Atherosclerosis remains the leading cause of morbidity and mortality in the Western world [1, 2]. It is usually regarded as a systemic disease and several well-identified risk factors (i.e., hypertension, hyperlipidemia, diabetes mellitus, and cigarette smoking) have been implicated in its pathogenesis. Noninvasive imaging of atherosclerosis, such as intimal wall thickening and plaque formation, is routinely available using a variety of imaging techniques. The causes of atherosclerosis are multifactorial and knowing them could allow earlier prevention and detection of the disease. The frequent occurrence of atherosclerotic plaques in well-recognized arterial districts, together with the focal distribution of these plaques in regions of curvature, bifurcation, and branching of the vessels, suggests that fluid dynamics and vessel geometry may play a localizing role in the cause of plaque formation [3]. In vitro and in vivo models have been used to study the flow patterns in a variety of arterial territories and to look for an association between areas of preferential atherosclerotic plaque formation and blood flow hemodynamics [4–7]. The magnitude and rate of change of blood flow close to a vessel wall, which can be expressed using the concept of wall shear stress, have been linked to the pathogenesis of atherosclerosis. Vessel segments with low wall shear stress or highly oscillatory wall shear stress appear to be at the highest risk for development of atherosclerosis. The purpose of this review is to familiarize the imagers with the concepts and principles underlying wall shear stress measurements. Wall shear stress mapping may someday become part of the multifactorial, multidisciplinary approach to early atherosclerosis detection.

We first review this hypothesized association between atherosclerosis and wall shear stress. We then review the use of phase-contrast velocity-encoded MR imaging and Doppler sonography to map velocity profiles in vascular structures. These hemodynamic parameters can be used to calculate how quickly the blood velocity increases when moving from the vessel wall to the center of the vessel. Estimation of wall shear stress is now possible with noninvasive imaging techniques such as MR imaging and Doppler sonography. MR imaging can be used to confirm, in vivo, what is known from in vitro hemodynamic studies and observations made at autopsy and in experimental models. Some day, this may help us better understand the importance of flow hemodynamics in the multifactorial etiology of atherosclerosis.

**Wall Shear Stress**

In nonpulsatile flow in a straight vessel, fluid does not move at the same velocity at every point in the vessel. Instead, fluid flow is fastest at the center and slowest close to the wall. The fluid velocities assume a parabolic profile referred to as the “laminar flow” profile [8] (Fig. 1). This pattern of flow is the result of friction within the fluid and between the fluid and the vessel wall, and is related to the fluid viscosity. This friction creates a tangential force exerted by the flowing fluid on the intimal surface of the artery and is referred to as the “wall shear stress” (Fig. 2). The magnitude of wall shear...
Effect of Wall Shear Stress on the Histology and Function of the Endothelial Cells

Evidence from in vitro and in vivo studies suggests that both low wall shear stress and high oscillatory patterns of wall shear stress cause intimal wall thickening [4–7, 11]. Some studies also suggest that these local hemodynamic factors act independently of other known risk factors for atherosclerosis. For example, in a prospective study by Gibson et al. [12] of 26 patients with 74 lesions, low local shear stress was significantly correlated with an increased rate of atherosclerosis progression in human coronary arteries independently of circulating lipoprotein values and systemic hemodynamics.

