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Mouthscope: Autonomous Detection of Oral Precancerous Lesions By Fluorescent Imaging

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Abstract

Oral cancer (OC), the third most prevalent cancer in India, is highly treatable when diagnosed at an early stage. In rural India, 60% of OC cases are diagnosed with advanced stages. The solution of mass early-stage screening currently requires experienced doctors and robust healthcare infrastructure. MouthScope -- uses AI to make OC screening more accessible by automating it. It scans the entire oral cavity for potentially cancerous lesions without professional intervention. Mouthscope works on the principle of auto-fluorescence. The device is portable and can be used with a mobile phone. The phone camera captures color differences caused by auto-fluorescence and sends it to the machine learning model which predicts with 96% accuracy. The device contains a long-pass filter, low-wavelength light-emitting diode (LED), a microcontroller, a cheek-retractor, and a phone holder. Mouthscope uses two machine learning models: resnet_v2, a Deep Residual Convolutional Neural Network (RCNN) and YOLOv5 based on the You Only Look Once (YOLO) architecture. The device allows for both real-time self-detection and mass screening, allowing for self-checkups for follow-up cases. Mouthscope has been tested with 24 patients out of which 4 are cancerous, and it was found that there was a clear visual distinction between the potentially malignant tissue and normal tissue, with malignant tissue having darker color. Moreover, the machine learning models were able to detect this distinction in 4 different lesions. By using a smartphone and classifying images through machine learning, Mouthscope eliminates the need for extensive infrastructure for mass screening of OC, making it more attainable for rural India.

Keywords: Oral Cancer, Classification, Auto-fluorescence, RESNET_V2, YOLOV5

1. Introduction

Oral cancer (OC) is a prevalent issue in rural India due to very high consumption of tobacco [1]. Moreover, low medical awareness among the general population and a lacking medical infrastructure means that most cases of

OC are diagnosed late and have a low cure rate [2]. Above that, the cost of diagnosis for OC in India is about ₹60000 and the surgery cost can be as high as ₹2,35,000 to ₹5,00,000 [3]. Thus, an effective device for early-stage, affordable and accurate detection of OC is essential.

In this direction, the authors have developed Mouthscope which is an engineering project targeted at improving the condition of OC screening in rural India. To maximize the potential of such a device, certain key targets and features were set before designing the device. The target features set that would make this goal possible included:

1. Low cost: to make mass-screening affordable
2. Rapid detection: to permit regular screening at primary health care centers
3. Minimum professional intervention: requiring professional intervention only to confirm detection results, with no special training to use the device itself
4. Self-assessment: allow real time detection for follow-up checks in patients and self-diagnosis
5. High sensitivity

1.1. Motivation and Novelties

The ultimate goal of this engineering project is to develop a non-invasive device that can rapidly and accurately detect the presence of early stage premalignant OC with minimal professional intervention. While existing fluorescence techniques are accurate, they still require trained professionals. Introduction of deep learning (DL) to these techniques overcomes this barrier to open possibilities of low-intervention, mass screening.

The Mouthscope works on the principle of autofluorescence and DL. The autofluorescence is due to maximum excitation of Reduced Nicotinamide Adenine Dinucleotide Phosphate (NADPH) particles in the mouth consequently leading to the optimal autofluorescence. The camera captures the autofluorescent images of the oral cavity which are then fed to the two DL models to detect the OC. The DL models that are employed for detecting OC are resnet_v2 and YOLOv5. Finally, the device Mouthscope is tested on 24 patients with the goal of validating it.

The rest of the paper is drafted as such: Section 2 reviews the contemporary literature which is followed by the problem statement in section 3. Section 4 of the paper describes the steps for developing the prototype and its working principle. Section 5 is the results and discussion where the results obtained are described in brief. Also the section draws a comparison with other devices that are available in the market. Finally, section 6 concludes the paper.

