

MEASUREMENT OF PLAQUE PROGRESSION

Presented as a poster at the International Atherosclerosis Society meeting, Kyoto, September 2003

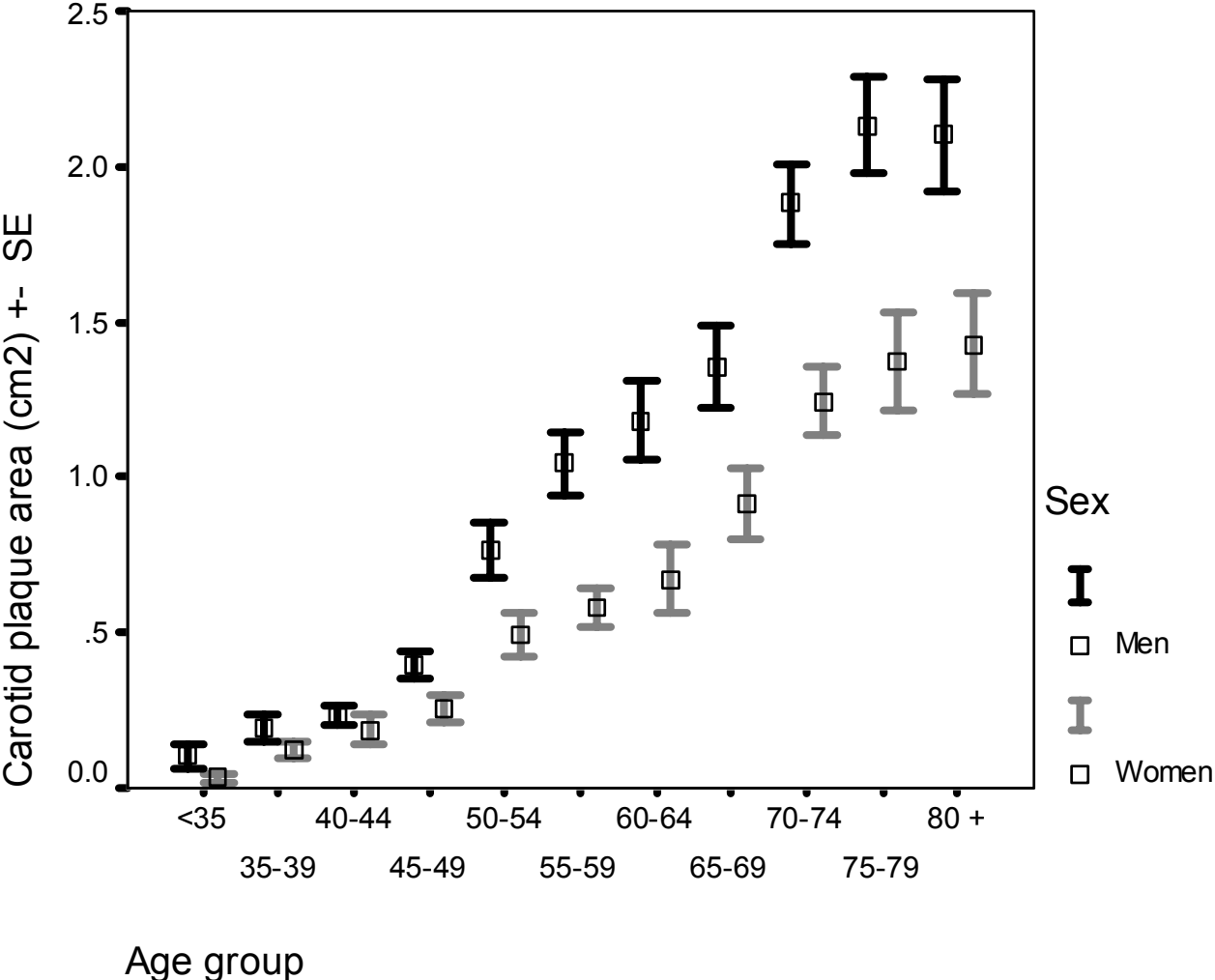
We have shown that measurement of carotid plaque is useful for stratifying risk¹², for evaluating response of patients to therapy¹³, and for genetic research¹⁴⁻¹⁷.

