Three-Dimensional Assessment of Extracranial Doppler Sonography in Carotid Artery Stenosis Compared With Digital Subtraction Angiography

Tiemo Wessels, MD; Judith U. Harrer, MD; Susanne Stetter, MD; Michael Mull, MD; Christof Kloetzsch, MD

Background and Purpose—Difficulties in data presentation, data storage, and a high interobserver variability may influence color-coded Duplex sonography assessment of internal carotid artery stenosis (ICAS). The aim of our study was to evaluate the between-method agreement of ICAS using 3D color Doppler sonography (CDS) compared with digital subtraction angiography (DSA).

Methods—Forty-nine patients with 64 ICASs (age 64±9 years) were involved. The patients were investigated with a color-coded duplex system using the power mode. The 3D system consists of an electromagnet that induces a low-intensity magnetic field near the patient’s head. A magnetic position sensor is attached to the probe and transmits the spatial orientation to a personal computer.

Results—A total of 62 ICASs were reconstructed successfully with 3D CDS in 47 of 49 patients. High agreement for 2 independent observers was found in 3D CDS (weighted κ coefficient of 0.88). Three-dimensional CDS slightly underestimated the mean stenotic degree (mean 3D CDS 68.47±10.5 versus DSA 71.3±10.0). The intermethod agreement comparing DSA with 3D CDS was analyzed with the Bland and Altman test, which showed good agreement. Mean sensitivity of 3D CDS was 93%, mean specificity 82.5%, mean positive predictive value 82%, and mean negative predictive value 98%.

Conclusions—The 3D CDS findings demonstrated good agreement compared with the gold standard, DSA, yielding higher accuracy than CDS alone. Compared with angiography or magnetic resonance angiography, 3D CDS can be performed easily on critically ill patients in stroke or intensive care units and may therefore provide a useful tool for patients unable to undergo more invasive imaging techniques. (Stroke. 2004;35:1847-1851.)

Key Words: carotid stenosis ▪ ultrasonography, Doppler ▪ cerebrovascular disorders ▪ imaging, three-dimensional

The degree of stenosis in symptomatic carotid artery disease is highly correlated to the risk of cerebral infarction.1–3 Color duplex sonography (CDS) has become the most widely used noninvasive method to screen for internal carotid artery stenosis (ICAS).1,4–6 The difficult assessment of critical ICAS attributable to low intrastenotical velocities with frequency-based sonography was improved by using the power mode.7 Several methods have been described to estimate the degree of ICAS with CDS.1,4,5,8,9 Nevertheless, the method is highly dependent on investigator experience.10 Doppler techniques are safe and can be used as a bedside technique. However, when compared with digital subtraction angiography (DSA), CDS shows a lower sensitivity, ranging from 65% to 87%, and a specificity ranging from 71% to 91% to detect different degrees of carotid stenosis or stenosis that would require surgery.11,12 Pitfalls include overestimation of the stenotic degree in case of contralateral ICAS with duplex ultrasound by means of hemodynamic criteria and overestimation by grading ICAS using morphological information from evaluation of the diameter to assess the stenotic degree with duplex ultrasound.10–12 Furthermore, image presentation and reliability are important features of a technique, especially in the interdisciplinary approach concerning ICAS therapy with vascular surgeons and interventional neuroradiologists.

Because of these limitations, DSA is still regarded as the gold standard technique to demonstrate the exact stenotic degree. However, the method is an invasive procedure and is associated with radiation exposure. A morbidity rate of 1% to 4% and a 1% risk of peri-interventional stroke accounts for increasing numbers of centers using predominantly magnetic resonance angiography (MRA) before surgery in carotid
artery disease. Several preliminary reports concerning 3D ultrasound in carotid artery disease already demonstrate encouraging results.

Several limitations of the different published methods (time-consuming data reconstruction, space-occupying personal computers necessary for data acquisition, and low quality of reconstructed pictures) have been reported herein. The aim of this study was to assess the between-method agreement for the degree of stenosis obtained with 2D CDS, 3D reconstruction, and DSA.

