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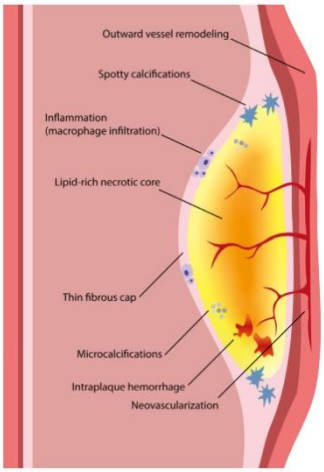
VULNERABLE PLAQUES

What is it?	Atherosclerotic plaques are asymmetric focal thickenings of the intima, consisting of connective-tissue elements, lipids, and debris. Their formation and destabilization are the main hallmarks of atherosclerotic disease. Vulnerable plaques are defined as nonobstructive atherosclerotic lesions that are prone to rupture, causing arterial thrombosis and leading to, for example, acute coronary syndromes (ACS) and stroke. Features of this kind of plaque include inflammation, thin fibrous caps, large necrotic lipid core, positive remodelling, neoangiogenesis, intraplaque hemorrhage and endothelial denudation. The starting point of atheroma formation is believed to be an endothelial dysfunction or activation. However, earlier studies have proposed that the main factor that dictates the formation of plaques is the response associated to lipoprotein retention within the arterial wall. Potential contributors to early atherogenesis are: increased cholesterol entrapment and deposit in the intima, which led to enchanced stimulation of ox-Lp(a); foam cell formation; induced monocyte-chemostatic activity which promote smooth muscle cell proliferation and potentially is associated with necrotic core progression, carotid stenosis and occlusion. Inflammation plays an important role in plaque progression, where inflammatory tissue factors are key contributors to plaque thrombogenicity. Atherosclerotic plaques are characterized by hyperlipidemia and unresolved inflammation, tightly linked by complex innate and adaptive immune processes. Unresolved inflammation triggers plaque calcification, which further reduces mechanical stability of the plaque. Features of plaque instability include large necrotic core NCs (>24–50% of total lesion area), high amounts of inflammatory cells, thin fibrous caps (23 ± 19 μm), reduced extracellular fibrous matrix, abundant neovascularization and intraplaque hemorrhage and calcification.
Why do we measure it?	The majority of ACS arises from rupture or erosion of a coronary plaque leading to (sub)acute thrombosis. Together with vasoconstriction and increased coagulability, thrombosis may lead to acute cessation of the coronary blood flow and subsequent myocardial ischemia. Some coronary plaques are particularly prone to rupture. “Vulnerable plaques” are characterized by specific high-risk features that increase the risk for plaque rupture. The risk for plaque disruption depends more on plaque vulnerability (plaque type) than on degree of stenosis (plaque size). Lipid-rich and soft plaques are more vulnerable and prone to rupture than collagen-rich and hard plaques. They are also highly thrombogenic after disruption because of high content of tissue factor. There seems to be three major determinants of a plaque's vulnerability to rupture: 1) the size and consistency of the lipid-rich atheromatous core, 2) the thickness of the fibrous

	cap covering the core, and 3) ongoing inflammation and repair processes within the fibrous cap. Lipid accumulation, cap thinning, lack of smooth muscle cells (smc), and macrophage-related inflammation destabilize plaques, making them vulnerable to rupture. In contrast, smc-related healing and repair processes stabilize plaques, protecting them against disruption. Plaque size or stenosis severity tell nothing about a plaque's vulnerability. Many vulnerable plaques are invisible angiographically due to their small size and compensatory vascular remodeling.
How can it be measured	By noninvasive and intravascular imaging including: Histopathology: identification of lipid plaque with a fibrous cap that is < 65 µm thick and is heavily infiltrated by inflammatory cells and macrophages. Computer tomography (CT) angiography: enables the assessment of plaque characteristics, which are categorized as positive remodelling, low attenuation plaques and spotty calcification. Magnetic resonance imaging (MRI) is capable of detecting features of vulnerable plaque noninvasively, such as intraplaque hemorrhage, a component of the American Heart Association's definition of type VI plaque and coronary artery plaques. This feature is observed as a high signal of T1-weighted imaging and has been associated with strokes of carotid origin. Intravascular ultrasound (IVUS) delivers 100-µm axial resolution images of the arterial wall. IVUS features that are associated with plaque vulnerability include the presence of an echolucent zone, calcium deposits, and positive remodeling. Virtual histology (VH) IVUS data are collected with a 20-MHz, 2.9-F phased-array transducer catheter that acquires ECG-gated IVUS data. Briefly, VH-IVUS uses spectral analysis of IVUS radiofrequency data to construct color-coded tissue maps that label plaque into four major components. The catheter-based near-infrared spectroscopy (NIRS) has the potential to identify and quantify lipid core plaques, as it can penetrate blood and several millimetres into the tissue but it is unable to indicate the depth of lipid core plaques. The current NIRS system is combined with IVUS as a single catheter. Intravascular OCT is a near-infrared light-based imaging system that delivers images with 10- to 20-µm axial resolution. It therefore enables visualization of blood vessel wall microstructures in vivo at an unprecedented level of detail.
Where is it measured?	Noninvasive Methods to Image Vulnerable Plaques in the Carotid Arteries, using ultrasound, MRI, nuclear imaging, and x-ray multidetector computed tomography (MDCT). Such methods benefit from the accessibility of carotid plaques and the availability of tissue obtained after carotid endarterectomy to serve as the gold standard for the assessment of imaging results. Noninvasive Methods to Image Vulnerable Plaques in the Coronary Arteries: CT methods can assess the degree of coronary artery calcification, which adds prognostic information beyond that provided by the Framingham Risk Score. New MDCT

	instruments can detect coronary artery stenoses noninvasively, but characterization of the composition of plaques (beyond detection of calcium) is not yet possible. MRI has also been used for non-invasive characterization of coronary plaques. Unfortunately, the length of time required for study is considerable, and the resolution is insufficient for optimal characterization of coronary plaques. Invasive Imaging of Vulnerable Plaques in the Coronary Arteries: have a great advantage over non-invasive methods in assessment of coronary plaques. Intracoronary catheters have an excellent vantage point close to the tissue of interest, and their movement is similar to that of their target.
Figure	Figure from a publication:  *Van Veelen. Detection of Vulnerable Coronary Plaques Using Invasive and Non-Invasive Imaging Modalities. Reviews in Cardiovascular Medicine. DOI: 10.3390/jcm11051361. Figure 1.*
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