8 Carotid Arteries

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8.1 Introduction

According to clinical trials in symptomatic (North American Symptomatic Carotid Endarterectomy Trial Collaborators 1991) or asymptomatic patients (Executive Committee for the Asymptomatic Carotid Atherosclerosis Study 1995), the prevalence of significant (>50%) stenosis of the carotid bifurcation in symptomatic patients is 18–20%, while that in asymptomatic patients referred for carotid imaging is 14%. The prevalence of internal carotid artery disease (Grant et al. 2003) in the asymptomatic group, therefore, approaches that found in symptomatic patients. Both the above-mentioned studies proved the benefit of carotid endarterectomy in patients with severe symptomatic carotid artery stenosis. Recent publications have demonstrated that subgroups of patients with a 50%–69% stenosis may also expect a small benefit from carotid endarterectomy (European Carotid Surgery Trialists' Collaborative Group 1991).

Color Doppler ultrasound (US) has dramatically increased the accuracy and feasibility of US carotid examination and is now the screening examination of choice in the detection of extracranial carotid artery stenosis (Grant et al. 2003). Considerable gains have been made in the quality of US examinations of the carotid arteries, such as improved gray-scale resolution due to use of speckle-reducing modes, tissue harmonic and compound imaging, and Doppler methods with improved sensitivity to slow flows. Nevertheless, color Doppler US is nondiagnostic in a small but significant number of cases. The more frequent causes of nondiagnostic color Doppler US are borderline stenosis or preocclusive internal carotid artery stenosis.

Intra-arterial digital subtraction angiography (DSA) is considered the reference procedure in the assessment of carotid stenosis, and DSA has become the standard of reference for selecting patients for carotid surgery (Nederkorn et al. 2003). However, DSA has several drawbacks, e.g., patient discomfort, its invasive nature, and the risk of complications. According to previous reports there is a 4% risk of transient ischemic attack or minor stroke, a 1% risk of major stroke, and even a small (<1%) risk of death (Hankey et al. 1990; Davies and Humphrey 1993). Therefore, noninvasive or minimally invasive techniques such as three-dimensional (3D) time-of-flight (TOF) magnetic resonance (MR) angiography and contrast-enhanced MR angiography (Back et al. 2000; Nederkorn et al. 2003) are increasingly being used as supplements to duplex US in the diagnosis of carotid artery stenosis. Recently, contrast-enhanced US, performed after the injection of a microbubble-based agent, has been proposed for the assessment of carotid artery stenosis (Kono et al. 2004).

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8.2 Carotid and Vertebrobasilar Color Doppler US

The NASCET (1991) and ECST trials (1991) showed the strong benefit of endarterectomy in appropriate symptomatic patients with 70-90% internal carotid artery stenoses. In the NASCET method, the smallest internal carotid artery lumen diameter is compared to the distal internal carotid artery diameter, while in ECST the smallest internal carotid artery lumen diameter is compared with the estimated lumen diameter of the normal carotid bulb.

Numerous imaging and Doppler parameters are currently used at various laboratories for the evaluation of internal carotid artery stenosis, including peak systolic velocity (PSV), end-diastolic velocity (EDV), the ratio of PSV of the internal and the common carotid artery, EDV in the common carotid artery, and the ratio of EDV in the internal and the common carotid artery. The PSV measured in the internal carotid artery stenosis and the presence of plaque on gray-scale and/or color Doppler US are the parameters that should be used when diagnosing and grading stenosis (Grant et al. 2003). The other parameters may be employed when the PSV may not be representative of the extent of disease owing to technical or clinical factors such as the presence of tandem lesions, contralateral high-grade stenosis, discrepancy between visual assessment of plaque and the PSV in the internal carotid artery, elevated velocity in the common carotid artery, hyperdynamic cardiac state, or low cardiac output (Grant et al. 2003).

Analysis of the spectral Doppler waveforms has been successful in the detection of stenosis even though this is an indirect method of evaluating the degree of narrowing. Color and power Doppler US provide angiographic-like images of the carotid arteries that help delineate the lumen but are limited by low temporal or spatial resolution, angle dependence, and susceptibility to artifacts (Kono et al. 2004). Although Doppler imaging is reasonable in a number of situations, the represented flow and the vessel wall do not overlap in conditions in which flow is turbulent or disturbed by plaque or clot or when vascular tortuosity is present. Furthermore, regions of slow or small-volume flow, as occur in very tight stenoses and long narrow channels, may be invisible at Doppler imaging.

8.3 Contrast-Enhanced US of the Carotid Arteries

Microbubble-based contrast agents may be imaged by dedicated gray-scale contrast-specific modes such as phase inversion or multipulse techniques. The phase-inversion harmonic technique was found to be superior to the second harmonic technique for vascular imaging because of its higher spatial resolution, more effective tissue suppression, and higher sensitivity to flow (Steinbach 1999).

Gray-scale filling of vessels with a microbubble-based agent was shown to be more reliable and more accurate than filling of vessels with color Doppler signal both in vitro and in an animal model (Sirlin et al. 2001), and in humans (Mattrey and Kono 1999). The normal carotid bulb and the internal and external carotid arteries (Fig. 8.1) are clearly depicted by contrast-enhanced US, with accurate delineation of the external and internal borders of the carotid wall (Fig. 8.2).

