Characterization of Carotid Artery Plaques Using Real-time Compound B-mode Ultrasound

Rolf Kern, MD; Kristina Szabo, MD; Michael Hennerici, MD; Stephen Meairs, MD

Background and Purpose—Real-time compound ultrasound imaging is a new technique for improving the image quality of B-mode scanning. We investigated the value of this method for the characterization of atherosclerotic plaques in the internal carotid artery.

Methods—Thirty-two patients (22 men, 10 women; mean age, 75 years) with plaques of the internal carotid artery as identified by high-resolution B-mode scanning were investigated with real-time compound ultrasound imaging with the use of a 5- to 12-MHz dynamic range linear transducer on a duplex scanner. Two independent observers rated plaque morphology according to a standardized protocol.

Results—The majority of plaques was classified as predominantly echogenic and as plaques of irregular surface, whereas ulcerated plaques were rarely observed. The interobserver agreement for plaque surface characterization was good for both compound ultrasound (κ=0.72) and conventional B-mode (κ=0.65). For the determination of plaque echogenicity, the reproducibility of compound ultrasound (κw=0.83) was even higher than that of conventional B-mode ultrasound (κw=0.74). According to a semiquantitative analysis, real-time compound ultrasound was rated superior in the categories plaque texture resolution, plaque surface definition, and vessel wall demarcation. Furthermore, there was a significant reduction of acoustic shadowing and reverberations.

Conclusions—Real-time compound ultrasound is a suitable technique for the characterization of atherosclerotic plaques, showing good general agreement with high-resolution B-mode imaging. This advanced technique allows reduction of ultrasound artifacts and improves the assessment of plaque texture and surface for enhanced evaluation of carotid plaque morphology. (Stroke. 2004;35:870-875.)

Key Words: carotid artery plaque ■ reproducibility ■ morphology ■ ultrasonography

Ultrasonographic imaging of the carotid arteries allows assessment of both early and advanced atherosclerotic disease. This noninvasive technique has played a central role in many recent epidemiological studies and is being used increasingly for evaluating the efficacy of atherosclerosis prevention trials. Moreover, there is evidence that ultrasonographic B-mode characterization of plaque morphology may be useful in assessment of the vulnerability of the atherosclerotic lesion,1–5 although a confident and reproducible classification of “dangerous” plaques is still not available. Despite the strong role of diagnostic ultrasound in cerebrovascular disease, significant deficits remain. The correlation between ultrasonographic features and the histological evaluation of carotid plaques is often poor.6–7 Limiting factors responsible for such deficits include low spatial resolution and ultrasound artifacts. Thus, improving ultrasonographic image quality is an important goal because this may allow acquisition of additional information for elucidation of stroke pathophysiology, ultimately leading to better primary and secondary stroke prevention.

One approach to improving ultrasonographic image quality in cerebrovascular applications may be to average several images taken from different perspectives. This hypothesis is supported by the results of in vitro B-mode imaging studies showing that combining scan information from more than 1 angle leads to a significant reduction in the amount of random noise or speckle.8,9 This technique, termed compounding, has been used in experiments to increase signal-to-noise ratio in 3-dimensional ultrasound imaging.9,10 Compound imaging has also been applied in an in vivo 3-dimensional system registering irregularly sampled ultrasound images obtained from different perspectives to maximize vessel wall information of the carotid artery.11 The major obstacle for implementation of compound imaging in routine clinical practice, however, has been the time-consuming offline processing of image data common to all systems. Recently, real-time spatial compound imaging has been made possible through substantial improvements in the computational power of modern ultrasound equipment. First experience with this technique in the field of cerebrovascular ultrasound imaging has demonstrated its ability to improve visualization of atherosclerotic plaques in vitro.12 These experiments were recently complemented by studies in patients with carotid artery disease to
show better intraobserver and interobserver reproducibility in the evaluation of atherosclerotic disease. We hypothesized that real-time compound imaging, by reducing speckle and ultrasound artifacts, could improve the in vivo characterization of carotid artery plaque morphology.

