## Depiction of Carotid Plaque Ulceration and Other Plaque-Related Disorders by Intravascular Sonography: A Flow Chamber Study

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**PURPOSE:** To evaluate the ability of intravascular sonography to depict plaque ulceration and to identify the limitations of and the artifacts associated with this technique. **METHODS:** Twenty-eight human carotid arteries were mounted in a pulsatile flow chamber and examined with intravascular sonography. We compared 140 intravascular sonograms with gross pathologic and histologic sections. Ulcerations with a diameter or depth of at least 0.5 mm were sought. **RESULTS:** All eight arteries with ulcerated plaques and nine of 10 individual ulcerations were depicted by intravascular sonography. One artery (one of 140 arterial cross sections) with a small mural thrombus was misinterpreted as ulcerated. Our intravascular sonographic measurements underestimated the gross ulceration dimensions by 22% (depth) and 17% (orifice diameter). **CONCLUSIONS:** Intravascular sonography is highly accurate for the diagnosis of plaque ulceration. The central position of the high-frequency transducer within the target vessel facilitates high resolution of the arterial lumen–wall border, permitting more powerful definition of small ulcerations than available by other diagnostic methods. However, the utility of invasive intravascular sonography for detecting carotid ulcerations cannot be determined until the pathologic significance of plaque ulceration is clearly defined.

Index terms: Arteries, carotid; Arteries, ulceration; Arteries, ultrasound

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According to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (1), the primary determinant of the need for carotid endarterectomy is the degree of arterial stenosis. The NASCET investigators also considered plaque ulceration an important factor in lesions with high-grade stenosis (2). Carotid plaque ulceration may be a cerebral embolic source, even when the degree of stenosis is less than 70% (3–6). Carotid ulcerations are thought to increase the risk for cerebral embolism by acting as thromboembolic substrates or by allowing plaque components to fracture into the

AJNR 17:1881–1890, Nov 1996 0195-6108/96/1710–1881 © American Society of Neuroradiology lumen. Their detection may therefore dictate the treatment method used. Unfortunately, current neurovascular imaging methods, such as angiography (7, 8) and Doppler sonography (9), are unreliable for the detection of ulceration. Color Doppler flow sonography has been described as highly sensitive and specific for showing large ulcerations (10), but its ability to show small ulcerations, which are also thought to be clinically significant (11), has not been documented. The ability of intravascular sonography to delineate clearly the arterial lumen– wall border and wall layers (12, 13) prompted us to assess its accuracy in showing carotid plaque ulcerations.

### **Materials and Methods**

### Study Design

We sought to determine the reliability and spatial accuracy of intravascular sonography for detecting ulcerations by examining human carotid arteries in a flow chamber. To obtain intravascular sonograms that were suitable for subsequent comparison with gross pathologic and histologic arterial cross sections, we developed a comparison tech-

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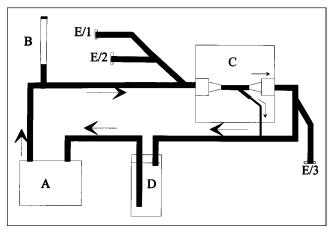


Fig 1. Flow chamber diagram. A, Harvard pump; *B*, pressure buffering tube (which mimics vessel elasticity); *C*, Plexiglas chamber with carotid artery branches mounted on plastic cones; *D*, fluid reservoir; E/1 through E/3, rotating hemostatic valves for injection of contrast agent, introduction of the catheter, or other applications; *arrows* show direction of flow.

nique based on angiographic roadmap images and continuous video recording. Interpretations of the intravascular sonograms were made in a blinded fashion, allowing unbiased comparisons with the cross sections.

#### Specimen Preparation

Twenty-eight carotid arteries were removed from human cadavers fixed with 95% ethyl alcohol (mean age, 74.4  $\pm$  9.7). The cadavers were not preselected for carotid artery disease. The arteries were kept fixed in 10% buffered formalin. After excess connective tissue was removed from the arteries, they were mounted by their common, internal, and external arterial branches on plastic cones in a Plexiglas flow chamber filled with saline (Fig 1). We used a Harvard pump to produce pulsatile flow in the arteries during the examinations. The circulating fluid was 40% glycerin, which closely approximates the viscosity of blood.

