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A low-cost Point-of-Care Diagnostic for Premature Oral Cancer Screening

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A low-cost Point-of-Care Diagnostic for Premature Oral Cancer Screening

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Abstract

Oral cancer is a cancerous growth in the oral cavity. More than 90% of all oral cancers are squamous cell carcinoma. Oral squamous cell carcinoma has the highest mortality ratio compared to other carcinomas. The high mortality rate is mainly due to detection of the cancer in an advanced stage on account of its initial asymptomatic nature. In addition, the methods currently in place for oral cancer detection involve expensive complex laboratory procedures and usually longer wait times for patients leading to late diagnosis. Further, the treatments for advanced staged cancers are costly and less effective in terms of the post-treatment survival rates. Thus, society needs an easy-to-use tool for assessing oral cancers at an early stage. The aim of the project is to develop an easily accessible point-of-care kit which will assist in early detection of oral cancer at a low cost. The kit will consist of a complete home-based test which could be easily operated by vulnerable individuals. The test will be based on the patient's salivary sample and to obtain an oral cancer risk-analysis with detailed statistics on an app. Furthermore, the app will also feature a digital pathology test for an analysis of potential malignancies based on image(s) of the oral cavity. The chemical aspect of the tool will be based on a thermal reaction of formulated Thiobarbituric Acid reagent along with a spectroscopy sensor. The app will be connected to the sensor via Bluetooth and the image screening will be based on deep learning using deep convolutional neural network.

Keywords

oral cancer, early detection, at home testing, deep learning

Overview and background

Currently, the data from Center of Disease Control (CDC) suggests that the most effective way to control oral cancer is to combine early diagnosis and appropriate treatment in a timely manner. However, the issue lies in the early detection of the disease and is the most challenging part of the entire treatment procedure. Usually, the initial stage of oral cancer goes under negligence of the patient due its asymptomatic nature and the symptoms may appear to be a benign cause. According to the Oral Cancer Foundation, there is no comprehensive program in the US to opportunistically screen for the disease, and without that late-stage discovery is more common. Talking about the major cause of this disease, smoking or use of tobacco in any form is the culprit. When a person smokes, they generate Reactive Oxygen Species (ROS). The Reactive Oxygen Species induced cell damage leads to lipid peroxidation which is implicated in the development of oral cancer. This mostly affects the polyunsaturated fatty acids leading to alteration in the function and structure of cell membranes. As a result, Malondialdehyde (MDA) is formed as the product of lipid peroxidation. So, MDA can be used for measuring the degree of lipid peroxidation that took place. An increase in the presence of MDA in saliva is widely reported in pre-oral cancers and cancers in the initial stage. A study conducted in October 2020 had concluded that "It has been shown that saliva has great potential for the development of diagnostic and prognostic tests for oral cancer" (Shamsher and Prabhu 2020; Radhika et al. 2016) . Moving on to the deep learning aspect of the project, recent studies have concluded that deep learning algorithms are able to exceed the performance of human experts in many disease recognition scenarios (Tschandl et al. 2019a, Tschandl et al. 2019b; Mobadersany et al. 2018). For some background information, oral squamous cell carcinoma which originates as an epithelial dysplasia, generally develops from precursor lesions termed as oral potentially malignant disorders (OPMDs). However, all OPMDs do not always develop into malignancies. Recent studies (Speight et al. 2018;Dost et al. 2013) have concluded that when OPMD changes to a nonhomogeneous presentation, it has a greater risk of malignant transformation compared to homogenous presentations (lesions). As stated before, initial symptoms of oral cancer can mimic the characteristics of a benign cause leading to misguidance when it is observed by a non- cancer specialist such as a dentist in routine cleanings. However, there are specialists who can differentiate between benign and malignant lesions and they are concentrated in more developed regions of the world. This leads to a lack of access to proper guidance in areas which might not be completely developed. Hence, the concept of "digital pathology" is gaining widespread popularity in the world. Digital pathology refers to a cost-effective screening strategy as a support to current procedures in place. With the rapid development of imaging and sensing technologies in camera systems of consumer smartphones, they are a good candidate to be used as a screening device. These improved smartphone camera systems have higher quality, low-noise and faster camera modules in them. So, smartphone-based white light inspection methods are good solutions for acquiring oral images (Camalan et al. 2021;Welikala et al. 2020).

