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Advances in Intravascular Ultrasound

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ABSTRACT

Since its inception, intravascular ultrasound (IVUS) and optical coherence tomography (OCT) have played a significant role in evaluating the pathophysiology of coronary artery disease (CAD) guiding the interventional and medical management of CAD improving outcomes in patients. Although the benefits of each of these modalities have been proven, due to some limitations, no single intravascular imaging technique has been proven to provide a detailed and complete evaluation of all CAD lesions. The use of different intravascular imaging modalities sequentially may lead to complications, which are cumbersome, consume time, and add financial burden to the patient. Recently, hybrid imaging catheters that combine OCT and IVUS benefits have been developed to limit these problems. Intravascular imaging techniques we are using currently have some drawbacks that hinder accurate assessment of plaque morphology and pathobiology as demonstrated in many histological studies, causing difficulty in identifying high-risk plaques. To overcome these limitations, great efforts have been put into developing hybrid, dual-probe catheters by combining imaging modalities to get an accurate analysis of plaque characteristics, and high-risk lesions. At present, many dual-probe catheters are available including combined IVUS-OCT, near-infrared spectroscopy-IVUS that is available commercially, the OCT-near infrared fluorescence (NIRF) molecular imaging, IVUS-NIRF, and combined fluorescence lifetime-IVUS imaging. Application of this combined multimodal imaging in clinical practice overcomes the limitations of standalone imaging and helps in providing a comprehensive and accurate visualization of plaque characteristics, composition, and plaque biology. The present article summarizes the advances in hybrid intravascular imaging, analyses the technical hindrances that should be known to have a use in the different clinical circumstances, and the till date shreds of evidence available from their first clinical application aiming to bring these modalities into the limelight and their potential role in the study of CAD.

Keywords: Coronary artery disease, Intravascular ultrasound, Optical coherence tomography

INTRODUCTION

In the early 1990s, intravascular imaging was introduced for the 1st time for the evaluation of intravascular atheroma burden and detection of plaque characteristics.[1] With the usage of intravascular ultrasound (IVUS) and optical coherence tomography (OCT) in clinical practice, there was an improvement in patient outcomes.[2-5] The potential role of IVUS and OCT in assessing plaque morphology and pathophysiology has been proven in many studies.[6-9]

However, usage of a single intravascular imaging technique does not provide a complete picture of the plaque morphology and characteristics. IVUS and OCT when used sequentially on separate catheters showed an incremental advantage in the assessment of plaque morphology and burden during percutaneous coronary intervention (PCI).[10-12] This sequential usage of multiple imaging modalities led to increased risk, time, and cost of the procedure. To alleviate this problem, hybrid imaging techniques have been introduced.[13]

The major offset of using a single imaging technique in the assessment of plaques was proven in large-scale studies and histopathology-based studies (i.e., the positive predictive value of IVUS-derived variables for the detection of progression of lesion which required revascularization was 41% in PREDICTION trail vs. 18.2% in the PROSPECT study).

The strengths and drawbacks of IVUS and OCT modalities are listed in [Table 1]. OCT has higher resolution and lesser tissue penetration as it has higher frequency when compared with IVUS.[14-17] OCT needs clearance of blood and proper engagement of catheter for image acquisition. Due to its higher resolution, OCT has the potential to precisely identify the etiology of acute coronary syndrome (plaque rupture, plaque erosion, or calcified nodule),[17-19] as well as inflammatory cells.[20] OCT's ability to accurately identify thin cap fibroadenomas (TCFA) is still limited when histology is used as the reference method.[21,22] Consequently, the accuracy of TCFA detection is increased by the combined use of OCT and IVUS.

The daily practise of using IVUS and OCT for improved optimization and guidance during PCI has increased globally. These techniques offer useful information about the lesion's properties, the stents size, the landing zones, the expansion of the stent, the edge dissection, and acute complications.[23] The guidewire's crossing point through the stent struts, toward the side branch, can be found due to OCT's greater resolution in comparison to angiography and IVUS, this makes it the best option when doing bifurcation lesion interventions. In addition, 3D OCT aids in determining the proper placement of the wire throughout the procedure.[24-26]

Usage of OCT in large vessels with proximal or ostial lesions is hindered by the difficulty in engaging catheter, hence difficulty in blood clearance which is important for optimal imaging.[27,28] In contrast, IVUS is thought to be suitable for such lesions. IVUS catheter can be passed into the side branch located just proximal to chronic total occlusion for examining the site of wire penetration under real-time imaging.[29,30]. As there are limitations of both IVUS and OCT, combination of both modalities is useful. Vessel border visualization is good with IVUS due to penetrating ability, whereas the OCT clearly delineates the lumen border. Combining the both modalities improves the accuracy of plaque burden estimation in clinical settings.