### Intravascular Sonographic Examination Technique

We used a Sonos intravascular sonographic unit (Hewlett-Packard, Andover, Mass) with Sonicath 30 MHz 3.5F sonographic catheters (Boston Scientific, Natick, Mass). The catheter was fed into the internal carotid artery via the common carotid artery. The radiopaque transducer of the catheter was positioned at the junction of the artery and the mounting cone. At this position, an initial roadmap image of each specimen was made. Intravascular sonograms were obtained by a continuous, calibrated withdrawal of the catheter (14). The calibration was accomplished by dictating each millimeter traversed by the catheter to the microphone on the sonographic unit. At selected areas, the withdrawal was momentarily interrupted so that angiograms could be obtained to record the position of the transducer. The magnification factor for these angiograms was set to 1.0 by filming a radiopaque metric ruler. In this way, the dictated position of the transducer and the angiographic reference images allowed us to determine the precise location represented by each cross-sectional sonogram. This technique was used to section the artery at selected locations corresponding to relevant sonographic images.

### Definition of a Plaque Ulceration

We defined an ulceration as an indentation, fissure, or erosion on the luminal surface of a plaque, exposing a portion of the inner plaque to direct contact with circulating blood. We set the lower limit of the orifice diameter and depth of an ulceration to 0.5 mm, a distance that we could accurately measure on gross examination, and that was within the resolution limits of the intravascular sonographic system (Fig 2).

### Interpreting Intravascular Sonograms

A neuroradiologist experienced in intravascular sonographic image interpretation reviewed the sonograms in a blinded fashion (without knowledge of gross pathologic and histologic findings). Specific features were evaluated, including the shape of the lumen–wall border and the irregularity of the plaque surfaces. The depth and diameter of each suspected ulceration were measured via the software in the sonographic unit. Other plaque-related abnormalities, such as intimal flaps and dissections, were also observed.

### Gross Pathologic and Histologic Evaluation

The arteries were cross sectioned for gross pathologic and histologic analysis, primarily at levels appearing abnormal on the intravascular sonograms. The regions that appeared nonpathologic on intravascular sonograms were longitudinally sectioned and examined for ulcerations that may have been overlooked by the interpreter. A total of 140 arterial cross-sectional segments, each approximately 3 mm thick, were produced. Gross observation, which was used to determine the presence of plaque ulcerations, is considered more accurate than histologic examination (7), because the preparation of tissue for histologic study can produce endothelial artifacts. However, sections stained with hematoxylin-eosin and trichrome were used to verify the authenticity of the ulcerations found by gross examination. We measured the dimensions of the ulcerations on the gross specimens.

### Statistical Analysis

Mean lesion size and standard error of the mean were calculated for gross and intravascular sonographic measurements. Sensitivity, specificity, positive predictive value, accuracy, and prevalence were calculated.

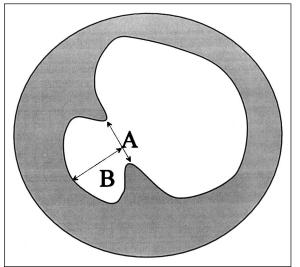


Fig 2. Definition of depth and diameter of the orifice of an ulcer. *A*, orifice diameter; *B*, depth of ulceration.

TABLE 1: Statistical analysis based on cross-sectional intravascular sonograms

| Definition of ulceration size | ≥0.5 mm                       |
|-------------------------------|-------------------------------|
| Validated by                  | Gross pathology               |
| System used                   | 30 MHz 3.5F sonographic probe |
| Number of cross sections      | 140                           |
| Sensitivity                   | 9/10 = 90%                    |
| Specificity                   | 129/130 = 99%                 |
| Prevalence                    | 10/140 = 7%                   |
| Positive predictive value     | 9/10 = 90%                    |
| Accuracy                      | 138/140 = 99%                 |

## Results

Our results are summarized in Table 1. Of the 28 arteries, 23 (82%) contained plaques, and eight of those (35%) had at least one ulceration. Two of the eight arteries had two ulcerations in the same artery. Of the 140 arterial cross sections examined, 81 (58%) contained plaque and 10 (7%) had plaque ulceration. We accurately identified all eight ulcerated arteries and nine of 10 individual ulcerations with intravascular sonography (90% to 100% sensitivity). One artery (of 140 arterial cross sections) that had a small mural thrombus was misinterpreted as ulcerated (95% to 99% specificity).

The mean average depth of the ulcerations was  $1.05 \pm 0.44$  mm, and the mean average diameter of the orifice was  $1.95 \pm 0.72$  mm, according to gross measurements. The mean dimensions of all 10 ulcerations as measured on intravascular sonograms were  $1.00 \pm 0.36$  mm (depth) and  $1.76 \pm 0.59$  mm (orifice diameter). The average of the absolute values of the differ-

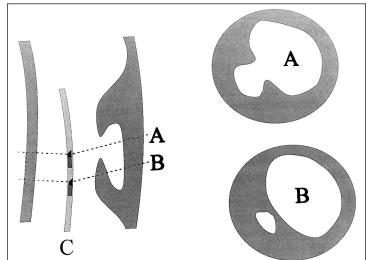


Fig 3. Cul-de-sac. *A*, midsection; *B*, proximal margin; *C*, longitudinal view, position of transducer at *A* and *B* cross sections.

ences between the gross and intravascular sonographic measurements was 0.23 (22%)  $\pm$  0.23 mm for depth, and 0.33 (17%)  $\pm$  0.28 mm for diameter.

