Computer analysis in oral lichenoid reactions

Ulf Mattsson, Guy Heyden, Artur Chodorowski, Tomas Gustavsson, Mats Jontell and Folke Bergquist

Department of Oral Pathology, Department of Endodontology/Oral Diagnosis, Mednet Laboratory, University of Göteborg; Department of Applied Electronics, Chalmers University of Technology; and Hasselblad Electronic Imaging AB; Göteborg, Sweden

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To improve diagnostic procedures and facilitate clinical decision-making, computer-assisted image analysis was performed on color slides from 30 patients with histopathologically verified oral lichenoid reactions. Areas from white hyperkeratotic and adjacent red inflamed areas of the lesions were selected and subjected to image analysis. The digitization of the color slides was done by means of an image scanner, and the digital information was transmitted to a personal computer for subsequent feature extraction and analysis. The different oral lesions were characterized as the difference in mean values between white hyperkeratotic and red inflamed areas, respectively, compared with clinically normal tissue. Statistical analyses were made on three different color systems: Red-Green-Blue (RGB), normalized red-green-blue (rgb), and Intensity-Hue-Saturation (IHS). The results showed statistically significant differences in all color systems for both the hyperkeratotic areas and adjacent inflammatory reactions. A linear correlation was obtained when the results of the image analysis of color variations were compared with a clinical score system for hyperkeratosis and inflammation evaluated by two investigators independently. □ *Computer analysis; dentistry; mouth diseases; mucosal lesions*

Ulf Mattsson, Department of Oral Pathology, Faculty of Odontology, University of Göteborg, Medicinaregt. 20, S-413 90 Göteborg, Sweden

Modern camera equipment for clinical macrophotography has proved to be a valuable tool for the clinical analysis of oral soft tissue lesions over time (1). The interpretation of color slides is, however, limited by our ability to discriminate between changes in color and express differences objectively and quantitatively. Computer processing of color slides may improve this interpretation and facilitate diagnostic procedures and clinical decision-making. Assisted scientific analyses of oral mucosal lesions would also contribute to our understanding of temporal changes of these lesions.

Computer-assisted methods for image analysis are currently being used in several fields of science, such as modern oral radiology, forensic dentistry, and oral pathology. The objectives of introducing image processing and feature analysis have varied, but the technique is used as a valuable aid in different forms of analyses. Feature analyses of digitized images are used to evaluate and compensate for differences between observers (2, 3). It can also be used as an instrument for direct measurement (4, 5) or to identify image features indicating pathologic conditions (6).

The purpose of the present study was to elaborate and evaluate a method of standardized image processing and analysis of color slides of clinically recognized hyperkeratosis and inflammation in histopathologically confirmed oral lichenoid reactions. The possibility of correlating the clinical judgement of hyperkeratinization and inflammation to changes in image data was to be evaluated.

Materials and methods

In the present study oral lichenoid reactions included both lesions of oral lichen planus and adverse reactions to amalgam fillings. The clinical criteria of oral lichen planus and lichenoid reactions differed only with regard to their involvement of the oral mucosa. Oral lichen planus was found in the buccal mucosa and in at least one additional area, whereas the adverse reactions appeared in the buccal mucosa as solitary lesions closely associated with amalgam fillings.

The diagnosis of the lesions had been histopathologically verified and classified in accordance with the criteria recommended by WHO (7). Color slides of 30 patients (mean age, 54 years; SD, 11 years) were randomly selected from a slide collection of oral mucosal lesions at the Department of Endodontology/Oral Diagnosis, University of Göteborg. Slides with lesions showing both a clearly visible hyperkeratotic area and an adjacent inflammatory zone were included in the study. The photographs were taken during a period from 1987 to 1991.

Image digitization

The colour slides were digitized using a stepmotor-controlled 2048 linear CCD sensor (Dixel 2000, Hasselblad Electronic Imaging AB, Göteborg, Sweden). The digitized images were represented by 512 × 368 pixels with 24 bits per pixel and 8 bits per color. Each pixel contained red (R), green (G), and blue (B) values on a scale ranging from 0 to 255. This information was then transmitted to an IBM-compatible PC with an extended graphics card (ATVista Truevision Inc., Indianapolis, Ind., USA) and later subjected to image analysis.

Image feature extraction and classification of image data

Image data were collected in three steps.

1) In all slides image features were extracted from an area adjacent to the lichenoid reaction, in a region considered by the operator as normal tissue. These data would later serve as reference values in the following statistic analysis.

