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# Miniaturised all-optical ultrasound probe for thrombus imaging

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## ABSTRACT

All-optical ultrasound (OpUS) has emerged as an imaging paradigm well-suited for minimally invasive procedures. In particular, OpUS has demonstrated potential in endovascular imaging due to its high degree of miniaturisation and mechanical flexibility, high imaging resolution and immunity to electromagnetic interference. Here, we present the first human thrombus imaging using an OpUS device, which was performed on an extracted clot. The results demonstrate the feasibility of using OpUS for thrombus imaging, with the ultimate goal of guiding minimally invasive endovascular clot retrieval procedures.

**Keywords:** Optical ultrasound, Photoacoustic, Minimally invasive surgery, Thrombus imaging

## 1. INTRODUCTION

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), is the third most common cardiovascular disease with an overall annual incidence of 100–200 per 100,000 people.[1,2] If untreated, acute PE is associated with a significant mortality rate, and accompanying humanistic and economic burden. Early thrombus removal with minimally invasive interventions reduces the risks of VTE complications. However, the thrombus age and molecular characteristics including its fibrin composition may determine the success of interventions.[3,4] Therefore, peri-operative objective assessment of the thrombus age and molecular characteristics will help improve the clinical decision making, risk stratification, treatment including anti-coagulation regimen, and reduce complications. There is no such assessment tool available currently, and clinical decision is based solely on subjective history and conventional imaging. The challenge we propose is to develop a pre- or peri-operative biomedical imaging and sensing material that can objectively determine the age and molecular characteristics of *in vivo* venous thrombus.

All-optical ultrasound (OpUS) is emerging as an alternative paradigm which is well suited for minimally invasive cardiovascular procedures. With this technique, ultrasound waves are both generated and received using light.[5] OpUS can provide broad ultrasound transmission bandwidths and high reception sensitivity for high-resolution interventional imaging.[5,6] Additionally, the use of optical fibres for light delivery allows for miniaturisation of the device and immunity to electromagnetic interference.[7] When integrated into a medical catheter, these devices are well-suited for imaging within the human body, in areas such as intravascular imaging, where space constraints are crucial. Furthermore, OpUS devices utilise low-cost materials and fabrication processes which are ideal for single use devices.

Previously, OpUS has been used for 2D imaging of vascular tissues *ex vivo*[5] and for M-mode intracardiac imaging *ex vivo*.[6,7] Recently, rotational, side-viewing OpUS imaging has shown strong potential for intravascular imaging.[8] In this study, we performed a feasibility study for OpUS imaging of an *ex vivo* human thrombus,

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extracted from a peripheral vessel of a patient during a clot retrieval procedure. The OpUS device used here comprised two optical fibres; a multimode fibre with an optically absorbing composite coating for ultrasound generation via the photoacoustic effect, and a single mode fibre with a plano-concave microresonator for ultrasound reception. The high-resolution images acquired by the OpUS device demonstrated imaging through the full thickness of the thrombus. These first-of-their-kind images of *ex vivo* human tissue represent a first step towards using OpUS for diagnosis and treatment guidance during endovascular surgery.

## 2. MATERIALS AND METHODS

### 2.1 Optical ultrasound imaging system

The all-optical ultrasound imaging system comprised two parts: the fibre-optic device and an opto-electronic console for interrogation (Figure 1). The fibre-optic device comprised two optical fibres; one for ultrasound generation and one for ultrasound reception. For ultrasound generation, a 400 µm core multimode optical fibre delivered photoacoustic excitation light to a composite coating consiting of reduced graphene oxide (rGO) and polydimethylsiloxane (PDMS). The fabrication process for the composite and transmitter was described in a previous work.[9] In brief, a solution of rGO and xylene was prepared by adding 500 mg rGO to 2.5 ml xylene. Then, the prepared optical fibre with a flat end face was dipped into the rGO and xylene solution and removed to form a coating on the fibre end face. The coated fibre was left for 24 h in ambient conditions to dry.