2. Literature review

A review of the relevant literature confirms the extent of the problem of OC in India. The study carried out by Priya and Lando confirms that the culture of consuming tobacco is deeply rooted in rural India, and hence in the future, OC cases are likely to only rise. The article demonstrates a close correlation between OC and tobacco in rural India. The situation is made worse due to late-stage detection of OC being commonplace in India [4]. In the literature [5], it is reported that 60-80% of OC cases are diagnosed at an advanced stage. As a result, the study concluded that early-stage detection techniques will not only improve the cure rate but also lower the cost and morbidity rate. The importance of early diagnosis of OC and limitations of the recent diagnostic aids in achieving it are highlighted in [6]. In the study, the authors raised the need for detection techniques which are not invasive, accurate, and cheap as a first step towards positive impact on survival of OC patients. Established literature also pointed out drawbacks in the existing techniques. Biopsies are the most used method for diagnosis. However, biopsy is expensive, time-consuming, and requires expert technicians. Hence in literature [7], the authors concluded that despite multiple studies, non-invasive, portable, easy-to-use, rapid, cost-effective techniques that do not require a skilled professional to process, analyze, and interpret the test results are still not available in India.

In the literature, there exists works that used the principle of fluorescence in detecting cancer. In the article [8], the authors have suggested that the autofluorescence techniques show high sensitivity and selectivity, yet they are limited only to clinicians with sufficient professional experience and training. Thus, elimination of this requirement will pave the way for better oral cancer screening.

Literature reviewed was also conducted to determine the machine learning (ML) models which were to be used. In [9], it was concluded that YOLOv5 is a lightweight, low-inference time object detection model, which is significantly faster than competing models, and comes pretrained on the Coco dataset. Similarly, resnet_v2 which was conceptualized in [10] that it is based on the deep residual neural network architecture and provides high accuracy for image recognition and classification. More papers were reviewed but limiting the literature only to the most recent and most specific papers.

3. Problem Statement

There is currently a major gap in affordable, rapid and accurate OC screening in rural India. More than half of rural Indian males, approximately 57%, consume tobacco [11]. This is a leading cause of the prevalence of OC in rural India, as more than 90% of OC cases in India report using tobacco products [12]. This prevalence is not adequately met by sufficient screening infrastructure. Less than 1.5% of the Rural Indian Population goes through an oral Cavity Examination, and as a result OC is detected in the later stages where it is difficult to treat: Based on the Tumor, Nodes, and metastases (TNM) classification, 60-80% of the OC cases are detected in the later stages [5]. The late screening leads to high morbidity of OC in India, as 5 people die of OC every hour [13]. To solve the problem, the authors have conceptualized to develop and manufacture an accurate, non-invasive, low cost and significantly fast device that can detect oral precancerous cells.

Mouthscope aims to address this gap in OC screening through three main ways. Firstly, through early fast and accurate predictions for OC at an early stage. OC is highly treatable when diagnosed at a precancerous or early-stage. The survival rate is 80% for stage I OC patients, whereas only 20% of patients with stage IV OC survive after 5 years [14]. Early-stage detection lowers not only the morbidity rate of OC but also the cost of treatment.

Mouthscope is also targeting automation of lesion screening. In India, there is a mismatch between people susceptible to OC i.e. the ones who fall into risk categories like tobacco consumers and smokers and infrastructure available for diagnosis to them, especially in rural areas. In India, 79% of tobacco consumers live in rural areas [15]. Mouthscope aims to solve this by eliminating the need for expensive diagnostic tools and specially trained doctors and requiring only one affordable device with a target price set at ₹15,000 only for accurate detection having target accuracy of 95% in a non-invasive manner.

By making OC screening more accessible, Mouthscope aims to retain the screening as a part of routine testing in primary healthcare centers, where testing can be performed by a general physician or nurse without the need of special training.

The Mouthscope also addresses the problem of follow-ups. Follow-ups are essential after treatment, as the recurrence rate of squamous cell carcinoma is 32.7% [16]. However, there is a lacking medical infrastructure, especially in rural areas, to facilitate the recommended number of follow-ups. Being a device that can attach directly to a smartphone, the Mouthscope can provide reliable self-detection for follow-ups without requiring much infrastructure.

