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Miniature integrated optical coherence tomography (OCT) - ultrasound (US) probe for intravascular imaging

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SUMMARY

A miniature integrated optical coherence tomography (OCT) – ultrasound (US) probing system for real-time intravascular imaging has been developed. The outer diameter of the integrated probe is 0.69 mm, which is small enough for imaging in human coronary arteries. This probe, which has high resolution and deep tissue penetration, is designed to identify vulnerable atherosclerotic plaques in coronary arteries. The first *in vivo* images of a rabbit abdominal aorta obtained by the integrated OCT-US probe are presented.

Keywords: atherosclerosis, vulnerable plaque, intravascular ultrasound, optical coherent tomography

ABSTRACT

Coronary artery atherosclerosis is a major public health problem associated with high clinical morbidity and mortality. For over 20 years, intravascular ultrasound (IVUS) imaging has been a standard diagnostic tool for atherosclerosis[1]. Recently, optical coherence tomography (OCT) with high resolution, has been applied to intravascular imaging because it enables direct imaging of thin fibrous cap[2], one of the key feature of vulnerable atherosclerotic plaque, and tissue responses to stent implantation[1]. The combined use of OCT and IVUS is hypothesized to remarkably increase diagnostic accuracy[3-5].

Here, we report on a miniature integrated optical coherence tomography (OCT) –ultrasound (US) probe, which is small enough for imaging in coronary artery. The OCT probe design permits light from a single mode fiber to be focused by a 0.35-mm-diameter gradient-index (GRIN) lens and then reflected by a 0.25-mm-diameter micro prism into the sample. A 0.5mm × 0.5mm 35MHz PMN-PT side-viewing ultrasound transducer is combined with the OCT probe for ultrasound imaging. By arranging the OCT probe and US transducer sequentially, the outer diameter of the integrated OCT-US probes has been decreased significantly to 0.69 mm. This miniature integrated probe simultaneously provides both OCT and ultrasound imaging. By adopting a two-channel data acquisition board, external clock and GPU parallel computing, a truly integrated OCT-US system is achieved allowing real time data acquisition, processing and display. The first in vivo imaging of a rabbit abdominal aorta and *in vivo* imaging of a pig coronary artery acquired by combined OCT-US probe demonstrates the utility of this miniature integrated OCT-US probe.

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1. INTRODUCTION

Atherosclerosis is the leading cause of morbidity and mortality in the United States and is becoming the preeminent health problem worldwide. Detection and diagnosis of atherosclerosis relies on medical imaging techniques[6]. Intravascular ultrasound (IVUS) imaging[7,8] has become a standard imaging modality for atherosclerosis diagnosis since it provides direct visualization of vessel walls. Recently, optical coherence tomography (OCT) has been applied to intravascular imaging because it offers new insights into the micro structure of atherosclerosis and tissue responses to stent implantation[9-11]. Research has been conducted to compare diagnostic accuracy of OCT and IVUS during which separate OCT and IVUS systems were used to image the same sites of interest[3,4]. It has been pointed out that OCT and IVUS are complementary in the application of intravascular imaging, and the combination of the two can offer advantages which cannot be achieved by using either modality alone[5].

An integrated OCT-US system will be capable of offering high resolution, which is essential for visualizing microstructure of a plaque, and also large penetration depth which is necessary for visualizing structures deep within the vessel wall. Thus, enhanced diagnostic accuracy can be obtained. Moreover, improved safety for the patient can be achieved since only a minimum amount of flushing agent will be needed for OCT under the guidance of US. An integrated OCT-US probe can provide both OCT and ultrasound imaging simultaneously so that both cost and the physician's time will be reduced significantly compared to using separate probes.

Previously, our group has developed different types of integrated intravascular imaging probes combining OCT with US [12-14]. In Yin *et al* and Yang *et al* [13,14], the OCT probes and the US transducers were put side by side and had outer diameters of 2.4 and 2.8mm, respectively. In Li *et al* [12], the OCT probe was inserted into a centric hole of the US transducer to achieve co-registered OCT-US imaging. This probe had an outer diameter of 2.5mm. The imaging capabilities of previous OCT-US probes were demonstrated by successful imaging of normal rabbit aorta. In this paper, we report on a novel probe design and improvement of the whole system. By arranging the OCT probe and US transducer sequentially, the overall size of the integrated OCT-US probes has been decreased significantly. Furthermore, data acquisition and image display are in real-time for both OCT and US due to modified hardware and software design. The capability of our integrated OCT-US imaging system is demonstrated by *in vivo* imaging of a rabbit abdominal aorta and *in vivo* imaging of a pig coronary artery.