2) In the next step image features were extracted from the hyperkeratinized part of the lesion. Parallel to the extraction of quantitative image information a classification was made by the operator on the basis of the visual appearance of the hyperkeratosis within the extracted object. It was classified as mild (i), moderate (ii), or pronounced (iii) in accordance with the clinical criteria below.

i) A white slightly translucent area with no elevation of the lesion above the surface.

ii) A distinct white area with no translucency and no obvious elevation compared with adjacent tissue.

iii) A compact white area with no translucency and with an elevation compared with adjacent tissue.

3) Finally, image features were extracted from the inflamed area surrounding the hyperkeratinized region. The inflammation was classified in accordance with the score system described below as mild (i), moderate (ii), or pronounced (iii).

i) A thin pale red area with only slight visible difference in redness compared with adjacent clinically normal tissue.

ii) A broader and distinct red area adjacent to hyperkeratosis.

iii) An intensely red area adjacent to and extending wide from the white areas.

When hyperkeratinization or inflammation appeared heterogeneous, image features were extracted from more than one area of the lesion.

Methods of analysis

In the analysis three color systems were used. This was done to evaluate whether any of the systems presented advantages for the interpretation of obtained image features when compared with the histopathologic changes analyzed in the study. The color systems used were as follows:

I. Red (R)–Green (G)–Blue (B) values (RGB) that represented the originally digitized values for each pixel on a scale from 0 to 255.

II. Normalized red (r)–green (g)–blue (b) values (rgb). The color system describes the relative amount of Red (R), Green (G), and Blue (B), respectively, for each pixel.

Table 1. Comparison between registered mean values and standard errors (SEM) in hyperkeratotic areas in lichenoid reactions and normal tissue through computerized analysis. Differences are measured in digitized Red-Green-Blue values (RGB), normalized red-green-blue values (rgb), and in Intensity-Hue-Saturation (IHS)

	Hyperkeratotic area		Clinically normal tissue		Difference		
	Mean (n = 74)	SEM	Mean (n = 38)	SEM	Mean (n = 74)	SEM	P value
R	241.9	2.1	242.9	3.1	−2.2	1.4	NS
G	161.0	5.8	143.2	6.6	15.9	3.5	<0.001
B	167.2	5.1	132.1	6.5	33.1	2.9	<0.001
r	110.7	1.8	122.3	2.9	−10.7	1.2	<0.001
g	69.7	1.1	68.4	1.4	0.9	0.8	NS
b	73.2	0.7	62.8	1.6	9.8	0.6	<0.001
I	189.7	4.2	172.4	5.2	15.6	2.5	<0.001
H	177.4	1.1	185.0	1.0	−7.8	0.7	<0.001
S	46.1	3.2	65.8	4.8	−18.1	4.3	<0.001

$$r = 255 \times R/(R + G + B) \quad 0 \leq r \leq 255,$$
$$g = 255 \times G/(R + G + B) \quad 0 \leq g \leq 255 \text{ and}$$
$$b = 255 \times B/(R + G + B) \quad 0 \leq b \leq 255.$$

Each pixel could thus have a value from 0 to 255. An area with a high normalized r value and low g and b values is visually percepted as a red color.

III. Intensity-Hue-Saturation values (IHS). This color system is composed of perceptive parameters. The Hue value (H) describes a specific color, such as red or green. The Intensity (I) shows the brightness or darkness of the color, and the Saturation value (S) describes to what extent the color is mixed with white. A highly saturated color contains very little white. In accordance with Ledley et al. (8), the following algorithms were used for the IHS parameters.

$$I = (R + G + B)/3 \qquad 0 \leq I \leq 255,$$
$$H = \arctan(\sqrt{3} \times (G - B)/(2R - G - B))$$
$$H = H + 180 \qquad 0 \leq H < 360 \text{ and}$$
$$S = 1 - 3 \times \min(r,g,b) \qquad S = 255 \times S$$
$$0 \leq S \leq 255$$

All three color systems consequently use the same digitized values, and systems II and III are only transformations of the original RGB values.

For each of the objects mean values and standard errors for the extracted features were computed. Data from each hyperkeratinized and inflamed area were compared with data from an adjacent area regarded as clinically normal. The mucosal lesions were quantitatively expressed as the difference in mean values in hyperkeratinized and inflamed areas, respectively, compared with normal tissue.

A standard t test was used in the statistical analysis, and a p value <0.05 was regarded as statistically significant. Linear correlation analysis was performed to examine whether there was a correlation between the values obtained in the image analysis and the clinical characterization of the lesions.