Patients and Methods
A total of 49 patients (36 male, 13 female) with a mean age of 64±9 years (±SD) were included in the study. The patients were referred for ultrasound examination after stroke (12 patients), after transient ischemic attack (16 patients), after screening (12 patients), or for other reasons (9 patients). Bilateral CDS of all extracranial and intracranial brain-supplying vessels was performed by an experienced investigator using a power-based CDS system (Acuson XP128/10; 5-Hz linear probe for the first 22 patients, and afterward, Agilent HP Sonos 5500 with an 11-3L linear shear probe). Velocity waveforms of each vessel were obtained routinely. The stenotic degree investigated by 2D CDS was graded using peak systolic velocities (PSVs), poststenotic velocities, and morphological criteria. The stenotic degree was graded using the following accepted protocol: mild, 0% to 39% (PSV normal, only morphological criteria); moderate, 40% to 59% (PSV <150 m/s); high-grade, 60% to 79% (PSV 150 to 250 m/s); critical, 80% to 99% (PSV >250 m/s); and occlusion, 100%.

After CDS, all patients were examined with 3D CDS of the stenotic vessel; vessel occlusions were not included in the study. The 3D CDS was performed in power mode. For a precise 3D visualization of the vessel, it was important to change some parameters of the duplex machine. The color persistence and the color Doppler gain had to be enhanced slightly to achieve optimal color filling. The probe was placed in the transversal plane. The entire vessel volume was scanned starting with its caudal portion, including the distal common carotid artery up to the cranial segment of the internal carotid artery (ICA), always keeping the ICA lumen in the center of the monitor screen. The free-hand system (Echotech 3D Imaging Systems) used in this study is adaptable to every commercially available color-coded duplex system. The 3D system consists of an electromagnet that induces a low-intensity magnetic field near the patient’s head. The composite magnetic field is generated from an array of 3 coils at 90° angles to each other to produce 3 magnetic fields, yielding a 3D orientation. A magnetic position sensor is attached to the ultrasound probe and transmits the spatial orientation (x, y, and z axes) of the probe to a personal computer workstation, which also receives the corresponding 2D images from the video port of the duplex machine. During a 30- to 40-s interval, 200 2D images, together with the spatial information, were stored on the hard disk of the workstation. During offline analysis, a reconstruction algorithm was used to extract the color-coded information from the 3D data set. The Windows-based software provides a photorealistic surface rendering of the investigated vessels (Figures 1 and 2). Use of different threshold values and filtering tools makes it possible to reduce artifacts. Volume- and surface-rendering techniques facilitate spatial orientation between small arterial segments and animated sequences of reconstructed arteries, which are useful to distinguish between flow patterns of close neighboring vessels.

In addition, all patients underwent 4-vessel DSA for medical reasons (time interval 1 to 7 days). After femoral puncture, all 4 extracranial brain-supplying vessels were catheterized, and ~8 mL of an iodinated nonionic contrast agent (Solutrust 300, Iopamidol; Amersham) was administered to display the vessels. The rate of angiography-related complications (neurological and at the puncture site) was recorded.

Calculation of ICAS degree evaluated by means of 3D CDS and DSA was based on the North American Symptomatic Carotid Endarterectomy Trial criteria measuring intrastenotic and distal vessel diameter. Categorization into different grades was equal to the above classification of stenosis obtained by CDS. Two independent experienced ultrasound investigators, blinded to 2D CDS and DSA results, categorized the grades of stenosis obtained by 3D CDS and DSA for statistical evaluation. We used SPSS 12.0 software (SPSS). To estimate the agreement of 3D CDS measurements and DSA as well as 3D CDS and CDS, we used the Bland and Altman procedure. This procedure was also used to assess intraobserver repeatability for evaluation of 3D CDS. Furthermore, intermethod and interobserver agreement was expressed with the weighted κ coefficient (κw). The Spearman correlation coefficient (r) was applied additionally for correlation analysis of percentage stenosis. Sensitivity, specificity, and positive and negative predictive values to detect high-grade and critical ICAS were calculated for 2D CDS and 3D CDS and compared with DSA. A P value of <0.05 was considered statistically significant.
Results

Three-dimensional CDS offline reconstruction could be performed on 47 of 49 patients. In 2 patients, 3D CDS reconstruction was impossible because of massive calcification and acoustical shadowing. A total of 15 patients showed bilateral ICAS. In a total of 62 ICASs, 3D CDS were compared with DSA. No angiographic-related or puncture site complications were recorded. Four patients had a tandem lesion distal to the carotid bifurcation, rendering 2D CDS evaluation impossible. Two examples of 3D reconstruction are demonstrated in Figures 1 and 2. Mean reconstruction time (including the scanning procedure) was 7.1 minutes (±3.1).

