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Zhang, Tianyu; Shepherd, Simon; Huang, Zhihong; Macluskey, Michaelina; Li, Chunhui

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Development of an intraoral handheld optical coherence tomography-based angiography probe for multi-site oral imaging

TIANYU ZHANG, SIMON SHEPHERD, ZHIHONG HUANG, MICHAELINA MACLUSKEY, AND CHUNHUI LI

1 Centre for Medical Engineering and Technology, University of Dundee, Dundee DD1 4HN, UK
2 School of Dentistry, University of Dundee, Dundee DD1 4HN, UK
* c.li@dundee.ac.uk

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Oral cancer, primarily oral squamous cell carcinomas (OSCC), is a major health concern worldwide. The current gold standard for the diagnosis of OSCC is biopsy and histopathological analysis, which is invasive and can place a huge financial burden on the healthcare system. Optical coherence tomography-based angiography (OCTA) is a non-invasive imaging technique that shows promise as an imaging modality to aid the diagnosis of OSCC. This Letter outlines the development of a handheld intraoral OCT probe applied to a swept-source OCT system with an angiography function for oral applications. The probe has a thin body with a diameter of 17.8 mm and a two-lens system with a working distance that is adjustable from 20.92 mm to 24.08 mm, a field of view 9 mm in diameter, an imaging depth of 1.7 mm, and resolutions of 39.38 µm (laterally) and 33.37 µm (axially). This probe was used to scan 14 oral sites to evaluate its ability to scan various sites in the oral cavity. This system has the potential to reduce invasive procedures and aid early OSCC diagnosis.

Oral squamous cell carcinoma (OSCC) is highly prevalent and was associated with a high mortality of 177,757 in 2020 globally [1]. Oral potentially malignant disorders (OPMD) often precede and may develop into OSCC. Should the malignant transformation be diagnosed early, subsequent treatments of OPMD may reduce the increased morbidity associated with late diagnosis [2]. Therefore, early diagnosis of OSCC or even preventing OPMD from developing into OSCC plays an important role in fighting against oral cancer. The current gold standard for the clinical evaluation of oral lesions is physical examination followed by biopsy and histological evaluation [3,4]. However, oral biopsies are invasive, which can induce risks of inflammation, bleeding, and infection, and can also cause significant discomfort to patients and place burdens on healthcare systems [3,5]. Therefore, an economically robust and transformative technology that can improve diagnostic efficiency and reduce the need for invasive biopsy could be transformative for patients diagnosed with oral mucosal lesions, including OPMD. There are several imaging techniques that have the potential to allow the early detection of OSCC or OPMD, such as mucoscopy [6], high-frequency ultrasound imaging [7], fluorescence photography [8], confocal endomicroscopy [9], and orthogonal polarization spectral imaging [10]. However, these techniques have limitations—either the image resolution is too low or the imaging depth is too shallow to provide reliable image-based markers—and none have been proven to be equivalent or superior to the current clinical examination for the early detection of oral lesions [11,12].

Optical coherence tomography (OCT) is a non-invasive imaging technique offering high-resolution images of biological tissue [13]. However, its structural signals are not sufficient for diagnosis or differentiating lesions [14]. Angiogenesis, the formation of new blood vessels, plays a vital role in supporting tumor cells and has been identified as a potential diagnostic tool for OSCC [15–17]. OCT-based angiography (OCTA), a functional OCT application, can detect the microvascular network within tissue [18]. OCTA has proven useful in the early detection and monitoring of various cancers [19,20]. Therefore, it is suggested that OCTA has the potential to be helpful in the early detection and imaging of OSCC or OPMD. Among recent oral applications of OCTA [21–25], although results have been promising and the potential of intraoral OCTA imaging has been demonstrated, access to all areas and sufficient OCTA mapping of the oral cavity to image a clinical lesion remain unproven. Specifically, the scanning probe designed by Wei et al. is similar to a dermatological OCT scanning probe and is too thick to image the entire oral cavity, only its outer surfaces (e.g., gingiva and lips) [25]. In addition, although Choi and Wang designed a small and thin probe with a reflective mirror which would be able to scan some difficult oral areas, this probe is only 23 mm long, which, as a result, cannot reach less accessible regions of the oral cavity [23]. Tsai et al. designed a handheld OCT probe that protrudes 92 mm and is 10 mm thick [24]. However, it has a limited field of view (FoV), 2 × 2 mm². Lastly, although Le et al. firstly used a wide-view OCT probe which would be too large for intraoral imaging [21] and then designed an intraoral probe [22],
their study only presented the results of dental hard tissue assessment and did not explore the possibility of full-site oral imaging.

