Changes in Internal Carotid Artery Flow Velocities with Cerebral Vasodilation and Constriction

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SUMMARY Non-invasive Doppler-shift ultrasound, together with spectral analysis, have been used to study the changes in internal carotid artery flow velocity patterns that occur with cerebral vasoconstriction and vasodilation provoked by over-breathing and breath-holding. Significantly different waveform shapes, characteristic for each vessel, were demonstrated from the internal and external carotid arteries, making identification of the internal carotid certain. In 5 healthy subjects over-breathing for 3 minutes significantly lowered the mean height of the internal carotid waveform by an average of 32% (p < 0.001). Breath-holding for 40-60 seconds raised the mean height by an average of 31% (p < 0.001). The pulsatility index of the waveforms varied inversely to mean height. These results show that the effects of cerebral dilation or constriction are easily detected by flow-velocity changes in the internal carotid artery.

DOPPLER-SHIFT SIGNALS from the internal carotid artery have been studied previously in healthy volunteers and in patients with cerebral arteriosclerosis, induced hypertension and following administration of vasodilator drugs. In these investigations the signals were processed by a sound spectrograph (Rion model SG — 04A) or an envelope detector linked to an ink oscillograph. More recently a spectral analyzer (Spectrascribe) has been developed in our laboratory. This analyzer is capable of displaying and printing the Doppler-shift signals immediately and continuously onto light-sensitive paper so that changes in flow velocities can be observed when signals are monitored over long periods, even several hours.

For an ultrasonic pen torch arrangement, e.g. coplanar transmitter and receiver crystals, the relationship between the Doppler-shift frequency (Δf) of back-scattered radiation from a blood corpuscle moving with velocity v is given by the equation:

\[ Δf = \frac{2f v \cos \phi}{c} \] (1)

where f is the transmitted frequency, c is the velocity of sound in tissue (≈1500 ms\(^{-1}\)) and \(\phi\) is the angle between the incident ultrasound beam and the direction of blood flow. The Doppler-shift frequency is positive for blood flowing toward the crystals and negative for blood flowing away from them. For a beam frequency in the range 1-10 MHz the Doppler-shift frequencies for normal physiological blood flow (v < 1.0 ms\(^{-1}\)) lie in the audible range and can therefore be monitored with headphones. To measure the absolute velocity of each blood corpuscle it is necessary to know the angle (\(\phi\)) between the ultrasound beam and vessel axis (equation 1). However, by clamping the pencil probe at a constant angle to the skin surface throughout each examination it is possible to obtain quantitative information on changes in blood flow velocities during a procedure such as breath-holding or hyperventilation.

Carbon dioxide is a powerful vasodilator of cerebral vessels. Breath-holding raises the arterial Paco\(_2\) tension which causes active dilatation of cerebral arterioles and an increase in cerebral blood flow. Conversely, over-breathing lowers Paco\(_2\) and constricts cerebral arterioles with a consequent decrease in flow. These stimuli were used to test the possibility of detecting such induced changes in cerebrovascular impedance by direct observation of flow velocities in the internal carotid artery.

Materials and Methods

The portable apparatus consisted of a Parks (701) 5 MHz unidirectional continuous-wave Doppler velocimeter and a cassette tape recorder (Sony 124CS). Signals were monitored with a pair of headphones, recorded on magnetic tape, processed by the Spectrascribe (Medishield Corporation, UK, Hammersmith, London) and printed out continuously on light sensitive paper (Kodak, Linagraph Direct Print type 1895) in the form of a sonagram (figs. 1, 2).

The sonagram is a display of the Doppler-shift frequencies received from all blood corpuscles moving in the ultrasound beam over a period of as many cardiac cycles as required. Doppler-shift frequency is displayed along the y axis, time is along the x axis and trace intensity relates to the number of corpuscles moving at a given velocity. The outline of the sonagram is, therefore, equal to the maximum frequency shifts which are proportional to the maximum flow velocities at each instant during the cardiac cycle. This outline is referred to as the maximum frequency envelope or the sonagram waveform shape.

Two parameters were calculated from the maximum frequency envelope of each sonagram, mean height (\(\bar{h}\)) and Pulsatility Index (PI). Mean height (\(\bar{h}\)) is equal to the area under the sonagram outline.
PI — Peak-Peak

**Figure 1.** (a) Sonagram for one cardiac cycle from the internal carotid artery of a healthy male aged 28 years. The waveform displays 3 peaks. Systole is from the foot of the first peak to the end of the second peak. (b) Waveform shape redrawn to show derivation of Pulsatility Index (PI = 0.7).