Subjects and Methods
Real-time Compound Ultrasound: Technical Aspects
Speckle artifact can be described as noise due to the interference of returning echoes from tissue. Speckle is an inherent artifact and reduces image contrast and detail resolution. Spatial compounding can be used to suppress speckle noise. As a result, contrast is improved. As multiple echoes return, they contain speckle information from different locations. By averaging out the speckle and other noise information, the signal-to-noise ratio can be improved for the target location information. The averaging process favors real data and reduces the visual representation of speckle and noise. Real-time compound imaging uses computed beam steering technology to steer ultrasound beams "off-axis," providing multiple transmit angles in the course of a single scan. The averaging process provides multiple transmit angles in the course of a single scan. Pipeline signal-processing architecture is used to accurately render these steered frames into the appropriate display geometry and update the compound image in real time as each new frame is acquired.

Ultrasound Studies
Consecutive patients with internal carotid artery (ICA) stenosis >40% diameter reduction were included in the study and examined by an experienced ultrasonographer. A standardized protocol was used that comprised high-resolution B-mode and real-time compound ultrasound scans from standardized planes of the ICA. Sequential perpendicular cross sections along the axis of the ICA at the maximum extent of the atherosclerotic lesion and parallel longitudinal sections, including the carotid bulb, were displayed. In every case, additional examinations with frequency- and power-based color-coded duplex ultrasound were obtained to determine the degree of the stenosis and to detect ulcers and anechogenic plaques that might be missed in B-mode scans. The average scan time for the complete ultrasound protocol was 10 minutes for each carotid artery, with the scan times of compound ultrasound and conventional B-mode being approximately the same length. All ultrasound investigations were performed on a Philips HDI 5000 duplex scanner (Philips Medical Ultrasound, NL) with a 5- to 12-MHz dynamic range linear transducer. Third-generation SonoCT Real-time Compound Imaging software was applied for compound ultrasound.

The degree of ICA stenosis was determined according to the measured maximum flow velocity and to the local narrowing in percent diameter reduction at the maximum of the stenosis, calculated according to the formula \((1 - A/B) \times 100\%\), where \(A\) represents the tightest diameter of stenosis and \(B\) the suspected former vessel diameter. For later subgroup analysis, atherosclerotic plaques were stratified for the localization as lesions limited to the far wall, lesions limited to the near wall, and both far and near wall lesions. The results of each ultrasound investigation were stored digitally. Before presentation to the observers, each image was cropped to exclude patient information and scan specification, referring to the applied technique. The observers were requested to classify each atherosclerotic plaque regarding echogenicity and plaque surface and regarding image quality in 5 different categories. The criteria of data classification are explained below in detail.

Plaque Characterization
The classification of atherosclerotic plaques was performed according to the criteria established by the Consensus Conference concerning the morphology and the risk of carotid plaques. Thus, plaque echogenicity and texture are determined in categories from I to V, ranging from the homogeneous, uniformly anechogenic (class I) plaque to the homogeneous, uniformly echogenic (class IV) plaque, as well as mixed forms with the heterogeneous, predominantly hypoechogenic (class II) and the predominantly echogenic (class III) plaques. Unclassified plaques, for example due to excessive shadowing, are considered class V plaques. The appearance of the plaque surface is defined as (1) smooth and regular; (2) mildly irregular when height variations between 0.4 and 2 mm are seen along the contour of the lesion; or (3) ulcerated when flow vortices with evidence of reversed flow in the color-coded duplex scan and recesses with an extent of at least 2 mm in depth and 2 mm in length and a well-defined back at its base are present.

Assessment of Image Quality
To compare the image quality and visualization of the atherosclerotic plaque, the residual vessel lumen, and surrounding structures of both B-mode techniques, we used a semiquantitative scale of image quality in the 5 categories regarding (A) the determination of the plaque texture resolution, (B) the definition of the plaque surface, (C) the vessel wall demarcation, (D) the amount of acoustic shadowing, and (E) the level of reverberation artifacts.

Categories A to C
In these categories, image quality was rated as good, moderate, or poor by each of the 2 observers in both methods. The determination of plaque texture resolution (A) was considered to be of good quality if the internal structure of the plaque could be visualized entirely and an attribution of the plaque class was easily possible. A good quality of plaque surface definition (B) was assigned if the surface of the plaque was visible in its whole extent without areas of shadowing or other confounding artifacts. Vessel wall demarcation (C) represents a descriptive category for the depiction of arterial walls that might be compromised by artifacts as well as anatomic peculiarities such as, for example, deep localization.