To explore the feasibility of full-site oral imaging using OCTA, in this study we designed an intraoral handheld scanning probe with an OCTA capability for oral imaging applications. We used the probe to scan 14 oral locations in 3 healthy participants: the buccal mucosa, upper lip, lower lip, hard palate, soft palate, posterior floor of the mouth, anterior floor of the mouth, lower labial (outside) gingiva, lower lingual (inside) gingiva, upper labial gingiva, upper palatal (inside) gingiva, dorsal surface of the tongue, lateral border of the tongue, and ventral surface of the tongue. These locations were chosen as they are high-risk oral sites that are prone to OSCC [26]. This study was reviewed and approved by the Research Ethics Committee of the University of Dundee. Informed consent was obtained from all subjects before scanning.

The imaging system used in this study is a lab-built, portable, non-invasive swept-source optical coherence tomography (SSOCT) system with an OCTA function, which was demonstrated in previous studies [27]. This system utilizes a swept-source vertical-cavity surface-emitting laser (SL132120, Thorlabs Inc., Newton, MA, USA) with a center wavelength of 1300 nm, a bandwidth of 100 nm, and a sweeping rate of 200 kHz. The laser is firstly split by a 50/50 beam splitter into reference and sample arms. The sample arm is integrated into a handheld probe designed for ease of use and portability. This system was operated with LabVIEW, while the post-processing was performed on MATLAB.

The scanning probe was specifically designed with a slender, elongated, and rounded profile (diameter of 17.8 mm) to facilitate the scanning of hard-to-reach areas within the oral cavity. A cross-sectional optical diagram of the probe is depicted in Fig. 1(A), and a photograph is presented in Fig. 1(B). The scanning probe comprises a collimator, a display screen, a CCD camera, a set of XY galvo mirrors (6210H, Cambridge Technology, Bedford, MA, USA), an objective optical tube, and a scanning tip. The display screen and CCD camera can help with accurate targeting during scanning, while the optical tube contains a two-lens system that functions as an objective lens. The rear lens (AC254-125-C, Thorlabs Inc., Newton, MA, USA) is an achromatic doublet with a focal length of 125 mm and a diameter of 25.4 mm. The front lens (AC127-075-C, Thorlabs Inc., Newton, MA, USA) is also an achromatic doublet, possessing a focal length of 75 mm and a diameter of 12.7 mm. While the optical tubes are supplied by Thorlabs, an adjustable tube (SM05V05, Thorlabs Inc., Newton, MA, USA) is positioned between the two lenses. Consequently, the distance between the front and rear lenses varies from 76.69 mm to 84.69 mm, resulting in an effective working distance for this two-lens system ranging from 20.92 mm to 24.08 mm. A 3D-printed side-viewing scanning tip, containing a reflective mirror (ME05S-P01, Thorlabs Inc., Newton, MA, USA), is situated at the optical tube’s end, enabling easy access to regions within the oral cavity that a conventional forward-viewing probe cannot reach. The biocompatible 3D-printed (material: ABS-M30) scanning tip is disposable and replaced for each volunteer, ensuring compliance with infection control practices. The designed probe can achieve maximum FoV with a diameter of 9 mm.

Measurements were recorded to evaluate the performance of the scanning probe. Firstly, the point spread functions (PSFs) were measured at different imaging depths in air to evaluate the roll-off sensitivity of this system, which is shown in Fig. 2(A). Additionally, the full width at half maximum (FWHM) of each PSF was calculated as the axial resolution value, as shown in Fig. 2(B). The mean FWHM value is 33.37 µm, which is considered the axial resolution of this intraoral scanning probe. In addition, the lateral resolution was also tested with a 1951 USAF test target (R3L3S1PR, Thorlabs Inc., Newton, MA, USA). The resolved element based on the Rayleigh criterion [28] was group 4 element 5, which corresponds to a lateral resolution of 39.38 µm.

![Fig. 1. (A) Optical diagram and (B) photo of the intraoral probe in this study.](image)

![Fig. 2. (A) Logarithmic plot of the measured sensitivity profiles at various imaging depths in air. (B) Axial resolution values, defined as the FWHMs of the PSFs, at various depths in air.](image)
Fig. 3. Cross-sectional structural results for a number of scanning sites within the oral cavity: (A) buccal mucosa, (B) upper lip, (C) lower lip, (D) healthy hard palate, (E) hard palate with a burn wound, where the wound area is indicated by a dashed rectangle, (F) soft palate, (G) posterior floor of the mouth, (H) anterior floor of the mouth, (I) lower labial (outside) gingiva, (J) lower lingual (inside) gingiva, (K) upper labial (outside) gingiva, (L) upper palatal (inside) gingiva, (M) dorsal surface of the tongue, (N) lateral border of the tongue, (O) ventral surface of the tongue. All scale bars represent 500 µm.

