Opacity Pulse Propagation Measurements in Humans: Atraumatic Screening for Carotid Arterial Occlusion

BY ALBERT F. HECK, M.D., AND THOMAS R. PRICE, M.D.

Abstract:
Opacity pulse propagation times to areas of facial skin supplied by internal carotid (medial supraorbital area) and external carotid arteries (lateral supraorbital areas, cheeks, etc.) were carried out in 27 patients with cerebrovascular symptoms, 16 of whom had normal four-vessel angiographical studies and 11 of whom had unilateral carotid occlusion. In most persons with normal extracranial vessels, no significant difference is found between mean values of propagation time to internal carotid beds on the two sides of the face or between homologous areas of the face supplied by external carotid branches. With unilateral internal carotid occlusion, mean propagation time is prolonged to the medial supraorbital (internal carotid) area on the side of occlusion, while mean propagation times to external carotid beds do not differ significantly. Occlusion of the common carotid artery results in prolongation of mean propagation time to both internal and external carotid beds on the side of the arterial obstruction. Limitations of the technique and possible sources of error are discussed. The preliminary results reported suggest that this technique may be useful in atraumatic evaluation of patients for carotid arterial disease.

ADDITIONAL KEY WORDS
stroke angiography characteristics of screening techniques

Stenosis or occlusion of the carotid arteries occurs commonly in the general population.\textsuperscript{1,2} The contribution of carotid occlusive disease to the compromise of collateral cerebral circulation and to the pathogenesis of cerebral infarction in some stroke patients is widely appreciated. It is desirable to have atraumatic techniques which could accurately detect those patients with cerebrovascular symptoms in whom further definitive investigation of the carotid arteries by angiography might be justified.

The purpose of this communication is to describe the application of opacity pulse propagation measurement techniques\textsuperscript{3} to this problem and to present preliminary results of studies in both normal persons and in patients with angiographically verified unilateral carotid occlusion.

Rationale and Hypothesis
Use of these techniques in humans represents direct application of observations from animal experiments during the last several years in which carotid artery compression resulted in differential prolongation of pulse propagation times to internal and external carotid beds.\textsuperscript{4}

\begin{itemize}
\item Stenosis or occlusion of the carotid arteries occurs commonly in the general population.\textsuperscript{1,2}
\end{itemize}
The anatomical rationale for application in human studies is identical to that upon which thermometric screening techniques have been based. The frontal and supraorbital arteries normally supplying facial skin over the medial supraorbital areas are branches of the ophthalmic artery, a branch of the internal carotid artery, whereas other areas of facial skin, including the lateral supraorbital areas, are supplied by branches of the external carotid.

The technique involves passing light into tissue and monitoring the change in opacity of the tissue during each cardiac cycle by means of highly sensitive photocells. The amount of light falling on the photocell, when converted by the cell to voltage for recording, takes the form of a wave—the opacity pulse wave (fig. 1). By recording the electrocardiogram concurrently, one can measure the interval from electrical ventricular systole—the R wave—until the arrival of the opacity pulse wave at the site monitored. This interval, the pulse propagation time, can be measured for each beat of the heart at several locations in the body during the same cardiac cycle.

It is postulated that, in persons with normal, fully patent carotid arterial vessels, mean values of opacity pulse propagation times to homologous areas of skin on the two sides of the face will not be significantly different, whereas in persons with arterial obstruction somewhere between the pulse-generating organ, i.e., the heart, and the cutaneous site monitored, prolongation of propagation time to that site, when compared to the side opposite, will occur. Further, it might be expected that the asynchrony between opacity pulses derived from internal versus external carotid beds,
OPACITY PULSE PROPAGATION MEASUREMENTS

FIGURE 2

Probe locations on the face: RMO-LMO, right and left medial orbits; RLO-LLO, right and left lateral orbits; RC-LC, right and left cheek; RCH-LCH, right and left chin.

previously described in animals, will be reflected to some degree in opacity pulses recorded from facial skin supplied by external and internal carotid arteries respectively.

Method

Equipment for derivation of opacity pulses in human studies employs the same photometric principle utilized in animal experimentation. Light is carried into the skin of the face; change in intensity of light back-scattered from the skin is converted by a photocell to voltage for polygraphical recording. The transducer (Prototypes, Inc.) is a light-pipe housed in an opaque light shield. The cadmium selenide photocell (peak spectral response 7350Å) is placed concentrically in the transducer, the photocell providing a variable resistance in a circuit of linear bridge configuration. A self-testing circuit allows for equalization of sensitivity of the photosensors in the two channels of the apparatus. Transducers are placed on the face at the locations shown in figure 2 by means of dry transfer tape (3M Company, No. 465). The translucent adhesive allows firm attachment to the skin without concomitant pressure artifact. Photometer channels are balanced after each application of the transducers.