Categories D and E
Reduction or suppression of certain artifacts that typically occur in ultrasound may lead to superior visualization of anatomic or pathological structures. The amount of artifacts was rated as high, low, or absent by each of the 2 observers in both methods. Acoustic shadowing (D) emerges when parallel ultrasound beams hit structures with high attenuation. Extensive shadowing may severely diminish image quality or completely erase the information behind such a structure. In carotid artery plaques, shadowing frequently arises in regions of calcification. Reverberations (E) are artifacts due to incoherent wave interference arising at structures with differing echo intensity and lead to spurious echoes and a granular appearance within an otherwise homogeneous region.

Statistical Analysis
The intraobserver and interobserver reproducibility of compound ultrasound and conventional B-mode was determined by the analysis...
of plaque echogenicity and plaque surface. For plaque surface analysis, we used unweighted \( \kappa \) statistics since the 3 categories are nominal scales. For plaque echogenicity consisting of 5 categories, a weighted \( \kappa \) \((\kappa_w)\) was calculated that weighted disagreements involving distant values more heavily than disagreements involving more similar values.\(^9\) For plaque classes I to IV, ratings of I and IV for the same plaque were weighted heavily \((w=1)\), disagreements between I and III or II and IV were weighted as \(w=2/3\), and all other disagreements were given low weightings \((w=1/3)\). Since class V represents unclassifiable plaques, ratings of class V and any other class all were weighted equally \((w=1/3)\). \(\kappa\) and \(\kappa_w\) were indicated including 95% CIs.

For comparing image quality, semiquantitative data from the aforementioned categories (A to E) were analyzed stratified by observer. A \(\chi^2\) test was performed to determine differences between the methods. A value of \(P<0.05\) was considered statistically significant. Statistical analysis was performed with the SAS software package (version 8.2).

### Results

**Patient Selection**

Thirty-two patients treated in our Stroke Unit were included in the study (22 men, 10 women; mean age, 75 years). In 43 of the 64 insonated ICAs, significant atherosclerotic changes were observed. We found small plaques with 40% to 50% degree of stenosis in 10 of 43 patients, moderate (50% to 70%) stenoses in 18 cases, and high-grade (70% to 90%) stenoses in 7 cases. Subtotal stenoses were seen in 2 and occlusions in 6 of the cases.

### Definition of Plaque Echogenicity and Surface

An overview of the interobserver agreement for both compound ultrasound and conventional B-mode is given in Tables 1 and 2. The majority of plaques was classified as predominantly echogenic and as plaques with irregular surface. Plaque ulcers were rarely observed. Fifteen atherosclerotic plaques were limited to the near vessel wall, 11 lesions were limited to the far wall, and 17 lesions involved both far and near walls.

Table 1 illustrates the results for the characterization of plaque echogenicity. \(\kappa_w\) values indicate a good reproducibility for both methods, with even higher values when compound ultrasound was used. The intraobserver reproducibility was also good with \(\kappa_w=0.66\) (95% CI, 0.63 to 0.70) for observer 1 and \(\kappa_w=0.78\) (95% CI, 0.73 to 0.82) for observer 2.

In a subanalysis comparing the reproducibility in atherosclerotic lesions according to their position in the vessel wall, the interobserver agreement with the use of conventional B-mode had a tendency toward higher values in the far wall \((\kappa_w=0.92;\ 95\% \ CI, 0.76\ to\ 1.0)\) than in the near wall \((\kappa_w=0.57;\ 95\% \ CI, 0.27\ to\ 0.87)\). With the use of compound ultrasound, the reproducibility was excellent in the far wall \((\kappa_w=1.0)\) but also high in the near wall \((\kappa_w=0.70;\ 95\% \ CI, 0.38\ to\ 1.0)\). The significance of this subanalysis is limited by large and overlapping CIs from the small sample size.

### Comparison of Image Quality

Table 3 shows the overall results of the semiquantitative analysis of image quality evaluated in different categories with the use of real-time compound ultrasound and conventional B-mode. With the use of compound ultrasound, plaque texture resolution (A) was rated superior in 41.9% by observer 1 and in 44.2% by observer 2. The plaque surface definition (B) was considered superior in 41.9% and in 32.6%, respectively. Vessel wall demarcation (C) was improved in 39.5% and in 44.2%. The amount of acoustic shadowing (D) was considered to be less in 30.2% and in 44.2%. The level of reverberation artifacts (E) was reduced in 48.8% and in 55.8%. For all 5 categories (A to E), the difference between the 2 observers reached the level of statistical significance. The strongest improvement of image quality was noted for plaques that produced shadowing artifacts (classes III and IV), followed by hypoechoic plaques (class I). The improvement was of lesser importance in class II plaques, and the improvement was equally distributed in the plaque surface categories. Two examples of ICA plaques visualized by both sonographic techniques are given in Figures 2 and 3.

