Measurement of Carotid Blood Flow in Man and its Clinical Application

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SUMMARY  With the use of a new ultrasonic volume flow meter (VFM), over 8000 measurements of common carotid blood flow were made in 120 normal control subjects and 550 patients with various neurological disease. The accuracy of the flow meter in measuring blood flow on an experimental model ranged from 93 to 97%.

In normal subjects, common carotid blood flow varies with age. It increased from newborn to age 20 and gradually decreased thereafter. In normal healthy subjects, the flow varies within ± 6.7% (2SD) at one sitting (intrasession) and ± 21.2% (2SD) from week to week (intersession study). Carotid blood flow varies linearly with $P_{CO_2}$ and increased markedly in response to endotracheal intubation. In healthy adults, the flow ratio between the two common carotid arteries is 1.07 ± 0.052. This ratio increases in patients with transient ischemic attacks to 1.28 ± 0.23 ($p < 0.05$) and in patients with intracranial space occupying lesions to 1.46 ± 0.39, ($p < 0.01$).

In 26 consecutive cases of carotid endarterectomies, the preoperative common carotid blood volume flow was 5.1 ± 1.0 cc/sec. All cases preoperatively had at least 30% stenosis and ranged from 30 to 100% stenosis. The carotid blood volume was significantly increased post-operatively ($p < 0.001$). The overall accuracy in detecting carotid and cerebral arterial disease is 89% with sensitivity of 96% and the specificity of 71%.

Our clinical experience indicates that this device is not only a valuable noninvasive diagnostic tool for evaluation of carotid disease but also appears to be useful in assessing cerebral blood flow.

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ULTRASONIC DOPPLER FLOW METERS have been used extensively in recent years in the evaluation of the hemodynamics of the vascular system. However, the currently routinely used devices have not been able to determine the actual amount of blood flow in cc/sec. In our previous paper, we have reported the accuracy of a new Doppler device, the transcatheter Doppler Flow Meter-VFM, in measuring the actual flow in cc/sec on an experimental model.1 In this paper we summarize our experiences in the use of this device in assessing common carotid blood flow in various clinical states.

Principle

The device was developed by Furuhata and his coworkers with collaboration of Hayashi-Denki Co., Kawasaki, Japan in 1978.2 An A-mode transducer is used to measure the diameter of the pulsating artery in real time, and "an angle-independent"2 Doppler ultrasound technique to measure the velocity of blood flow at a cross-section of the common carotid artery.2,3 The diameter is measured and tracked by a phase-locked echo-tracking method.4 The operator selects a point in the A-mode echo of the artery wall and moves a tracking gate to coincide with it. The tracking gate will then lock onto and track the motion of a single cycle from the echo of the wall of the artery. The diameter of the pulsating artery is calculated every 2 msec from the distance between two tracking gates. The system is capable of measuring arteries 2 to 30 mm in diameter at a depth of 3–70 mm, with a resolution of 0.5 mm.1,5

In order to measure the true diameter of the artery, the angle of the sound beam of A-mode has to be maintained at 90 degrees relative to the longitudinal axis of the artery. This is accomplished by having the echo from the vessel wall register on the cathode ray tube (CRT) only if the incident angle is within ± 5 degree from the desired 90 degree.1,5 A carrier frequency of 5 MHz at 10 KHz repetition rate is used for the Doppler probe. A sharp cut-off crystal filter extracts the Doppler frequency band of interest. The band-width of the crystal filter limits the velocity range of this device to between 9 and 105 cm/sec.

The received values are processed by a built-in computer to calculate the volume of blood flow. The Volume Flow Meter (VFM) provides a CRT, a hardcopy analog and a digital display of the data. The data consists of mean and range of flow (cc/sec) and velocity (cm/sec) and range of wall motion of the artery (mm), in real time and averaged across 5 heartbeats.5

Previously, the uncertainty of the angle between the probe and the blood vessel has prevented accurate flow measurements with the Doppler Techniques. The new device circumvents this problem by deducing the true velocity using a probe with a known fixed angle between two receiving transducers and a transmitting transducer. The mathematical formula derived is shown in figure 1.

Reliability of the Device on Experimental Models

(1) Comparison with Electromagnetic Flow Meter (EMF)

(A) Static Flow. In a series of experiments carried out in a model system the volume flow meter described above was compared with flow measurements ob-
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Comparison between VFM flow readings and true flow measurement by constant flow pump. A known volume of blood specimen was transferred from one graduated cylinder to another by a constant flow pump through a 5 mm Teflon tube. The flow reading by VFM and the actual amount of blood specimen collected in the cylinder correlated well.

