The Role of Venous Digital Subtraction Angiography of the Carotid Bifurcation in the Evaluation of Patients with Reversible Ischemic Attacks or Stroke

JOSEPH TH.J. TANS, M.D.,* Peter H. HOOGLAND, M.D.,† and ERIK J. JONKMAN, M.D.‡

SUMMARY The diagnostic value of venous digital subtraction angiography (VDSA) was evaluated in 168 consecutive patients with suspected or known atherosclerotic lesions of the internal carotid artery. The VDSA findings were correlated with that of arterial angiography (AA) in 50 patients, yielding a sensitivity of 84%, a specificity of 93% and an accuracy of 89%. Correlation of the results of Doppler with that of AA and VDSA provided support for the reliability of VDSA. Clinical data relevant to the selection of angiographic technique was collected, comparing patients who underwent only VDSA, only AA and VDSA followed by AA.

The conclusions of our study are: 1) If the image quality is good a normal VDSA practically excludes the presence of surgical lesions in the internal carotid artery and obviates the need for AA. 2) The presence of therapeutically relevant obstructive disease is reliably detected by VDSA, but the degree of obstruction cannot be determined accurately enough to proceed with cerebrovascular surgery without AA. 3) Patients with ischemic events in the carotid territory who are potential candidates for surgery should undergo VDSA when the non-invasive tests are normal and AA when these tests indicate the presence of a stenosis or occlusion.

VISUALIZATION of the extracranial part of the carotid system was the first and most important application of intravenous digital subtraction angiography (VDSA). Several authors have compared VDSA with conventional arterial angiography for examination of the carotid bifurcation and reported high percentages of sensitivity, specificity and accuracy. However, clinicians do not seem to have accepted VDSA as readily as their radiological colleagues and its role in the diagnostic evaluation of patients with ischemic events in the territory of the carotid arteries is by no means established. We have attempted to evaluate the usefulness of VDSA by:

1. Determining its accuracy. The results of VDSA were compared with those of arterial angiography (AA) and Doppler examination.
2. Analyzing the changes in the application of angiographic techniques arising from the introduction of VDSA. We have tried to determine why VDSA was performed and what was done with its results, particularly with respect to AA.

Patients and Methods

In the first 9 months after the introduction of VDSA 168 patients with suspected or known atherosclerotic lesions of the carotid system were examined. All examinations were carried out with an Angioskop and Angiotron (Siemens). The contrast material was administered through a pigtail catheter placed in the superior vena cava. Each patient received 4 to 6 injections of 30 to 50 ml Telebrix 38®, administered via a pressure injector at a rate of 17 ml/sec.

To evaluate the cervical region 1 posterior-anterior and 2 posterior-oblique views were always obtained. In order to obtain adequate visualization of both carotid bifurcations the oblique views had to be repeated at another angle in a number of patients. Depending on the clinical problem the examination was completed by views of either the aortic arch or the intracranial vessels. In 50 cases AA was performed during the same period. For 39 of these patients the angiographic evaluation started with VDSA followed by arterial digital subtraction angiography (ADSA) within 4 weeks. The remaining 11 patients underwent conventional arterial angiography first and follow-up VDSA within 6 months.

Although the angiograms were reviewed, we only used the original neuroradiological reports for this study. All reports of the VDSA examinations included an evaluation of image quality, taking into account contrast density, motion artifacts and vessel overlap. VDSA images were rated as good when the carotid bifurcation was well visualized in two different views. When the carotid bifurcation was well visualized in only one view or when both views showed a suboptimal contrast density, a mild degree of motion artifact or some vessel overlap, the study was qualified as diagnostic. The examination was rated as poor when contrast density, motion artifact and/or vessel superimposition yielded non-diagnostic images. The extracranial part of each internal carotid artery was classified into one of the following categories: 1 = normal, 2 = atherosclerosis without stenosis, 3 = stenosis of <30%, 4 = stenosis of 30–70%, 5 = stenosis of >70% or 6 = occlusion. The degree of stenosis was determined by measuring the arterial diameter relative to the normal diameter of the internal carotid artery at the site of the stenosis. When the degree of stenosis measured from the posterior-anterior and the posterior-oblique views differed, the mean of both measurements was calculated. VDSA was considered to be correct if the assigned category agreed with that of AA. In order to calculate sensitivity, specificity and
accuracy of VDSA relative to AA categories 1, 2 and 3 were presumed to be normal and categories 4, 5 and 6 abnormal.

