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ORIGINAL ARTICLE

Oral leukoplakia evaluation through clinical photography: classification, interactive segmentation, and automated binarization before going on Artificial Intelligence algorithms

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Abstract:

Oral leukoplakia (OL) evaluation through photographs can be performed with the aid of Artificial Intelligence (AI). Supervised Machine Learning (SML) processes, which are based on labeling, are indicated to ensure a reliable computational mechanism of lesion identification. Thus, OL classification and demarcation within a photograph are crucial for SML. Objective: To label OL lesions in homogeneous and non-homogeneous using photographs, and to test a segmentation procedure, aiming for its use in a trustworthy dataset. Methods: Fifty-five OL photographs were inserted into Fiji/ImageJ, and a region of interest (ROI) was defined to obtain a three-dimensional plot of pixel color clustering. Then, the photography and the plot were used for OL classification by a panel of 5 experts in Oral Medicine. The segmentation process was performed by two operators which created a second ROI for evaluation of the lesion by area, perimeter, centroid, and circularity. The intraclass correlation coefficient was calculated and a comparative analysis was performed (Mann Whitney and Unpaired t-test). Then, segmentation was accomplished by creating a computer code including the precise information of the lesional site, in an automated binarization fashion. Results: The experts agreed in 53% of the cases regarding OL classification. An excellent level of operator agreement related to the size and site of the lesion was found. Although, differences were found comparing the lesion's area, perimeter, and centroid ($p<0.05$). The code was effective for the segmentation separating the lesion from the background. Conclusion: The agreement on OL classification among experts accounted for half of the cases. The lesion segmentation was possible using a computer code based on interactive drawing. With an excellent agreement between operators, the manual delimitation of lesional sites can be used for SML, but the differences regarding lesional perimeter and its classification should be considered before labeling and creating a good dataset.

Keywords: Artificial Intelligence; Photography; Leukoplakia, Oral

INTRODUCTION

Oral squamous cell carcinoma (OSCC) can be preceded by a potentially malignant disorder, one being oral leukoplakia (OL)[1,2], considered one of the most common oral potentially malignant disorder[3]. A meta-analysis revealed that OL overall prevalence worldwide was 4.11% among adults[2]. OL can be classified as homogenous (homogeneous white plaque presentation) and non-homogenous (lesions including erythematous areas beyond the white plaques, such as the erythroleukoplakia, and lesions with altered texture)[4]. The non-homogeneous lesions suggest a significantly increased risk of malignant transformation[5].

In face of the large variation in OL clinical presentation, its diagnosis and management could be challenging for health professionals. In this way, intraoral photography has been gaining attention due to its key role in the diagnosis and monitoring of patients with these lesions[6,7]. Machine learning (ML) – a subset of Artificial Intelligence (AI) – appears as a prominent tool to improve the prediction and diagnosis of different types of oral lesions, usually combining clinical information with the physical aspects of the lesion[8,9].

ML is based on pattern identification and recognition, which considers all the information within an image – without involving human experience. At one point, it is necessary to check the reliability of this recognition, and the supervised Machine Learning (SML) takes place, with the insertion of crucial information based on the labeled images[10]. OL photographs correspond to clinical images containing information about the lesion, which includes the lesion's color, size, margins, appearance, texture, and exact site, meaning, the location on the mucosa affected by the lesion and that could be delimitated/demarcated[7]. For SML, labeling is necessary so that the algorithm could be somehow trained based on the raw information contained in the images, also considering their allocation in different groups. In this way, the aim of the study was to label the OL lesions using photographs, considering their classification into homogeneous and non-homogeneous, with the aid of a 3D pixel clustering plot. In addition, to create a binarized mask of the OL lesion based on an interactive segmentation, and to check the agreement between individuals who performed the manual segmentation of the lesion, prospecting its use for SML.

MATERIALS AND METHODS

Fifty-five OL photographs were obtained from the archives of the Hospital Dentistry Service of the Polydoro Ernani de São Thiago University Hospital (HU-UFSC), and of the Oral Diagnosis Center of the School of Dentistry of the University of São Paulo (FOUSP). The OL photographs were selected based on the following parameters: images in TIFF and JPEG format; with substantial quality allowing the identification of the whole OL lesion; with no blurred spots on the lesion surface; and with no excessive brightness which could interfere on the lesion analysis. OL lesions included both homogeneous and non-homogeneous presentation, the last ones also including images of patients diagnosed with Proliferative Verrucous Leucoplakia (PVL). The project was approved by both Institutional Research Ethics Committee (UFSC - CAAE: 46527321.0.0000.0121, with the Approval number: 4.798.415; FOUSP – CAAE: 46527321.0.3001.0075, with the Approval number: 4.831.275).

