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Authors

Heidari, Andrew Emon
Sunny, Sumsum P
James, Bonney L
[et al.](#)

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Optical Coherence Tomography as an Oral Cancer Screening Adjunct in a Low Resource Settings

Andrew E. Heidari, Sumsum P. Sunny, Bonney L. James, Tracie Lam, Anne V. Tran, Junxiao Yu, Ravindra D. Ramanjinappa, Uma K, Praveen Birur, Amritha Suresh, Moni A. Kuriakose, Zhongping Chen, Petra Wilder-Smith

Abstract— Oral cancer is the sixth most common cancer worldwide, predominantly seen in low and middle-income countries (LMIC). Two thirds of all cases are detected at a late stage when prognosis and treatment outcomes are poor. Oral lesions are commonly detected by visual inspection, followed by invasive surgical biopsy and time-consuming histopathological analysis. Optical coherence tomography (OCT), a minimally invasive tomographic imaging technology, can be used to non-invasively identify premalignant or malignant change in the oral mucosa. In this study, a mobile OCT imaging system was designed, constructed and tested for its performance as a point-of-care oral diagnostic device in a LMIC. Twenty patients with suspicious oral lesions and 10 healthy subjects were enrolled in this pilot study. Two dimensional OCT images as well as clinical examination data, risk habit history and histopathology were collected. OCT images for healthy oral mucosa, dysplasia and malignancy were evaluated in a blinded fashion by visual scoring and computed image processing techniques. It was found that the OCT image processing algorithm performed at or exceeded the performance of visual observer scoring of OCT images.

Index Terms— image classification, cancer, biomedical optical imaging, biomedical image processing, optical coherence tomography

I. INTRODUCTION

ORAL squamous cell carcinoma (OSCC) ranks as the sixth most common cancer worldwide, accounting for approximately 400,000 new cancer cases annually [1]. Two-thirds of OSCC cases originate in low-resource countries of the world [2]. The high morbidity and mortality of OSCC are attributed primarily to late diagnosis, with more than two thirds of OSCC cases diagnosed at loco-regionally advanced states [3]. Prognosis of OSCC is stage dependent, with an average five-year disease-free survival rate of 80-90% if diagnosed at stage I and II and only 20% if diagnosed at stage III and IV [1]. Thus, early detection and prompt treatment offer the greatest hope to patients with oral cancer, providing the best chance of minimally invasive treatment and better disease outcomes.

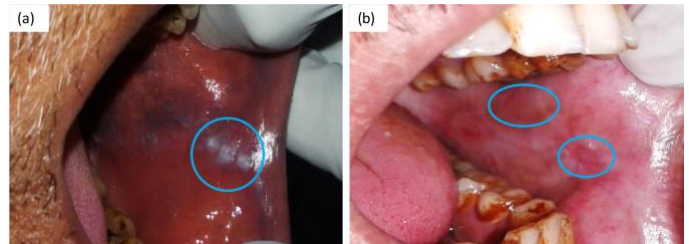


Fig. 1. (a) Left buccal mucosa leukoplakia circled in blue (b) Left buccal mucosa erythroplakia circled in blue.

A. Oral Cancer Clinical Unmet Need

Oral cancer is frequently preceded by oral potentially malignant lesions (OPML) which typically present as red, white or speckled lesions as can be seen in Fig. 1. Although 1.5%-20% of these lesions progress to OSCC over 5 years [4-5], malignant transformation rates may be as high as 51% for individual lesions such as erythroplakia [5]. The mechanism of malignant transformation remains unclear, and there are no clear prognostic markers informing on risk in individual patients or to guide the specialist's treatment plan [7]. Therefore, patients with OPMLs require frequent and careful monitoring to ensure early detection of malignant transformation. Currently, monitoring is performed by visual examination and incisional/excisional biopsy. The diagnostic accuracy of visual examination is unreliable. In addition, biopsies have poor patient compliance and require specialist skills as well as expensive laboratory facilities that are typically limited to high-resource environments [4]. The key challenge to reducing the mortality and morbidity of OSCC is to generate strategies to identify and detect OSCC at an early stage and to develop a non-surgical means of monitoring lesions that are at risk of malignant transformation. By overcoming this barrier, OSCC outcomes will improve considerably. In LMICs, this need is particularly urgent in remote areas due to the very limited availability of oral cancer specialists.

Approximately two-thirds of OSCCs occur in LMICs, with very high rates in South and South-East Asia (e.g., in Bangladesh, India, Malaysia, Nepal, Pakistan, Sri Lanka, Thailand, and Vietnam) [7]. Tobacco smoking and chewing, betel quid use, alcohol abuse and poor oral hygiene are the primary factors for greater oral cancer prevalence [8]. India has the 8th highest age-adjusted death rate of head and neck cancers in the world, and among females the rate is the highest in the

world [9]-[13]. The Indian sub-continent accounts for one-third of the world burden [14]. Oral cancer is the most common cancer in India, accounting for 40% of all cancers overall, and for more than 50% of all cancers in some areas of the country [14]. While the 5-year survival rate in the U.S. for OSCC is 62%, the survival rate is only 10-40% and the cure rate is approximately 30% in the developing world [15].