In the past we have measured 2-D plaque area, summing the cross-section of plaques measured in longitudinal views. We have shown that plaque progresses along the axis of the vessel 2.4 times as fast as it thickens¹⁸. For this reason measuring plaque is much more sensitive to change than is measuring IMT.

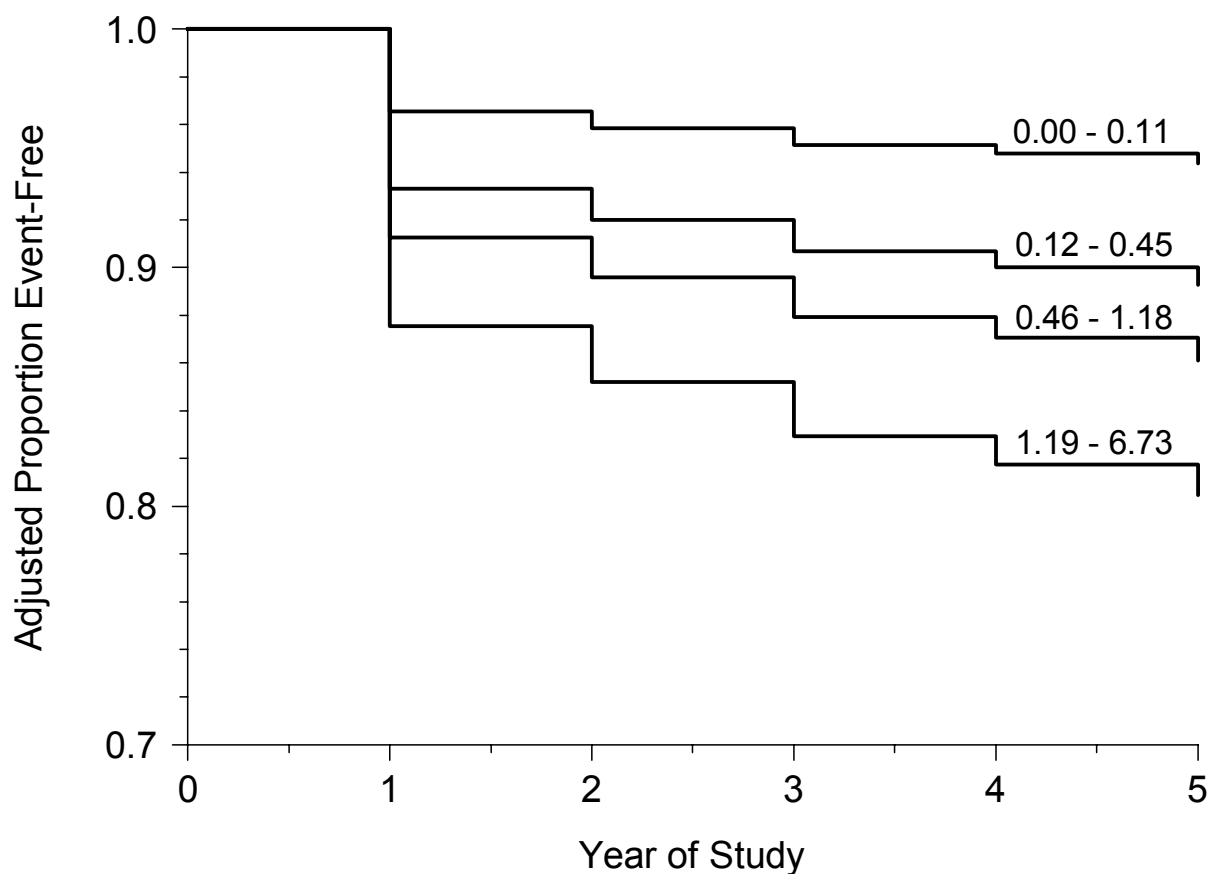
Patients in the top quartile of baseline plaque area have a relative risk of 3.5 for stroke, myocardial infarction or death during average followup of 2.5 years, after adjustment for traditional risk factors, and patients with progression of plaque have twice the risk of events in followup compared to those with stable plaque¹².