Doppler examination was performed with a Kranzbühler 760 bidirectional Doppler device with emitter frequencies of 4 and 8 mHz. Twenty-nine patients not examined at our institution were excluded from analysis. The flow velocities were measured in both common carotid arteries and the peripheral branches of the ophthalmic arteries. The Doppler findings were classified as stenosis/occlusion by the neurophysiologists when differences of ≥30 percent were measured between the right and left side or when the middiastolic flow velocity was below the range of normal values employed at our laboratory.4

In 44 patients AA was performed first and the subsequent VDSA served to follow known obstructive lesions of the internal carotid artery or evaluate the results of carotid endarterectomy. This group of patients was excluded from analysis, leaving 124 patients for whom VDSA was the first angiographic examination. As mentioned above, 39 patients underwent ADSA after VDSA and 85 patients were not subjected to AA at all. We were able to collect 27 patients with an ischemic event in the carotid system who had AA without VDSA during the same 9-month period.

The final clinical diagnosis was obtained from chart review. Sixty seven patients had a reversible ischemic attack (RIA = transient ischemic attack or reversible ischemic neurologic deficit), 69 patients suffered from a mild to moderate stroke and 15 patients presented a severe stenosis on AA. Finally a group of 6 carotid arteries with a mild to moderate stenosis on VDSA and a severe stenosis on AA. Finally a group of 6 carotid arteries could be identified the VDSA of which was interpreted as normal or atherosclerosis while the AA indicated moderate to severe stenosis.

Having defined a stenosis of ≥30% as clinically significant, we calculated for VDSA a sensitivity of 84%, a specificity of 93% and an accuracy of 89%. The relationship between reliability and image quality of VDSA is shown in table 3. Both good and diagnostic images yielded true negative and true positive studies.

The most important finding, however, was that only one of the 7 false negative VDSA examinations exhibited good image quality. In addition, the false positive rate of 2 of the 3 false positive results was only diagnostic, emphasizing again the importance of obtaining optimal pictures.

Relating Doppler to AA, the Doppler proved to be a very sensitive method for detecting high grade stenosis (table 4). A stenosis >70% or an occlusion of the internal carotid artery was missed by Doppler in only 5 of the 194 (3%) arteries examined. False positive Doppler examinations, i.e. an abnormal Doppler associated with an AA classified as normal, atherosclerosis or stenosis <30%, were found in 3% of the arteries. It is generally assumed that the Doppler will identify carotid artery stenoses exceeding 50%. Therefore it is not surprising that a normal Doppler was observed in almost half of the arteries with a stenosis of 30–70%.

Compared with AA the proportion of normal VDSA examinations was high, but otherwise a similar correlation was found between VDSA and Doppler as between AA and Doppler. The percentages of false negative and false positive studies were nearly identical; the accuracy of the doppler relative to AA was 89% and to VDSA 91%. It may be argued that no definite conclu-

### Table 1: Venous Digital Subtraction Angiography (VDSA) of Extracranial Part of Internal Carotid Artery (No. = 326)

<table>
<thead>
<tr>
<th>VDSA findings</th>
<th>No. of arteries</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. normal</td>
<td>156</td>
<td>48</td>
</tr>
<tr>
<td>2. atherosclerosis</td>
<td>46</td>
<td>14</td>
</tr>
<tr>
<td>3. stenosis &lt;30%</td>
<td>29</td>
<td>9</td>
</tr>
<tr>
<td>4. stenosis 30–70%</td>
<td>36</td>
<td>11</td>
</tr>
<tr>
<td>5. stenosis &gt;70%</td>
<td>30</td>
<td>6</td>
</tr>
<tr>
<td>6. occlusion</td>
<td>39</td>
<td>12</td>
</tr>
</tbody>
</table>

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1. RIA = transient ischemic attack or reversible ischemic neurologic deficit.
2. Atherosclerotic ulcerations, in only 14% of the 36 patients were associated with a detectable degree of stenosis. Atherosclerotic lesions were classified as either atherosclerosis or stenosis. Stenosis of varying degree was seen in 26% and occlusion in 12% of the arteries, the obstructions being located almost exclusively in the proximal part of the internal carotid artery.