B. Optical Coherence Tomography as a Potential Solution

Optical coherence tomography, a minimally invasive, non-ionizing imaging modality, can generate high-resolution cross-sectional images of near-surface abnormalities in complex tissues [16]. It can be compared to ultrasound imaging conceptually. Ultrasound generates tomographic images through resolving the time-of-flight acoustic reflections caused by differences in acoustic impedance of tissue anatomy. Given the relatively slow speed of sound in air and tissue, 330m/s to 1,540m/s respectively, conventional electronic analog to digital circuitry can be used to calculate the delay and intensity between the emitted ultrasonic waves and the reflected echo from the tissue sample [17]. Similarly, OCT can provide tomographic images through resolving the ballistic back scattered light based echoes generated by differences in tissue refractive indices. Since the speed of light through air and tissue is several hundred thousand orders of magnitude larger than sound at 299,700km/s and 222,000km/s respectively, alternative approaches such as low coherent interferometry must be used to resolve light based echoes [18]. For a typical spectral-domain OCT system (SD-OCT) light from a low-coherent superluminescent diode light source is coupled into a fiber based Michelson interferometer comprised of a static reference reflector, 2-D scanning probe sample arm, and spectrometer. Low-coherent light is initially split into a reference and sample beam where their reflections are later combined, interfered, and detected by a spectrometer. The difference in the distance traveled between the two interference arms will cause shifts in frequency that are captured in the interference fringe pattern. From the relationship between frequency and path length of the light traversed, the interference fringe pattern is converted into cross-sectional tomographic images of tissue generated at near histologic resolution with <15 μm depth resolution. The images show the macroscopic characteristics of the epithelial and sub-epithelial structures. With an oral mucosal penetration depth of approximately 2mm, the imaging range of OCT is suitable for interrogating the thin (0.2-1mm) human oral mucosa.

C. Optical Coherence Tomography Oral Cancer Prior Art

There exists a substantial body of prior work utilizing OCT to diagnose and classify normal, dysplastic and malignant lesions in both animal and human in-vivo studies [19-22]. Previous studies have shown that the oral mucosa clearly loses its well stratified structure as it progresses from normal to invasive squamous cell carcinoma. Such studies have acquired OCT images and visually compared them to corresponding histopathology. Specifically within the last 10 years, researchers have further investigated quantitative parameters that are sensitive to classify OCT images removing the subjectivity of visual scorers. It has been noted that as tissue

progresses from normal to potentially pre-malignant, the squamous epithelium thickens with respect to a baseline normal [23]. Other groups have investigated the intensity distribution in the depth and lateral direction of OCT B-scans where they have discovered that cancerous cell morphologies tend to resemble a more random depth resolved intensity distribution of the OCT signal than their healthy counterparts [24]. The goal of this study was to develop and deploy a low-cost, mobile OCT imaging system and probe capable of triage output for diagnosing OPMLs and OSCC in Bangalore, India. The initial milestone of this study was to train health care personnel to collect OCT image data for healthy, dysplastic and malignant oral tissue with corresponding histopathology. The data would then be used to develop and assess the accuracy of an algorithm capable of classifying normal, dysplastic and cancerous tissue building upon the prior art of quantitative analytic approaches.

II. METHODS

This prospective clinical study was initiated after obtaining IRB Approval from The Narayana Health Medical Ethics committee (NHH/MEC-CL-2015-279). Patients referred to the Mazumdar Shaw Cancer Center, Bangalore, India, and clinically diagnosed to have OPMLs and malignant lesions were enrolled in the study. Patient overview is shown in Table I.

TABEL I
STUDY PATIENT POPULATION DEMOGRAPHIC AND RISK HABITS

Variables	Frequencies (n=30)	Percentages
Sex		
Male	17	57
Female	13	43
Age		
>40	16	53
<40	14	47
Risk Habits		
None	10	33
Tobacco	20	67
Drinking	0	0
Normal	10	33
Mild dysplasia	5	18
Moderate dysplasia	3	10
Severe dysplasia	2	6
OSCC	10	33

A. Clinical Study Design

After a conventional oral clinical exam, the following six areas were imaged with 2-D OCT: left and right buccal mucosa, dorsal and lateral surfaces of tongue, labial mucosa, and floor of mouth. Two to three averaged 2-D OCT B-scans 500 A-lines in length were acquired at each site as can be seen in Fig. 2. Punch biopsies were then collected as per standard of care from any areas that appeared clinically suspicious and were subsequently processed for histopathological processing. The OPML and malignant lesions were reported as non-dysplastic, mild, moderate or severe dysplasia, or invasive carcinoma based on the World Health Organization criteria [19].

B. OCT Imaging System and Probe

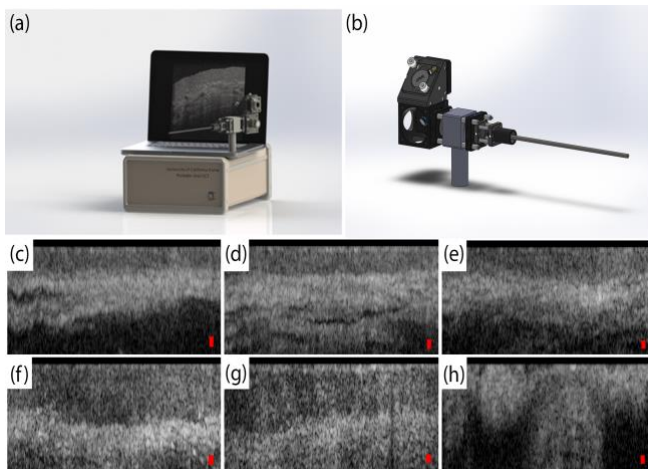


Fig. 2. (a) Portable low cost optical coherence tomography system and probe (b) Close up isometric view of the 2-D forward viewing OCT probe. 2D OCT B-Scans of various area acquired with such probe of the oral cavity including: (c) Floor of the mouth (d) Labial mucosa (e) Gingiva (f) Lateral surface of the tongue (g) Right buccal mucosa (h) Dorsal surface of the Tongue. Red scale bars indicate a height of 100 μ m. OCT images shown clearly provide distinctions between the squamous epithelium, basement membrane, and lamina propria.

