Atherosclerosis Disease Management
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Part I
Histology, Pathologies and Associated Risks
Chapter 1
Introduction to the Pathology of Carotid Atherosclerosis: Histologic Classification and Imaging Correlation

Naima Carter-Monroe, Saami K. Yazdani, Elena Ladich, Frank D. Kolodgie, and Renu Virmani

Abstract  Understanding the natural history of carotid atherosclerosis is essential in the management of patients at risk for stroke. Atherosclerotic plaque at the carotid bifurcation is the underlying cause of the majority of ischemic strokes and the degree of carotid stenosis is strongly associated with stroke risk in symptomatic patients. Pathologic studies comparing symptomatic and asymptomatic carotid plaques have demonstrated that specific plaque characteristics are associated with ischemic brain injury and the mechanisms underlying plaque instability in the carotid circulation are similar to those in the coronary circulation. This chapter will focus on the morphologic classification of carotid atherosclerosis based on a modification of the AHA classification system (with a comparison to atherosclerosis in the coronary vasculature) and will consider morphologic differences between carotid plaques in asymptomatic vs. symptomatic patients. In addition, we provide brief overview of the burgeoning number of imaging modalities used in the characterization of carotid plaques, as they compare to histologic studies.

Keywords  Atherosclerosis • Fibroatheroma • Thin-cap fibroatheroma • Plaque rupture • Plaque erosion • Carotid • Endarterectomy • Plaque morphology • Inflammation • Magnetic resonance imaging • Angiography • Doppler ultrasound

1.1  Introduction

Despite advances in diagnostic and therapeutic interventions aimed at eradicating the scourge of cardiovascular disease, in the year 2006 alone, one out of every six deaths was due to coronary artery disease, with a total mortality of 425,425 persons in the US population. For the same year, in approximately 1 out of every 8.6 death certificates, or a total of 282,754 deaths, heart failure was recorded as an underlying cause of death or a precipitating factor. Current projections on cardiac-related disease...
in the US estimate that 785,000 people will have a new coronary event, 470,000 will have recurrent disease, and 195,000 will have a silent first myocardial infarction for 2010 [1].

As the third leading cause of death in the USA, stroke proves to be just as devastating given that in 1 year approximately 795,000 people will suffer a new or recurrent stroke. Of these cases, approximately 500,000 are first attacks and 200,000 recurrent attacks. In 2006, stroke contributed to approximately 1 in 18 deaths in the USA [1]. Ischemic stroke accounts for the largest number of new strokes (88%) followed by intracerebral hemorrhage (9%) and subarachnoid hemorrhage (3%) [2]. Atherosclerotic plaque at the carotid bifurcation is the underlying cause of the majority of ischemic strokes and the degree of carotid stenosis is strongly associated with stroke risk in symptomatic patients [3]. However, the degree of stenosis does not always predict those patients who will develop vulnerable lesions as low-grade lesions may also result in cerebrovascular events. Pathologic studies comparing symptomatic and asymptomatic carotid plaques have demonstrated that specific plaque characteristics are associated with ischemic brain injury and the mechanisms underlying plaque instability in the carotid circulation are similar to those in the coronary circulation [4, 5]. In fact, plaque morphology is considered an additional independent risk factor for cerebral infarction.

Before launching into a discussion of the pathological aspects of atherosclerotic disease of the carotid, the rich history of the medical assessment of atherosclerosis and evolution of pathological evaluation will be presented. The pathology and natural history of atherosclerotic carotid disease in light of our current knowledge of coronary atherosclerosis will follow. While the precise sequence of events leading to carotid plaque vulnerability is as yet unknown, certain early lesions and more advanced progressive lesions have been characterized and will be presented according to a modified classification scheme originally devised for the coronary circulation. In addition, the screening and current medical imaging modalities to assess carotid atherosclerosis and correlation with histologic findings will be discussed.

