| | |
|---|---|
| CT | Computed Tomography |
| DSCT | Dual Source Computed Tomography |
| MDCT | Multidetector Computed Tomography |
| HU | Hounsfield units |
| bpm | Beats per Minute |
| IVUS | Intravascular Ultrasound |
| NPV | Negative Predictive Value |
| PPV | Positive Predictive Value |

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## Aim of the work :

We assessed the potential of a quantitative approach for non-calcified plaque characterisation, using a histogram analysis of the Hounsfield Units (HU) distribution within coronary plaques with the aim to accurately classify non-calcified plaques into fibrous and lipid-rich as compared to intravascular ultrasound (IVUS).

# مقارنة بين الأشعة المقطعية متعددة المقاطع و الموجات الصوتية الوعائية فى تقييم اللويحات الناتجة عن تصلب الشرايين التاجية

رسالة
توطئة للحصول على درجة الدكتوراة فى أمراض القلب و الأوعية الدموية


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# Discussion

The accurate characterization of coronary atherosclerotic plaques remains challenging, even when using invasive modalities such as IVUS. The detection of lipid-rich plaques is of potential relevance owing to their propensity to rupture and cause future cardiac events. This information could therefore affect risk stratification and subsequent treatment decisions. Motoyama et al. showed in a follow up study of intermediate duration, that patients with atherosclerotic plaques showing positive remodelling in CT as well as low attenuation areas - interpreted as lipid-rich content - were more prone to develop acute coronary syndromes (ACS).[111]

We analysed 55 non-calcified coronary atherosclerotic plaques in 40 patients using contrast enhanced DSCT and IVUS. The mean CT density for lesions classified as predominantly fibrous in IVUS was significantly higher than lesions considered predominantly lipid-rich. These results are in line with previous observations looking at mean CT attenuation of fibrous and lipid-rich plaques.[83, 84, 86, 97, 100] In our study, we observed close but not identical CT

attenuation values for coronary atherosclerotic plaques as compared to earlier studies. Mean CT density for lipid-rich plaques in our cohort was 67 HU versus 96 HU for fibrous plaques. Earlier studies reported mean densities ranging from 11-99 HU for lipid-rich plaques versus 77-121 HU for fibrous plaques.[83, 84, 86, 96, 97, 99-101] This difference could be explained by a higher contrast concentration within the coronary system as well as different image reconstruction parameters which both have been shown to significantly influence density measurements.[102, 103, 145] Even when image acquisition parameters are kept constant, there is substantial variability concerning the mean CT attenuation in different plaque types. This has been shown in previous studies and was reproduced in our patient group.100 For example, density values for lipid rich plaques ranged from 20 to 200 HU. Hence the area under the ROC curve (0.3) displayed a limited ability of this parameter to discriminate between lipid-rich and fibrous plaques. Recently Takahashi et al. analysed 77 coronary atherosclerotic lesions imaged with a 320-detector row system and used integrated backscatter IVUS as the gold standard.[146] Similar to previous findings, significant differences were observed for

densities of lipid-rich and fibrous plaques, however with an overlap in the density values (-18 to 69 HU for lipid-rich pool vs. 44 to 195 HU for fibrous pool). Using a ROC-curve analysis, they found that a cut-off of 56 HU could discriminate between lipid pool and fibrosis with a sensitivity of 93% and a specificity of 90%. The authors explain the better results in their study due to the less interobserver variability in plaque characterization using integrated backscatter IVUS compared to conventional grey-scale IVUS.[146] However, in their study, only the lipid volume quantified in CT correlated with IVUS measurements whereas the fibrous pool showed no significant correlation. [146] Furthermore, in an ex-vivo setup of 3 donor hearts, Maurovich-Horvat et al. assessed coronary CT angiography and invasive imaging modalities (IVUS and optical frequency domain imaging) as regards characterization of plaque composition using histopathological examination as the gold standard.[147] In their study, coronary CT angiography and IVUS were reasonably associated with histopathological findings, whereas optical frequency domain imaging was strongly associated to histopathological findings. These results support the

potential use of optical imaging as a reference standard for plaque characterization, rather than IVUS.

Beyond the mere analysis of 'mean densities' as performed in previous studies, we used quantitative histogram analysis to calculate the percentage of pixels with attenuation values ≤30 HU within each plaque. This parameter was found to be significantly different in predominantly lipid-rich plaques vs. predominantly fibrous plaques, and a cut-off value of 5.5% allowed differentiation between both plaque types with high sensitivity and specificity (95% and 80% respectively, area under ROC curve 0.9). Histogram analysis may therefore be helpful for coronary atherosclerotic plaque characterisation using CT angiography and seems to be more accurate than the analysis of mean plaque densities.