In-vivo OCT images were acquired using an SD-OCT system and prototype 2-D scanning long GRIN rod probe Fig. 2(a)-(b). The SD-OCT system using center wavelength of 930nm has an axial resolution of 7.0 μ m and lateral resolution of 15.0 μ m in air. Using a 1.2kHz 1024-point CCD line-scan camera on the spectrometer detection arm, an imaging speed of 2 frames/second was achieved with 500 A-lines/frame. The 2-D long GRIN rod (Gradient lens corporation, Tremont NY) probe is comprised of a gold coated galvanic scanning mirror, a pair of scan lenses, a rigid one pitch gradient refractive index (GRIN) rod and an objective lens. A long rigid one pitch GRIN rod was used in this study to relay light from the proximal portion of the probe to the patient's tissue. For this study, the GRIN rod on the probe was designed to be longer to provide approximately 60cm of separation between the clinician and the patient to ensure social gender appropriateness for a rural population in India.

C. OCT Image Analysis

Retrospective data from 10 subjects each with representative OCT images for healthy, dysplastic and malignant oral mucosa were selected by a non-blinded investigator. These coded OCT images were scored by a blinded visual scorer who had been pre-standardized to 95% agreement with histopathology using 200 standard OCT images with matching histopathological diagnoses from our University of California Irvine OCT image database. After scoring completion, the evaluator was unblinded and then provided advice on optical criteria that could be useful to define normative optical characteristics to generate a diagnostic algorithm for distinguishing between healthy, dysplastic and malignant mucosa. Finally, image data was

evaluated using an image-processing algorithm created in MATLAB (Natick, Massachusetts).

III. IMAGE PROCESSING METHODS

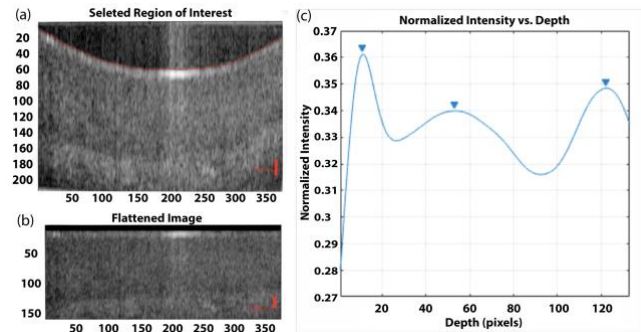


Fig. 3. (a) Edge detection with dynamic programming (b) Flattened ROI (c) Smooth depth intensity distribution. Scale bars indicate a length of 106 μ m.

Preprocessing of OCT images was necessary as imaging artifacts caused by spherical and chromatic aberration in the probe design resulted in distorted OCT images Fig. 3(a). To remove the distorted shape of the oral mucosa an edge detection and flattening algorithm was utilized [20]. OCT images were then classified as normal, dysplastic, and malignant through a two-step decision tree. Initially, OCT images were categorized into two categories: non-malignant (normal and dysplastic) vs malignant through a comparison of optical tissue stratification. Subsequently, the “non-malignant” group was broken down into characterization as either “healthy” or “dysplastic” by observing changes in the deviation of the identified basement membrane at the epithelium- lamina propria junction.

A. Healthy and Dysplastic vs. Malignant

From a superficial observation, the presence of clear and organized epithelial stratification with demarked boundaries in OCT images can readily give the viewer a sense of tissue classification with regard to “non-malignant” vs “malignant”.

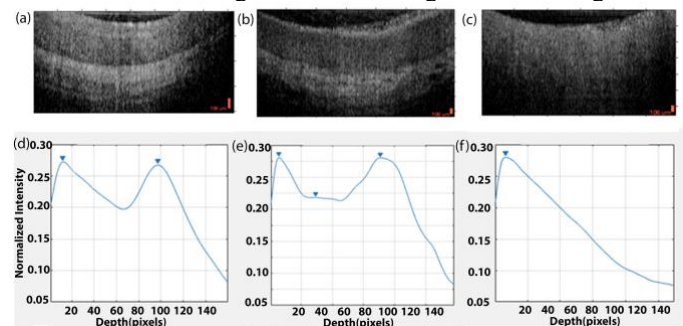


Fig. 4. (a) Normal (b.) Dysplasia (c.) Malignant OCT images of oral mucosa with corresponding depth resolved intensity plots. This series of images illustrates the loss of tissue stratification observed between normal/dysplastic and malignant oral mucosa.

Non-malignant tissue were represented in OCT images by a clear tissue stratification and an intact basement membrane as seen in Fig. 4(a,b). However, as seen in Fig. 4(c) malignant lesions of the oral mucosa lacked tissue stratification and basement membrane delineation. Based on these observations

an algorithm was developed to analyze the depth resolved intensity distribution to distinguish images of non-malignant tissues from those of malignant sites.

