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EDITORIAL COMMENT

Approaching Automated 3-Dimensional Measurement of Atherosclerotic Plaque Volume*

J. David Spence, MD, MBA

Early efforts to quantify atherosclerosis by ultrasound began in the mid-1980s with measurement of intima-media thickness (IMT), first in monkeys (1) and then in human subjects (2). When measured in the far wall of the distal common carotid at a site where there is no plaque, IMT does not represent atherosclerosis; it is a biologically distinct phenotype, with different relationships to risk factors and genes (3). It is also a very weak predictor of cardiovascular risk. Studies that include plaque thickness in the measurement of IMT, combining some participants with plaque and those without plaque, confuse the issue by conflating plaque with IMT. Rundek et al. (4) reported that plaque thickness predicted cardiovascular risk in the Northern Manhattan Study.

Measurement of total plaque area (TPA) was first carried out in my lab by Maria DiCicco, RVT, in 1990. Persson et al. (5) published a method in 1992 after hearing about this, and then TPA was used in 1996 to assess the effect of mental stress on atherosclerosis (6). In 2002, it became apparent that among patients attending vascular prevention clinics, TPA was a strong, graded predictor of cardiovascular risk. After adjusting for age, sex, cholesterol, systolic blood pressure, smoking (pack-years), homocysteine, diabetes, and treatment of blood pressure and lipids, the 5-year risk of stroke, myocardial infarction, or vascular death by quartile of TPA was 5.6%, 10.7%, 13.9%, and 19.5%, respectively. Patients with plaque progression in the first year of follow-up (one-half of the patients) had twice the risk of events, after adjusting for the same panel of risk factors. These findings were validated in a large ($n > 6{,}000$) population-based study, the Tromsø study, in 2007, with regard to myocardial infarction (7) and, in 2011 (8), with regard to stroke. Carotid TPA is a stronger predictor of risk than percentage of stenosis (9,10).

It has become increasingly apparent that measurement of plaque burden is a much stronger predictor of cardiovascular risk than IMT, with a much greater dynamic range (0 to 1,200 mm^2 for TPA vs. approximately 0.5 to 1.5 mm for IMT), and is much more sensitive to the effects of therapy than IMT. In the High-Risk Plaque Study, carotid plaque burden was highly correlated with coronary calcium score (11) and as predictive of events (12), whereas IMT was neither.

Carotid plaques are focal and grow along the artery in the axis of flow twice as quickly as they thicken; they also grow and regress circumferentially. Sample sizes and duration of studies of therapies are therefore much smaller for 3-dimensional (3D) carotid ultrasound than for IMT, carotid magnetic resonance imaging studies, and even coronary intravascular ultrasound studies (13). For studies of participants with no plaque, measurement of 3D vessel wall volume is a better choice than IMT is (14,15). The history of the development of measurement of plaque burden was recently reviewed (16).

Recognition that plaque progressed in one-half of the patients despite treatment according to guidelines and that those with progression had twice the risk led to a new approach to vascular prevention: "treating arteries instead of treating risk factors" (17,18). In high-risk patients with asymptomatic carotid stenosis, implementation of that approach was associated with