Pulsatility Index (PI) is defined by peak-to-peak height divided by mean height \( \bar{h} \) as shown in figure 1 and is independent of the angle \( \phi \) between transducer and vessel over a wide range of angles. Hence \( \bar{h} \) and PI are inversely related. Both parameters were calculated on a sonagram waveform digitizer (Autograph) designed and built in our laboratory. In these experiments the probe was fixed in a clamp so as to maintain angle \( \phi \) constant. Hence from equation (1), as \( f \) and \( c \) are constant, the Doppler-shift frequency \( \Delta f \) is proportional to the blood corpuscle velocity \( v \). Therefore, under these conditions, as \( \bar{h} \) is equal to the maximum blood flow velocities averaged over the cardiac cycle, changes in \( \bar{h} \) are equal to changes in these maximum flow velocities. Comparisons of \( \bar{h} \) and PI before and after the breath-holding and hyperventilation procedures were performed on a Monroe 1930 calculator using Student's t-test for paired values.

**Examination Procedure**

Each subject lay supine for at least 10 minutes before recordings were made. An ultrasound coupling gel was applied to the tip of the probe which was then placed lightly on the surface of the neck just below the angle of the jaw. At this level the internal carotid is usually posterolateral to the external carotid artery. We have found it easier to insonate first the external carotid artery, with the probe pointing toward the head, and then the internal carotid is insonated by keeping the probe tip at the same position on the skin and moving the opposite end of the probe slightly medially. The 2 vessels were easily distinguished from each other by both the different character of their audible signals and their sonagram waveform shapes (fig. 2). When a clear signal from the internal carotid artery was obtained, the probe was fixed in a clamp to maintain it at a constant angle to the skin throughout the experiment.

Four healthy volunteers were examined during normal breathing (control readings) followed by hyperventilation for 3 min and then a further 3 min of normal breathing. Another healthy subject (GH) hyperventilated for a period of 5 min and recordings were continued for a further 5 min. During hyperventilation the volunteers were requested to breathe more deeply than usual but to maintain their normal rate of respiration. This protocol minimized any Doppler detector movement caused by the maneuver and allowed continuous deep breathing for periods of 3 or 5 min as required. Five healthy subjects inspired to approximately two-thirds maximum inspiration and held their breath for 40–60 sec. Recordings were continued for a further 20 sec after breath-holding ceased.
TABLE 1 Effects of Hyperventilation on h and PI Relative to Each Subject's Control Value Taken as 100%

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age yrs.</th>
<th>After hyperventilation</th>
<th>Period of hyperventilation (mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RP</td>
<td>30</td>
<td>79 ± 4</td>
<td>129 ± 9</td>
</tr>
<tr>
<td>MM</td>
<td>20</td>
<td>56 ± 4</td>
<td>141 ± 15</td>
</tr>
<tr>
<td>RJ</td>
<td>20</td>
<td>62 ± 6</td>
<td>160 ± 12</td>
</tr>
<tr>
<td>JC</td>
<td>32</td>
<td>67 ± 2</td>
<td>137 ± 10</td>
</tr>
<tr>
<td>GH†</td>
<td>21</td>
<td>77 ± 5</td>
<td>143 ± 17</td>
</tr>
<tr>
<td>Mean</td>
<td>25</td>
<td>68 ± 4</td>
<td>142 ± 13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>h (%)</th>
<th>PI (%)</th>
</tr>
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<tbody>
<tr>
<td>After hyperventilation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Period of hyperventilation (mins)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean ± 1 SD Control; h = 100 ± 5, PI = 100 ± 8, (for 10 successive cardiac cycles).
All values of h and PI above have p < 0.001 compared with their control value.
† = same examination.

Results

Hyperventilation

A reduction in mean height h of the internal carotid artery sonagram, ranging from -21% to -44%, was found in all subjects after over-breathing for 3 min. This was statistically significant at the level of p < 0.001 (table 1). The corresponding PI values of the sonagram waveforms increased markedly (29-60%, p < 0.001). These effects increased further in subject GH who hyperventilated for a period of 5 min (see fig. 3).

