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EDITORIAL COMMENT

Googling the Coronary: Fiberoptics and a Computer Provide the Answers*

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In this issue of *iJACC*, Tearney et al. (1) provide stunning images of the coronary arteries obtained with the first use of optical frequency domain imaging (OFDI) in patients. As has been done with internet searching, the authors have used major advances in optical methods and computerized data processing to retrieve and present information in a novel manner. The use of OFDI makes it possible to perform 3-dimensional optical microscopy in the difficult conditions of the coronary artery of a beating heart.

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Optical frequency domain imaging is a fast version of optical coherence tomography (OCT), neither of which is a familiar acronym to the cardiology community. The fundamental method of OCT starts with the delivery of near-infrared (NIR) light via a fiberoptic catheter to the wall of the coronary artery (2,3). The structures in the wall (luminal boundary, lipid cores, calcifications, macrophages, stents, and other targets) absorb and scatter this light to different degrees. This interaction of the light with the tissue results in return of the light to the detector after varying time intervals. The delay is identified by interference patterns created by interactions of the returning waves of light with the incident light. The result is a microscopic image with a resolution of approximately 10 μm. Two limitations of OCT with NIR light are: 1) it cannot be used in the presence of blood; and 2) the penetration into tissue is limited to approximately 1 mm.

These limitations were not of importance in the field of ophthalmology in which OCT has been widely used for over 6 years to examine the retina. In the coronary arteries, however, the need to remove blood from the field of view has been a major limitation. The technique in the coronary arteries requires either a balloon occlusion followed by a saline flush, or a saline flush alone, to interrogate specific locations in the coronary tree. Although remarkable images of coronary features have been obtained, the slow rate of measurement with OCT prevented scanning of a significant length of a coronary artery during a single flush.

Tearney et al. (1), who pioneered the use of OCT in coronary patients, turned to OFDI to markedly accelerate the speed of data acquisition and thereby enable scanning of longer segments of the coronary arteries during a single flush. In contrast to OCT, which uses a broadband light source, OFDI uses light of a narrow waveband whose frequency varies rapidly during the interrogation. This variation in the frequency of the light delivered makes it possible to obtain 100 frames of data in a second versus fewer than 10 frames/s that could be obtained with a conventional OCT system. Hence, as demonstrated in the 3 cases in this report, scans of 3 to 7 cm could be obtained during single saline flushes.

The use of OFDI provides far more information about the coronary artery than does a coronary angiogram, the current standard of care. Lumen dimensions are easily determined as are stent expansion and dissection. The unusual circumstance in which the authors were able to

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image both a new stent and a stent placed 9 years earlier documents that OFDI is able to identify neointimal hyperplasia covering a stent. The ability of OFDI to visualize a thin single cell layer covering a stent, which would suggest that a stent is no longer prone to thrombosis, is not proven.

In addition to identifying structural features, OFDI provides information about plaque composition and thrombosis. Users of the technique were able to identify calcium, macrophages, lipid pool, and thin fibrous cap by using optical features validated in previous OCT studies (4–8). Had significant thrombus been present, it would have been easily identified by OFDI (9).

Both OCT and OFDI have been compared with intravascular ultrasound (IVUS) because all 3 techniques provide structural information about the coronary artery. Although IVUS can obtain measurements through blood, which is a major advantage, the resolution of IVUS is not nearly as good as that of OCT/OFDI (100 μm for IVUS vs. <10 μm for OCT/OFDI). However, IVUS can penetrate much further into tissue, which gives it an advantage over OCT/OFDI for detection of the external elastic membrane and identification of expansive remodeling (10), a sign suspected to reflect plaque vulnerability. In addition to OCT/OFDI, other optical methods can be used to characterize coronary plaque. Diffuse reflectance NIR spectroscopy has been developed for the identification of lipid core plaque, and Raman spectroscopy is under study as a means to identify the individual chemical constituents of plaques (11,12). As noted by the authors, combinations of modalities are likely to be required to provide a full characterization of the artery.

Current OFDI technology has additional limitations. The impressive 3-dimensional images presented require several hours of manual and semiautomated analysis of the cross-sectional and longitudinal optical images. Such analysis currently requires the use of trained readers. In addition, the OFDI sign of lipid is an attenuation of reflectance rather than a positive signal indicative of lipid. Also, signals indicating lipid pools and calcified areas must be distinguished based on the sharpness of their borders with surrounding tissue. Efforts are currently underway to address these limitations (13).

Although OFDI is not yet approved for clinical use, there are many purposes for which it is likely to be adopted. The clear high-resolution images of stents makes it likely that OFDI can be used to document that a stent is adequately expanded, which may decrease the risk of late stent thrombosis. Both OCT and OFDI are uniquely useful for the detection of thrombus and assessment of fibrous cap thickness, 2 important imaging goals that cannot be achieved as well with other imaging modalities. Eventual usage for documentation of endothelialization of stents is also likely. Although OFDI is not yet available for clinical use, a commercial OCT system is available for routine usage outside the U.S.

In addition to these stenting-related uses, it is likely that OFDI will undergo intensive study in patients already undergoing stenting for its ability to identify plaques suspected to be vulnerable to rupture and causation of a second coronary event. As discussed previously in this editorial comment, OFDI is able to scan an artery for the presence of macrophage-rich thin-capped fibroatheromas, such as inflamed thin cap fibroatheromas (TCFA), that are suspected to be the cause of most acute coronary syndromes. The use of OFDI could provide the diagnostic method for both a natural history study and a randomized treatment trial for these structures.

Finally, if success is achieved in secondary prevention in patients undergoing stenting, it is possible to envision a role for ODFI in a much-needed strategy for primary prevention of coronary events. The steps, which require validation in controlled studies, would be as follows: 1) Screen the population with improved genetic tests and demographics to identify high-risk individuals; 2) perform noninvasive imaging in these high-risk individuals, most likely with multidetector computed tomography or magnetic resonance, to determine whether an inflamed TCFA might be present; 3) perform OFDI to confirm that such a structure is present; and 4) treat the inflamed TCFA with a stent, a novel pharmaceutical, or other method, before it causes a coronary event.

The unfortunate premature death of Tim Russert, who had passed a stress test only a month earlier, highlights the need for improved methods to interrogate the coronary arteries, methods that could be developed with currently available high technology. Google-used fiberoptics, lasers, and advanced computerized algorithms to develop an improved method to locate and present information from the world-wide web. In a similar manner, OFDI uses these same tools to collect millions of pieces of information about the coronary and then presents the data in a form that is useful to the cardiologist. The amazing views provided by OFDI *may* make it possible to find and treat a dangerous plaque before it causes a catastrophic coronary event.

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Key Words: optical microscopy ▪ OFDI ▪ optical frequency domain imaging ▪ OCT optical coherence tomography ▪ fibroatheroma ▪ thin cap.