Theoretical Background to Automated Diagnosing of Oral Leukoplakia: A Preliminary Report

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1. Introduction

Oral leukoplakia represents the most common oral potentially malignant disorder [1]. It is a white patch or plaque that cannot be characterized clinically or pathologically as any other disease. It is a classical definition of leukoplakia presented by the World Health Organization. Etiology of leukoplakia is multifactorial. Most important factors are alcohol, smoking cigarettes, poor oral hygiene, electro-galvanic currents, and spicy food irritating oral mucosa. Possibility of malignant transformation of leukoplakia is in the range between 0.2% and 5% [2]. Due to the risk of malignant transformation, it is important to take a proper diagnosis. The golden standard of diagnosis is still histopathological examination, but invasiveness is a main disadvantage of that examination. Fluorescence or autofluorescence of lesions are used in some of the diagnostic systems, such as ViziLite®, ViziLite®PLUS, VELScope®, Identafi®, and Orascoptic DK [3, 4]. The huge wave of electro-optical devices is a base for alterations in oncological prophylaxis in oral squamous cell cancer. There are simple analogous apparatus, such as VELScoope and Microlux, which utilize fluorescence or led light. Unfortunately their specificity is very low.

Digital images are consisted of pixels. Pixels build patterns which create texture. Mathematical and statistical analysis of texture patterns is known as texture analysis (TA). Methods of TA are based upon the mathematical analysis of the matrix that represents the distribution of pixel brightness within the image. Texture analysis may be divided into four methods: statistical, structural, model-based, and transform [5, 6]. TA is commonly used in medicine to analyze X-ray photos, computed tomography images, or magnetic resonance images. Intraoral digital photos of leukoplakia seem to be a good material for texture analysis, which will be helpful in early diagnostic.

On the one hand, nowadays, intraoral macrophotography with a digital single lens camera or compact system...
camera is popular in dentistry. On the other hand, endo-
scoping image acquisition is possible in oral cavity by
maxillofacial surgeons, ENT doctors, or gastroenterologists
too. Previously mentioned methods may be the potential
source of images which can be analyzed using TA.

Electronic, tele-, and automated diagnosing is possible in
the decade when each physician possess a smartphone.
Proper small cameras and LED light are in all telephones,
and many electrooptical devices are available in dental or
medical centers. The minor development is noted in the field
of specialized software.

The aim of this study was to create a base of the remote
diagnosis system of oral leukoplakia.

2. Materials and Methods

2.1. Patients. Thirty-five patients affected by leukoplakia
were included into this study. All lesions were histopatho-
logically verified (with standard hematoxylin and eosin
staining) after taking the specimen from pathologically
changed oral mucosa under local anesthesia. The mean age
of the study group was 58 years. Exclusion criteria was a high
grade dysplasia.

Intraoral photography of normal oral mucosa and
leukoplakia was taken using a Canon EOS 500D (Canon,
Ota, Tokyo, Japan) digital camera with a macro ring
13 mm, 50 mm, f1.8 lens (Canon, Ota, Tokyo, Japan) and
ring flashlight YN-14EX (YONGNUO Photographic
Equipment, Longhua District, Shenzhen, China). All
photos were taken from the same distance (focus distance
was locked to achieve it), and optical axis of lens was
perpendicular to examined lesion. A polarized filter on
the camera lens was applied to reduce any reflections.
Directly before taking photo, affected mucosa was getting
dry to decrease the risk of reflections.

All procedures were conducted after obtaining the ap-
proval of the Ethics Committee of Wroclaw Medical Uni-
versity, Poland (approval No. KB-367/2014).

2.2. Image Preprocessing. All of graphical operations were
performed in GIMP version 2.10.8 (GNU Image Ma-
nipulation Program, https://www.gimp.org/). In the
center of the lesion, the region of interest (ROI) with
300 × 300 pixels was selected. Leukoplakia ROI was se-
lected at the center of the lesion, without reference
healthy mucosa. Reference mucosa ROI was selected from
the same region, for example, if lesion was at the tongue,
reference ROI was selected at the tongue. Such prepared
fragment of image was cut-off from the original photo.
To achieve maximum possible contrast of photography, a
high-pass filter was applied. After that, level tools were
used to equalize image histogram (to unify contrast of all
images). Next, images were converted into the 4 bits grey
scale. File was saved into TIFF format without any
compression algorithms. All graphical operations are
shown in Figure 1. The region of interest was chosen
without any visible reflections in all of cases.