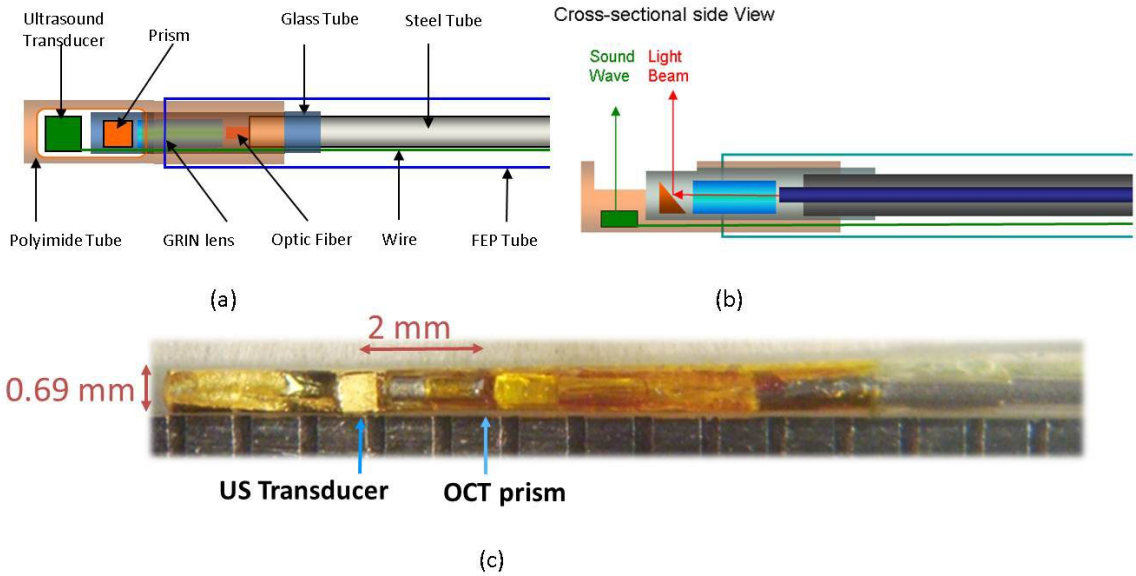

Fig1. (a) The schematic of the distal end of the miniature OCT-US probe, front view. (b) The schematic of the distal end of the miniature OCT-US probe, cross-sectional side view. (c) Photograph of the miniature OCT-US probe.

2. MATERIAL AND METHODS

The major challenges behind the integration of the OCT-IVUS system come from three aspects. First, an integrated probe that combines OCT components with US components needs to be designed and fabricated. Second, the design of the catheter should be engineered for satisfying the same requirements for clinical procedures of IVUS catheter imaging. Last but not least, a truly integrated system requires simultaneous OCT and US data acquisition, processing and image display which are mainly discussed by the presentation in OCT session named "Advances in a fully integrated intravascular OCT-ultrasound system for cardiovascular imaging" with 3D imaging of cadaver coronary artery tissue.

