

Imaging of the Carotid Artery Vulnerable Plaque

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Abstract Atherosclerosis involving the carotid arteries has a high prevalence in the population worldwide. This condition is significant because accidents of the carotid artery plaque are associated with the development of cerebrovascular events. For this reason, carotid atherosclerotic disease needs to be diagnosed and those determinants that are associated to an increased risk of stroke need to be identified. The degree of stenosis typically has been considered the parameter of choice to determine the therapeutical approach, but several recently published investigations have demonstrated that the degree of luminal stenosis is only an indirect indicator of the atherosclerotic

process and that direct assessment of the plaque structure and composition may be key to predict the development of future cerebrovascular ischemic events. The concept of “vulnerable plaque” was born, referring to those plaque’s parameters that concur to the instability of the plaque making it more prone to the rupture and distal embolization. The purpose of this review is to describe the imaging characteristics of “vulnerable carotid plaques.”

Keywords Carotid artery · Vulnerable plaque · CTA · MRA · US-ECD

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Introduction

Atherosclerosis involving the carotid arteries is a disease with a high prevalence in the population, particularly in elderly patients, and carotid artery narrowing has been reported in up to 75 % of men and 62 % of women aged 65 years [1]. Atherosclerotic disease of the carotid arteries is a significant condition as accidents of the carotid artery plaques have been associated with the development of cerebrovascular events [2]. For this reason, detection of carotid atherosclerotic disease and identification of those determinants that are associated to an increased risk of stroke are critical components to the prevention of stroke.

The degree of luminal stenosis typically has been considered as the most important element to grade the severity of carotid atherosclerotic disease. However, several recent investigations have demonstrated that the plaque structure and composition may represent a more direct biomarker for the development of cerebrovascular ischemic events [3–6]. From a conceptual point of view, this is easy to understand: the majority of ischemic infarcts occur because emboli originating from the heart or a carotid plaque occlude an

arterial vessel of the brain and not because there is a reduced blood flow from a luminal stenosis, usually well-compensated thanks to the Circle of Willis and other cerebral collateralization.

In the late 1980s, coronary artery angiographic studies showed that coronary artery plaques causing only a moderate degree of stenosis can lead to an acute myocardial infarction [7, 8], confirming that *luminal narrowing* was not the cause of the myocardial infarction. Histopathological studies demonstrated that erosion and disruption was present in those plaques associated with myocardial infarction. Similar conclusions were reached for the carotid arteries as studies found that cerebrovascular events also can occur in patients with carotid plaques causing low-grade stenosis (<30 %) and with no other identifiable cause for their stroke [9–11].

These findings have generated tremendous interest for the development of noninvasive methods that can measure the total volume of the plaque and reliably identify the morphologic features of “vulnerable plaques” [12–14]. Another significant observation is that carotid artery plaques change over time: the composition of carotid plaques varies with the progression of atherosclerotic disease, and some phases seem to be more prone to plaque accidents and cerebrovascular events [15]. The American Heart Association (AHA) proposed a 6-stage plaque classification, which is considered to reflect the temporal natural history of the disease (Table 1).

The Concept of Vulnerable Plaque and its Clinical Impact

A number of carotid plaque features have been associated with an increase risk of stroke [16, 17], whereas others are associated with a reduced risk of ischemic events [18]. Howard et al. found that different types of plaque are associated with different types of ischemic events. Carotid

plaques from patients treated with endarterectomy because of previous ocular ischemic events have fewer vulnerable plaque features than those from patients with recent cerebral ischemic events, possibly explaining some of the differences in risk of stroke between these groups [19].

Morphological characteristics of vulnerable plaques encompass a number of features, including the presence of a thin fibrous cap (FC) with a large lipid core, intraplaque hemorrhage (IPH), and the presence of intraplaque active inflammation [3, 20]. Unstable plaques also tend to be characterized by an eccentric distribution, an irregular surface without erosion of the intimal layer or superficial ulcerations with intimal exposure (Fig. 1). These features are strongly associated with significant hemodynamic changes and shear stress. The presence of plaque inflammation increases the potential vulnerability of the plaque, as chronic inflammation (histologically visible as the presence of macrophages and T lymphocytes) promotes vasa vasorum weakening, plaque connective-tissue rupture, and arterial wall thrombosis. Finally, the concept of remodeling, initially described for atherosclerotic lesions in coronary arteries, is now largely accepted for carotid arteries. Unstable plaques can show either positive or negative remodeling. Positive remodeling is a dilation of the vessel wall in response to an increase in the plaque/wall volume in order to maintain sufficient lumen diameter [21]. When this compensatory enlargement is inadequate to ensure a sufficient lumen size, negative remodeling with lumen stenosis occurs.

Plaque Surface Morphology

The morphology of the luminal surface of carotid plaques, classified as smooth, irregular or ulcerated (Fig. 2), is a determinant of the risk of embolic event [4, 22]. A *smooth surface* configuration refers to a regular luminal

Table 1 AHA classification and imaging techniques

Stage	Definition	US	CT	MR
I	Incorporation of scattered macrophages and foam cells within the arterial wall triggered by intralésional atherogenic lipoprotein	+	+	+
II	Development of fatty streaks	++	++	++
III	Extracellular fats that break up cell–cell connections in smooth muscle layers	+	++	++
IV	The classic atheroma that contains a fatty necrotic core. The presence of atheroma may not narrow the vascular lumen since that the affected vessels can compensate for the increase in plaque volume through a widening of their external circumference rather than protrusion of plaque into the vascular lumen	++	+++	+++
V	Stage V is further classified as three different classes: Stage Va indicates those plaques having a fatty core as well as a multilayered thick fibrous cap (fibroatheroma); Stage Vb lesions are largely calcified; and Stage Vc lesions are predominantly fibrous	+	+++	++
VI	“Complex” plaque: there are areas of internal haemorrhage or focal apposition thrombosis. These lesions may undergo repeated cycles of rupture, thrombosis, and remodelling	+	++	+++