Oral leukoplakia classification

The OL images were inserted on the Fiji/ImageJ software (ImageJ 1.53q, Wayne Rasband, National Institute of Health, USA), followed by the delimitation of a ROI with a square format, with a dimension of 125x125 pixels (Figure 1A and 1B). The color scale was adjusted to 8-bits, with values between 0-100. Using the plugin "Color Inspector 3D (v2.5)" for ImageJ, a three-dimensional plot was created containing the color clustering information of the selected ROI. The 3D plot based on color clustering reveals spheres of different sizes within a cube. Pixels with the same color value are grouped creating a cluster, represented by a sphere on the plot. The more pixels of those color values, bigger the sphere. The spheres are organized within the plot in a central line, so whitish colors are disposed more on the top of the cube, and reddish spheres are on the bottom of the cube (Figure 1C and 1D).

With these plots, a presentation was organized with each OL image and its correspondent plot. A questionary was realized with the stomatologists of the project to verify their concordance on the lesion's classification in homogenous and non-homogenous. The 5 stomatologists classified the lesions considering their clinical experience, and received the orientation to use the 3D plot as an auxiliary tool.

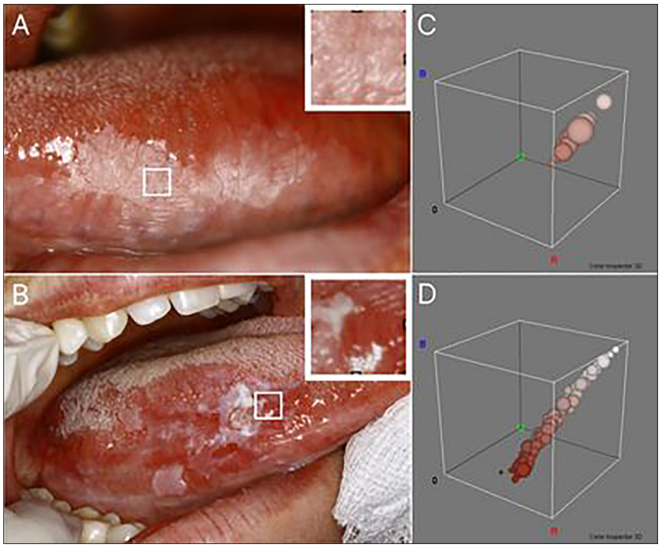

Figure 1. A) Clinical image of homogenous OL localized at side edge of tongue, permeated by pinkish mucosa under normal conditions. B) Clinical image of non-homegenous OL (eritroleukoplakia) containing both white and reddish areas. C and D) 3D plot containing spheres of different sizes representing the color clustering variation observed, ranging from white to red colors.

Interactive segmentation and binarization

The interactive segmentation of the OL lesional site within the image was also performed using the Fiji/ImageJ software. Two calibrated operators (one undergraduate student – first author - and one master student – second author) received previous orientation about the use of ImageJ tools and how to perform the manual drawing of the whole lesion site in the clinical image (Figure 2A). Both operators realized the interactive segmentation of the lesions individually and saved each ROI in a separate folder. The delimitation of the ROIs was based on the full extent of the lesion using the tool "Polygon Selection", with the brush tool size of 25 pixels (Figure 2A). Regions that could make it confused for delimitation, such as the ones including shadows, inflammation areas, possible traumatic associated lesions, or regions with intense bright areas generated by camera flash were excluded. In addition, lesion sites were considered individually, meaning that distinct sites with healthy mucosa between lesions were considered two sites. After segmentation, the ROIs were analyzed by the parameters: area and perimeter of the lesion (in pixels), centroid (localization of the most central pixel of the lesion on the x and y axis in the image) and circularity. For the measurements, the "Measure" tool on ImageJ was used (using the command Ctrl+M, previously defined in "Set measurements" for: Area, Perimeter, Shape descriptors and Centroid).

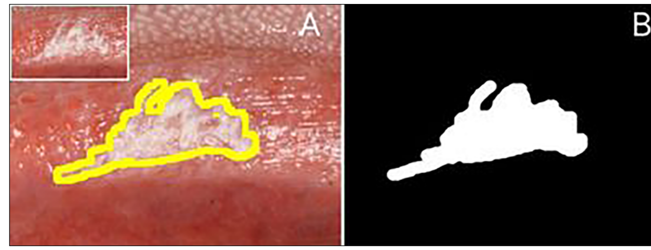

Figure 2. Scheme demonstrating the process of creating the mask for binarization using the program Visual Studio Code. A) Initial clinical image of homogeneous OL and a ROI created through the lesion interactive segmentation phase - limits of the lesion perimeter can be seen delimited in yellow. B) Binary mask created through the computer code based on the initial clinical image and its respective ROI, made in the Visual Studio Code program.