Table 1: Comparsion of IVUS and OCT.

	IVUS	OCT
Imaging through blood	+++	–
Imaging entire plaque burden	+++	+
Imaging near field adjacent to the catheter	–	+++
Detection of TCFA/vulnerable plaque	+	+++
Detection of deep calcium	+++	–
Assessment of calcium thickness	–	+++
3D reconstruction/bifurcation	+	+++
Real-time imaging	+++	+
Assessment of stent strut apposition/structure	++	+++
Assessment of stent coverage	+	+++

IVUS: Intravascular ultrasound, OCT: Optical coherence tomography

In daily practise, consecutive OCT and IVUS imaging is uncommon. The advantages of additional imaging have not well been evaluated and its value may be underestimated. However, sequential intravascular imaging needs the expertise to find and match the exact corresponding cross-sections in the vessel (co-registration) and rotated images (co-alignment). This has that the additional risk of complications, time delay, higher cost, improper co-registration, and co-alignment of the two imaging modalities leads to confusion and adds to cumbersomeness during the procedure. These issues might be resolved using a hybrid IVUS-OCT catheter.

OCT aids in the characterisation of the plaque components including lipid pools, calcium, fibrotic tissue, and thrombus. OCT helpfulness is demonstrated in many studies for calcific lesions,[31,32] but due to its heterogenous composition requires good experienced that operator is required to interpret properly.[27,33] Sometimes severe coronary stenosis with calcification may be seen with angiogram and OCT, but combination of OCT with IVUS delinates the mixed plaque morpohology in better why, which may change our decision in preforming the PCI from rotablation to cutting balloon. Os also, occationally nodular calcification may be misinterpreted as red thrombus on OCT, but hybride OCT with IVUS can detect attenuated plaque which was previously interpreted as nodular clacification.[34,35]

Sometimes, optical frequency domain imaging (OFDI) may show a mass that protruding into the lumen with uneven surface with signal attenuation, which may be interpreted as a red thrombus. However, IVUS will help in this situation, if it is a superficial calcification but not thrombus then acoustic shadowing of that mass will be there, which facilitates to select the proper treatment strategy.

There are numerous hybrid probes being created and evaluated in both *ex vivo* and preclinical *in vivo* settings. Californian engineers created the first hybrid probe integrating OCT and IVUS in 2010.[36] The optical and ultrasound transducers on this probe are fixed side by side. It was investigated in the aorta of a rabbit. Due to this hybrid catheter's bigger size (outside diameter 2.4 mm, 7.2 Fr) and greater rigidity, there were some restrictions on how it could be used. Later, smaller probes (outside diameter 1.18 mm, 3.6 Fr) were created (outer diameter 1.18 mm, 3.6 Fr) [Figure 1a].[37] It was discovered that there was an issue with the image's co-registration due to the longitudinal offset between the ultrasonic and optical imaging planes, particularly when taking catheter motion during the procedure into account.[38] Advanced hybrid catheters with