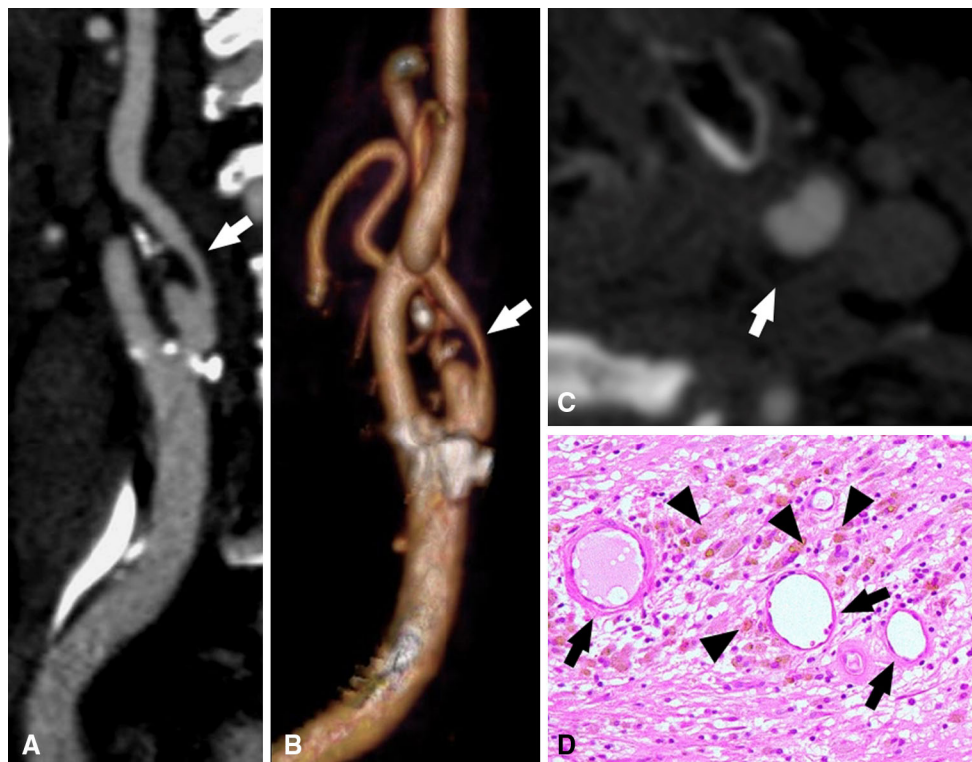


Fig. 1 Unstable plaques often are characterized by eccentric stenosis caused by a soft plaque with ulceration of the intima. **a** MIP reconstruction shows the presence of a wide ulcerated carotid plaque causing severe stenosis of the lumen (*arrow*). **b** Volume rendering of

the same carotid plaque. CTA axial image **c** demonstrated a hypodense plaque (HU value 14), whereas the histological section **d** showed the presence of neovessels (*black arrows*) and macrophages (*black arrowheads*)

morphology at the level of the plaque without any sign of ulceration or irregularity; it indicates a stable plaque. An *irregular surface* configuration represents a risk factor for embolism and is associated with an increased risk of TIA/stroke [23]. The third type of morphology indicates the presence of frank *ulcerations*. This condition significantly increases the risk of cerebrovascular events as demonstrated in the NASCET study [24, 25]. Lovett et al. [11] suggested a classification for carotid artery ulcerations where type 1 ulcerations point out perpendicular to the lumen, type 2 ulcerations have a narrow neck and point out proximally and distally, type 3 ulcerations have a neck proximally and point out distally, whereas type 4 ulcerations have a neck distally and point out proximally.

Several studies compared different imaging techniques to assess carotid plaque ulcerations [26, 27], and the best imaging modality for this purpose is CTA [22, 28, 29]. Saba et al. [22, 28] showed in 2007 that CTA had significantly better sensitivity compared to US-ECD for the detection of plaque ulcerations (93 vs. 37.5 %). The use of post-processing techniques, especially volume-rendering algorithms, may further help in the detection/characterization of carotid plaque ulcerations [28]. One of the limitations of CTA in the assessment and detection of small

ulcerations is the presence of a halo or edge blur that may mask these ulcers [30, 31].

MRI can detect the presence of carotid plaque ulcerations with sensitivity similar to the CTA [32]. In a recently published paper by Etesami et al. [32], contrast-enhancement MR was superior to time-of-flight (TOF) MRA for the detection of carotid ulcerations; the latter has a sensitivity of only 55 %, whereas contrast-enhancement MR has a sensitivity of 81.5 %. The false negatives on TOF MRA were related to ulcer orientation, location relative to point of maximum stenosis, and neck-to-depth ratio.

The Fibrous Cap

The FC plays a critical role in determining vulnerability of atherosclerotic plaques; particularly, the thickness and morphology are important predictors of rupture. Histologically, the FC is constituted by smooth muscle cells within a collagen-proteoglycan matrix associated with macrophages and T lymphocytes [33]. Inflammatory cells are also present at the interface with the underlying necrotic core [34]. According to histological findings, whereas an

