Role of Computed Tomography Coronary Angiography in the Detection of Vulnerable Plaque, Where Does it Stand Among Others?

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Abstract

Recently, there has been a growing interest in identification of coronary “vulnerable plaques” that are prone to rupture; this potentially would help identify patients with higher risk of development of cardiac events. Recent advances in cardiac imaging modalities have been successful in studying various plaque vulnerability features to variable degrees, strengths and limitations. Computed Tomography Coronary Angiography (CTCA) has gained an increasing popularity in studying plaque anatomy, morphology and composition by the virtue of its widespread availability and non-invasiveness. CTCA has been validated against histology and IVUS with reasonable correlation; moreover, some follow-up studies have shown a significant association to the development of acute coronary syndromes. Nevertheless, attention should be paid to the whole patient big picture that includes other factors operating on other extra-coronary axes that involve inflammation, immunity, coagulation and neuroendocrine systems.

Introduction

Atherosclerotic cardiovascular diseases are still the leading cause of deaths in industrialized Countries and Coronary Artery Disease (CAD) accounts for the majority of this toll [1]. Cardiac events are typically caused by disruption of coronary plaques where plaque rupture occurs in about two thirds of cases, while the remaining third of cases are caused by plaque erosion with formation of occluding thrombus [2]. Thus, a clinically relevant definition of a rupture-prone (or what has been termed the “vulnerable”) plaque, is a lesion that places a patient at risk for future major adverse cardiac events, including death, myocardial infarction, or progressive angina.

On the other hand, the histopathological features that have been associated with vulnerable plaques and defined them, include: 1) A large eccentric necrotic lipid core, occupying approximately one-quarter of the plaque area [3], 2) A thin fibrous cap (<65 μm thick) [4], 3) Heavy infiltration by large number of inflammatory cells (macrophages and T cells) particularly at the shoulder region of the plaque [5], 4) Spotty calcification, 5) Neovascularization due to proliferation of the vasa vasora and formation of immature and leaky microvessels, with subsequent rupture and intra-plaque hemorrhage [6], finally, 6) In contrast to eroded plaques, rupture-prone plaques usually are non- or mildly obstructive, yet the size of the plaque may be substantial due to the phenomenon of positive remodeling [7]. Yet, some of these aforementioned features, namely calcification and positive remodeling are still controversial about their actual role in plaque stability.

Invasive coronary angiography, though presumably considered as the gold standard for the diagnosis of CAD, is a mere luminogram that focuses mainly on the stenosis severity rather than plaque characteristics. Moreover, other traditional non-invasive stress tests as stress echocardiography or myocardial perfusion imaging only help detect hemodynamically significant lesions rather than non-obstructive potentially vulnerable plaques.

Obstacles in detection of vulnerable plaques include their small size and being localized within the rapidly moving coronary arteries. In addition, plaque vulnerability is a dynamic process, a plaque that appears rupture-prone today could rather be stable tomorrow, even ruptured plaques do not always lead to coronary events as many ruptures occur and heal silently. Therefore, there has been a growing interest for detection and characterization of coronary atherosclerotic plaques. The aim of the present review paper is to shed some light on different diagnostic modalities used for the assessment of plaque vulnerability, with specific focus on the Multi-Detector Computed Tomography (MDCT) as an evolving tool in that field with all its strengths and limitations.

Imaging Modalities used for Assessment of Vulnerable Plaques

Direct visualization of atherosclerotic plaques in vivo is the only way forward for studying the natural history of atherosclerotic disease. The imaging techniques currently used are generally able to provide adequate information on the lumen diameter reduction or its functional significance. So, different imaging techniques; both invasive and non-invasive, have been developed to reliably evaluate plaque composition and identify its vulnerable features, thereby allow implementation of treatment strategies to prevent adverse coronary events. Table 1 lists different invasive and non-invasive imaging modalities with main strengths and limitations.

