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Letters

RESEARCH LETTER

Accuracy of OCT Core Labs in Identifying Vulnerable Plaque

It has been demonstrated that the identification of vulnerable plaque during cardiac catheterization can predict future coronary events. Intravascular optical coherence tomography (IVOCT) is the ideal imaging platform because it has a greater resolution, allowing for the identification of vulnerable plaque features, such as thin-cap fibroatheroma (TCFA), macrophages/foam cells, neovascularization, necrotic cores, and plaque erosion, that are not identifiable by other imaging techniques.[1] Although the OCT appearances of these features have been defined in consensus papers based on histology,[2,3] there are a limited number of studies that have determined the accuracy of OCT readers in identifying vulnerable plaque. We organized a blinded study with histologic truth to determine the accuracy of the interpretation of plaque components by leading international OCT core labs.

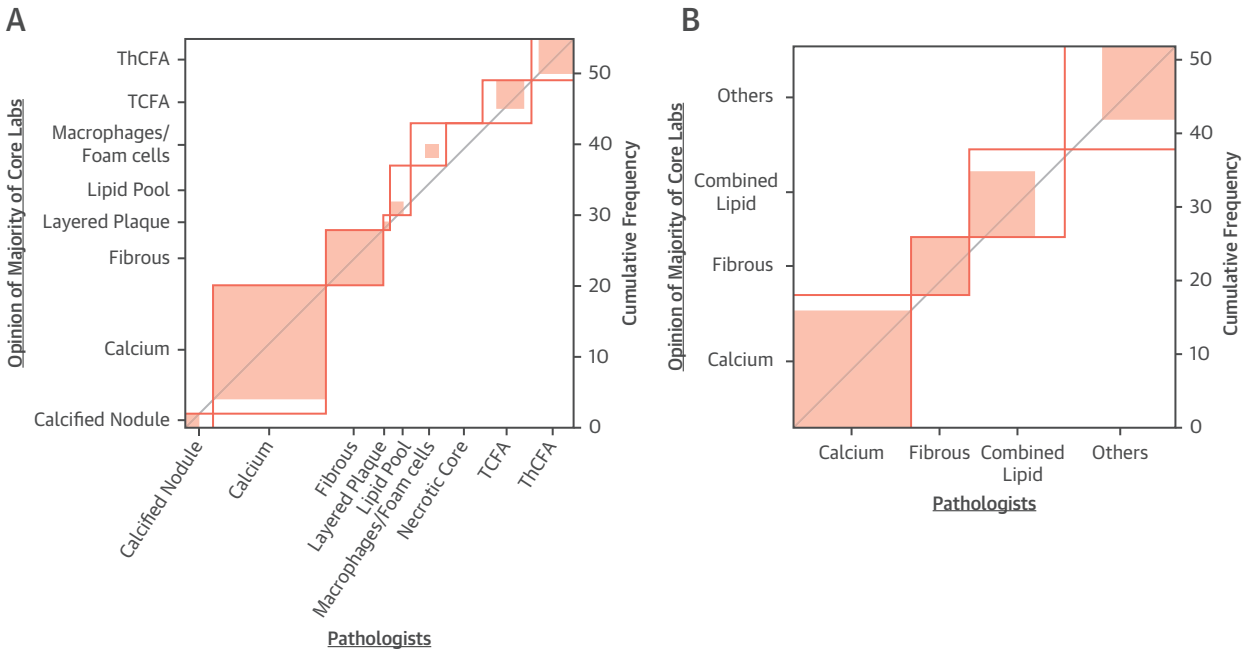
Forty-three human hearts were obtained from patient donors within 24 hours of death. Coronary arteries were harvested, imaged during saline perfusion with an Ilumien IVOCT system (Abbott), and processed for serial histologic sectioning (hematoxylin and eosin, Movat's pentachrome; CD68 antibody). IVOCT frames were coregistered to histology and manually segmented into plaque components by 2 expert readers (T.H. and M.D.F.) and 2 senior pathologists (D.V. and L.M.B.). Each of the 7 core labs (in Japan, the Netherlands, Switzerland, and the United States) was provided 51 OCT video clips of 7 consecutive frames with 9 possible components of both stable and unstable plaques: fibrous tissue, lipid pool, necrotic core, macrophages/foam cells, calcification, calcified nodule, TCFA, thick-cap fibroatheroma (ThCFA), and layered plaque. All readers blindly identified plaque features and filled out an answer sheet. No histology or thresholding guidance for the measurements was provided. Accuracy was assessed by the OCT core lab agreement on each plaque component with 3 pathologists (D.V., L.M.B., and S.L.) from 2 independent sites. The kappa coefficient (κ) was used to measure intrareader agreement, where $\kappa < 0.20$ means weak agreement, and $\kappa > 0.75$ represents excellent agreement. Statistical analyses were performed by a biostatistician (J.M.) using SAS software (SAS Institute).