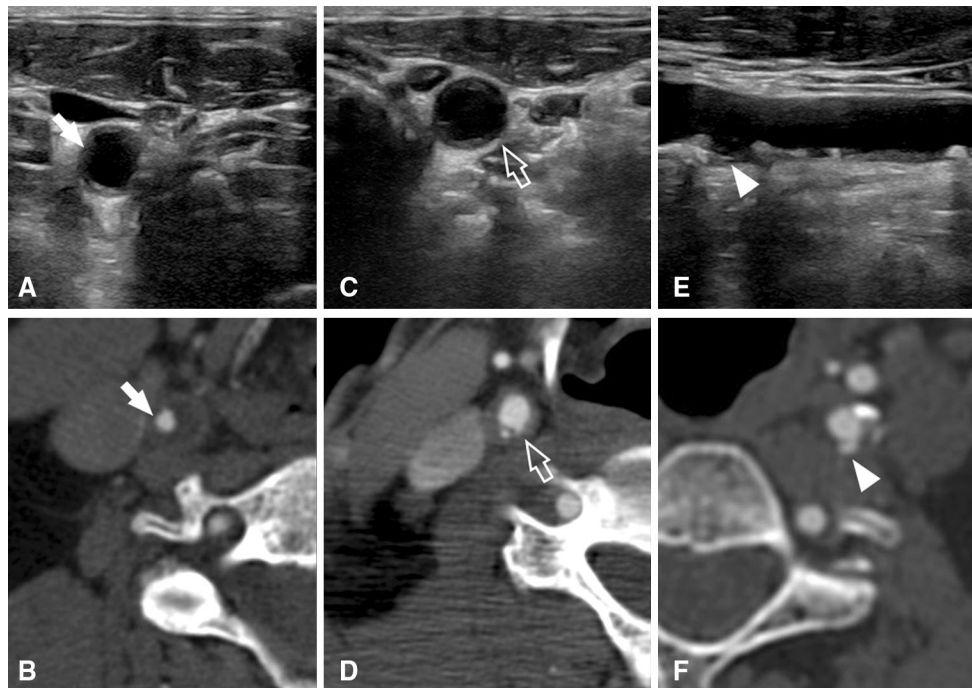


Fig. 2 Examples of different luminal morphology of the carotid artery plaques imaged using CT and US. **a, b** Smooth luminal surface (*white arrows*) for CT and US respectively. **c, d** Irregular luminal

surface (*white open arrows*) for CT and US respectively. **e, f** Smooth plaque ulcers (*white arrowheads*) for CT and US respectively

intact FC is associated to a low-risk plaque rupture, a thin FC is associated to a mild-risk plaque rupture and a fissured FC, to a high-risk plaque rupture.

Unstable and vulnerable plaques are thus characterized by a thin FC covering a large necrotic core containing macrophages and interstitial collagen. After the FC rupture, the exposure of thrombogenic subendothelial plaque constituents to the luminal blood flow represents a critical event that eventually leads to thromboembolic complications.

The imaging technique that best assesses the status of the FC is MRI, which allows defining the FC as normal, thin, or fissured/ruptured [35–37]. Thick FCs appear as a juxtaluminal band of low signal on TOF MR images, whereas in plaques with thin FCs, this dark juxtaluminal band is absent [37] (Fig. 3). When FC rupture occurs, the absence of a dark band between the lumen and the plaque core is accompanied by the presence of a bright gray region adjacent to the lumen, corresponding to plaque hemorrhage and/or mural thrombus. The lumen surface may or may not appear irregular, depending on the extent of the plaque rupture and mural thrombus formation. Using MRI, Demarco et al. [35] found a strong and statistically significant association between fissured FC and ipsilateral symptoms ($p < 0.01$). Authors also tried to use CT to identify the FC [38], but the results were suboptimal because of the halo or edge blur effects that reduce the contrast resolution by

masking the FC. Currently, no imaging studies have been used ultrasonography to assess the FC.

Intraplaque Hemorrhage

IPH is currently recognized as a high risk factor for plaque instability, because it contributes to plaque progression and destabilization [39, 40], causing complications by promoting vulnerability, luminal occlusion or embolic events. Several studies have found a strong association between IPH and cerebrovascular events [41–43]. Gross and microscopic pathological investigations suggested that IPH occurs more often in symptomatic patients undergoing CEA and that the age of the hematoma correlates with the timing of the symptoms [44, 45]. Histopathological examinations have revealed the association between IPH and the presence of neovessels [46]. Particularly, a study suggested the possible rupture of neovessels as cause of production and expansion of IPH [47].

The appearance of IPH on MRI depends on the hemoglobin structure and oxidative state. Different timing patterns are known for IPHs: early and acute hemorrhage contains intracellular meta-hemoglobin, whereas extracellular meta-hemoglobin is commonly found in subacute hemorrhage; finally, chronic hemorrhage is characterized by the presence of hemosiderin (Fig. 4). MR can age IPH

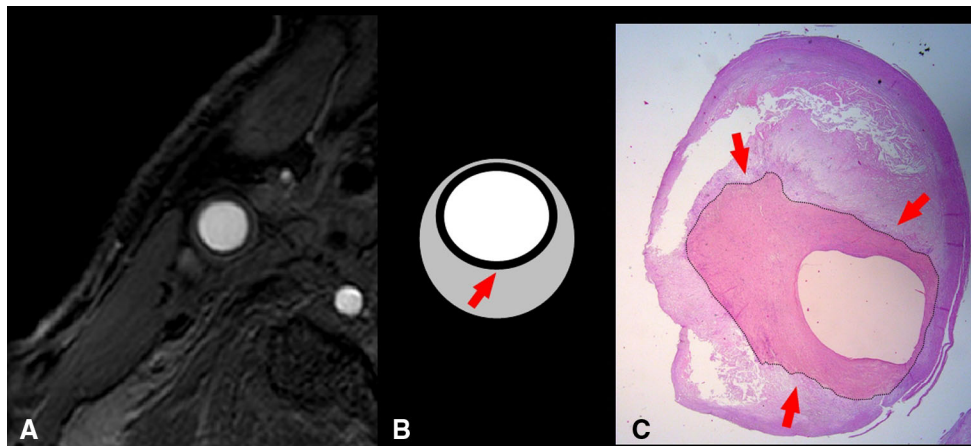


Fig. 3 **a** Thick fibrous caps appear as a juxtaluminal band of low signal in time-of-flight (TOF) MR images. **b** Schema is demonstrated (*red arrow*). **c** Histological image of a thick fibrous cap (*red arrows*)