The scanning protocol employed in this study was the B-M scan, which has been utilized in previous research [27]. Each OCTA scan is composed of numerous A-lines, with each A-line providing structural depth information along the axial axis (Z axis) at a specific location. The X galvo mirror can manipulate the laser orientation along the X axis, enabling the acquisition of multiple A-lines that coalesce into a single B-frame. By repeatedly capturing B-frames at the same position, angiography information can be extracted [27]. The Y galvo mirror facilitates the B-M scan on a line-by-line basis, generating a 3D volume dataset encompassing both structural and angiography information. In this study, each OCTA scan comprised one OCT data cube with dimensions of 400 × 400 × 960 × 3 (X × Y × Z × N in pixels), which took about 4 seconds in total. These scanning parameters correspond to an en-face scanning range of 5.2 × 5.2 mm². The imaging depth is ∼1.7 mm.

A post-processing pipeline was utilized to extract angiography information and visualize vascular networks. Firstly, the interference signals were subjected to the Fourier transform, and then the windowed eigen-decomposition (wED) algorithm [27], which can extract the angiography signals. When selecting layers along the Z axis, the epithelium and lamina propria layers were selected, which contain the vascular information for the tissue, and are widely used in the assessment of oral diseases [16,29]. Lastly, en-face projection results were generated by using a green-red depth-encoded maximum intensity projection (MIP) algorithm.

In this study, 14 areas inside the oral cavity were scanned to demonstrate the full-site oral imaging ability of our intraoral OCTA probe. Figure 3 shows cross-sectional structural scan results from the various oral sites. Cross-sectional views of normal, healthy mucosa and mucosa with a burn wound are shown in Figs. 3(D) and 3(E), respectively, where the wound area is indicated by the dashed rectangle. The OCTA results are presented as en-face MIP images in Fig. 4. These MIP results are depth encoded in green-red color coding. The full imaging depth...
range in Fig. 4 is from 26 µm to 1700 µm, which corresponds to the hue changing from green to red, as shown in the color bar. The intensity of each hue value represents the OCTA intensity. Both Figs. 4(D) and 4(E) show results from the hard palate; these exhibit normal, healthy mucosa and mucosa with a burn wound, respectively. The dashed square in Fig. 4(E) indicates the wounded area.

This study demonstrated the feasibility of implementing OCTA imaging within the oral cavity. Furthermore, a specially designed scanning probe facilitated ready access to multiple oral sites to assess the potential for comprehensive oral cavity imaging. While a limited number of OCT studies have addressed in vivo OCTA imaging of the human oral cavity [21–25], none have successfully achieved full-site oral imaging. Our design of intraoral scanning probe has a slender, elongated, and rounded profile and a side-viewing scanning tip to facilitate the scanning of hard-to-reach areas within the oral cavity. High-resolution structural cross sections and microvascular networks with depth information on 14 intraoral sites were demonstrated using the designed probe.

Although this study successfully imaged the microcirculation within the oral cavity, the current probe design is difficult to stabilize due to the probe weight (719 g) and subject motion. We are aiming to develop a motion-tracking system for further clinical study. Another potential solution involves replacing the existing swept-source laser with one featuring a higher sweeping rate, which would decrease the scanning time and thus reduce the motion artifacts during scanning. Moreover, although the designed probe’s FoV may not cover the whole lesion area, a 3D stitching algorithm [30] from our previous study can be applied. Additionally, enhancing the lateral resolution to the capillary level (<8 µm) is crucial for accurately resolving microvessels and ensuring the reliability of quantitative analysis, such as vessel diameter and density. However, increasing the resolution may increase the sensitivity of OCTA measurements to bulk motion in the tissue due to its enhanced resolving capability, resulting in a reduced flow contrast of the angiogram. Hence, we did not try to achieve super-high resolution with our probe design. Based on clinical needs, modified probes with more compact sizes or better lateral resolution can be developed for more accurate vascular mapping. To further evaluate our probe design, quantitative analysis of a database with more healthy participants will be needed as a continuation of our research.

In conclusion, this study represents the first in vivo examination of comprehensive oral-cavity angiography imaging using a purposefully designed intraoral probe with an SS OCT system for scanning oral sites that are prone to oral mucosal disease, OPMD, and OSCC. The use of such a probe by primary care practitioners would allow early referral of high-risk lesions to specialist care. In a specialist environment, this could reduce the need for invasive biopsy and help delineate the full scope of a lesion. Should its sensitivity and specificity be demonstrated in future work, this system has the potential to replace invasive biopsy procedures and detect oral cancers at an earlier stage, leading to improved patient outcomes.

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Data availability. Data underlying the results presented in this paper are not publicly available at this time but may be obtained from the authors upon reasonable request.

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