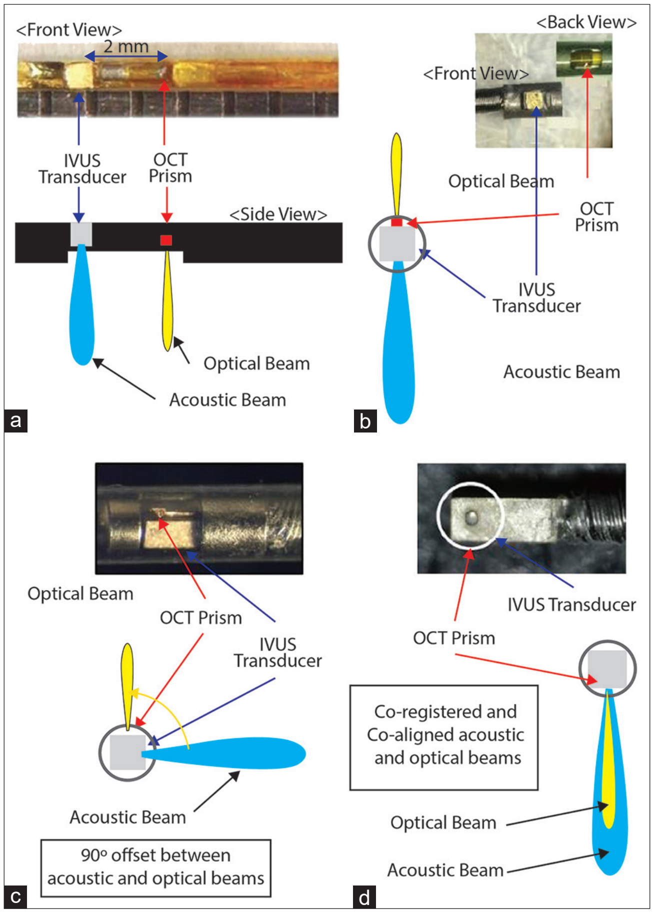

Figure 1: Four different types of hybrid intravascular ultrasound-optical coherence tomography (OCT) catheter tips are shown in pictures and schematics. (a) Modified, smaller hybrid catheter with a 2 mm longitudinal offset between the IVUS and OCT imaging planes was created at the University of California, Irvine, CA, in the United States (outer diameter 1.18 mm, 3.6 Fr). (b) In Irvine, California, the University of California developed a cutting-edge hybrid catheter. The IVUS transducer and OCT prism were placed back to back. (c) A hybrid catheter created by Toronto, Canada;s Sunnybrook Research Institute. IVUS transducer and OCT prism were used together side by side. (d) Conavi Medical Inc. (Toronto, Ontario, Canada) and Sunnybrook Research Institute together developed an innovative hybrid catheter (Novasight HybridTM system). This technology uses an IVUS transducer with an incorporated OCT prism to produce coincident imaging beams.

back-to-back OCT and ultrasonic transducers were created to prevent this.[39,40] [Figure 1b]. In this cutting-edge hybrid catheter, the IVUS transducer and OCT prism were placed back to back. At Sunnybrook Research Institute in Canada, a different hybrid system was created and verified using human cadaver specimens.[41] In a 4 Fr probe, an OCT prism and an ultrasonic transducer were both implanted side by side. The acoustic and optical beams scanned the same cross-section of tissue with 90° offset to each other [Figure 1c]. Recently, a 2.8 Fr hybrid catheter was developed by Sunny-brook Research Institute and Conavi Medical Inc., which had a 40 MHz ultrasound transducer at the tip of the catheter along with an embedded OCT optic cable [Figure 1d]. In this Novasight Hybrid™ system, the technology uses an IVUS transducer with an incorporated OCT prism to produce coincident imaging beams. This design helps in producing coincidental optical and ultrasound beams that facilitate simultaneous image acquisition at the same cross-section in the vessel at same time and eliminated errors of co-registration due to cardiac motion or variable rotational motion of the hybrid imaging catheter. With this catheter-derived images were comparted with the autopsy speciments of same artery, there was good correlation of the histopathology and hybride catheter imaging, non-uniform rotational distortion during operation may have a possibility of causing inaccurate image co-registration *in vivo*.

At present, terumo corporation is working to create a hybrid IVUS and OFDI system with a 2.6 Fr imaging catheter and built-in IVUS analysis software. In 2018 Sheth *et al*. reported, the first hybrid IVUS-OCT images of the coronary arteries in humans using a Novasight Hybrid™ system.[42] Studies frequently showed the acquisition of evocative, infrequently unexpected images illustrating the synergistic benefits of an IVUS-OCT hybrid device, not only in plaque characterization but also during PCI, despite the fact that current experiences were restricted to a small number of cases with simple lesions on coronary angiograms. In [Table 2], the limitations of these invasive imaging modalities are mentioned.