The schematic of the miniature OCT-US probe is shown in figure 1. Unlike our previously published designs which had a parallel or coaxial arrangement, this new version of the probe design features a sequential arrangement of the US transducer and OCT probe so that over-all probe size is significantly decreased by roughly 4-fold. Within the OCT probe, a 0.35mm-diameter gradient index (GRIN) lens was used for light focusing, followed by a 0.3mm-diameter micro-prism for reflecting the focused light beam into tissue. All the optical components were fixed in a polyimide tube with an outer diameter (OD) of 0.41mm and wall thickness of 0.02mm. The working distance of the OCT probe was about 3mm. The ultrasonic transducer with an aperture size of 0.5mm × 0.5mm was built using a PMN-PT single crystal which has superior piezoelectric properties for building high sensitivity US transducers in a small size. The center frequency of the ultrasound transducer was 35 MHz with a fractional bandwidth of 51%. The two way insertion loss was measured to be 15 dB at the center frequency. The transducer was fixed in the proximal end of a thin-wall polyimide tube (OD 0.69mm, wall thickness 0.025mm) within which the OCT probe was also fixed. A window was made on the tube to let both the light beam and soundwave exit. Finally, the transducer wire and optical fiber were sealed in a thin-wall fluorinatedethylenepropylene (FEP) tube (OD 0.61mm, wall thickness 0.05mm). The maximum outer diameter of the fully integrated probe was 0.69mm. It was known beforehand that the transducer and prism were 2mm apart, thus co-registered OCT and US images could easily be matched from a 3-D data set by offsetting OCT and US images by this distance. The measured axial and lateral resolutions (based on FWHM) of the OCT system with the probe were 8μm and 30μm, respectively. Resolutions of the US part were 60μm and 420μm, respectively, measured from 6μm wire phantom.

The OCT-US probe was connected to the integrated OCT-US system via a semi-homemade rotary joint which consisted of a fiber optic rotary joint (Princetel, Inc., Pennington, NJ) and an electric slip ring (Prosperous. Co., Hangzhou, China). The optical portion of the OCT sub-system has been previously reported (12-14). As for the US sub-system, a Panametrics pulser/receiver (Olympus NDT, Inc., Kennewick, WA) was used to drive the ultrasound transducer and also to receive the echo signals. The light source generated a 20 KHz trigger signal which drove a function generator (Agilent Technologies, Inc., Santa Clara, CA) serving as a frequency divider to provide 4 KHz triggers to synchronize the data acquisition board and the pulser/receiver. Both OCT and US signals were digitized by a two-channel, 12 bit data acquisition board (Alazar Technologies Inc., Pointe-Claire, QC, Canada) working at a sampling rate of 250 MHz. OCT-US software was developed to handle both OCT and US data acquisition, processing, image display and data saving. Real-time OCT-US image display was achieved thanks to multi-threaded computing techniques. Our home-developed OCT-US program was capable of handling simultaneous OCT-US data processing and image display at a speed of 20 frames per second (1000 A-lines per frame for both OCT and US). Due to the rotational speed limitation of the slip ring, actual imaging speed was turned down to 4 frames per second. Three-dimensional scanning was obtained by using a rotational motor and a translational stage.

In order to satisfy the requirements of clinical procedure, our catheter (including the probe and outer sheath) shares the following characteristics. First, a 0.65mm outer diameter double wrapped torque coil is used outside optics fiber and electrical wire for protection instead of stainless steel tube[12]. This torque coil transmits the rotation of the proximal end accurately to the distal tip. Furthermore, its flexibility allows the torque coil to maintain performance even in bent sections. As such, the catheter is possible to be used in clinical study where coronary artery is accessed through femoral artery and the catheter is required to make a ~ 180-degree sharp bend. Second, as the same design as IVUS catheter, the probe was spinning within a 3.6 Fr catheter sheath [figure 2] to protect the probe from contamination and also help avoid causing trauma to the inner vessel wall. As to the integrated OCT-IVUS catheter, a special material for sheath needs to be used, which is not only transparent to US but also IR light to avoid noise in US or OCT images. Third, the precise position of the imaging probe is identified by 2 X ray-detectable marker bands and a 0.40mm inner diameter channel are engineered at the distal end of the sheath for the catheter, to work as standard guide wire rail. Last but not

least, with over 160cm usable length, where the catheter is inside body, 15~20cm of intracoronary length is able to achieve during procedure.