1.2 Atherosclerosis: A Historical Perspective

Atherosclerosis is an “ancient disease” with a fascinating history, beginning with its characterization in medical works of ancient Egyptians, Greek, and Romans (both atherosclerosis and cardiovascular disease in general). Roman Emperor Hadrian (76–138 AD) according to accounts by classical historian Dio Cassius (recorded 80 years after Hadrian’s death), died from congestive heart failure secondary to hypertension and coronary atherosclerosis [6]. This fascinating history leads up to a duel of ideas between Rudolf Virchow and Carl von Rokitansky in the middle of the nineteenth century. Both observed cellular inflammatory changes in atherosclerotic lesions of the vessels they examined. Rokitansky held that these inflammatory changes were secondary in nature. Virchow, however, postulated that inflammation played a primary role in the process of atherogenesis [7].
Conventional wisdom has cast atherosclerosis to be a disease of modern man secondary to modern diet and stress despite the historical evidence outlined above and (more extensively) in other texts. However, paleopathology paints different picture, with findings of atherosclerotic lesions in mummies [8]. Microscopic examination of preserved vessels extracted from the mummified remains of the ancients showed evidence of atheroma, lipid deposition, medial calcification. Radiological exam revealed calcification of aorta and other large vessels. Allam et al. utilized whole-body, six-slice computed X-ray tomographic imaging (CT) to visualize calcium hydroxyapatite in vessel walls on 22 mummies kept at the Egyptian National Museum of Antiquities in Cairo, Egypt. Presence of calcium hydroxyapatite in a clearly defined artery upon CT imaging considered diagnostic for atherosclerosis (based on current convention) [9] and calcification along an artery’s probable course considered “probable atherosclerosis.” In these mummies, who lived between 1981 BCE and 334 CE, CT imaging found definite evidence of atherosclerosis in the form of calcium hydroxyapatite deposition in 5 of 16 mummies (30%), and probable atherosclerosis in 4 of 16 (25%). Calcification was more prevalent in those mummies who died at age 45 years or older (87%) as opposed to those dying before age of 45 (25%) [10].

1.3 Introduction to Carotid Artery Atherosclerosis

1.3.1 Pathologic Evaluation of the Carotid Endarterectomy Specimen

Carotid endarterectomy (CEA) has become the principal technique for cerebral revascularization in symptomatic and asymptomatic patient with extracranial carotid occlusive disease. CEA has become the most commonly performed vascular operation with an estimated 117,000 procedures performed annually in the USA. While the precise sequence of events leading to carotid plaque vulnerability is as yet unknown, certain early lesions and more advanced progressive lesions have been characterized and will be presented according to a modified classification scheme originally devised for the coronary circulation. It is in the interest of the pathologist to evaluate the endarterectomy specimen optimally, as only a detailed histologic examination of the carotid plaque specimen may demonstrate the underlying plaque morphology responsible for the disease, especially in symptomatic lesions.

Most surgeons remove the carotid plaques from the carotid artery bifurcation along with 10–15 mm of the internal and, if necessary, the external carotid artery. In all cases, the fixed specimens should be X-rayed to allow not only the identification of calcification but also provide information as to the extent of the luminal narrowing. Since most specimens are calcified, there is a necessity for most specimens to be decalcified in EDTA before histologic studies (Fig. 1.1). After decalcification, the specimen is cut transversely at 3–4 mm intervals beginning at the bifurcation. The entire specimen should be evaluated, as the culprit lesion
may not be limited to the most severely narrowed segment. Carotid plaque types share similarities with those found in the coronary circulation and may be classified according to AHA guidelines or by the simplified classification scheme described below [11].