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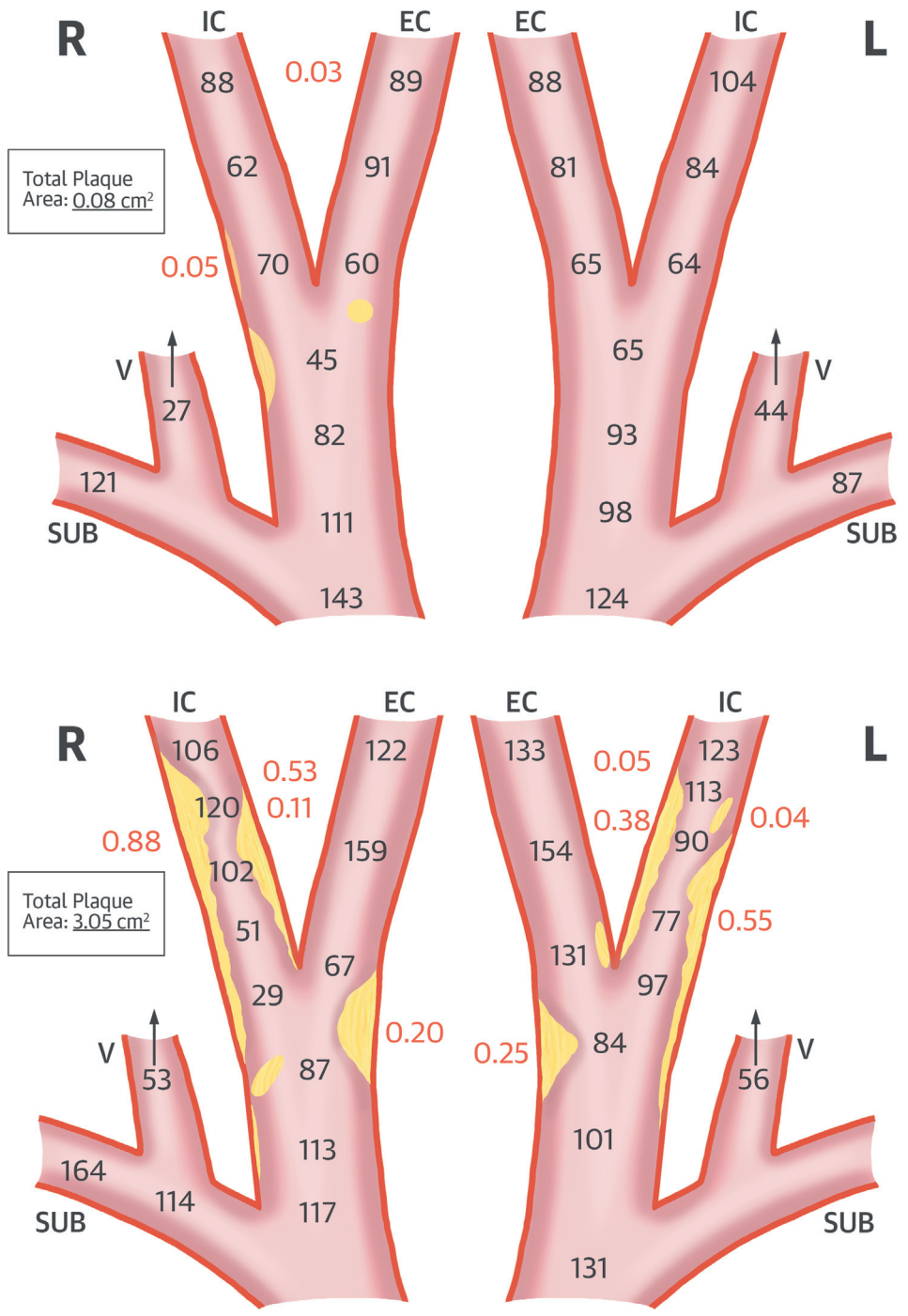
From the Stroke Prevention and Atherosclerosis Research Centre, Robarts Research Institute, Western University, London, Ontario, Canada. Dr. Spence is an officer of Vascularis Inc., a dormant company.

FIGURE 1 **Dynamic Range and Location of Carotid Plaques**



Composite drawings in an ultrasound report from the Stroke Prevention and Atherosclerosis Research Centre, London, Canada. They show the location of plaques **(in yellow)** on a template of the carotid arteries. Individual plaque areas (in cm^2) are shown in **orange numbers;** the **black numbers** within the lumen are peak velocities at each location. Total plaque area is expressed as **black numbers** on the left. **(Top)** A 76-year-old woman with only 8 mm^2 of plaque and no stenosis. **(Bottom)** A 67-year-old man with 305 mm^2 of plaque; there is approximately 50% stenosis of both external carotids. EC = external carotid; IC = internal carotid; SUB = subclavian; V = vertebral.