The agreement between the 2 pathology sites was almost perfect ($\kappa = 0.81 \pm 0.07$; 95% CI: 0.70-0.93). Overall agreement on different plaque components varied between individual core labs (κ from 0.22 to 1.0, with a median of 0.67 ± 0.07). The highest level of agreement with pathologists was achieved in identifying plaques with stable components, including fibrous (0.93), calcium (0.83), and ThCFA (0.63) (**Figure 1A**). However, the lowest level of agreement was in identifying vulnerable plaque features. The median κ values across the 7 core labs for these categories were TCFA: 0.22; necrotic core: 0.22; macrophages/foam cells: 0.39; lipid pools: 0.35; and calcified nodule: 0.50. Because the differentiation of lipid pools from necrotic cores by OCT is controversial, we included in our study only 4 images (7.8%) identified by pathologists as necrotic cores. As a result, only 3 of the 7 OCT core labs have identified these features.

Also, we demonstrated that all core labs individually were able to read moderately well 3 traditional categories—calcium (0.83); fibrous (0.93); and combined lipids (0.58), comprising all lipid subcategories (lipid pools, necrotic cores, and TCFAs). The agreement between the majority of OCT core labs and pathologists for these categories was substantial ($\kappa = 0.76 \pm 0.07$; 95% CI: 0.62-0.9) (**Figure 1B**).

Despite the superior resolution of IVOCT, which can provide images close to the resolution of histology, image evaluation of vulnerable plaques can be challenging. It requires dedicated training in cardiovascular imaging and is always subject to considerable inter-reader variability. Our study shows that leading OCT readers from core labs can accurately read stable plaque components, including fibrous, calcium, and ThCFA. However, their accuracy diminishes when they try to identify specific features of vulnerable plaque, including TCFA, lipid pools, necrotic cores, calcified nodules, and macrophages/foam cells. It known that lipids are the most difficult plaque feature to identify with OCT because they are often mixed with other plaque components such as calcification and fibrous tissue, but they also have many presentations, including lipid pools, TCFAs, and necrotic cores. Our study supports this conclusion. For example, when all lipid subcategories were

FIGURE 1 **OCT Core Lab Performance in Reading Histologic Plaque Components**



(A) Agreement between 7 OCT core lab majority opinions and pathologists on all 9 histologic plaque components ($\kappa = 0.67 \pm 0.07$; 95% CI: 0.54-0.81). (B) Agreement between 7 core lab majority opinions and pathologists on 3 traditional plaque components—calcium, fibrous, and combined lipids (lipid pool, TCFA, and necrotic core) ($\kappa = 0.76 \pm 0.07$; 95% CI: 0.62-0.9). The size of the box indicates the number of images assigned to each plaque type. The dark blue area indicates exact agreement. The larger the blue area, the greater the agreement. OCT = optical coherence tomography; TCFA = thin-cap fibroatheroma; ThCFA = thick-cap fibroatheroma.

combined into one called combined lipid (similar to how OCT core labs report their findings), reading accuracy improved from fair to substantial. Several research programs are developing methodologies to aid in the identification of plaque components. One promising approach is the use of AI-based methods to identify plaque high-risk features automatically, within minutes, consistent with the speed of the catheterization laboratory environment.[4,5]

Despite some limitations (some high-risk features of vulnerable plaque, such as microcalcification, neovascularization, plaque hemorrhage, and positive remodeling, were not included; rulers were not provided; and only 7 consecutive frames instead of entire pull backs were used), our study implies that if expert readers have difficulty identifying vulnerable plaques, then interventional cardiologists may have similar issues. As a result, many OCT users in the catheterization laboratory are reluctant to characterize plaque composition.

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