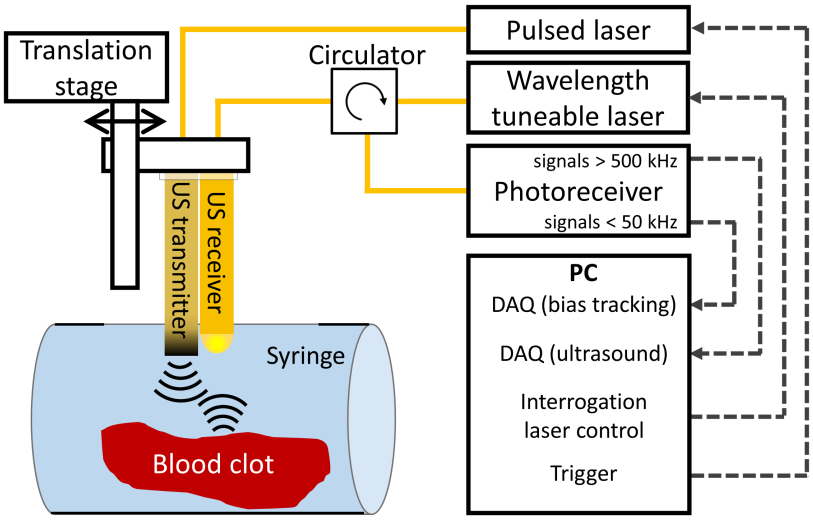


Figure 1. The schematic of the OpUS system for thrombus imaging. DAQ: data acquisition.

Subsequently, the coated fibre was dipped into a PDMS solution (MED-1000, Polymer Systems Technology, UK) and directly removed. The rGO and PDMS coated fibre was left to cure in ambient conditions for a further 24 h. The fabricated ultrasound transmitter generated ultrasound peak-to-peak pressure in excess of 1 MPa, with corressponding bandwidth of $>$ 20 MHz, allowing for promising ultrasound wave penetration depth and high imaging resolution. The optical ultrasound receiver comprised a plano-concave microresonator on a single mode optical fibre using the design and fabrication process described in previous work.[10] Briefly, a dielectric mirror was deposited onto the end face of the single mode fibre. Subsequently, the fibre was coated with an epoxy dome and then another dielectric mirror was deposited. For protection, a Parylene C overcoat was applied to the distal fibre end. The optical ultrasound imaging console that controlled ultrasound generation and interrogated the plano-concave microresonator comprised two lasers. A Q-switched Nd:YAG laser (SPOT-10-500-1064, Elforlight, UK) with wavelength of 1064 nm, a pulse width of 2 ns, pulse energy of 30 µJ, and repetition rate of 100 Hz was used to irradiate the rGO-PDMS composite coating for ultrasound generation. For ultrasound detection, a wavelength tuneable laser (Tunics T100S-HP CL, Yenista Optics, France) with operating wavelength ranging from 1500 nm to 1600 nm was used to interrogate the plano-concave microresonator. The laser was connected via a fibre optic

circulator, allowing the reflected light to be detected by a photoreceiver that split the output into DC ($< 50$ kHz) and AC ($> 500$ kHz) components. The DC component was used to track the optimum bias point, whilst the AC component recorded the modulation of the reflected optical power caused by impinging ultrasound waves. To optimise the sensitivity of the plano-concave microresonator, the wavelength of tuneable laser was biased to a local maximum derivative of the interferometer transfer function (ITF). In this case, the received ultrasound signal can be converted from the variations of the reflected optical power induced by impinging ultrasound waves. To form the OpUS device, the fibre optic ultrasound transmitter and receiver were held together using the heat shrink tubing and their end faces were aligned at the same level (Figure 1). The total lateral dimension of the device was less than 1 mm.

### 2.2 *Ex vivo* human thrombus imaging

Research ethical approval for obtaining human clots was obtained from the Royal Free London NHS Foundation Trust and UCL Biobank (REC reference: 21/WA/0388). For imaging *ex vivo*, the thrombus sample was placed in a syringe (10 ml) filled with saline. The syringe had a customised window (30 mm $\times$ 20 mm) on the side wall. The OpUS device was mounted on a motorised stage (MTS50/M-Z8, Thorlabs, UK) and placed above the thrombus sample through the window on the syringe (Figure 1). During imaging, the OpUS device was translated laterally, across the whole segment of the thrombus sample with a step size of 50 µm. For each step, an ultrasound A-line was acquired. Prior to display, the signals acquired underwent several image processing steps. The A-lines were concatenated and underwent bandpass filtering (Butterworth, 10-40 MHz, 4th order). The cross-talk signals originating from the direct transmission of ultrasound wave from the coating were reduced using a general linear model.[5] Subsequently, image reconstruction was performed using a k-space method.[11] Finally, envelope detection was effected with the Hilbert transform; logarithmic transformation was performed prior to display.