As shown below, 3-D ultrasound measurement of plaque volume is even more sensitive to effects of treatment, as it captures change not only in thickness and length, but also circumferential growth or regression.

Distribution of carotid plaque area by age and sex



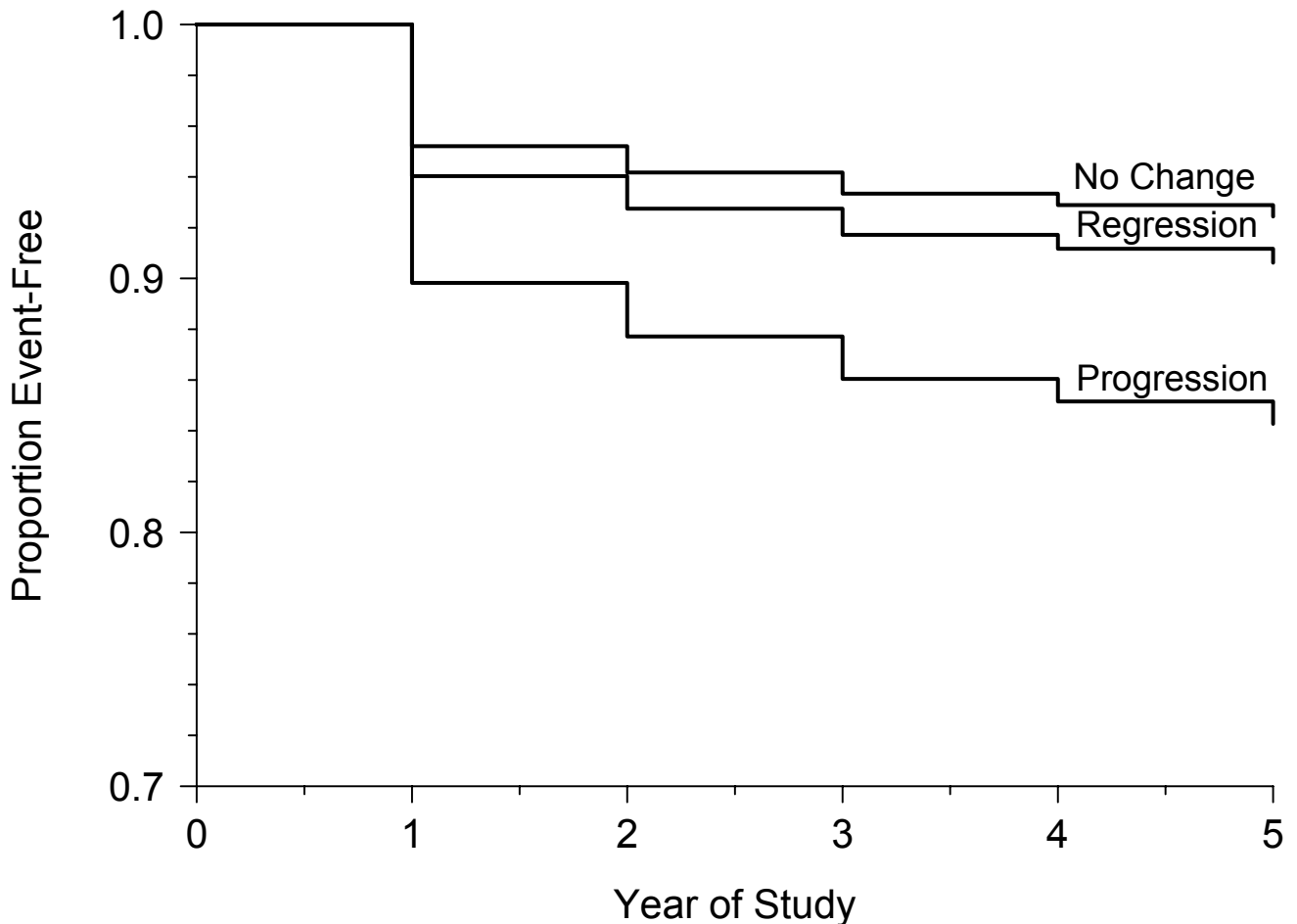
Risk stratification by carotid plaque measurements (total plaque area)



