Limited studies have investigated symptomatic patients with bilateral carotid plaques. In this specific population, 18F fluoro-D-glucose positron emission tomography–computed tomography examination has demonstrated higher inflammation in symptomatic plaques compared with the contralateral.1,2 Thus, inflammation seems to play a major role in progression and destabilization of the culprit plaque in patients with symptomatic carotid stenosis.

Recent studies with a new method, microwave radiometry (MWR), revealed that in vivo noninvasive temperature measurements of carotid plaques can be obtained, reflecting plaque inflammatory activation.3 Because higher plaque inflammation is associated with plaque vulnerability in carotid arteries,2,4 we hypothesized that in patients with acute ischemic stroke, culprit carotid arteries will exhibit higher temperature compared with the contralateral carotid arteries.

The aim of the present study was to investigate in patients with acute ischemic stroke and bilateral carotid plaques (1) whether the culprit carotid artery has higher inflammation as detected by MWR compared with the contralateral artery and (2) the predictive accuracy of MWR in culprit carotid artery identification.

Methods
Consecutive patients with acute anterior circulation ischemic stroke because of large artery atherosclerosis were included in the study. Carotid arteries of all patients were evaluated by carotid ultrasound and MWR.

Results
In total, 50 patients were included in the study. Culprit carotid arteries had higher ΔT compared with nonculprit arteries (0.93±0.58 versus 0.58±0.35°C; P<0.001). The addition of ΔT to a risk prediction model based only on ultrasound plaque characteristics increased its predictive accuracy significantly (c-statistic: 0.691 versus 0.768; Pdiff=0.05).

Conclusions—Culprit carotid arteries show higher thermal heterogeneity compared with nonculprit carotid arteries in patients with acute ischemic stroke and bilateral carotid plaques. MWR has incremental value in culprit carotid artery discrimination. (Stroke. 2015;46:272-274. DOI: 10.1161/STROKEAHA.114.007526.)

Key Words: acute stroke ■ carotid atherosclerosis ■ inflammation
Three segments of 20 mm were considered along each carotid artery. The middle segment was the region of common carotid bifurcation (bifurcation segment) and was used as a marker. The segment of each carotid artery with the highest plaque thickness was designated as target segment for the following MWR measurements.

**Microwave Radiometry Measurements**

A microwave computer-based system (RTM 01 RES, Bolton, UK) was used for the performance of MWR measurements. The system measures temperature from internal tissues at microwave frequencies. Basic principles of MWR have been previously described. MWR measurements were performed at both culprit and nonculprit carotid arteries over the segments previously defined in ultrasound imaging, including the target segments. Temperature difference (\(ΔT\)) of each carotid artery was assigned as the temperature of the target segment minus the minimal temperature of each carotid (reference temperature) as previously determined.

**Statistical Analysis**

Probability values are 2-sided from the Student t test or Wilcoxon test for continuous variables, depending on the normal or not distribution of the variables (SPSS Inc., Chicago, IL, USA). Noncontinuous values were compared by \(χ^2\) test. A value of \(P<0.05\) was considered significant. Multiple logistic regression analysis was used to determine those factors which are independently associated with culprit carotid arteries.

Several prediction models were also considered for culprit carotid artery identification and were compared with the use of Harrell’s c-statistic as measure of discrimination: (1) traditional risk factors plus plaque thickness (sex, age, smoking, dyslipidemia, arterial hypertension, diabetes mellitus, and family history), (2) traditional risk factors plus \(ΔT\), 3) traditional risk factors plus plaque thickness plus \(ΔT\).

**Results**

In total, 100 carotids from 50 patients with anterior cerebral circulation ischemic stroke with bilateral carotid plaques on the ground of large artery atherosclerosis were included in final analysis (Table 1).

Max plaque thickness in culprit carotid arteries was higher compared with nonculprit carotid arteries (3.76±2.03 versus 2.53±1.09 mm; \(P<0.001\)). By multivariate logistic regression analysis, culprit carotid arteries had higher max plaque thickness compared with nonculprit, after adjustment for sex, age, arterial hypertension, diabetes mellitus, and family history (odds ratio, 1.60; 95% confidence interval, 1.12–2.28; \(P=0.01\)).