It has long been hypothesized that low wall shear stress and the resultant stagnation of blood permit increased uptake of atherogenic blood particles as a result of increased residence time [13]. More recent research has provided us with a better understanding of the mechanisms underlying this. It has been shown that wall shear stress can change the morphology and orientation of the endothelial cell layer. Endothelial cells subjected to elevated levels of wall shear stress tend to elongate and align in the direction of flow, whereas those experiencing low or oscillatory wall shear stress remain more rounded and have no preferred alignment pattern [14, 15]. Moreover, exposure of the arterial wall to a relatively low wall shear stress may increase intercellular permeability and consequently increase the vulnerability of these regions of the vessel to atherosclerosis [16]. Levels of the vasoactive substances released by endothelial cells (prostacyclin, nitric oxide, and endothelin-1) are strongly influenced by shear stress. An acute increase in wall shear stress in vitro elicits rapid cytoskeletal remodeling and activates a signaling cascade in endothelial cells, with the consequent acute release of the vasodilators nitric oxide and prostacyclin [17]. Nitric oxide in particular appears to be a key mediator in the atheroprotective effect of high wall shear stress [18]. High laminar shear stress sharply reduces endothelial cell levels of precursor proendothelin mRNA. This decreases the level of endothelin-1 peptide, which exerts a constricting and mitogenic effect on vascular smooth muscle cells [19]. Finally, prolonged oscillatory shear stress induces expression of endothelial leukocyte adhesion molecules, which are important in mediating leukocyte localization in the arterial wall [20].

The overall picture is that nonpulsatile high shear stress promotes release of factors from endothelial cells that inhibit coagulation, migration of leukocytes, and smooth muscle proliferation, while simultaneously promoting endothelial cell survival. Conversely, low shear stress and flow reversal shift the profile of secreted factors and expressed surface molecules to one that favors the opposite effects, thereby contributing to the development of atherosclerosis [16]. This complex endothelial cell response to shear stress may also provide a mechanism by which known risk factors act to promote atherosclerosis [18].

Clinical Applications

The relation between wall shear stress and the development of atherosclerosis has been studied using wall shear stress values derived in vivo from phase-contrast MR imaging, pulsed Doppler sonography, or quantitative arteriography. The relationship between wall shear stress and other known risk factors for atherosclerosis has also been investigated. Wall shear stress inversely relates to age, systolic blood pressure, and body mass index, factors directly implicated in the pathogenesis of atherosclerosis [21].

The theory of low shear stress and cyclic variations in shear stress is one that is gaining popularity. What is clinically relevant is the location of atherosclerotic lesions. This knowledge was available long before wall shear stress was being measured. Whether the knowledge of wall shear stress will have any clinical relevance is subject to discussion and is still hotly debated. However, wall shear stress mapping may become one of several screening tests for a multifactorial approach to atherosclerosis prediction in the future, and as such is receiving much attention from agencies that fund research in the early detection of atherosclerosis.

We will review the available preclinical applications of wall shear stress measurement in important vascular territories often affected by atherosclerosis.

Abdominal Aorta

The distribution and severity of atherosclerosis in the abdominal aorta is not uniform: it preferentially involves the posterior wall of the infrarenal abdominal aorta. Several investigators have measured wall shear stress in the abdominal aorta to look for an explanation. Oshinski et al. [22] calculated wall shear stress in the suprarenal and infrarenal abdominal aorta in eight healthy volunteers as summarized in Table 1. The mean and peak wall shear stress were higher...
in the suprarenal aorta than in the infrarenal aorta, with the lowest wall shear stress measured along the infrarenal posterior wall. Furthermore, a correlation was seen between the oscillatory component of wall shear stress and the development of atherosclerosis. Similar results were obtained by Oyre et al. [23] in six healthy volunteers, as summarized in Table 2.

Moore et al. [24] studied blood flow patterns in the abdominal aorta. They showed that in the suprarenal aorta the velocity profiles were mostly forward and axisymmetric, whereas in the infrarenal aorta extensive flow reversal was noted throughout diastole near the posterior wall (Fig. 3). This persistent diastolic flow was not seen in the suprarenal aorta. This localized diastolic reversal of flow is the result of the curvature of the aorta and the high percentage of flow taken away by major anterior aortic branches distal to the diaphragm [25]. Moore et al. postulated that the aortic curvature causes the velocity profile to be skewed toward the outer wall of the curvature, with the fluid near the inner wall moving at relatively low velocities. This velocity pat-

### Table 1: Wall Shear Stress Values in Human Abdominal Aorta as Measured by Oshinski et al. [22]

<table>
<thead>
<tr>
<th>Wall Shear Stress</th>
<th>Suprarenal Aorta (dynes/cm²)</th>
<th>Infrarenal Aorta (dynes/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anterior Wall</td>
<td>Posterior Wall</td>
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</tr>
<tr>
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<tr>
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<td>10.4 (2.9)</td>
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</tbody>
</table>

Note.—Measurements are mean (SD). 1 dyne/cm² = 0.1 Pa = 0.1 N/m².

