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Article

Quantitative vs. Qualitative Assessment of the Effectiveness of the Removal of Vascular Lesions Using the IPL Method—Preliminary Observations

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1. Introduction

Skin laser therapy is currently one of the most frequently performed treatments for improving the condition of the skin [1–10]. High-energy light is commonly used to reduce vascular lesions such as erythema, telangiectasias or small venectasias located on the lower limbs [6,11–17].

One of the most common reasons for visiting cosmetology, aesthetic medicine or aesthetic dermatology clinics are vascular lesions located on the face. A large group of patients are people with a complexion that gets red easily and are hyperreactive. The most common defects include telangiectasias and erythematous changes, initially in the transient form, eventually turning into permanent erythema with the accompanying telangiectasias. The typical location of vascular lesions is the skin of the nose and cheeks, but in some cases the lesions may include other areas of the face, such as the ears, neck and décolleté [6,11–21].

The difficulty in assessing the severity of lesions objectively is one of the main challenges in developing more effective therapies for telangiectasia and erythematous lesions.

Even experienced physicians present variability in assessing the severity of vascular lesions. The lack of an objective methods for assessing clinical improvement is particularly problematic in the case of studies that compare and evaluate various treatments, including those searching for optimal parameters for laser devices and IPL. In addition, the assessment and monitoring of vascular and erythematous lesions treatment may be difficult to standardize as most clinical evaluation systems are susceptible to inter-observer variability. Therefore, objective, reliable and preferably non-invasive measurement tools are needed. The currently used methods of assessing the severity of vascular and erythematous lesions have a number of limitations. One of the most popular procedures is dermatoscopy. Dermoscopic analysis is not quantitative; it requires interpretation by the operator, as the applied polarized light negatively affects the image resolution [22,23]. Another popular technique is capillaroscopy, but it is also a qualitative method [24]. Optical coherence tomography enables the registration of skin images with high resolution; however, all skin irregularities, often present within vascular lesions, negatively affect the resolution and quality of the images [25]. Ultrasonography, including high-frequency ultrasonography, has a relatively low resolution and does not quantify lesions [26].

The method that currently offers the greatest potential for quantifying vascular lesions is the use of computer-aided image analysis [27–30]. Nevertheless, the algorithms proposed so far are sensitive to changes in illumination, other chromophores present in the field of view (mainly melanin) and have relatively low sensitivity and specificity in relation to vascular lesions and do not refer to the physiological features of the skin/vessels.

The aim of the study is to develop a methodology for objectively assessing the response of dilated skin blood vessels to treatments using high-energy light. The main aim of the research was to develop objective, repeatable methods of assessing the effectiveness of erythema treatments. The currently used methods are either qualitative or only semi-quantitative. The quantitative assessment of the effectiveness of the treatment will not only allow to compare different technologies with each other, but at the same time—after completing the tests—indicate which initial parameters of the patient’s skin may affect the effectiveness of the treatment. This may allow the treatment parameters to be optimized in relation to individually defined (quantified) characteristics of the patient’s skin.

The more specific aims are to verify the hypothesis about the advantage of the cross-polarized light imaging technique over non-polarized light imaging technique for the quantitative analysis of vascular lesions; development of mexametric signal acquisition methods, which would allow to verify the hemoglobin concentration factor in the skin before and after a series of treatments; development and optimization of image analysis and processing algorithms that would allow for the quantitative evaluation of vascular lesions in the skin of the face; and verification of the hypothesis about the possibility of using methods in image analysis and processing for the quantitative assessment of the response of vascular lesions to high-energy light treatments.

2. Materials and Methods

2.1. Study Participants

The study included 13 patients (12 women and 1 man), aged 20 to 54, that struggled with vascular and erythematous lesions in the course of rosacea.

The inclusion criteria were voluntary participation and the occurrence of erythematous and/or vascular skin lesions within the face eligible for high-energy light treatments. The erythematous lesions in were at the severe stage in 60% of patients, and at the moderate stage in 40% of patients. Increased erythematous lesions were mainly located on the cheeks and chin, and only moderately around the nose. Telangiectasias were observed in all patients on the nose and in some patients on the chin and cheeks.