Firstly, a region of interest (ROI) was selected from the original OCT image. An edge detection algorithm previously developed was applied on the ROI to obtain the edge of the first layer. The tissue under consideration was then flattened to a given height with respect to the edge previously found. After flattening, averaging was conducted in the lateral scanning direction of the image. The intensity of every 5 vertical A-lines was averaged together to remove speckle artifacts. Lastly, the intensity of every 20 horizontal segments in the depth axis were averaged together to remove the small peaks in intensity along the depth axis seen in Fig. 3(c). A pre-built function in MATLAB was then utilized to determine the number of peaks in the resulting smoothed depth resolved intensity profile.

B. Healthy vs. Dysplastic

Further differentiation within the “non-malignant” tissue group to distinguish healthy from dysplastic areas was achieved by evaluating the epithelium-to-lamina propria junction seen in the OCT images. During the development and progression of dysplasia, the squamous epithelium thickens and begins to grow down into the underlying lamina propria [22]. This downward growth is realized as a change in basement layer morphology seen in Fig. 5(c). Thus, the images of non-malignant oral tissues were analyzed for vertical deviation in the basement membrane. From the flattened images previously described, the algorithm prompts the selection of an ROI that covers the boundary of the epithelium and lamina propria. The area is then subjected to the previously described edge detection algorithm to outline the epithelium-lamina propria boundary. The average height of this edge is computed to then calculate the deviation from this value to epithelium-lamina propria boundary. The absolute value of the deviation from the average height position of the edge is determined for all points across the edge and averaged. The standard deviation of the deviations along the identified edge are calculated and utilized as a classification criterion in addition to the average deviation.

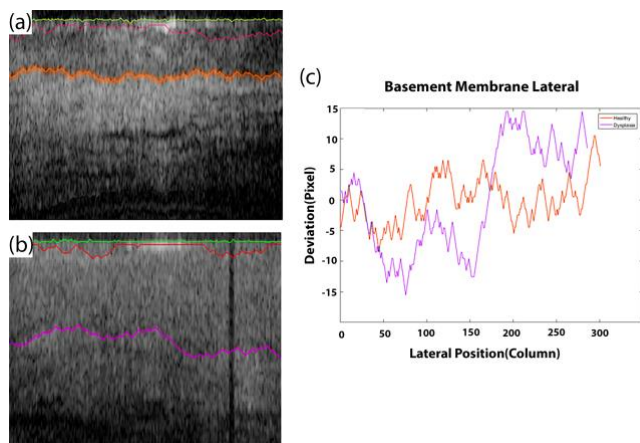


Fig. 5. (a)-(b) Segmented healthy and dysplastic tissue, respectively. Epithelium-lamina propria junction denoted in blue (c) Epithelium-Lamina propria boundary lateral deviation with respect to layer average height.

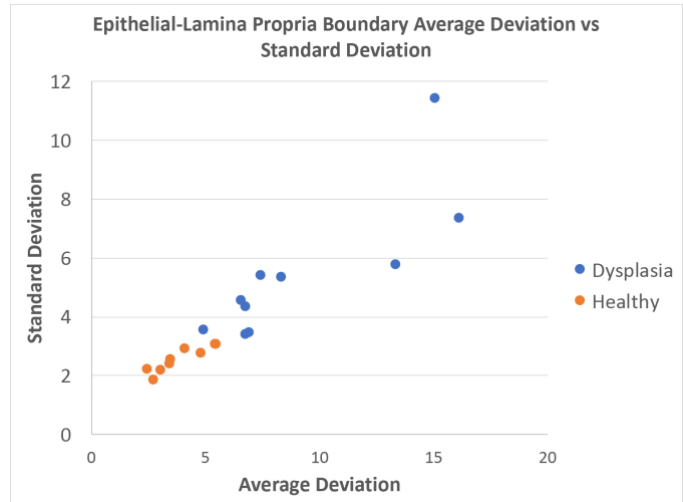


Fig. 6. Scatter plot showing separation between health and dysplastic OCT images based upon the average deviation of the epithelium-lamina propria junction and the standard deviation of the distribution of deviations per boundary

IV. RESULTS AND DISCUSSION

Malignant and pre-malignant or healthy lesions were classified based on the number of peaks identified in the depth resolved intensity distribution. It was found that a minimum of two peaks were observed in the non-malignant oral mucosal images, while only one peak was observed in images of cancerous tissues presented in Fig. 4(c). From this analysis, the number of peaks with a threshold of two peaks were identified as primary diagnostic decision criterion between cancerous and potentially pre-malignant. The loss of heterogeneity between potentially pre-malignant lesions and cancer agrees well with previously published work [25].

Pre-malignant or dysplastic and healthy OCT image classification was achieved through the previously discussed epithelium-lamina propria boundary deviation. As can be seen in Fig. 6, the dysplastic and healthy OCT image data is well separable using the average deviation and edge standard deviation parameters. An average deviation value of 6 provided a sensitivity and specificity of 90 and 100% for the classification between dysplastic and healthy OCT images. The average deviation values for the dysplastic and healthy group provided statistical significance in a student t-test with a p-value of 1.2×10^{-4} . When considering the standard deviation of the distribution of deviations, a standard deviation of 3.3 provided a sensitivity and specificity of 100 and 90% respectively. The standard deviation values for the dysplastic and healthy group also were statistically significant with a p-value of 5×10^{-3} .

Diagnostic agreement with the histopathological gold standard was determined through the Cohen’s kappa coefficient of agreement (κ) as well as diagnostic positive predictive value (PPVs), negative predictive value (NPVs), sensitivity, and specificity for the diagnostic classifications of the clinical scorer and algorithm. The results are summarized in Table II.