The ratio between the value of the VFM reading and the actual flow was 2% lower with a standard error of 0.4%. The ratio was higher in flows of under 2 cc/sec and over 18 cc/sec. We repeated the experiment for flows of less than 2 cc/sec using a 2 mm tube to obtain velocities comparable to newborns whose average artery diameter is 3 to 4 mm. There was a static error of 11% and a coefficient error of 22%. However, the correlation coefficient was 0.99.*

Materials and Methods

1. Subjects
A total of 670 cases were studied. Of these, 120 were normal subjects from newborns to over 60 years of age and the remaining 550 cases were patients with various neurological conditions, such as peripheral nerve disease, intracranial lesions, transient ischemic attacks (TIAs) and extracranial vascular diseases. The examination was carried out with the subject relaxed in a supine position. A transducer was placed over the common carotid artery one to two finger breadths above the upper edge of the clavicle. After setting the gates on optimum near and far side wall echoes of the artery and obtaining good quality velocity waves, the computation switch was activated (fig. 3).

2. Variability of the Common Carotid Blood Flow
Serial intrasession (at one sitting) variability and intersession (week to week) variability and left and right difference in flow was evaluated in 5 normal volunteers.

The mean and standard deviation was calculated from the 5 readings taken on each common carotid artery. All the data was then normalized using the subject mean reading as "1.00." From this the standard deviation of all the data was calculated. This is the standard deviation of all the subject’s data expressed as

FIGURE 1. Schematic diagram of probe and device to measure volume flow. The probe consists of four piezoelectric transducers. An A-mode transducer measures the diameter of the artery. Rb., T. and Ra. are Doppler transducers and determine the velocity of the blood flow. These values are processed by a built-in computer to calculate the volume of the blood flow in cc/sec, using the formula shown in the diagram.

FIGURE 2. Comparison between VFM flow readings and true flow measurement by constant flow pump. A known volume of blood specimen was transferred from one graduated cylinder to another by a constant flow pump through a 5 mm Teflon tube. The flow reading by VFM and the actual amount of blood specimen collected in the cylinder correlated well.

Human blood sample from a blood bank was pumped through a Teflon tube (2 and 5 mm in diameter) by a constant flow pump. The transducer of the VFM was placed 15 mm away from the tube to monitor the flow. Five hundred to seven hundred cc of blood was pumped from one graduated cylinder to another. Based on the time required to transfer the known amount of blood, the actual flow rate was calculated. The ratio between the value of the VFM reading and the actual flow is shown in figure 2. With the 5 mm tube, the ratio was nearly one to one. Flow was adjusted in incremental amounts from 2 to 18 cc/sec. The VFM value was 2% lower with a standard error of

*Measurement of pulsatile arterial flow. A by-pass between the abdominal aorta and the inferior vena cava in an anesthetized dog was used. VFM/EMF ratio for the pulsating arterial specimen was 0.98. The correlation coefficient was 0.94 on the 5 mm diameter artery. A similar high ratio and coefficient were observed on an 8 mm vessel and the irregular branching iliac and abdominal artery.†

(2) Actual Flow Measurement by Constant Flow Pump
Human blood sample from a blood bank was pumped through a Teflon tube (2 and 5 mm in diameter) by a constant flow pump. The transducer of the VFM was placed 15 mm away from the tube to monitor the flow. Five hundred to seven hundred cc of blood was pumped from one graduated cylinder to another. Based on the time required to transfer the known amount of blood, the actual flow rate was calculated. The ratio between the value of the VFM reading and the actual flow is shown in figure 2. With the 5 mm tube, the ratio was nearly one to one. Flow was adjusted in incremental amounts from 2 to 18 cc/sec. The VFM value was 2% lower with a standard error of 0.4%. The ratio was higher in flows of under 2 cc/sec and over 18 cc/sec. We repeated the experiment for flows of less than 2 cc/sec using a 2 mm tube to obtain velocities comparable to newborns whose average artery diameter is 3 to 4 mm. There was a static error of 11% and a coefficient error of 22%. However, the correlation coefficient was 0.99.*

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DIGITAL DISPLAY

FIGURE 3. A view of the VFM examination in a laboratory setting. A probe is placed over the common carotid artery just above the clavicle (below the carotid bifurcation). After obtaining good arterial wall echoes and velocity waves on the CRT, the switches for measurement (1), computation (2) and printout (3) are pressed.

3. Criteria for Interpretation of Angiogram and VFM

(A) Angiographic Criteria for Abnormality

1. Carotid Stenosis. More than 40% reduction of the diameter of the carotid artery measured in either of two planes at the level of the most severe stenotic area compared to the nearest normal portion of the artery.