The exclusion criteria were being underage, tendency to keloid and hypertrophic scars; a fresh tan; viral, bacterial and fungal skin diseases; vitiligo; implanted pacemaker or defibrillator; untreated diabetes; cancer; pregnancy and lactation; use of drugs or herbs with photosensitizing properties; taking anticoagulants; tattoos; permanent makeup; the

use of filler in the last 6 months and botulinum toxin in the last 2 weeks; and surgical procedures in the treatment area in less than 3 months.

The study was approved by the Bioethics Committee (Medical University of Silesia KNW/0022/KB1/27/16).

2.2. Erythema Reduction Treatments

Treatments aimed at reducing the erythema were carried out using the Lumecca device™ (InMode MD Ltd., Yokneam, Israel), emitting polychromatic intense pulsed light (IPL) in the range from 400 to 1200 nm, where—according to the manufacturer’s declaration—40% of the total energy in the 500–600 nm band is useful for erythema reduction.

Each patient was subjected to three treatments and breaks between treatments lasted from 3 to 4 weeks, in accordance with the manufacturer’s recommendations.

The treatments were carried out on the volunteers’ cheeks, giving a total of 26 treatment spots—two cheeks for each volunteer. Before each treatment, the skin was cleansed and a coupling gel was applied, which has cooling properties and reduced the reflectance of radiation at the skin/air interface. Then, the skin reaction was assessed in response to the applied physical factor. Treatment parameters were selected individually. The first-pass energy density during the 1st treatment was on average 12.23 ± 0.725 J/cm² of skin. In people whose reaction after the first cheek treatment was not intense (no intense redness and swelling, as well as no milky color of the vascular areas), the treatment was repeated in the most erythematous spots (the so-called second pass) with a simultaneous reduction in energy density. The second pass during the 1st treatment was performed in 10 patients using radiation with an energy density of 9.70 ± 0.483 J/cm². For the 2nd and 3rd treatment, the first-pass energy density was 13.31 ± 0.630 J/cm² and 14.31 ± 0.7514 J/cm² of skin, respectively, while the second-pass energy density was 11.42 ± 0.669 J/cm² (12 patients) and 12.08 ± 0.862 J/cm² skin (13 patients).

2.3. Image Acquisition and Mexametry

Photographic documentation and mexametry measurement of the patients’ skin were performed before each treatment and one month after the third (last) treatment. Image acquisition was carried out in constant temperature conditions, around 20 °C, in the morning. After reaching the test site, the patient was asked to rest in a sitting position for 20 min before the measurements. The photos were taken under artificial lighting, where all lighting parameters were precisely controlled, including color temperature, lamp power, light direction, and light polarization.

The FOTOMICUS system (Elfo, Łódź, Poland) was used for the acquisition of skin images, the software of which enables to take photographs with strictly defined parameters. Study participants had a series of clinical photographs taken in non-polarized light for documentation purposes, and in cross-polarized light for further image processing and analysis. The photographic documentation included 5 images in cross-polarized light and 5 images in non-polarized light before the series of treatments, and 5 images in cross-polarized light and 5 images in non-polarized light after the series of treatments. Cross-polarization of light allows to reduce the scattering and reflection of light from the sebaceous layer on the skin, enabling better visualization of the changes in the epidermis and skin, which are important for the analysis of dilated blood vessels.

Mexameter® from Courage-Khazaka Electronic (Köln, Germany) was used to assess the melanin and hemoglobin content in the skin.

2.4. Image Processing and Analysis

In the first stage, the RGB images were recorded and decomposed to individual channels: red, green and blue (ImageJ version 1.52a, NIH, Bethesda, MD, USA). Then, the output image (RGB) and its individual channels were transformed into images in shades of gray (MATLAB Version 7.11.0.584 (R2010b), 2018).

The next step was image normalization; i.e., broadening the dynamic range to increase the contrast of the images. Normalization was performed for the entire set of 520 recorded images. It consisted of identifying the brightest pixel in the whole set of images, which was given a brightness of 255, and the darkest pixel, which was given a brightness of 0. The remaining pixels were assigned the appropriate gray levels in the range from 0 to 255.

The GLCM and QTDECOMP algorithms operating in the MATLAB Version 7.11.0.584 (R2010b) environment were used for the quantitative analysis of vascular lesions.

2.4.1. GLCM Analysis

GLCM analysis, i.e., the so-called the gray-level co-occurrence matrix, determines how many times a pixel of an image with a given brightness is adjacent to a pixel with a different brightness. The vascular lesion is most visible when the contrast between the lesion and healthy skin is the highest. Thus, the subjective perception of vascular lesions is affected by the number of vascular lesions in a particular spot, the color of the lesion and the contrast between the lesion and healthy skin [31].