In addition to being expensive and in need for specially trained personnel, invasive techniques by their very nature, have a lower level of patient acceptability than non-invasive modalities which may provide a good alternative. Collectively, factors that characterize an ideal non-invasive technique would include; patient-related factors: 1) wide range of clinical indications, 2) absence of ionizing radiation, 3) unnecessary administration of contrast media and 4) not precluded by metallic devices or leads, and technical factors: 1) Rapid image acquisition, 2) high temporal, spatial and contrast resolution, 3) ability to provide both anatomic and metabolic information, and 4) accurate and reproducible [26].
<table>
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<tr>
<th>Modality</th>
<th>Mechanism</th>
<th>Spatial resolution</th>
<th>Strengths</th>
<th>Limitations</th>
<th>Relevant Studies</th>
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<td><strong>Invasive Modalities</strong></td>
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<tr>
<td>Intravascular ultrasound (IVUS) [8-11]</td>
<td>The intensity of the backscattered signal is processed into gray scale differ among different plaque components</td>
<td>150 µm</td>
<td>Provides information on plaque anatomical features and composition to lesser extent [12]</td>
<td>-Invasiveness -Limited temporal resolution -Limited spatial resolution -So cannot recognize thin cap fibroatheroma (TCFA) -Gray scale IVUS cannot accurately differentiate elements of plaque composition</td>
<td>-Features of plaque vulnerability include: eccentric pattern, echolucent core, positive remodeling, presence of thrombi, plaque length, lumen narrowing and spotty calcification [13,14]</td>
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<td>IVUS-RF (radiofrequency) analysis e.g. Virtual histology (VH) [8-11]</td>
<td>RF data are more in direct relation to the interaction of ultrasound with tissue</td>
<td>100-200 µm</td>
<td>-Ability to differentiate between different tissue types in plaques: dense calcium, fibrous, fibro-fatty and necrotic core [15] -Identification of TCFA</td>
<td>-Invasiveness -Limited spatial resolution</td>
<td>-When compared to histology, sensitivity, specificity and predictive accuracy of VH to detect necrotic core, a vulnerability feature were 67%, 93% and 88% respectively [16] -PROSPECT study showed a correlation between presence of TCFA and future major adverse cardiac events (hazard ratio: 3.35) [17,18]</td>
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<td>Paligography (intravascular elastography) [8,10]</td>
<td>Measures the local strain rate of vessel wall and plaque (fibrous plaques are stiffer than lipid-rich ones) high strain regions denote more vulnerable plaques</td>
<td>200-400 µm</td>
<td>Identification of thin fibrous caps</td>
<td>-Invasiveness -Limited spatial resolution -Cardiac motion</td>
<td>Human studies have shown a strong correlation between number of highly deformable plaques and both the clinical presentation (ACS Vs. stable patients) [18]</td>
</tr>
<tr>
<td>Intravascular MRI (IV-MRI) [8]</td>
<td>Calculates the water diffusion coefficient: lipid-rich &lt; fibrous plaques</td>
<td>120 µm</td>
<td>Detection of plaque composition</td>
<td>-Invasiveness</td>
<td>There was a good correlation between MRI and histology with sensitivity and specificity of 100% and 99% [19]</td>
</tr>
<tr>
<td>Angioscopy [8-11]</td>
<td>Direct visualization of the endothelial surface. The intensity of the yellow color detected is used for plaque characterization</td>
<td>200 µm</td>
<td>Precise visualization of plaque surface detecting disrupted plaques (ulcers, fissures)</td>
<td>-Invasiveness -Limited tissue penetration and spatial resolution</td>
<td>Number of yellow plaques were shown to be a strong predictor of ACS [20]</td>
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<td>Optical coherent tomography (OCT) [8-11]</td>
<td>Light-based imaging, measures the amplitude of backscattered light (optical echoes) from a sample as a function of time delay</td>
<td>4-20 µm</td>
<td>-Highest spatial resolution, able to resolve thin fibrous caps &lt;65 µm -Only technique able to detect eroded plaques -Accurate detection of plaque composition</td>
<td>-Invasiveness -Limited tissue penetration (1.25 mm), however, the most relevant morphologic findings are primarily localized within the first 500 µm under lumen surface</td>
<td>Second generation OCT e.g. Optical Frequency Domain Imaging has shown a good potential to define plaque constituents compared to histology [21]</td>
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<tr>
<td>Near Infrared spectroscopy (NIRS) [8,10,11,22]</td>
<td>Different molecules absorb and scatter near-infrared light differently allowing for the chemical characterization of biological tissues</td>
<td>N/A</td>
<td>Detection of plaque composition</td>
<td>-Invasiveness -Limited tissue penetration -Cardiac motion</td>
<td>When compared to histology, sensitivity and specificity of NIRS to detect lipid core, thin cap and inflammatory cells were 77%-90%, and 89%-93% respectively [23]</td>
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<tr>
<td>Thermography [8,10]</td>
<td>Plaque inflammation and neoangiogenesis produce heat measured at the surface of the plaque</td>
<td>500 µm</td>
<td>Detection of plaque inflammation and neoangiogenesis</td>
<td>-Invasiveness -Limited tissue penetration and spatial resolution -Cooling effect of blood underestimates temperature differences</td>
<td>Thermal heterogeneity has been correlated with features of vulnerable plaque like positive remodeling [24]</td>
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<td><strong>Non-invasive modalities</strong></td>
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<td>MDCT [8,10,25,26]</td>
<td>-Detects plaque morphology and composition by measuring local tissue attenuation -Molecular imaging using new contrast agents is under study</td>
<td>500 µm (200-300 µm in dual-source CT)</td>
<td>-Widely available -Detection of lumen narrowing accurately -Detection of plaque morphology and composition (within limits) -High spatial and temporal resolution</td>
<td>-Ionizing Radiation -Contrast agent -Artifacts e.g. blooming -Overlap in the attenuation spectrum of non-calcified plaque components (lipid and fibrous)</td>
<td>See later for details</td>
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</table>
Systematic comparison between invasive and non-invasive modalities for coronary plaque characterization in ex-vivo specimens demonstrated that CTA and IVUS are reasonably associated with plaque composition and lesion grading according to histopathologic findings, while Optical Frequency Domain Imaging (a second generation of OCT) was strongly associated.

