Supplemental Material

Manuscript title: Intravascular Polarimetry in Patients with Coronary Artery Disease

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Supplementary Methods

Intravascular PS-OFDI

All procedures were performed according to standard practice in the Erasmus MC catheterization laboratory.[1] Briefly, the imaging system operated at a center wavelength of 1300 nm with a wavelength scanning range of 110 nm, corresponding to a radial resolution of 9.4 μm, assuming a refractive index of 1.34. The intravascular catheter was pulled back at a rate of 20 mm/s with continuous injection of non-ionic contrast solution at a rate of 3-4 mL/s, and images were acquired at a rate of 100 frames/s, each consisting of 1024 radial scans.

Intravascular PS-OFDI offers insight into tissue composition by quantifying birefringence and depolarization through standard intravascular imaging catheters, as described in detail previously.[2] In short, the imaging system employed a polarization diverse receiver to determine the polarization state of the light scattered by the tissue, and an electro-optic polarization modulator to vary the polarization state of the light illuminating the vessel wall between consecutive radial scans. Polarimetric analysis was performed offline with spectral binning to reconstruct maps of tissue birefringence and depolarization.[3] **Birefringence** is the unitless ratio of change in retardation (phase delay between two principle polarization states) per propagation distance traveled by light. It corresponds to the difference of the refractive indices experienced by light polarized parallel and orthogonal to the fibrillary components, such as collagen fibers and layered smooth muscle cells.[4] In the present study, birefringence is displayed in the rage of $0\text{-}1.8\times10^{-3}$. **Depolarization** corresponds to a randomization of the detected polarization states, induced by propagation and scattering of light inside tissue.[2,5] As a measure of tissue depolarization, we computed the complement to 1 of the degree of polarization.

Depolarization ranges from 0 for completely polarized light without any randomness to 1 for completely depolarized, i.e. randomized light.

Comparison of polarization properties with plaque burden and stenosis severity

To investigate the association of polarization properties with stenosis severity, we examined the correlation of birefringence and depolarization with percent area stenosis. Plaque cross-sectional area (CSA) was defined as IEL CSA minus lumen CSA and computed only in normal artery and FP. Percent plaque CSA ($\%CSA_{plaque}$) was calculated as plaque CSA divided by the IEL CSA. The GEE approach was employed to determine the relationship between polarization properties, percent area stenosis for all plaque types and $\%CSA_{plaque}$ for normal artery and FP, respectively.

Supplementary References

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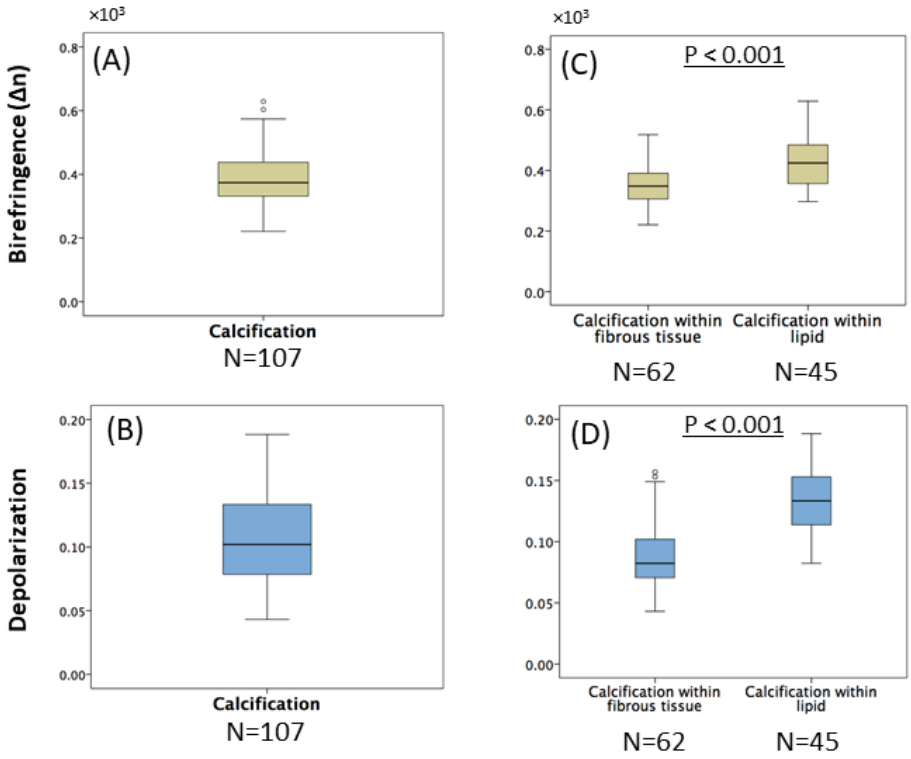
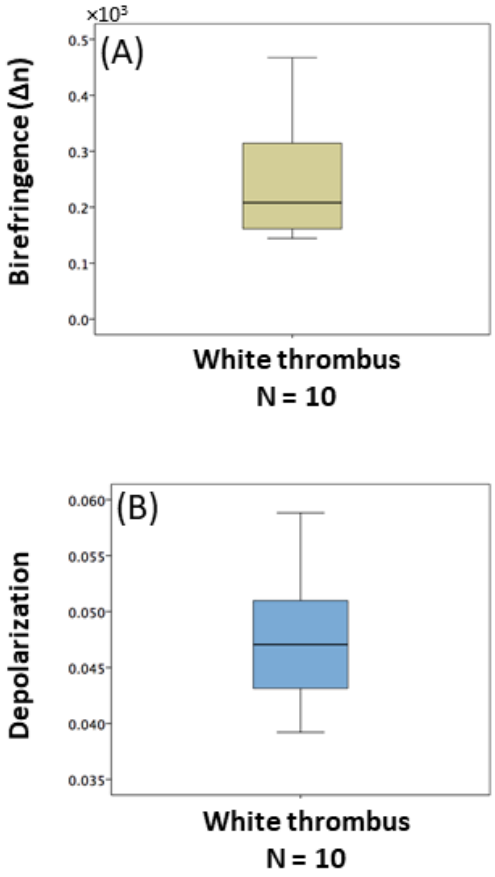