In the GLCM matrix, the number of columns and rows equals the number of gray levels (G). Image analysis can be performed in different directions: vertically (90°), horizontally (0°) and diagonally (45° or 135°). In this study, pixels in the horizontal direction ($\theta = 0^\circ$), located in the immediate vicinity ($d = 1$), were examined.

The performed GLCM analysis included contrast and homogeneity.

GLCM contrast according to Formula (1) is a measure of the local brightness variation among pixels in an image. The result of the analysis is an assessment of how many times pixels of a defined brightness are adjacent to each other. For example, Figure 1 shows how many times in the matrix—in a horizontal projection—pixels with a brightness of 1 and 2 appear next to each other. For the examined images, the matrix had a size of 256×256 , and the analyses were carried out for 8-bit color depth (Figure 1).

$$\sum_{i,j} P_{i,j} (i - j)^2 \quad (1)$$

where:

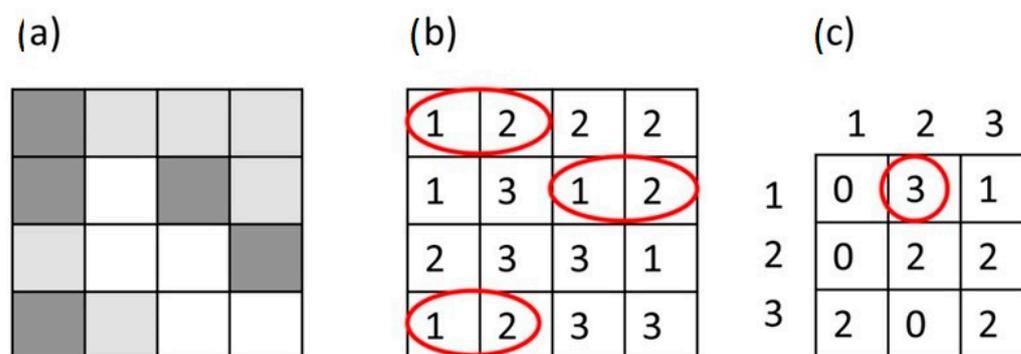


Figure 1. Scheme of the GLCM matrix: (a) a fragment showing adjacent pixels; (b) the complex pixel configuration; (c) the number of pixel pairs in this configuration.

i —brightness of the tested pixel;

j —brightness of the adjacent pixel.

In the patients' photos, the spots, including the vascular lesions (ROI), were identified arbitrarily and were a subject for further analysis. Then, the following channels were separated from the image: red (R), green (G) and blue (B). Then, all images were converted to grayscale. It was assumed that the vascular lesions correspond mainly to the red (R) channel.

The analysis of the GLCM homogeneity of the image was aimed at determining the homogeneity of the pixels' brightness within the entire ROI; i.e., the intensity of the lesions in the entire studied spot. Homogeneity in the adopted research model was understood as:

$$\sum_{i,j} \frac{p(i,j)}{1 + |i - j|} \quad (2)$$

where:

i —brightness of the tested pixel;

j —brightness of the adjacent pixel.

The greater the homogeneity and the lower the contrast, the more consistent the skin color, which means less or no vascular changes. Contrast and homogeneity are given in relative units (as above).

2.4.2. Quadtree Decomposition

Quadtree decomposition (QTDECOMP) is an image processing and analyzing function that divides the image into four equal-sized square blocks, and then automatically analyses the fulfilment of an arbitrarily given brightness difference criterion by these blocks. Dividing the image into equal blocks is repeated iteratively until each block meets the assumed arbitrary criterion. If the block meets the criteria, it is not further divided. If it does not meet the criteria, it is split into four blocks again and the test criterion is applied to those blocks (Figure 2). A brightness value of 8 in the presented research model was adopted as the threshold of the decomposition division. This means that in the grayscale range from 0 to 255, the blocks were divided until the adjacent partition fields did not differ in mean brightness greater than 8. For this arbitrarily assumed value, the most representative quantitative results of the analysis were obtained.