### 1.3.2 Localization of Plaque at the Carotid Bifurcation

The earliest pathologic studies described the occurrence of atherosclerosis near branch ostia, bifurcations and bends, suggesting that flow dynamics play an important role in its induction. Atherosclerotic plaque tends to occur at regions where flow velocity and shear stress are reduced. It has been demonstrated that blood flow is disturbed at the carotid bifurcation where it departs from a laminar unidirectional pattern. The greatest atherosclerotic plaque accumulation typically occurs on the outer wall of the proximal segment and the sinus of the internal carotid artery, in the region of the lowest wall shear stress (Fig. 1.2). Plaque thickness is the least on the flow divider side at the junction of the internal and external carotid arteries where wall stress is the highest [12]. Thus, the unique geometrical configuration and flow properties of the carotid bifurcation contribute to the formation of atherosclerotic plaque, which may lead to critical carotid stenosis. However, plaque complications, regardless of the degree of the stenosis, are frequently the critical determinant of clinical consequences. At the carotid bifurcation, hemodynamic
1.4 Classification of Atherosclerotic Disease

1.4.1 The AHA Classification Scheme

The earliest classification system for atherosclerotic disease consisted of only two categories – the “fatty streak” and the atheromatous plaque. Considered as the precursor lesion to the atheromatous plaque, the fatty streak was defined as a lesion consisting of smooth muscle cells, lipid laden macrophages, and other inflammatory cells embedded within a proteoglycan–collagen matrix. The atheromatous
plaque represented a continuation from the fatty streak stage, as a raised lesion with a lipid-rich necrotic core and an overlying fibrous cap. Within this necrotic core, varying amounts of cholesterol and cholesterol esters are deposited [13].

In a series of three reports, the AHA classification scheme was introduced using a numerical classification to stratify the various forms of coronary lesions [14–16]. This scheme was more sophisticated and focused on linear progression of human atherosclerotic disease progressing from unaffected normal intima (and adaptive intimal changes/thickening), to pre-atherosclerotic intimal lesions (Types II, III) to advanced disease (IV, V, VI). In brief, the first category or the Type I lesions represented the very initial changes, with only an increase in intimal macrophages and appearance of the foam cell – macrophages filled with lipid droplets. Type II lesions are grossly identifiable as “the fatty streak” layers of foam cells and lipid droplets interspersed within layers of intimal smooth muscle cells. Type III lesions are considered intermediate lesions (a bridge between Type II and Type IV), characterized by pools of extracellular lipid [16]. The atheroma as the first of the advanced lesions, falls within the Type IV category, and is characterized by a larger, confluent, and more disruptive lipid core. Next in the sequence is the fibroatheroma, or Type V lesion, in which the lipid core remains sequestered from the lumen by layers of fibrous connective tissue, with (Type Va) or without (Vb) calcification. Some variants of the Type V lesion have minimal lipid deposition (Vc). The Type VI lesion extends the Type V lesion to include plaques with fissure, hematoma, and/or thrombus formation [15].

This scheme assumes that the “atheroma” is a stable lesion, following Virchow’s deduction that the “atheroma,” is a fatty mass encapsulated within a fibrous cap much like purulent material in an abscess is encapsulated within a capsule [17]. This capsule must be disrupted in order for the thrombogenic core to gain exposure to the vascular lumen and cause initiation of the coagulation cascade. It is based on this paradigm, that the concept of plaque rupture as the critical event leading to atherosclerotic death has been accepted [18]. In one autopsy-based study, evidence of plaque rupture associated with thrombosis was identified in 73% of cases, plaque fissure with intraplaque fibrin deposition and hemorrhage seen in 8% of cases, and 19% with no evidence of thrombi [19].