Outputs of the photometer channels are led to a Grass EEG polygraph with matched amplifiers; ECG is recorded from limb electrodes through a jack-box, the signal input led into three of the matched amplifiers (fig. 1). After pens are checked for alignment, recordings are made at chart speed of 60 mm/sec, or 16.7 msec/mm.

Data Handling

Since the time interval monitoring system used to measure propagation time in the animal laboratory is neither inexpensive nor generally available, a method of manual measurement of propagation times, readily performed using equipment available in most medical institutions, was devised. Measurements are made by drawing a line through the peaks of ECG R-waves and measuring in millimeters the interval until occurrence of inflection points of the corresponding opacity pulse waves (fig. 1). This electrical null point is not affected by amplification (fig. 3) and can be measured with an accuracy of 0.5 mm or approximately 8 msec.

Thirty consecutive measurements are made for each channel and the mean value of propagation time is calculated. The statistical significance of the difference of these means is then evaluated by approximate T-test. The range of individual measurements during each sampling is noted and, for purposes of rapid calculation, the standard deviation is estimated as one-third of this range. These results are periodically checked by long calculation of formal T-test, which shows that the approximate test tolerates about 5% false positives.

Allowing an error of 8 msec (i.e. 0.5 mm) in individual manual measurements, a sample based on 30 consecutive measurements will insure that error in the difference of the means will be no more than 5 msec at \( p = 0.05 \) or 6 msec at \( p = 0.01 \) if the range of individual measurements does not exceed 33.4 msec. If the range of individual measurements is greater than 33.4 msec, but does not exceed 50.1 msec, then a difference of means greater than 7 msec is significant at \( p = 0.05 \), while a significance level at \( p =0.01 \) is insured at differences greater than 9 msec.

Subjects

Studies reported here concern 27 patients with symptoms of cerebrovascular disease in whom four-vessel angiography was performed; 16 of
these had angiographically normal carotid systems and 11 had unilateral carotid arterial occlusion. Three patients with unilateral occlusion also had stenosis of the opposite carotid artery. In addition, 70 studies have been performed without angiographical correlation in subjects aged four to 81 without symptoms, bruits or neurological findings; 39 of these were under age 20, an age group which, except for congenital anomaly or migraine, might reasonably be expected to have normal carotid arteries.

Results
In most normal humans and in 14 of 16 patients with cerebrovascular symptoms but angiographically normal carotid arterial systems, mean values of propagation time to medial orbits on either side were not significantly different (fig. 1, tables 1 and 2). Neither is there a statistically significant difference, in most normals, between propagation values in external carotid beds on the two sides (fig. 4, table 1). Further, the stability of mean levels of propagation time from one minute to the next, found in animals in the resting state,6,7 is also found in humans in both internal and external carotid beds, as shown in aggregate values of all cardiac cycles occurring during successive minutes over a five-minute period (table 2).

In eight of 11 patients with unilateral carotid occlusion, prolongation of mean propagation time to the medial orbit in excess of 7 msec occurred on the side of occlusion (fig. 5, table 1). These differences were significant at probability less than 1%. In two of the remaining three patients with total carotid occlusion, differences greater than seven milliseconds were found between times to the medial orbits, but prolongation occurred on the side opposite the total internal carotid occlusion. The first of these two patients also had 50% stenosis of the opposite internal carotid
OPACITY PULSE PROPAGATION MEASUREMENTS