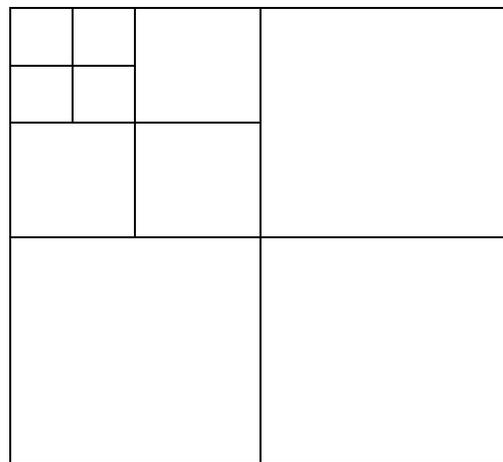


Figure 2. Scheme of dividing the ROI for quadtree decomposition.

2.5. Statistical Analysis

The statistical analysis was based on the results obtained from the tests performed before the first (before) and after the third (final) treatment (after).

Statistical analysis was performed using Statistica 10.0 StatSoft for Windows software. To evaluate statistical significance, a Wilcoxon test was performed. Significance was set at $p < 0.05$.

3. Results

Sample photos of a patient captured in cross-polarized light before a series of treatments and after three IPL treatments are shown in Figure 3.

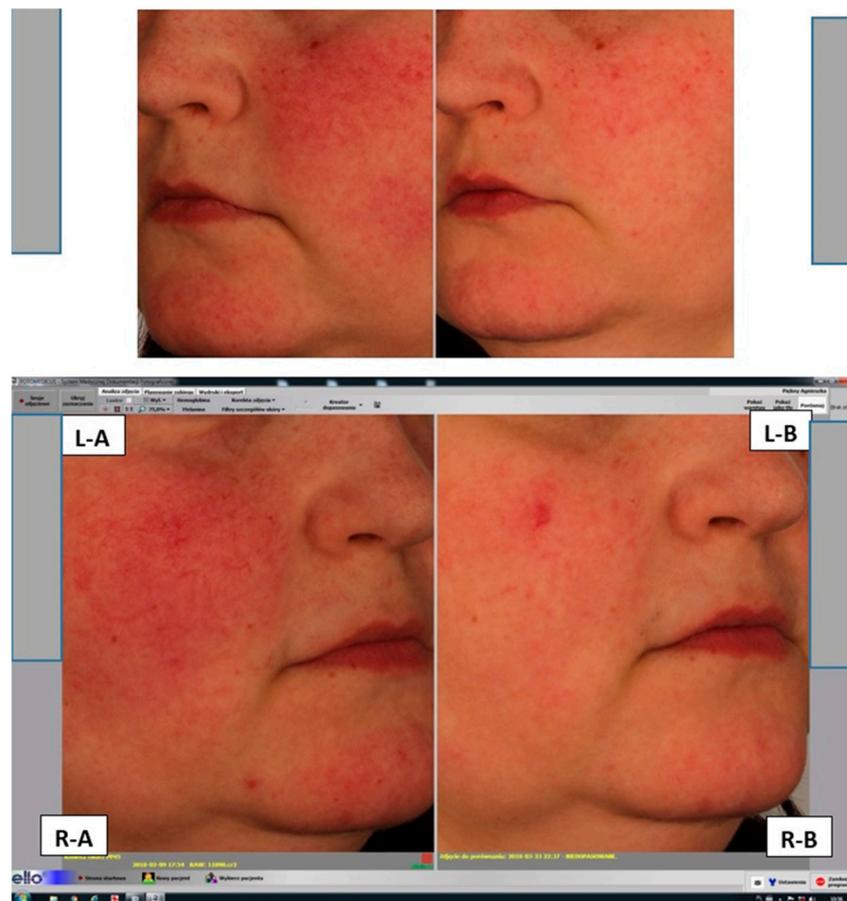


Figure 3. The left cheek (L) and the right cheek (R) before the first treatment (A) and after the third treatment (B), in cross-polarized light.

3.1. Mexametry

The analysis of vascular lesions based on mexametric data (measurements of melanin and hemoglobin content) did not show any statistically significant differences between the condition of the skin before and after the series of treatment. The melanin content in the skin did not change; the median before the first treatment was 123.5 arbitrary units (a.u.) at the interquartile range of 48 a.u. (Q1 = 97; Q3 = 145), and after a series of 3 treatments, 126.5 a.u. and 14.0 a.u. (Q1 = 121; Q3 = 135), respectively. The mean content of hemoglobin in the skin slightly decreased; the median before the procedures was 376.5 with a quartile range of 41 a.u. (Q1 = 302; Q3 = 443), and after the procedures 335.5 a.u. and 52 a.u. (Q1 = 264; Q3 = 416), respectively.