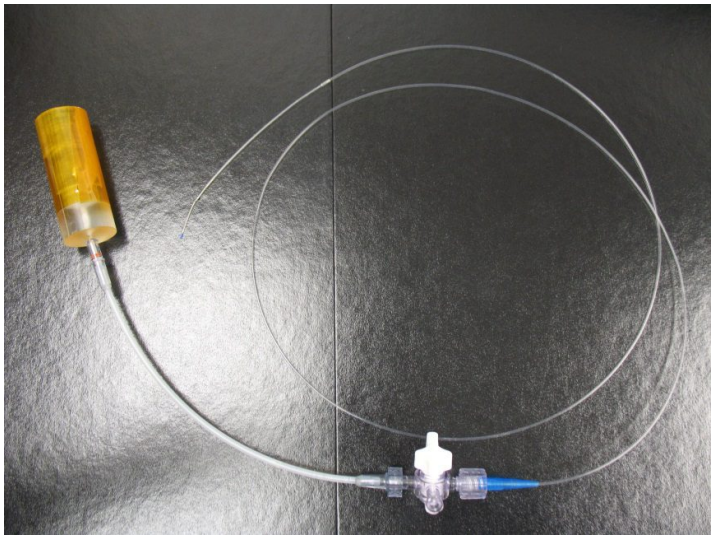

Fig2. Photography of OCT-US catheter sheath

For the *in vivo* rabbit experiment, a male New Zealand white rabbit weighing 3.9 kg was anesthetized and intubated during the surgical and imaging procedures. Details of the surgical procedure can be found in Hoang *et al* (13). Perfluorocarbon (PFC) was used as a flushing agent for OCT. The images were acquired with Newport inc. linear stage to automatic pull back at a rate of 0.2mm/s.

For the *in vivo* swine experiment, a 54.0kg female Yorkshire white swine is anesthetized by Ketamine and xylazine. An oblique skin incision was made into the right groin above the area overlying the femoral artery. The integrated OCT-IVUS catheter was inserted into the coronary artery from Femoral right with the lead of x-ray detection. Data were recorded after the 2 marker bands were detected by Phillips Family R2 BV Pulsera C-Arm. Perfluorocarbon (PFC) was used as a flushing agent for OCT.

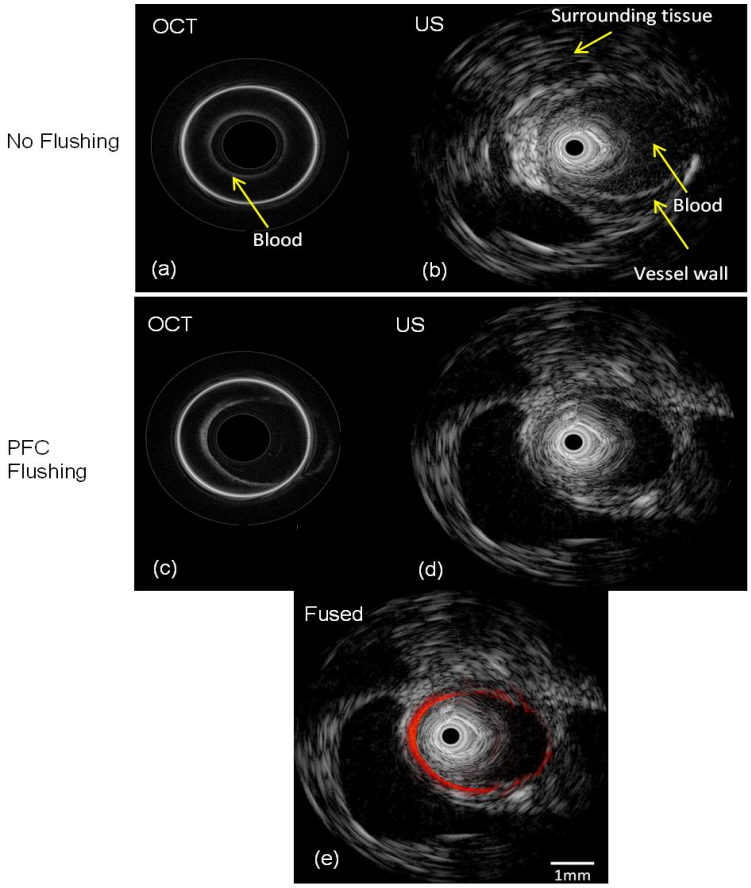

Fig 3. OCT (a) and US (b) images of a rabbit abdominal aorta without Perfluorodecalin (PFD) flushing. OCT (c), US (d) and combined (e) OCT-US images with PFD flushing

3. RESULTS AND DISCUSSION

In vivo imaging of the normal rabbit abdominal aorta was performed using this miniature probe and integrated system. Figures 3(a) and (b) show the OCT and US images without flushing. Since blood is highly scattering for OCT but serves as natural transmission media for US, no vessel structure could be seen in the OCT image [figure 3(a)] but was clearly visualized in the US image [figure 3(b)]. When using PFC as a flushing agent, a clear view was obtained for OCT as shown in figure 3(c). Again, the fused image as shown in figure 3(e) shows that the OCT and US images match well. We can see the aorta surface with fine resolution in the OCT image and deep penetration depth into the aortic wall in the US image.