### Table 2: Wall Shear Stress Values in Human Abdominal Aorta as Measured by Oyre et al. [23]

<table>
<thead>
<tr>
<th>Wall Shear Stress</th>
<th>Suprarenal Aorta (dynes/cm²)</th>
<th>Infrarenal Aorta (dynes/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimal</td>
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<td>–10.0</td>
</tr>
<tr>
<td>Peak</td>
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<td>27.2</td>
</tr>
<tr>
<td>Mean</td>
<td>6.3</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Note.—1 dyne/cm² = 0.1 Pa = 0.1 N/m².

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Fig. 3.—Graphs show velocity profiles measured in infrarenal aorta in vivo (top row) and in vitro (middle row) using MR imaging at five points (A, B, C, D, and E) during cardiac cycle. Horizontal axes are in millimeters (anterior to posterior, right to left), and points in time when each image was taken are on volume flow rate waveforms (bottom row). Vertical axes are velocity (cm/sec) for the top and middle rows, and in vitro flow (ml/sec) for the bottom row. Note that most extensive flow reversal was located along posterior wall. (Reprinted with permission from [24])

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pattern is caused by centrifugal forces moving the fluid around the curve. The branches along the anterior wall of the aorta pull a significant amount of fluid away from the posterior wall, also creating a region of relatively low flow in that location. At the aortic bifurcation, two peaks of flow reversal were also noted near the lateral posterior walls, and the lowest velocities were located near the lateral wall. These flow patterns help explain the influence of wall shear stress on the progression of atherosclerosis in the abdominal aorta. The strongest flow reversal (the posterior wall of the infrarenal aorta and the lateral posterior walls of the aortic bifurcation) corresponds to the locations with the most atherosclerotic lesions and intimal thickening [24].

In addition, Moore et al. [26] documented that the near-wall diastolic flow reversal seen in the infrarenal aorta and aortic bifurcation during rest was nearly eliminated during simulated exercise. They assumed that the changes in wall shear stress during exercise might account for some of the reduction in atherosclerosis progression seen clinically in association with exercise. It is unknown how patient positioning (erect versus supine during an MR study) might affect these flow patterns.

Ascending Thoracic Aorta

The pattern of flow in the ascending thoracic aorta is more complex than in the descending abdominal aorta. Helical flow and extensive flow reversal are consistent features of aortic flow in healthy subjects that result, at least in part, from the curvature of the arch and the strong pulsatility of flow [27–29]. Bogren et al. [28] studied 24 healthy subjects using MR velocity mapping. Systolic velocity maps were similar in the proximal aorta and the mid ascending aorta, with maximum early systolic flow along the left posterior wall. Toward the end of systole and throughout diastole, a channel of reverse flow developed in the same region in the mid ascending aorta, but in the proximal aorta it split to enter the sinuses of Valsalva, predominantly the left and right coronary sinuses. Mean percentage ratio of retrograde-to-antegrade flow was 6.3%, with most retrograde flow occurring in early diastole. Bogren et al. suggested that retrograde aortic flow assists coronary flow. Even though the flow reversal in the ascending aorta is expected to result in low wall shear stress, the ascending aorta is known to be less affected by atherosclerosis than the abdominal aorta. The reason for this contradictory observation is not known but may point to the presence of other factors besides low wall shear stress responsible for the development of atherosclerosis.