The results of VDSA and AA could be compared in 90 of the 100 carotid arteries examined by both techniques (table 2). Ten carotid arteries were not or poorly visualized by either venous or arterial angiography. For two thirds (67%) of the carotid arteries the categories of VDSA and AA agreed. The degree of stenosis was overestimated by VDSA in 12%. For most of these carotid arteries VDSA and AA differed by only one category. An important finding was that 3 carotid arteries appeared to be occluded on VDSA, whereas a subsequent AA showed that the arteries were still open. These cases of subtotal stenosis were successfully treated by endarterectomy. The radiological abnormalities were underestimated by VDSA in 21% of the arteries, the discrepancy between the categories of VDSA and AA being greater. We observed 5 carotid arteries with a mild to moderate stenosis on VDSA and a severe stenosis on AA. Finally a group of 6 carotid arteries could be identified the VDSA of which was interpreted as normal or atherosclerosis while the AA indicated moderate to severe stenosis.

Having defined a stenosis of ≥30% as clinically significant, we calculated for VDSA a sensitivity of 84%, a specificity of 93% and an accuracy of 89%. The relationship between reliability and image quality of VDSA is shown in table 3. Both good and diagnostic images yielded true negative and true positive studies. The most important finding, however, was that only one of the 7 false negative VDSA examinations exhibited good image quality. In addition, the false positive rate of 2 of the 3 false positive results was only diagnostic, emphasizing again the importance of obtaining optimal pictures.

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DIAGNOSTIC VALUE OF VDSA/Tans et al

1. normal
2. atherosclerosis
3. stenosis <30%
4. stenosis 30-70%
5. stenosis >70%
6. occlusion

TABLE 2
Venous Digital Subtraction Angiography (VDSA) Related to Arterial Angiography (AA) (No = 90)

<table>
<thead>
<tr>
<th>VDSA</th>
<th>Degree of stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;30%</td>
</tr>
<tr>
<td>1. normal</td>
<td>20</td>
</tr>
<tr>
<td>2. atherosclerosis</td>
<td>4</td>
</tr>
<tr>
<td>3. stenosis &lt;30%</td>
<td>3</td>
</tr>
<tr>
<td>4. stenosis 30-70%</td>
<td>3</td>
</tr>
<tr>
<td>5. stenosis &gt;70%</td>
<td>2</td>
</tr>
<tr>
<td>6. occlusion</td>
<td></td>
</tr>
</tbody>
</table>

Changes in the Application of Angiographic Techniques Arising from the Introduction of VDSA

We tried to establish from clinical data why patients presenting with RIA or stroke in the carotid system were subjected to VDSA or AA as the first angiographic examination. Patients in whom there was uncertainty about the diagnosis of reversible ischemic attack and patients with concomitant disease, not or marginally satisfying the criteria for cerebrovascular surgery, underwent VDSA (table 5). An age > 60 years and cardiac disease as a possible source of emboli also proved to be an important factor in favor of VDSA. The results of Doppler did not seem to play an important role in the choice of angiographic technique during the period of investigation. Sixty-five percent of the patients selected for VDSA appeared to have a normal Doppler examination, but a normal Doppler was also found in 56 percent of those who underwent AA first. Finally in a number of patients in good condition, VDSA was performed primarily to compare its results with that of AA.