In addition to the ulcerations, we found four intimal flaps, two dissections, four mural thrombi, and one (postendarterectomy) Dacron graft within an arterial wall.

### Discussion

## Pathogenesis of Ulcerations

The size and severity of an ulceration may vary greatly. The smallest ones are the result of partial endothelial cell loss and are visible only by microscope. Deep ulcerations may expose and release subendothelial plaque contents. Ulcerations are caused by various influences, including inflammatory cell accumulation, toxic substances, proteolytic enzymes released by macrophages, plaque weaknesses, and hemodynamic factors (15).

The pathogenesis of carotid ulcerations may include the intraplaque hemorrhage and acute plaque rupture mechanism caused by the Bernoulli effect (16). Neovascularization often develops near atheromatous lesions (17, 18). If a plaque causes a significant stenosis, the local flow velocity will increase while the intramural pressure decreases, a result predicted by Bernoulli's equation (16). The thin-walled capillaries of the neovascularization may rupture if the pressure gradient between the capillaries and the plaque becomes too large. An intraplaque hemorrhage will result and act as a positive feedback mechanism, further increasing the stenosis and the pressure gradient. The plaque's fibrotic cap may tear and be unable to protect the plaque from an acute rupture. If the cap is strong enough to resist rupture, the intraplaque hematoma undergoes maturation and fibrosis. Proliferating smooth muscle cells, rich in rough endoplasmic reticulum (15) and macrophages, always appear near intraplaque hematomas. These activated cells can weaken the fibrotic cap by releasing proteolytic enzymes such as collagenase, elastase, and stromelysin (19). As a result of these hemodynamic and biochemical factors, the plaque may rupture, leaving behind an ulceration. Ulceration in plaque types that lack intraplaque hemorrhage may occur by a similar weakening of the fibrotic cap.

## Prevalence of Plaque Ulceration

Streifler et al (7) and Fürst et al (10) studied select groups of endarterectomy patients with high prevalences of ulceration (58% and 48%, respectively). In our unselected group, 29% of the arteries had at least one ulceration. This prevalence indicates that ulceration is a common feature of carotid plaque, and therefore warrants investigation for its dangers. Only a reliable detection technique can facilitate an accurate assessment of the dangers of ulcerated plaques.

# Intravascular Sonographic Patterns of Ulcerations

Intravascular sonography typically shows an ulceration as a small cavity in the plaque. In some cases, the ulceration continues as a diverticulum, parallel to the longitudinal axis of the artery. Fisher and Ojemann (20) refer to this as a "cul-de-sac" (Fig 3). The diverticulum changes appearance in the adjacent cross sections to an apparent hole in the plaque on the intravascular sonogram. This pattern is a hallmark sign of ulcerations (Fig 4). In other cases, the ulceration appears as a deep indentation or as a shallow lesion of the intima with an irregular surface (Fig 5).

## **Overview of Different Imaging Methods**

The ability of different systems to show plaque ulceration varies tremendously. Digital

subtraction angiography has good spatial resolution but poor contrast resolution and can only provide a limited number of planes. Its strength is its ability to show large ulcerations while showing the flow pattern within and near an ulcerated lesion. Another advantage is that a long segment of the artery can be seen at once. For these reasons, this technique will most likely remain a vital tool for investigations of invasive carotid disease.

B-mode sonography, like intravascular sonography, is based purely on the echogenicity of tissues. However, unlike intravascular sonography, B-mode sonography gives an external view of the blood vessels only, and access to certain views is limited and highly investigator dependent. Yet this method is cheap, quick, noninvasive, and easily reproducible. It is a good screening method for carotid stenosis. Its ability to show plaque ulcerations is limited by its resolution and by the factors mentioned above.

