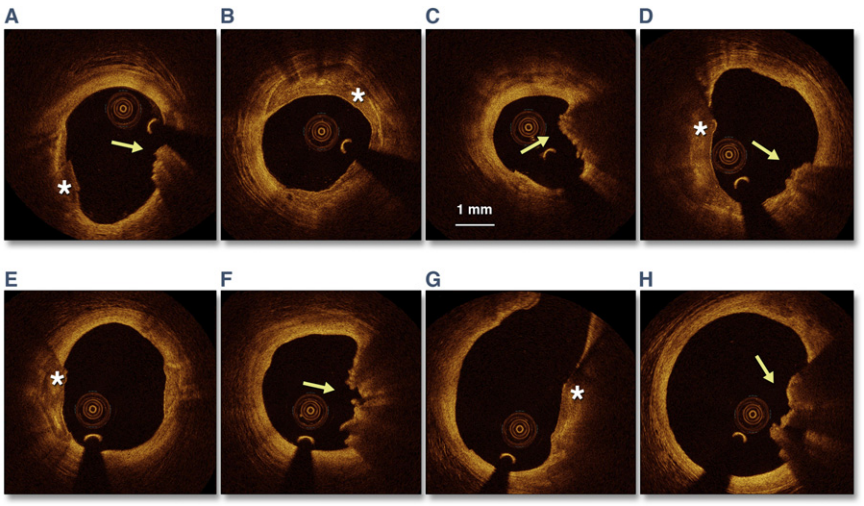

Figure 2. Optical Coherence Tomography

Optical coherence tomography cross-sectional images from the sites shown in Figure 1 (Online Video 2). **(A, C, D, F, and H)** Presence of red thrombus **(yellow arrows)** in areas of fibrocalcific plaque **(asterisks)** in the absence of plaque rupture. **(B, E, G)** Sharp protrusions of calcium into the lumen **(asterisks)** with very thin, or absent overlying intimal layer.

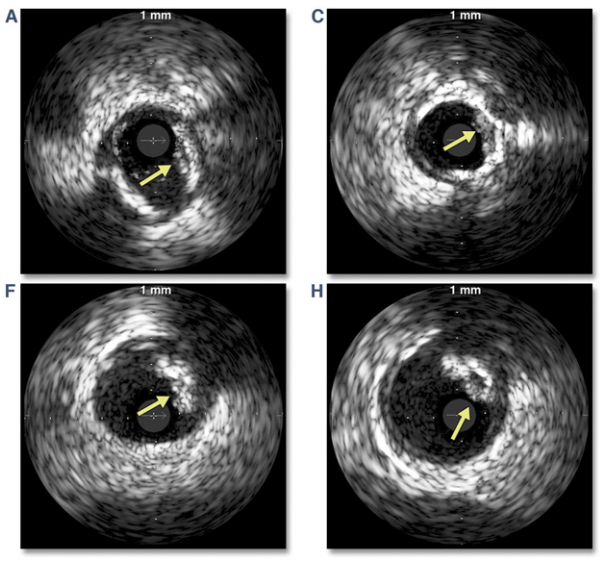

Figure 3. Intravascular Ultrasound

Intravascular ultrasound cross-sectional images corresponding to sites **A, C, F,** and **H** of Figure 1. **Arrows** indicate the presence of thrombus adjacent to calcific protrusions.

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APPENDIX

For supplementary videos and their legends, please see the online version of this article.

Reproducibility of In Vivo Measurements for Fibrous Cap Thickness and Lipid Arc by OCT

Thin fibrous cap and lipid pool are thought to be major determinants of plaque instability. However, current imaging modalities such as angiography, intravascular ultrasound, and angioscopy do not have sufficient resolution to accurately measure them. It is widely accepted that optical coherence tomography (OCT) is the in vivo "gold standard" imaging modality for the measurement of fibrous cap thickness. However, its reproducibility has never been systematically studied. Therefore, we attempted a systematic investigation of interobserver agreement and intraobserver reproducibility of fibrous cap thickness and lipid arc measurements.

Fifty frames and 25 pullback runs of OCT were randomly selected for frame analysis and plaque analysis, respectively, from the Massachusetts General Hospital OCT Registry database. Each selected frame included 1 lipid plaque and each run included 1 or more lipid plaques with a total length of 30 to 50 mm. OCT images were analyzed by 4 independent observers who were blinded to the selections of frames and runs of OCT using the proprietary software for offline analysis (LightLab Imaging Inc., Westford, Massachusetts).