![Figure 3](http://stroke.ahajournals.org/)

**Figure 3. Hyperventilation — a typical subject (GH). (a)** Mean height (h) of sonograms from the internal carotid artery normalized by taking mean control value as 100%. Vertical bars denote standard deviation averaged over 10 cardiac cycles. (b) Pulsatility Index (PI) of sonagram waveform shape normalized to control value of 100% for the same cardiac cycles as in (a).

Table 2(a) Effect of Apnea on h Relative to Each Subject's Control Value Taken as 100%

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age yrs.</th>
<th>Recording</th>
<th>h 10 secs after start apnea</th>
<th>PI 40-60 secs after start apnea</th>
<th>Period of apnea (secs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RP</td>
<td>30</td>
<td>1</td>
<td>91 = 1*</td>
<td>131 = 4*</td>
<td>55</td>
</tr>
<tr>
<td>MM</td>
<td>20</td>
<td>1</td>
<td>82 = 3*</td>
<td>129 = 6*</td>
<td>55</td>
</tr>
<tr>
<td>JC</td>
<td>32</td>
<td>1</td>
<td>80 = 5*</td>
<td>145 = 7*</td>
<td>60</td>
</tr>
<tr>
<td>GH†</td>
<td>21</td>
<td>1</td>
<td>77 = 4*</td>
<td>139 = 13*</td>
<td>60</td>
</tr>
<tr>
<td>Mean</td>
<td>26</td>
<td>1</td>
<td>86 = 3</td>
<td>131 = 7</td>
<td>50</td>
</tr>
</tbody>
</table>

Mean ± 1 SD Control = 100 ± 5, PI = 100 ± 8 (10 cardiac cycles for control, 6 cardiac cycles for other measurements). * = p < 0.001.
† = 0.001 < p < 0.01.

Table 2(b) Effect of Apnea on PI Relative to Each Subject's Control Value Taken as 100%

<table>
<thead>
<tr>
<th>Subject</th>
<th>Recording</th>
<th>h 10 secs after start apnea</th>
<th>PI 40-60 secs after start apnea</th>
<th>Period of apnea (secs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RP</td>
<td>1</td>
<td>130 = 7*</td>
<td>66 = 11*</td>
<td>55</td>
</tr>
<tr>
<td>MM</td>
<td>2</td>
<td>135 = 4*</td>
<td>54 = 4*</td>
<td>55</td>
</tr>
<tr>
<td>JC</td>
<td>1</td>
<td>114 = 5*</td>
<td>69 = 5*</td>
<td>40</td>
</tr>
<tr>
<td>DD</td>
<td>1</td>
<td>157 = 16*</td>
<td>71 = 11*</td>
<td>60</td>
</tr>
<tr>
<td>JB</td>
<td>1</td>
<td>89 = 10</td>
<td>67 = 5*</td>
<td>60</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>134 = 9</td>
<td>69 = 9</td>
<td>50</td>
</tr>
</tbody>
</table>

Mean ± 1 SD Control = 100 ± 10, PI = 100 ± 10 (10 cardiac cycles for control, 6 cardiac cycles for other measurements). * = p < 0.001.
† = 0.001 < p < 0.01, other 3 values were not significant at this level.

Voluntary Apnea

In all subjects mean height h was raised by 19-47% after breath-holding for 40-60 sec (p < 0.001) (table 2a). Peak-to-peak measurements of the waveform shape varied inversely to mean height, thus causing PI to change by up to 61% from the control reading (table 2b). These effects are shown for subject RP (1st recording) in figure 4.

Four subjects showed a decrease in mean height of up to 23% within the first 10 sec of breath-holding (p < 0.001) after which there was a steady rise to maximum levels.
by arteriography, as well as in healthy volunteers, and we have now examined these vessels in patients with carotid artery disease. Several reports refer to differences between the flow velocity waveform shapes of Doppler-shift signals recorded from the internal and external carotid arteries. We have now examined these vessels in patients with carotid artery disease demonstrated by arteriography, as well as in healthy volunteers, and have found that the internal and external carotid arteries are easily distinguishable from each other by listening to their audible Doppler signals and simultaneously inspecting their sonagram waveform shapes. The waveform shape detected from each vessel is principally determined by the flow velocity wave from the heart together with the effects of reflected waves from distal arterial junctions and the periphery. Changes in vessel wall compliance that occur with age or the presence of any arterial disease will further modify the waveform pattern. The internal carotid waveform is a combination of both internal and external carotid waveforms as this artery supplies the face and scalp. The internal carotid sonagram is characterized by a relatively higher diastolic flow velocity level which is compatible with the uniform diameter of this vessel until it divides into the low impedance vascular beds of the brain. The common carotid waveform is a combination of both internal and external carotid waveforms as this artery supplies both these vascular systems.