Patients in the top quartile of baseline plaque have a relative risk of 3.5 vs the lowest quartile, after adjustment for traditional risk factors age, sex, blood pressure, cholesterol, smoking, diabetes and homocysteine

Spence JD, Eliasziw M, DiCicco M, Hackam DG, Galil R, Lohmann T. Carotid Plaque Area: A Tool for Targeting and Evaluating Vascular Preventive Therapy. Stroke 2002;33:2916-2922.

Risk stratification by progression of carotid plaque area

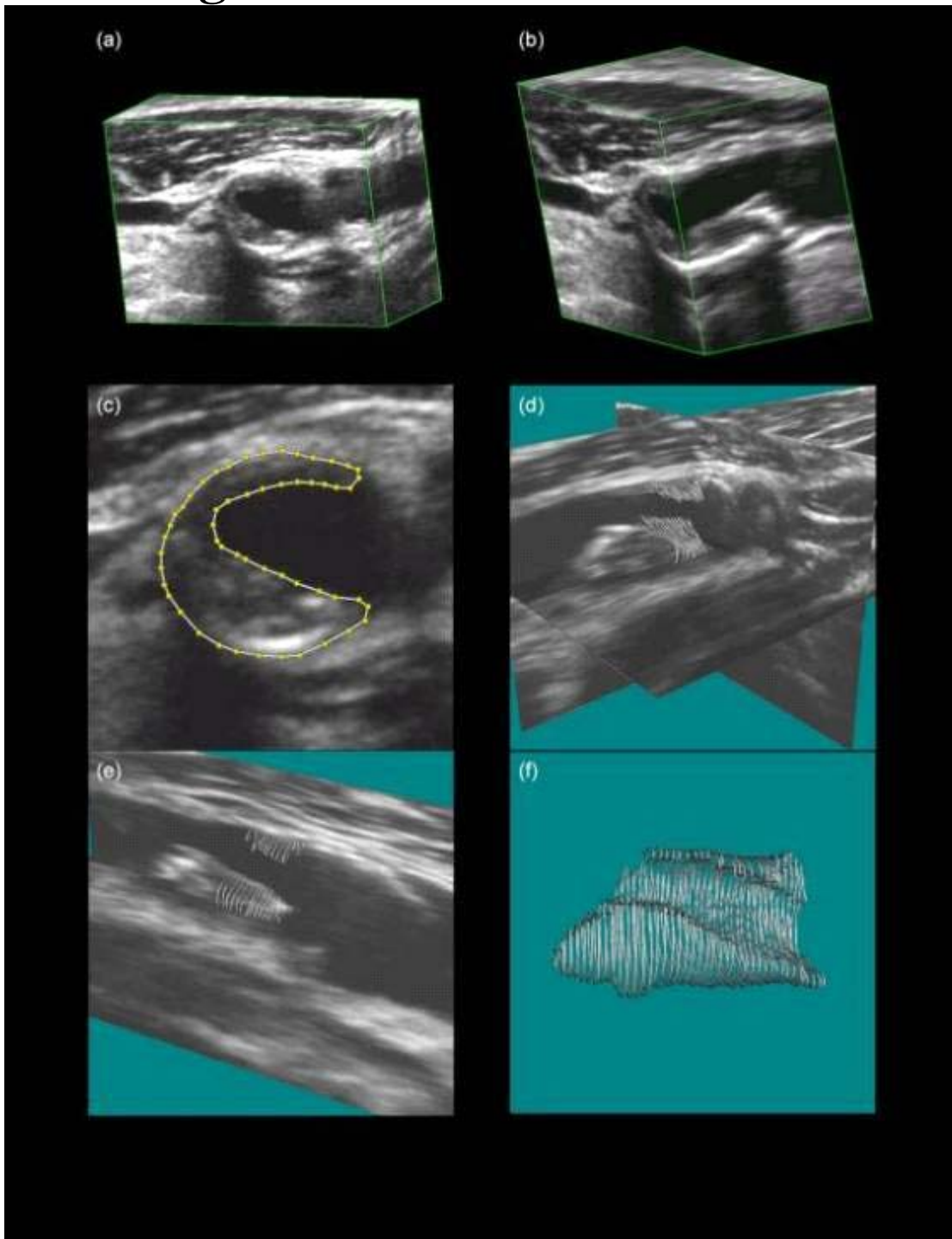