To conclude the segmentation, the binarization was performed in order to separate the lesion from the whole image background (Figure 2B). A computer code was created in Python language for obtention of binary masks of the OL lesional sites. The Visual Studio Code program was used with the aid of Jupyter Notebook program for the creation of mask named create_mask_from_roi (https://github.com/ricardocaldas/maskimg). This code was formulated using Python 2.8 language with resources offered on Numpy, OS, Shutil, Tempfile, Matplotlib, Roifile, CV2. The code create_mask_from_roi was intended to fill regions of interests in white, matching with the lesional sites, and regions of non-interest in black, meaning the whole other sites in the image. The functionality "create_mask_from_dir" was created for execution and the result of "create_mask_from_roi" was completed in a separated directory. A visual evaluation of each mask created and the match with the lesional site within the image was confirmed for the 55 images tested.

Statistics Analysis

The data was inserted into Excel and analyzed using GraphPad Prism 9.0. The Shapiro-Wilk normality test was performed for all variables. The comparations were performed using the Mann-Whitney test (for the parameters: area, perimeter, and circularity) and the Unpaired t-test (for the parameters of the centroid of the X and Y axes). The concordance between operators was calculated with the intraclass correlation coefficient (ICC). A significance level of 5% was considered.

RESULTS

Oral leukoplakia classification

From the 55 images obtained from both Institutions, 51 met the inclusion criteria and were used for classification agreement. The four excluded images were removed from the final analysis because the 3D plot was identified to be not representative of the whole lesion extension once the ROI selection was difficult to be defined. Through the questionary containing each clinical image of the OL lesions and its corresponding plot, a total agreement of 53% was obtained for all five experts, with 12 cases for homogeneous and 15 non--homogeneous. A partial agreement of 47% was found for the other lesions. In 6 cases the partial agreement was found to be classified equally by four experts, and only one disagreed with the classification. In the other 18 cases, there was an agreement among 3 experts and a disagreement between 2 professionals.

Regarding the 3D plot, it was observed that most parts of the homogeneous lesions revealed the pixel's clustering forming big spheres, most of them being white and whitewish colors, and some of them with light pink and beige colors. Non-homogeneous cases revealed red spheres on the plot, mostly concentrated on the bottom corner of the cube. These spheres were smaller than the other spheres. In all plots, the spheres were usually disposed of in a linear arrangement.

Lesion interactive segmentation and binarization

The interactive segmentation between operators (OP1 = MA and OP2 = TR) revealed great concordance for all analyzed parameters – area, perimeter, centroid axis x, centroid axis y – except for circularity (ICC, Table 1). However, comparative tests revealed significant difference for parameters area ($p<0.0001$), perimeter ($p<0.001$) and centroid axis X ($p<0.03$), as seen in Table 2.

The agreement between operators on the delimitation process allowed proceeding with the binarization process. At this point, the ROIs designed by the first operator were chosen for the final segmentation step, being the creation of binarized masks, which consists in the separation of the whole lesion from the background. The computer code created was then used and after running, the 55 binary masks were created, with the lesional site in white and the background in black. The whole process for the binarization was conducted in less than 1 minute.

Table 1. Intraclass correlation between the two operators regarding the results of the interactive segmentation.

Parameters	ICC	*p*
Area	**0.876**	**<0.001**
Perimeter	**0.810**	**<0.001**
Centroid (X axis)	**0.970**	**<0.001**
Centroid (Y axis)	**0.973**	**<0.001**
Circularity	0.410	0.60

Significant agreement in bold.

DISCUSSION

This study analyzed the photographs obtained during patient care on the clinical evaluation of oral leukoplakia. These photographs were not only taken for diagnosis, but for lesion monitoring during the follow--up, mostly aiming to identify alterations in the lesion's clinical appearance. First, for classification, even with the use of a 3D additional plot with information on the color distribution, it was noted that an agreement among experts could not be present in all cases. Similar to our results, a recent study of Araújo et al. (2023)[9], conducted on 46 clinical images of patients diagnosed with oral potentially malignant disorders, revealed that the subjective clinical assessment may explain the source of interobserver discordance on the classification and annotation of the lesions, and that this subjectivity is based on human observation, a variable criteria that suffered from adjustments over the years, different educational backgrounds, and personal experience.

The creation of a 3D plot with information on the number of pixels of each color within the lesion area might be a tool that can be used in the OL classification process into homogenous and non-homogenous. The result of 3D plots created in this study showed a noticeable difference between lesions that were considered homogenous and non-homogenous, revealing colored spheres with different sizes. However, the classification of OL lesions, even with the use of the mentioned plot, only revealed 100% agreement among the experts in half of the cases. This finding could be justified because, besides color, OL classification contemplates other clinical aspects, such as surface texture and lesions boundaries. Another study revealed that besides color, other features in the clinical evaluation were also important, meaning size, margin, surface appearance, and irregularity[11]. Another fact is that during the questionary, it became notable that the experts based the classification mostly on their own experience and did not really hold on to the 3D plot interpretation. One could assume that this image interpretation regarding pixel clustering is usually not applicable in clinical practice. Ilhan et al. (2020)[12] revealed that the application of filters and contrast enhancement in clinical imagens of lesions - in addition to the 8bit scale used in our study - may be a viable alternative

Table 2. Comparative analysis of the results obtained by the two operators related to the lesion characteristics within the image.