2.3. Texture Analysis. Optical images (300 × 300 pixels) from
35 cases were transformed to the 4 bit grey scale graphical files
imported in MaZda 4.6 (Technical University of Lodz, Poland)
software, and texture analysis was performed (Figure 2) [7, 8].
Six textural features were selected: two of run length matrix
(long run emphasis inverse moments and short run emphasis
inverse moments), two of co-occurrence matrix (entropy as
shown in Figure 3 and difference entropy calculated in distance
of 5 pixels), and two of Haar wavelet transformation (wavelet
energy after a two-dimensional low-pass filter and scale 5 and
scale 6 of the transformation) [9–11].

Let \( p(i, j) \) be the number of times there is a run of
length \( j \) having grey level \( i \). Let \( N_g \) be the number of grey
levels, and \( N_r \) be the number of runs [12]. Definitions of
the parameters of the run length matrix \( p(i, j) \) are given
below.

Long run emphasis inverse moments:

\[
\text{LngREmph} = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} j^2 p(i, j)}{C}. \quad (1)
\]

Short run emphasis inverse moments:

\[
\text{ShrtREmph} = \frac{\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i, j)j^2}{C}, \quad (2)
\]

where the coefficient \( C \) is defined as

\[
C = \sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i, j). \quad (3)
\]

The co-occurrence matrix-derived parameters are de-
defined by the equations that follow, where \( \mu_x, \mu_y \) and \( \sigma_x \) and \( \sigma_y \) denote the mean and standard deviations of the row
and column sums of the co-occurrence matrix, respectively,
which are related to the marginal distributions \( p_x(i) \) and
\( p_y(j) \).

Entropy:

\[
\text{Entropy} = -\sum_{i=1}^{N_g} \sum_{j=1}^{N_r} p(i, j)\log(p(i, j)). \quad (4)
\]

Difference entropy:

\[
\text{DifEntrp} = -\sum_{i=1}^{N_g} p_{x-y}(i)\log(p_{x-y}(i)). \quad (5)
\]

For discrete Haar wavelet transformation, the calculation
of energy for frequency 2D subband after passing a low-
pass filter (\( L \)) in scales 5 and 6 was performed:
$E_{\text{subband, scale}} = \frac{\sum_{x,y\in \text{ROI}} (d_{x,y}^{\text{subband}})^2}{n}$, \hspace{1cm} \hspace{1cm} \hspace{1cm} (6)

where $d$ is the wavelet coefficient, and $n$ is the number of pixels in region of interest (ROI, i.e., whole image presented in Figure 3 in the upper raw), both at 5$^{\text{th}}$ and 6$^{\text{th}}$ scales and subband LL. ROIs are reduced in successive scales in order to correspond to subband image dimensions. Output of this procedure is a vector of features containing energies of wavelet coefficients calculated in subband LL at 5$^{\text{th}}$ and 6$^{\text{th}}$ scales.

Figure 1: Graphical operations of source intraoral photography of leukoplakia.
ANOVA was performed in Statgraphics Centurion XVI software. Next, procedure uses a probabilistic neural network (PNN in Statgraphics Centurion XVI software) to classify cases into different diagnosis, based on 3 input variables (input factors were the strong distractors of this image analysis: short run emphasis inverse moments, entropy, and wavelet transformation energy in scale 5 of the 35 cases (Figure 4).

2.4. Statistical Analysis. The Shapiro–Wilk test was applied to checking normality. One-way analysis of variance (ANOVA) was applied. The difference was considered as significant if $p < 0.05$. Statgraphics Centurion 18 ver.18.1.12 (StarPoint Technologies, Inc., Virginia, USA).

3. Results

Summary statistics of selected textural features of oral mucosa are presented in Table 1. Frequency of short run emphasis inverse moments artifacts decreases significantly in leukoplakia lesion ($p < 0.005$). Both methods of calculation of the entropy reveals their decrease in pathology (difference entropy $p < 0.005$ and entropy $p < 0.001$, Figure 5). The superimposition on texture pattern is the highest

Figure 3: Analyzed images. Left column: leukoplakia of oral mucosa. Right column: normal oral mucosa. In top: raw photographic images. In second row: images after transformation to the 8 bit normalized grey scale. Third row: short run emphasis inverse moments map (number of short lines of similar pixels increased in some regions of leukoplakia-left image). In bottom: maps of entropy distribution in the image (inside leukoplakia, foci are dark areas of low entropy mixed with high entropy plates; in normal mucosa, entropy is distributed regularly).
The energy is the highest as far as Haar wavelet transformation considered in scales 5 and 6.