Carotid Bifurcation

Atherosclerosis in the carotid artery bifurcation has been extensively studied because of its great clinical importance. An inverse relationship exists between the in vivo measured wall shear stress and the arterial wall thickness in the carotid arteries [21, 30]. Gnasso et al. [30] measured the peak and mean wall shear stresses in the carotid arteries of 23 patients with evidence of stenosis and found that wall shear stress is lower in the arteries in which plaques are present than in plaque-free arteries. Because of the vital importance of blood flow in patients with stroke, great efforts have also been made to develop complex computer modeling of blood flow in the carotid bulb. Milner et al. [31] used such an approach to get a detailed map of variations in wall shear stress in the carotid bulb. They reconstructed three-dimensional (3D) models of the carotid bifurcation lumen from serial black blood MR images of two healthy volunteers. Common and internal carotid artery flow rate waveforms were determined from MR imaging phase-contrast velocity imaging in the same subjects and were used for the computational model. Subject-specific velocities and wall shear stresses were computed with a finite element-based model, yielding maps of a variety of wall shear stress indexes. Maps of the average wall shear stress magnitude in the carotid bifurcation of two healthy volunteers were included in this study (Figs. 4A and 4B). Hoeks et al. [32] calculated the wall shear rate in the common carotid arteries in volunteers presumed to be healthy, in

Fig. 4.—Drawings show time-averaged wall shear stress for carotid bifurcation geometry. A and B, Drawings are derived from in vivo MR imaging data from 28-year-old volunteer (A) and 32-year-old volunteer (B). Anterior and posterior views are provided to identify asymmetry of patterns. Notice contour levels. Scale of wall shear stress values is shown on bottom right side. Darker shades correspond to higher time-averaged wall shear stress, indicative of lower probability for atherosclerotic change. Comparison of A and B illustrates individual variability in wall shear stress patterns and carotid artery geometry. (Reprinted with permission from [31])
two categories: young age group (20–30 years old; \( n = 8 \)) and old age group (60–70 years old; \( n = 6 \)). These researchers found that although the peak shear rate decreases with age, the mean shear rate averaged over the cardiac cycle is the same for both age groups. They assumed that the reduced relative change in diameter, associated with a reduced elasticity of the arterial wall at older age, does not result in a higher mean wall shear rate because of the increase in diameter. This assumption corroborates earlier observations about the possible interaction between mean wall shear rate and the caliper of the artery.

Coronary Arteries

The coronary arteries are also commonly affected by atherosclerosis. The coronary arteries are unique in the body because blood flow is intermittent and shows wide phasic variations as a result of systolic contraction of the heart. Coronary systole and diastole are out of phase with systemic systole and diastole. Approximately 50% of the total coronary blood flow occurs in early diastole, 25% in late diastole, and only 25% in systole [33]. The anatomic curvatures inherent in the coronary circulation add to the complexity of the flow pattern because major epicardial arteries curve gently around the border of the heart [3]. Pathologic examination of coronary arteries reveals that the atherosclerotic plaques are located mainly along the inner side of the curved coronary arteries [3, 34–36]. The composite effects of these hydraulic factors seem to be significant in the predisposition of the coronary arteries to atherosclerotic changes and in the selection of the site of involvement [3]. Krams et al. [37] evaluated wall shear stress and vessel 3D geometry as factors determining the development of atherosclerosis in curved coronary artery segments in which atherosclerotic plaques are mainly localized on the inner curvature. They found that areas of maximum shear stress were close to the outer wall and areas of minimum shear stress were close to the inner curve.

Wall Shear Stress Measurement: Techniques and Challenges

As discussed, multiple experimental studies confirm the association between wall shear stress and early atherosclerosis. Simplistic measurements of wall shear stress seem to be adequate to help predict areas at risk. However, the precise role played by hemodynamics and wall shear stress in the development and progression of vascular disease remains unclear, in large part because of lack of in vivo studies with humans. The inability to conclusively identify the hemodynamic quantities that influence atherosclerosis may be attributed in part to the fact that flow studies are typically carried out in idealized models with averaged flow parameters, whereas sites predisposed to atherosclerosis are identified from averaged postmortem measurements [31]. The flow pattern in a blood vessel can be complex and can vary with time, as seen in the pulsatile flow pattern in the infrarenal abdominal aorta (Fig. 3). We will provide a review of how to use the velocity profiles to estimate the wall shear rate. We will then review some of the methods used to obtain blood velocity data non-invasively in vivo and discuss the limitations of the methods and how to overcome them. The methods considered will be phase-contrast MR imaging and Doppler sonography. Older approaches using quantitative arteriography will not be discussed.