Parameters	Operator 1	Operator 2	*p*
Area (pixels)	348089 (93227 – 884005)	436548 (176318 – 1340426)	0.08
Perimeter (pixels)	3149594 (1567313 – 6276177)	4483750 (2250664 – 6800856)	0.16
Centroid (pixel location)			
X axis	1345884 (±567298)	1283075 (±531234)	0.61
Y axis	955365 (±368411)	969999 (±402251)	0.86
Circularity (#)	0.40 (0.30 – 0.42)	0.30 (0.20 – 0.50)	0.52

for standardizing and defining the plots, maybe increasing the concordance rate among the experts. In sum, regarding our results, the need to consider subjectivities during the OL classification process before proceeding with AI algorithms should be taken into account.

Besides classification, the separation of the lesion from the background in an image could be tricky, mostly because the definition of the lesion's borders could not be similar considering different operators. The agreement on the lesional site defined by the two operators was excellent, however, carrying the differences in the manual drawing related to the lesional perimeter. All these together suggest that it could be a real challenge to label an oral leukoplakia using its photograph, mainly because of its prospection to use this information in labeling before the creation of a dataset of good quality aiming its use on AI algorithms.

Concerning the segmentation process, it was demonstrated in our study that the definition of the precise demarcation of the lesion boundaries can be challenging. Mirzaalian Dastjerdi et al. (2019)[13] verified that the interactive segmentation process for skin lesions, outlining the surface of lesions, depends on clinicians' opinion and experience and may vary between different operators. Our results were in accordance once differences in the manual drawing of the lesions revealed significant differences between the two operators regarding area, perimeter, and the centroid of the lesions, and the two operators had different experience levels. However, there was an excellent level of agreement between both professionals, meaning, they were in accordance concerning the differentiation amongst big and smaller lesions, and in defining the lesion site within the image.

Once the agreement was found, it was enabled to proceed with the continuation of the methodology, which allowed the creation of a binary mask through a computational code. The binarized masks faithfully separated the lesion area from its background based on an operator's segmentation. The ROI definition is necessary for the following steps, including any other AI methodologies that will be used. In our study, the geolocation of the lesion within the image defined manually, and included within the computational code, could be used together with the OL classification to accomplish the labeling development. Besides SML, labeling is important also for other AI methods, such as convolutional neural networks (CNNs). In the study of Gomes et al. (2023)[14], the authors performed a manual delimitation and cropping of a rectangle ROI including the whole lesion, which was then used in the training CNN process, which was presented in a labeled and supervised way. In the end, it could be suggested that the labeling phase, before going on to the real AI algorithm creation and training, could be challenging and may need a team of experts and students to perform the manual drawing of the lesions, something that could be really time-consuming. Welikala et al. (2020)[15] reported that automated detection and classification of oral lesions for the early detection of oral cancer is a task that faces several issues, including the difficulty of accessing labeled datasets.

The present study aimed the creation of mechanisms that will improve OL labeling using clinical images. The use of AI – mainly SML – still needs human involvement for the perfect calibration and the use of datasets with reliable information. Our results point to the fact that the human experience in both classification and segmentation was crucial to increase the quality of the datasets that will be used for any AI methods. Moreover, SML are susceptible to requiring overfitting and careful validation in addition to labeled data and training[16].

The limitation of this study was mostly related to the use of OL photography captured in an intraoral approach can result in an image with lower quality. The clinical images that were obtained from the archives of the institutions presented different saturation, color scale, brightness, size, and amount of tissue adjacent to the lesion which can reduce the efficiency of classification.

CONCLUSION

In conclusion, labeling oral leukoplakia lesions in clinical images is a challenging process that needs the evolvement of students and experts. The classification into homogeneous and non-homogeneous was in total agreement among the experts in half of the cases, and the 3D plot of color clustering was helpful in some way. Manual delimitation of the lesion for segmentation was revealed to be different between the two operators regarding the lesion's boundaries, even though there was an agreement on the lesion's size and location within the image. Binarization was possible in an automated fashion through the creation of a computational code, based on the manual drawing of the whole lesion. Information on the classification and the precise lesion location in the photography is crucial for the labeling process, improving the quality of the dataset, before starting with the creation of an artificial intelligence algorithm.

Compliance with Ethical Standards: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the Declaration of Helsinki from 1964 and its later amendments or comparable ethical standards.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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