The decision to perform AA in patients who already had VDSA was based mainly on the results of VDSA (fig. 1). Of the 37 patients with VDSA examinations classified into categories 3, 4, 5 and 6 and without contra-indications for AA, 34 subsequently underwent AA. Obviously, it was thought necessary to confirm the presence of an obstructive lesion in the appropriate carotid artery and determine more accurately its degree by means of AA. In patients showing abnormalities only in the internal carotid artery contralateral to the ischemic event, AA was considered to be contra-indicated. Refusal of AA was also classified as a contra-indication for AA in this analysis. Nevertheless, the number of patients exhibiting relative or absolute contra-indications for AA was comparatively high. Since these contra-indications are much the same as that for cerebrovascular surgery, we conclude that during this introduction period the use of VDSA was somewhat too liberal.

Of the patients with a VDSA interpreted as normal or atherosclerosis and without contra-indications for AA, we draw particular attention to those 23 in which image quality was classified as good. Although all of these patients were potential candidates for cerebrovascular surgery, they had no AA because it was felt that surgical lesions were sufficiently excluded by a normal VDSA of good quality.

Discussion

A number of authors have reported on the VDSA examination of the carotid bifurcation. Image quality was a major issue in most of these reports. Chilcote et al and Earnest et al observed good to excellent visualization of both carotid arteries in 60 to 75%, Wood and coworkers found that for 1000 internal carotid arteries the image quality was excellent in 48%, diagnostic in 44% and unsatisfactory in 8%. Motion artifacts of various types, inadequate levels of contrast medium due to diminished cardiac or pulmonary function and superposition of vessels appear to be unavoidable, even as experience with this technique grows, and tend to occur more often in the elderly patients for whom VDSA is such an attractive alternative.

In two studies normal VDSA examinations were reported in 22% and 36% of the internal carotid arteries examined. Our rather high percentage of carotid arteries interpreted as normal, has to be attributed to patient selection and to a conservative way of interpretation, hesitating to describe minor lesions on VDSA as abnormal. Normal conventional arterial angiograms are encountered in a small proportion of patients inves-

TABLE 3
Results of Venous Digital Subtraction Angiography (VDSA) Related to Image Quality

<table>
<thead>
<tr>
<th>Results of VDSA</th>
<th>No. of arteries</th>
<th>Image quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>True negative*</td>
<td>42</td>
<td>25</td>
</tr>
<tr>
<td>True positive†</td>
<td>38</td>
<td>19</td>
</tr>
<tr>
<td>False negative</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>False positive</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

*Normal, atherosclerosis, stenosis <30%.
†Stenosis 30-70%, stenosis >70%, occlusion.
tigated for cerebral ischemia in the carotid territory. For patients with transient ischemic attacks the ipsilateral carotid bifurcation was reported to be normal in 12%, 7 for patients with RIA's or stroke 20% of the carotid arteries was normal and 33% showed irregularities of the vessel wall. 8 Comparison of these figures with our VDSA examinations, showing normal carotid arteries bilaterally in 32% and atherosclerotic lesions without stenosis in only 14%, suggests that many small ulcers and other minor abnormalities were not detected by VDSA or nor appreciated as such.

Soon after the introduction of DSA at our institution its great value for intraarterial angiography was recognized and conventional arterial angiography was rarely used thereafter. The carotid bifurcation can be visualized by ADS A as well as by conventional arterial angiography, but ADS A requires less contrast material and less selective catheterization and it is faster, cheaper and more expedient.

Analysing the results of VDSA the 2 authors with the largest series distinguished 5 grades of stenosis. 1-2 It has been demonstrated that interpretations of the degree of carotid artery stenosis are not very accurate, especially with lesions compromising less than 50% of the arterial lumen. 9 Also it is evident from the findings at surgery that arterial angiography is not the never-failing golden standard. 10 Therefore we used only 3 categories, drawing the dividing line at 30% and 70% because patients with a stenosis <30% are usually not operated upon and patients with a stenosis >70% almost always are.

Comparing VDSA and AA high percentages of agreement between both examinations were found and sensitivity, specificity and accuracy of VDSA ranged from 94 to 99%. 1, 2 However, VDSA was considered to be correct by these authors if it agreed with or was within one category of the degree of stenosis on AA. 1, 2 VDSA examinations of lesser quality were not included 1 and patients with moderate stenosis were regarded as having no disease. 2 For instance, taking together the VDSA studies interpreted as good or excellent and poor by Chilcote et al, 1 yields a sensitivity of 91%, a specificity of 90% and an accuracy of 90%, percentages rather similar to ours.

