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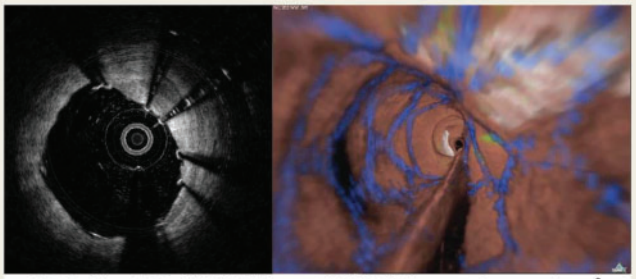
Intravascular optical coherence tomography

Shedding light on the coronary wall to reveal plaque features and improve percutaneous coronary interventions (PCI)

Intravascular optical coherence tomography (IVOCT) began at MIT in the early 1990's with the recognition that OCT could be used for clinical applications other than ophthalmology. Initial steps made there towards IVOCT feasibility included the acquisition of cadaver arterial images demonstrating the capacity of OCT to visualize depth-resolved architectural detail of plaque[5] and the development of the first mechanical scanning catheter.[6] Early histopathologic correlation studies from cadaver arteries demonstrated that IVOCT was capable of distinguishing the major fibrous, fibrocalcific, and lipid-rich plaque types and also potentially identifying inflammation as manifested by macrophage accumulations.[7,8]

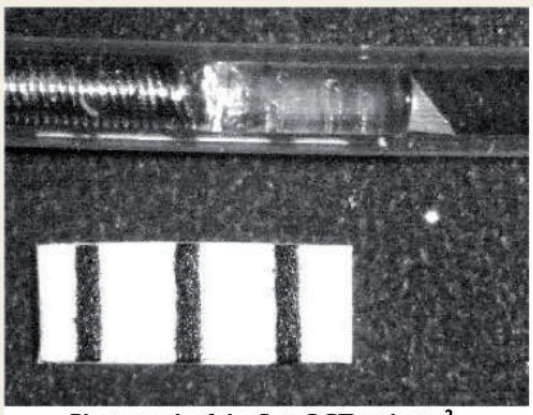


2D (left) and 3D (right) high-speed IVOCT images from patients[3]

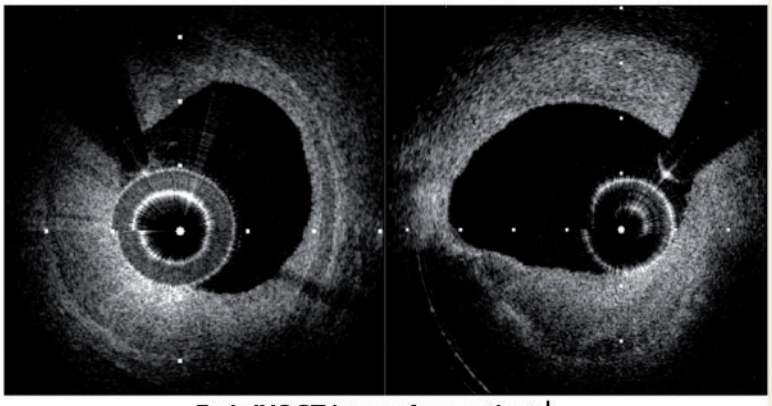
Data from the first patients[1] acquired at Massachusetts General Hospital and in Korea (Asan Medical Center, St. Mary's Hospital) at the turn of the millennium showed the potential of this technology to obtain high-resolution images of coronary plaque pathology, but the relatively low imaging speed combined with a short 2-s blood clearance following saline/radiocontrast flushing primarily relegated it to research applications. The advent of much higher speed OCT technology in the mid-2000's made non-occlusive flushing and high-quality 3D IVOCT acquisition practical in the catheterization lab, leading to commercially available clinical instruments and its place alongside intravascular ultrasound (IVUS) as a tool for interventional cardiologists to visualize the structure of the coronary artery wall. Intravascular optical coherence tomography quickly found a sizeable niche in assessing tissue response to stents through the measurement of stent strut coverage. Yet, much of the early motivation for the development of IVOCT was the detection of the vulnerable plaque/patient. Compared to IVUS, IVOCT was thought to be particularly promising for identifying high-risk plaques because of its higher resolution that enables the identification of thin caps, easier discrimination of lipid-containing plaques, and visualization of macrophage accumulations. Acting on asymptomatic lesions has proven elusive so far though due to missing pieces of the puzzle, including insufficient precision of imaging and a lack of established, targeted therapeutic options. Thus, the focus of intravascular imaging has evolved to improving the outcome of PCI. As exemplified by Räber *et al.* in this is issue of EHJ,[9] consensus documents have now been written summarizing what we know and do not know about IVOCT imaging as well as establishing standards for interpreting and ultimately using this technology to improve individual PCI outcomes. Studies have been done and are underway[9] to determine the evidence that is needed to make this application of intravascular imaging the standard of care.

