The combination of Color Flow imaging with the parietal motion depicts the mechanical interaction of the two components of the vascular dynamics, i.e. tube and fluid. This approach provides fundamentally new information on the physical mechanisms of carotid plaque rupture, and will make it possible to find new predictive indicators of clinical stroke based on the biomechanical arterial behavior.

A new ultrasound technique

The Arterial Wall Motion (AWM) technique is based on Tissue Doppler Imaging (TDI) technology, tracking procedures, and advanced signal/image processing algorithms.
AWM allows dynamic visualization of relative motion variations at different points.

It offers a new way of interpreting mechanical interactions between different components of the vascular structure. The preliminary clinical investigations performed to evaluate this new technique already provide an interesting insight into the biomechanical processes that are probably responsible for plaque rupture.

The technique provides simultaneous measurements made on multiple diameters along an arterial segment of interest (typically, every 0.5 mm along an arterial segment with a length of 40 mm) repeated continuously throughout the cardiac cycle (50–100 frames per second). This approach allows dynamic visualization of relative motion variations at different parts of the arterial walls, and identification of regions in which there is high (axial and/or lateral) relative deformation. The instantaneous positions of the arterial wall borders along a 2D longitudinal scan are measured with very high accuracy/resolution (50 to 100 times greater than that obtained from grayscale imaging). When these instantaneous measurements are superimposed as zoomed curves on a real-time Cineloop image, they reveal novel and impressive information (both visual and quantitative) about the state of the arterial segment under investigation. In a healthy artery, all the points exhibit synchronized and homogeneous motion. On the other hand, the presence of a region with different mechanical properties, such as atheromatous plaque, is marked by localized spatio-temporal motion discontinuities.

AWM provides unique information on the state of the artery.

The AW M measurement technique provides unique information. No previous attempts have been made to obtain such information using ultrasound, and it would not be possible to obtain equivalent data using other imaging modalities such as MRI or CT.

Data acquisition and measurements

The heart of the AW M technique is Tissue Doppler Imaging (TD I). TD I measures the tissue velocity and displays it as a color-coded superimposition on the corresponding grayscale anatomical image. A series of high-frequency ultrasound echoes are reflected by the anatomical structures. A change in the position of the structures induces phase shifts in the reflected echoes. These phase shifts are processed to estimate the local velocity of the objects under examination.

TD I has been mainly developed in the context of cardiology, where it has generated strong research interest due to its high accuracy in quantifying myocardial contractility.

There have been no previous studies defining the role of TD I in vascular applications, because the commercially available technology would require modifications to enable it to measure arterial wall motion rather than cardiac muscle motion. In our investigations, appropriate modifications of the scanning parameters were made in an ATL HDI 5000 ultrasound system, in order to apply TD I to the movements of the carotid arteries. These modifications change the characteristics of the echo sequences in both time and space, providing an adequate frame rate and an appropriate velocity range.

The carotid artery prototype is based on a linear array vascular probe (5–12 MHz). The ultrasound probe position is adjusted to acquire longitudinal views of the artery, in which the walls are clearly seen on the B-mode image. An image sequence of the carotid artery is acquired, with a duration of 2 to 10 seconds. The sequence comprises B-mode grayscale images of tissue, as well as simultaneous TD I color images of tissue motion.

Off-line data processing

Arterial wall motion imaging

The TD I image sequence is processed off-line, according to the following steps:

- The user indicates a point inside the artery on one of the images of the sequence. The edges of the vessel walls are then extracted automatically from all the B-mode images of the sequence.

- The position of the arterial structures is then reported on the TD I data planes. Based on the location of the moving structures, the algorithm is now able to perform local time and space integration of velocity values provided by TD I. It computes the wall displacement curves as a function of time throughout the cardiac cycle, and as a function of position along the arterial axis. A high degree of accuracy is achieved.

- The excursion of the artery is superimposed on the B-mode image in graphic form, allowing the
displacements to be analyzed as a function of position along the axis of the artery with time.

Two static lines represent the reference positions of the arterial walls at the beginning of the cardiac cycle. The wall displacements are displayed relative to these reference lines, for each frame during the cardiac cycle, with distances proportional to the wall displacement. The user can display dynamic sequences, or go through the sequence of B-mode images step by step.

The principle of the AWM technique is shown in Figure 1.

Parietal strain imaging
The compressive strains on the tissue within the plane of the ultrasound scan are calculated by applying a gradient operation to the tissue velocity data, perpendicularly to the arterial axis, and integrating it in time. This provides image sequences of strain accumulation within the tissue occurring during a cardiac cycle. The information on the intraparietal strain (i.e., strain within the thickness of the arterial wall) is mixed in color on the B-mode image. Red corresponds to compression, blue to distension.

Quantification
Figure 2 illustrates the preliminary quantification tools available. Arterial dilation, arterial wall motion and motion gradients are displayed as time and space curves. Part A of the quantification package displays an image of the sequence. Part B is the superposition of the dilation curves measured simultaneously on the diameters of the arterial segment. The user can choose a particular time of the sequence on this graph using a track ball or a mouse, and the displayed image is updated on part A. Part C shows the particular cardiac cycle and the corresponding time portion of the dilation curves. Part D, displayed under the image, is the representation of the dilation excursion (minima-maxima) during the selected cardiac cycle along the arterial axis. The user can compare the dilation amplitudes along the arterial axis caused by the discontinuities of the mechanical properties of the artery.