4. Methodology

The Mouthscope device was designed on computer-aided software called Autodesk Fusion 360. There were 6 prototypes and 30 sketches. These models were 3-D printed using a resin material. The final design consists of a

450 nm dichroic long-pass filter (Edmund Optics filter #69-876), LEDs of wavelength 405 nm, a microcontroller (Arduino nano), a cheek retractor that helps capture the entire oral cavity and a universal phone holder with a spring lock mechanism which allows any phone to be used. The conical device was designed to fit into the mouth and scans the entire oral cavity for potentially cancerous lesions without professional intervention, and in a non-invasive manner. The conical design also prevents external light from entering. Moreover, the device has a multi-directional phone adjustment mechanism which allows the camera of any phone to be adjusted to an appropriate height and length such that its camera is aligned with the filter. The device also has a variable resistor to control the intensity and wavelength of the LEDs, allowing real time optimization. The labelled diagram of the Mouthscope device is shown in Figure 5. Mouthscope itself works on 2 working principles: autofluorescence and machine learning.

4.1 Autofluorescence

Autofluorescence begins with the emission of light from the 405 nm LEDs in the device, which is directed towards the mouth. Inside the mouth, this light excites fluorophores in the normal oral tissue which thus emit light of a higher wavelength than 405 nm but not in the cancerous tissue. On re-entering the device, only the light above 450 nm can pass through the dichroic filter. Thus, the cancerous tissue appears much darker than the mouth, and this color difference can be captured in the device. Multiple tests were performed to optimize autofluorescence.

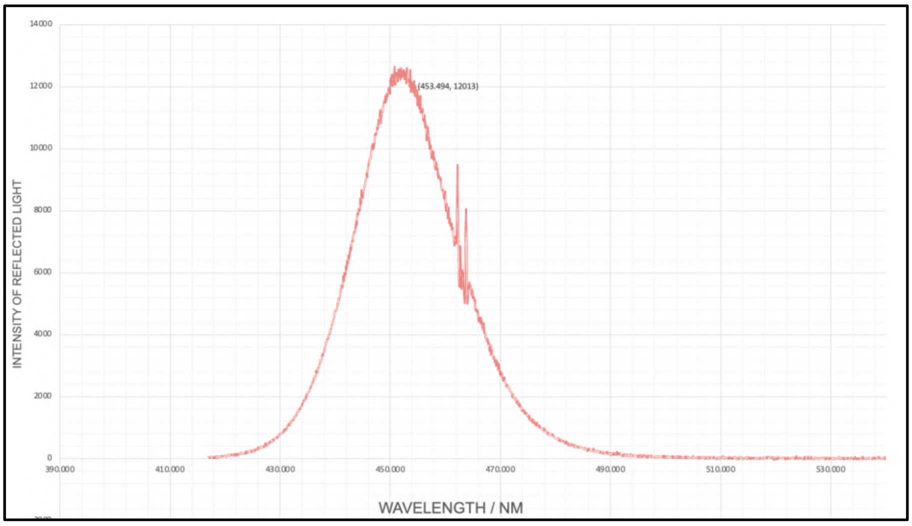

Figure 1: Fluorescence Spectroscopy of the Mouth

To determine the filter set to be used, fluorescence spectroscopy of the oral cavity was carried out. A 405 nm wavelength light was used to excite the oral mucosa and captured the reflected light with a fibre spectrometer. The peak was observed at 453.494 nm, with the graph seen in Figure 1. Thus a 450 nm wavelength dichroic filter was selected.