FUSION OF INTRAVASCULAR IMAGING AND COMPUTED TOMOGRAPHIC CORONARY ANGIOGRAPHY

van der Giessen *et al.*[43] first introduced a model to fuse IVUS and computed tomographycoronary angiography (CTCA). To determine the position and orientation of IVUS images relative to the extracted centerline, the proposed method, which is similar to methodologies proposed to fuse X-ray and intravascular imaging, combines 3D centreline data from CTCA and anatomical landmarks visible on both IVUS and CTCA. IVUS-CTCA derived parameters offer an effective alternative for endothelial shear stress (ESS) computation, IVUS-CTCA hybrid imaging makes it easy to evaluate coronary artery bifurcations thereby data on shear stress at the site of bifurcation.[44] Combined IVUS imaging and CTCA showed that at the site of coronary bifurcations plaques are exposed to more shear stress beginning from nascent stages of formation and that high shear stress is associated with plaque rupture.[45]

In a study using CTCA-IVUS imaging, it was found that thicker plaques were found at sites of low ESS, and IVUS demonstrated that these lesions had fibrofatty plaques.[46] Simulation of stent deployment in coronaries was made possible by the fusion of IVUS and CTCA which was demonstrated in a study.[47]

Table 2: Advantages and limitations of the existing invasive imaging modalities and the available hybrid imaging techniques.

Features associated with increased plaque vulnerability	**Imaging modalities**										
	IVUS+X-ray	**OCT+X-ray**	**IVUS+CTCA**	**OCT+CTCA**	**NIRS-IVUS**	**IVUS-OCT**	**OCT-NIRF**	**IVUS-NIRF**	**OCT-NIRS**	**IVUS-IVPA**	**IVUS-FLIm**
Lumen dimensions	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
Plaque burden and positive remodelling	+++	+	+++	+	+++	+++	+	+++	+	+++	+++
Lipid component	+	++	+	++	+++	++	++	+	+++	++	++
Cap thickness	+	+++	+	+++	++	+++	+++	+	+++	+	+++
Neo-angiogenesis	–	++	–	++	–	++	++	–	++	+	–
Inflammation	–	+	–	+	–	+	+++	+++	+	++	++
ESS assessment	+++	+++	+++	+++	–	–	–	–	–	–	–
Fast analysis	–	–	–	–	++	+	NK	NK	NK	NK	NK
Current status	Implemented to evaluate the efficacy of CTCA in assessing plaque morphology	Limited applications	Implemented to evaluate the efficacy of CTCA in assessing plaque morphology	Limited applications	Commercially available	*In vivo* validation	First in man studies	Under development	*Ex vivo* validation	*Ex vivo* validation	*In vivo* validation

(+++) Indicates excellent performance of the modality, (++) Moderate performance of the modality, (+) Poor performance of the modality, (–) The modality is unable to provide this information, (NK) Not known. EES: Endothelial shear stress, IVUS: Intravascular ultrasound, RF-IVUS: Radiofrequency analysis of the IVUS backscattered signal, OCT: Optical coherence tomography, NIRS: Near-infrared spectroscopy, CTCA: Computed tomographic coronary angiography, NIRF: Near-infrared fluorescence imaging, IVPA: Intravascular photoacoustic, FLIm: Fluorescence life time imaging, ESS: Endothelial shear stress

Reconstruction of both the vascular lumen and the vessel wall at coronary bifurcation can be done, and models can be applied to simulate stent deployment. This study paved the pathway for the development of *in silico* methodologies to plan and optimize and execute the procedure of stenting in complex coronary lesions. Similar methodologies can be applied to fuse the images obtained by OCT and CTCA. Karanasos *et al*. used hybrid CTCA and IVUS, and CTCA and OCT data to demonstrate that post-bioresorbable scaffold implantation high shear stress (ESS) at the end of 2 years lead to formation of plaques with thicker fibrous caps at 5 years,[48] demonstrating that ESS is a determinant in predicting the response of the vessels treated with these scaffolds in long term.