TABLE 1
Mean Pulse Propagation Times—Four-Vessel Angiography: Correlations

<table>
<thead>
<tr>
<th></th>
<th>RMO</th>
<th>LMO</th>
<th>Δ</th>
<th>RLO</th>
<th>LLO</th>
<th>Δ</th>
<th>RMO</th>
<th>LLO</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal angiogram</td>
<td>126.9</td>
<td>124.6</td>
<td>2.3</td>
<td>132.1</td>
<td>132.1</td>
<td>0</td>
<td>131.6</td>
<td>124.9</td>
<td>6.7</td>
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<tr>
<td>Rt. int. carot. occlusion 60 yr. ♀</td>
<td>173.7</td>
<td>156.2</td>
<td>17.5</td>
<td>140.8</td>
<td>140.0</td>
<td>0.8</td>
<td>155.6</td>
<td>142.3</td>
<td>13.3</td>
</tr>
<tr>
<td>Rt. com. carot. occlusion 62 yr. ♀</td>
<td>170.3</td>
<td>158.9</td>
<td>11.4</td>
<td>171.1</td>
<td>162.3</td>
<td>9.4</td>
<td>175.6</td>
<td>162.8</td>
<td>12.8</td>
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TABLE 2
Mean Pulse Propagation Times and Heart Rate: Successive One Minute Aggregates

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<tr>
<th>Diurnal time</th>
<th>Sample</th>
<th>X</th>
<th>Range</th>
<th>X</th>
<th>Range</th>
<th>X</th>
<th>Range</th>
<th>Heart rate</th>
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</thead>
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<tr>
<td>0:00-1:00</td>
<td>112</td>
<td>123.6</td>
<td>(108.6-150.3)</td>
<td>126.9</td>
<td>(116.9-141.9)</td>
<td>534.4</td>
<td>(501.0-559.5)</td>
<td>112</td>
</tr>
<tr>
<td>1:01-2:00</td>
<td>113</td>
<td>126.9</td>
<td>(116.9-141.9)</td>
<td>126.9</td>
<td>(116.9-141.9)</td>
<td>524.4</td>
<td>(509.4-542.8)</td>
<td>115</td>
</tr>
<tr>
<td>2:01-3:00</td>
<td>108</td>
<td>122.8</td>
<td>(116.9-141.9)</td>
<td>126.9</td>
<td>(116.9-141.9)</td>
<td>527.9</td>
<td>(509.4-559.5)</td>
<td>113</td>
</tr>
<tr>
<td>3:01-4:00</td>
<td>88</td>
<td>124.9</td>
<td>(116.9-141.9)</td>
<td>127.9</td>
<td>(116.9-141.9)</td>
<td>544.4</td>
<td>(526.1-567.8)</td>
<td>110</td>
</tr>
<tr>
<td>4:01-5:00</td>
<td>110</td>
<td>122.6</td>
<td>(116.9-133.6)</td>
<td>124.4</td>
<td>(116.9-141.9)</td>
<td>534.9</td>
<td>(509.4-551.1)</td>
<td>112</td>
</tr>
<tr>
<td>7:00-8:00</td>
<td>111</td>
<td>124.7</td>
<td>(116.9-150.3)</td>
<td>111.1</td>
<td>(100.2-125.3)</td>
<td>540.4</td>
<td>(517.7-551.1)</td>
<td>110</td>
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<tr>
<td>8:01-9:00</td>
<td>111</td>
<td>121.4</td>
<td>(108.6-133.6)</td>
<td>109.5</td>
<td>(100.2-116.9)</td>
<td>536.5</td>
<td>(516.0-549.4)</td>
<td>111</td>
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<tr>
<td>9:01-10:00</td>
<td>109</td>
<td>120.5</td>
<td>(108.6-133.6)</td>
<td>109.7</td>
<td>(100.2-116.9)</td>
<td>533.7</td>
<td>(501.1-559.5)</td>
<td>112</td>
</tr>
<tr>
<td>10:01-11:00</td>
<td>101</td>
<td>122.2</td>
<td>(108.6-133.6)</td>
<td>109.7</td>
<td>(100.2-125.3)</td>
<td>546.0</td>
<td>(517.7-584.5)</td>
<td>109</td>
</tr>
<tr>
<td>11:01-12:00</td>
<td>92</td>
<td>118.7</td>
<td>(108.6-133.6)</td>
<td>109.4</td>
<td>(100.2-125.3)</td>
<td>526.1</td>
<td>(507.7-541.1)</td>
<td>114</td>
</tr>
</tbody>
</table>

artery; the second patient, with left internal carotid occlusion, had previously had severe trauma to the right orbit with a large scar over the right medial orbital area. The remaining patient, with occlusion of the left internal carotid artery, showed no significant difference between medial orbits (Δ = 3.1 msec and 2.1 msec on two separate runs), but also had plaques bilaterally in the common carotid arteries.