2. Cerebral Arteriosclerosis. Unequivocal reduction in the diameter of major cerebral (the anterior and middle cerebral) arteries due to spasm, vasculitis or atherosclerosis with or without retrograde flow.

3. Abnormal Carotid Artery Other Than Stenosis. Severe looping, obvious plaque or narrowing resulting in less than 20% reduction in the diameter of the internal carotid arteries.

(B) Primary Criteria. a) Less than 6.0 cc/sec of common carotid flow per side. b) High to low flow ratio between the two carotids greater than 1.20. c) Excessively high mean volume flow (over 15 cc/sec) with greater than 30% fluctuation in the flow.

(B) Secondary Criteria. a) Irregular velocity wave form. b) Mean velocity higher than 20 cm/sec. c) Over 30% decline of carotid flow upon compression of the ipsilateral superficial temporal and facial arteries. d) Velocity less than 10 cm/sec. e) Arterial diameter of greater than 9.0 mm.

When any of the primary criteria, or two of the secondary criteria are observed the test is defined as a positive. A positive secondary criterion occurring alone may identify technical errors.

Results

1. Normal Control

1. Variation With Age

In the 32 newborns with age of 2.9 ± 2.3 days the volume flow was 1.6 ± 0.46 cc/sec. The flow then increased to an average of 3.9 ± 0.5 cc/second at one month and to 7.4 ± 0.3 cc/sec at three years. The blood flow reaches the highest level between 5 to 20 years of age with a mean of 8.5 ± 1.3 cc/sec. The flow begins to decline thereafter. From 21 to 40 years of age the flow is 7.99 ± 1.5 cc/sec. In the 40 to 60 years age group the mean flow is 7.21 ± 1.15 cc/sec while in the group of age over 60, it decreased to 6.7 ± 0.49 cc/sec. The overall range of acceptable normal values for flow was 6 cc/sec to 11 cc/sec over the age range of 5 to over 60 years (table I).

2. Reproducibility

(A) Intrasession Reproducibility: The standard deviation of repeated intrasession measurement was 3.8%. This indicates that if a patient has repeated readings on one side, he will have a reading that could be within plus or minus 7.6% (2SD) variation.

(B) Intersession Reproducibility — The standard deviation was 10.6%. This indicates that if a patient is tested on different days from week to week, his readings could fluctuate over a range of ± 21.2% (2SD) from the average flow. However, even with this fluctuation the flow remains within the normal range of flow of 6 cc/sec to 11 cc/sec (fig. 4).

3. Side to Side Flow Variation and Ratio

The high to low flow ratio between the two carotids was 1.07 ± 0.052. Correlation between the left and right side between sessions was calculated to see if the variations were due to a symmetric change in cerebral blood flow or due to lateralized changes. The relatively low correlation of 0.63 suggested that both occur. There were no consistent left to right differences in flow.
TABLE 1

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean flow cc/sec</th>
<th>High to low flow rate</th>
<th>Mean diameter</th>
<th>Wall motion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(L)</td>
<td>(R)</td>
<td>(L)</td>
<td>(R)</td>
</tr>
<tr>
<td>Normal control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Newborn(2.9 ±2.3 days old)</td>
<td>1.6 ±0.46</td>
<td>1.6 ±0.30</td>
<td>1.03</td>
<td>3.9 ±0.65</td>
</tr>
<tr>
<td>5-20 (2.9 ±10.3)</td>
<td>8.5 ±1.30</td>
<td>8.5 ±1.28</td>
<td>1.07 ±0.07</td>
<td>6.7 ±0.64</td>
</tr>
<tr>
<td>21-40 (4.1 ±13.1)</td>
<td>7.99 ±1.5</td>
<td>7.67 ±1.3</td>
<td>1.07 ±0.13</td>
<td>7.2 ±0.50</td>
</tr>
<tr>
<td>41-60 (4.1 ±13.1)</td>
<td>7.21 ±1.15</td>
<td>7.48 ±1.10</td>
<td>1.10 ±0.07</td>
<td>7.5 ±0.77</td>
</tr>
<tr>
<td>61-over (4.1 ±13.1)</td>
<td>6.7 ±0.49</td>
<td>6.6 ±1.30</td>
<td>1.09 ±0.05</td>
<td>7.16 ±0.65</td>
</tr>
<tr>
<td>Subnormal control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post partum (24 ±5 y.o.)</td>
<td>6.9 ±1.0</td>
<td>6.4 ±1.1</td>
<td>1.08 ±1.1</td>
<td>7.05 ±0.49</td>
</tr>
<tr>
<td>Peripheral nerve and spinal disease (41 ±13 y.o.)</td>
<td>8.5 ±1.3</td>
<td>8.2 ±0.60</td>
<td>1.04 ±0.05</td>
<td>7.5 ±0.50</td>
</tr>
</tbody>
</table>