Figure 2: Modified Device used to determine distance from the mouth

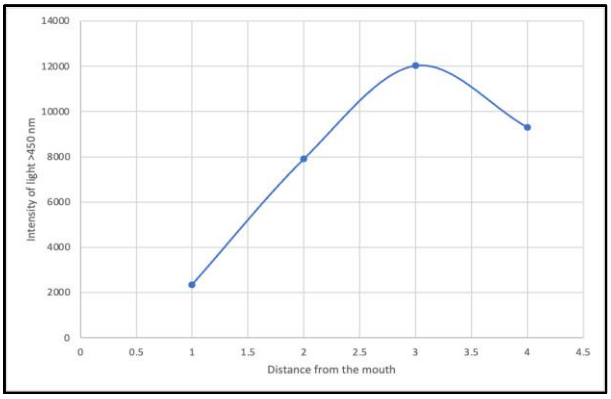

Figure 3: Distance from the mouth vs Intensity of light > 450 nm

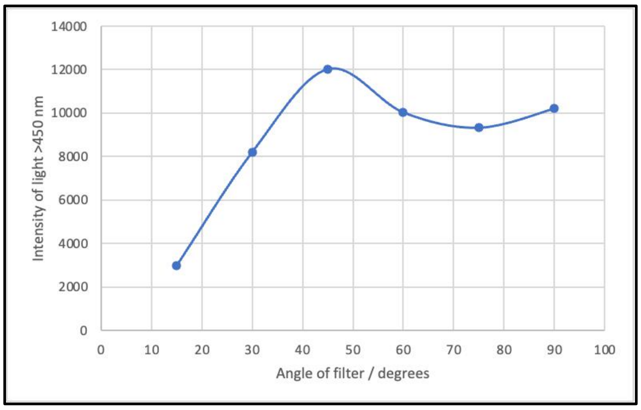

Figure 4: Angle of the filter vs Intensity of light > 450 nm

A modular prototype was also developed to determine position and angle of the filter, seen in Figure 2. For the distance of the filter from the mouth, the device was marked at 1 cm intervals from 1 to 6 cm from the mouth and the filter was suspended inside. The relative fluorescence was subsequently recorded at 1cm intervals. The optimal distance was determined as 4 cm, as seen in Figure 3. Similarly, for the angle of the filter, the filter was suspended inside the device, and robotically rotated at 15-degree intervals with relative fluorescence being recorded. The optimal angle was found to be 45º, as seen in Figure 4.

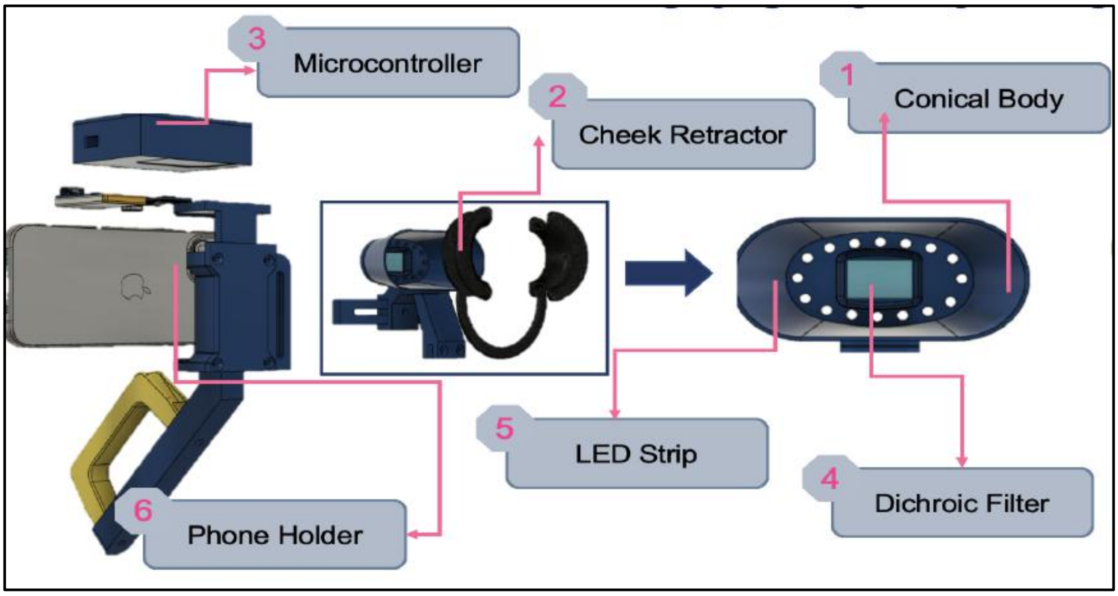

Figure 5: Final Prototype, with labeled parts

The final prototype and its major parts can be seen in Figure 5. The names of the parts along with their uses are summarized in Table 1.