Imaging features that were associated with advanced lesions were, mixed plaque at CTA, calcification at IVUS and lipid-rich plaque at OFDI. Moreover, OFDI showed a better diagnostic accuracy differentiating early from advanced coronary lesions, with area under the curve (AUC) of 0.8 compared to AUC of 0.63 and 0.68 for IVUS and CTA respectively [21].

**Multi-detector Computed Tomography**

First-generation scanners, or “conventional” CT, utilized a single X-ray source and single X-ray detector cell. Over the past two decades with the tremendous advances in technology, MDCT presented a breakthrough in cardiac CT imaging technology by 1) increasing the number of detector rows from 4 to 320 thus increasing the coverage in the Z-axis up to 16 cm in a single heart beat with a single gantry rotation, 2) speeding up the gantry rotation, enough to freeze the cardiac motion by capturing images within the relatively brief period of cardiac diastasis. the use of dual-source MDCT system has markedly improved the temporal resolution to approximately 85 msec, resulting in a shorter scan time and 3) decreasing the thickness of the detectors to 0.5-0.625 mm thus increasing the spatial resolution to image sub-millimeter structures. This has allowed more accurate and detailed imaging of coronary plaques morphology and composition.

MDCT has caught up with coronary angiography, showing an excellent diagnostic accuracy in diagnosis of obstructive CAD when compared to coronary angiography as the gold standard. In a recent meta-analysis of 188 studies (from 2004 to 2011), the mean sensitivity and specificity of MDCT were 97% and 87% respectively [31].