Patients with progression of plaque area in the first year (>0.05 cm^2 ; i.e. the median rate of progression) had twice the risk of stroke, death or myocardial infarction over a mean followup of 2.5 years, vs patients with stable plaque or regression.

Spence JD, Eliasziw M, DiCicco M, Hackam DG, Galil R, Lohmann T. Carotid Plaque Area: A Tool for Targeting and Evaluating Vascular Preventive Therapy. *Stroke* 2002;33:2916-2922.

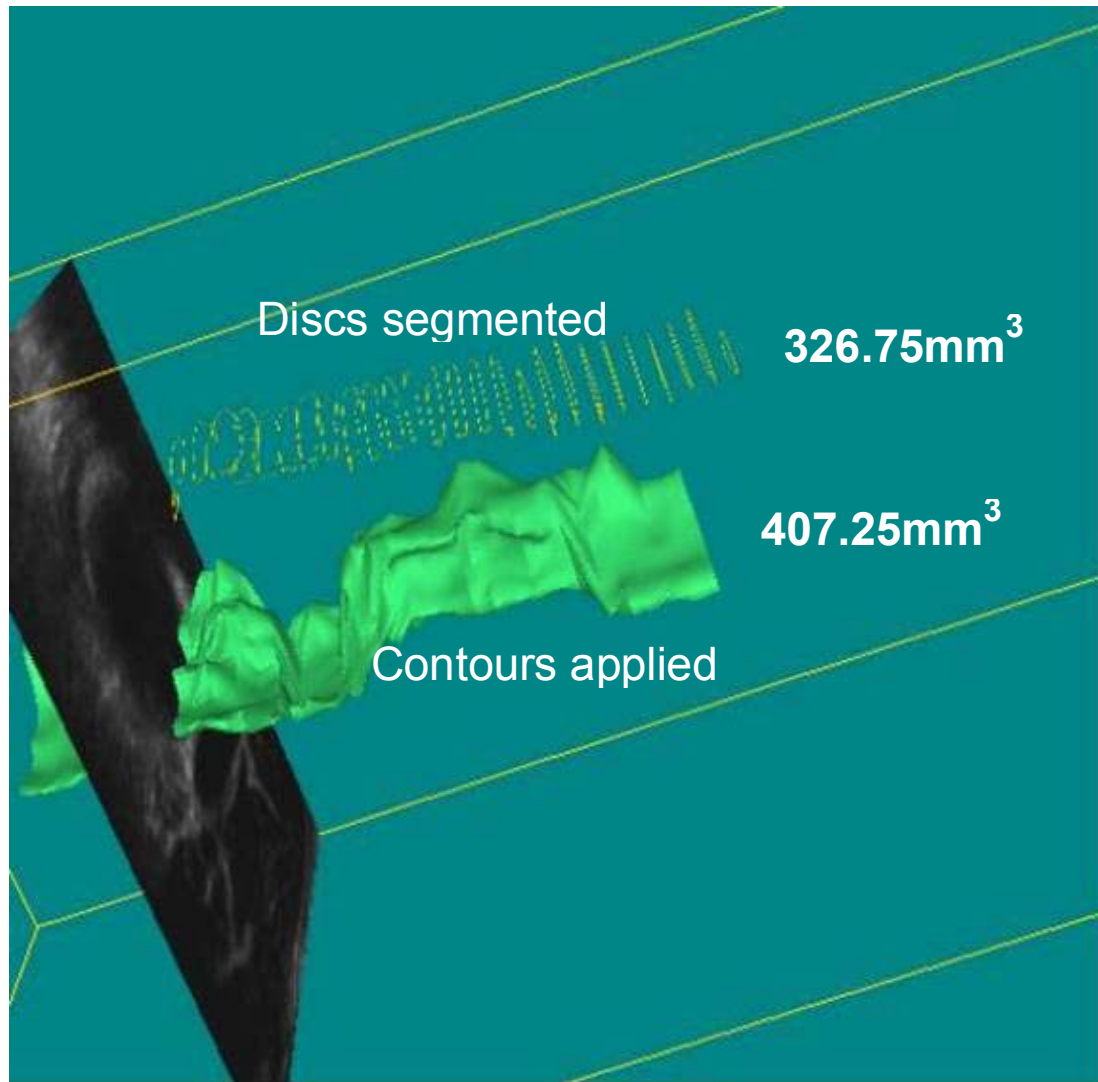
Measurement of 3-Dimensional plaque volume