TABLE II
DIAGNOSTIC ACCURACY OF OCT IMAGES ANALYZED BY A
CLINICAL OBSERVER AND DIAGNOSTIC ALGORITHM WITH A
GOLD STANDARD OF HISTOPATHOLOGY

	Clinical Observer				
	Sens	Spec	PPV	NPV	κ
Healthy vs. Cancer and Dysplasia	89%	100%	1	0.83	0.90
Cancer vs. Dysplasia	91%	89%	0.91	0.89	0.89
	Diagnostic Algorithm				
Healthy vs. Cancer and Dysplasia	95%	100%	1	0.91	0.95
Cancer vs. Dysplasia	91%	100%	1	0.89	0.90

From Table II we can see that the diagnostic algorithm has a higher κ , PPV, and NPV when differentiating both normal from dysplasia/cancerous lesions and dysplasia from cancerous lesions in comparison to the clinical observer. These results suggest that the diagnostic algorithm could provide a higher level of agreement with the gold standard of histopathology compared to the diagnostic conclusions determined by the clinical observer.

A. OCT Image Analysis: Diagnostic Algorithm vs. Clinical Observer

Diagnostic sensitivity and specificity by the visual scorer were accurate due to extensive scorer training and pre-standardization. Since this study was designed to provide the foundation for developing the basis for a diagnostic algorithm with the goal of identifying “typical” optical parameters for healthy, dysplastic and malignant tissue images acquired with histopathological correlation were included in the study. Sensitivity for differentiating between healthy and dysplastic/cancerous tissue via the image processing algorithm out-performed the clinical scorer by 6%. This could be explained by the notion that clinicians may tend to over-diagnose their patients to prevent a missed diagnosis. However, over-diagnosis can lead to unnecessary tissue biopsy, and possibly reduced patient compliance with any future biopsy recommendations for the purposes of surveillance or diagnosis. It also results in unnecessary cost and use of valuable specialist time and resources.

The diagnostic specificity for differentiating cancer and dysplastic tissues for the clinical observer vs. the diagnostic algorithm differed by approximately 11%, with the algorithm performing better than the clinical scorer. The reduced accuracy of visual scoring in this context could be attributed to the challenge of identifying the visually less evident changes in the OCT image that are typical for dysplasia vs oral squamous cell carcinoma. These results suggest that the OCT system, probe and image processing methods developed can inform on triage and provide diagnostic guidance when specialists for biopsy and histopathological evaluation are not available. By using a standardized image-processing algorithm with identical work flow between patient’s OCT images, the interpretation

uncertainty in a clinical observer’s diagnosis could be removed to permit qualitative analysis of tissue features that may not be obvious to the naked eye.

B. Comparison of OCT to Other Oral Screening Methods

One can observe the diagnostic and screening potential of OCT imaging paired with an image processing algorithm when comparing sensitivity and specificity of other well documented oral cancer screening tests. A conventional method of oral examination (COE), using incandescent light is a long standing standard method for oral cancer screening [26]. For COE typical sensitivity and specificity measured across multiple large scale clinical trials measured 85% sensitivity and 97% specificity [28]. The OCT imaging system and image processing algorithm used in this study evidenced better diagnostic performance than COE. Thus, the proposed OCT-based approach can be a potential adjunct to improve the sensitivity and specificity of COE. However, in a resource rich environment, OCT may not provide similar benefit. In this circumstance the accessibility to biopsy and histopathological processing and interpretation would provide the highest achievable sensitivity and specificity. However, OCT can be used to guide clinical decision making and biopsy in the oral cavity, an area with high functionality for speech and swallowing and conservation of tissues is an importance.

Several existing oral cancer screening tests use narrow-emission tissue fluorescence approaches [29]. Typically, their sensitivity is considerably better than their specificity. Two such devices are the VelScope™ and the Identafi™ [29], [30] systems. For both systems, the user is required to make a subjective conclusion based on what he/she perceives from the fluorescent images. This in-turn creates the need of training a specialist, which would limit the usability of the device in a remote, underserved or non-specialist setting [5,7]. Lastly, a Stanford research group has recently developed Oscan, an illumination attachment for oral cancer screening. The low cost of the Oscan device makes it an attractive option to be used in LMIC health care settings, but poses several limitations previously discussed. Similar to the VelScope device, the Oscan system cannot access the posterior regions of the oral cavity including the oropharynx providing an incomplete screening of oral health.

In contrast to high power 1W UV source (400-460) that is used for the VelScope, OCT utilizes a safe, low-power near infrared light source (5mW 1310nm) that do not pose any safety hazards to the physician or patient during operation, yet provides comparable sensitivity and specificity. OCT devices, similar to the probe and system presented in this work, are configurable to specifically image hard to reach oral regions that are not readily accessible with current fluorescence based imaging systems. With further improvements in the imaging probe lateral resolution, and spherical aberration it is likely that an OCT system will provide excellent triage guidance for oral pre-cancer and cancer in non-specialist settings. However, in resource rich areas it would still be advantageous to conduct the typical workflow of conventional oral examination