High-frequency (5–10 MHz) linear-array transducers have to be employed to assess carotid arteries,

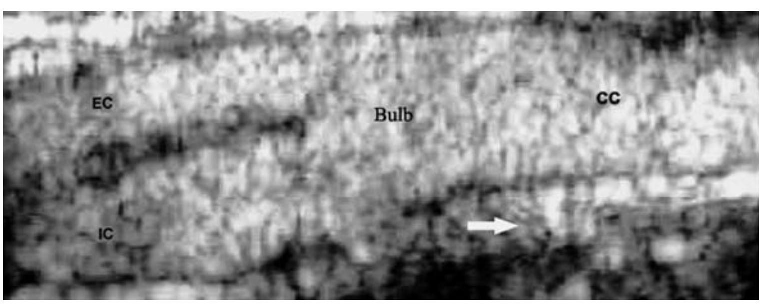


Fig. 8.1. Contrast-enhanced US angiography of the normal carotid bulb. Contrast-tuned imaging (Esaote, Genoa, Italy) with a high-frequency (3–10 MHz) linear transducer and low acoustic power insonation after the injection of sulfur hexafluoride-filled microbubbles. The common carotid (*CC*), internal carotid (*IC*), and external carotid (*EC*) arteries are clearly depicted by enhancing the acoustic backscattering from blood. A moderately high acoustic power (mechanical index = 0.3) is employed to increase the signal produced by microbubbles, in part from microbubble resonance and in part from microbubble destruction. However, the increased insonation power results in incomplete suppression of the background signal from stationary tissues (*arrow*).

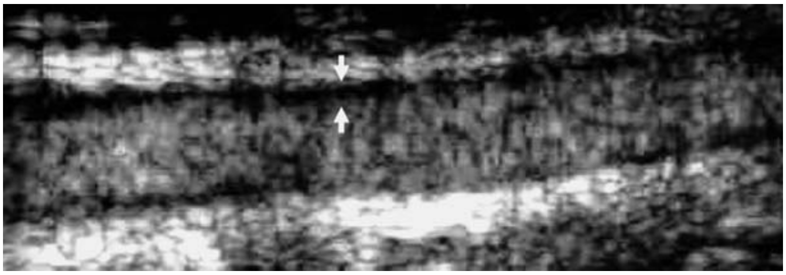


Fig. 8.2. Contrast-enhanced US angiography of the normal common carotid artery. Contrast-tuned imaging (Esaote, Genoa, Italy) with a high-frequency (3–10 MHz) linear transducer and low acoustic power insonation after the injection of sulfur hexafluoride-filled microbubbles. The vessel wall of the common carotid artery, at both the intimal and the adventitial side, is accurately delineated by the enhanced acoustic backscattering from blood owing to the microbubbles.

including after the injection of microbubble-based agents (Fig. 8.1). Nowadays, high-frequency linear-array transducers display lower sensitivity to microbubble resonance than do low-frequency curved-array transducers. This is because the resonance frequency is related to the diameter of the microbubbles, and most microbubbles present a resonance frequency of around 3–3.7 MHz, which is closer to the center frequency transmitted by low-frequency transducers than to that transmitted by high-frequency transducers. Consequently, the insonation produced by a high-frequency transducer results in the resonance of fewer microbubbles with a smaller diameter, and in the production of a lower signal. For these reasons, in contrast-enhanced US of carotid arteries it is reasonable to slightly increase the acoustic power of insonation (e.g., mechanical index of 0.3–0.4) in order to increase the signal, produced partly from microbubble destruction and partly from microbubble resonance. Nevertheless, this results in an incomplete suppression of the background signal from the stationary tissues (Fig. 8.1), which produce signal if the acoustic power insonation presents a mechanical index exceeding 0.15–0.2.

8.4 Advantages of Contrast-Enhanced US Compared to Baseline Color Doppler US

8.4.1 Quantification of Internal Carotid Artery Stenosis

Correct quantification of the percentage reduction in the carotid lumen by a plaque may be obtained by contrast-enhanced US (Figs. 8.3, 8.4). Correct quantification of internal carotid artery stenosis may be