DSA revealed no mild ICAS, 9 (14%) moderate, 36 (58%) high-grade, and 17 (27%) critical ICAS. One moderate ICAS was categorized as mild by 3D CDS. Of 36 high-grade ICASs, 4 were classified erroneously as moderate and 1 as critical. The tendency to underestimate the stenotic degree became more obvious in the critical ICAS group: 10 of 17 (58%) critical ICASs were classified as high-grade (Table 2). In summary, 15 of 62 (24%) angiographically proven ICASs were underestimated by 3D CDS by 1 grade.

Bland and Altman analysis expressed in percentage points showed good intermethod agreement for 3D CDS and DSA (bias −0.02; 2 SD limits of agreement −0.13 and 0.08; Figure 3), which was found to be better than agreement of 2D CDS and DSA (bias −0.03; 2 SD limits of agreement −0.28 and 0.22; Figure 4). Agreement between 2D and 3D CDS was moderate (bias −0.05; 2 SD limits of agreement −0.28 and 0.21; Figure 5). The combined information of 3D CDS and 2D CDS was largely congruent with DSA (bias <0.01; 2 SD limits of agreement −0.16 and 0.16). The degree of agreement comparing semiquantitative grades of stenosis acquired with DSA and 3D CDS resulted in a $\kappa_w$ of 0.69 ($P<0.001$) and hence a reasonable congruence (Table 1). The additionally evaluated Spearman correlation coefficient showed good correlation of DSA and 3D CDS findings ($r=0.74$; $P<0.001$).

For 3D CDS, an excellent intraobserver repeatability was calculated (bias 0.01; repeatability coefficient 0.07) using the Bland and Altman method. Interobserver reliability was found to be high ($\kappa_w=0.88$).

### Table 1.
Comparison of 3D CDS Against DSA Showed Moderate Intermethod Agreement

<table>
<thead>
<tr>
<th></th>
<th>3D CDS</th>
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<tbody>
<tr>
<td></td>
<td>0%–39%</td>
</tr>
<tr>
<td>DSA</td>
<td></td>
</tr>
<tr>
<td>0%–39%</td>
<td>0</td>
</tr>
<tr>
<td>40%–59%</td>
<td>1</td>
</tr>
<tr>
<td>60%–79%</td>
<td>0</td>
</tr>
<tr>
<td>80%–99%</td>
<td>0</td>
</tr>
<tr>
<td>Occlusion</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
</tr>
</tbody>
</table>

$\kappa_w=0.69; P<0.001; n=62.$
TABLE 2. Sensitivity and Specificity, Positive and Negative Predictive Values for High-Grade and Critical ICAS With 2D CDS and 3D CDS Compared to DSA

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPVs (%)</th>
<th>NPVs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D CDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>60</td>
<td>97</td>
<td>58</td>
<td>95</td>
</tr>
<tr>
<td>High-grade</td>
<td>78</td>
<td>86</td>
<td>84</td>
<td>78</td>
</tr>
<tr>
<td>Critical</td>
<td>92</td>
<td>80</td>
<td>80</td>
<td>92</td>
</tr>
<tr>
<td>3D CDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>66</td>
<td>92</td>
<td>67</td>
<td>92</td>
</tr>
<tr>
<td>High-grade</td>
<td>99</td>
<td>67</td>
<td>75</td>
<td>99</td>
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<tr>
<td>Critical</td>
<td>87</td>
<td>98</td>
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<td>98</td>
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PPVs indicates positive predictive values; NPVs, negative predictive values.

For comparison of 3D CDS results with the diagnostic value of “classic” 2D CDS, a $\kappa$ of 0.78 was calculated apart from the Bland and Altman procedure. The $\kappa$, for 2D CDS compared with DSA was 0.68 ($P<0.001$). Correlation of the 2 techniques resulted in $r=0.86$.

We calculated the mean sensitivity, specificity, and the positive and negative predictive values for 2D CDS and 3D CDS for detecting high-grade and critical stenosis by using DSA as the reference standard. The 3D CDS yielded a sensitivity of 93%, a specificity of 83%, a positive predictive value of 82%, and a negative predictive value of 98% (Table 2). For 2D CDS, the following mean values were calculated: sensitivity 85%, specificity 83%, positive predictive value 82%, and negative predictive value 95% (Table 2).

**Discussion**

The usefulness of CDS as a screening tool for carotid artery disease is unquestioned, but compared with DSA, the demonstration of vessel disease through use of screenshots or video clips of CDS examinations is often not easy to interpret for those who are unfamiliar with the technique.