In the context of chemical oral cancer test, existing research has been done on the Malondialdehyde (MDA) - Thiobarbituric Acid (TBA) reaction and their properties. It is known that one molecule of MDA reacts with two molecules of TBA in an acidic medium to produce a colored adduct at high temperatures. In this research, 0.375 g of TBA was dissolved in 85% Ortho-Phosphoric acid (1 ml) and 1% Trichloro-Acetic Acid (1 ml). In addition, specimens of salivary samples were taken to note and compare the color changes in different groups such as smokers and nonsmokers. A connection between higher lipid peroxidation was noted in smokers compared to non-smokers and a LPI chart was derived. The results obtained from this research suggest a promising approach to develop a home-based test kit for oral cancer (Shamsher and Prabhu 2020). However, the presented solution uses a 1.5 Liter water bath as the source of heat leading to a heavy and bulky testing kit. The use of a water bath also leads to a longer reaction time. Also, it requires human intervention to read the color of the adduct and compare it with the LPI chart to get a result. In recent years, studies (Tschandl et al. 2019b, Tschandl et al. 2019a) have concluded that deep learning algorithms are able to exceed the performance of humans in many screening scenarios. Majority of the previous experiments on oral cancer detection rely on the use of an expensive medical device. These devices can also be inaccessible in some parts of the world, and it requires a physician consultation.

Objectives

This proposed solution will consist of an automated, quick and efficient chemical test along with a physical inspection for oral cancer. The first part will consist of the chemical test. Based on the previous research data, the proposed test will consist of a thermal reaction (100 degrees Celsius) taking place between the formulated TBA reagent and salivary sample of the patient resulting in the color change based on the malondialdehyde concentration in the provided sample. The heating device used will be a thermoelectric Peltier cooler. This will eliminate the 1.5 Liter water bath, leading to a quick and lightweight product. A spectroscopy sensor will be then used to determine the MDA concentration (Optical density at 532 nm) thanks to the color changing nature of the adduct. The sensor will communicate with the desgined app via Bluetooth. Based on the data shared from the spectrometer sensor and an initial user survey, the MDA concentration value and a risk analysis of “probability of potential malignancies” will be displayed to the patient (using LPI chart)(Shamsher and Prabhu 2020). Moving on to the next part, the app will prompt the patient to capture any lesions or unusual features present in their oral cavity. In this case, the patient can either self-capture the lesions or someone can help them in this process to obtain an analysis of their lesions (if any). In recent years, there have been some promising results on the concept of digital pathology. My solution for the image analysis will consist of a simple image-capturing method for consistent lesion position and focal distance over different images. This method will allow a direct focus on the important parts of the image for disease recognition without using any region proposal methods (Welikala et al. 2020). This idea proposes to use one of the latest convolutional neural networks (HRNet) for a better classification of malignancies compared to commonly used classification models such as VGG16, ResNet50, and DenseNet169. This design will eliminate use of any expensive medical screening device. In addition, the use of an app will also open more options in the future which could be implemented in a home-based test such as collecting patient data for research purposes.

Impact

If the idea is useful, it would combine the previous work done on oral cancer screening to a next level by building a lighter /stable product, decreasing the wait time, automating the testing process, and eliminating the use of expensive medical devices to inspect one's oral cavity for potential malignancies.

Implementation

For building the chemical test prototype, I intend to build a wireless mini-test kit in a small box. A cuvette will be prefilled with the TBA reagent in a dock. A thermoelectric Peltier will be located beneath the dock to heat the solution. The thermoelectric Peltier will be powered to set the temperature of the saliva – TBA solution to about 100 degrees Celsius by using Arduino Uno R3, a temperature sensor (DS18B20) and a custom program to control the temperature. I will tweak the program developed in (Laganovska et al. 2020) for the needs of this project. For the spectrometer, a setup will be prepared consisting of a power supply (I will use DC power for both heating and spectroscopy sensor), Arduino Nano, a Bluetooth module and a led. I will tweak the Android application as prepared for the Android app interface. The circuit and other heat-sensitive parts can be placed behind the "cooler" side of the Peltier cooler to prevent them from malfunctioning from excessive heat as it is basically a heatsink.

To build the automatic oral cancer detection algorithm, I will first need a dataset. In the dataset, there will be 5 categories for the images to fall under:

1. Normal;
2. Aphthous Ulcer;
3. Low Risk OPMD;
4. High Risk OPMD and
5. Oral Cancer.

In addition, for each lesion there will be a single image. So, if someone has multiple lesions, they will need multiple lesion-specific images. The next step is annotation. The images in my dataset will need to be annotated by an oral disease expert (this would be the best since it will ensure high quality annotation in my dataset). Also, any "controversial cases" will be excluded based on the annotation from the dataset. In addition, it is recommended to set higher split ratios of the "High Risk OPMD" and "Cancer" classes as these are the most harmful conditions compared to the other three classes for producing the experimental results. The proposed design consists of a custom developed software in Python and implemented using open-source PyQT and PyTorch libraries. So, a CNN-based system will take one image as an input and will output the probabilities for each of the five types of categories specified before following "preprocessing". It is important to note that one will need to adjust the range of each pixel in the input image. The program will be using the recently introduced high-resolution representation learning network (HRNet), which is pretrained on the ImageNet (Deng et al. 2009; Zhang et al. 2021) and then with transfer learning from the ImageNet and obtained dataset, the input is analyzed to output the probabilities of each the 5 classes. Finally, the result will be based on the class with the highest probability.