a

b

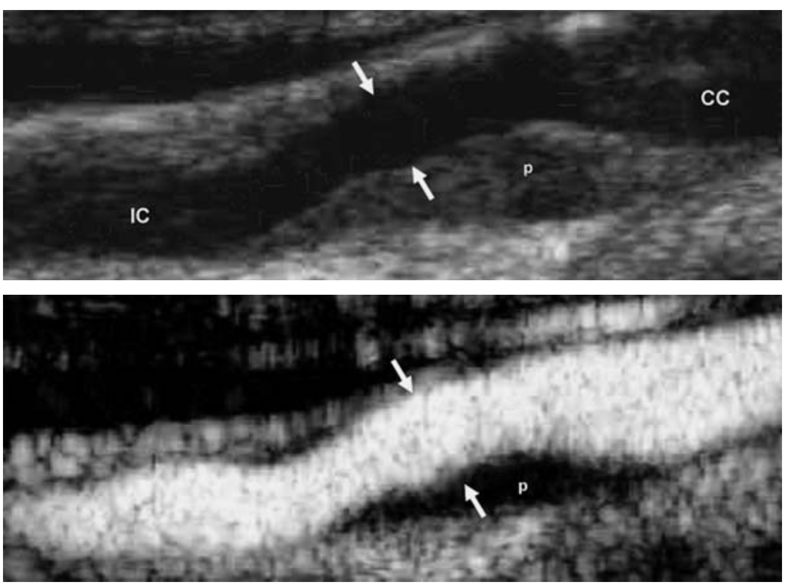
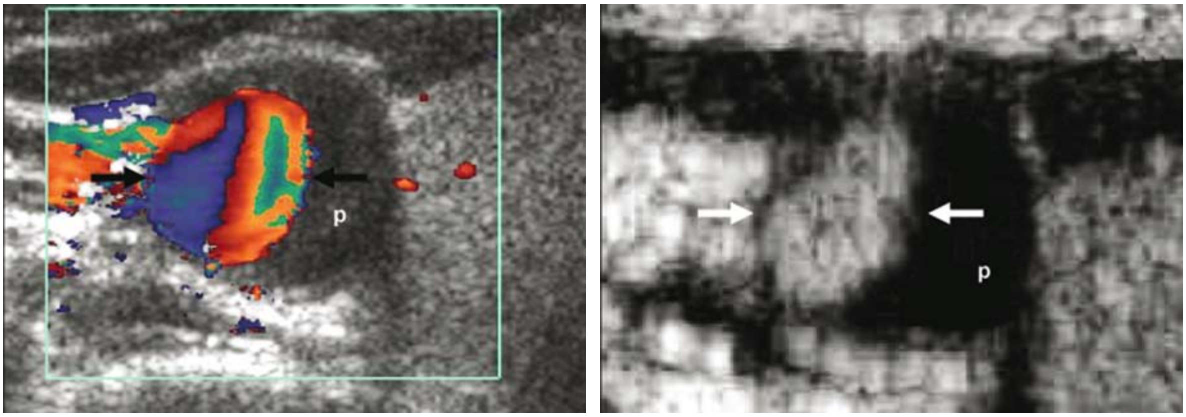


Fig. 8.3a,b. Contrast-enhanced US angiography of a fibrous plaque (*p*) in the carotid bulb. Baseline US (**a**) and contrast-enhanced US (**b**) after the injection of sulfur hexafluoride-filled microbubbles. Longitudinal plane. The residual lumen (*arrows*) of the vessel is clearly depicted by the enhanced acoustic backscattering from blood owing to the microbubbles. *CC* common carotid artery, *IC* internal carotid artery.



a b

Fig. 8.4a,b. Contrast-enhanced US angiography of a fibrous plaque (*p*) in the carotid bulb. Baseline color Doppler US (**a**) and contrast-enhanced US (**b**) after the injection of sulfur hexafluoride-filled microbubbles. Axial plane. The residual lumen (*arrows*) of the vessel is clearly delineated by both color Doppler US and contrast enhanced US.

achieved by means of contrast-enhanced US after microbubble injection. According to the NASCET method (1991), the smallest internal carotid artery lumen diameter at the stenosis level is compared to the distal internal carotid artery diameter (Figs. 8.5, 8.6). Significant agreement has been shown between contrast-enhanced US and intra-arterial digital subtraction angiography in the quantification of internal carotid artery stenosis (Kono et al. 2004).

The ability to visualize the entire internal carotid artery lumen allows the accurate depiction of stenoses, with percentage stenosis values that are highly correlated with those obtained using conventional DSA (Kono et al. 2004). Furthermore, because US images also show the outer wall, the full thickness of the plaque is displayed (Fig. 8.4), which allows accurate monitoring of disease regression or progression (Sirlin et al. 2001).

The ability to depict the outer and inner margins in the transverse plane allows the measurement of percentage area reduction at the point of maximal narrowing. Percentage area narrowing values are more reliable than the percentage diameter stenosis because they are measured at the point of interest rather than at the distal vessel, where findings may or may not be normal (Kono et al. 2004). Furthermore, because stenoses can be eccentric, one would expect them to be more accurately measured on two-dimensional projections, as has been demonstrated by ex vivo measurements of resected carotid plaque at MR imaging (Kono et al. 2004).

The principal application of contrast-enhanced US in carotid artery disease is in differentiating tight stenoses from complete occlusion (Fig. 8.7). In particular, regions of slow flow or small-volume flow, such as channels in recanalized clots or very tight preocclusive stenoses, may not be identified by Doppler but are clearly depicted by contrast-enhanced US due to its higher spatial and time resolution (Sirlin et al. 1997). The correct differentiation of a preocclusive internal carotid artery stenosis from internal carotid artery occlusion is of fundamental importance for the decision on whether to adopt a surgical or a conservative approach.

8.4.2 Assessment of the Distal Internal Carotid Artery

Contrast-enhanced US also allows more effective assessment of the distal part of the internal carotid artery in comparison with color Doppler US. In particular, the part of the internal carotid artery immediately outside the cranium may be effectively assessed by contrast-enhanced US (Fig. 8.5c,d). Although contrast-enhanced US is not impaired by artifacts, such as the blooming that occurs in color Doppler US, acoustic shadowing or signal attenuation may be identified if a large dose of microbubbles has been employed (Kono et al. 2004).