Estimation of Wall Shear Rate: The Need to Interpolate from Discrete Velocity Measurements

The first step in estimating wall shear stress requires velocity measurements derived from duplex Doppler sonography, velocity-encoded cine MR imaging, or quantitative angiography. These velocity measurements are made at a discrete number of points and must be interpolated or extrapolated to obtain the velocity profile [38]. Velocity is a vector quantity, and the appropriate component of the vector must be used to calculate wall shear stress. The vector is zero at the vessel wall. The wall shear rate calculation requires an estimate of the slope of a velocity profile from at least two, preferably three, velocity values obtained near the vessel wall [22]. The accuracy of wall shear stress is a function of the spatial resolution of the velocity estimates [39] and the interpolation algorithm used. A review of several interpolation techniques for wall shear stress calculation was made by Lou et al. [38]. They compared the techniques used to estimate wall shear rate based on one, two, or three velocity measurements near the vessel wall.

The interpolation methods used can be classified according to the degree of polynomial curve fitting of the velocity profiles [38]. The simplest interpolation, called the linear method, assumes a linear velocity distribution and measures the velocity component in a single point away from the wall. If \( v \) is the component of velocity parallel to the wall measured at a distance \( dr \) from the wall, then the wall shear rate can be approximated with the following equation:

\[
\text{wall shear rate} = \frac{v}{dr}
\]

The second method, called the quadratic method, is based on a quadratic fit between two velocity measurements, \( v_1 \) and \( v_2 \), at distances \( dr_1 \) and \( dr_2 \) from the wall [38]. In another method, a third velocity is measured at a point between the two points used in the quadratic method. A least-squares fit method is adopted to accommodate all three points, or four points if the point at the wall is included, in a parabolic velocity profile. The benefit of the extra point is doubtful because it forces the velocity profiles to comply more with the data in the region farther away from the wall than with the data closer to the wall. A higher order polynomial, however, is generally less robust. As the order of the curve fitting increases, the result becomes sensitive to small amplitude, more or less randomly distributed errors in the data [38].

Pulsed Doppler Sonography

Pulsed Doppler sonography is noninvasive and is routinely used to determine the velocity distribution in the human arterial system in vivo. The Doppler technique measures the velocity component along the direction of insonation. A correction is then made to determine the velocity component along the axis of the vessel. This approach is subject to error that will propagate to the wall shear stress calculation. Pulsed Doppler sonography measures average velocities in the sensitive volume of the focused acoustic wave. This averaging is referred to as the “sample volume sensitivity function.” Velocity profiles determined from Doppler measurements are generally not known with sufficient accuracy as a result of numerous errors affecting both spatial and velocity measurements: errors in the positioning of the sonographic probe and its sample volume, alteration of the signal-to-noise ratio, echoes of the distal wall, and inadequate spatial resolution that interferes with the accuracy of velocity profile determination, particularly near the wall in which the velocity gradient is often high and has to be determined accurately [40]. We will review several of the proposed solutions to overcome these limitations.

The wall shear rate can be calculated using one central velocity and vessel diameter measurements. This simple approach was used by Gnasso et al. [21, 30] to calculate the peak and mean wall shear rates using an assumed parabolic model of velocity distribution across the arterial lumen. Some of these measurements thus represent temporal and spatial averages. Echo Doppler sonography examination to measure arterial diameter, intima-media thickness, and blood flow velocity was performed using ECG-triggered high-resolution sonography. The researchers found that Doppler sonography measurement of wall shear stresses in the com-
mon carotid arteries in vivo was reproducible [21]. The major drawback of their approach is the assumption of a linear velocity distribution and the fact that only the central peak velocity is used to measure the wall shear rate.