3.2. GLCM Analysis

As a result of the IPL treatments, the mean GLCM contrast decreased statistically significantly both for the all RGB range (before: Me = 6.6, Q1 = 5.7, Q3 = 8.5; after: Me = 6.0, Q1 = 5.4, Q3 = 7.3) and for each channel ($p < 0.01$) (Figure 4). The highest GLCM contrast before the series of treatments was recorded for the green channel: Me = 7.2, Q1 = 6.0, and Q3 = 9.3; however, after the third treatment, the results approached the results in the other channels: Me = 6.2, Q1 = 5.5, and Q3 = 7.6. The values obtained for other color channels were as follows: Red—before: Me = 6.8, Q1 = 6.0, and Q3 = 9.1, after: Me = 6.2, Q1 = 5.5, and Q3 = 7.4; Blue—before: Me = 6.9, Q1 = 5.8, and Q3 = 8.7, after: Me = 6.3, Q1 = 5.7, and Q3 = 7.6 (Figure 4).

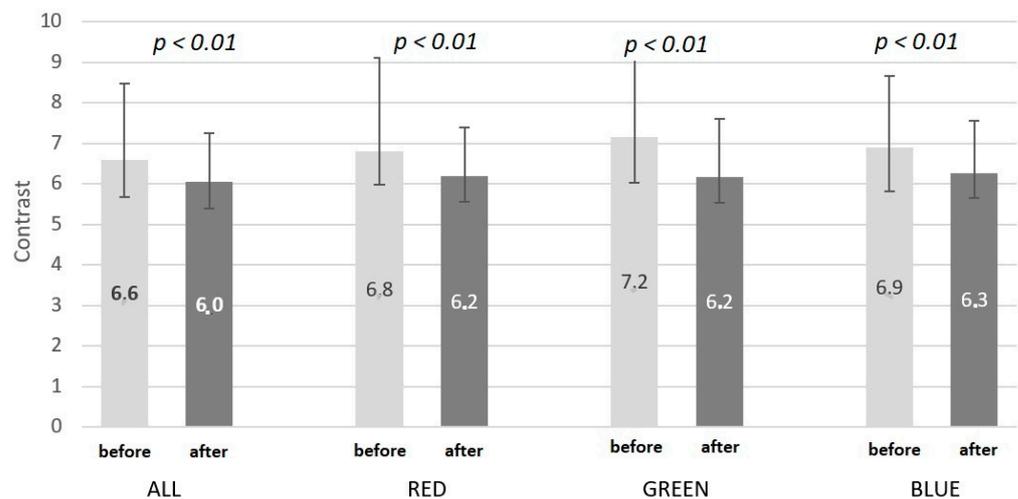


Figure 4. Average GLCM contrast of the treatment spot images in the full color range (ALL) and in red, green and blue channels after conversion to gray levels, in cross polarized light; before—before the first treatment; after—after third treatment.

The GLCM homogeneity of the skin identified in the RGB image and individual channels increased statistically significantly ($p < 0.01$), which confirms the decrease in contrast and indicates a reduction in the visibility of vascular lesions as a result of the series of IPL treatments (Figure 5).