### Table 1: Characteristics of different imaging modalities used for detection of vulnerable plaques.

<table>
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<tr>
<th>Imaging Modality</th>
<th>Characteristics</th>
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<tr>
<td>High resolution MRI [8,10,25,26]</td>
<td>Uses different contrast weightings (T1, T2, proton-density and time-of-flight) to evaluate the biological features of plaque components. Molecular imaging using specific agents like paramagnetic nanoparticles targeting: • Fibrin: in plaque disruption and thrombosis • Cellular markers as E-selectin and vascular cellular adhesion molecule (VCAM): in inflammation and • Integrin αvβ3 in angiogenesis. 1 mm (improves to 350 µm in carotids)</td>
</tr>
<tr>
<td>Nuclear imaging (SPECT/PET) [8,10, 25,26]</td>
<td>Molecular imaging targeting: • Macrophages: in inflammation using 18F-Fluorodeoxyglucose (FDG) • Apoptotic cells: using Annexin V • Vasocostricting peptides: using 18F-Endothelin-1 (ET-1) PET: 4-5 mm SPECT: 1-1.6 cm</td>
</tr>
<tr>
<td>Contrast-Enhanced ultrasonography [8,10,25]</td>
<td>Acoustically active microbubbles (3-4 µm in diameter) that act as pure intravascular tracers, when exposed to ultrasound field, they produce a strong backscatter signal and specific nonlinear signal that differentiates them from surrounding tissues. • Molecular imaging; microbubbles labeled monoclonal antibodies targeting endothelial surface molecules e.g. VCAM-1 3-4 µm</td>
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The potential for MDCT evaluation of coronary plaques is enormous, given its noninvasive nature and its ability to evaluate the entire coronary arterial tree in contrast to IVUS. MDCT can help detect the suggested triad of the main features associated with plaque vulnerability namely; positive remodeling, low attenuation (<30 HU), and spotty calcifications [32-35]. Other imaging phenomenon, that has been reported to be pathologically related to thin cap fibroatheromas the "napkin ring" sign, defined as the presence of a ring of high attenuation around plaque; with a higher CT attenuation than those of calcium depositions [36] (Figures 1 and 2).

### Plaque morphology

Assessment of the plaque size rather than the luminal size is a more logical approach especially in plaques that show substantial positive remodeling, potentially indicating a higher risk for events than plaques with lesser extent of remodeling. Motoyama et al. [35] calculated the remodeling index and reported positive remodeling when the diameter at the plaque site was at least 10% larger than reference segment, it was shown that the frequency of positive remodeling among patients with acute coronary syndrome (ACS) was significantly higher than those with stable angina (87% Vs. 12%, P<0.0001) [35]. Similar finding was
confirmed when Pflederer et al. [37] showed a significantly higher remodeling index in ACS patients when compared to those with stable angina (1.6 ± 0.4 Vs. 0.97 ± 0.17, P<0.001) [37]. When validated against IVUS, The diagnostic accuracy of MDCT in detection of positive remodeling was excellent where area under the curve was >0.9 with excellent sensitivity and specificity of 100% and 90% respectively [38]. Interestingly, in a recent paper that used coronary artery simulation models, vessel wall stress concentrations were always predicted to be higher in the fibrous cap of plaques with positive remodeling compared to those with negative remodeling independent of the fibrous cap and the degree of stenosis [39].

Invasive coronary imaging is the gold standard for detection of disrupted plaques, the angiographic hallmark of complex lesions was characterized by “Ambrose criteria” including haziness, ulceration, intraplaque dye penetration and intraluminal filling defects, these features correlated with both histology and IVUS [40]. There are only scant data regarding the ability of Computed Tomography Coronary Angiography (CTCA) to identify features of plaque disruption; ulceration and/or intraplaque dye penetration. When compared to IVUS, MDCT was less accurate for the detection of plaque disruption in coronary arteries; sensitivity 57%, specificity 71% [41]. A more recent study that used the invasive angiography as the gold standard, MDCT has shown a good specificity (82-95%) but modest to good sensitivity (53%-58%). The lower sensitivity is likely attributable to the lower spatial resolution of CTCA compared with invasive angiography and presence of plaque calcification [42].