Culprit carotid arteries had higher \(ΔT\) compared with asymptomatic carotid arteries (classification based on clinical criteria; 0.93±0.58 versus 0.58±0.35°C; \(P<0.001\); Figure). By multivariate logistic regression analysis, culprit carotid arteries exhibited higher \(ΔT\) values compared with nonculprit, after adjustment for sex, age, vascular risk factors, and \(ΔT\) values (odds ratio, 1.60; 95% confidence interval, 1.56–22.63; \(P=0.01\)).

In Table 2 are summarized the results of c-statistics of the various models. The addition of \(ΔT\) to the model of traditional risk factors+plaque thickness increased the predictive ability of the model significantly.

**Discussion**

In the present study, we showed that in patients with acute atherothrombotic stroke and bilateral carotid artery disease (1) culprit carotid arteries have increased plaque thickness and higher inflammatory activation compared with nonculprit

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**Table 1. Study Population**

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical variables</strong></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>68.48±12.43</td>
</tr>
<tr>
<td>Male sex</td>
<td>36 (72)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>24 (48)</td>
</tr>
<tr>
<td>Smoking</td>
<td>24 (48)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>10 (20)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>38 (76)</td>
</tr>
<tr>
<td>Family history</td>
<td>14 (28)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>18 (36)</td>
</tr>
<tr>
<td><strong>Previous medication</strong></td>
<td></td>
</tr>
<tr>
<td>ASA</td>
<td>24 (48)</td>
</tr>
<tr>
<td>ADP-inhibitors</td>
<td>10 (20)</td>
</tr>
<tr>
<td>ACE</td>
<td>2 (4)</td>
</tr>
<tr>
<td>ARB</td>
<td>26 (52)</td>
</tr>
<tr>
<td>(β)-Blockers</td>
<td>12 (24)</td>
</tr>
<tr>
<td>Statins</td>
<td>24 (48)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Ca-antagonists</td>
<td>10 (20)</td>
</tr>
</tbody>
</table>

All values are expressed as mean±SD or n (%). ACE indicates angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers; ASA, acetylsalicylic acid; and Ca-antagonists, calcium antagonists.

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**Table 2. C-Statistic Values of Various Models for Culprit Carotid Artery Prediction**

<table>
<thead>
<tr>
<th>Model</th>
<th>C-Statistic</th>
<th>95% CI</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRF+plaque thickness</td>
<td>0.691*†</td>
<td>0.588–0.794</td>
<td>0.001</td>
</tr>
<tr>
<td>TRF+(ΔT)</td>
<td>0.747†</td>
<td>0.644–0.850</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TRF+plaque thickness+(ΔT)</td>
<td>0.768*†</td>
<td>0.666–0.870</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* indicates confidence interval; and TRF, traditional risk factors.

\(†\) indicates comparison, 0.05.
arteries and (2) ΔT offers incremental predictive value in culprit carotid artery identification.

The findings with MWR regarding the inflammatory status of the culprit carotid artery are in accordance with the studies using 18F fluoro-2-deoxyglucose positron emission tomography—computed tomography. Indeed, recent studies with limited number of patients with acute ischemic stroke have shown that inflammatory activation interferes significantly in plaque progression and destabilization.1,2,4

The addition of a functional characteristic in the diagnostic algorithm, such as an accurate marker of local inflammation, increased the diagnostic accuracy of the culprit plaque.

Quantification of plaque inflammation could potentially contribute significantly to primary and secondary prevention of stroke. Indeed, functional carotid artery assessment, additionally to morphological characteristics, could better stratify patients in risk for stroke. Although 18F fluoro-2-deoxyglucose positron emission tomography scan is the most accurate noninvasive method for detection of local inflammation, radiation exposure and other technical issues hamper its wide application, especially for serial evaluations. Thus, a new noninvasive method, simple in application, such as MWR, would be a useful tool in primary and secondary prevention.

Study Limitations

All patients had ipsilateral to the cerebral symptoms carotid plaques, where the events were attributed. However, other sources of atheroemboli, such as the aortic arch, cannot be excluded because our patients did not undergo transeosophageal echocardiography.

Conclusions

In patients with acute ischemic stroke and bilateral carotid plaques, MWR offers incremental predictive value in culprit carotid artery identification.

Disclosures

None.

References

Incremental Predictive Value of Carotid Inflammation in Acute Ischemic Stroke
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Konstantinos Spengos, Christodoulos Stefanadis, Elias Siores and Dimitrios Tousoulis

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