(4) Physiological Variation

(A) Hyper and Hypoventilation and Sit-up Exercise. Common carotid blood flow was monitored before, during and after hyper and hypoventilation and sit-up exercises. Hyperventilation tended to lower carotid flow in all of the cases. However, hypoventilation or exercise did not cause significant change in 5 subjects without evidence of cerebral, cardiovascular, or intracranial diseases. In a typical response from a 30 year old female, the flow decreased from 9.6 cc/sec to 4.67 cc/sec within 10 deep rapid respiratory cycles. The flow rapidly returned to baseline at the cessation of hyperventilation.

(B) With Response to Controlled Ventilation Changes. The common carotid blood flow was monitored at an average of 4 readings per minute, and arterial blood gases determined in 6 patients without clinical evidence of carotid or cerebral arterial disease during general anesthesia. At the lowest P\textsubscript{aCO\textsubscript{2}} of 17 torr, the carotid flow decreased from baseline value of 9.0 cc/sec to 5.3 cc/sec and at the highest P\textsubscript{aCO\textsubscript{2}} of 49 torr the flow reached 12.02 cc/sec. The correlation coefficient between P\textsubscript{aCO\textsubscript{2}} and carotid flow is between 0.777 and 0.929. The response of carotid blood flow to P\textsubscript{aCO\textsubscript{2}} is indicated by the slope of the regression line (fig. 5).

(C) In response to endotracheal intubation. The common carotid blood flow, in general, is relatively stable during the course of general anesthesia, except during intubation. Flow is markedly elevated (double to triple baseline value) in response to the endotracheal intubation (fig. 6). Frequently used pharmacologic agents such as sodium pentothal, and neuromuscular blocking agents do not change flow significantly. However, sodium nitroprusside induced hypotension produced an unexpected increase in carotid flow, as measured by the VFM within the range of autoregulation.

2. Patient Controls (without cerebrovascular pathology)

(1) Other neurological disease

Twelve patients with peripheral nerve and musculoskeletal disease without any evidence of cerebrovas-
cular disease were examined. The mean carotid blood flow was $8.22 \pm 0.60$ cc/sec. The high to low flow ratio was $1.04 \pm 0.54$. These values were comparable to the values of an age matched normal control group.

(2) In the postpartum period

Thirty subjects averaging 2.4 days post delivery either by spontaneous vaginal or by caesarian section were studied. There was no statistical difference in the common carotid flow between the two groups ($t = 0.58$, N.S.).

3. Patients with cerebrovascular pathology

(1) Carotid and/or cerebral arterial disease

Seventy-seven consecutive patients (154 carotids) with cerebrovascular symptoms were evaluated with VFM with reference to volume flow, velocity and flow ratio. All patients had bilateral biplane carotid arteriograms. The degree and character of the carotid stenosis was assessed using the above criteria for interpretation of the angiogram and VFM. Although the statistical analysis included only cases with greater than 40% stenosis for purposes of comparison of the flow and/or ratio to the degree of stenosis, in figures 7 and 8 cases with 21–40% stenosis were included.

(A) Unilateral. 32 cases had unilateral 20% or greater reduction in the diameter of the artery, the average was 67.6% (Range: 25% to 100%).

a) Internal carotid

The mean high to low ratio between the two carotids was $1.3 \pm 0.2$ in cases with 21 to 40% stenosis, $2.1 \pm 0.5$ with 41 to 70% stenosis, $2.6 \pm 1.5$ with 71 to 90% stenosis and $4.2 \pm 3.7$ with cases of 91–100% stenosis (fig. 7).

The mean volume flow in the common carotid artery was $6.4 \pm 0.7$ cc/sec with 21–40% stenosis, $5.7 \pm 0.9$ with 41 to 70% stenosis, $5.5 \pm 1.8$ with 71 to 90% and $3.5 \pm 1.8$ cc/sec with 91–100% stenosis (fig. 7).

The mean velocity in the common carotid artery was $16.0 \pm 5.4$ cm/sec with 21–40% stenosis, $10.2 \pm 2.5$ on 41 to 70% stenosis, $10.7 \pm 1.8$ with 71 to 90% stenosis and $2.5 \pm 2.7$ with 91 to 100% stenosis. The degree of stenosis and flow volume was correlated inversely, as expected with the correlation coefficient of $-0.73$ ($p < 0.01$).

b) Common Carotid

There was marked fluctuation or abnormally high velocity (over 20 cm/sec) in all 4 cases with stenosis of the common carotid artery when the probe was placed near or at the stenotic site. Zero flow was observed in two cases of complete occlusion of the innominate artery.