Results

Hyperkeratinized versus normal tissue

A comparative analysis was performed on data from 74 hyperkeratinized areas and 38 reference values from normal tissues (Table 1).

RGB values. Significant changes were noted for G and B values, whereas the difference in R value was small and not statistically significant. Changes were greater for the B value than for the G value.

Normalized rgb values. The greatest differences were noted for r and b values. No significant change could be recorded for g

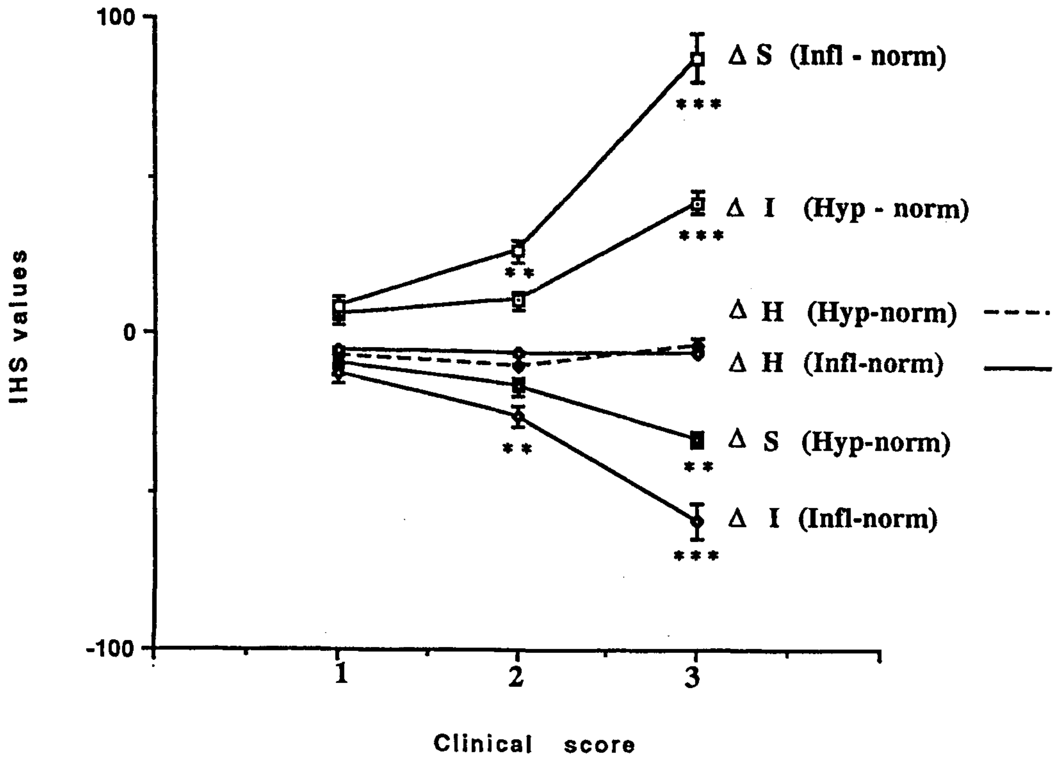

Fig. 1. Distribution of mean values and standard errors (SEM) for the difference in Intensity (I), Hue (H), and Saturation (S) between hyperkeratinized and inflamed areas in lichenoid reactions compared with clinically normal tissue. The clinical classification of hyperkeratosis and inflammation is shown as mild (1), moderate (2), and pronounced (3). The statistical significance between classes is shown as ** = $p < 0.01$ and *** = $p < 0.001$.

values. The r value was lower in the hyperkeratinized area, whereas the b value was increased.

Intensity-Hue-Saturation (IHS) values. The Intensity value (I) was higher in the hyperkeratinized area than in normal tissue, and the difference correlated well with the clinical score of hyperkeratosis (Fig. 1). The Hue value (H) was lower on the color scale in the hyperkeratinized area than in normal tissue in 70 of 74 observations. The Saturation value (S) was lower in the hyperkeratinized area in 63 of 78 observations.

Linear correlation analysis demonstrated a statistically significant relationship ($p < 0.001$) between difference in image data from hyperkeratinized to clinically normal areas compared with the clinical score system. This relationship was demonstrated in all three color systems used in the analysis for all variables except Hue value (H) and normalized r value (r).

Inflamed tissue versus clinically normal tissue

A comparative analysis was performed on image data from 78 objects extracted from inflamed areas (Table 2).

RGB values. All three variables demonstrated significant differences, which were most pronounced for G and B values. The differences increased with subjectively evaluated degree of inflammation.