On the other hand, in carotid arteries, the introduction of MDCT did improve the detection of ulceration improving the sensitivity of single slice CT from 60 to 87% and specificity from 74 to 98% [43-46].

**Plaque composition**

By virtue of MDCT ability to measure local tissue attenuation, MDCT also allows imaging of the vessel wall, potentially providing insights into plaque composition rather than the physiology [47]. Identification of plaque composition is based on measuring the attenuation coefficient which is displayed as a CT number relative to the attenuation of water (0 Hounsfield units HU) and air (~1000 HU) [48]. Calcifications appear as hyperdense, fibrous tissue as isodense and lipid core, intra-plaque hemorrhage and thrombus as hypodense. However, using the absolute CT numbers to define different plaque constituents, especially of soft plaques, is influenced by various factors that could limit its accurate assessment, rendering the exact definition of low attenuation plaque values with the currently available techniques more challenging. These factors include; attenuation of intracoronary contrast medium, tube voltage, degree of stenosis, use of different reconstruction filters [49]. Table 2 shows some studies that reported CT attenuation values of various coronary plaque types in relation to IVUS. Of note, the reported CT numbers showed significant differences in densities of plaque components, yet, with substantial overlap.

Coronary artery calcium (CAC) is defined as a hyper-attenuating lesion >130 HU within an area of ≥ 3 pixels. Agatston score has been widely used to quantify CAC score by multiplying the lesion area (mm²) by a density factor (between 1 and 4) [54]. CAC score with its clinical and prognostic implications will be discussed later.

Different classifications of morphological patterns of calcification have been used in previous reports, one classification was as: speckled (calcified nodules), fragmented (shell-like, linear, or wide, single focus of calcium >2 mm in diameter), or diffuse (≥ 5-mm segment of continuous calcification) [55]. Calcified nodules have been well described on IVUS studies and identified as a less common cause of
plaque disruption (2-7%). On CTCA, Calcified nodules were observed in association with only 6% of obstructive stenotic lesions (>50%), whereas 44% of non-obstructive lesions showed this calcification pattern [55].

Other studies described classification patterns as spotty and dense calcification. Spotty calcification was defined and sub-classified according to their length on curved multiplanar reconstruction into: small spotty (<1 mm), intermediate spotty (1-3 mm), and large spotty calcifications (≥ 3 mm). Dense calcifications were defined as a plaque with high CT density, completely calcified and with calcifications present bilateral on cross-sectional axial slices [33,56,57]. A recent study, used high-resolution micro-computed tomography to identify micro-calcifications in the cap proper of 62 human coronary fibroatheromas, it showed that micro-calcifications were abundant in lipid pools. However, those calcifications observed in the fibrous caps increased the risk of rupture by introducing a stress concentration effect [58]. From the clinical viewpoint, this is highlighting the notion that it is not the micro-calcifications per se that are dangerous but their locations in the cap.

When validating MDCT studies, both histology and IVUS have been used as reference standard. Though histology is a better reference standard, IVUS is considered an accepted method for evaluation of the coronary arteries, where histology cannot be obtained.

When compared to histology, MDCT has shown a strong correlation for detection of calcification and fibrous tissue, while correlation was moderate for the detection of the amount of lipid core and fibrous tissue when compared to IVUS (Table 3). Also, MDCT could accurately detect calcified plaques with excellent sensitivity and specificity reaching 100% in a carotid study by Wintemberg et al. [46]; however, the detection of calcifications alone is not enough for the assessment of vulnerable plaques. As previously mentioned, due to some technical limitations, the soft tissue contrast of CT is low, resulting in a moderate diagnostic accuracy with a sensitivity range of (62%-94%) and specificity range of (74%-100%) [41,45,46].