More complex signal processing can be used to obtain more realistic velocity profiles, as done by Brands et al. [10], who described a method to estimate noninvasively the time-dependent wall shear rate in vivo. They evaluated the velocity distribution using off-line signal processing of the sonographic signal. The off-line processing was performed in the radiofrequency (RF) domain and consisted of an RF domain velocity estimator preceded by an adaptive vessel wall filter. The latter was adopted to get an optimal discrimination between the slowly moving structures, like vessel walls, and the slowly moving blood near the vessel wall. This in vivo estimate of the time-dependent wall shear rate was reproducible, but only in relatively straight blood vessels, because in curved vessels the peak velocity shifts toward the outer wall of the vessel, thus making the wall shear stress estimate more complex. Hoeks et al. [32] used a similar approach for the measurement of wall shear stress in the carotid arteries.

Several other methods have been proposed to improve the accuracy of pulsed Doppler sonographic measurements of velocity profiles. Spatial resolution can be improved by applying a deconvolution process. Corrected deconvoluted velocity profiles have allowed noticeable improvement in the estimation of wall shear rate when compared with the uncorrected Doppler profiles [40, 41].

Even more complex approaches using 3D reformatting, mainly from Doppler and sonographic measurements, have been tested. Chandran et al. [42] performed computer simulation of 3D velocity profiles and wall shear stress distribution in a morphologically realistic 3D reconstruction of an arterial segment. They used intravascular sonography with a constant pullback technique in the abdominal aorta of dogs to obtain the velocity profiles [42]. Similarly, Krams et al. [37] combined 3D reconstruction from angiography and intravascular sonography with computational fluid dynamics and were able to measure wall shear stress and wall thickness in the right coronary artery in vivo [37].

**MR Imaging**

MR velocity measurements typically provide less temporal resolution than pulsed Doppler sonographic measurements, but MR imaging can be used to examine almost any vessel in the body without regard to overly-bone or bowel gas. Furthermore, the velocity data can be precisely matched with anatomic pictures, providing an integrated anatomic and functional examination [8]. Velocity-encoded phase-contrast MR imaging relies on the phase shift of spins moving along the direction of a bipolar velocity-encoding gradient. Phase-contrast MR imaging allows direct measurement of flow velocity, and volume flow rate can be obtained [43].

MR imaging velocity measurement represents an average value of the velocity over the entire pixel, including both moving and stationary structures. One important source of error when using MR velocity measurements for the calculation of wall shear stress is that the position of the vessel wall within the edge pixel (the pixel that is partially covered with moving blood and partially with stationary tissues) is not known because of limited spatial resolution. If the wall position in the edge pixel is not correctly estimated, an error of 34% in wall shear stress measurement can be made [22]. Another lesser source of error is the limited temporal resolution of the velocity measurements, which is more a limitation of MR imaging than of sonography. Sonographic measurements are made about every 1 msec, whereas MR imaging measurements are made every 30 msec or more [8].

Several methods have been proposed to overcome the problem of inadequate spatial resolution in the evaluation of wall shear stress by MR imaging. Strang et al. [44] suggested ignoring the edge pixel when determining the slope of the velocity profile from a polynomial fit to the velocity points. Frayne and Rutt [45] attempted to overcome extrapolation-based techniques using Fourier velocity encoding to determine the velocity distribution in a voxel that straddles the blood–vessel wall interface. These researchers found, by appropriate processing, that the velocity distribution could both determine the location of the interface in the voxel and estimate the velocity profile across the spatial extent of the voxel. From this information, estimates of shear rate were obtained with a mean error of 15% compared with 73% obtained by extrapolation of the velocity profile over multiple voxels. However, the total image acquisition times were lengthy (approximately 2 hr), which probably excludes the in vivo application of the technique to humans [45].