(B) Bilateral. There were twenty-four cases (48 arteries) in this series. The degree of reduction of the diameter on the higher stenotic side was 86.3% (Range: 50–100%) and on the lower stenotic side was 51% (Range: 26–100%). The mean high to low ratio was $2.4 \pm 3.7$ (range = 1.06 to 19.79). The mean flow on the more severely stenotic side was $7.0 \pm 4.6$ cc/sec, (range = 0.7 to 30 cc/sec) significantly different from age matched controls ($p < 0.01$) for both flow ratio and volume flow. Abnormally high velocity may be registered with as low as 30% stenosis when the probe is placed near or at the stenotic site. The magnitude of fluctuation of velocity does not correlate with the degree of stenosis. The degree of reduction of flow or the flow ratio between the carotids could not distinguish the grade of stenosis of the carotid artery when the stenosis was present bilaterally. Some cases had a wide range of flow fluctuation from a maximum of 95 cc/sec.
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Volume flow in cases of unilateral and bilateral carotid stenosis and cerebral arteriosclerosis. Degrees of the unilateral carotid stenosis are compared.

to a minimum of 3 cc/sec. The flow ratio of these cases ranged from 3.24 to 19.79.

c) Cerebral arteriosclerosis and looping of the carotid artery

There were 14 cases in this series. The mean flow ratio was 1.4 (Range: 1.03 - 2.40). The flow on the lower side was 6.2 ± 1.6 cc/sec and the velocity was 13.2 ± 3.4 cm/sec for the group with cerebral arteriosclerosis or carotid disease with or without carotid stenosis less than 20%. There was no significant difference in flow ratio or volume flow from age matched controls (t = 1.59, N.S.). These cases included loops or kinks or multiple plaques in the internal carotid, narrowing of the intracranial internal carotid, or major cerebral occlusions (anterior or middle cerebral artery). There was one additional case of fibromuscular dysplasia.

d) TIA's without cerebral angiographic confirmation

In the early phase of this study, nineteen consecutive cases of suspected TIA were evaluated. The mean age was 59 ± 10.1. The flow ratio between the two carotids was 1.28 ± 0.4 (2 SD). The normal value for the same age group is 1.077 ± 0.08 (2 SD) (fig. 9). There was significant difference from age matched control (p < 0.05).

e) Follow-up flow study after carotid endarterectomy

There are 26 consecutive cases for this study. Twen-

ty cases had unilateral stenosis ranging from 30% to 100%, mean 73 ± 20.5 and 5 cases of bilateral stenosis ranging 40 to 100%. The preoperative blood volume flow was 5.1 ± 1.0 cc/sec, and 6 days postoperatively the flow was increased to 8.4 ± 3.6 cc/sec (p < 0.001). During 3 to 9 months follow up study the flow did not significantly change (8.8 ± 3.5 cc/sec). Two cases however, had artificially high flow (17.4 to 22 cc/sec). This finding suggests either severe stenosis of the common carotid artery or near complete occlusion of the internal carotid artery (fig. 10).

(2) Other cerebrovascular disease (AVM)

There were 2 cases of arteriovenous malformation. The volume flow was markedly elevated to 11.04 cc/
Carotid flow in a case of brain death just before, during and after resuscitation. The flow of 3 to 4 cc/sec is approximately equal to the flow of the external carotid artery. DEFIB.:defibrillation. O:Normal flow (estimated).

4. Accuracy for assessment of cerebral and carotid disease

The result of the VFM was compared with bilateral carotid angiogram to evaluate the VFM ability to detect significant carotid stenosis and cerebral or carotid arterial disease. For statistical purposes the primary criteria of flow and ratio or combined have been included in the calculations because of their objectivity. Velocity values and the secondary criteria are supplemental in individual instances but do not enter into or influence the statistical evaluation of the accuracy of the VFM. The accuracy of the VFM was defined in terms of its sensitivity (ability to detect the presence of disease) and specificity (ability to recognize the absence of disease). Within the framework outlined in table 2 the results shown in table 3 were obtained. This table defines the sensitivity and specificity using a single criterion of either flow or ratio. For purposes of screening the results obtained were greatest considering flow alone. For purposes of evaluating symptomatic carotid disease, the results were greatest considering either ratio alone or combining ratio and flow. When comparing flow alone, we have considered the total number of arteries. However, for calculations using ratio between the carotids and the combined data we have considered the total number of patients (74 patients).

