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Clinical Characterization of Coronary Atherosclerosis With Dual-Modality OCT and Near-Infrared Autofluorescence Imaging

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ABSTRACT

OBJECTIVES We present the clinical imaging of human coronary arteries in vivo using a multimodality optical coherence tomography (OCT) and near-infrared autofluorescence (NIRAF) intravascular imaging system and catheter.

BACKGROUND Although intravascular OCT is capable of providing microstructural images of coronary atherosclerotic lesions, it is limited in its capability to ascertain the compositional/molecular features of plaque. A recent study in cadaver coronary plaque showed that endogenous NIRAF is elevated in necrotic core lesions. The combination of these 2 technologies in 1 device may therefore provide synergistic data to aid in the diagnosis of coronary pathology in vivo.

METHODS We developed a dual-modality intravascular imaging system and 2.6-F catheter that can simultaneously acquire OCT and NIRAF data from the same location on the artery wall. This technology was used to obtain volumetric OCT-NIRAF images from 12 patients with coronary artery disease undergoing percutaneous coronary intervention. Images were acquired during a brief, nonocclusive 3- to 4-ml/s contrast purge at a speed of 100 frames/s and a pullback rate of 20 or 40 mm/s. OCT-NIRAF data were analyzed to determine the distribution of the NIRAF signal with respect to OCT-delineated plaque morphological features.

RESULTS High-quality intracoronary OCT and NIRAF image data (>50-mm pullback length) were successfully acquired without complication in all patients (17 coronary arteries). The maximum NIRAF signal intensity of each plaque was compared with OCT-defined type, showing a statistically significant difference between plaque types (1-way analysis of variance, $p < 0.0001$). Interestingly, coronary arterial NIRAF intensity was elevated only focally in plaques with a high-risk morphological phenotype ($p < 0.05$), including OCT fibroatheroma, plaque rupture, and fibroatheroma associated with in-stent restenosis.

CONCLUSIONS This OCT-NIRAF study demonstrates that dual-modality microstructural and fluorescence intracoronary imaging can be safely and effectively conducted in human patients. Our findings show that NIRAF is associated with a high-risk morphological plaque phenotype. The focal distribution of NIRAF in these lesions furthermore suggests that this endogenous imaging biomarker may provide complementary information to that obtained by structural imaging alone. (J Am Coll Cardiol Img 2016;■:■–■) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

DCF = double-clad fiber

LAD = left anterior descending coronary artery

LCx = left circumflex coronary artery

NIRAF = near-infrared autofluorescence

NIRS = near-infrared spectroscopy

NSD = normalized SD

OCT = optical coherence tomography

PCI = percutaneous coronary intervention

TCFA = thin-cap fibroatheroma

ThCFA = thick-cap fibroatheroma

Intravascular optical coherence tomography (OCT) is a high-resolution imaging technique that is increasingly being used in interventional cardiology for the investigation and management of coronary artery disease (1,2). OCT enables the visualization of the artery wall microstructure, including morphological features related to coronary events such as lipid-containing regions, macrophage accumulations, thin-cap fibroatheromas (TCFAs), erosions and ruptures, and thrombi and calcified nodules (1,2). Owing to its capability to enable a clear view of the detailed arterial morphology and implanted arterial stents, OCT has also been used to assess the response of the artery wall after percutaneous coronary intervention (PCI) (1,2).

Even though OCT provides an unprecedented level of morphological detail, it does have limitations that constrain its diagnostic capabilities. Key plaque features such as lipid, for example, manifest as low OCT signal. The use of negative contrast features can confound diagnosis because signal loss may arise from a variety of different sources such as macrophage shadowing, intraluminal debris, and image artifacts (3,4). Furthermore, the capability of OCT to differentiate non-necrotic intracellular and extracellular lipid accumulations from necrotic core lipid has never been shown and therefore remains an unanswered question in the field (2,4). This ambiguity is problematic because studies have shown that a definitive diagnosis of necrosis is needed to distinguish rupture-prone lesions (5). In addition, microstructure alone does not provide a complete understanding of coronary artery disease, as the underlying mechanisms of coronary plaque development that lead to disruption and acute thrombosis are multifactorial, involving a complex interaction between structural, compositional, and biomechanical characteristics and cellular and molecular processes in the vessel wall (5).

Fluorescence molecular imaging has been proposed to complement OCT for studying plaque pathobiological mechanisms (6,7). Intravascular near-infrared fluorescence using targeted molecular agents has been shown to elucidate inflammatory activity and fibrin accumulation in mice (8) and rabbit (7,9) arteries, but these agents are not yet approved for human use. Detection of fluorescence from naturally occurring molecules, also known as autofluorescence, is closer to clinical application because it can be detected without the administration of exogenous agents. Autofluorescence excited in the ultraviolet and the visible portions of the electromagnetic spectrum has been studied in human plaques ex vivo where the signal relates to elastin, collagen, and nicotinamide adenine dinucleotide (10,11). Recently, red-excited (633-nm) near-infrared autofluorescence (NIRAF), with emission detected between 700 and 900 nm, has been shown in cadaver coronary arteries to be specifically elevated in advanced necrotic core-containing lesions (12), including thin-cap fibroatheroma (TCFA), the most common type of plaque implicated in acute coronary syndromes and acute myocardial infarction.

Based on the potential of the OCT and NIRAF combination to improve our detection of necrotic core lesions and specifically TCFAs, we developed a human-use OCT-NIRAF system and catheter. Here we describe a first-in-human safety and feasibility study of this multimodality intravascular imaging technology in patients and report our findings regarding the spatial distribution of the NIRAF signal with respect to colocalized OCT images of tissue microstructure in vivo.

METHODS

PATIENTS. Patients undergoing PCI at Massachusetts General Hospital (Boston, Massachusetts) were enrolled between July 2014 and January 2015. All patients provided informed consent, and the study was approved by the Massachusetts General Hospital (Partners Healthcare) institutional review board.

DUAL-MODALITY OCT-NIRAF IMAGING SYSTEM. We created a dedicated, dual-modality OCT-NIRAF system that implements state-of-the-art OCT (1,250 to 1,370 nm) and NIRAF, excited at 633 nm and detected between 675 and 950 nm (Online Figure 1). This system acquires synchronized OCT and NIRAF data at a rate of 100 frames/s. The OCT-NIRAF coronary imaging procedure is identical to that of

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