Oshinski et al. [22] proposed an attractive method for estimating the position of the vessel wall in the edge pixel that then allows the estimation of shear rate in the aorta in humans using MR phase velocity mapping (Fig. 5). In their method, the flow volume through a pixel is measured by multiplying the MR imaging–measured velocity through the pixel by the pixel surface area ($d^2$ for a square pixel), even if the entire pixel is not

**Fig. 5.**—Drawing shows simplified representation of velocity interpolation method for estimating wall shear stress proposed by Oshinski et al. [22]. Vertical axis represents velocity. Horizontal axis represents one axis in cross-section of vessel. $v_1$ and $v_2$ are average velocities measured by MR imaging in edge pixel and first interior pixel, respectively; $v_c$ is calculated velocity at inner side of edge pixel; $x$ is estimate of position of vessel wall within edge pixel.
Wall Shear Stress and Early Atherosclerosis

occupied by flowing material. The volume flow \( Q \) through the edge pixel thus can be measured as:

\[
Q = v_h d^2
\]

where \( Q \) is the flow rate (ml/sec) through the edge pixel, \( v_h \) is the average velocity (cm/sec) in the edge pixel, \( v_f \) is the pixel dimension (cm) for a square pixel. Next the velocity \( v_h \) at the inner side of the edge pixel is estimated. The assumption is made that the velocity profile near the vessel wall is linear, and therefore \( v_h \) is the average value of \( v_f \) and \( v_2 \) (\( v_2 \) is the velocity [cm/sec] measured with MR imaging in the first interior pixel).

\[
v_h = \frac{v_f + v_2}{2}
\]

Using the estimate of \( v_h \) and the fact that the velocity is zero at the wall, the expression for the flow in the edge pixel can be rewritten as:

\[
Q = \frac{1}{2} v_h x d
\]

Next the distance \( x \) between the vessel wall and the inner side of the edge pixel is estimated (Fig. 5). By combining equation 3 with equation 5, the location of the vessel wall in the edge pixel can be determined as:

\[
x = \frac{2 v_f d}{v_h}
\]

Using this estimate of the position of the vessel wall in the edge pixel, the wall shear rate can be determined with high accuracy. An important assumption in the theory is that the radius of the artery is large enough that a straight line, instead of a curved line, can represent the edge of the vessel in the edge pixel, and consequently this method is not applicable to medium- and small-sized vessels. The principal advantage of the technique proposed by Oshinski et al. [22] is its speed. A major drawback is that shear rate is calculated using linear interpolation and velocity measurements from adjacent voxels and, thus, the accuracy of the technique is still intrinsically coupled to the voxel size [45].

Moore et al. [26] calculated the wall shear stress from MR velocity measurements of pulsatile flow in an anatomically accurate model of the human abdominal aorta. Fluid velocities were measured with a phase-velocity-encoding gradient-echo sequence. In another study by Moore et al. [24], a variant of phase-contrast MR angiography called “free induction decay acquired echoes” (FAcE) sequence was used for velocity quantification based on the phase of the MR imaging sequence. This variant is a sequence with separate sampling of the left and right K-space half-planes that allows very short TEs with inherent motion compensation of the frequency-encoding gradient. Thus, both motion-related dislocation artifacts and signal voids caused by coherence loss in regions with irregular flow are minimal [46]. Oyre et al. [23] used the same FAcE sequence for the measurement of wall shear stress in the abdominal aorta. In both studies, measurement of wall shear stress was based on simple edge detection.

In 1998, Oyre et al. [9] described a new method for determination of wall shear stress based on circumferential subpixel edge detection. These researchers applied a priori knowledge of the parabolic blood velocity distribution in the thin boundary layer of the vessel wall to velocity data from the whole circumference of the vessel. A standard ECG gradient-echo pulse sequence with bipolar velocity-encoding gradients was used to obtain the velocity data. By this technique, a 3D paraboloid model could be fitted to the large number of velocity data obtained in the parabolic boundary layer. Position of the lumen vessel wall, wall shear stress, and volume flow were then determined at a subpixel level from the 3D paraboloid model. To assess the validity of their concept, in vitro lumen area was measured in a glass tube using MR velocimetry with a mean error of 0.6%. These researchers then measured the wall shear stress in the common carotid artery in seven healthy volunteers, the first attempt of MR imaging to estimate wall shear stress in a two-dimensional configuration. A 3D approach for the measurement of wall shear stress in areas where the blood flow is more complicated, as in the ascending aorta, was described in 1998 by Suzuki et al. [47]. They measured axial and nonaxial wall shear rates using MR velocity mapping and were able to successfully do vector analysis of the wall shear rate.