Similar to positive remodeling, low attenuation plaque value (defined as <30 HU) and spotty calcification (defined as <3 mm in size) were significantly more frequent in ACS patients than in stable disease (79% Vs. 9%, p<0.0001 and 63% Vs. 21%, p=0.0005 respectively) [35]. The concomitant presence of the 3 high risk features was associated with a high positive predictive value for culprit lesions in ACS (95%) while their absence showed a high negative predictive value (100%) [35]. Of note, in a study where dual source CTCA was used, both spotty calcification and napkin ring signs were exclusive to ACS patients [37].

The role of calcification in determining the stability of individual plaque and its likelihood to rupture causing an event is still controversial. Some authors have assumed calcification to be protective against plaque rupture and a sign of healed plaques, especially that plaques with erosions (a less frequent mechanism of acute coronary syndromes) are often not calcified [65]. On the other hand, others have shown that the presence of small hard-rock calcium adjacent to soft tissues create forces that contribute to plaque instability and coronary events [66-69]. In the majority of patients with acute coronary syndromes, some CAC was detected, with a substantially greater score than in matched control subjects without coronary artery disease [70].

CAC score has been shown to have a high prognostic power being associated with hard cardiac events and total mortality in follow up studies. While the zero calcium score was associated with very low event rate <0.03% per year in metaanalysis studies [71], the hazard ratio for major coronary events went up to 3.89 and 7.1 in patients with CAC score between (1-100) and (101-300), respectively when compared to individuals without calcium [72].

It is worth noting that in spite of the relationship between CAC and plaque burden, there is only a weak correlation between the amount of CAC and the angiographic stenosis severity. Large amounts of CAC are not necessarily associated with the presence of significant stenoses. Even the absence of CAC, though makes the presence of significant stenosis relatively unlikely, ‘zero’ calcium score cannot be used to rule out coronary stenoses in symptomatic individuals, especially when they present at young age and with acute symptoms [73].

Detection of Vulnerable Plaque in Asymptomatic “Vulnerable” Subjects

The current appropriateness criteria do not recommend using computed angiography as a screening tool in asymptomatic population considering the risk of radiation and contrast media, cost and lack of supporting evidence. Motoyama et al. studied 1059 asymptomatic subjects by MDCT where atherosclerotic plaques were analyzed for the presence of the three vulnerability features; the plaque characteristics of lesions resulting in ACS during the follow-up of 27 ± 10 months were evaluated. It was shown low attenuation and/or positive remodeling independently predicted ACS (hazard ratio=22.8, CI=6.9-75.2, p<0.001) with a significantly higher likelihood of ACS than 2 feature-negative plaques or no plaques (p<0.001) [74]. Since HIV patients show high rates of MI and sudden cardiac deaths, a recent study has assessed the plaque vulnerability in asymptomatic relatively young HIV-infected subjects versus non-HIV-infected controls who were cardiovascular risk matched. The study concluded that the HIV-infected group has higher prevalence of

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of plaque and its measured attenuation value</th>
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<tbody>
<tr>
<td>Shroeder et al. 2001 [50]</td>
<td>Soft: 14 ± 26 HU</td>
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<tr>
<td></td>
<td>Intermediate: 91 ± 21 HU</td>
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<tr>
<td></td>
<td>Calcified: 419 ± 194 HU</td>
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<tr>
<td>Rasouli 2006 [51]</td>
<td>Soft: 23 ± 71 HU</td>
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<tr>
<td></td>
<td>Fibrous: 108 ± 79 HU</td>
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<tr>
<td></td>
<td>Fibro-calcified: 299 ± 112 HU</td>
</tr>
<tr>
<td></td>
<td>Calcified: 404 ± 264 HU</td>
</tr>
<tr>
<td>Motoyama et al. 2007 [52]</td>
<td>Soft: 11 ± 12 HU</td>
</tr>
<tr>
<td></td>
<td>Fibrous: 78 ± 21 HU</td>
</tr>
<tr>
<td></td>
<td>Calcified: 516 ± 198 HU</td>
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<tr>
<td>Pohle et al. 2007 [53]</td>
<td>Hypo-echogenic: 58 ± 43 HU</td>
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<td>Hyper-echogenic: 121 ± 34 HU</td>
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Table 2: MDCT studies showing attenuation values of different coronary plaques types.