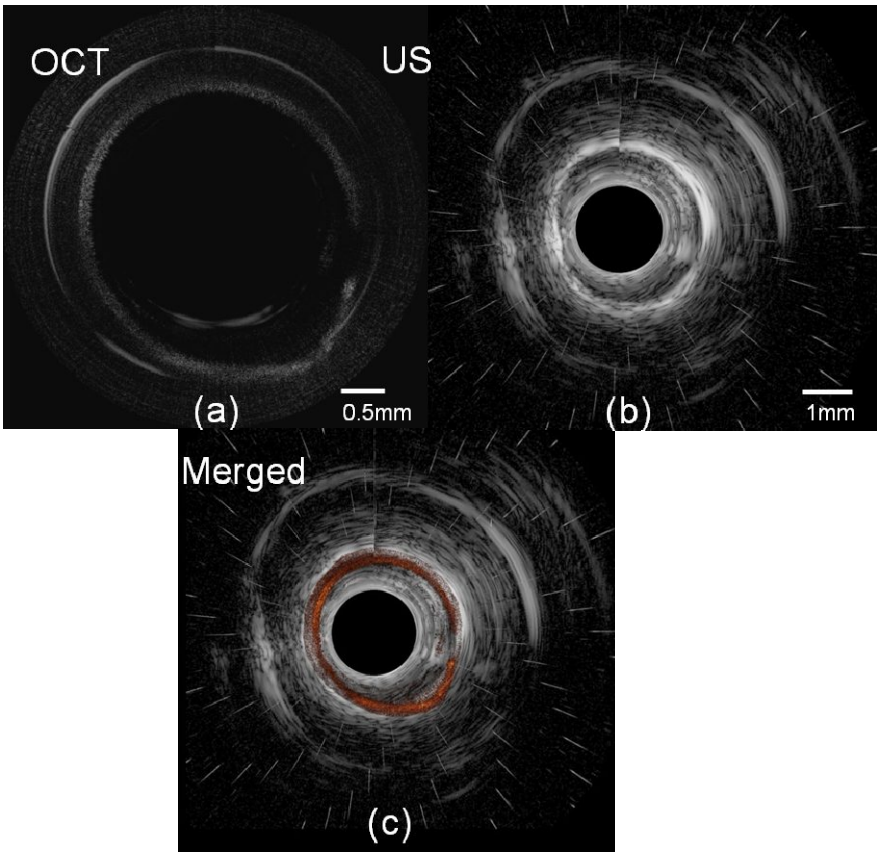

Fig 4. OCT (a), US (b) and merged(c) images of a swine coronary artery with Perfluorodecalin (PFD) flushing.

OCT and US images of a porcine coronary artery specimen with calcified plaque is shown in figure 4. The coronary artery can be identified in both images. The structure of inner layer of artery wall is clearly seen in OCT image [figure 4(a)] due to the high axial resolution and high contrast of OCT. However, the OCT system could not visualize the entire depth of the vessel wall, and its maximum penetration depth in this image was about 0.4 mm. But the US [figure 4(b)], penetration depth was much deeper than that of OCT (the radius of the image is 4.5mm). The contour of the vessel in the OCT image matches very well with that in the US image, as shown in figure 4(c) which indicates that the two images were taken at approximately the same site.

4. CONCLUSION

We have successfully developed a miniature integrated OCT-US probe with an outer diameter of 0.69mm which is suitable for *in vivo* imaging. *In vivo* imaging of both rabbit and swine demonstrates the feasibility of our system for intravascular imaging. The results of these experiments hold promise for this integrated system to be used in clinical study, providing high resolution and high penetration depth for better assessment of vulnerable plaque,.

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