



Imaging atherosclerotic plaque composition with intracoronary optical coherence tomography

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Optical coherence tomography (OCT) allows highly accurate diagnosis of atherosclerotic plaques, including measurement of the thickness of fibrous caps, permitting an assessment of the risk of rupture. While the OCT image presents morphological information in highly resolved detail, it relies on interpretation by trained readers for the identification of tissue type. We developed a method for quantitative classification of atherosclerotic plaque constituents. The optical attenuation coefficient μ_t distinguishes different tissue types: necrotic core and macrophage infiltration exhibit strong attenuation, $\mu_t \geq 10 \text{ mm}^{-1}$, while calcific and fibrous tissue have a lower $\mu_t \approx 2\text{-}5 \text{ mm}^{-1}$. (Neth Heart J 2009;17:448-50.)

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It is generally accepted that the majority of acute coronary events are precipitated by the rupture of a vulnerable atherosclerotic plaque in the coronary system, and subsequent

thrombogenesis.¹⁻³ The thin-cap fibroatheroma is currently hypothesised to be the most likely class of arterial wall pathology to constitute a vulnerable plaque.^{4,5} The key to plaque vulnerability is still elusive,⁷ even though recent technological advances in intravascular imaging technology have enabled the collection of a wealth of data on unstable atherosclerosis in all its stages of development,⁸ both in clinical and in *ex vivo* settings. It appears very likely that combined information on physiological, anatomical, chemical, and mechanical parameters⁹⁻¹¹ is needed for a reliable assessment of the proneness of a specific lesion to rupture. Some of these parameters may be accessible through intravascular imaging methods.¹²⁻¹⁶ In addition, plaque type and morphology prior to intervention significantly influence the long-term procedure outcome.¹⁷ The parameters that influence plaque vulnerability include the thickness of the fibrous cap overlying the necrotic core, inflammation, intraplaque haemorrhage, and composition.^{10,18} Data on plaque composition and stability, complementing the image, may inform the decision on if and how to treat a particular section of coronary artery.

Optical coherence tomography (OCT)¹⁹ is rapidly becoming the method of choice for assessing arterial wall pathology *in vivo*. It has an image resolution of about 10 to 15 μm , an order of magnitude better than intravascular ultrasound. Atherosclerotic plaques can be diagnosed with high accuracy,²⁰ including measurement of the thickness of fibrous caps,²¹ moving a step towards *in vivo* assessment of the risk of rupture. Insight into the physiology of a plaque is complementary to the structural information offered by the OCT greyscale image.

While the OCT image presents morphological information in highly resolved detail, it relies on interpretation of the images by trained readers for the identification of vessel wall components and tissue type. We have developed a framework to aid the recognition of these atherosclerotic plaque constituents, based on the optical attenuation coefficient of the tissue. This coefficient describes the signal loss with depth in the OCT image. We demonstrate the principle, and show results for different plaque types using histopathology for validation.

The detected OCT signal intensity can be analysed using a simple equation, which models the signal strength as a

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function of depth according to a Lambert-Beer exponential decay curve, multiplied by a coupling factor:²²

$$I_d(z) = I_0 T(z) \exp[-\mu_s z] \quad (1)$$

The coupling factor $T(z)$ is needed to take into account the focusing properties of the lens in the distal tip of the catheter. We are interested in the attenuation coefficient $\mu_s(z)$, appearing in the exponent of this relation. The scale factor I_0 depends on the incident intensity and the backscattering coefficient μ_b . The backscatter efficiency is a tissue property that can be measured independently in homogeneous media.²³

Equation (1) describes the OCT signal in a homogeneous medium. The vessel wall, and biological tissue in general, is a heterogeneous structure. An OCT A-line $I_d(z)$ usually samples more than one tissue type. Hence, the signal intensity has to be fitted in windows, of a length that is unknown *a priori*.²⁴ Here, variations in $\mu_s(z)$ may confound the analysis of $\mu_s(z)$. In addition, the presence of speckle means that the contrast-to-noise ratio (CNR) in the image is inherently low.²⁵ We present here the results of an *in-vitro* study of human coronary arteries.