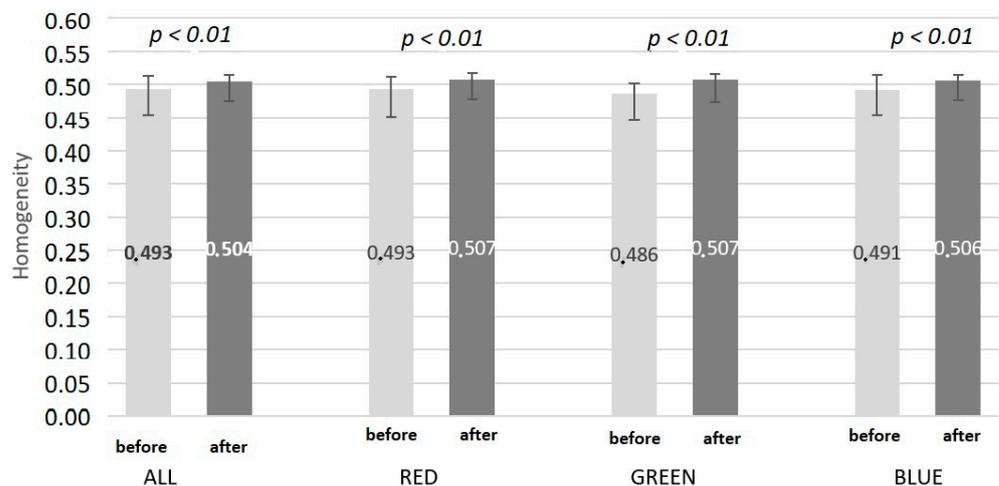


Figure 5. Average GLCM homogeneity of the treatment spot images in the full color range and in the red, green and blue channels after conversion to gray levels, in cross polarized light; before—before the first treatment; after—after third treatment.

3.3. Image Brightness Analysis

In order to quantify vascular lesions within the facial skin, the method of analyzing the brightness of the examined spots recorded in the RGB color space was also used, and then converted to gray levels. Brightness has been specified on a scale from 0 to 255, where 0 represents black and 255 represents white.

The brightness of the skin increased, indicating a lightening of the skin spots after three IPL treatments, but the changes were not statistically significant. Table 1 shows the mean gray levels (brightness) for the left and right cheek images captured under cross-polarized light.

Table 1. Average brightness (a.u.) of the RGB images of the left and right cheeks and the red, green and blue channels after conversion to gray levels before treatments (BEFORE) and after series of treatments (AFTER); \bar{x} = mean; SD = standard deviation; p = level of statistical significance; ns = not significant.

		RGB		Red Channel		Green Channel		Blue Channel	
		BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
Left cheek	\bar{x}	151.3	154.8	207.9	211.3	136.6	141.0	109.0	112.1
	SD	10.2	14.1	11.1	14.6	12.3	16.1	9.4	13.0
	p	ns		ns		ns		ns	
Right cheek	\bar{x}	156.2	157.1	213.3	213.4	141.4	143.3	113.8	114.5
	SD	10.2	12.0	9.8	11.7	13.0	13.7	10.0	12.4
	p	ns		ns		ns		ns	

3.4. Quadtree Decomposition

Tables 2 and 3 and Figures 6 and 7 show the quadtree decomposition results (QTDECOMP) of images of the left and right cheeks recorded in polarized light. The QTDCOM analysis shows that the IPL treatments resulted in an increase in the number of blocks with a larger area and a decrease in the number of blocks with a smaller area for all channels and the image not subjected to RGB decomposition. The increase in the number of blocks with a long side (8×8 and 16×16 pixels) compared to squares with a shorter side (2×2 and 4×4 pixels) indicates that the images of vascular lesions after a series of IPL treatments have become more homogeneous.

Table 2. The number of blocks with sides of 1×1 , 2×2 , 4×4 , 8×8 , 16×16 and 32×32 pixels, resulting from the quadtree decomposition of the left cheek image recorded with a cross-polarization filter before the series of treatments (BEFORE) and after the series of treatments (PO). Me = median; Q1 = lower quartile; Q3 = upper quartile; p = level of statistical significance; ns = no significance.

	1×1		2×2		4×4		8×8		16×16		32×32	
	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
Me	12	34	111	107	269	263	479	458	79	98	2	1
Q1	4	8	91	75	240	198	285	179	40	56	0	0
Q3	41	48	314	166	584	452	660	572	474	348	22	37
p	ns		ns		=0.05		<0.05		ns		ns	

Table 3. The number of blocks with sides of 1×1 , 2×2 , 4×4 , 8×8 , 16×16 and 32×32 pixels, resulting from the quadtree decomposition of the right cheek image recorded with a cross-polarization filter before the series of treatments (BEFORE) and after the series of treatments (PO). Me = median; Q1 = lower quartile; Q3 = upper quartile; p = level of statistical significance; ns = no significance.