8.4.3 Characterization of Atherosclerotic Plaques and Detection of Carotid Plaque Ulceration

Color Doppler US does not allow correct assessment of the surface of thrombotic atherosclerotic plaques owing to the limited spatial resolution, the presence

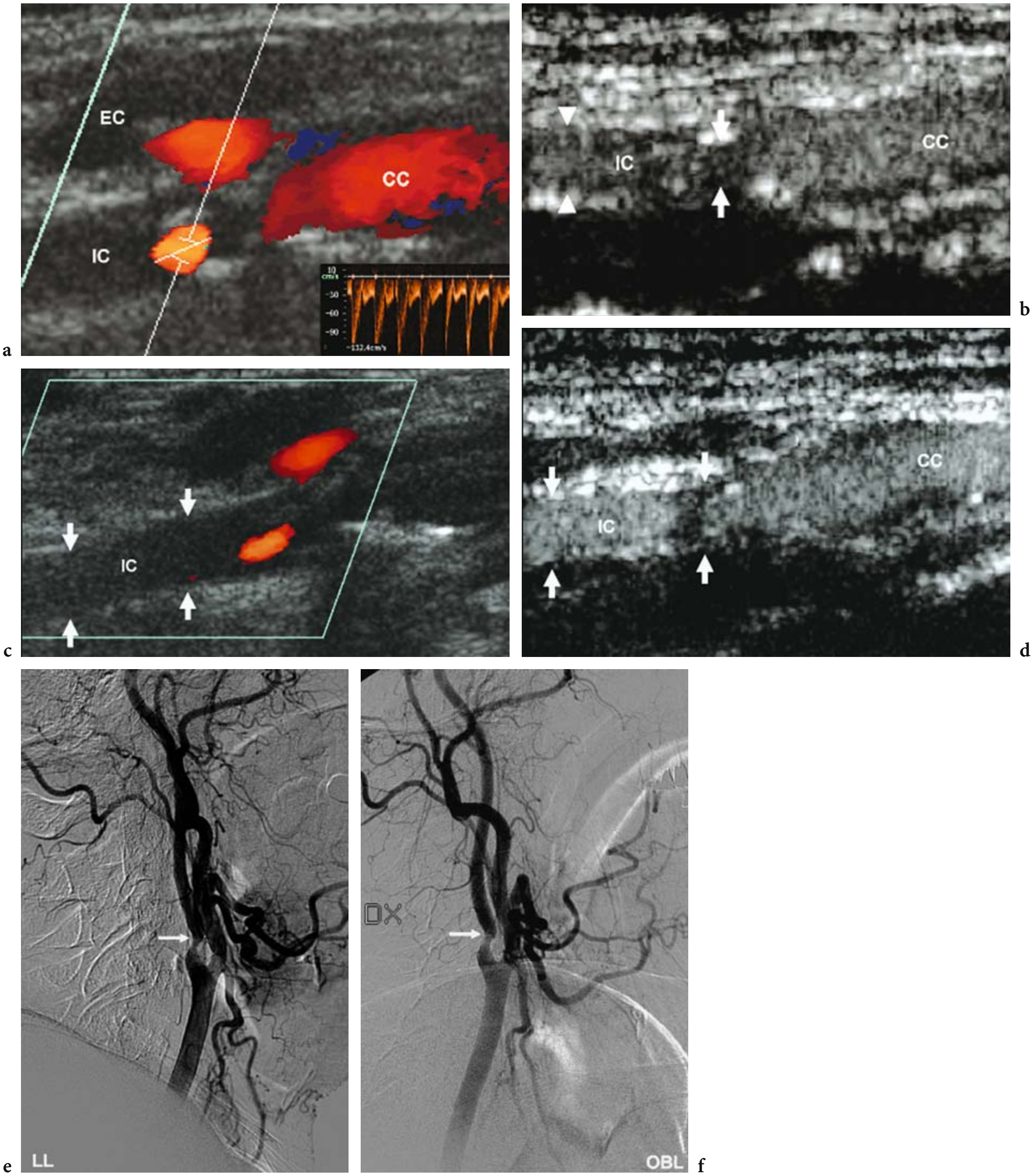


Fig. 8.5a–f. Improvement in the assessment of internal carotid artery stenosis and of the distal arterial segment by contrast-enhanced US in comparison with baseline color Doppler US. **a** Baseline power Doppler US does not allow accurate assessment of the right internal carotid (*IC*) artery stenosis (*arrows*) for the presence of a fibrocalcific plaque in the carotid bulb. **b** Contrast-enhanced US after the injection of sulfur hexafluoride-filled microbubbles allows assessment of the residual lumen of the internal carotid artery. Quantitation of internal carotid artery stenosis is performed by comparing the smallest diameter (*arrows*) of the arterial stenotic segment to the diameter of the distal internal carotid artery (*arrowheads*) according to the NASCET method (about 60% stenosis). **c** Baseline color Doppler US does not allow evaluation of the right internal carotid artery segment (*arrows*) distal to the fibrocalcific plaque in the bulb. **d** Contrast-enhanced US clearly depicts the distal internal carotid artery, revealing normal patency. **e, f** Right lateral (**e**) and oblique (**f**) intra-arterial digital subtraction angiography confirms the stenosis (about 60%) (*arrow*). *CC* common carotid artery, *EC* external carotid artery.