Discussion

This non-invasive flow meter allows simultaneous measurement of artery diameters by A mode ultrasound and velocity measurements by an angle insensitive doppler technique in the same cross sectional area to allow the calculation of volume flow in cc per sec. Dynamic change in flow in cc/sec secondary to emotional change, hyperventilation etc., hence can be evaluated quantitatively. It further has the capability of following carotid flow changes occurring in a variety of disease states affecting the cerebral circulation. These include focal stenosis of the carotid artery as well as diffuse decreases secondary to increased intracranial pressure or cerebral arteriosclerosis. Disorders resulting in significant increase in flow (such as AVM) can also be detected.

Previously, carotid flow data have been available only by the use of an electromagnetic flow meter. This requires surgical exposure of the vessel. Our previous in-vitro experiments have shown a high correlation between EMF measurements and those recorded by the VFM. In addition we have documented the accuracy of the VFM with actual measurements of flow obtained by a constant flow pump. Other methods of measuring cerebral blood flow, such as the Xenon isotopic methods, allow measurements of total or regional cerebral blood flow but not of carotid blood flow. They also have poor temporal resolution and may not be suitable for rapid serial studies.

There are several technical criteria which must be met in order to achieve accurate recordings. These are: good far and near side echoes from the walls of the carotid artery, and high quality velocity tracings from the two receiving transducers on the Cathode Ray Tube.
(CRT) display during the computation period of 5 heartbeats. Sufficient coupling gel should be used. An experienced operator can easily locate the common carotid artery. At least four flow determinations are taken for each patient to assure reproducibility of the readings. The device is simple to operate and the results are immediately available. Our normal values for the common carotid flow for newborns and adults correspond well with published values obtained by venous occlusion plethysmography, electromagnetic flow meter, and Xe 133 clearance technique. Total cerebral blood flow in man, as reviewed in many literature sources, average 54 mls/min/100 g brain tissue. With an average brain weight of 1400 g. This is equivalent to 6.3 cc/sec/side.

The internal carotid to common carotid artery flow estimates to be 70% and the external carotid flow is approximately that of vertebral flow (30%). Hence, common carotid arteries flow which this device measures indirectly, represents cerebral blood flow. It should be pointed out however, that our comparison to cerebral blood flow figure in literature is limited by the availability of accurate data relating common carotid flow to cerebral blood flow.

Our data showing a decline of 21% in the group over age 60 compared to the 21–40 age/group (8.5 cc/sec/side to 6.7 cc/sec/side) is close to the 25% drop between ages of 20 to 70 reported by Naritomi et al.

The large week to week variability in common carotid artery flow suggests that dynamic changes in cerebral circulation take place even in the resting, awake, healthy individuals, hence, minor changes in flow should not be over-interpreted. Our data of plus or minus 21% change correlates well with the study by Obrist et al using 133 Xe inhalation method. Similar large test-retest coefficients of variation have been reported from the internal carotid injection method. However, Austin et al and Prencipe reported a variation of only ± 14% by intravenous or intracarotid Xe injection method respectively. Because those

### Table 2 Outline Used for Statistic Analysis of the Accuracy

<table>
<thead>
<tr>
<th>Ratio Alone</th>
<th>ANGIOGRAM RIGHT</th>
<th>ANGIOGRAM LEFT</th>
<th>INTERPRETATION</th>
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<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>True Negative</td>
</tr>
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<td>+</td>
<td>+</td>
<td>True Positive</td>
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<td>-</td>
<td>+</td>
<td>False Negative</td>
</tr>
</tbody>
</table>

**Flow Alone**

<table>
<thead>
<tr>
<th>ANGIOGRAM</th>
<th>INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>True Positive</td>
</tr>
<tr>
<td>-</td>
<td>True Negative</td>
</tr>
<tr>
<td>-</td>
<td>False Negative</td>
</tr>
<tr>
<td>+</td>
<td>False Positive</td>
</tr>
</tbody>
</table>

**Combined**

<table>
<thead>
<tr>
<th>Abnormal Flow and/or Ratio With Positive Angiogram:</th>
</tr>
</thead>
<tbody>
<tr>
<td>True Positive</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormal Flow and/or Ratio With Negative Angiogram:</th>
</tr>
</thead>
<tbody>
<tr>
<td>False Positive</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal Flow and Ratio With Positive Angiogram:</th>
</tr>
</thead>
<tbody>
<tr>
<td>False Negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal Flow and Ratio With Negative Angiogram:</th>
</tr>
</thead>
<tbody>
<tr>
<td>True Negative</td>
</tr>
</tbody>
</table>
TABLE 3  Four Cases were Excluded from this Statistical Analysis; Two Arteriovenous Malformation, One Brain Tumor with Carotid Stenosis, and One with Incomplete Arteriographic Study. This Statistical Analysis was Done Using the Two Primary Criteria; Flow or Ratio Alone or Combined.