As shown by 10–15% non-culprit lesion major adverse coronary events (MACE) in PCI patients, found in natural history studies conducted over the past decade such as PROSPECT,[10] pre-emptively treating asymptomatic, non-flow limiting lesions still remains a large, untapped opportunity for intravascular imaging. We have also now learned that structure seen by IVUS and OCT is important but not sufficient for completely determining the fates of individual coronary lesions. As a result, there has been a large amount of research to develop technologies that uncover other plaque features that add predictive value.

While near infrared spectroscopy (NIRS) has shown a capacity to sensitively detect lipid through flowing blood, one of the key consequences of the introduction of IVOCT was that it revealed that high-resolution optical imaging can be safely done in human coronaries using



Photograph of the first OCT catheter[2]

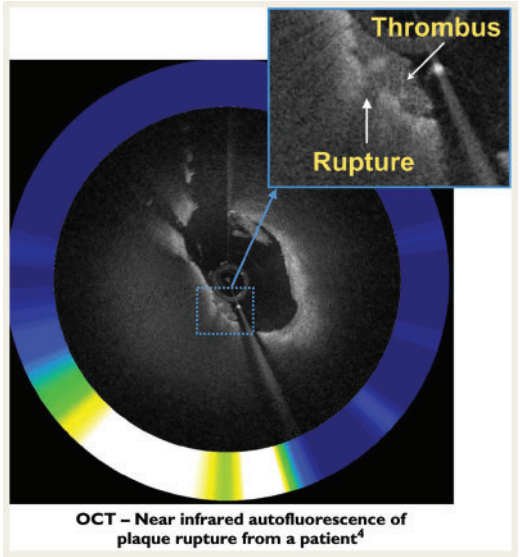


Early IVOCT images from patients[1]

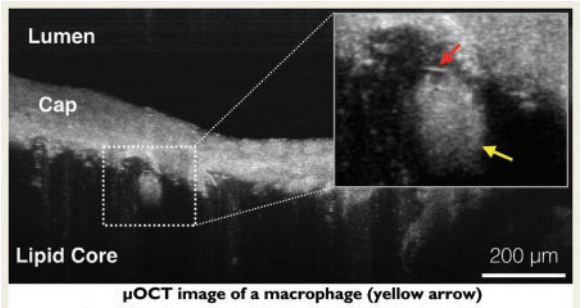
a saline or radiocontrast flush to clear blood from the imaging field. This advance has opened up the possibility of deploying other optical imaging modalities that provide more information about plaques that could increase precision. Studies have recently shown that autofluorescence of plaques provide information on plaque composition that is complementary to structure.[11,12] The field is awaiting the introduction of targeted fluorescent molecular labels[13] that will highlight specific mechanistic aspects that lead to accelerated plaque destabilization. Spectroscopy and fluorescence are now being done in concert with OCT, using a single catheter, providing co-localized information on both structure and chemical/molecular composition where the whole is greater than the sum of the individual parts. An additional benefit of the blood flushing with OCT is the clear delineation of the lumen that enables efficient computation of endothelial shear stress[14] a measure of the pathobiological milieu that promotes plaque progression.

Some newer developments have involved improvements in IVOCT itself. Recently, polarization-sensitive OCT (PS-OCT) that measures oriented structures in tissue has been demonstrated in patients[15] and shown to provide an additional mode of contrast that may facilitate plaque characterization and measurements of features such as fibrous caps.[16] The speeds of some research-based IVOCT systems have increased further, allowing an entire pullback to be conducted in a single cardiac cycle, removing motion artefacts from 3D reconstructions.[17,18] Image analysis has also advanced, enabling additional quantitative information on plaque composition to be automatically extracted from the images.[19]

Another significant advance involves imaging coronaries at the cellular level with a new 1-μm-resolution technology called micro-OCT (μOCT). In cadaver coronaries imaged on a bench top microscope, μOCT has been shown to see individual smooth muscle cells, macrophages, monocytes, leukocytes, and subcellular elements such as singular platelets, crystals, and fibrin strands.[20] Its capacity to visualize stents is also unparalleled, allowing for example the body's inflammatory response to drug eluting stent (DES) polymer coatings to be clearly seen. Recently a catheter has been developed that enables intracoronary μOCT in patients.[21] While only time will tell whether there are useful clinical applications of μOCT, it is likely that it will be important for increasing our understanding of coronary artery disease and interventions, driving the field forward at a faster pace.



OCT – Near infrared autofluorescence of plaque rupture from a patient[4]



μOCT image of a macrophage (yellow arrow) phagocytosing a crystal (red arrow) in a cadaver coronary

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References are available as supplementary material at *European Heart Journal* online.