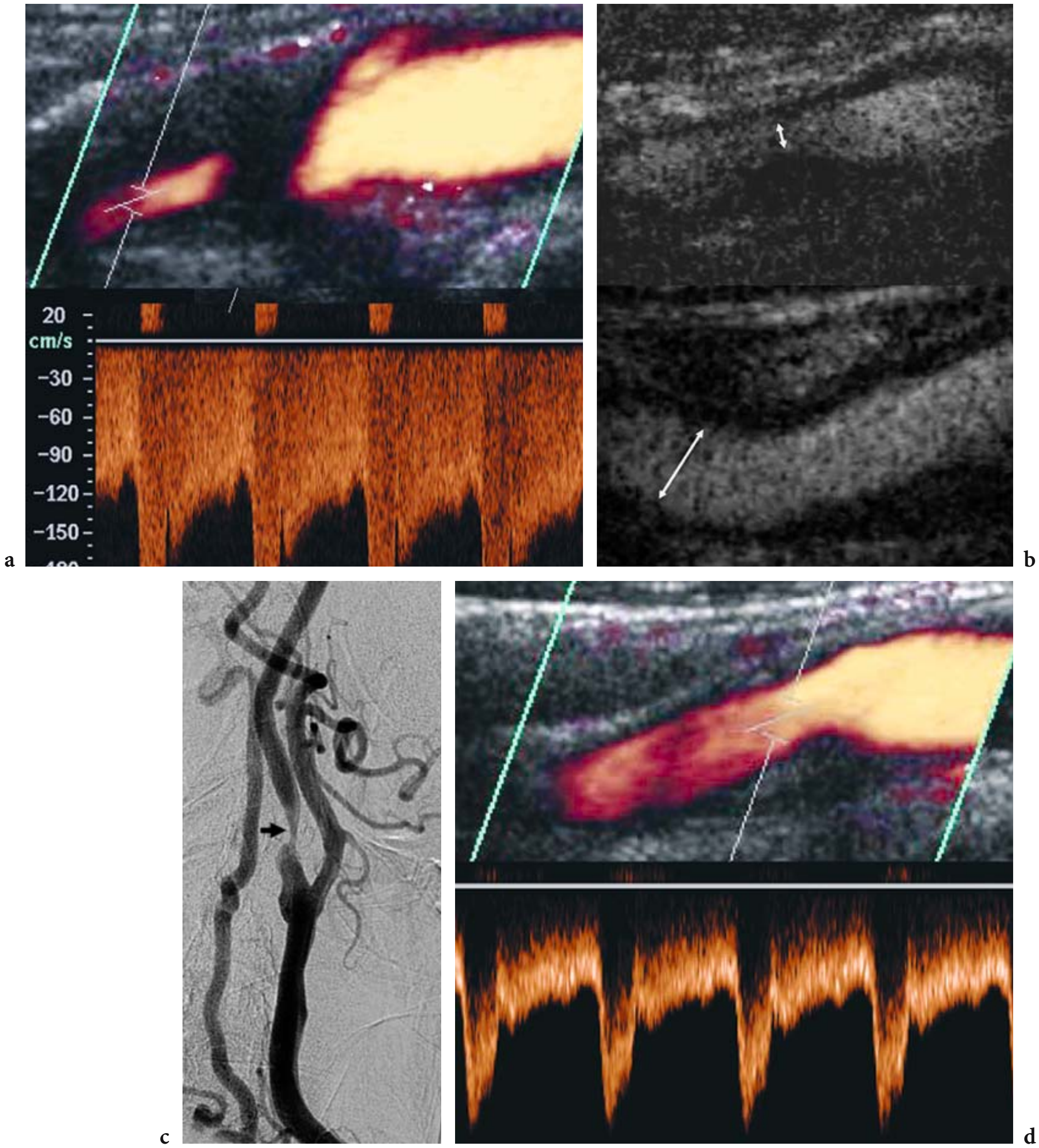
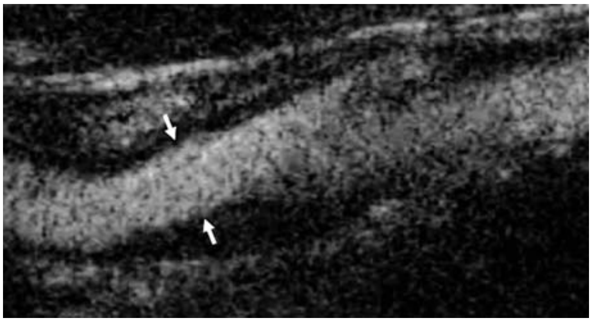


Fig. 8.6a–f. Further examples of improvement in the assessment of internal carotid artery stenosis and of the distal arterial segment by contrast-enhanced US in comparison with baseline color Doppler US. **a** Baseline power Doppler US does not allow assessment of the right internal carotid artery stenosis for the presence of a fibrocalcific plaque in the carotid bulb. Doppler interrogation (Doppler volume) is possible exclusively downstream of the calcific plaque, revealing high peak systolic velocity with spectral trace broadening. **b** Contrast-enhanced US after the injection of sulfur hexafluoride-filled microbubbles allows assessment of the residual lumen (*arrows*) of the internal carotid artery. By comparing the internal carotid artery lumen diameter at the stenosis (above) to the downstream internal carotid artery diameter (below), according to the NASCET method, the right internal carotid artery stenosis is quantified as 90%. **c** Lateral view of the right internal carotid artery on intra-arterial digital subtraction angiography. The high-grade stenosis (90%) of right internal carotid artery (*arrow*) is confirmed. **d** Baseline color Doppler US identifies a moderate stenosis caused by a fibrotic plaque in the left internal carotid artery (Doppler volume).


e


f

continued Fig. 8.6. e Contrast-enhanced US allows a clear depiction of the residual lumen of the left internal carotid artery. The stenosis is quantified as 40%. **f** Lateral view of the left internal carotid artery on intra-arterial digital subtraction angiography. The low-grade stenosis of the left internal carotid artery (*arrow*) is confirmed.