Both duplex and color Doppler flow sonography have a high-frequency (7.5 to 10 MHz) transducer for B-mode image production, but their real strength lies in their Doppler capability. However, the frequency of the Doppler measurements (3.5 to 5 MHz) is usually lower than B-mode measurements. Doppler measurements also require an assignment of sample size (or volume) of at least 1 mm in order to keep noise level low. As a result, the spatial resolution of the Doppler measurements is greater than the assigned sample size, and this may result in the false interpretation of an ulceration, especially if disturbed flow is present. Furthermore, Doppler studies can yield only longitudinal views, some of which are difficult to obtain. The easy detection of disturbed flow in stenotic or ulcerated regions gives color Doppler imaging a clear advantage over duplex systems, making it a superior yet more expensive screening method.

The ability of computed tomographic angiography to show plaque ulcerations is thought to be similar or slightly better than conventional angiography (21). However, a large series has never been evaluated with this method or with magnetic resonance angiography.

# Imaging Capabilities of B-Mode Sonographic Systems

To quantify the capabilities of other imaging methods, we compared the B-mode resolution

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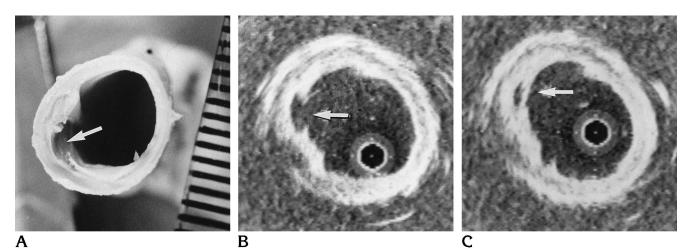




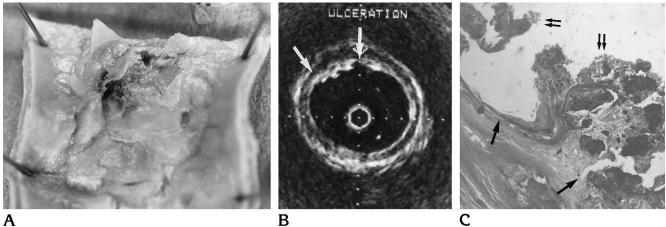
Fig 4. Deep plaque ulceration (cul-de-sac).

A, Gross photograph.

B, Intravascular cross-sectional sonogram across the orifice. The ulceration is clearly seen as an invagination of the lumen into the wall (arrow).

*C*, Intravascular cross-sectional sonogram below the orifice. The deepest portion of the ulceration is seen as an echolucent hole in the intima (arrow).

*D*, Histologic section (trichrome, magnification  $\times 25$ ).



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Fig 5. Shallow ulceration.

A, Gross photograph.

*B*, Intravascular sonogram shows irregularity of the arterial wall (between *arrows*).

C, Histologic section shows loss of endothelium, microulcerations and fissures (single arrows), and small thrombi (double arrows) near these ulcerations (trichrome, magnification  $\times 25$ ).

| System<br>Resolution     | 30-MHz Intravascular<br>Sonography Single Rotating<br>Crystal |                  | 10-MHz Linear Array<br>Transducer |                  | 5-MHz Linear Array<br>Transducer |                  |
|--------------------------|---|------------------|-----------------------------------|------------------|----------------------------------|------------------|
|                          | Calculated  | Company<br>Data* | Calculated                        | Company<br>Data† | Calculated                       | Company<br>Data† |
| Axial, mm<br>Lateral, mm | 0.08  | ≤0.2<br>0.2      | 0.23                              | 0.3<br>0.3       | 0.46                             | 0.3<br>0.4       |

 TABLE 2: Comparison of transducer frequency and resolution in B-mode sonography

\* Hewlett-Packard Sonos 2000 using Boston Scientific 3.5F sonographic probes.

† OEC-Diasonics (Salt Lake City, Utah) VST Masters Series System service manual.

limits of each. The resolution values shown in Table 2 are those of the VST Masters Series sonographic system (OEC-Diasonics, Salt Lake City, Utah). The maximum theoretical axial resolution can also be calculated according to the equation

resolution<sub>max</sub> (m) = 
$$\frac{3\lambda}{2} = \frac{3\frac{V_t}{f}}{2} = \frac{3v_t}{2f} = \frac{2310(m/s)}{f(1/s)}$$

where *m* indicates meter; *s*, second;  $\lambda$ , wavelength of the emitted ultrasound; f, frequency of the transducer; and  $v_t$ , speed of the ultrasound beam in the arterial wall (1540 m/s) (22). This equation states that the axial resolution of a system depends primarily on the frequency of the transducer (and secondarily on the spatial pulse length). The lateral resolution of a sonographic system is usually lower than its axial resolution; however, the latest phased-array units may have similar lateral and axial resolutions (23). The lateral resolution of the single rotating crystal of the transducer rapidly decreases with depth because the ultrasound beam cannot be focused electronically. However, at a distance of 2 to 3 mm (the distance between the intimal surface of the carotid artery and the transducer if the catheter is in a central position), a 30-MHz sonographic system performs well.