Table 1: Parts and their uses

Part	**Use**
Conical Body	Scatters light from the LEDs to the entire mouth. Prevents entry of external light. Focuses entering light on filter.
Disposable Cheek Retractor	Exposes entire oral cavity, also single use and can be sterilized
Variable Resistor and Microcontroller	To control the intensity and wavelength of LEDs, and calibrate as necessary
450 nm dichroic long-pass filter at 45º	Only allows light above 450 nm wavelength to pass through
LED Strip of 405 nm LEDs,	Illuminates mouth and excites oral tissue
Adjustable Phone Holder, with a spring lock mechanism	Multidirectional adjustability with a spring-locking mechanism to hold the phone in place. Allows multiple sizes of phones to be used while ensuring the camera is flush with filter

4.2 Machine Learning

Mouthscope uses 2 machine learning models: resnet_v2, a Deep RNN and YOLOv5. Resnet_v2, which has a high prediction time, is dedicated to screening purposes. The YOLOv5 model, with rapid inference allows detection of lesions in real-time such as for follow-up checks in patients. Both models were trained on a self-collected dataset which was acquired through primary data collection with a control group of 24 patients including four cancer patients, which produced 1200 images (and 899 labels); in addition to pretrained weights. The primary dataset was augmented through rotations, and use of background images (non-cancerous cases) with non-labelled classes to minimize false positives. Both models were deployed to an application interface using Swift. The app allows users to view the YOLOv5 model's predictions in real-time, allowing a focus on self-detection. The app also inputs information about the patient. The models' predictions can also be verified (ideally by a doctor) and then models are retrained based on feedback.

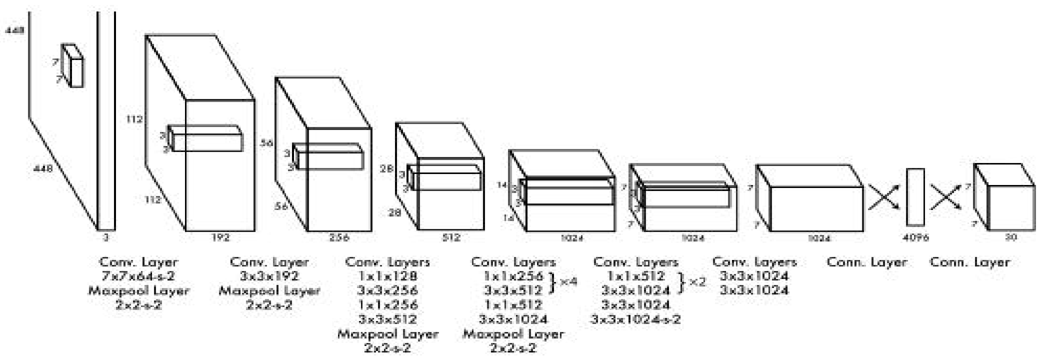

Figure 6: YOLOv5 network architecture [17]

YOLOv5 works on the 'You only look once' architecture, based on a CNN with only single forward propagation through a neural network. The architecture approaches inference as a regression problem, producing bounding boxes for the entire image in a single run. This architecture is visually summarized in Figure 6. Alternatively, resnet_v2 is a deep RCNN, working on image classification, with several deep convoluted neural layers and residual connections. Resnet_v2's performance was tested using a confusion matrix and YOLOv5's performance was tested using mAP (mean average precision).

4.3 Device Testing

The device itself was also tested with 24 patients. 4 patients who were pre-diagnosed with OC lesions namely Erythroplakia, Leukoplakia, Squamous cell carcinoma, and Submucous fibrosis and 20 apparently healthy patients used for validation of the device. All patients gave informed consent. The mean age was 36 years old, with a max of 78 and a min of 21. The male-female ratio was 70:30, chosen to roughly approximate the ratio of OC incidence in India. Oral tobacco consumers represented 20% of the dataset.