1.4.2 Limitations of the AHA Classification

Over time and with observation of more lesions, many have noted limitations to the AHA classification. Specifically, one limitation entails the lack of direct, experimental human or animal studies to prospectively model the progression of atherosclerotic disease. Animal models rarely progress beyond Type IV, the atheroma, which is considered to be the most stable of the advanced lesions. This is not the case in humans, where clinically evident lesions fall in the type V and VI categories, and type IV lesions are usually clinically silent except in cases of severe lipidemia in which the atheromatous core can become occlusive because of increase in size alone [20].
A second limitation involves the analysis of human arteries, primarily from autopsy material. Several studies involving the analysis of autopsy derived human coronary specimens have shown exceptions to the classification rules of the AHA system, including a study by van der Wal et al. [21] involving a series of 20 patients undergoing sudden cardiac death with plaque rupture seen in 60% of the coronary lesions. The remaining 40% of lesions showed “superficial erosion” – a diagnostic category not addressed in the AHA schema. In approximately half of the cases of “superficial erosion,” a fibrous cap heavily infiltrated by macrophages and T-lymphocyte and overlying a necrotic core was identified. The second series of studies evaluated coronary vessels from greater than 200 cases of sudden coronary death [22–26]. “Sudden coronary death” is defined as an unexpected death witnessed within 6 h of the onset of symptoms or death of a person known to be in stable condition <24 h before death [25]. Surprisingly, only one-third of the lesions in this series could be classified as plaque rupture, and 35% of lesions with thrombi failed to show a rupture site. And many of these lesions did not show significant inflammation.

We have proposed modifications to the AHA classification to address the aforementioned issues, mainly to the classification of the “intermediate” and “advanced” categories of plaque morphology [11]. This modified system includes seven categories as detailed in Table 1.1 including intimal xanthoma, intimal thickening, pathological intimal thickening, fibrous cap atheroma (fibroatheroma), thin cap fibrous cap atheroma, calcified nodule, and fibrocalcific plaque. Although both the AHA and Modified AHA classification systems explicitly refer to coronary artery atherosclerosis, observation shows that there are sufficient similarities between atherosclerotic lesions in the carotid and femoral vasculature in order to extend this classification system to those vascular beds. Figure 1.3 provides various examples of the lesion types according to the modified classification.

### Table 1.1 Modified classification based on morphologic description

<table>
<thead>
<tr>
<th>Early nonsymptomatic carotid disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse intimal thickening</td>
</tr>
<tr>
<td>Intimal xanthoma</td>
</tr>
<tr>
<td><strong>Intermediate lesion</strong></td>
</tr>
<tr>
<td>Pathologic intimal thickening</td>
</tr>
<tr>
<td>Progression of atherosclerosis leading to plaque enlargement</td>
</tr>
<tr>
<td>Plaque hemorrhage (+/− calcification)</td>
</tr>
<tr>
<td>Thin cap fibroatheroma (+/− calcification)</td>
</tr>
<tr>
<td>Lesions with thrombi</td>
</tr>
<tr>
<td>Plaque rupture with luminal thrombus</td>
</tr>
<tr>
<td>Plaque rupture with ulceration</td>
</tr>
<tr>
<td>Plaque rupture with organizing thrombus</td>
</tr>
<tr>
<td>Plaque erosion</td>
</tr>
<tr>
<td>Calcified nodule</td>
</tr>
<tr>
<td>Stable atherosclerotic plaque</td>
</tr>
<tr>
<td>Healed rupture/erosion</td>
</tr>
<tr>
<td>Fibrocalcific plaque</td>
</tr>
<tr>
<td>Total occlusion</td>
</tr>
</tbody>
</table>
1.4.3 Pathologic Features of Atherosclerosis and Modifications to the AHA Classification

1.4.3.1 Early, Asymptomatic Lesions

Intimal Thickening and Intimal Xanthoma

Both intimal thickening and intimal xanthomas are considered the earliest, prelesional stage of the disease. “Intimal xanthoma” replaces the type I “fatty streak” or “initial lesion” in the AHA classification and is characterized by focal accumulations of lipid laden macrophages noticed in the arterial walls of the very young and known to regress with time. Adaptive intimal thickening replaces the Type II “intimal lesion” or “intimal thickening” characterized by smooth muscle cells and proteoglycan matrix with variable amounts of lipid and absent to minimal infiltrating inflammatory cells. In the carotid intimal thickening and plaque formation have been demonstrated to predominate occur at the outer wall of the proximal segment and at the sinus of the internal carotid artery. Both regions experience the lowest wall shear stress in the carotid and share the distinction of being areas of maximal plaque burden in cases of advanced atherosclerotic disease. As postulated
for coronary vessels, it is the intimal mass lesion that serves as the most likely precursor of advanced atherosclerotic lesions [27].