<table>
<thead>
<tr>
<th>&gt;40% STENOSIS WITH ASCVD</th>
<th>RATIO ALONE</th>
<th>FLOW ALONE</th>
<th>COMBINED</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRUE POSITIVES (D)</td>
<td>51</td>
<td>58</td>
<td>58</td>
</tr>
<tr>
<td>TRUE NEGATIVES (A)</td>
<td>15</td>
<td>51</td>
<td>6</td>
</tr>
<tr>
<td>FALSE POSITIVES (C)</td>
<td>6</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>FALSE NEGATIVES (B)</td>
<td>2</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>TOTAL (A + B + C + D)</td>
<td>74</td>
<td>148</td>
<td>74</td>
</tr>
</tbody>
</table>

OVERALL ACCURACY: \( \frac{(A + D)}{(A + B + C + D)} \) 89% 74% 86%

SPECIFICITY: \( \frac{A}{(A + C)} \) 71 85 46

SENSITIVITY: \( \frac{D}{(B + D)} \) 96 66 95

NEGATIVE PREDICTIVE VALUE:
- \( \frac{A}{(A + B)} \) 88% 63% 67%
- \( \frac{D}{(C + D)} \) 89 87 89

studies did not evaluate short term (intrasession) test-retest reliability, it is difficult to differentiate patient variability from instrument uncertainty.

On the other hand, despite our 21% variability, all the readings fall within the well defined limits of 6–12 cc/sec range of normal controls. This suggests that despite the fluctuations, abnormal cerebral vascular disease may be recognized and that this method is useful in defining pathological low flow or high flow states.

In-vitro studies of flow performed on a 2 mm tube helps to validate its use in infants whose common carotid arteries are on the order of 3 to 4 mm in diameter. Currently, there is no widely accepted method in measuring the carotid cerebral blood flows in the infant. The venous plethysmography method of measuring cerebral blood flow is highly dependent on the compliance of the calvarium, thus making it unsuitable for use in older children once skull sutures have been closed. In the normals, there is a large increase in common carotid flow from newborn to age 3.

It has been shown previously that carotid blood flow is also profoundly affected by the changes in arterial \( P_{CO_2} \) in conscious man as well as under anesthesia. Over the range of 17 to 47 torr, carotid blood flow varies linearly with \( P_{CO_2} \). The marked elevation of carotid blood flow observed with endotracheal intubation is clinically important. In certain conditions the volume flow may not be associated with other hemodynamic changes, such as arterial hypertension and tachycardia. The rapid rise of the volume flow may be hazardous to patients with increased intracranial pressure or cerebral aneurysm.

The preliminary results for detection of carotid and cerebral arterial disease are encouraging. When the test is used for screening asymptomatic population with a low incidence of carotid disease, it is preferable to have a high specificity and a high positive predictive value to avoid unnecessary arteriography. Therefore, from our data it is preferable to use the single criterion of flow alone. Our data indicates with flow alone as the criterion a specificity of 85% and a positive predictive value of 87%. On the other hand, if the population has a high probability of symptomatic carotid disease, high sensitivity and high negative predictive value are important to avoid missing clinically important lesions. Therefore, from our data it is likewise preferable to use the single criterion of ratio alone or the combined criteria. Our data indicates with ratio alone a sensitivity of 96% and a negative predictive value of 88%. Using the combined criteria our data indicate a sensitivity of 95% and a negative predictive value of 67% (table 3). A relatively low negative predictive value is due mainly to the fact that the carotid flow may be lowered by diseases which may not be demonstrable by carotid angiography. The accuracy of the volume flow meter is enhanced in our opinion by the additional use of the secondary criteria as defined above, although, we have not considered these in our statistical analysis. In particular in the negative case with a high index of suspicion it has been found that compression study of the superficial temporal and facial artery is valuable by identifying a large drop in flow in cases where there is severe carotid stenosis.

Mean high to low flow ratio increased with the degree of stenosis. The ratio between the group with 41
to 70% stenosis and over 70% stenosis was statistically significant ($p < 0.001$) (fig. 11). The VFM however, was unable to estimate the precise degree of stenosis in individual cases. Paradoxically high velocity readings are frequently seen in complete occlusion of the internal carotid and in brain death. This may be due to turbulence and flow reflux.8

Cerebral angiography is not necessarily a good standard for evaluating this technique. Fell et al27 noted that intra and inter observer repeatability in the interpretation of angiograms for low grade carotid stenosis is low (75% and 57% respectively). In this series to maintain consistency of the measurements all were done by a single observer (one of the authors; SU). In assessing the percent of stenosis, the portion of the carotid artery that is taken as reference is subjective. The tortuosity of some carotids makes single plane angiogram determination difficult. A severely tortuous or looped artery may have decreased flow due to a kink in hypertensive or normotensive states. During angiography the high pressure injection of contrast material may expand the kinked portion and gives the impression of a highly patent artery.