Normalized rgb values. Significant changes were noted for all three variables. The differences were most pronounced for the r value. The r value increased, whereas

Table 2. Comparison between mean values and standard errors (SEM) in inflamed areas surrounding the lichenoid reaction and clinically normal tissue through computerized analysis. Differences are measured in digitized Red-Green-Blue values (RGB), normalized (red-green-blue) values (rgb), and Intensity-Hue-Saturation (IHS)

	Inflamed tissue area		Clinically normal area		Difference		
	Mean	SEM	Mean	SEM	Mean	SEM	
	($n = 78$)		($n = 41$)		($n = 78$)		*P* value
R	227.1	3.1	243.0	2.7	15.7	2.2	<0.001
G	97.1	6.1	142.0	6.4	−43.2	3.5	<0.001
B	98.5	5.9	131.7	6.1	−31.5	3.3	<0.001
r	147.9	4.1	122.6	2.7	24.4	2.8	<0.001
g	52.2	2.2	68.1	1.3	−15.5	1.5	<0.001
b	53.5	2.0	62.8	1.5	−8.9	1.3	<0.001
I	140.6	4.9	171.9	5.1	−30.1	2.9	<0.001
H	178.8	0.5	184.7	1.0	−5.8	0.4	<0.001
S	103.5	6.4	66.1	4.7	36.2	4.2	<0.001

the g and b values decreased in the inflamed area.

Intensity-Hue-Saturation (IHS) values. The Intensity value (I) was lower in the inflamed area than in the clinically normal tissue (Fig. 2). The Hue value (H) was lower on the color scale in the inflamed area in 73 of 78 observations compared with the adjacent clinically normal tissue, with a mean difference of 5.8 degrees (SEM, 0.4; $p < 0.001$). The Saturation value (S) was higher in the inflamed area, and the difference increased with increased clinical evaluation of the degree of inflammation (Fig. 2).

A statistically significant linear relationship was found between differences in image data from inflamed areas and clinically normal tissue, and the observed inflammation scored from 1 to 3. The relationship was statistically significant ($p < 0.001$) for all variables except Hue value (H).

Hyperkeratinized versus inflamed tissue

The Hue value (H) was strikingly lower in the hyperkeratinized area than in normal tissue in 70 of 74 comparisons. The same pattern was found when analyzing inflammatory reactions peripheral to the keratotic area. The Hue value was lower in 73 of 78 comparisons. A comparative analysis was therefore performed to evaluate whether difference in Hue (H) existed between hyperkeratinized areas and adjacent inflamed areas. The results showed a mean difference in Hue of only 1.7 degrees (SEM, 0.8; $p < 0.05$; $n = 75$). The Intensity (I) was higher and the Saturation (S) lower in the hyperkeratinized area than in the adjacent inflamed area in all observations.

Discussion

The aim of the study was to elaborate a method whereby the hyperkeratinizing and inflammatory tissue reactions in lichenoid mucosal lesions could be evaluated by image analysis. The results showed that both types of reaction pattern could be expressed by quantitative image data in all three color systems. A linear correlation was obtained when the results of the image analysis of color variations were compared with the clinical score system for both hyperkeratosis and inflammation.

It has been demonstrated that the thickness of the epithelium differs with age and sex (9, 10). It can therefore be assumed that interindividual differences exist in the visual appearance of clinically normal intraoral mucosa, and this had to be taken into consideration when elaborating a method that enabled evaluation of a lesion in individual patients. Tissue change was therefore expressed as the difference in color values between pathologically affected area and clinically normal tissue in each patient.

The results of the statistical analyses performed in our study showed that both the hyperkeratotic and inflammatory tissue reactions could be expressed in terms of quantitative image data. Hyperkeratosis in oral lichenoid reactions may, thus, be defined as an area with higher (I), a lower (H), and a lower (S) value, compared with an adjacent area of tissue regarded as clinically normal. Inflammation, on the other hand, presented with a decreased value (I), an increased