For frame analysis, all 4 observers measured the fibrous cap thickness and lipid arc on a selected frame. For plaque analysis, all observers selected 1 lipid plaque that they thought had the thinnest fibrous cap in the entire length of each OCT pullback and then measured the fibrous cap thickness at the thinnest part in the chosen plaque. Observers also measured the lipid arc at every 1-mm interval over the entire length of the selected plaque and recorded both the maximum and average lipid arc. All measurements were

Figure 1. The Representative OCT Images for Measurements of Fibrous Cap Thickness and Lipid Arc

Representative cases of optical coherence tomography (OCT) measurements for fibrous cap thickness **(A)** and for lipid arc **(B)** from 4 independent observers. For plaque analysis, all 4 observers selected the same plaque from the OCT run; however, there were differences in the frame that they selected to measure the thinnest fibrous cap and value of fibrous cap thickness measurements (43.3 μm for #327, 53.3 μm for #289, 53.3 μm for #305, and 60 μm for #261, clockwise).

performed at 3 different times and average values were calculated. In addition, the analyses were repeated at intervals of at least 2 weeks by the first observer.

Interobserver agreement of the OCT measurements was assessed by intraclass correlation coefficient (ICC) based on the random effects analysis of variance model. The same method was applied to assess the intraobserver reproducibility of a single observer. The PROC NLMIXED procedure of SAS version 9.2 (SAS Institute, Cary, North Carolina) was used to calculate inter- and intra-ICC with 95% confidence intervals (CI).

All 50 frames had 1 lipid plaque, and 25 pullback runs had an average of 2.7 lipid plaques within each pullback. The representative OCT images for measurements of fibrous cap thickness and lipid arc in lipid plaque from observers is shown in Figure 1. For frame interobserver analysis, the ICC was 0.85 (95% CI: 0.79 to 0.91) for fibrous cap thickness and 0.95 (95% CI: 0.92 to 0.97) for lipid arc (Table 1). For plaque interobserver analysis, all 4 observers selected the same plaque in each of 25 runs. The ICC was 0.49 (95% CI: 0.26 to 0.69) for fibrous cap thickness and 0.77 (95% CI: 0.53 to 0.97) and 0.71 (95% CI: 0.55 to 0.86) for maximum and average lipid arc, respectively (Table 1).

Intraobserver reproducibility was high for fibrous cap thickness and lipid arc in both frame (ICC = 0.99) and plaque analyses (ICC = 0.99).

Several studies have evaluated the correlation for fibrous cap thickness between OCT and histological examination in animals and human cadavers (1,2), as well as a difference of fibrous cap thickness in different clinical presentations using OCT (3). However, the reproducibility of OCT for in vivo measurements of fibrous cap thickness and lipid arc has never been tested. This is the first in vivo study of OCT reproducibility for measurements of lipid plaque components. Whereas frame analysis showed very similar measurements of fibrous cap thickness from 4 independent observers (ICC = 0.85), the degree of agreement for plaque analysis was not high (ICC = 0.49). For plaque analysis, it was not difficult for 4 observers to select the same plaque that they believed contained

Table 1. Distribution and Interobserver and Intraobserver ICC for Fibrous Cap Thickness and Lipid Arc

	Frame Analysis (n = 50)		Plaque Analysis (n = 25)		
	Fibrous Cap Thickness, μm	Lipid Arc, °	Fibrous Cap Thickness, μm	Average Lipid Arc, °	Maximum Lipid Arc, °
Mean*	70.3 ± 24.3	184.2 ± 67.2	60.5 ± 14.2	169.2 ± 42.3	239.7 ± 79.7
Maximum/minimum*	170/29	360.0/65.2	120/35	259.1/65.6	360.0/90.4
Interobserver ICC	0.85	0.95	0.49	0.71	0.77
Intraobserver ICC	0.99	0.99	0.99	0.99	0.99

Values are mean ± SD. *Summary statistics included 200 analyzed frames and 100 analyzed plaques. The analysis took into account the quadruplets measured by the 4 independent observers.
ICC = intraclass correlation coefficient.

the thinnest fibrous cap in each pullback. However, there was inconsistency in selecting the frame that had the thinnest fibrous cap (Fig. 1A). This may be a possible explanation for the attenuated agreement value in plaque analysis as compared to frame analysis. On the other hand, lipid plaque has a diffuse border, and it is challenging to detect the inner border of lipid pool within the plaque for cap measurement.

The agreement levels in lipid arc measurement were higher and more consistent for both frame and plaque analyses than those in the fibrous cap thickness. Such a discrepancy may be due to the difference in measurement unit scale between the two (degree of angle vs. length [μm]).

In conclusion, caution should be exercised when OCT images are interpreted, especially for the measurement of fibrous cap thickness in lipid plaques.

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