Differences in the Measured Wall Shear Stress

Most of the in vivo measurements of wall shear stress show qualitative agreement. However, differences exist in absolute values for the measured wall shear stress among different investigators. To illustrate this point, we compared published wall shear stress measurements in the common carotid arteries (Table 3). The variation in measured wall shear stress can be attributed to many factors. First, different techniques were used to obtain the blood velocity data. Second, the interpolation algorithms used to estimate wall shear stress differed. Gnasso et al. [21, 30] assumed a linear velocity distribution and estimated wall shear stress in the common carotid arteries from one central velocity measurement and a vessel diameter measurement. However, both Oyre et al. [9] and Hoeks et al. [32] found that blood flow in the common carotid artery was blunt (i.e., velocity profile was flat-topped) in peak systole and does not assume the full paraboloid pattern presumed by Gnasso et al. [21, 30]. When data of Oyre et al. [9] were analyzed in the same way as the studies by Gnasso et al., the peak wall shear stress was underestimated by 50% and the mean wall shear stress was underestimated by 22%. Third, the sites of wall shear stress measurement were inconsistent. Gnasso et al. measured wall shear stress in the common carotid artery 1–2 cm proximal to the bulb, whereas Hoeks et al. measured it 2–3 cm proximal to the tip of the flow divider. Wide quantitative variation in the measured wall shear stress along the same vessel was reported by several investigators; thus, the measured wall shear stress values should be regarded as site-specific [22, 31]. Fourth, individual variations existed because wide variation in the measured wall shear stress among different individuals was reported [22, 31]. This fact may partly explain why some individuals are more prone to atherosclerosis, because the etiology is multifactorial. Fifth, age-related changes exist in wall compliance. Also, wall excursion changes during the cardiac cycle, and the effects of

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Note.—Measurements are mean (SD) and are expressed as dynes per square centimeter. 1 dyne/cm² = 0.1 Pa = 0.1 N/m².

a Calculated from the wall shear rate values in young age group assuming blood viscosity of 3.5 mPa.s.
wall excursion changes on wall shear stress variations have not been studied. For example, the coronary wall diameter can change by 10% as a result of pulsatile flow.

Conclusion

The relation between wall shear stress and the development and progression of atherosclerosis has been well established. The non-invasive in vivo measurement of wall shear stress using MR imaging is feasible. Despite the differences in the measured values of wall shear stress, most available methods show qualitative agreement, and some valuable clinical observations have been derived from these in vivo measurements of wall shear stress. Low and oscillating wall shear stress seems to favor the development of atherosclerosis as determined by the inverse relationship between wall shear stress and arterial wall thickness. Wall shear stress also seems to depend on age, blood pressure, and body mass index. The value of wall shear stress is subject-specific and vessel-specific. Wall shear stress varies along the same vessel and around the vessel circumference. More studies are needed to document variations in wall shear stress in different vascular beds both at rest and during exercise to better understand the early atherosclerotic process. These studies may provide more insight about the effect of known risk factors for atherosclerosis on wall shear stress and how changes in these risk factors affect wall shear stress.

Atherosclerosis has a complex multiparameter etiology. Wall shear stress mapping may someday become a factor in the screening of patients predisposed to the development of atherosclerosis because of anatomic variations in the blood vessel resulting in localized areas of low or oscillatory wall shear stress. Many more clinical studies in larger patient groups are needed to validate this theory and to establish reproducibility of the technique in vivo.

References

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