Disk segmentation method



Measurements are made in the axial plane (c); the perimeter of the plaque in each slice is traced (d and e); slices are made at 1-mm intervals, and the slices are stacked up to form a volume, and the surface contour is mapped for measurement of plaque surface roughness (f).¹⁹⁻²²

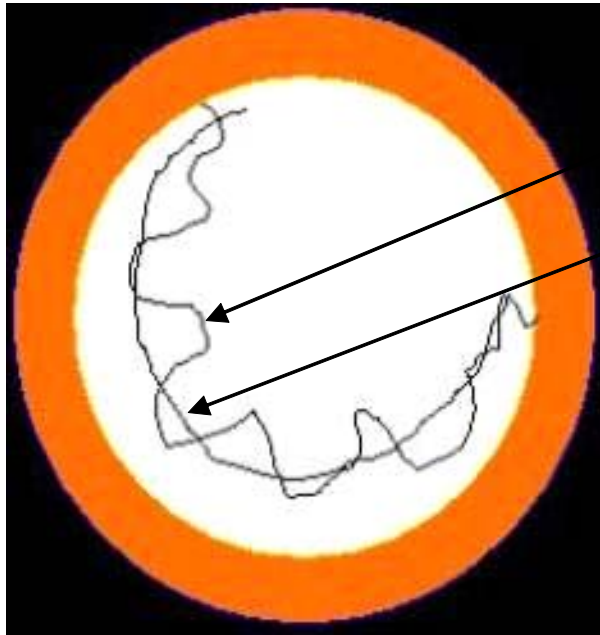
Measurement of 3-Dimensional plaque volume



This view shows two plaques in the left carotid, in a patient with unstable carotid plaque manifested by microemboli on transcranial Doppler. The plane shown at left (in black) is a slice in the common carotid; the plaques shown extend into the internal carotid. The upper plaque (326.75mm^3) has had each slice traced in cross-section (plaque envelopes in yellow); the next step is mapping of the contours, shown in the lower plaque (407.25mm^3). Longitudinal and cross-sectional views of this patient's ulcerated left carotid artery are shown below.