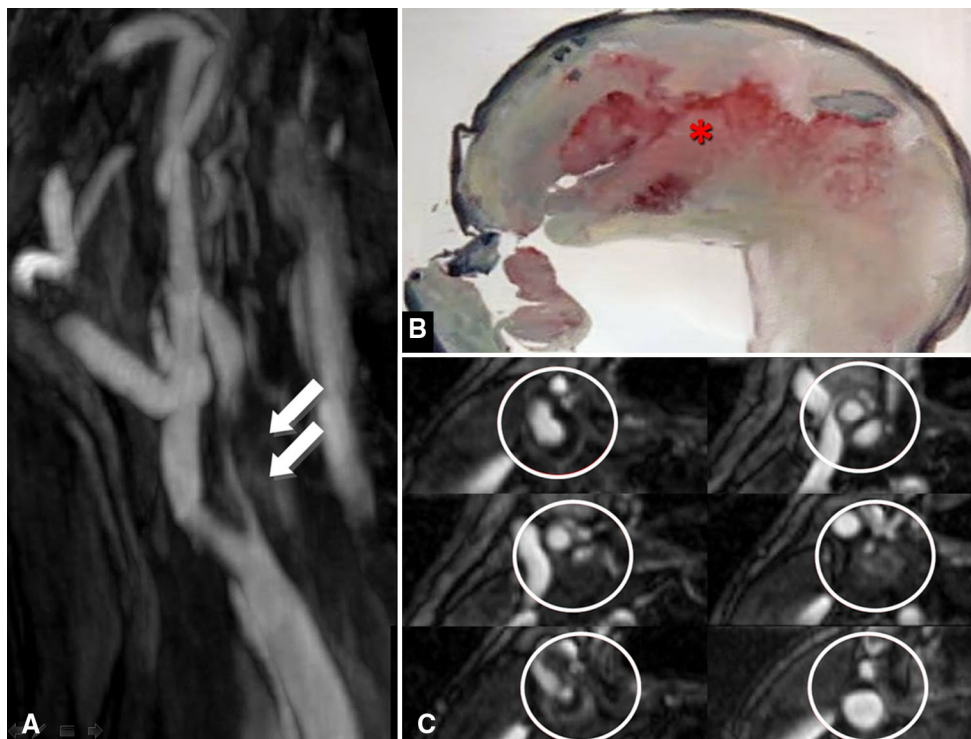


Fig. 4 High-resolution T1-weighted images acquired during the equilibrium phase of gadolinium. **a** The presence of a long and eccentric plaque with regular surface but enhancement of the inner plaque component (*arrows*), compatible with the presence of

inflammation and haemorrhage. **b** The correspondent histological section confirmed the presence of haemorrhage within the plaque core. **c** Axial reformatted images show the localization of enhancement area within the plaque

[48–50] by distinguishing different patterns on T1-w, T2-w, PD, and TOF images. Authors tried to identify IPH using CT and found a strong correlation between very low HU value and IPH [51, 52].

The Plaque Composition

Carotid artery plaques are constituted by different components and the relative proportion of these components

can vary greatly from one plaque to the other. These differences are important because different types of plaque are associated with different risks of stroke. Ultrasound, and especially CT and MRI, can offer information about the carotid artery plaque composition.

On CT, carotid atherosclerotic plaques are classified, according to their HU density, in fatty (<60 HU), mixed (60–130 HU), and calcified (>130 HU) plaques [53] (Fig. 5). Very low HU value in the plaque (<0 HU) are associated with the presence of intraplaque haemorrhage [53, 54]. The presence of fatty plaques are associated with an increase risk of stroke [55], whereas the presence of calcium in the carotid artery plaques seems to be a protective factor [18, 56], which is unlike the coronary arteries [57, 58]. It is hypothesized that calcium in the carotid atheromatous plaques confers stability, resulting in a protection against the biomechanical stress and the disruption. The presence and the amount of calcium in the carotid artery plaque can be assessed using different imaging techniques but the most sensitive technique is CT because of the high attenuation of X-rays by calcium hydroxyapatite, which leads to a high density structure in the plaque. For the CT analysis of calcified plaques, it is extremely

important to correctly select the window of visualization (level and center) [59].

On ultrasonography, the analysis of the echogenicity is the main parameter that reflects the plaque composition. One of the most used method is the Gray-Weale's classification modified by Geroulakos [60] that classifies the plaque in five types according to the level of echogenicity: type 1 (anechogenic with echogenic FC); type 2 (predominantly anechogenic but with echogenic areas representing less than 25 % of the plaque); type 3 (predominantly hyperechogenic but with anechogenic areas representing less than 25 % of the plaque); type 4 (echogenic and homogeneous plaque); and type 5 (unclassified plaques reflecting calcified plaques with areas of acoustic shadowing which hide the deeper part of the arterial layers). It was demonstrated that types 1 and 2 are similar to CT fatty plaques, types 3 and 4 as mixed plaques, and type 5 as calcified plaques [61, 62] (Fig. 5).

MRI can depict carotid artery plaque composition but, as described in the previous section, its best potential lies in its ability to identify the presence of haemorrhage within a plaque and to characterize its age [40]. The type of the plaque is associated not only with the potential