Neural network discrimination shows (Figure 6) full leukoplakia recognition (sensitivity 100%) and specificity 97%. All of leukoplakia images were described properly, and one normal mucosa image was classified as pathological lesion.

4. Discussion

Sambandham et al. applied the ViziLite system in case of leukoplakia diagnosis. Their study shows that sensitivity and specificity of ViziLite is about 77.3% and 27.8%, respectively [13]. McIntosh et al. revealed that the Microlux/DL system showed a sensitivity of 77.8% and a specificity of 70.7% in case of leukoplakia diagnosis [14]. Ibrahim et al. revealed that even adding toluidine blue dye did not improve the effectiveness of the Microlux/DL system. At the same study, they showed that the sensitivity was 100% and specificity was 32.4% of Microlux/DL for visualization of suspicious pre-malignant lesions when considering biopsy as a golden standard [15].

Lalla et al. confirmed that it is possible to detect oral epithelial dysplasia using reflectance spectroscopy (Identafi and DentalEZ). Their study showed that Identafi’s system under violet light offered a sensitivity of 12.5% and specificity of 85.4% for detection of oral epithelial dysplasia. It is important to know that high level of clinical experience is required to interpret the results of autofluorescence examination [16].

Chan et al. used texture analysis in case of micro-calcifications detection on mammograms. Their result indicates that computerized texture analysis can extract mammographic information that is not apparent by visual inspection. These studies reveal that the level of specificity was 39% and the sensitivity level was 100% [17]. Our results were the same at the level of sensitivity but much higher in aspect of specificity (97%). Li et al. studies confirmed too that mammographic texture analysis was a reliable technique for differential diagnosis of benign and malignant breast tumors. Furthermore, the combination of imaging-based diagnosis and texture analysis can significantly improve diagnostic performance [18].

Short run length emphasis inverse moments detect short lines of pixels which have similar lightness. Their presence in mucosal image is the normal status. As the short lines disappeared, the leukoplakia develops. Similarly, entropy and difference entropy indicate the regions where the fine nest of mucosal surface texture exists. In pathological lesion, that fine texture disappears transforming into white regions, i.e., leukoplakia areas. Haar wavelet transformation results indicate that the pathological lesions of leukoplakia are quite extended due to a significant scale of wavelet transformation (scale 5 and scale 6), which can be superimposed on the pathological

![Figure 4: Schema of the probabilistic neural network used for discrimination the leukoplakia lesion from normal mucosa.](image-url)

Table 1: Summary statistics of textural features in normal oral mucosa and leukoplakia lesions.

| Textural feature                        | Reference mucosa          | Leukoplakia lesion | ANOVA |
|-----------------------------------------|---------------------------|--------------------|-------|
| Long run emphasis inverse moments       | 9.70 ± 15.38*             | 13.93 ± 8.90       | F = 1.99; p = 0.16 |
| Short run emphasis inverse moments      | 0.64 ± 0.14*              | 0.56 ± 0.08        | F = 10; p < 0.005 |
| Entropy                                 | 1.73 ± 0.12               | 1.62 ± 0.10        | F = 16; p < 0.001 |
| Difference entropy                      | 0.56 ± 0.09               | 0.50 ± 0.07        | F = 11; p < 0.005 |
| Wavelet transformation energy LL scale 5| 57.44 ± 2.61              | 67.75 ± 1.52       | F = 462; p < 0.0001 |
| Wavelet transformation energy LL scale 6| 56.12 ± 2.61              | 65.65 ± 1.86       | F = 309; p < 0.0001 |

* Lack of normal distribution.
texture. That again points that the oral mucosa lost its physiological fine textural appearance.

That objective analysis in the neural network revealed that involving 3 textural features into optical analysis of the oral mucosa leads to proper diagnosis of leukoplakia. One normal sample of oral mucosa was recognized as pathology probably due to subclinical development of pathology in mucous membrane.

The proposed 5 or less features of oral mucosa texture observed in natural or artificial light can be used for developing simple application for a smartphone to significantly improve possibility of oral mucosa leukoplakia.

5. Conclusions

Application of texture analysis for oral leukoplakia versus healthy mucosa is a promising diagnostic method, which may be a base of the remote and semiautomatic diagnosis system.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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