### Discussion

This study investigated the value of compound imaging for evaluation of atherosclerotic plaques in the ICA. The results demonstrate advantages of this technique over conventional high-resolution B-mode imaging, namely, improved visualization of plaque texture, better demarcation of plaque surface, and reduction of ultrasound artifacts. Compound ultrasound shows a good reproducibility in the evaluation of plaque morphology and provides an even higher interobserver agreement than conventional B-mode in the classification of plaque echogenicity. Our findings support previous
work demonstrating better intraobserver and interobserver reproducibility in evaluation of atherosclerotic disease of the carotid artery with compound imaging.\textsuperscript{13}

Improved visualization of the plaque surface and better delineation of vessel walls with compound imaging should provide new opportunities for enhanced detection and characterization of plaque ulcerations. Previous attempts to describe plaque surface structure with B-mode ultrasound have been disappointing. Although a relatively good differentiation between smooth, irregular, and ulcerative plaque surfaces has been obtained for postmortem carotid artery specimens,\textsuperscript{16} the in vivo accuracy compared with findings at carotid endarterectomy has been considerably poorer.\textsuperscript{7,17,18} B-mode imaging has not provided a satisfactory diagnostic yield for ulcerative plaques, with a sensitivity of $<50\%$.\textsuperscript{17} It is important to remember, however, that our current concepts on the role of

<table>
<thead>
<tr>
<th>Categories</th>
<th>Observer 1</th>
<th>Observer 2</th>
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<tr>
<td></td>
<td>Compound Ultrasound</td>
<td>B-mode Ultrasound</td>
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<tr>
<td>A Good</td>
<td>30 (69.8%)</td>
<td>14 (32.6%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>11 (25.6%)</td>
<td>25 (58.1%)</td>
</tr>
<tr>
<td>Poor</td>
<td>2 (4.7%)</td>
<td>4 (9.3%)</td>
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<tr>
<td>$P&lt;0.001$</td>
<td>$P=0.001$</td>
<td>$P=0.001$</td>
</tr>
<tr>
<td>B Good</td>
<td>18 (41.9%)</td>
<td>9 (20.9%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>20 (46.5%)</td>
<td>18 (41.9%)</td>
</tr>
<tr>
<td>Poor</td>
<td>5 (11.6%)</td>
<td>16 (37.2%)</td>
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<td>$P=0.001$</td>
<td>$P=0.08$</td>
<td>$P=0.001$</td>
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<tr>
<td>C Good</td>
<td>23 (53.5%)</td>
<td>14 (32.6%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>16 (37.2%)</td>
<td>19 (44.2%)</td>
</tr>
<tr>
<td>Poor</td>
<td>4 (9.3%)</td>
<td>10 (23.2%)</td>
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<td>$P=0.001$</td>
<td>$P=0.001$</td>
<td>$P=0.001$</td>
</tr>
<tr>
<td>D High</td>
<td>1 (2.3%)</td>
<td>9 (20.9%)</td>
</tr>
<tr>
<td>Low</td>
<td>29 (67.4%)</td>
<td>26 (60.5%)</td>
</tr>
<tr>
<td>Absent</td>
<td>13 (30.2%)</td>
<td>8 (18.6%)</td>
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<td>$P&lt;0.001$</td>
<td>$P=0.004$</td>
<td>$P&lt;0.001$</td>
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<td>E High</td>
<td>3 (7.0%)</td>
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<tr>
<td>Low</td>
<td>24 (55.8%)</td>
<td>23 (53.5%)</td>
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<tr>
<td>Absent</td>
<td>16 (37.2%)</td>
<td>7 (16.3%)</td>
</tr>
<tr>
<td>$P=0.017$</td>
<td>$P=0.003$</td>
<td>$P=0.003$</td>
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Figure 2. Example of a 70% carotid artery stenosis caused by a heterogeneous, predominantly echogenic plaque with the use of real-time compound ultrasound in the longitudinal (A) and the transversal (B) planes. The corresponding high-resolution B-mode scans are shown below (C and D). Both the plaque structure and the delineation of the surface are depicted better with the use of compound imaging.