COMBINED NEAR-INFRARED SPECTROSCOPY IVUS IMAGING

Combination of NIRS-IVUS imaging is the only intravascular imaging that is currently approved for clinical use in the USA and other countries. It provides reliable data on plaque pathobiology and morphology. The combination of NIRS and IVUS with good co-registration and simultaneous acquisition offers a vast information, as IVUS details about plaque structure, whereas lipid-rich plaques may be reliably and precisely detected by NIRS.[49] NIRS-IVUS, which is now marketed, combines NIRS and rotating IVUS at 50 MHz with a single 3.2 Fr monorail catheter. The tip of the catheter includes two NIRS fibres that transmit and collect near-infrared light, as well as a rotating intravascular ultrasonic transducer that operates at 50 MHz with an extended bandwidth. The chemogram, which is the result of the NIRS catheter, is co-registered with the IVUS data to provide hybrid pictures that enable assessment of the dimensions of the lumen, outer vessel wall, and plaque, including the burden of the plaque, as well as concurrent evaluation of the longitudinal and circumferential distribution of the lipid component.

Several studies have used NIRS-intravascular ultrasonography to evaluate the impact of statins on plaque burden and composition.[50,51] A high-risk lipid plaque signature may be linked to sudden cardiac events, according to studies using NIRS and IVUS that revealed the culprit lesions in patients with non-ST or ST-elevation myocardial infarction have specific morphological characteristics (such as an increased lipid component and plaque burden).[52,53] Some preliminary data suggest that NIRS-IVUS can identify plaque characteristics related to future events.[54] Two significant trials (Prospect II and the Lipid Rich Plaque Study) are underway to more thoroughly and formally test this theory. The inability of IVUS to resolve finer measurements such as cap thickness or neointimal coverage of stent struts, loss of the IVUS imaging signal behind calcific tissue, irregular lumen border definition in the presence of thrombus, and the necessity of priming and occasionally flushing the imaging catheters are some of the limitations of NIRS-IVUS. Since NIRS does not explicitly reveal the depth of the lipid core plaque, it is impossible to discern between superficial and deep lipid in the same arc using this information alone.

COMBINED IVUS AND INTRAVASCULAR PHOTOACOUSTIC (IVPA) IMAGING

An analytical chemical diagnostic method called IVPA imaging appears to be able to identify the lipids like cholesterol esters that make up atherosclerotic plaques depth-resolved composition. Since the same transducer can be used to do a traditional pulse-echo measurement, IVPA pictures are intrinsically collocated with tissue structure obtained by IVUS and can detect the struts of stents and provide chemical information on plaque composition. When compared to NIRS, the depth resolution of IVPA imaging has the benefit of allowing for the precise spatial location and volume of the lipids within the plaque relative to the lumen boundary imaged by IVUS.

There have been various hybrid IVUS-IVPA imaging prototypes presented over the past 5 years. An optical fibre is added to an IVPA catheter to supply light to excite the IVPA signal, making it functionally comparable to an IVUS catheter. The optical beam crosses over to overlap with the acoustic beam due to sideways reflection. Early designs using phased-array transducers or rotational IVUS catheters were somewhat large.[55,56] Miniaturized intracoronary scanning probes with high-frequency transducers that could provide images with a 35 mm resolution came after them.[57] Recently, flexible catheters that are appropriate for real-time imaging were demonstrated, bringing the picture acquisition time on par with that of existing commercial IVUS systems.[58,59] Extensions to triple-modality IVPA-IVUS-OCT combinations may be possible in the future.

The first *in vivo* IVPA applications[60,61] have shown that this modality can be a valuable tool for determining plaque vulnerability and quantifying the response to various forms of intervention (device, pharmaceutical, and lifestyle changes) with great chemical detail.[62,63] However, there is a problem to solve before it can be applied in the clinical setting, there are a number of technological and regulatory obstacles.[64] The requirement for blood clearance because blood weakens signals and IVPA's limited capacity to visualize the entire plaque when there are big lipid cores is two additional drawbacks of the designs that are currently in use.

COMBINED FLUORESCENCE LIFETIME IMAGING AND IVUS

Recent research has shown that the fluorescence lifetime values obtained from measurements of diseased arteries

Table 3: Technical characteristics of the combined intravascular imaging catheters.