Pathological Intimal Thickening

These lesions mark the transition from the early pre-atherosclerotic lesions (the “intimal mass” or “intimal xanthoma”) to the more advanced lesions (i.e., the fibroatheroma) discussed below. Both we and the authors of the AHA classification scheme agree that the majority of human atheromatous lesions originate as preexisting intimal masses, and not from the intimal xanthoma seen in juvenile patients [28]. When these lesions progress to the pre-atheromatous or “pathological” stage, they are characterized by acellular regions located within the deeper intimal layers (close to the media) filled with proteoglycans and extracellular lipid pools. In this lesion we begin to notice the presence of inflammatory cells, as macrophages and T-lymphocyte aggregate toward the luminal side of the intima at the periphery of the lipid pools [11, 16]. The lipid pools most often arise from areas of adaptive intimal thickening, AHA Type III lesions fit into this category and are commonly observed in the coronary, carotid, and iliofemoral arteries.

1.4.3.2 Advanced Symptomatic Lesions

Fibrous Cap Atheroma

This category encompasses plaques categorized as AHA Type IV and V lesions and includes those lesions with a “fibrous cap” overlying a lipid core [11, 15]. This fibrous cap consists of smooth muscle cells embedded in a proteoglycan matrix with infiltration by variable numbers of macrophages and/or T-lymphocyte. The underlying lipid core is composed of variable amounts of extracellular lipid, necrotic debris, and cholesterol crystals often surrounded by macrophages (Fig. 1.4).

Progression of Atherosclerosis Leading to Plaque Enlargement

Intraplaque Hemorrhage

Intraplaque hemorrhage is common in advanced coronary atherosclerotic disease. It is believed to arise from the disruption of thin-walled microvessels (vasa vasorum) that are lined by discontinuous epithelium without supporting smooth muscle cells. Several investigators have suggested that intraplaque hemorrhage and rupture of the fibrous cap are associated with an increased density of microvessels [24, 29]. In the carotid circulation, the incidence of intraplaque hemorrhage has been reported as higher in symptomatic patients (84% vs. 56% of asymptomatic) [4]. Several studies in fact have cited intraplaque hemorrhage as an important process...
associated with carotid plaque progression and the development of neurologic symptoms suggesting that hemorrhage may be related to disruption of the plaque or may lead to critical stenosis [30–33]. Plaque vascularity has been shown to correlate with intraplaque hemorrhage and the presence of symptomatic carotid disease [29]. These new blood vessels could play an active role in the metabolic activity of the plaque and ultimately control the processes that govern plaque progression. In addition, fibrin is a common finding in mature atherosclerotic lesions and most likely represents chronic hemorrhage within the plaque.

**Thin Cap Fibrous Atheroma (Vulnerable Plaque)**

This category expounds upon the fibrous cap atheroma to include those cases not included explicitly in the AHA classification with a quantifiably thinner fibrous cap, defined as a thickness <65 μm, and a relatively large necrotic core, often representing approximately 25% of the plaque area [26]. Studies have shown that the “thin cap” experiences loss of both extracellular matrix and smooth muscle cells, often accompanied by hemorrhage, calcification and abundant vasa vasorum [23, 34].
It is this thinning of the fibrous cap that leading to fissures and ruptures that results in total fibrous cap disruption in the coronary [11, 35], carotid [4], aortic [36], and femoral arteries. And it is this disruption of the fibrous cap, exposing the highly thrombogenic substances of the underlying necrotic core to the lumen, that is one factor responsible for luminal thrombosis. Given that 75% of thrombi in patients experiencing sudden coronary death are secondary to plaque rupture, early recognition and treatment of the thin cap fibroatheroma is of the utmost importance in the fight against premature death secondary to coronary atherosclerotic disease [35].