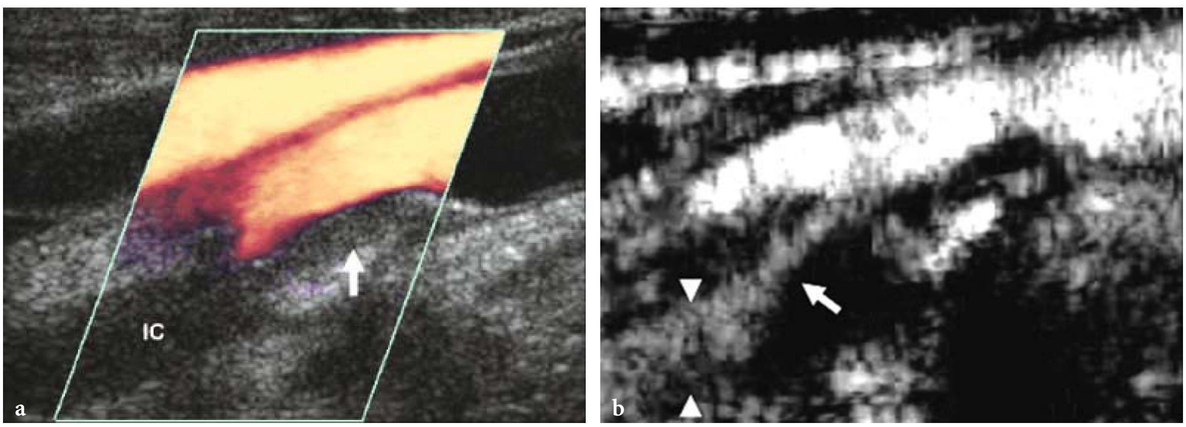


Fig. 8.7a–d. Improvement in the assessment of preocclusive internal carotid artery stenosis by contrast-enhanced US in comparison with baseline color Doppler US. **a** Baseline power Doppler US reveals a fibrous plaque (*arrow*) in the right carotid bulb without revealing the residual lumen of the internal carotid (*IC*) artery. **b** Contrast-enhanced US after the injection of sulfur hexafluoride-filled microbubbles allows correct visualization of the residual lumen of the internal carotid artery (*arrow*), revealing a reduction in the lumen diameter of about 90–95%. The quantitation is performed by comparing the smallest diameter (*arrow*) of the stenotic segment to the diameter (*arrowheads*) of the distal internal carotid artery according to the NASCET method. **c, d** Right anteroposterior (**c**) and laterolateral (**d**) intra-arterial digital subtraction angiography confirms preocclusive internal carotid artery stenosis (about 95%) (*arrow*).

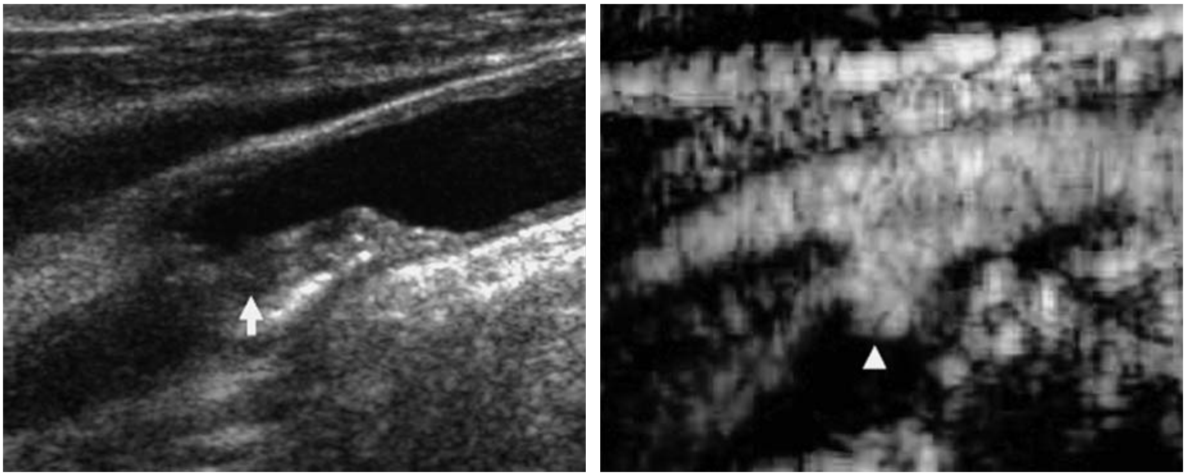


Fig. 8.8. a Baseline US reveals a fibrotic plaque in the right carotid bulb (*arrow*). **b** Contrast-enhanced US after injection of sulfur hexafluoride-filled microbubbles reveals ulceration (*arrowhead*) in the plaque in the carotid bulb.

of artifacts and superimposition of color pixels at the plaque borders. Nowadays, contrast-specific modes offer high spatial resolution and permit the elimination of artifacts. For these reasons, the border of a complicated plaque, such as an ulcerative or hemorrhagic plaque (Fig. 8.8), may be effectively identified and characterized after microbubble injection.

Contrast-enhanced US can clearly depict plaque ulcerations and recanalization not detected on Doppler US images because of the effect of turbulence, flow disturbance, or slow flow (Kono et al. 2004). Moreover, contrast-enhanced US has further advantages over color Doppler US, such as independence from the angle of incidence and absence of the technical parameters necessary for optimal filling of vessels on color Doppler US (Kono et al. 2004).