### Comparison of Different Imaging Methods

To compare our data with other methods (7, 10, 24, 25), we also performed a statistical analysis, which treated the arteries as individual entities (as opposed to cross sections). The results are in Table 3. On the basis of these calculations, intravascular sonography was 100% sensitive, but one artery had two lesions and we were able to detect only one of them. Of the techniques listed in Table 3, only color Doppler

flow sonography rivals intravascular sonography in ability to show ulcerations; yet we accurately detected four of four lesions with diameters less than 2.0 mm, the lower limit detected by Fü rst et al (10). The ulceration that we were unable to detect had a diameter of 3.0 mm but a depth of only 0.5 mm. None of the other authors listed in Table 3 considered depth as a criterion for ulceration size. It is particularly surprising that Fürst et al (10) did not include depth, considering that the flow signal registered on color Doppler flow sonography also relies on lesion depth. Shallow lesions, such as the one shown in Figure 5, may not be visible with color Doppler flow sonography, but they are with intravascular sonography, and can be of interest pathologically. All four of the ulcerations we detected with diameters less than 2.0 mm also had depths less than 2.0 mm (0.5, 1.0, 1.0)1.5, and 1.5 mm, respectively), so the size of these lesions is clearly below the lateral and axial resolution capabilities of color Doppler flow sonography. Since the ability of intravascular sonography was not diminished by our low limits for both depth and diameter (0.5)mm), we believe it is a more powerful and accurate method than color Doppler flow sonography.

## Capabilities of Intravascular Sonography

The main advantage of intravascular sonography is its ability to provide images from inside blood vessels. Although intravascular sonographic systems are capable of giving crosssectional views only, there are methods to reconstruct longitudinal views, or even threedimensional views, from cross-sectional data (26). In the absence of such capabilities, longitudinal mapping of a portion of an artery by pushing and pulling the catheter may be investigator dependent. Angiography must simulta-

TABLE 3: Comparison of intravascular sonography, digital subtraction angiography, B-mode and duplex sonography, and color Doppler flow sonography: data validated by gross pathology (results of different authors)

|                             | Intravascular<br>Sonography | Digital<br>Subtraction<br>Angiography | B-Mode<br>Sonography  | Duplex<br>Sonography | Color Doppler<br>Flow<br>Sonography |
|-----------------------------|-----------------------------|---------------------------------------|-----------------------|----------------------|-------------------------------------|
| Study                       | Our results                 | Streifler et al,<br>NASCET (7)        | O'Leary et al<br>(25) | Young et al (24)     | Fürst et al (10)                    |
| Definition of<br>ulceration |                             |                                       |                       |                      |                                     |
| size                        | ≥0.5 mm                     |                                       | ≥1 mm                 |                      | ≥2 mm                               |
| Validated by                | Gross pathology             | Gross pathology                       | Gross pathology       | Gross pathology      | Gross pathology                     |
| System                      | 30-MHz 3.5F                 | Biplane                               | 7.5- or 10-MHz        | 10-MHz               | 5.0- or 7.5-MHz                     |
| used                        | sonographic<br>probe        | angiography                           | transducer            | transducer           | transducer                          |
| No. of                      | 1                           |                                       |                       |                      |                                     |
| arteries                    | 28                          | 500                                   | 47                    | 12                   | 89                                  |
| Sensitivity                 | 8/8 = 100%                  | 130/283 = 46%                         | 7/18 = 39%            | 0/2 (=0%)*           | 41/43 = 95%                         |
| Specificity                 | 19/20 = 95%                 | 146/197 = 74%                         | 21/29 = 72%           | 8/10 (=80%)*         | 46/49 = 94%                         |
| Prevalence                  | 8/28 = 29%                  | 290/500 = 58%                         | 18/47 = 38%           | 2/12 (=17%)*         | 43/89 = 48%                         |
| Positive<br>predictive      |                             |                                       |                       |                      |                                     |
| value                       | 8/9 = 89%                   | 130/181 = 72%                         | 7/15 = 47%            | 0/2 (=0%)*           | 41/44 = 93%                         |
| Accuracy                    | 27/28 = 96%                 | 278/500 = 56%                         | 28/47 = 60%           | 8/12 (=67%)*         | 84/89 = 94%                         |

\* Sample size insufficient for statistical analysis.

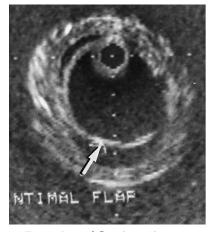


Fig 6. Intimal flap (arrow).