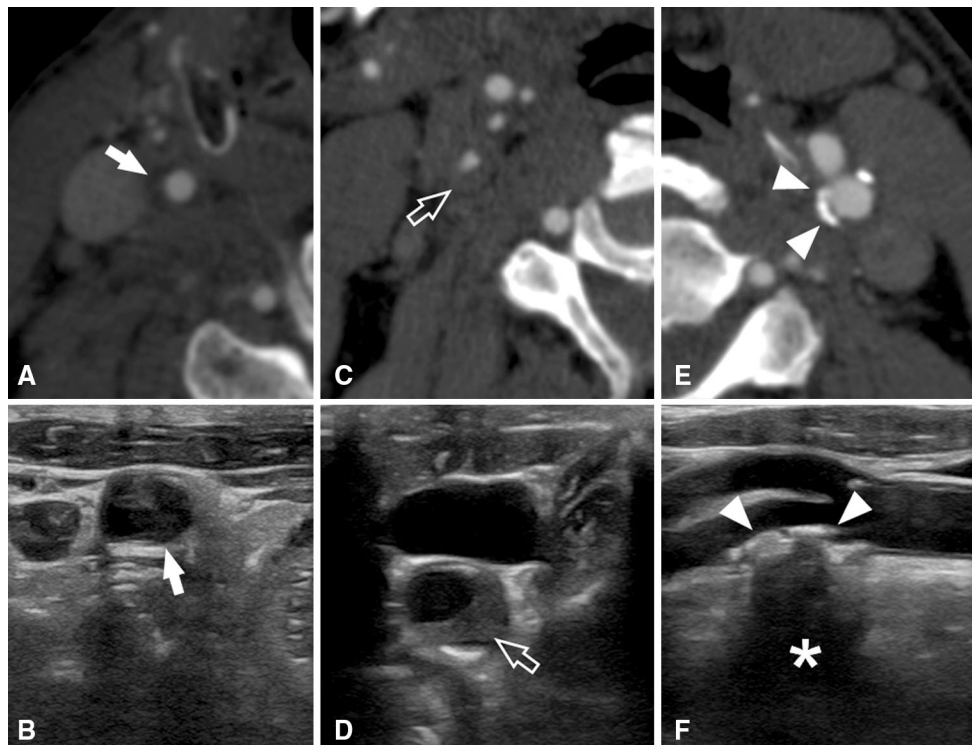


Fig. 5 Different plaque types of the carotid artery plaques imaged using CT and US. **a, b** Fatty plaques (*white arrows*) on CT corresponding to the Geroulakos class 1 on US. **c, d** Mixed plaques

(*white open arrows*) on CT corresponding to the Geroulakos class 3 on US. **e, f** Calcified plaques (*white arrowheads*) on CT corresponding to the Geroulakos class 5 on US

development of cerebrovascular events but also with the presence of other conditions that affect the brain such as cerebral micro-bleeds and leukoaraiosis [63–65].

This information also is extremely important for risk assessment of carotid artery stenting (CAS) because some conditions (circumferential calcification or large necrotic cores with thin or ruptured FC) are considered as a counterindication to the CAS procedure. In particular, Kamenskiy et al. [66] recently found that patients with circumferential, heavily calcified plaques, located in the distal portion of the internal carotid artery are most likely to have poststenting geometric changes and complications, whereas Tsutsumi et al. [67] found that in those calcified plaques that were treated with CAS there were multiple fragmentations of the calcifications (assessed by MDCT) in 94.4 % of the cases.

The Plaque Volume

Recent studies have demonstrated that the volume of the carotid artery plaque, driven by the remodeling that occurs in the time, is a critical determinant of the plaque “vulnerability” and risk of rupture. Some authors have hypothesized that the plaque volume may be a better descriptor of the severity of atherosclerotic disease than the degree of stenosis it causes [68]. Noninvasive in vivo assessment of atherosclerotic plaque volume and the relative contribution of the different plaque components have important clinical implications, in terms of ischemic event risk assessment. Nowadays, dedicated CTA-based software can calculate the volume of the carotid artery plaque and

determine the volume of the subcomponents. These software are based on the HU threshold, so that the operator can select for which HU a plaque can be considered fatty, mixed, or calcified. A new study published in 2013 addressed this type of quantification using MRI, but the results were less convincing because of the lower spatial resolution of MRI compared to CT [69] (Fig. 6).

The lipid component volume appears to be associated with the presence of plaque ulcerations, which represent a significant risk factor for the development of cerebrovascular events [70]. The plaque composition changes with increasing plaque volume. More specifically, there is an increase in the proportion of lipid and calcification with increasing plaque volume.

The Plaque Neovascularization

Several histopathological studies revealed that the ectopic neovascularization in the intima and media is a hallmark of advanced atherosclerotic lesions [71]. The presence of neovascularization in carotid artery plaques is considered as an element of vulnerability because these microvessels are prone to rupture, and IPH has been shown to accelerate plaque evolution [72].

Carotid contrast-enhanced ultrasonography (CEUS) can offer some information about the presence of neovascularization [73] in particular when microbubbles are used [74, 75]. However, the reproducibility and utility of this modality for clinical care are not well established [76]. On CT, the identification of plaque neovascularization is based on few studies [77–81] that demonstrated the ability of CT

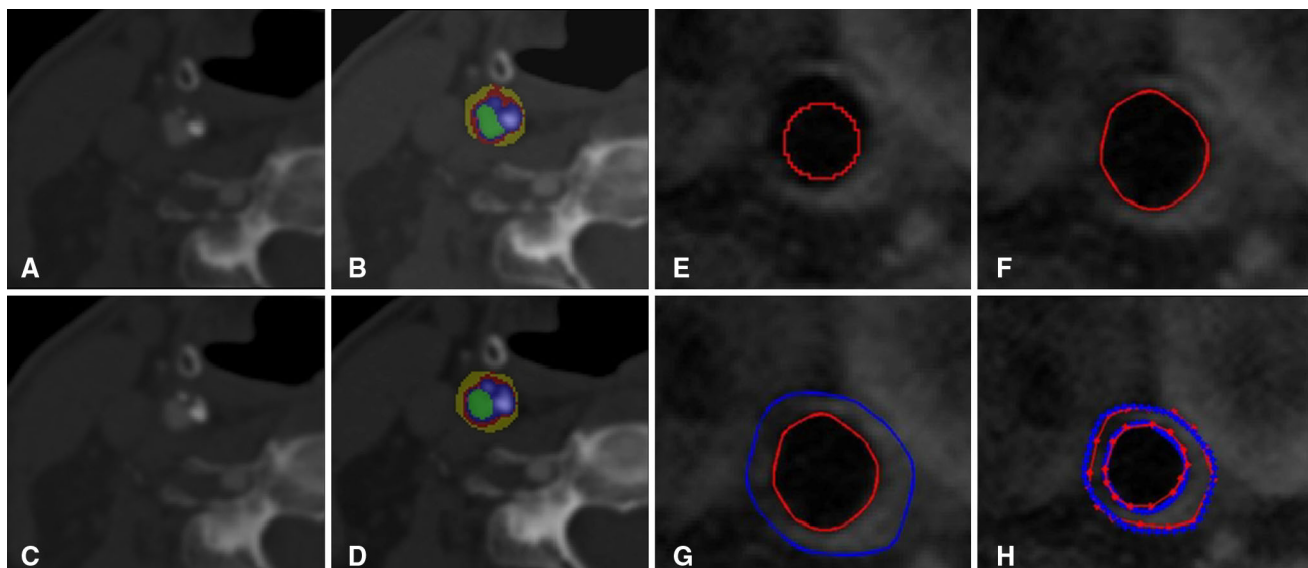


Fig. 6 Carotid CTA axial images (a, b) with automated carotid artery plaque segmentation (c, d). MR axial images (e, f) with automated carotid artery lumen detection (g, h)