C. Cost and Performance of the OCT Imaging System

The cost of the imaging system was considered in this study to produce a suitable price point for systems deployable in LMICs. The material cost for the imaging system used in this study including a 2-D imaging probe and laptop totaling \$23,500. As previously mentioned the axial and lateral resolution of this imaging system was $7.0\mu\text{m}$ and $15\mu\text{m}$ respectively, with 2 frames/second at 500 A-lines per frame. The Imulux Niris OCT imaging system and flexible endoscopic forward viewing probe with axial and lateral resolution of $10\mu\text{m}$ imaging at 1 frame/second was priced at \$65,000. The Niris OCT system was used in the earlier work investigating the use of OCT to discern differences between healthy and abnormal oral mucosa [19,31]. This imaging system could be considered the first push towards a commercially available OCT system and probe. However, its high price tag with lacking performance make it a less than ideal OCT system compared to the system used in this work. Recently, S. kim *et al* published their design of a low-cost portable OCT system at a \$7,164 price point [32]. The compact OCT imaging system and probe achieve comparable performance to the system presented in this work with an axial and lateral resolution of $7.0\mu\text{m}$ and $17.6\mu\text{m}$ respectively. The low-cost system achieves an imaging rate of 12 frames per second pushing ahead of the 2 frame/second imaging rate of the system used in this study. However, their probe design does not account for the miniature form factor necessary to image the oral cavity. Utilizing the imaging system core with the proper probe form factor and scanning optics presented in this study, would be the ideal candidate for compactness, value, and performance.

V. CONCLUSION

A mobile OCT imaging platform and long GRIN rod scanning probe were developed and deployed at a healthcare center in Bangalore, India. Oral mucosal health was diagnosed by visual analysis of OCT images via a standardized blinded scorer and an image-processing algorithm, with biopsy and histopathology serving as the gold standard. In this pilot study of 30 patients, similar levels of diagnostic sensitivity and specificity resulted from image analysis by a blinded clinical scorer and a novel diagnostic algorithm. This work suggests that our image processing algorithm and mobile imaging system could provide a useful screening and triage tool for basic level field screeners where specialist expertise and facilities are not available. Future work will focus on improving the imaging speed and cost of the compact mobile system and the discriminatory abilities of the image-processing algorithm.

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Andrew E. Heidari has completed his Bachelors in Biomedical Engineering with a specialization in bio-photonics from the University of California Irvine(UCI). After graduating with his B.S he worked at OCT Medical Imaging, an academic startup aimed at commercializing OCT endoscopic technology for. He then perused his masters graduate degree in Biomedical Engineering at the UCI that eventually led him to continue towards the completion of his Ph.D. He is now a Ph.D. candidate at UCI working under the mentorship of Professor Zhongping Chen at the Beckman Laser Institute where he is developing new biomedical imaging probes and methods for disease diagnosis and monitoring. His work primarily involves highly collaborative research with physicians in head and neck cancer and interventional pulmonology. His research interests include identifying clinical unmet needs that can be supplemented with developed research that can be translated from the bench to bedside. He has extensively worked on imaging and characterizing the formation of bacterial biofilms and oral cancer using OCT. After completing his Ph.D., he plans on applying for SBIR/STTR government funding to kick start his startup ventures aimed to commercialize the use of OCT for head and neck cancer resection as well as bacterial management in critically ill patients.

Dr. Sumsum P Sunny was born in Kerala, Indi in 1984. He completed his Bachelors in Dental Sciences in 2010 from Amrita VishwaVidhyapeetham, Kochi. His post-graduate training was in MDS (Oral Medicine and Radiology) and was completed in 2013 from K.L.E.s' Institute of Dental Sciences, Rajiv Gandhi University of Health Sciences, Bangalore.

Dr. Sumsum P Sunny is currently working as Senior House Officer in Head and Neck Oncology at the Mazumdar Shaw Medical Center, Narayana Health. His primary responsibilities have been to lead the departmental cancer outreach programs and oral care management of head and neck oncology patients. His focus is to facilitate outreach programs for early detection and prevention of oral cancer. His research group focuses on the development of non-invasive technique for early detection of oral cancer. The Welcome Trust/DBT India Alliance awarded Research Training Fellowship for him in 2016. He is also working in DSRG-5, Integrated Head and Neck Oncology Program, at Mazumdar Shaw Center for Translational Research (MSCTR), Narayana Health, Bangalore as Research Fellow since 2013. He is also a part of two NIH grant collaborated with University of California, Irvine (2013) and University of Arizona, Arizona (2016) focusing on oral cancer and precancerous imaging towards the development of point of care diagnostics.

Dr. Sunny has received prizes for his paper and poster presentation in Nation and International conferences. He has National and International publications. He is a visiting scholar in Biomedical and Electronic Engineering System Laboratory, IISc, Bangalore and adjunct faculty in KLES, Dental Sciences, Banaglore.

Bonney L. James was born in Kerala, India in 1987. She has completed her B. Tech in biotechnology and biochemical engineering from Kerala University and M. Tech in genetic engineering from SRM institute, Chennai, India. She is currently working towards her PhD degree.

She is working as a senior research fellow in Head and neck research, Mazumdar Shaw center for translational research since 2014. She has worked in two projects involving early cancer detection and is currently working on identifying markers for lymph node metastasis. She is part of four publications and also part of one of the chapter of the book titled "Contemporary Oral Oncology" (Dr. Moni Abraham Kuriakose, 2017, Springer). Her research interest includes lymph node metastasis & immune surveillance in oral cancer. Ms. Bonney Lee James is a recipient of the best poster award from Federation of head and neck oncology in the year 2015.

