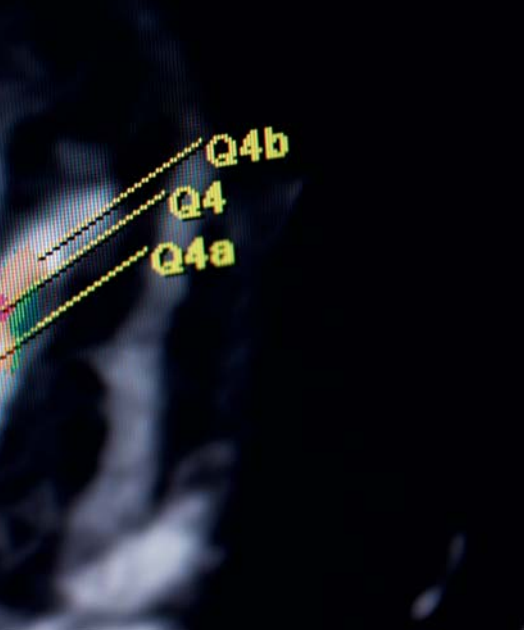
Virtual Histology with Dual Source CT

In Tübingen, Germany, the partnership between radiologists and cardiologists at the University Clinic at Schnarrenberg – aided by Siemens imaging technology – is making great strides in the identification of vulnerable plaques.

By Hildegard Kaulen, PhD



Histology based on Dual Source CT is a new development.

Every fourth heart attack comes completely unexpected and cannot be explained by classic risk factors such as hypertension, hyperlipidemia, smoking, diabetes mellitus or genetic factors. Usually, the cause is the rupture of a vulnerable plaque. The exact risk of some atherosclerotic plaques has, until now, been very unpredictable. A study with the Dual Source SOMATOM Definition CT, at the clinic of the University of Tübingen in Germany indicates that this situation could soon change.

It's not uncommon that a fruitful collaboration stands at the beginning of an interesting new development. At Schnarrenberg, a hill that offers an unobstructed view over the surrounding countryside, radiologists working with Prof. Claus D. Claussen, MD, and cardiologists working with Prof. Meinrad P. Gawaz, MD, came together to perform an illuminating study. The goal was to use computed tomography to more accurately determine the extent and composition of atherosclerotic plaques. For this purpose, two procedures were compared: virtual histology using intravascular ultrasound (IVUS), and virtual histology using Dual Source CT.

IVUS histology has been the gold standard for characterizing atherosclerotic plaques for the past three years. Histology based on Dual Source CT is, in contrast, a new development. The assessment of plaque volume and composition rests upon Hounsfield Unit (HU)-based color mapping. With the comparison, the two responsible physicians, radiologist Harald Brodoefel, MD, and cardiologist Christof Burgstahler, MD, entered new territory and obtained some fascinating results. With plaque volume assessment, the methods delivered almost identical results. With the determination of plaque composition, there were discrepancies that have apparent causes. Visual assessment, which is typically in use, almost always resulted in an overestimation of the plaque burden and an underestimation of vascular lumen.

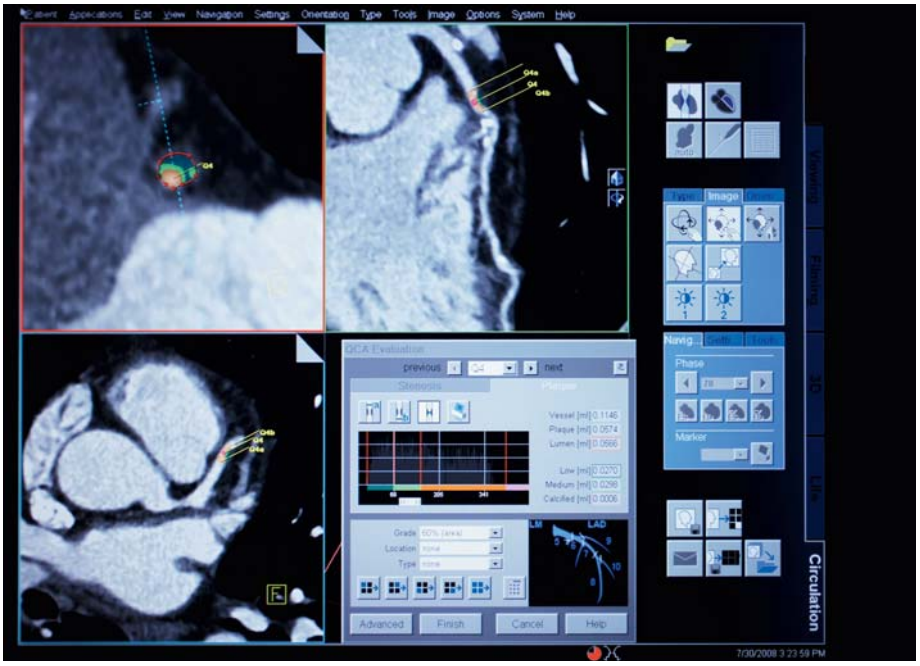
"We can well determine plaque volumes using DSCT based virtual histology."