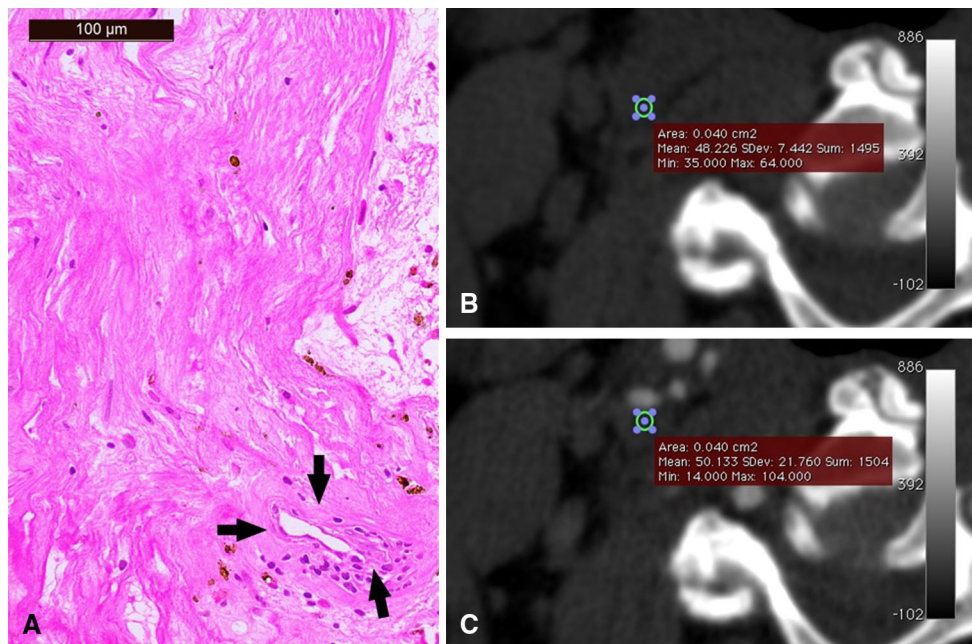


Fig. 7 Carotid contrast plaque enhancement. **a** Histological slice of a 67-year-old patient who underwent carotid endarterectomy where neovessels are visible (*black arrows*). **b** CT axial image of the same

patient is given and in the plaque there is an HU value of 48. **c** Same section as (**b**) obtained after administration of contrast material: the plaque HU values are higher

to detect contrast plaque enhancement (CPE) related to the degree of neovascularization (Fig. 7).

MRI also can assess the presence of neovasculature in carotid artery plaques [82–85]. A recent study by Gaens et al. [85] showed that dynamic contrast-enhanced MR of carotid atherosclerotic plaques can assess plaque neovasculature and that the Patlak model is well-suited for describing carotid plaque enhancement; the authors found that the $K(\text{trans})$ is an indicator of plaque microvasculature (validated by histology) and that the reproducibility of $K(\text{trans})$ was good.

Contrast Enhancement (US–MRI–CT)

Contrast-Enhanced Ultrasound

CEUS represents a simple and noninvasive technique for the evaluation of plaque vascularization, allowing for the detection of plaque vasa vasorum that are abundant in vulnerable plaques [86–88].

Different ultrasound contrast agents are commercially available. They differ basing on their composition (protein, lipid, phospholipid, or sulfur hexafluoride microbubbles), but they have the common characteristic that they resonate when exposed to an ultrasound wave. The enhancement of the arterial lumen allows to assess the degree of stenosis and to evaluate luminal irregularities, dissections, or ulcerations. At the same time, the technique allows direct

visualization of the adventitial vasa vasorum and intraplaque angiogenesis. A recent article by Staub et al. [89] concluded that vulnerable plaques frequently have a greater degree of neovascularization and that the presence of plaque neovessels correlates with lesion severity and with morphologic features of plaque instability. Therefore, contrast-enhanced ultrasound can represent a valuable tool for risk stratification of unstable plaques [89].

High-Resolution and Contrast-Enhanced Magnetic Resonance Imaging

High-resolution magnetic resonance imaging is a useful noninvasive tool for characterizing atherosclerotic plaque composition and provides excellent images of the arterial wall. The high field strength (1.5–3 T), the high-contrast resolution and the use of dedicated surface radiofrequency coils that increase the signal-to-noise ratio allow to go beyond the assessment of stenosis degree and to depict plaque components (FC, lipidic core, calcification, IPH). Contrast-enhanced magnetic resonance angiography (CE-MRA) has been demonstrated to be a very accurate non-invasive test for the detection of significant (70–99 %) symptomatic carotid artery stenosis [90]. Different contrast agents are currently used to characterize carotid plaque. Gadolinium-chelates contrast agents are most commonly used for MRA examinations; for the assessment of unstable plaques, the vascular enhancement of the carotid plaques themselves has been demonstrated to hallmark the presence

of an increased endothelial permeability due to plaque inflammation that facilitates the entry of contrast agents [83, 91–95].

A study by Kerwin et al. confirmed the usefulness of contrast-enhanced MR imaging in both the depiction of plaque inflammation and the differentiation of the plaque components such as fibrous or necrotic portions. Moreover, they showed that early plaque enhancement is due to the presence of internal neovessels, while late enhancement is related neovasculature supply and endothelial permeability [94]. The correlation between the degree of plaque enhancement and the degree of neovascularization, which is itself linked to the degree of plaque inflammation, also was confirmed at histology in a recent study by Millon et al. [96].