There are a number of limitations to be acknowledged. Only data sets of excellent or good image quality were included in this analysis, apart from the relative small sample size. Another important limitation is that IVUS has limitations in differentiating plaque compositions and is not considered a true gold standard.[148]

We did not analyze partly calcified plaques. However, such calcifications have substantial impact on the mean density within plaques. It can be expected that this new method of identifying lipid-rich plaque – while it may need some adjustment – may in fact be more accurate than the analysis of mean plaque attenuation. Moreover, these results can only be applied with caution to other scanner technologies or scan protocols, where differences in spatial and temporal resolution as well as differences in slice thickness and convolution kernel used for reconstruction would influence density measurements. As a consequence, the cut-off adopted in our study (pixels with attenuation ≤30 HU) to differentiate between plaque subtypes, can only be applied with caution to other scanner technologies and scan protocols. However, to our knowledge, this is the first study to report on the potential role of a quantitative histogram analysis in coronary atherosclerotic plaque characterisation using coronary CT angiography. Plaque characterisation using histogram analysis of the distribution of pixels with attenuation ≤30 HU may contribute

towards more reliable classification of non-calcified plaque by coronary CT angiography.

# Dual Source-CT Coronary Atherosclerotic Plaque Characterization using Histogram Analysis: a comparative study to IVUS

Thesis submitted for partial fulfillment of M.D. degree in

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## Introduction:

Coronary heart disease is a major cause of morbidity and mortality worldwide. “Acute coronary syndrome” is the term used to collectively describe acute manifestations of coronary heart disease; this includes a spectrum ranging from unstable angina to acute myocardial infarction. Acute coronary syndromes result from the sudden rupture or erosion of atherosclerotic plaques, and therefore the increasing interest in coronary plaque imaging, quantification and characterization.

Multi- detector row computed tomography for the assessment of coronary atherosclerosis has been intensely researched in the past few years. Its feasibility to detect coronary stenosis (1-6), lipid-rich plaques (7) and measuring the vessel area by manual tracing has been reported (8).

Determining the CT-densities within an atherosclerotic plaque principally allows the differentiation between lipid-rich (potentially vulnerable) and fibrotic plaques (i.e eventually more stable) coronary atherosclerotic lesions (9-13). However the mean densities of the different types of atherosclerotic plaques lie close

to each other; in addition the measured densities are extensively affected by the surrounding tissues, which is due to interpolation during image acquisition (14-15).

A study conducted by the CT-group in Erlangen, Germany, concerning ex-vivo analysis of atherosclerotic plaques using multislice computed tomography, showed that complex analysis of the distribution of CT densities within atherosclerotic plaques to identify potentially vulnerable plaques is promising.

## Aim of the work:

To evaluate the accuracy of dual source CT coronary angiography in detecting “lipid-rich” plaques as validated by Intravascular Ultrasound (IVUS) as the gold standard.

## Patients and Methods:

Patients involved in the study will be subjected to both contrast agent enhanced dual source CT coronary angiography as well as IVUS studies. 50 patients will be included in the study.

**Dual source CT examination:**

Patients will be scanned with a dual source CT scanner (DSCT, DEFINTION, Siemens Medical Solutions, Forchheim, Germany). Gantry rotation time of 330 ms. X-ray data will be simultaneously acquired in 2 x 64 slices with 0.6 mm collimation, with a tube voltage of 120 kV and a tube current of 400 mAs per tube.

**Intravascular Ultrasound technique:**

IVUS examination will be done in the context of invasive Coronary angiography. For each patient a single coronary artery will be studied (40 MHz IVUS Catheter, Boston Scientific (Natick, MA, USA) with a diameter of 3.2 F). After intracoronary injection of nitrates, an auto-pullback of 0.5 mm/s through the examined coronary with an image acquisition rate of 30 Hz will follow. Examinations will be digitally recorded. Recordings will then be further processed and analyzed and finally as avi-data saved.

**Dual source CT analysis**:

For every identified plaque, a series of multiplanar reconstructions perpendicular to the vessel axis and in intervals of 1.0 mm will be rendered. Using special software on the post-processing workstation, it would be possible to obtain for every cross-section within the segmented area, the total area of pixels, whose density lies between two free chosen values. In this manner, a histogram for the CT–densities for every cross section within the atherosclerotic plaque (in categories of 10 HU) could be obtained. By summing up the different values obtained from all cross sections of the plaque, a volumetric distribution of the CT densities within this plaque could be obtained.

**IVUS analysis:**

IVUS data will be interpreted by two experienced readers. Every identified plaque will be visually assessed and then in consensus will be determined whether the plaque -apart from the calcified segments- is predominantly “hyperechoic” (signal strength more than the surrounding adventitia) or “hypoechoic” (signal strength