Imaging modality	Probe size	Probe arrangement	Probe characteristics[a]	Image depth	Image axial resolution	Frame rate	Technical limitations restricting clinical applications	Histological evidence
NIRS-IVUS (66)	3.2 Fr	IVUS transducer and NIRS optics at 180° apart	NIRS: 800–2500 nm IVUS: 50 MHz	NIRS: <3 mm IVUS: 16 mm	IVUS: 20 µm	NIRS: 150 spectra/s IVUS: 16/s	None	The NIRS ability to detect lipid core was 86% in the only prospective validation study of its kind
IVUS-OCT (67)	7.2 Fr	Side by side	IVUS: 40 MHz OCT: 1310 nm	NA	IVUS: 38 µm OCT: 8 µm	1/s	Large catheter size Poor image quality acquisition rate	*In vitro* feasibility study in a rabbit aorta
	4 Fr (68)	Side by side 90° apart	IVUS: 42.5 MHz OCT: 1325 nm	OCT: 1 mm within tissue	NA	5/s	Increased artefacts/ moderate image quality Low frame rate Poor co-registration in case of NURD	Qualitative validation in human cadavers
	3.6 Fr (69)	Sequential arrangement–2 mm apart	IVUS: 35 MHz OCT: NA	IVUS: 4.5 mm OCT: NA	IVUS: 60 µm OCT: 8 µm	20/s	Large catheter size Inaccurate co-registration of IVUS and OCT	Feasibility study in human cadaver and *in vivo* in the aorta of a rabbit
	2.7 Fr (70)*	Back to back	IVUS: 45 MHz OCT: NA	NA	NA	10/s	Low image acquisition rate	Feasibility study in human and swine cadavers
	3 Fr	Co-linear ultrasound and optical beams	IVUS: 40 MHz OCT: 1320 nm	NA	NA	100/s	None	Feasibility in pre-clinical *in vivo* models
OCT-NIRF	2.4 Fr (71)	Dual clad fibre with a single-mode OCT core and an inner NIRF cladding	OCT: 1320 nm NIRF: 750 nm	NIRF: 3 mm	OCT: 7 µm	25.4/s	Low image acquisition rate	Feasibility study in cadaveric human coronary artery and *in vivo* in rabbits
	2.6 Fr (72)	Dual clad fibre with a single mode OCT core and an inner NIRF cladding	OCT: 1290 nmNIRF: 749–790 nm	OCT: 1–2 mm	OCT: 7 µm	100/s	None	Feasibility study *in vivo* in rabbit models
IVUS-NIRF	4.2 Fr (73)	Side by side	IVUS: 45 MHz NIRF: 750 nm	IVUS: 4 mm NIRF: 2 mm	IVUS: NA	30/s	Large size catheter	*In vitro* validation in phantoms and feasibility study *ex vivo* in porcine carotids
OCT-NIRS	2.4 Fr (74)	Side by side	OCT: 1282 nm NIRS: 1230–1330 µm	OCT: 1.5 mm	OCT: 10 µm	24/s	None	Feasibility study in a cadaveric human coronary artery

(Contd...)

Table 3: *(Continued)*.

Imaging modality	Probe size	Probe arrangement	Probe characteristics[a]	Image depth	Image axial resolution	Frame rate	Technical limitations restricting clinical applications	Histological evidence
IVUS-IVPA	3.6 Fr (75)	Parallel alignment	IVUS: 35 MHz IVPA: 532 μm	IVUS: 5 mm	IVUS: 59 μm	NA	The need for blood removal for IVPA imaging	*In vitro* validation in a wire phantom model and a feasibility study in a rabbit aorta
	3.6 Fr (75)	Parallel alignment	IVUS: 80 MHz IVPA: 532 μm	IVUS: 4 mm	IVUS: 35 μm	NA	The need for blood removal for IVPA imaging	*In vitro* validation in a wire phantom model and a feasibility study in a rabbit aorta
	8.7 Fr (76)	IVPA probe within the IVUS probe	IVUS: 35 MHz IVPA: 1197 μm	NA	NA	1/s	Large catheter size The increased time needed for IVPA imaging	*In vitro* validation in phantom models and a feasibility study in a pig iliac artery
	2.7 Fr (77)	Sequential arrangement	IVUS: 40 MHz IVPA: 1210 μm	IVUS: 4.5 mm IVPA: 4.5 mm	IVUS: 100 μm IVPA: 100 μm	5/s	The increased time required for IVPA imaging	*In vitro* validation in phantom models and a feasibility study in a stented rabbit iliac artery
IVUS-FLIm	7 Fr (78)	Side by side	IVUS: 40 MHz FLIm: 300 μm	NA	NA	FLIm: 6.7/s IVUS: 30/s	Large catheter size The need for balloon inflation to obstruct flow	Feasibility study *in vivo* in the femoral artery of a pig model
	5 Fr (79)	Side by side	IVUS: 40 MHz FLIM: 390–629 μm	NA	FLIm: 160 μm	IVUS: 30/s FLIm: 40/s	The need for blood flow obstruction Inaccurate co-registration of FLIm and IVUS data The offline analysis of the FLIm data	*Ex vivo* validation in cadaveric coronary arteries (sensitivity and specificity range: 84–100% for all plaque types) and in a swine coronary arteries 68