With occlusion above the level of the common carotid bifurcation, values in the external beds on the two sides were not significantly different, as in normal subjects (table 1). In patients with occlusion below the bifurcation, propagation times on the occluded side differed at significance levels of 1% in both internal and external beds when compared to homologous points on the unoccluded side (table 1). Interestingly, in this latter situation, the asynchrony between internal and external pulses (fig. 4, table 2) is preserved on the side of common carotid occlusion (table 1).

Discussion
A technique useful as a clinical screening procedure should ideally possess several characteristics. These include: accuracy, meaningfulness and simplicity of data interpretation; rapidity of test performance; simplicity of instrumentation and procedure; continuity of observations in time; stability of transducers employed; lack of trauma, stress or potential danger to the subject screened; and a low or negligible degree of physiological reactance. Physiological reactance concerns the effect induced by the presence of the transducer or by the making of the measurement upon the
Normal activity and reactivity of the system being monitored. The technique described satisfies requirements of simplicity and stability of instrumentation and procedure, rapidity of performance, continuity of observations and lack of trauma, stress or potential danger. In studies presented here, data are both meaningful and easily interpretable. Several possible sources of error must, however, be considered.

Local vasodilatation results in prolongation of opacity pulse propagation time. Excessive heating of the skin locally under the transducer, whether by retention of the heat normally lost by radiation or by the effect of light from the transducer, could cause local vasodilatation, thereby inducing error. Application of the transducer and light for periods of five minutes results in a rise in local skin surface temperature of only 2°C. In the data presented, it would appear that the degree of physiological reactance which might be induced by this small change in temperature is not sufficient to interfere with accuracy of the results obtained.

This technique, in its present state of development, is limited, however, by the nature of the pathological process it was designed to detect. Occlusive arterial disease characteristically occurs in more than one location and commonly affects the carotid arteries bilaterally. Qualitative comparison of opacity pulse propagation measurements in the presence of bilateral carotid disease in some cases might, therefore, be expected to show no difference between the two sides (false negative), as perhaps in the patient noted above who showed occlusion of the left internal carotid artery, plaques bilaterally in the common carotid arteries, and no significant difference in mean
Opacity pulse recordings from right medial orbit (RMO) and left medial orbit (LMO) in a patient with angiographically verified left internal carotid arterial occlusion. Mean values in lower right corner. Opacity pulses on the left lag those on the right by a mean difference of 13 msec.

Propagation times to the medial orbits on either side.

Conversely, with occlusive disease of smaller arterial branches, as, for example, the frontal or supraorbital arteries or the ophthalmic artery proximal to the origin of the former, the resulting prolongation of propagation time would represent a false positive result with respect to cerebrovascular involvement. Occlusive disease of these smaller branches might account for the finding of significant differences in propagation times to the medial orbits in two of 11 patients with normal four-vessel angiograms reported above. This explanation is difficult to verify, however, since these small arteries are poorly demonstrated in most angiograms and were not visualized in the patients concerned. Further, it should be noted that prolongation of propagation time in both of these "false positives" occurred on the same side as middle cerebral artery occlusions in these patients. Occlusion of supraorbital and frontal arteries secondary to orbital trauma, on the other hand, was mentioned by Austin and Sajid as source of error during direct thermometric screening for carotid occlusive disease. In the series reported here, one patient with left internal carotid occlusion showed significant prolongation of propagation time to the right medial orbit, where an extensive scar secondary to old orbital trauma was present. Traumatic occlusion of small arteries and escarification of this area could very likely account for the false lateralization found in this patient.

The vagaries of newly formed collateral circulation from external carotid vessels of the face and, possibly, via the nasal septum to skin over the medial orbits after internal carotid occlusion are poorly understood and
must be considered as yet another possible source of error. In the latter case, however, preliminary data suggest that when such collateral develops, propagation times to medial and lateral orbits on the involved side may be equal, in contradistinction to the normally occurring asynchrony between the two beds.

Results reported here concern only the two extremes of a pathological continuum, i.e., no stenosis versus occlusion, since for purposes of initial presentation of these new and unfamiliar techniques, demonstration of the abnormality detected is clarified by the existence of a situation in which carotid blood flow is either unimpeded or unequivocally impaired. Perhaps of greater clinical importance is the demonstration of lesions causing only partial occlusion, and studies to determine the minimal degree of carotid stenosis which can be detected by these techniques are presently in progress. The preliminary results reported, however, suggest that these techniques are capable of atraumatically detecting abnormalities in the carotid arterial circulation and may, therefore, be useful in screening of patients requiring further diagnostic evaluation.

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References
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