Fusion of AWM and blood flow imaging
As blood enters a stenosis, it accelerates to maintain the volume flow. This acceleration creates a velocity at the output which, in the case of a 70% stenosis, is ten times higher than that in a normal artery. The kinetic energy of the moving blood is very high, and this occurs at the expense of the pressure, which falls, and can even fall below the pressure outside the vessel. This creates contraction of the artery rather than dilation during the systolic phase. With a very tight stenosis in the carotid bifurcation, the vessel will collapse, resulting in fatigue of the plaque structure with the likelihood of rupture. This mechanism could be illustrated if blood flow imaging and arterial wall motion measurements were performed simultaneously. It is not feasible because the scanning sequence configurations for each of these echographic modes are not compatible.
However, it is possible to create a composite representation using a combination of a color flow sequence and a wall motion sequence. Wall motion and color flow acquisition data sets are acquired consecutively, but the sequences are automatically synchronized by analyzing the arterial dilation curves and the flow images (Fig. 3).

Technical validation

The validation was performed using an arterial wall phantom to assess the accuracy of the wall motion measurements. The phantom is computer-controlled, with a mechanical movement that simulates the motion of the artery walls. A comparison between known wall motion and that measured by the ultrasound prototype allowed an objective assessment of the prototype’s accuracy and precision.

The phantom specifications are consistent with the characteristics of arterial wall motion: high acceleration (200 m/s²), translation range (5 mm) and accuracy (± 1 µm). The motorized translation stage is linked to a plane, covered by a material with similar characteristics to biological tissue, that moves up and down. A stationary plane parallel to the first one mimics the second arterial wall.

The targeted accuracy for the ultrasound measurement of carotid wall motion is 10 %, or 50 µm for a typical maximum carotid dilation of 500 µm. Multiple ultrasound acquisition configurations have been tested to establish a quantitative description of the system parameters related to the wall motion measurements. This has allowed objective optimization of the ultrasound machine settings (e.g. frame rate, color line density).

Clinical tests

The clinical problem

Surgical management of asymptomatic carotid stenosis is highly controversial. One randomized controlled trial (ACAS) has suggested that in patients with asymptomatic stenoses > 60 %, carotid endarterectomy (CEA), in combination with the best medication, is associated with a significant reduction in subsequent ischemic stroke when compared with the best medication alone. However, on the basis of a stenosis > 60 %, the number of CEAs required to prevent one stroke would be very high. In fact, up to 19 out of 20 patients would be undergoing an ‘unnecessary’ operation. In an attempt to develop better predictors of stroke risk in this patient group, attention has turned to plaque morphology. Specifically, it has been postulated that plaque rich in lipid is much more likely to cause stroke than plaque that is fibrous. Until now no pre-operative, non-invasive technique has been able to discriminate plaque types or stratify stroke risk with sufficient reliability to support clinical decision-making.

In this context, the necessary clinical validation of Arterial Wall Motion imaging should determine whether plaque strain is able to distinguish between high- and low-risk plaques with sufficient accuracy to allow clinical decisions regarding the appropriateness of CEA for individual patients. The correlative goal will be to investigate whether the plaque motion characteristics are related to...
plaque structure. These tests should also determine whether, in asymptomatic carotid stenoses, plaque strain is related to progression of stenosis in terms of cross-sectional area reduction, development of cerebral infarcts and clinical symptoms.

Preliminary clinical validation

Preliminary investigations have been performed in vivo on atherosclerotic carotid arteries. The AWM technique has been successfully tested on over 50 normal carotid arteries and 40 carotid arteries with >70 % stenosis. The several examples presented here are in accordance with the mechanical behaviors postulated in the literature, which have not been demonstrated in vivo using other techniques. The investigations reveal longitudinal discontinuities of wall displacements and heterogeneous internal strains, due to variations in arterial tissue elasticity caused by plaque development.

**N.B.** The corresponding movie sequences are included in the enclosed CD-ROM.

Case 1 corresponds to a 90 % degree stenosis with a calcified plaque. Figure 4 a represents the wall motion display at the systolic peak. The characteristics are an overdilation proximal to the stenosis and a large wall displacement gradient at the edge of the plaque. The display of strain (Figure 4 b) inside the wall and plaque tissue demonstrates that intraparietal distension coincides with large lateral strains in the arterial wall. Another observation is that calcified structures are not compressed when surrounding tissues are strongly stressed.

Case 2 (Fig. 5) shows a very narrow channel obstruction. The strength of the output blood flow jet causes the artery to bend. There is no dilation at the location of the stenosis.

**Fig. 5.** Case 2. Narrow obstruction. The strength of the output blood flow jet causes the artery to bend. There is no dilation at the location of the stenosis.

**Fig. 6.** Case 3. Localized discontinuity of the posterior wall, with a change in the direction of motion between two adjacent segments, suggesting a possible rupture in the plaque.

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Case 2 (Fig. 5) shows a very narrow channel obstruction. The strength of the output blood flow jet causes the artery to bend. There is no dilation at the location of the stenosis.

**Fig. 6.** Case 3. Localized discontinuity of the posterior wall, with a change in the direction of motion between two adjacent segments, suggesting a possible rupture in the plaque.

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Case 2 (Fig. 5) shows a very narrow channel obstruction. The strength of the output blood flow jet causes the artery to bend. There is no dilation at the location of the stenosis.

**Fig. 7.** Case 4. Severe stenosis with high jet velocities.

**N.B.** The corresponding movie sequence is included in the enclosed CD-ROM.

Case 4 corresponds to a severe stenosis with high jet velocities.
Conclusion

These examples demonstrate the very innovative potential of this technique. Other related vascular applications will be investigated, such as iliac and femoral artery stenosis, stents, graft anastomoses, aortic aneurysm and therapy follow up. The Arterial Wall Motion technique gives access to new functional parameters of the vascular process, and may lead to a complete renewal of the vascular exam. Further investigation and validation are required to fully understand the mechanical processes imaged by this technique.

It is hoped that the Arterial Wall Motion technique will offer new, pertinent criteria for the characterization of arterial lesions.
References