Blood-pool contrast agents (characterized by a long intravascular circulation times) and contrast agents that are characterized by an increased R1 relaxivity allow for “steady-state,” T1-weighted images with increased spatial (isotropic) resolution, during the equilibrium phase of contrast circulation after the initial first pass [97]. The use

of the steady state sequences combined with the first-pass study can provide additional diagnostic information comparable to that obtained with CT angiography [98] (Fig. 8).

Finally, small particles-based contrast agents (iron oxide) can be used to evaluate the presence of plaque inflammation because of their ability to enter atherosclerotic plaques with an increased endothelial permeability and accumulate in migrated macrophages [99]. High-risk inflamed plaques may be identified with a focal area of signal loss visualized on MR images, due to contrast accumulation [100]. Moreover, ultrasmall superparamagnetic iron oxide (USPIO)-enhanced MR imaging has been experimentally used as a biomarker for the screening and the assessment of therapeutic response to statins treatment.

Computed Tomography Angiography

The widespread availability of multi-detector-row CT scanners has made CT angiography the most used noninvasive technique to assess carotid arteries after color-

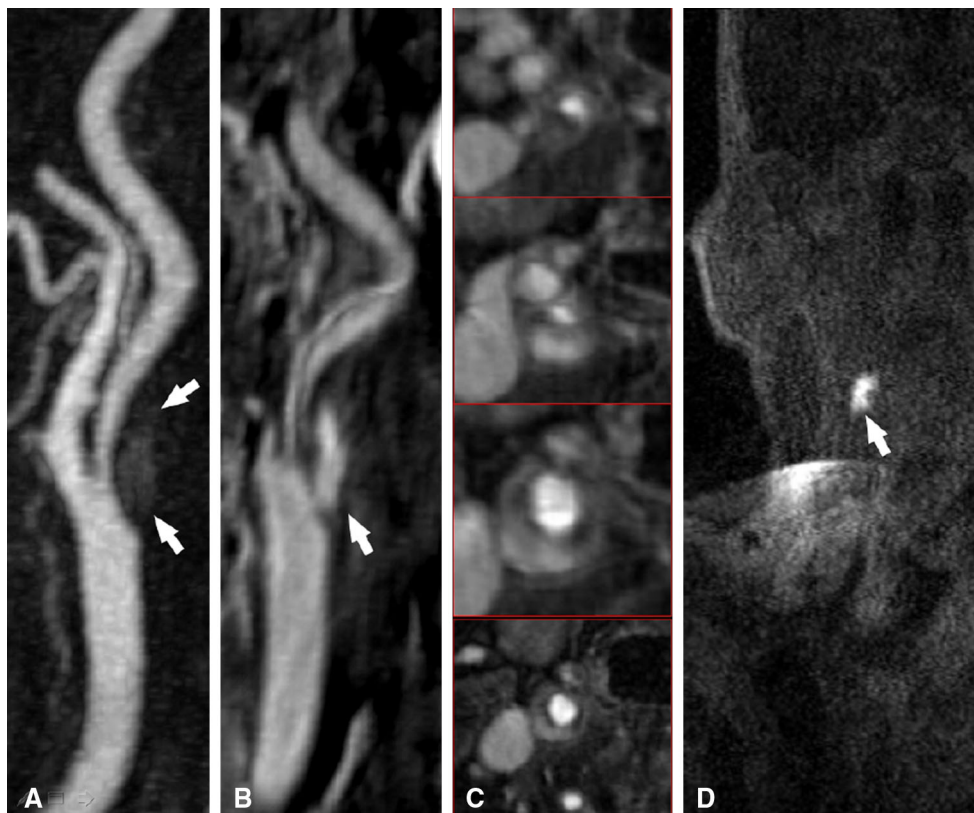


Fig. 8 CE-MRA of a vulnerable carotid plaque performed after injection of a high-relaxivity contrast agent. The use of high-resolution, T1-weighted sequences acquired after the first-pass study, during the equilibrium phase, can provide additional diagnostic information, such as the presence of signs of plaque vulnerability (inflammation or haemorrhage). During the first pass of the contrast agent (a), a soft and regular plaque is depicted at the carotid

bifurcation (arrows). High-resolution, T1-weighted sequences (b) show the presence of an enhancing area within the plaque (arrow) corresponding to intraplaque haemorrhage. Axial reconstruction (c) shows the location of the enhancing area and the stenosis degree. A hyperintense area corresponding to the intraplaque haemorrhage was also visible on precontrast T1-weighted images (arrow in d)

duplex ultrasound. The advantages of this technique are several: velocity of execution, large Z-axis coverage, possibility to use several postprocessing techniques, and the high confidence of the clinicians and surgeons with the CT images. The high spatial resolution combined with very short acquisition times make computed tomography angiography (CTA) of the carotid arteries a very useful tool for the assessment of carotid plaque burden.

A meta-analysis conducted by Koelemay et al. reported sensitivity and specificity values for CTA of 97 and 99 %, respectively, in terms of characterizing the degree of carotid stenosis. In particular, CTA was accurate to characterize 70–99 % stenoses and for the diagnosis or exclusion of occlusions [101]. The ability to scan with very thin slices allows for the accurate evaluation of carotid plaques and of possible intimal irregularities or ulcerations. In terms of CT characterization of plaque components, the presence of high-calcified plaques can hamper a correct estimation of the other components (lipidic core and initial signs of inflammation) because of the blurring artifacts. This limit does not exist for soft plaques.

Finally, CTA is particularly useful for the evaluation of carotid artery remodeling (modifications of lumen diameters following the development of a wall plaque) [102]. The main disadvantage of CTA is the radiation dose delivered to the patient. It is important to underline that the radiation dose can significantly change according to the

type of the CT scanner used. In particular, there is a difference between the use of the single source CT versus the dual source CT technology. In a recently published paper [103], the CDTI of single source CT was 12.5 mGy, whereas using dual energy CT system was 10.64 mGy.