In the carotid artery, our laboratory has measured a mean vulnerable cap thickness of 72 ± 24 μm. Therefore, we have defined carotid vulnerable plaque thickness as less than 120 μm. Another recent study has defined carotid vulnerable plaque thickness as less than 165 μm based on a mean (±SD) cap thickness of 70 ± 47 μm [37]. Carotid plaques follow a similar pattern of disruption with fibrous cap thinning and infiltration of macrophages (Fig. 1.5). In a recent study, 47% of carotid ruptured plaque occurred in arterial segments with less than 70% luminal narrowing. Furthermore, a high prevalence of vulnerable plaques occurred in segments not significantly narrowed (80% of cases) [37]. These data suggest that the culprit

Fig. 1.5 Thin-cap fibroatheroma “vulnerable” plaque in the carotid artery. (a) A Movat Pentachrome-stained image of a thin cap fibroatheroma consisting of a relatively large necrotic core (NC) covered by a thin fibrous cap (FC). (b) Demonstrates a high-power image demonstrating infiltration of foamy macrophages in the fibrous cap. Macrophages (MACΦ) can be more clearly seen on oil-red-o staining in (c) (modified from [85]).
lesions and their precursors occur more commonly in less severely narrowed vessels. Moreover, the data highlight the important tenet that plaques may progress to a substantial size before significant luminal stenosis occurs.

Lesions with Thrombi

This category includes lesions shown by observation to predispose to luminal thrombosis. As will be discussed further, these lesions are not mutually exclusive and thus can co-exist in the vascular bed and even in the same plaque.

**Plaque Rupture with Luminal Thrombus/Organizing Thrombus**

“Plaque rupture” is a descriptive term for phenomenon in which the fibrous cap becomes disrupted and an overlying luminal thrombus is in continuity with the underlying necrotic core. Ruptures typically have an enlarged necrotic core and the area of fibrous cap disruption shows both loss of smooth muscle cells and infiltration by macrophages and lymphocytes (Fig. 1.6). An acute thrombus is

![Fig. 1.6](image-url) Plaque rupture with ulceration in the carotid artery. (a) A Movat Pentachrome-stained image demonstrates a disrupted fibrous cap (arrow) with a relatively large necrotic core (NC). (b) shows a lack of actin-positive smooth muscle cells (ASMA) in the region of rupture. (c) demonstrates an abundance of CD-68 positive macrophages (MACΦ) at site of rupture (modified from [85])
characterized by platelet aggregates with few red blood cells and scattering of acute inflammatory cells. Over time, the thrombus may become organized, a process which involves infiltration of endothelial and smooth muscle cells and neovascularization. In cases of sudden coronary death, at least 75–80% of patients dying suddenly show the presence of acute or organized thrombi, while the rest demonstrate “critical” (≥75%) cross-sectional area luminal narrowing [38]. While plaque rupture with luminal thrombus is considered to be the major etiology of stroke, thrombi occupying large portions of the lumen in the carotid are unusual [4]. Spagnoli et al. identified thrombotically active plaques in 74% of patients with ipsilateral stroke [5].

**Plaque Rupture with Ulceration**

Most investigators agree that plaque rupture with ulceration is the dominant mechanism that leads to thrombus formation with subsequent embolization and cerebral ischemic events [4, 31]. Because of the differing hemodynamic properties of the carotid vs. coronary circulation, ulceration is a more common phenomenon in the carotid artery where shear stress is higher compared to the coronary circulation. Ulceration is defined by an excavated necrotic core with a discontinuous fibrous cap. Thrombus, if present, is found lying in the excavated crater.