8.5 Limitations of Contrast-Enhanced US in the Assessment of Carotid Arteries

Contrast-enhanced US of the carotid arteries does have various limitations. First, like color Doppler US, contrast-enhanced US is of limited value in the presence of grossly calcific plaque, the only possible solution being to examine the vessels before and after the acoustic shadowing caused by the plaque. This limitation is obvious, given that US transmission is almost completely arrested behind a calcific interface, and severe calcifications hinder full visualization of the residual carotid lumen even in comparison with color Doppler US (Figs. 8.9, 8.10).

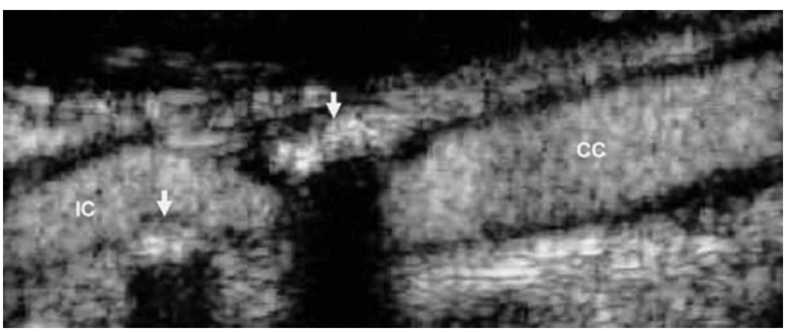


Fig. 8.9. Example of the limitations of contrast-enhanced US angiography in the presence of extensively calcified plaques (*arrows*) of the carotid bulb. Contrast-tuned imaging (Esaote, Genoa, Italy) with a high-frequency (3–10 MHz) linear transducer and low acoustic power insonation after injection of sulfur hexafluoride-filled microbubbles. At the level of carotid blub, the lumen of the vessel cannot be assessed owing to the posterior acoustic shadowing caused by the calcific component of the plaque. *CC* common carotid artery, *IC* internal carotid artery.