Dual-Energy Imaging

Recently, a new type of CT scanner was introduced: dual-energy CT. This technology allows to obtain the attenuation value of a tissue at multiple energy levels and to postprocess the dataset to evaluate the tissue attenuation determined for specific keV values [104] (Fig. 9).

Mannelli et al. [105], in a recently published “ex vivo” study, compared the size of the calcifications in the carotid artery plaques measured on the different keV images to a histological standard and found that calcium area measured on the 80 keV image set was most comparable to the amount of calcium measured on histology. Saba et al. [106] assessed “in vivo” the effect of the multispectral imaging in terms of carotid artery plaque classification and found that the HU values of carotid artery plaque significantly change according to the selected keV. Results from this study demonstrated that the HU-based plaque type (fatty and mixed) classification can be improved with the use of multienergy imaging.

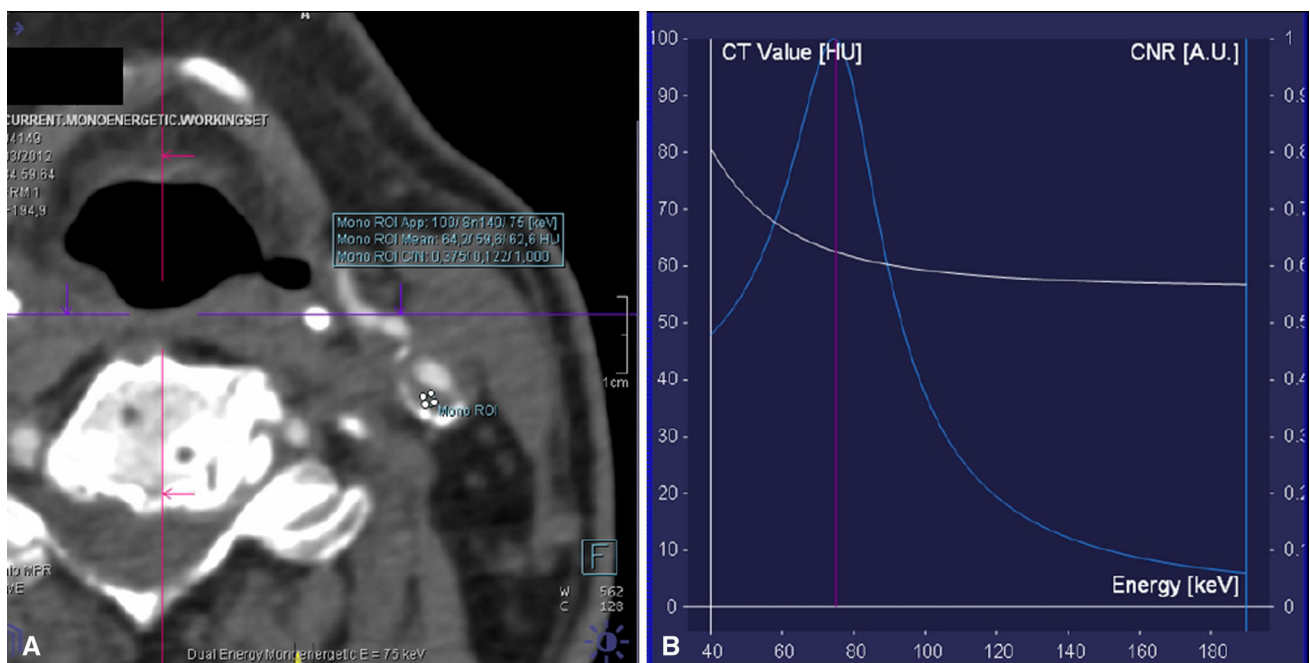


Fig. 9 The effect of the different keV levels is visible. The CTA axial image of a 62-year-old patient with a mixed plaque (a) and the variation of the HU value due to the variation of the keV is clearly visible (b)

Clinical Practice and Results from the Scientific Studies

In the past years, several studies have demonstrated that the degree of luminal stenosis represents only one of the parameter that can determine the ischemic stroke and gradually we have evolved to the concept of vulnerable plaque from the concept of risk arising from the degree of stenosis [9, 10, 107]. However, currently there is a discrepancy between these scientific studies and clinical practice; despite of many publications and discussions, plaque imaging techniques are not really the basics of clinical decision making or current guidelines and in the majority of cases decision towards revascularization are not based on plaque morphology but on the degree of stenosis [108–110]. Evaluation of the role of predictive effects of the previously described imaging parameters are needed and further studies are necessary to incorporate the potential of the advanced imaging techniques in the identification of the vulnerable plaque to selection of the therapeutical approach. Only in this way the identification of the features of plaque vulnerability will have a bigger clinical impact. Another important issue is the economic impact of the application of CTA or MRA in the diagnostic flowcharts. Previous study demonstrated that the cost of digital subtraction angiography is very high and it can be replaced by CTA or MRA [111]; however, there is no consensus when these techniques should be used and more data are required to define the economic impact of these techniques [112].

Conclusions

Nowadays, imaging can identify and characterize determinants of carotid atherosclerotic plaque vulnerability and stratify the risk of stroke for patients affected by atherosclerotic disease of carotid arteries. Ultrasound imaging can offer valuable information about the general composition of the plaque and also about the presence and degree of neovascularization within the plaques, when combined with the use of microbubble contrast agents. CT imaging allows assessment of several characteristics of the vulnerable plaques: total volume (and the volume of the sub-components), classification of the plaque types (fatty, mixed, calcified), analysis of the neovascularization. MRI offers the best level of assessment of carotid artery plaques by analysing features, such as the status of the FC and the presence of IPH. The use of specific contrast agents can target specific cell population, such as macrophages, which are a marker of the inflammatory process within vulnerable plaques. Further studies are necessary to incorporate the potential of the advanced imaging techniques in the identification of the vulnerable plaque to selection of the therapeutical approach.

Conflict of interest The authors declare that they have no conflict of interest.

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