**Plaque Erosion**

Although plaque erosions account for approximately 30–35% of cases of thrombotic sudden coronary death, plaque erosion is an infrequent cause of thrombosis in carotid atherosclerotic disease [4, 5]. It has been proposed that the rarity of plaque erosions may be related to the higher flow in the carotid location vs. the coronary circulation. It is believed that erosion is the result of vasospasm and loss of endothelial cells. Because the carotid artery is a large vessel, it is not surprising that erosions are very infrequently observed in the carotid atherosclerosis and is the least frequent cause of carotid thrombosis.

**Calcified Nodule**

The “calcified nodule” represents the least frequent cause of luminal thrombus accounting for 2–5% of coronary thrombi [38]. This term refers to a lesion with fibrous cap disruption and thrombi associated with eruptive dense calcified nodules. The plaque is heavily calcified consisting of calcified plates and a surrounding area of fibrosis in the presence or absence of a necrotic core (Fig. 1.7). The luminal region of the plaque shows the presence of breaks in the calcified plate, sometimes even bone formation, and interspersed fibrin with a disrupted surface fibrous cap. Although still infrequent in the carotid location, it is more frequently observed in carotid plaque ruptures vs. coronary accounting for 6–7% of thrombi (RV unpublished data).
1.4.3.3 Stable Atherosclerotic Plaque

Healed Rupture/Erosion

Healed lesions define a third category of atherosclerotic disease. These consist of healed plaque ruptures (HPRs), erosions and total occlusions. Multiple HPRs are also described in the carotid arteries and similar to the coronary circulation the degree of luminal narrowing may be related to the layering of multiple healed repair sites. In a recent study, it was demonstrated that healed ruptures were present in 13.9% of stroke patients, 11.5% of TIA patients, and 16.6% of asymptomatic patients [37]. While it has been shown that in coronary artery disease progressive narrowing occurs because of thrombosis, thrombus does not typically occupy a large portion of the carotid lumen and may explain why the prevalence of multiple HPRS appears to be somewhat less frequent in the carotid artery.
Fibrocalcific Plaques

These lesions are characterized by thick fibrous plaques overlying extensive accumulation of calcium in the intima close to the media. This form of plaque is normally seen in patients with stable angina. Coronary calcification correlates highly with plaque burden but its effect on plaque instability is less evident. Those that are >75% narrowed likely represent burnt-out lesions. Since necrotic core is usually minimal to absent in these plaques, this lesion is not considered a true fibroatheroma. However, it is possible that the fibrocalcific lesion is the end stage of a process of atheromatous plaque rupture and/or erosion with healing and calcification.

In carotid plaques, calcification is more likely to begin at the surface, resulting in eruption of calcified nodules. Also, asymptomatic carotid plaques are, in the majority of cases, fibrocalcific plaques.

Chronic Total Occlusion

Chronic total occlusions may demonstrate varied histology depending on the age of the lesion. Older lesions demonstrate luminal obstruction characterized by dense collagen and/or proteoglycan with interspersed capillaries, arterioles, smooth muscle cells, and inflammatory cells. These lesions may also show earlier phases of organizing thrombi containing fibrin, red blood cells, and granulation tissue. Total occlusions often demonstrate shrinkage of the artery, perhaps due to the effect of collagen within plaque and/or adventitia. This is not as common a lesion in the carotid location as in the coronary arteries, which is likely the effect of high flow causing thrombus to embolize.

1.4.4 Carotid vs. Coronary Disease: Differences in Plaque Morphology

Despite the many similarities demonstrated in plaque morphology between the carotid and coronary circulation, there are several unique features of carotid plaque morphology related to the high flow rates and the shear forces caused by the bifurcation of the common carotid artery into the internal and external carotids. One of the most important is the ulcerated plaque, which is rare in the coronary artery circulation but relatively common in the carotid and other elastic arteries. While ulceration is associated with thrombotic lesions in symptomatic patients, thrombus is not always present at the ulcerative site, a phenomenon most likely related to embolic mechanisms in the carotid circulation.

Plaque hemorrhage in the carotid artery is much more frequent than in the coronary arteries and may be related to high flow rates and pressures in the lumen.