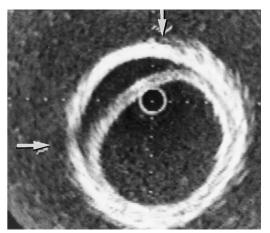


Fig 7. Dissection of the arterial wall (between arrows).

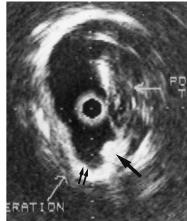


Fig 8. A thrombus is attached near the apex of the bifurcation (*single black arrow*). The cleft (*double arrows*) between this thrombus and the normal wall was misinterpreted as an ulceration.

neously accompany the intravascular sonographic investigation to validate the level of the findings and to direct the catheter.

# Intravascular Sonographic Patterns of Other Plaque-Related Disorders

An intimal flap is seen as a 0.5- to 1.0-mmthick intimal segment, partially detached from the arterial wall. The free edge makes a flapping movement during the cardiac cycle. We found four intimal flaps via intravascular sonography (Fig 6); all were validated by gross pathologic and histologic examinations; however, some of them may have been artificial.

Dissection appears as a lenticular layer within the arterial wall, which changes its shape during the cardiac cycle. Its echogenicity is similar to that of blood or, in this experiment, of circulating fluid. We accurately identified two dissections with intravascular sonography (Fig 7).

Mural thrombus appears as a thickened, echodense region attached to endothelium or to

Fig 9. Lateral impulse response artifacts (*arrows*).

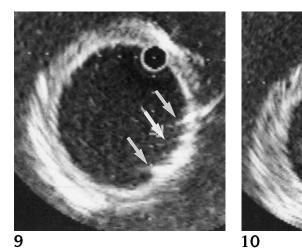


Fig 10. Origin of the superior thyroidal artery (*arrow*), which may mimic an ulceration.

an ulcerated surface. The echodensity and thus the visibility of the thrombus in vivo depends on its red blood cell content (27). We found two thrombi in conjunction with ulcerations. In one other case, however, a cleft created by a mural thrombus was misinterpreted as an ulceration (Fig 8).

One of the specimens had a postendarterectomy Dacron graft implanted within the carotid artery wall. The graft appeared as a hyperechogenic segment of the wall and was completely endothelialized on the histologic section.

## Limitations of Intravascular Sonography

The eccentric position of the sonographic catheter may result in the so-called lateral impulse response artifact, which can mimic an intimal flap or an ulceration (28) (Fig 9). Fortunately, this artifact can be recognized with experience, and we had no false-positive readings because of it. The frequency with which the lateral impulse response artifact occurs may be reduced when higher resolution probes become available.

Some variants of the origin of the superior thyroidal artery may be misinterpreted as ulcerations (Fig 10). Since it is easy to follow the lumen of the side branches on consecutive intravascular sonograms, side branches can be distinguished from ulcerations.

A definite limitation of every imaging method is the inability to show lesions below the resolution limit. Current intravascular sonographic systems have a maximum resolution of approximately 0.2 mm. Constantinides (11) claims that thrombotic processes in human arteriosclerotic arteries are always caused by breaks of plaque surfaces that are usually too small to see with current diagnostic methods. Ulcerations larger than 1 mm are associated with microembolism, but no relationship between plaque fissures smaller than 1 mm and microembolism detected by transcranial Doppler sonography has been established (6). Intravascular sonography is the only diagnostic method capable of showing submillimeter lesions of the arterial wall.

The 3.5F probe we used in our in vitro experiments is more rigid than a 3.0F microcatheter, but its rigidity is not much greater than that of a deflated dilatation balloon. Use of intravascular sonography before, during, and after angioplasty carries the risk of an extended procedure time. The probe must be advanced through stenotic, often tortuous lumen. Similarly rigid probes are widely used in cardiologic practice. However, since the danger of a thromboembolic complication in cerebral vessels is greater than in coronary vessels, we do not recommend the use of this particular probe in clinical cases. Further advances in probe technology, especially in catheter size and flexibility, are needed before they can be considered safe for clinical use.

### **Design Limitations**

The method used in our study provided a reproducible model of the arterial flow, pres-

sure, and pulsation of human carotid artery cir-Formalin fixation may produce culation. changes in the sonographic properties of plaques but not in the wall-lumen border. The acoustic properties of the glycerin solution we used as a circulating fluid differ from those of blood. This solution provides a completely echolucent conducting medium. Moving blood cell conglomerates produce random reflections in the lumen, which may result in a less accurate delineation of the arterial wall. However, the higher the frequency of the transducer, the greater the difference between the sonographic attenuation of blood and vessel wall (29).