<table>
<thead>
<tr>
<th>CT parameter</th>
<th>Correlation</th>
<th>P value</th>
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<tbody>
<tr>
<td>Histology</td>
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<tr>
<td>Calcification</td>
<td>r=0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fibrous tissue</td>
<td>r=0.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lipid core size</td>
<td>r=0.24</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Lipid core size (after excluding calcium)</td>
<td>r=0.81</td>
<td>&lt;0.001</td>
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<tr>
<td>IVUS</td>
<td></td>
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<tr>
<td>Necrotic core %</td>
<td>r=-0.539</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fibrous tissue %</td>
<td>r=0.571</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fibrofatty tissue %</td>
<td>r=0.074</td>
<td>0.512</td>
</tr>
<tr>
<td>Calcification %</td>
<td>r=0.113</td>
<td>0.316</td>
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Table 3: Summary of studies showing correlation between different CT plaque densities and histology or IVUS [50-53,59-64].
subjects with one or more vulnerability criterion. Moreover; there was a significantly higher number of low attenuation plaques and positive remodeling per subject [75].

Technical Limitations of CTCA

As previously highlighted in table 1, some technical factors might affect the role of CTCA in characterization of coronary plaques. These limitations include: 1) Radiation exposure; typical effective dose of radiation for retrospectively gated reconstruction is about 15 mSv, radiation doses delivered have markedly reduced to less than 2 mSv with the advent of newer prospective gating and ultra-low-dose protocols, these advances in technology are expected to further expand the CTCA applications and would permit follow-up studies to evaluate the progression of atherosclerotic plaques over time and with the use of interventional drugs like statins. 2) Contrast agents; currently used contrast media in CTCA are considerably safe, however, there is a minimal risk that should be anticipated and dealt with in patients with contrast allergy or those with advanced renal insufficiency. 3) Artifacts; various CT artifacts could limit the accuracy of CTCA in studying the plaque composition. Of note, dense calcification is a major limiting factor that could result in the blooming artifact phenomenon where calcium looks bigger than it actually is and 4) The significant overlap between tissue densities as previously discussed, rendering the accurate definition of plaque constituents more challenging [76].

Future Perspectives and Conclusions

The concept of “vulnerable plaque” has been introduced with the intention of detection of those high risk plaques that are potentially capable of causing acute cardiac events. Further risk stratification of asymptomatic or previously assumed low risk population is a complex process that goes far and beyond the mere use of risk score calculators or blood biomarkers. This process has been recently supported by the rapidly advancing imaging modalities that have shown some capabilities in visualizing various physical, chemical and biological aspects of atherosclerotic plaques that could define their vulnerability.

Among non-invasive modalities, MDCT seems to have the highest possibility of fulfilling the expectations of researchers and clinicians. In addition to its role in assessment of significant coronary obstruction with excellent diagnostic accuracy, it is getting popular as a promising non-invasive tool in detection of vulnerable features. This has been supported by studies that showed MDCT to have a good diagnostic accuracy and correlation when compared to histology and IVUS.A bigger role is expected from MDCT with the development of higher resolution scanners with lower radiation dose and the use of novel contrast media that could be targeted towards specific plaque constituents.

A major question after the identification of a vulnerable coronary plaque, should it be treated and how? At present there are no data to prove that interventional treatment strategies for those high risk but asymptomatic plaques are superior to conventional medical treatment. Data from large prospective studies will be needed to determine which approach will be beneficial.

Finally, we always should remember looking at the big picture accepting the idea that the pathogenesis of ACS does not involve only factors operating at the plaque level, but rather there is a concurrence of local and extra-coronary factors that involve coagulation, neuroendocrine, inflammatory and immune response of the vascular tissue.

References