## 3. RESULTS AND DISCUSSION

With the *ex vivo* human thrombus sample, the OpUS imaging provided visualisation through the full thickness of

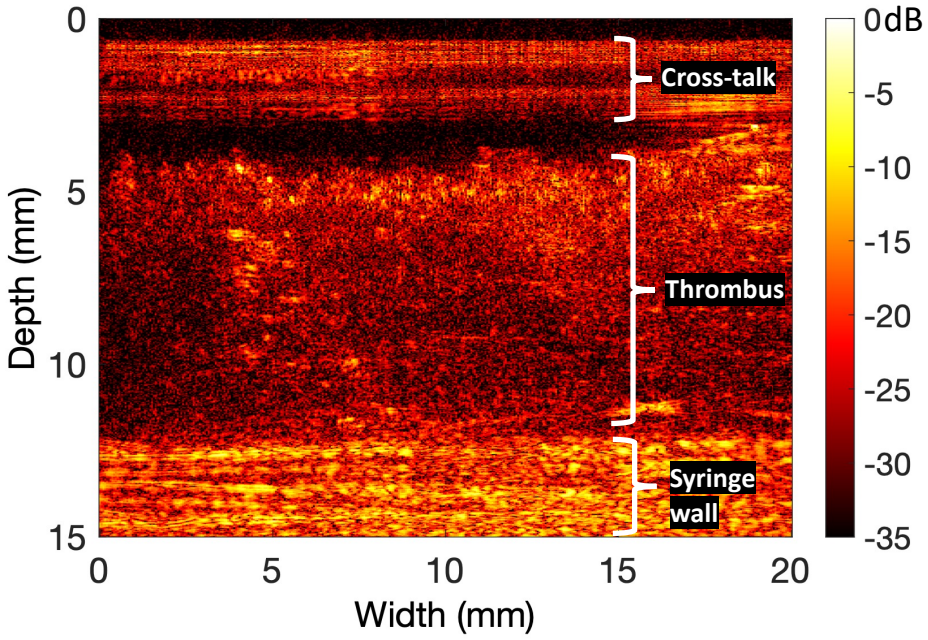


Figure 2. *Ex vivo* human thrombus OpUS image showing contrast throughout the full extent (7 mm) and beyond it to the syringe wall. The cross-talk arising from direct transmissions from the fibre-optic generator to the receiver is apparent in the first 3 mm.

the thrombus (7 mm), with a dynamic range of 35 dB (Figure 2). The OpUS image had a granular texture with several hyperechoic regions of unknown provenance. Speculatively, the texture and the ultrasonic attenuation charateristics obtained with OpUS could be used to provide information about the composition of a thrombus from within a vessel, which could in turn be used to determine its age (Figure 2). The age of a thrombus may influence the treatment strategy: acute and subacute thrombi can be treated with pharmacomechanical thrombectomy, while chronic thrombus can be treated with balloon angioplasty and stenting.[12,13] Additionally, OpUS could be used to determine the source of a thrombus, such as whether it was of arterial or venous origin, whether it was related to cancer or benign conditions, and whether it was caused by an embolus from cardiac arrhythmia or a localised rupture atherosclerotic plaque. This information could be useful in determining the underlying pathology and formulating an appropriate treatment plan. Furthermore, therapeutic modalities such as laser thrombolysis could be integrated, thereby providing concurrent treatment and imaging guidance. Future studies will explore the histological correlates of *ex vivo* thrombi of different ages and sources, and progress to *in vivo* imaging.

## 4. CONCLUSION

This study demonstrated the first-ever *ex vivo* human blood imaging by a miniaturised all-optical ultrasound device. With this device, high-resolution OpUS images containing potentially clinically relevant features were obtained. This proof-of-concept work provides a very early demonstration of the capability of OpUS imaging to visualise thrombi, and sets the stage for more detailed studies to assess the clinical utility of this modality for guiding endovascular treatment of venous thromboembolism (VTE) and deep vein thrombosis (DVT).

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