We imaged human coronary arteries (14 specimens; 12 LAD, 2 RCA) harvested at autopsy, within 24 hours post-mortem. The vessels were mounted on cannulas in a water bath at 37°C, and pressurised to 100 mmHg using a water column system. Imaging was performed with a commercial

intravascular OCT instrument (M2CV) and catheters (ImageWire 200; both from Lightlab Imaging, Westford, MA, USA). A vessel cross-section is imaged by an infrared light beam, central wavelength 1310 nm, which is swept along the vessel wall by the rotating catheter. The OCT system had an axial resolution of 14 μm , and a tangential resolution of 25 μm in the focus. The imaging depth was 3.3 mm. Each image line consisted of 752 pixels, corresponding to 4.5 μm per pixel. Sites of interest were marked with a needle. At every site, a stationary movie was recorded, of about 40 frames.

After imaging, the artery sections were pressure fixed at 100 mmHg in formaldehyde for 24 hours at room temperature, and subsequently stored in formaldehyde at 4°C for further processing. Vessels were partially decalcified for 24 hours in formic acid.²⁶ The tissue was embedded in paraffin and serially sectioned for histological staining. Each imaged cross-section was stained with Haematoxylin-Eosin (H&E), Picrosirius red, Elastic van Gieson (EvG) and immunohistochemical stain CD68. Histology was evaluated by two pathologists. We colour code the different tissue types in histology as follows: green for fibrous/smooth muscle cells (SMC); red for necrotic core; grey for calcium.

A schematic representation of the data analysis procedure can be seen in figure 1: the intensity profile along one radial OCT image line is averaged²⁷ over about all available frames to reduce speckle, and fitted in discrete windows using Equation (1).

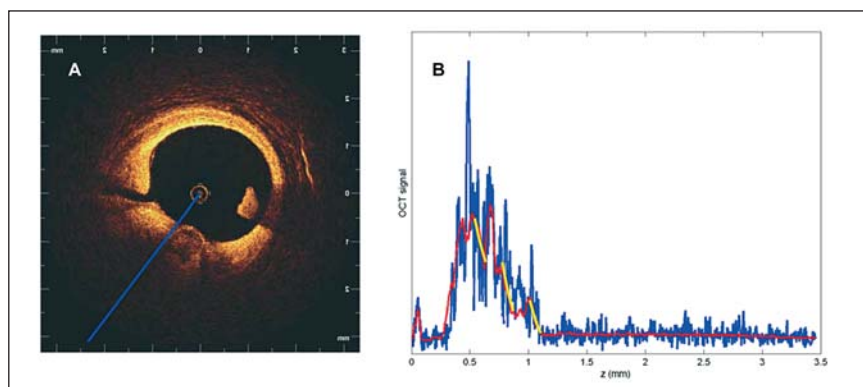


Figure 1. Illustration of the analysis procedure. **A)** OCT image of a heterogeneous plaque, showing a calcification (6 o'clock), platelet-rich thrombus (3 o'clock) and a small side branch (9 o'clock). The blue line indicates a single image line as acquired by the rotating catheter. **B)** Intensity profile along a single line. The OCT image (in blue) contains strong signal variations called speckle. Averaging ± 40 frames reduces the speckle (red), so the curve can be fitted in discrete windows (yellow lines in B). The tissue attenuation coefficient is derived from these fits.