Quantifying ulceration: plaque surface roughness

Plaque surface roughness:



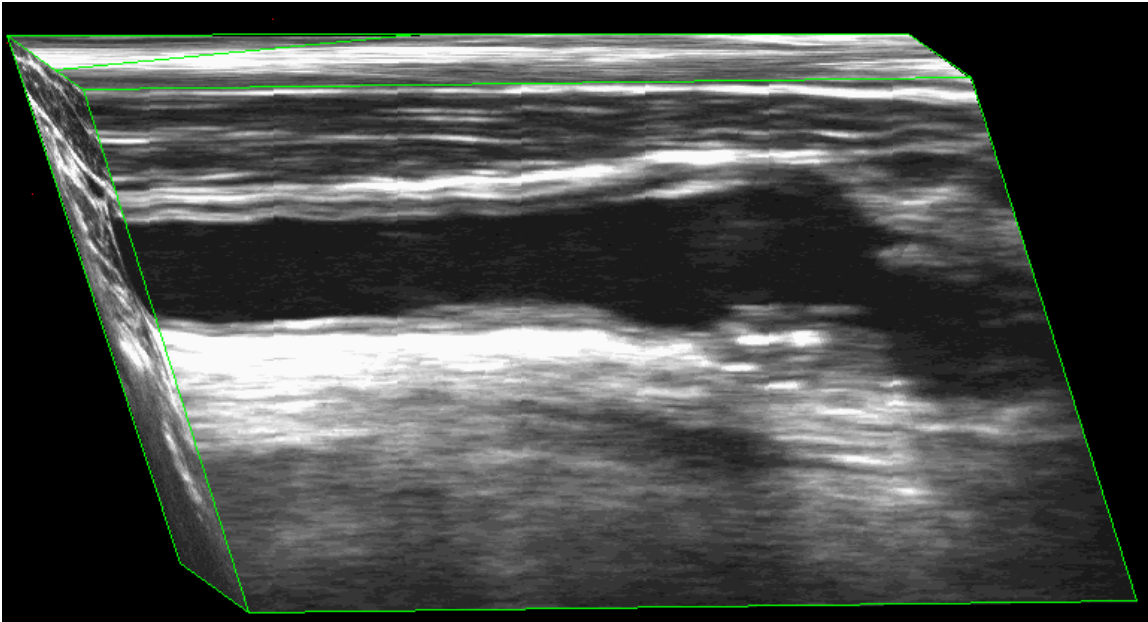
Actual plaque surface

Mathematically smoothed surface

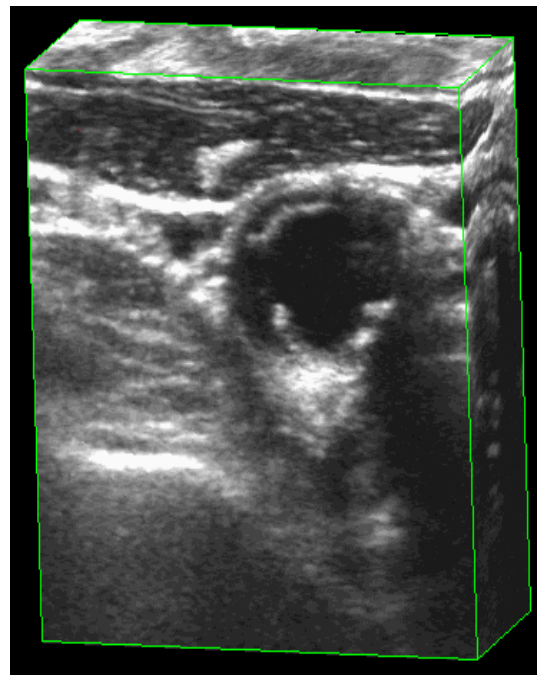
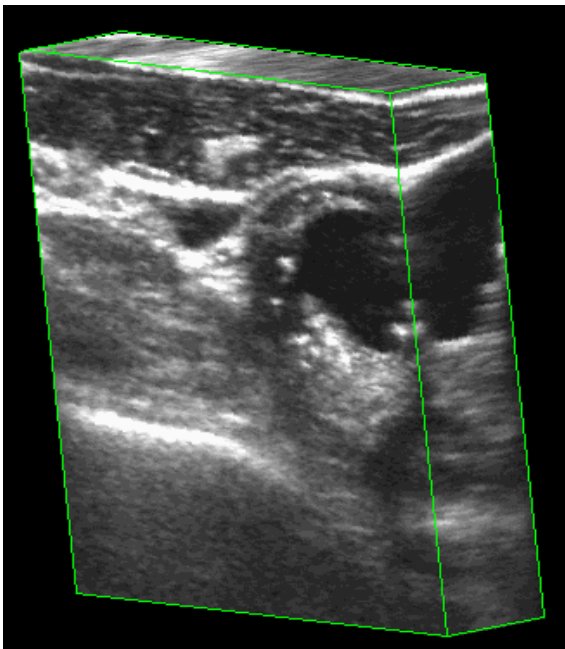
The difference between the two surfaces represents plaque roughness; this is a continuous variable, as opposed to ulceration, which is categorical

This 2-dimensional cartoon describes the concept; plaque roughness, however is a 3-dimensional quantity based on comparison of contours.

Ulceration in a patient with microemboli on TCD²³



Longitudinal view of the left internal carotid in a man with 70% stenosis and microemboli on TCD. Ulcers and fissures (below) likely explain the occurrence of microemboli



Results:

2. 3-D ultrasound carotid plaque volume: a tool for quickly measuring effects of treatment on atherosclerosis

In a study of 39 patients with carotid stenosis $>60\%$, age 69.42 ± 7.87 years, 15 female, randomly assigned to atorvastatin 80mg daily (n=18) vs placebo (n=21) we measured 3-D plaque volume at baseline and after 3 months, by disc segmentation of voxels representing carotid artery plaque, after 3D reconstruction of parallel transverse duplex US scans into volumetric 3D data sets^{22,24}.