4.4 Ethical and Safety Precautions

Throughout the testing of the device, certain safety and ethical protocols were maintained. These are listed below:

1. Use of separate, disposable cheek retractor for each patient
2. Sterilization of the device between each patient
3. The LEDs were ROHS certified, and each test was limited to 20 seconds of light exposure which is well within the safety limit of 1000 seconds for 405 nm light, prescribed by ACGIH. The TLV/BEI guidelines available in the website https://www.acgih.org/science/tlv-bei-guidelines/
4. A certified medical professional carried out all tests
5. Informed consent was taken from all patients
6. To ensure privacy, no identifying information of patients was used in the research

5. Results and Discussion

The device produced a visible color difference between the normal tissue and the potentially cancerous lesions in the patients' mouths.

Figure 7: Color difference between cancerous and non-cancerous tissues

As can be seen in Figure 7, in the case of normal oral mucosa, the image captured by the device had a bright green hue while the potentially cancerous lesion did not undergo autofluorescence and was visibly darker (the regions marked in red in the figure 7). The machine learning models were also able to detect these lesions. Out of the 24 patients that the device was with, autofluorescence from the device worked successfully on all 24, i.e. the device captures the color contrast between cancerous and healthy tissues. There was a similar degree of autofluorescence across ages (i.e. no impact of age on autofluorescence). Furthermore, the presence of tobacco in the mouth did not impact the efficacy of our solution.

The YOLOv5 model had 91% accuracy and Resnet_v2 had an accuracy of 96%. YOLOv5 allowed for rapid detection, with an inference of 23 frames per second. These models were tested with 4 different types of lesions namely erythroplakia, oral squamous cell carcinoma, leukoplakia, and oral submucous fibrosis. The 2 models were also successfully deployed on a mobile app.

5.1 Comparing with existing solutions

Comparing with the two main existing solutions in the market, mouthscope makes marked improvements. Biopsy of various types requires multiple professionals and large medical infrastructure. It is also invasive, time-consuming, and costly. Through earlier mass screening, mouthscope can reduce the number of patients who require biopsy, providing rapid and accurate detection with minimum intervention. As compared to other existing fluorescence-based solutions, Mouthscope has a lower cost approximately $170, and does not require any special training to be used. It also emphasizes early-stage detection.

6. Conclusions and Future Scope

At the end of the research, it could be concluded that the Mouthscope is a rapid, non-invasive, low-cost, and convenient device for OC screening. By reducing the infrastructure required to screen oral lesions, the Mouthscope can make both mass OC screening and remote detection (for follow-ups) more accessible to rural India. The cost of the product, its speed and its convenience ensure that it meets its vision of empowering rural India over OC.

There are 2 major future steps which can be taken to improve overall. Training and testing with a larger dataset size, specifically raising the number of cancer patients tested with. This will improve real-world accuracy by exposing the neural networks to a greater variety of lesions, preventing overfitting. Testing can also be focused on more ages, and more at-risk communities i.e., smokers and betel-nut chewers. It also aims to target inclusion of extra data-points, such as age and consumption of tobacco, within the model prediction. Addition of more data points will be good for accuracy.

Some further research must also be undertaken before the mouthscope is ready to be used as a routine detection device in primary health care centers. Fluorescence spectroscopy of a larger set of people to create a more generalized model of autofluorescence in the mouth will allow autofluorescence to be more universal.

Ethical standards:

The authors would like to declare that no financial support in any form is obtained for developing the prototype. Neither government nor private fundings is collected for the engineering project. The authors would also like to declare that proper written consent is taken from the patients while testing the prototype. Also, the authors declare that they have strictly abided by the TLV/BEI guidelines.

Credit authorship:

Aditya Mehta: Conceptualization, Writing, Coding, Software, Investigation; **Maanav Kothari**: Conceptualization, Writing, Coding, Software, Investigation; **Syed Abou Iltaf Hussain**: Editing, Reviewing and Supervision; **Reetu Jain**: Supervision

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