References

- Camalan S, Mahmood H, Binol H, Ara&uacute j, D. AL, Santos-Silva AR, Vargas PA, Lopes MA, Khurram SA, Gurcan MN (2021) Convolutional Neural Network-Based Clinical Predictors of Oral Dysplasia: Class Activation Map Analysis of Deep Learning Results. Cancers 13 (6): 1291. https://doi.org/10.3390/cancers13061291
- Deng J, Dong W, Socher R, Li L, Li K, Fei-Fei L (2009) ImageNet: A large-scale hierarchical image database. *IEEE Conference on Computer Vision and Pattern Recognition* https://doi.org/10.1109/cvpr.2009.5206848
- Dost F, L&ecirc C, A. K, Ford PJ, Farah CS (2013) A retrospective analysis of clinical features of oral malignant and potentially malignant disorders with and without oral epithelial dysplasia. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology 116 (6): 725-733. https://doi.org/10.1016/j.oooo.2013.08.005
- Laganovska K, Zolotarjovs A, V&aacute z, M. MD, K. L, J. B, H. K, V., Smits K (2020) Portable low-cost open-source wireless spectrophotometer for fast and reliable measurements. HardwareX 7: 00108. https://doi.org/10.1016/j.ohx.2020.e00108
- Mobadersany P, Yousefi S, Amgad M, Gutman DA, Barnholtz-Sloan JS, Vel&aacute zV, E. J, Brat DJ, Cooper LA (2018) Predicting cancer outcomes from histology and genomics using convolutional networks. Proceedings of the National Academy of Sciences 115 (13): 2970-2979. https://doi.org/10.1073/pnas.1717139115
- Radhika T, Jeddy N, Nithya S, Muthumeenakshi R (2016) Salivary biomarkers in oral squamous cell carcinoma - An insight. Journal of Oral Biology and Craniofacial Research 6: 51-54. https://doi.org/10.1016/j.jobcr.2016.07.003
- Shamsher N, Prabhu C (2020) QuitPuff: A simple method using lipid peroxidative changes in saliva to assess the risk of oral precancerous lesions and oral squamous cell carcinoma in chronic smokers. Indian Journal of Medical and Paediatric Oncology 41 (05): 670-676. https://doi.org/10.4103/ijmpo.ijmpo_127_19
- Speight PM, Khurram SA, Kujan O (2018) Oral potentially malignant disorders: risk of progression to malignancy. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology 125 (6): 612-627. https://doi.org/10.1016/j.oooo.2017.12.011
- Tschandl P, Codella N, Akay BN, Argenziano G, Braun RP, Cabo H, Gutman D, Halpern A, Helba B, Hofmann-Wellenhof R, Lallas A, Lapins J, Longo C, Malvehy J, Marchetti MA, Marghoob A, Menzies S, Oakley A, Paoli J, Kittler H, (2019a) Comparison of the accuracy of human readers versus machine-learning algorithms for pigmented skin lesion classification: an open, web-based, international, diagnostic study. The Lancet Oncology 20 (7): 938-947. https://doi.org/10.1016/s1470-2045(19)30333-x
- Tschandl P, Codella N, Akay BN, Argenziano G, Braun RP, Cabo H, Gutman D, Halpern A, Helba B, Hofmann-Wellenhof R, Lallas A, Lapins J, Longo C, Malvehy J, Marchetti MA, Marghoob A, Menzies S, Oakley A, Paoli J, Kittler H, (2019b) Comparison of the accuracy of human readers versus machine-learning algorithms for pigmented skin lesion classification: an open, web-based, international, diagnostic study. The Lancet Oncology 20 (7): 938-947. https://doi.org/10.1016/s1470-2045(19)30333-x
- Welikala RA, Remagnino P, Lim JH, Chan CS, Rajendran S, Kallarakkal TG, Zain RB, Jayasinghe RD, Rimal J, Kerr AR, Amtha R, Patil K, Tilakaratne WM, Gibson J, Cheong SC, Barman SA (2020) Automated Detection and Classification of Oral Lesions Using

Deep Learning for Early Detection of Oral Cancer. IEEE Access 8: 132677-132693. https://doi.org/10.1109/access.2020.3010180

- Zhang H, Li W, Zhang H (2021) An Image Recognition Framework for Oral Cancer Cells. Journal of Healthcare Engineering1-8. https://doi.org/10.1155/2021/2449128