Our results, like those of Earnest et al, 3 indicate that the degree of stenosis is underestimated more often than it is overestimated by VDSA. These authors also mentioned that the marked discrepancies between VDSA and arterial angiography were mostly due to incomplete or inadequate VDSA images. The number of false positive VDSA examinations was very low in

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**Table 4** Arterial Angiography (AA) and Venous Digital Subtraction Angiography (VDSA) Related to Doppler

<table>
<thead>
<tr>
<th>Angiography</th>
<th>Normal, atherosclerosis stenosis &lt;30%</th>
<th>Stenosis 30-70%</th>
<th>Stenosis &gt;70% occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of arteries</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>AA No = 194</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>101</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>stenosis/occlusion</td>
<td>5</td>
<td>14</td>
<td>57</td>
</tr>
<tr>
<td>Doppler</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>182</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>stenosis/occlusion</td>
<td>8</td>
<td>13</td>
<td>50</td>
</tr>
</tbody>
</table>

**Table 5** Clinical Features Relevant to the Selection of Venous Digital Subtraction Angiography (VDSA) as the First Angiographic Technique

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>VDSA (No = 124) No. of patients %</th>
<th>AA* (No = 27) No. of patients %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncertain ischemic event</td>
<td>25/22</td>
<td>—</td>
</tr>
<tr>
<td>Concomitant disease</td>
<td>32/28</td>
<td>2/7</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
<td>77/67</td>
<td>8/30</td>
</tr>
<tr>
<td>Cardiac emboli suspected</td>
<td>10/8</td>
<td>1/4</td>
</tr>
<tr>
<td>Normal Doppler</td>
<td>75/65</td>
<td>15/56</td>
</tr>
<tr>
<td>AA not feasible</td>
<td>9/7</td>
<td>—</td>
</tr>
<tr>
<td>VDSA performed to compare with AA*</td>
<td>21/17</td>
<td>—</td>
</tr>
</tbody>
</table>

*Arterial angiography.
all series reported so far; the number of false negative studies was limited, provided image quality was good. VDSA can therefore be regarded as a suitable and reliable screening technique.

Of particular importance are the VDSA examinations of 3 carotid arteries that were interpreted as being occluded. On arterial angiography these arteries showed pseudo-occlusion, a very severe stenosis of the internal carotid artery at the origin and slow antegrade flow distal to the stenosis. In one study pseudo-occlusion was found in almost 10% of cases initially diagnosed as occluded on the basis of routine conventional angiography. The subtotal stenosis can be identified by utilizing a long serial imaging run and subtraction or by ADSA. Since pseudo-occlusion is easily missed with conventional arterial angiography, it is not surprising that VDSA failed to reveal this condition. When such patients are operated upon without prior arterial angiography a superficial temporal to middle cerebral artery bypass will be performed, whereas carotid endarterectomy is the procedure of choice.

It is beyond the scope of this paper to discuss the merits of the Doppler examination for evaluation of carotid occlusive disease. We used the Doppler findings as a link between VDSA and arterial angiography for those patients who did not undergo both examinations. One should be cautious about weighing the reliability of an angiographic technique against that of Doppler. However, the nearly identical percentages of accuracy calculated for Doppler relative to AA and to VDSA are encouraging and support the undoubtedly more important findings obtained by direct comparison of VDSA and arterial angiography.

There is little debate about the usefulness of VDSA for follow-up of known carotid obstructions and carotid endarterectomy as well as for all those patients for whom arterial angiography is marginally indicated or even contraindicated. Various authors recommend VDSA for patients with asymptomatic carotid bruits, for the screening of asymptomatic high risk patients, for elderly patients, for patients with questionable ischemic events and for patients with ischemic events possibly caused by non-atherosclerotic conditions.