Although only a small number of subjects have been examined in this study the results show consistent and repeatable changes in internal carotid artery sonograms during over-breathing and breath-holding. During over-breathing, even allowing for the difficulty of maintaining the probe at a constant angle to the skin for 6-10 min, the results were as expected; a reduction in blood flow velocities due to cerebral vasoconstriction secondary to a lowered Paco₂. During voluntary apnea an unexpected finding was a diminution in sonogram mean height during the first 5-10 sec of breath-holding. However, the increase in intrathoracic pressure that occurs at the commencement of breath-holding causes an increase in intracranial pressure and a decrease in venous return to the chest resulting in a decreased cardiac output. These effects will reduce flow velocities in vessels perfusing the brain and probably account for the initial reduction in mean height observed in the internal carotid artery. The subsequent rise in mean height is attributed to vasodilatation following CO₂ retention.

The opposing changes in sonogram mean height of about 30% found for the stimuli used in this study are in accord with findings of Kety and Schmidt who showed a decrease in cerebral blood flow of 35% after 10 min voluntary hyperventilation and an increase of 75% by breathing a mixture of 5-7% CO₂ in air. The cerebrovascular reactivity to Paco₂ changes brought about by over-breathing, breath-holding or direct CO₂ inhalation may change in different physiological/pathological situations, for example in migraine, cerebral arteriosclerosis or response to cerebral vasodilator drugs.

Acknowledgments
We are indebted to the volunteers for their help, the Migraine Trust for a grant, and to all our colleagues in the Guy’s Non-Invasive Angiology Research Group for their help and advice.

References
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Flow Disturbances at the Apex and Lateral Angles of a Variety of Bifurcation Models and Their Role in Development and Manifestations of Arterial Disease

ALASDAIR D. MALCOLM, M.SC., F.R.C.P. (C) AND MARGOT R. ROACH, M.D., PH.D.

SUMMARY Dye flow patterns were studied in 12 glass model bifurcations with angles of 45, 90, 135, and 180°, and area ratios of 0.78, 1.03 and 1.27. At the apex, the dye formed a saddle zone, and streamlines from the core which entered this region were swept over the upper and lower surfaces to enter the lateral angles. Qualitatively, the shape and size of the apex played a key role in this effect. Boundary layer separation occurred in the lateral angles, and increased as flow into the branch was reduced. If the branch was occluded, a complex vortex developed in the first few diameters of the branch, and no flow occurred beyond this, even though the occlusion was about 20 diameters downstream. The results were comparable with steady and pulsatile flow. The implications of these results for the localization of atherosclerosis are discussed.

FLUID DYNAMIC FORCES are probably important in human atherogenesis, although the exact mechanism of production has not yet been determined. Lesions are most common near bifurcations and orifices.

Hot-film anemometry has been used to study blood flow in the arteries of large animals, and of man, with this method is that the probes are so large that additional flow disturbances are produced, particularly near the wall. Shear stress distribution at the wall of a rigid, plastic, arterial cast has been measured by an electrochemical technique with flush-mounted probes. Mathematical modelling has not yet been developed to the point at which comprehensive analysis of realistic 3-dimensional flows are possible. Open-channel model experiments with surface powder patterns or neutrally buoyant resin particles have been reported. However, flow in open channels and in 2 dimensions differs fundamentally from pipe flow since secondary motions cannot occur. Tubular glass models with tracer particles or dye streamlines are more comparable to the biological situation.

A wide range of configurations of bifurcations exists in the human arterial system. We have conducted a study in a family of glass model bifurcations in an attempt to determine if the differences in flow patterns could be due to variations in area ratio or to angle of bifurcation. We also restricted flow in parts of the bifurcation to examine the role of flow imbalance.
Changes in internal carotid artery flow velocities with cerebral vasodilation and constriction.
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Stroke. 1979;10:331-335
doi: 10.1161/01.STR.10.3.331

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