Tracie M. Lam was born and raised in Westminster, CA. She studied Business Economics and Biology during her undergraduate years at University of

California, Irvine (UCI) and Orange Coast Community College (OCC). Tracie has also participated in a Regional Occupational Program at the community college level to obtain a dental assistant and radiology certificate. Shown through her interests in dentistry, she applied to dental schools after receiving her bachelor's degree at UCI.

In 2010 to 2011, she was an undergraduate research assistant in Dr. John Longhurst's lab at UCI. From 2014 to 2017, she was a junior specialist in Dr. Petra Wilder-Smith's lab at Beckman Laser Institute. She started as a dental assistant in 2007 and has over 10 years of experience at various dental offices. She has been author and co-author on peer reviewed journal articles involving effects of dental gel on enamel surface recovery, dental plaque removal and re-accumulation, plaque removal and gingival health after use of a novel dental gel. She enjoys dental research involving clinical testing, methods and equipment to prevent or detect oral cancer, as well as dental products.

Ms. Tracie Lam had been in the Campuswide Honors program throughout college. She was a recipient of The Regents' Scholarships from 2009 to 2011 at UCI. She also published an honors thesis, Role of Nucleus Ambiguus and Cardiovascular Effects During Electroacupuncture in 2011 as part of the honors program. While at UCI, she was also a member in the national health pre-professional honor society, Alpha Epsilon Delta.

Anne V. Tran was born and raised in Fountain Valley, California. She received her B.S. degree in biological sciences at the University of California, Irvine in 2016 and will receive her D.M.D. degree in dental medicine from Western University of Health Sciences, Pomona, CA in 2020.

From 2015-2016, she was an undergraduate researcher with Dr. Petra Wilder-Smith's at the Beckman Laser Institute. Her research interests include oral cancer pathology and clinical dentistry that she has presented at the Undergraduate Research Opportunities Program Symposium in 2014 and 2015 at the University of California, Irvine, and American Society for Laser Medicine & Surgery in 2016 in Boston, MA.

Junxiao Yu received her B.S. degree in Biomedical Engineering from Illinois Institute of Technology, Chicago, IL, USA, in 2016. She is currently working toward the Ph.D. degree under the guidance of Dr. Zhongping Chen. Her research interests include optical coherence tomography and optical coherence elastography.

Ravindra D Ramanjinappa was born in Bengaluru, India in 1989. He has completed DMLT course certificate from Rajiv Gandhi University in 2008. He worked as a research assistant for 2 years in Nadathur Lab of Breast cancer research, St. Johns Research Institute after her graduation, till 2011. Currently he is working as Project assistant in DSRG-5, Integrated Head and Neck Oncology Program, at Mazumdar Shaw Center for Translational Research (MSCTR), Narayana Health, Bangalore since 2011. His research interest includes Immunofluorescence Immunohistochemistry and Fluorescence In Situ hybridization. Ravindra D R has more than ten International publication.

Uma K has received his MDS with a specialization in Oral Pathology from Mumbai University in 1994. He is currently Professor and Head of the Oral Pathology Department at K.L.E.S' Dental College and Hospital in Bangalore, India.

Dr. Praveen Birur is a Professor, & Head of the Department of Oral Medicine and Radiology at K.L.E.S' Institute of Dental Sciences, Bangalore, India. He is a consultant at Biocon Foundation and adjunct research scientist at Mazumdar Shaw Medical Centre. His special interests include "Prevention, Early Detection and Treatment of Oral Cancer". He has been involved in various health programs for down staging oral cancer in resource constrain settings in India. He has worked extensively with general dentists and non-professional health care workers to improve early diagnosis of oral cancer. He was the lead oral medicine specialist for their pilot mobile health project on oral cancer prevention and diagnosis. The early detection program has won numerous awards; few to be mentioned are NASSCOM – Innovation Award, Best Social Innovation Award, WHO – Public health Challenge award 2015 and IAOMR – Young researcher award 2016. He has also been conferred with Best Teaching Faculty for Academic excellence during 95th KLE Foundation day.

He is also a mentor to several trainees working on oral cancer research projects. He was the first Editor-in-chief for World Journal of Dentistry and is on the editorial board for various scientific journals. To his credit he has publications in both international and national journals and has authored three textbooks in Oral Medicine and Radiology.

Dr. Amritha Suresh was born in India in 1975. She completed her Bachelors in Science from the University of Kerala, India in 1996 and then her post-graduation professional degree from the Cochin University of Science and Technology, Kochi, India in 1998 after which she enrolled for her doctoral program. She completed her doctoral program (Life Sciences; molecular biology) in 2005 from Jawaharlal University, Delhi, India [Centre for Cellular and Molecular Biology, Hyderabad]. Her major fields of education have been in molecular biology, zoology and biochemistry.

She is currently a Principal Scientist of the Integrated Head and Neck Oncology Program, at the Mazumdar Shaw Center for Translational Research (MSCTR), Narayana Health, Bangalore. She is also a faculty of the Roswell Park-Mazumdar Shaw Cancer Center Collaborative Research program. Dr. Suresh completed her doctoral program from Center for Cellular and Molecular Biology (JNU) and served as a Research Associate at Head and Neck Institute, Amrita Institute of Medical Sciences and Research Center, Kochi during which period she was involved in setting up the research facility and the establishment of a Head and Neck tissue repository at the center. She has presented in multiple national and international conferences and has published in journals such as *Translational Oncology*, *Head & Neck*, *Genomics*, *Oral Oncology* and *Genome Research*. She has also co-authored a book on *Contemporary Oral Oncology*. Her major fields of interests include molecular mechanisms of oral carcinogenesis, drug resistance and recurrence, cancer stem cells in the processes of drug resistance, and development of molecular marker based assay systems for early detection, prognosis and prediction of treatment outcome.