The role of VDSA in the evaluation of patients with a reversible ischemic attack or mild to moderate stroke, who satisfy the criteria for cerebrovascular surgery, has not been determined. Among other things it depends on the attitude towards carotid endarterectomy. Aggressive surgeons who believe that any small ulcer should be removed will prefer arterial angiography, because minor atherosclerotic lesions are inadequately visualized by VDSA. Surgeons who only operate on moderate to severe stenoses may be content with VDSA as the sole preoperative examination but most clinicians require arterial angiography. Lusby and Ehrenfield performed 27 carotid endarterectomies based on the results of VDSA. Comparing the VDSA findings with radiopaque luminal casts of the surgical specimens they found agreement in 96% of the cases.

We hold the view that arterial angiography, preferably ADSA, is still mandatory whenever carotid endarterectomy or an extracranial-intracranial bypass operation is anticipated. It is evident from this study that carotid occlusions cannot be differentiated with certainty from severe stenosis and that the degree of stenosis may be inaccurately depicted by VDSA. Moreover we believe that detailed information on the intracranial circulation should be available. To decide which surgical procedure is indicated and which side to operate on, the collateral flow pattern must be known. In a few of our patients with carotid occlusion VDSA suggested the presence of abundant collateral flow from the contralateral carotid system, whereas subsequent ADSA showed that this flow originated from the ipsilateral external carotid artery. Intracranial obstructive lesions, particularly of the carotid syphons and the proximal parts of the middle cerebral artery, have to be excluded before embarking on carotid endarterectomy. The intracranial arteries may be clearly visualized by VDSA, but we as well as others have found that VDSA not infrequently fails to detect hemodynamically significant stenoses. Finally, the neurosurgeon contemplating a superficial temporal to middle cerebral artery bypass operation will require visualization of the donor and recipient vessels.

Analysis of the diagnostic process was somewhat hampered by the fact that in the first months after introduction of VDSA both neurologists and radiologists wanted to evaluate the potential of this new technique, that being an important reason to perform VDSA. Soon, however, clinical factors became decisive for the indication of VDSA. Furthermore the patient material was heterogeneous, comprising partly in- and partly out-patients, partly referred for VDSA by our own staff and partly by local neurologists, who did not share a common view on the application of VDSA. On the other hand this introductory period offered us the opportunity to investigate how a new diagnostic tool is accepted into clinical practice. In our experience this acceptance has not been as universally enthusiastic as reported by others. A VDSA examination of all patients who are possible candidates for cerebrovascular surgery is felt to be superfluous, because in many cases arterial angiography will be required anyway. The usefulness of VDSA for asymptomatic patients has to be questioned because therapeutic consequences are often lacking.

On the basis of the findings of this study we propose the following diagnostic scheme for patients with cerebral ischemia in the territory of the carotid artery (fig. 2). When the doppler and/or other methods of non-invasive testing indicate the presence of a stenosis or occlusion of the internal carotid artery, arterial angiography is performed. Particularly with the very sensitive Duplex scanning the occurrence of occlusive lesions can be predicted with a high degree of certainty. For patients without evidence of carotid obstructive disease and those with a marginal indication for arterial angiography VDSA is the method of choice. We have demonstrated that surgical lesions of the internal carotid artery are excluded with a sufficient degree of cer-
tainty by a normal VDSA examination, provided the image quality is good. Although it was not a subject of this study, we believe that with a normal VDSA of excellent quality it is even possible to exclude those hemodynamically significant intracranial stenoses considered to be an indication for a superficial temporal to middle cerebral artery anastomosis. However, when VDSA reveals a stenotic lesion or when the images are of lesser quality, arterial angiography is indispensable.

We want to stress that in view of the rapid developments in technology this diagnostic scheme will probably be valid for only a limited time. Already the number of good quality VDSA examinations is increasing and with that the number of patients requiring arterial angiography and hospital admission is decreasing. On the other hand it has been stated that improvements of the magnitude experienced during the evolution of computed tomography are unlikely for DSA and we do not share the optimistic view that VDSA will largely replace arterial angiography for the evaluation of patients with a reversible ischemic attack or stroke.

References
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