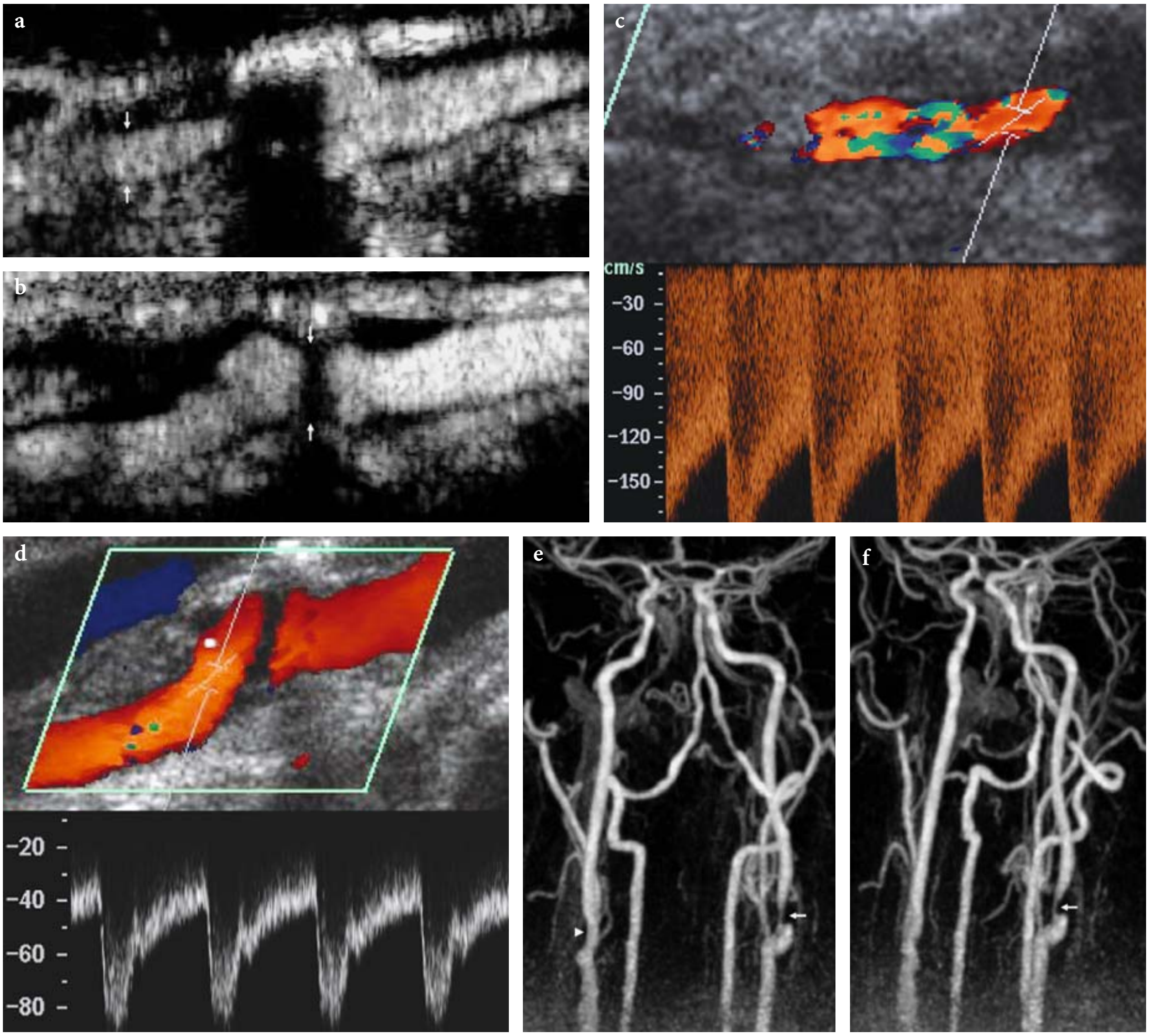


Fig. 8.10a–f. Further example of the limitations of contrast-enhanced US angiography in the presence of extensively calcified plaques of the carotid bulb. **a, b** Contrast-enhanced US angiography after the injection of sulfur hexafluoride-filled microbubbles. The tight stenosis of the left internal carotid artery (**a**) cannot be assessed owing to the posterior acoustic shadowing caused by the calcified component of the plaque, while the distal tract of the internal carotid artery (*arrows*) is clearly depicted. The presence of a calcified plaque in the right carotid bulb (**b**) resulted in posterior acoustic shadowing. **c** Color Doppler US of the left internal carotid artery with Doppler interrogation of the arterial segment immediately distal to the calcified plaque. The spectral broadening with an increase in the peak systolic velocity reveals a tight stenosis (about 90%). **d** Color Doppler US of the right internal carotid artery with Doppler interrogation. The regular Doppler trace allows exclusion of a significant stenosis. **e, f** Contrast-enhanced MR angiography confirms a tight stenosis of the left internal carotid artery (*arrow*) and a nonstenosing plaque (*arrowhead*) in the right bulb.

Second, contrast-enhanced US cannot assess velocimetric parameters related to the grade of stenosis but only geometric parameters related to carotid lumen reduction. Velocimetric parameters still have to be evaluated by Doppler interrogation of the vessels.

Third, dedicated contrast-specific modes have to be employed after the injection of microbubble-based agents. The use of contrast-enhanced color Doppler US is still not acceptable because of the presence of many artifacts, such as color blooming and spike artifacts in the Doppler trace (Fig. 8.11).

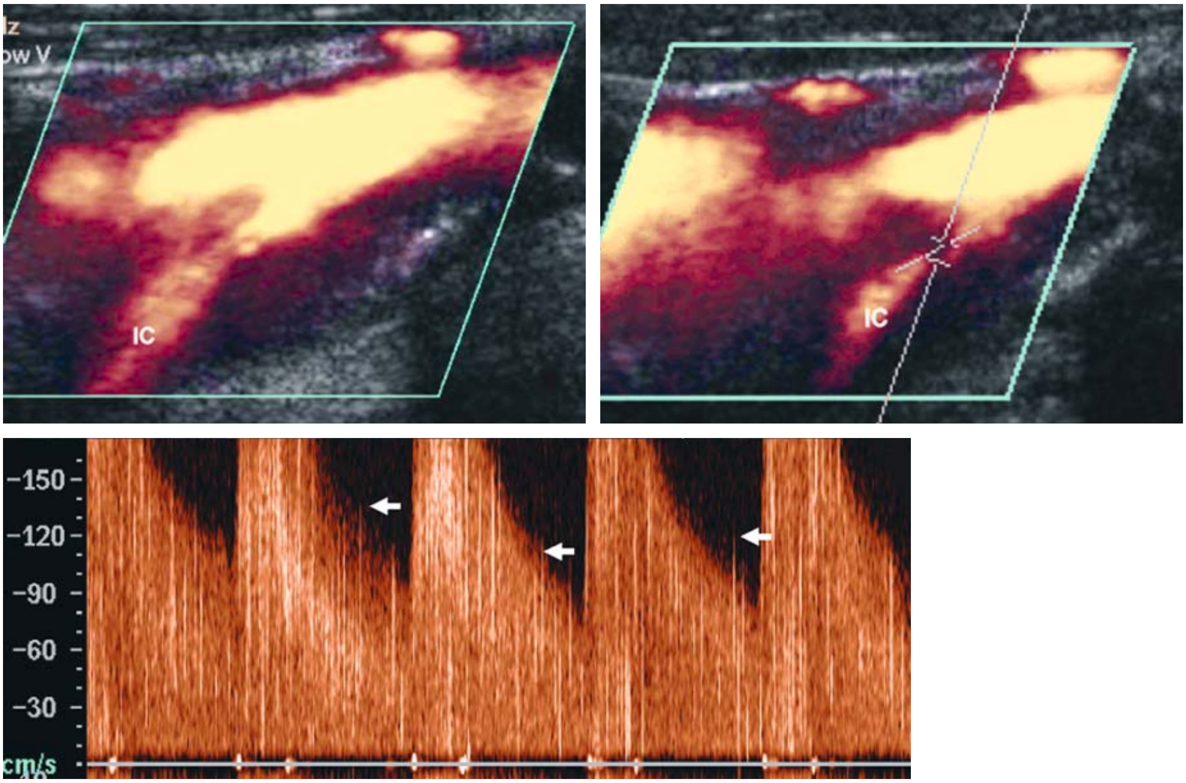
a b c


Fig. 8.11a–c. Power Doppler US with Doppler interrogation of the internal carotid artery after microbubble injection reveals spectral broadening with a markedly increased peak systolic velocity at the internal carotid artery. Extensive blooming artifacts, with color signal outside the vessel wall, are visible. Moreover, spike artifacts (*arrows*) from macrobubble aggregates or microbubble collapse are identifiable in the spectral trace (**c**).

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