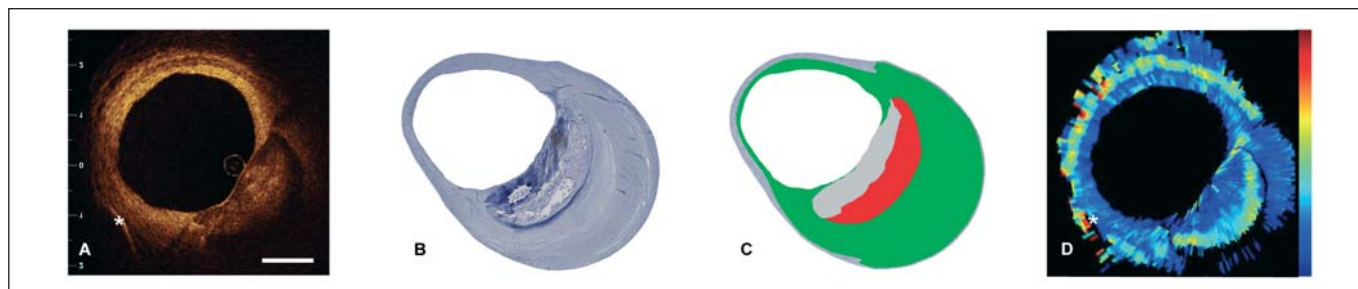


Figure 2. **A)** OCT image of a coronary atherosclerotic lesion *ex vivo*. * indicates the needle used for marking the imaged site; the length of the white scale bar is 1 mm. **B)** Corresponding histology, H&E stain. **C)** Cartoon histology, overlaid on the original histology slide, indicating an advanced necrotic core (red) behind a calcification (grey), and a slight fibrotic (green) circumferential intimal thickening. **D)** OCT derived attenuation coefficient μ_s , plotted on a continuous linear colour scale from 0 mm^{-1} to 15 mm^{-1} . The area corresponding to the necrotic core exhibits a higher attenuation coefficient (8-10 mm^{-1}) than the adjacent calcification or the surrounding fibrous tissue (2-3 mm^{-1}). Adapted from Van Soest *et al.*⁶

A total of 39 sites could be analysed. An example of a cross section with OCT data, histology, and attenuation image is displayed in figure 2. The example shown here illustrates that both fibrous and calcified tissues have a low attenuation coefficient, while necrotic material is more strongly attenuating. Healthy vessel wall, or mild intimal thickening (6-3 o'clock) is characterised by low attenuation bordered on the outside by a band of higher attenuation coinciding with the adventitial layer.

Figure 3 shows another cross section, where an eccentric plaque, consisting mostly of fibrous tissue and SMC, is infiltrated superficially with macrophages, a preatherosclerotic lesion type called intimal xanthoma. This example demonstrates the strong attenuation associated with macrophage accumulation. Macrophages have many and relatively large cell organelles, sustaining their high metabolic activity, and these tend to scatter light very efficiently. This leads to a high attenuation coefficient and also a high backscatter coefficient and thus a strong OCT signal, as is evident from the OCT image.

From a survey of the complete dataset, we conclude that a high attenuation coefficient in OCT, $\mu_t > 10 \text{ mm}^{-1}$, is associated with two markers of plaque vulnerability: presence of necrotic core, and macrophage infiltration. More stable forms of atherosclerotic tissue, and healthy vessel wall, have a low attenuation coefficient: $\mu_t \approx 2-5 \text{ mm}^{-1}$. These results demonstrate the possible advantage of imaging the attenuation coefficient for diagnosis of coronary plaques. We have succeeded in imaging the attenuation coefficient *in vivo*; an evaluation of the clinical value of this technique is currently ongoing. ■

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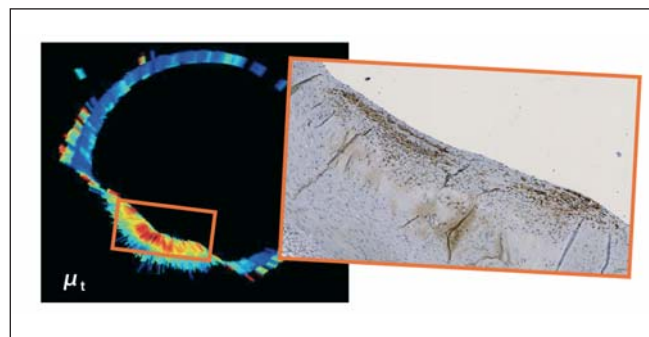


Figure 3. An intimal xanthoma case. High attenuation (colour scale 0-15 mm⁻¹ as before) in a fibrous lesion occurs due to macrophage infiltration, as evidenced by the CD68 stain in the inset. Adapted from Van Soest et al.⁶

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