NIRS: Near-infrared spectroscopy, IVUS: Intravascular ultrasound, OCT: Optical coherence tomography, NA: Not available, NURD: Non-uniform rotational distortion, NIRS: Near-infrared spectroscopy, NIRF: Near-infrared fluorescence imaging, IVPA: Intravascular photoacoustic imaging, FLIm: Fluorescence life time imaging. [a]All the multimodality imaging probes incorporated a rotational IVUS transducer. *The diameter of this prototype does not include the sheath that would protect the the rotating housing from the artery using time-resolved fluorescence spectroscopy or fluorescence lifetime imaging microscopy (FLIm) can be linked to pathological changes in the intima (250–300 mm depth), including accumulation of lipid both intracellular (in macrophages) and extracellular (lipid pool), elastin, and collagen, and so make it possible to distinguish between TCFA and thick cap fibroatheromas in terms of pathological characteristics.[65] This prompted the creation of a number of hybrid intravascular catheters for cardiovascular imaging applications that combine multispectral rotating FLIm and IVUS and enable simultaneous imaging of the morphological and biochemical characteristics of the artery wall [Table 3].

A rotating catheter that permits concurrent multispectral FLIm and IVUS imaging was described by Bec *et al*. This initial prototype's diameter was relatively enormous (7 Fr), making it impractical for intravascular imaging.[66,67] A completely automated and integrated FLIm-IVUS bimodal miniaturised (3.5 Fr diameter) that imaging device compatible with intravascular rapid imaging of coronary arteries was described by Ma *et al*. as a follow-up to this work.[68] The optic fiber and IVUS transducer were arranged in tandem in this design's huge oval shaft, which had a maximum diameter of 5 Fr. The commercial IVUS 3 Fr catheter's imaging components make up the ultrasonic and optical channels, together with a proprietary, total internal reflection, and side-viewing fibre constructed around a UV-grade silica fibre optic with a cap made of polymethylmethacrylate. The inactive channel can be drawn back into the shaft, while each modality is moved into the imaging portion to begin collecting data using helical scanning. *Ex vivo* intraluminal evaluation of diseased coronary arteries from 16 patients using the bi-modal catheter previously described showed that combined FLIm-IVUS imaging was more sensitive and specific (89%, 99%) at differentiating between different types of plaque than standalone FLIm (70%, 98%) or IVUS (45%, 94%).[68,69].The system has been improved, with a focus on removing blood from the optical channel in particular. Data acquisition during a bolus saline solution injection with a 7 Fr guide catheter was made possible by a quick data acquisition time (5 s for a 20 mm long coronary segment). While there were noticeable variations in intensity across the field of view that could be seen in the intensity images as a result of the mild changes in excitation and collection efficiency caused by vessel geometry and motion that occurred during the cardiac cycle, the computed average lifetime was uniformly distributed, as would be expected from a healthy artery (fluorescence dominated by elastin and collagen emission). The FLIm data and IVUS data could not be directly co-registered as in *ex vivo* investigations due to the cardiac motion.[67,68] The Marcu group is now developing a device that is compatible with *in vivo* intravascular imaging (single imaging core, 4 Fr), and this work lay the groundwork for further integrating FLIm and IVUS (UC Davis). Recent *in vivo* testing of this novel catheter in swine coronaries was done.

CONCULSION

Combination of different modalities of imaging which gives different information about the plaque morphology is useful to make as hybrid catheter. During this is hybridization, we have to take care of coplanar imaging of the two or three cathters. Simulataneously, the size of the hybrid catheters should be miniaturaed to be 6F guide compatable to apply clinically useful way, along with safety tesying in animal models.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflict of interest.

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