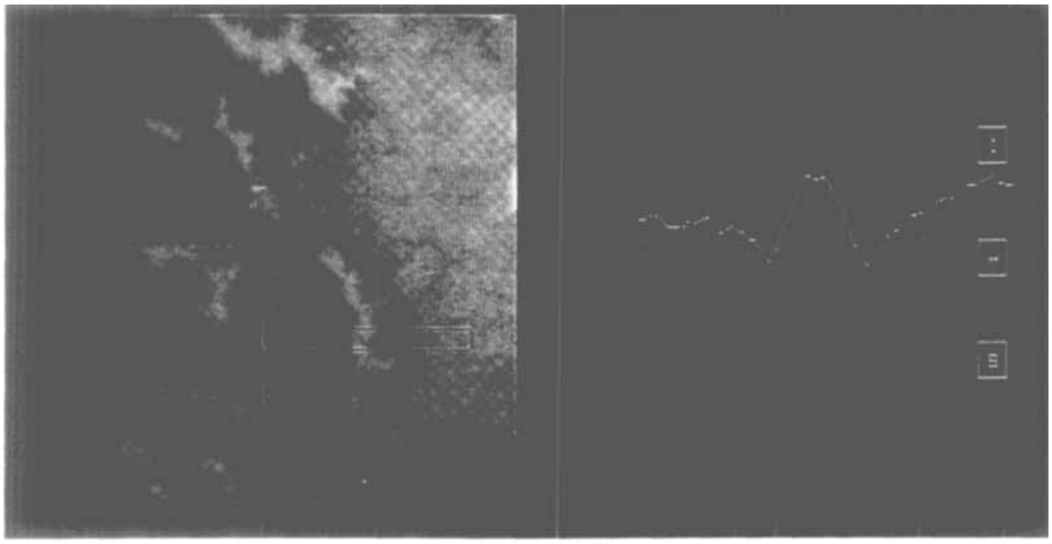

Fig. 2. Distribution of mean values in Intensity (I), Hue (H), and Saturation (S) from left to right in the marked area. Note the increase in I and decrease in S in the hyperkeratinized area while the opposite is obtained in the inflamed area immediately adjacent to the hyperkeratinized striae.

value (S), and with an (H) value that was lower than the adjacent normal tissue, as with hyperkeratosis (Fig. 2). The surrounding inflamed area showed essentially the same value in H as the hyperkeratinized tissue. It therefore seems reasonable to assume that the subepithelial inflammatory infiltrate may be identified by the difference in Hue between clinically normal tissue and the lesions. The increased thickness of the epithelium in the hyperkeratinized area alters I and S of the Hue present in the subepithelial area.

The increased 'redness' observed in the inflamed area may thus be explained by the presence of the inflammatory infiltrate in the lamina propria observed through an epithelium of equal or less thickness than an adjacent area that appeared clinically normal.

The linear correlations observed between image data and visual classification of hyperkeratosis may give a good visualization of the increased thickness and degree of keratinization of the epithelium, compared with neighboring normal tissue. To study this, a comparison of image data and data from histomorphometric analyses of exactly predetermined parts of lichenoid reactions should be performed in the future. Such evaluations could not be performed in the present material because the exact point in the mucosa from where biopsy specimen was taken was not marked before the surgical procedure. The correlation observed between image data and clinical impression of inflammation can be explained by two factors, separately or combined. The clinical classification of the degree of inflammation may reflect differences in the presence of blood vessels in the subepithelial area and/or differences in the thickness of the epithelium.

The use of clinical macrophotography is today a common technique to document changes in the oral tissues. When evaluating oral mucosal tissue changes in color slides there is, however, always a risk of differences in interpretation between observers. Addition of computer processing and feature analysis offers the advantage that measurements and analyses can be made more objectively and independently between observers. In the present study the analysis was limited to describe hyperkeratosis and inflammation by means of color features. If, however, other histopathologic tissue reactions of various oral mucosal lesions can be defined and biologically interpreted with image analysis, the computerized analysis can serve as a valuable tool in the understanding and clinical evaluation of a lesion. It may also, consequently, serve as an instrument in the clinical education of non-experienced clinicians.

The aim for the future is, therefore, to evaluate the possibility of distinguishing different oral mucosal lesions by image analysis. Such a system could be used as a complement to conventional histopathologic examination, but not as a substitution.

The need for adequate quality in the clinical photographs must be emphasized. The standard of the slides in the present study was good, but the photographs were not taken under standardized conditions, and the development procedures may have differed widely since the photographs were taken during a period from 1987 to 1991. An improved and more standardized method of photographic registration would further enhance the possibilities of computer-assisted image analysis. In the present study, however, the color slides could provide valuable information through the computerized analysis. Only small differences were recorded between slides in H value between hyperkeratinized and inflamed tissue areas, compared with clinically normal tissue. The I and S changes recorded in hyperkeratinized and inflamed areas demonstrated color changes that corresponded with the visual impression of the lesion. This indicates that the conditions under which the photographs in the present study were taken were adequate to permit statistically reliable image feature analysis. It can therefore be concluded that computer-assisted image analysis is to be regarded as a valuable means of evaluating and following up of intraoral lesions.

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