## Diagnostic Value of Intravascular Sonography

Intravascular sonography is a promising yet invasive method for detecting plaque ulceration. In establishing the clinical utility of intravascular sonography for the carotid arteries, its ability to differentiate plaque types (30, 31) and precisely measure stenosis (10) should also be considered. The true diagnostic value of intravascular sonography may be revealed by its influence on decision making. Stone et al (G. W. Stone, F. St Goar, M. A. Klette, T. J. Linnemeier, "Initial Clinical Experience with a Novel Low-Profile Integrated Coronary Ultrasound-Angioplasty Catheter: Implications for Routine Use," J Am Coll Cardiol 1993;21:134A, abstract) reported an altered treatment approach in 30% of their coronary angioplasty cases and Pichard et al (A. D. Pichard, G. S. Mintz, L. F. Satler, et al, "The Influence of Pre-intervention Intravascular Ultrasound Imaging on Subsequent Transcatheter Treatment Strategies," J Am Coll Cardiol 1993;21:133A, abstract) in 39% of their cases after examination with intravascular sonography. Physicians have yet to determine a standard method for treating ulcerated carotid lesions because an accurate diagnosis of ulceration has never been obtained. Knowledge of the presence of a plaque ulceration would not change the planned endarterectomy technique, but it may change its indication. Intravascular sonography may be valuable for endovascular treatment. A preexisting ulceration or an artificial fissure caused by angioplasty may pose thromboembolic danger. Based on results of intravascular sonography, a physician may decide to change balloon size or type, deploy a stent, or perform endarterectomy

instead of angioplasty. The result of angioplasty or stenting may be better assessed with intravascular sonography than with angiography (32). Because balloon angioplasty has not yet been evaluated in a large series, we lack reliable morbidity and mortality data for comparison with endarterectomy. However, the results of our clinical experience and those of cases reported in the literature suggest that the risk of endovascular treatment is not greater (33–36). If these preliminary results are an indication of procedural safety, balloon angioplasty may rapidly emerge as an alternative treatment method not only for high-risk patients but also for endarterectomy candidates. We believe that intravascular sonography, when rendered safe, may have a significant role in the prevention of thromboembolic complications arising from balloon angioplasty.

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### References

- North American Symptomatic Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;325: 445–453
- Eliasziw M, Streifler JY, Fox AJ, et al. Significance of plaque ulceration in symptomatic patients with high-grade carotid stenosis. *Stroke* 1994;25:304–308
- Sterpetti AV, Hunter WJ, Schultz RD. Importance of ulceration of carotid plaque in determining symptoms of cerebral ischemia. J Cardiovasc Surg 1991;32:154–158
- Dixon S, Pais SO, Raviola C, et al. Natural history of nonstenotic, asymptomatic ulcerative lesions of the carotid artery: a further analysis. Arch Surg 1982;117:1493–1498
- Harward TRS, Kroener JM, Wickbom IG, Bernstein EF. Natural history of asymptomatic ulcerative plaques of the carotid bifurcation. *Am J Surg* 1983;146:208–212
- Sitzer Mral microemboli in high-grade internal carotid artery stenosis. Stroke 1995;26:1231–1233
- Streifler JY, Eliasziw M, Fox AJ, et al. Angiographic detection of carotid plaque ulceration: comparison with surgical observations in a multicenter study. *Stroke* 1994;25:1130–1132
- Edwards JH, Kricheff II, Riles T, Imparato A. Angiographically undetected ulceration of the carotid bifurcation as a cause of embolic stroke. *Radiology* 1979;132:369–373
- Rubin JR, Bondi JA, Rhodes RS. Duplex scanning versus conventional arteriography for the evaluation of carotid artery plaque morphology. *Surgery* 1987;102:749–755