Dr. Suresh is the recipient of the young investigator grant from DBT apart from other grants from DBT and ICMR. She is a member of the American Association of Cancer Research, Head and Neck Cooperative group of India, and a life member of Foundation of Head and Neck Oncology, India a consortium involved in collaborative projects in head and neck cancer. Dr. Suresh is also the recipient of grants from Indian council of Medical Research, Scientific and Engineering Research Board for carrying out projects in Head and Neck Cancer. She is a reviewer for journals such as *Scientific Reports*, *International Journal of Oncology*, *Malaysian Journal of Medical Sciences*, *Journal of Proteomics and Bioinformatics* and *PLOS One*.

Dr. Moni A. Kuriakose was born in Kochi, India in 1959. He completed his Bachelors in Dental Sciences from University of Mysore and Bachelors in Medicine from University of Bristol, UK. He was a Resident in general surgery at the University of Newcastle, UK in maxillofacial surgery at the and completed a fellowship in head and neck Oncology from Roswell Park Cancer Institute, Buffalo.

He is Professor and Director of Surgical Oncology and Chief of the Head and Neck Oncology Program at the Mazumdar Shaw Cancer Center, Narayana Health, Bangalore. He is also the director of head and neck oncology translational research program at the Roswell Park Cancer Institute, Buffalo. Previously, he has served as Director of Head and Neck Oncology Translational Research program at the New York School of Medicine. He has been instrumental in establishing collaborations with national and international institutions/universities of complementary expertise to address the various issues with head and neck oncologic disease in a co-ordinated, multi-centric manner. He has chaired two international and four national conferences and has successfully carried out several projects in chemoprevention and translational research. His work is published in *Oral Oncology*, *Head and Neck*, *Journal of Applied genetics*, *Journal of Cancer Research and Therapeutics*, *Current Opinion in Otolaryngology and Head & Neck Surgery* and *Laryngoscope*. His primary interest is to use his experience to help to develop a model for universal, affordable and accessible cancer care in developing countries.

Dr. Kuriakose has served leadership positions in many national and international organizations including Secretary General of International Academy of Oral Oncology, Chairman of Oral Oncology special interest group of International Association of Oral and Maxillofacial Surgeons, Member of AO Research Review Commission, member of steering committee of HPV-AHEAD study of International Agency for Research in Cancer (WHO), secretary of Head and Neck Oncology Cooperative Research Group of India and Secretary of the Foundation of Head and Neck Oncology of India. He is the recipient of multiple research grants from NIH, Department of Biotechnology, ICMR, DHR, government of India. He is the Editor of *Contemporary Oral Oncology*.

Dr. Zhongping Chen received his B.S. degree in applied physics from Shanghai Jiao Tong University, Shanghai, China, in 1982, an M.S. degree in electrical engineering from Cornell University, NY, USA, in 1987, and his Ph.D. in applied physics from Cornell University in 1993. He is currently a Professor of biomedical engineering and the Director of F-OCT Laboratory at the University of California, Irvine, CA, USA. He is a cofounder and the board Chairman of OCT Medical Imaging, Inc. His research interests encompass biomedical photonics, microfabrication, biomaterials, and biosensors. His research group has pioneered the development of functional optical coherence tomography, which simultaneously provides high-resolution 3-D images of tissue structure, blood flow, and birefringence. He has published more than 220 peer-reviewed papers and review articles and holds a number of patents in the fields of biomaterials, biosensors, and biomedical imaging. Dr. Chen is a Fellow of the American Institute of Medical and Biological Engineering (AIMBE), a Fellow of SPIE, and a Fellow of the Optical Society of America.

Dr. Petra Wilder-Smith is Professor and Director of Dentistry at the University of California, Irvine's Beckman Laser Institute (BLI). She is a Fellow of the University of California, Irvine's Comprehensive Cancer Center, and Visiting Professor at Aachen University.

Professor Wilder-Smith's research interests include the development and validation of novel non-invasive optical techniques for oral diagnosis, especially early detection and monitoring of oral pre-cancerous and cancerous changes. Her work in this field over the past 25 years has resulted in much collaboration including more than 150 publications, 250 presentations at peer-reviewed scientific meetings, and 300 public lectures. Wilder-Smith is Co-Principal Investigator on an NIH-funded study to develop and test a low-cost portable screening device to detect possible oral cancer for use by field workers in India. Other funded research interests include oral biofilm, dental de- and remineralization, and pulpal vitality interrogation. Additional projects focus on the use of stem cells and other approaches to prevent or mitigate cancer-therapy-induced mucositis. Another area of interest in collaboration with Drs. Potma and Chen at BLI is the development and testing of novel miniaturized optical tools for interrogation of the nasopharyngeal mucosa as a predictor of inhalation damage to the entire airway. Wilder-Smith serves on many advisory boards, including the Medical Advisory Board to Cancer Research and Prevention Foundation, the Board of the American Society for Laser Medicine and Surgery, as well as the Editorial Boards of the journals *Lasers in Surgery & Medicine*, *Photomedicine and Laser Surgery*, and *Journal of Biomedical Optics*. Wilder-Smith has also served on the board of the Diagnostic Sciences Group for the International Association for Dental Research (IADR) and is currently President of this prestigious group.