Results: There were no significant differences in baseline risk factors. The rate of progression was $0.10 \pm 0.26 \text{ cm}^3$ in patients taking placebo, vs regression of $-0.055 \pm 0.15 \text{ cm}^3$ in patients taking atorvastatin (p=0.03)

Conclusions: 3-D plaque volume measurement can show large effects of therapy on atherosclerosis in 3 months, in sample sizes of 50-60 patients per group.

Baseline characteristics of patients randomized to atorvastatin vs placebo

		Mean	Std. Deviation	p value (ANOVA)
Age	Atorvastatin	68.89	8.11	0.64
	Placebo	70.19	8.79	
Cholesterol	Atorvastatin	4.41	1.053	0.84
	Placebo	4.47	.73	
Triglycerides	Atorvastatin	1.56	.76	0.66
	Placebo	1.69	1.03	
HDL	Atorvastatin	1.34	.41	0.64
	Placebo	1.28	.33	
LDL	Atorvastatin	2.38	.97	0.80
	Placebo	2.45	.64	
Homocysteine	Atorvastatin	10.65	4.44	0.11
	Placebo	13.69	6.49	
Systolic	Atorvastatin	148.11	21.30	0.42
	Placebo	142.62	20.98	
Diastolic	Atorvastatin	73.67	15.23	0.51
	Placebo	70.57	13.46	

	Atorvastatin N=18	Placebo N=21	p value (χ^2 - square)
Sex Male	9	15	0.15
Female	9	6	
Current smoker	2	7	0.10
Diabetic	3	5	0.44
Previous MI	2	2	0.15