- Fürst H, Hartl WH, Jansen I, Liepsch D, Lauterjung L, Schildberg FW. Color-flow Doppler sonography in the identification of ulcerative plaques in patients with high-grade carotid artery stenosis. *AJNR Am J Neuroradiol* 1992;13:1581–1587
- Constantinides P. Cause of thrombosis in human atherosclerotic arteries. Am J Cardiol 1990;66:37G–40G
- Tabbara M, Kopchok G, White RA. In vitro and in vivo evaluation of intraluminal ultrasound in normal and atherosclerotic arteries. *Am J Surg* 1990;160:556–560
- Foster FS, Ryan LK, Lockwood GR. High frequency ultrasound scanning of the arterial wall. In: Roelandt J, Bom N, Gussenhoven EJ, eds. *Intravascular Ultrasound*. Dordrecht, the Netherlands: Kluwer Academic Publishers; 1993:91–108
- Bom N, Lancé e CT, Rijsterborgh H, ten Hoff H, Roelandt JRTC. From idea to clinical application. In: Roelandt J, Bom N, Gussenhoven EJ, eds. *Intravascular Ultrasound*. Dordrecht, the Netherlands: Kluwer Academic Publishers; 1993:1–16
- Stary HC, Chandler AB, Dinsmore RE, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. *Arterioscler Thromb Vasc Biol* 1995; 15:1512–1531
- Beach KW, Hatsukami T, Detmer PR, et al. Carotid artery intraplaque hemorrhage and stenotic velocity. *Stroke* 1993;24:314–319
- 17. Fryer JA, Myers PC, Appleberg M. Carotid plaque hemorrhage: the significance of neovascularity. *J Vasc Surg* 1987;6:341–349
- Maravic CV, Kessler C, Maravic MV, Hohlbach G, Kö mpf D. Clinical relevance of intraplaque hemorrhage in the internal carotid artery. *Eur J Surg* 1991;157:185–188
- Lendon CL, Davies MJ, Born GVR, Richardson PD. Atherosclerotic plaque caps and locally weakened when macrophages density is increased. *Atherosclerosis* 1991;87:87–90.
- Fisher CM, Ojemann RG. A clinico-pathologic study of carotid endarterectomy plaques. *Rev Neurol (Paris)* 1986;142:573–589
- Cumming MJ, Morrow IM. Carotid artery stenosis: a prospective comparison of CT angiography and conventional angiography. *AJR Am J Roentgenol* 1994;163:517–523
- Kremkau FW. Diagnostic Ultrasound: Principles and Instruments. 4th ed. Philadelphia, Pa: Saunders; 1993:110–119
- Hedrick WR, Hykes DL, Starchman DE. Ultrasound Physics and Instrumentation. 3rd ed. St Louis, Mo: Mosby; 1994:44–59

- Young N, Soo YS, Fischer P. Comparison of duplex ultrasound with angiography in assessment of carotid bifurcation disease. *Australas Radiol* 1992;36:54–58
- O'Leary DH, Holen J, Ricotta JJ, Roe S, Schenk EA. Carotid bifurcation disease: prediction of ulceration with B-mode ultrasound. *Radiology* 1987;162:523–525
- Chandrasekaran K, Sehgal CM, Hsu T-L, et al. Three-dimensional volumetric ultrasound imaging of arterial pathology from twodimensional intravascular ultrasound: an in vitro study. Angiology 1994;45:253–264
- Frimerman A, Miller HI, Hallman M, Laniado S, Keren G. Intravascular ultrasound characterization of thrombi of different composition. *Am J Cardiol* 1994;73:1053–1057
- Finet G, Maurincomme E, Tabib A, et al. Artifacts in intravascular ultrasound imaging: analyses and implications. *Ultrasound Med Biol* 1993;19:533–547
- Lockwood GR, Tyan LK, Hunt JW, Foster FS. Measurement of the ultrasonic properties of vascular tissue and blood from 35–65 MHz. Ultrasound Med Biol 1991;17:653–666
- Fitzgerald PJ, Yock PG. Mechanisms and outcomes of angioplasty and atherectomy assessed by intravascular ultrasound imaging. J Clin Ultrasound 1993;21:579–588
- Jain SP, Jain A, Collins TJ, Ramee SR, White CJ. Predictors of restenosis: a morphometric and quantitative evaluation by intravascular ultrasound. *Am Heart J* 1994;128:664–673
- Wilson EP, White RA, Kopchok GE. Utility of intravascular ultrasound in carotid stenting. J Endovasc Surg 1996;3:63–68
- Guterman LR, Budny JL, Gibbons KJ, Hopkins LN. Thrombolysis of the cervical internal carotid artery before balloon angioplasty and stent placement: report of two cases. *Neurosurgery* 1996;38: 620–624
- Ferguson RDG, Ferguson JG, Lee LI. Endovascular revacularization therapy in cerebral athero-occlusive disease: angioplasty and stents, systemic and local thrombolysis. *Neurosurg Clin North Am* 1994;5:511–527
- Tsai FY, Matovich V, Hieshima G, et al. Percutaneous transluminal angioplasty of the carotid artery. AJNR Am J Neuroradiol 1986; 7:349–358
- Kachel R, Basche ST. Percutaneous transluminal angioplasty of supra-aortic arteries especially the internal carotid artery. *Neuro*radiology 1991;33:191–194