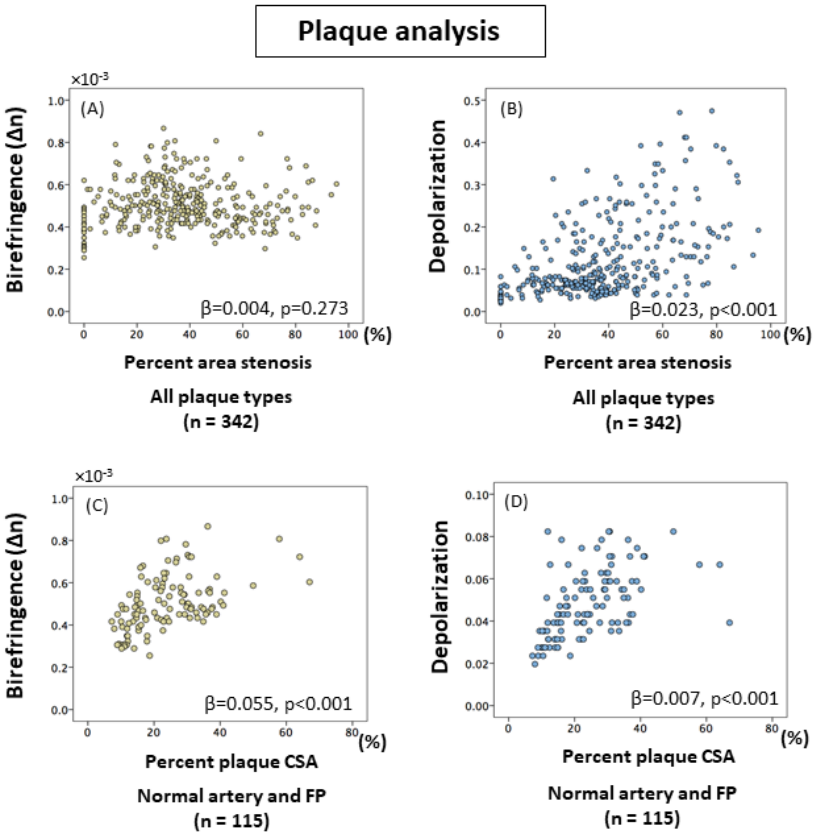
Supplementary Figure S1. Polarization properties of calcification

Median birefringence and depolarization were measured in calcifications, manually segmented in the intensity images of the 342 cross-sectional images of the plaque analysis. Calcifications were classified into 2 groups according to the presence or absence of lipid in the surrounding lesion (calcification within fibrous tissue or calcification within lipid). Calcifications exhibit low birefringence **(A)** and low depolarization **(B)**. **C** and **D** show comparisons of polarization properties of calcifications with and without lipid (fibrous tissue). **(C)** Calcifications in fibrous tissue exhibit lower birefringence compared to those in a lipid-rich lesion ($p < 0.001$). **(D)** Higher depolarization was observed in calcifications in lipid-rich tissue than in those located in fibrous tissue ($p < 0.001$). Association was tested by unadjusted generalized linear model using GEE. GEE = generalized estimating equation.



Supplementary Figure S2. Polarization properties of white thrombus

The plaque and cap analysis combined contained a total of 10 cross-sectional images with white thrombus. Based on intensity signal in conventional optical frequency domain imaging (OFDI), all the thrombus was classified as white thrombus. Manual segmentation, performed by tracing the boundary of the thrombus, revealed very low birefringence **(A)** and depolarization **(B)** in white thrombus.



Supplementary Figure S3. Associations between polarization properties and percent plaque Cross-sectional area

(A and B) Association between percent area stenosis and polarization properties for all cross-sections. **(C and D)** Association between percent plaque area and polarization properties in normal artery and FP. Association was tested by unadjusted generalized linear model using GEE. The percent area stenosis in all plaque types combined was significantly associated with depolarization ($\beta = 0.023$; $p < 0.001$), but not with birefringence ($\beta = 0.004$; $p = 0.273$) (Supplementary Figure 3A and 3B). Since $\%CSA_{plaque}$ can only be accurately calculated in normal artery and FP where the IEL is reliably identified in OFDI imaging, we also compared the polarization properties and $\%CSA_{plaque}$ in normal artery and FP. Birefringence ($\beta = 0.055$; $p < 0.001$) and depolarization ($\beta = 0.007$; $p < 0.001$) correlated positively with $\%CSA_{plaque}$ (Supplementary Figure S3-C and -D). CSA = cross-sectional area, FP = fibrous plaque, and GEE = generalized estimating equation.