Figure 3. Example of an irregular echogenic plaque located at the carotid bifurcation. Because of acoustic shadowing, the visualization of the plaque texture is poor in the conventional B-mode scans (C and D). The compound imaging scans show a reduction of shadowing (A and B).
Ultrasound imaging for detection and characterization of plaque ulceration stem primarily from studies performed >10 years ago. These studies were undertaken with equipment that does not provide image quality comparable to that of modern advanced ultrasound imaging techniques. We could not confirm the advantage of compound ultrasound for the assessment of plaque ulceration since ulcerated lesions were detected rarely in our population. This technique, however, might be the preferred imaging modality to use in new studies for characterization of the role of plaque ulceration as a marker of plaque vulnerability.

Real-time compound imaging may be equally beneficial for improved acquisition of 3- and 4-dimensional ultrasound data to perform 3-dimensional renderings and to analyze plaque motion. We have previously reported the usefulness of such techniques in evaluation of patients with ischemic stroke. By using real-time compound imaging, the quality of 3-dimensional images can be improved considerably because of better delineation of the arterial walls. Moreover, improved demarcation of the plaque surface allows superior performance of plaque motion algorithms (R. Kern, MD, et al, unpublished data, 2002).

The present study also demonstrates improved visualization of plaque echogenicity. Carotid artery plaques of homogeneous, moderate-intensity echogenicity consist mainly of fibrotic tissue. Such plaques rarely show ulceration, perhaps accounting for the lack of a significant correlation between homogeneous echogenicity and the occurrence of focal cerebral ischemia. Heterogeneous plaques represent matrix deposition, cholesterol accumulation, necrosis, calcification, and intraplaque hemorrhage. Several studies have demonstrated that high-resolution B-mode scanning can characterize echomorphologic features of carotid plaques that correlate with histopathological criteria. Although echolucent areas within the plaque may represent thrombotic material or hemorrhage, lipid accumulation may produce similar echogenicity. Recent studies using ultrasound integrated backscatter for the noninvasive assessment of plaque tissue composition reported promising results with a good correlation for different plaque components in comparison to histopathological analysis.

Plaque calcification produces acoustic shadowing. Depending on the location of the plaque and on the extent of calcification, acoustic shadowing can be a major obstacle for adequate ultrasonographic visualization. Furthermore, artifacts arising from clatter, side lobes, grating lobes, multi-path reverberations in the vessel lumen, and artifacts from intervening tissue between transducer and vessel may result in diminished perceptibility of an atherosclerotic lesion. Especially in hypoechoic plaques, those reverberations in the vessel lumen can make it difficult to judge the precise extent of the atherosclerotic lesion. The results of our study show that compound imaging can reduce the amount of acoustic shadowing and reverberations to allow enhanced evaluation of plaque structure.

Improved evaluation of plaque morphology with real-time compound imaging may aid in further studies designed to establish an association between plaque echogenicity and cerebrovascular events. Initial studies reported an association between heterogeneous plaques and the occurrence of cerebrovascular events. Other investigations of endarterectomy specimens also suggested a correlation between intraplaque hemorrhage and transient ischemic attacks and stroke. Other studies, however, could not confirm these observations. Whether differences in plaque echogenicity can distinguish between symptomatic and asymptomatic plaques continues to be a matter of debate. While some contend that heterogeneous carotid plaques are more often associated with intraplaque hemorrhage and neurological events, recent studies have provided good evidence that lipid-rich plaques are more prone to rupture and suggest that an association between intraplaque hemorrhage and a high lipid content as revealed in B-mode ultrasound may support this theory. The presence of hypoechoic ICA plaques has also been reported as an independent risk factor for cerebrovascular events. The application of compound B-mode imaging for enhanced evaluation of plaque morphology may additionally provide data to help elucidate the relationship between plaque echogenicity and the risk of plaque embolism.

The design and the sample size of this study were not intended to evaluate a possible association between the improvement of sonographic image quality and the prediction of recurrent strokes. Furthermore, our results were not compared with a standard control that would be a histopathological analysis of endarterectomy specimens. Nevertheless, this study provides useful information on the value of compound ultrasound in the clinical setting and implies that this technique has the potential to play an advantageous role in future investigations of plaque surface structure and plaque echogenicity as markers of plaque vulnerability.

In conclusion, this study demonstrates that real-time compound ultrasound is an advanced method for the characterization of atherosclerotic plaques with good agreement with high-resolution B-mode imaging. Image quality is improved because of better structural differentiation and suppression of artifacts. The potential of this method may involve better diagnostic confidence, including precise visualization of morphological details, identification of early lesions, and superior follow-up.

**References**


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