Prof. Claus D. Claussen, MD, University of Tübingen, Department of Radiology, Tübingen, Germany

Despite many advances in treatment, cardiovascular disease remains the number-one cause of death in western, industrialized nations. However, myocardial infarctions are often not the result of high levels of coronary stenosis, but rather stem from the rupture of a vulnerable plaque. Burgstahler says: "Stable lesions with high degrees of luminal constriction typically lead to exercise induced angina pectoris. Should the coronary vessel gradually be blocked, collateral vessels often arise, so that not every vascular blockage necessarily leads to an acute heart attack. In contrast, when a vulnerable plaque ruptures, it usually results in an acute vascular blockage, and thus in a heart attack. The patient may have been completely free of symptoms until this point. The identification of vulnerable plaques can therefore be an important parameter for risk stratification."

In order to estimate the threat of plaque rupture, one needs to know the plaque composition. The most dangerous are those with thin fibrous caps and large fatty cores, not the highly calcified plaques. Vascular calcification is simply a measure of the general vascular plaque burden. For a qualitative analysis, it is therefore necessary to be able to differentiate between fibrous tissue, lipids, calcification and necrotic tissues. This is where virtual histology comes into play. The team from Tübingen investigated whether Dual Source CT and the Plaque Analysis Program of the latest *syngo* Circulation Package represented a reasonable alternative.

With IVUS histology, the discrimination between different tissue types is not based on the conventional grey-scale image, but rather on the spectrum analysis of radio frequency data. Every histological class is assigned a color; thus there is one each for fibrous, necrotic, fatty-fibrous, and calcified material. The classification was previously validated by comparison with autopsy material. The fact that Dual Source CT can be considered for virtual histology has to do with its high level of spatial and temporal resolution. In both disciplines, the SOMATOM Definition sets industry stan-



SOMATOM Definition sets industry standards to visualize coronaries and plaque in the vessel wall.

dards with 83 ms temporal resolution to freeze any cardiac motion and 0.33 mm spatial resolution to visualize the coronaries and plaque in the vessel wall." Since it records images within a tenth of a second, produces hardly any motion artifacts from partial-volume effects and has highly homogenous Hounsfield Units, it possesses the technical prerequisites for virtual histology.

"Until now, intravascular ultrasound has been the gold standard for assessing vascular lumen, vascular wall and plaque burden," says Brodoefel. "Coronary angiography only gives information about the degree of stenosis. As an invasive procedure, IVUS has clear disadvantages. Every invasive procedure brings with it the risk of complications, and in addition, it is labor and cost intensive. Moreover, it is not possible to bring the ultrasound probe into every coronary vessel; some are too small and others have too high a level of stenosis. With Dual Source CT, the entire vascular tree with lumen and walls is represented. One can consequently observe the entire plaque situation. Finally, CT offers the opportunity to perform a more wide-ranging analysis than does intravascular ultrasound."

For Dual Source CT-based virtual histology, Burgstahler and Brodoefel first determined thresholds for the Hounsfield Unit based on IVUS data. For this, the doctors matched the determined color maps of some plaques with the spectrum analysis of the corresponding radio frequency data, and obtained the following thresholds: 10 to 69 HUs stand for the fatty compartment of an atherosclerotic plaque, 70 to 158 HUs for the fibrous compartment, 159 to 436 HUs for the vascular lumen, and 437+ for calcification. Additional plaques were subsequently analyzed using both procedures and the results compared. Burgstahler notes: "We found a good correlation with volumes. The sizes of plaques can thus be equally well determined with both Dual Source CT and intravascular ultrasound. With plaque composition, however, there was only limited correspondence. A possible reason is the lower spatial resolution in relation to IVUS. Calcification also presents a problem, since it respectively leads to excessive overexposure with CT and loss of ultrasound waves due to interference when using IVUS. Dual Energy mode possibly brings some advantages for determining the plaque composition. We have not yet evaluated this mode on the coronary vessels." The SOMATOM Definition can be used in Dual Source and Dual Energy mode. With Dual Source mode, both tubes run with the same energy level. Dual Energy mode allows better differentiation of tissues by subtracting two different energy levels, but results in reduced temporal resolution.

Noteworthy with this study was the high level of reproducibility of results. "The high inter-observer variability is a big problem with visually evaluating and manually segmenting atherosclerotic plaques," explains Brodoefel. "In contrast, a HU-based plaque analysis eliminates many investigator-dependent steps. In our work, high inter-observer variability could not only be achieved for plaque volume but also for plaque composition. It remains questionable, however, how robust the results for possible serial CT investigations of the same plaques will be. Here the always-different contrast of the vascular lumens presents us with great challenges."

Prof. Claussen also attributes great significance to the study. "We can well determine plaque volumes using Dual Source CT based virtual histology," he says. "The reproducibility is also high. For plaque composition analysis, we need improvements. In order to use virtual histology for screening or follow up controls, long-term studies are necessary anyway. They must demonstrate that there actually is a correlation between plaque compositions, determined using CT, and the risk of heart attack. We also need studies that show whether a specific intervention – such as statin therapy – changes plaque composition and thus positively influences risk. Furthermore, the levels of radiation exposure are still too high for screening or regular follow-up controls."

The study appears in: Brodoefel H, Reimann A, Heuschmid M, Tsiflikas I, Kopp AF, Schroeder S, Claussen CD, Clouse ME, Burgstahler C. Characterization of coronary atherosclerosis by dual-source computed tomography and HU-based color mapping: a pilot study. Eur Radiol. 2008 Nov; 18(11):2466-74. Epub 2008 May 20.

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