LETTERS TO THE EDITOR

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What is behind the calcium?
The relationship between calcium and necrotic core on virtual histology analyses

We read with great interest the investigative paper by Missel et al. We would like to thank the authors for furthering our knowledge in this field with their continued production of high-quality research. Our one reservation is with the creation of a necrotic core (NC) to dense calcium (DC) ratio from VH–IVUS data. We are proponents of this excellent tool, but we also have a healthy scepticism regarding its capability to accurately detect what is seen behind calcium in coronary lesions. We do agree that the spectral analysis of the backscatter radiofrequency ultrasound signal has 87–92% in vivo accuracy for the characterization of the four basic plaque components. We also do not doubt the ability of IVUS and VH to determine calcified areas. Our main concern involves the commonly seen appearance of NC behind areas of calcification. Only 21 region-of-interests containing NC were actually analysed in the initial accuracy evaluation of the SS/Eagle Eye VH classification tree. Is it possible that some areas appearing as NC are simply a manifestation of the attenuated echo signal behind calcium, which is subsequently classified to this tissue type by the VH algorithm? It is common to see NC coded in areas of echo loss behind stent struts (classified as calcium) if VH is switched on during motorized pullback through a stent. What did the authors do with their more calcified lesions? Were any excluded from the final analysis? If not, what are their thoughts about the contribution of sub-calcific echo dropout to NC percentages and ultimately their important NC/DC ratio?

We would be grateful for advice and expert opinion on these observations and whether or not this is a true limitation of the ‘current’ VH algorithm. We feel this is a very significant area in IVUS–VH research that could impact upon the important findings of this study and work continuing in our own department as well as other centres around the world.

References

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What is behind the calcium?
The relationship between calcium and necrotic core on virtual histology analyses: reply

In our recent study, the ratio of necrotic core to calcification (NC/DC ratio) detected by virtual histology intravascular ultrasound (VH-IVUS) in diseased coronary segments was related to known risk factors for sudden coronary death (SCD) in men, in line with previous observations that vulnerable plaques have more NC and less DC than stable plaques. We also demonstrated in a previous publication, also from the VH-IVUS registry, that the NC/DC ratio separated high-risk non-ST elevation ACS patients from low-risk patients.

This new IVUS-derived imaging method allows spectral analysis of backscattered radiofrequency (RF) ultrasound signal for the characterization of four basic plaque components: fibrous, fibro-fatty, DC, and a lipid-rich NC. However, concerns have been raised in regard to the efficacy of this method when calcified lesions are being analysed, specifically when plaque composition is assessed behind a large dense, calcium arc.

Highly calcified lesions are an anatomical limitation to IVUS assessment. However, it is important to differentiate cross-sectional area analysis from volumetric analysis. For greyscale IVUS, an arc of >90° makes IVUS measurements of plaque inaccurate owing to extensive shadowing caused by signal attenuation. This is true for a single cross-sectional frame at the minimum lumen area (MLA) site, but it may be not the case for a cross-section 2 or 3 mm away. We performed VH-IVUS volumetric analysis of the whole diseased segment, not merely selected single frames such as the MLA or maximum NC sites—volumes for each plaque component following the Simpson’s rule. Calcium arcs, as well as non-calcified segments, could be present along the vessel’s longitudinal axis. Therefore, we obtained the NC/DC ratio of the whole-vessel volumes, not just the area behind calcium. Signal attenuation behind calcium was ‘diluted’ longitudinally, not affecting the results significantly.

In addition, even when analysing single areas of interest, a highly calcified plaque would result in a much lower NC/DC ratio compared with a plaque with little, speckled calcification and a large NC, exactly the pattern of unstable lesions determined by histopathology of SCD subjects, reinforcing the usefulness of the NC/DC ratio not only as a vulnerability index, but also as a potential correcting factor for artefacts. The significant associations between the NC/DC ratio and the risk factors for SCD found in our study found are not only consistent with this concept, but also suggest that the balance between these components might be relevant in plaque vulnerability.

Finally, we share your scepticism regarding VH-IVUS analysis behind calcium. In fact, we studied this issue by analysing signals behind calcium in relationship to the background