MRA, and to a lesser extent CT angiography (CTA), is being used increasingly to avoid DSA. These modalities are likely to replace conventional angiography during the next several years.20–24 Compared with DSA, MRA, and CTA, the costs for 3D CDS are much lower, especially because currently, the necessary equipment is often implemented in high-end duplex scanners. Another advantage of 3D CDS, especially when compared with DSA, as well as with MRA and CTA, is independence from contrast agent application, the ability to conduct studies at the patients’ bedside, and a shorter examination time. The mean reconstruction time (including the scanning procedure) in our study was comparable to the results of the recently published article by Bucek et al.25 When comparing the average time (including scanning and reconstruction) needed for MRA (10 to 15 minutes), CTA (10 to 15 minutes), and DSA (15 to 30 minutes), additional time for transportation, patient preparation, informed consent, and checking laboratory values must be kept in mind. Because 2D CDS will be conducted for screening regardless, the time consumption for an additional 3D CDS investigation is indeed very low. Furthermore, for investigators trained in 2D CDS, the 3D scanning procedure and reconstruction can be learned easily.

Several previous studies on 3D ultrasound of ICAS have shown encouraging results.9,14,25 Keberle et al compared 3D power Doppler ultrasound with conventional color-coded sonography and DSA.9 A total of 26 ICASs (7 without stenosis, 4 low-, 4 middle-, and 11 high-grade stenoses) in 13 patients were examined. High correlation ($r=0.98; P<0.001$) between the 2 methods was observed. A greater number of patients were investigated by the work group of Bucek;25 a total of 32 patients with sonographically verified ICAS (30% to 99%) and 16 asymptomatic volunteers were included; 23 of the patients underwent DSA. Significant correlation was found between 3D CDS and 2D CDS ($r=0.85; P<0.001$) and 3D CDS and angiography ($r=0.57; P<0.01$). However, neither of the 2 studies comments on the level of intermethod agreement, which can be very different from the intermethod correlation. Thus, we provide results of both analysis procedures.

Our 3D CDS findings showed a good correlation with those provided by the gold standard DSA and supplied a superior diagnostic accuracy when compared with results of 2D CDS. The correlation analysis of our study ($r=0.74$) showed inferior results to the data published recently by Keberle9 ($r=0.98$) and a better correlation compared with the data of Bucek25 ($r=0.57$). The important difference in our study and the explanation for the lower correlation coefficient in comparison to the data by Keberle et al9 is that we investigated only patients with ICAS.

Considering a more exact statistical approach for analysis of intermethod agreement, the Bland and Altman plot19 allowed us to prove 3D CDS to be a reliable technique compared with DSA. We found a better intermethod agreement for 3D CDS and DSA than for 2D CDS and DSA, and furthermore, great agreement with DSA when both sonographic methods were used together.

The combination of 2D CDS and 3D CDS is far less susceptible to common pitfalls of Doppler ultrasound using hemodynamic criteria for stenosis grading because of the additive morphological information from many different visual angles. This is underlined by the very low bias ($<0.01$) for combined stenosis assessment calculated with the Bland and Altman procedure.

Method limitations include high-grade calcified plaques and profound kinking. Reconstruction was impossible in 2 cases because of massive calcification in our series. A serious drawback of the method was the distinct but frequent underestimation of high-grade ICAS (31%), which is the reason for the only moderate specificity and positive predictive values in high-grade ICAS. Underestimation of stenosis is a known feature of power Doppler,26,27 but power Doppler has also shown to be especially useful in preocclusive ICAS assessment.28 The power mode is more sensitive in detecting low flow near the vessel wall and is less disturbed by noise and clutter. However, in our opinion, the disadvantage of stenosis underestimation is by far outweighed by the excellent morphological information that is obtainable at virtually any arbitrary view angle, allowing precise information on plaque morphology and vessel routing.
Access to results of previous examinations is provided by storage on digital data media. This allows a second analysis of the raw data by a different investigator as well as animated data presentation as a 3D volume survey for interdisciplinary meetings and stent implantation or carotid endarterectomy planning.

3D sonography will not replace 2D CDS, but the combination of 3D images and hemodynamic assessment may improve carotid sonography reliability and will ease the demonstration of pathological sonographic findings to those who are not familiar with this technique. Three-dimensional demonstration of pathological sonographic findings to those of the raw data by a different investigator as well as animated storage on digital data media. This allows a second analysis of the precise grade of ICAS together with high-quality morphological information, a combination of 2D and 3D CDS is regarded as useful.

References
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