Because the intracerebral arterioles are the dominant resistance to flow, the human common carotid artery must be reduced in cross section area to 10–22% before blood flow is reduced.28 The angiogram does not identify the changes in the small arterioles. Pathology in the cerebral arterioles may change carotid flow. For example, Hachinski29 found, using an intracarotid 133 Xe method, a 35% decrease in cerebral flow over controls in a small series of patients with multi-infarct dementia.

Ultrasound volume flow determination may be especially useful for the following conditions.

1. Screening patients with symptoms of cerebrovascular disease and asymptomatic patients at risk for carotid disease, e.g. carotid bruit, strong family history, or hyperlipidemia.
2. Serial monitoring of carotid flow (cerebral blood flow)
   a. in response to vasodilators, changes in blood gas, pH and blood pressure
   b. in head trauma, intracranial bleeding, increased intracranial pressure or other acute processes affecting cerebral perfusion.
   c. in patients undergoing major surgery who may be at risk for cerebral vascular accidents or relative hypotension from prolonged anesthesia.
   d. Follow up study of the endarterectomy patients.

From our preliminary study, we conclude that this noninvasive ultrasonic flow meter (VFM) is an important advance in the assessment of carotid disease and in the quantitative physiological studies of carotid hemodynamics and cerebral blood flow.

Acknowledgments

We thank David H. Edwin, Ph.D. Department of Psychiatry the Johns Hopkins University School of Medicine for Statistical Analysis of our data in this text, and our special thanks to Ms. Harriet Grossman and Ms. Madalena Cesenaro for their secretarial help. Also thanks to our Neurometrics technicians Michael Trattner, RT, Fred Wolfe, RT, Erva Baden, RT, and Jay Wursta, RT, for their technical assistance.

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CSF Enzymes in Lacunar and Cortical Stroke

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AUSTIN E. DOYLE, M.D., F.R.A.C.P.,* and PETER F. BLADIN, M.D., F.R.A.C.P.‡

SUMMARY Cerebrospinal fluid enzyme levels of creatine kinase (CK), lactate dehydrogenase (LDH), glutamate oxaloacetate transaminase (GOT) and angiotensin converting enzyme (ACE) were studied in 40 acute stroke patients comprising 20 lacunar strokes and 20 cortical strokes. A marked elevation of at least one of the enzymes CK, GOT or LDH was seen in 80% of cases of cortical stroke. No elevation was seen in lacunar stroke with CK, GOT or ACE and only a slight elevation with LDH. Within the cortical group, there was a correlation between the site, size of infarction seen on CT scan and enzyme level. These findings may help to explain the previously noted unpredictability of rises in CSF enzymes in stroke patients. In certain instances, a study of CSF enzymes may be of use to distinguish cortical from lacunar stroke. A precise diagnosis of lacunar infarction is important for management purposes, entry into stroke treatment trials or description of new syndrome types.

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Patients, Materials and Methods

A total of 40 stroke patients were studied in two groups. The first group comprised 20 consecutive patients with lacunar syndromes in whom the site of infarction was documented on CT Scan. Further precision of diagnosis was established by the finding of a normal EEG and no abnormality on a standard battery of neuropsychological tests. The second group consisted of 20 consecutive patients with ‘cortical’ stroke; hemiplegia was accompanied by cortical signs such as dyspraxia, dysphasia and agnosia, focal abnormality on EEG contralateral to the physical deficit, abnormalities on neuropsychological testing and confirmation of the site of infarction on CT Scan.

A neurological score was devised for each patient based on motor and sensory deficit; a score of 0–6 was given for each of face, arm and leg (motor and sensory) ranging from no deficit (score, 0) to maximal deficit (score, 6). Thus maximal deficit involving face, arm and leg gave a total score of 36.

Lumbar puncture was performed within 48 hours of admission and estimates of creatine kinase (CK), Glutamic oxaloacetic transaminase (GOT), Lactic dehydrogenase (LDH) and angiotensin converting enzyme (ACE) were made. ACE was chosen because of its known concentration in the region of the basal ganglia. Total CSF CK has been shown to be almost entirely brain isoenzyme (CK BB). Serum for en-
Measurement of carotid blood flow in man and its clinical application.
S Uematsu, A Yang, T J Preziosi, R Kouba and T J Toung

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doi: 10.1161/01.STR.14.2.256

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