	1×1		2×2		4×4		8×8		16×16		32×32	
	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
Me	1092	1080	10301	8129	8216	8403	799	1053	3	6	0	0
Q1	476	616	4702	5394	4593	5007	598	833	2	2	0	0
Q3	1812	1392	12159	11012	8708	8927	1151	1394	6	9	0	0
p	ns		$p < 0.05$		ns		$p < 0.05$		ns		ns	

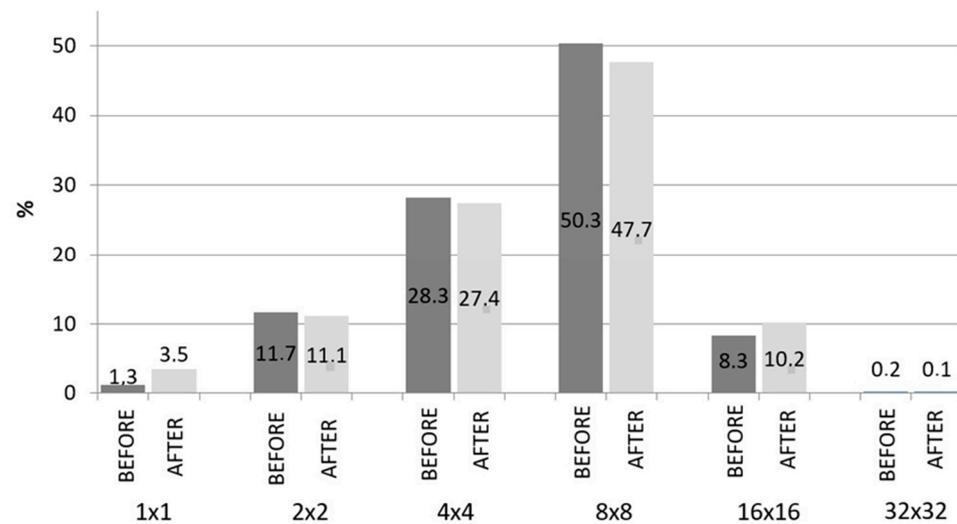


Figure 6. Change in the number of blocks with sides of 1×1 , 2×2 , 4×4 , 8×8 , 16×16 and 32×32 pixels, resulting from the quadtree decomposition of the left cheek image recorded with a cross-polarization filter.

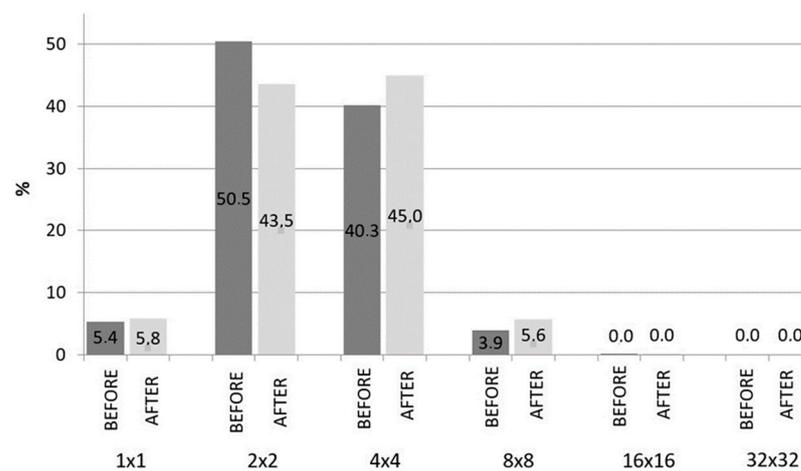


Figure 7. Change in the number of blocks with sides of 1×1 , 2×2 , 4×4 , 8×8 , 16×16 and 32×32 pixels, resulting from the quadtree decomposition of the right cheek image recorded with a cross-polarization filter.

4. Discussion

Commonly used methods of measuring the effectiveness of laser treatments are based on the subjective opinions of specialists performing the analysis. There are no clearly established criteria on which the scales are based; therefore, analyzing the results is difficult and ambiguous. Lesions are assessed visually, which allows for only a general assessment of the skin condition and may result in insufficient repeatability of the evaluation [32,33].

Currently used methods of identifying vascular lesions within the skin are based primarily on qualitative or semi-quantitative scales. The proposed method of examining vascular lesions allows for an objective, repeatable and quantitative assessment of the intensity of skin vascular lesions. The conducted research is the first in the world to use advanced image analysis and processing algorithms based on the co-occurrence matrix of gray levels and quadtree decomposition for the analysis of vascular lesions. It should be emphasized that the currently used simple methods of image analysis, such as image brightness analysis or brightness analysis of individual RGB image channels, do not allow obtaining unambiguous results. Similarly, the currently most popular method of measuring

the severity of erythema based on mexametric data analysis does not provide an objective assessment of lesions.

Commonly used methods of assessing the effectiveness of erythematous and/or vascular lesions reduction are most often based on a subjective assessment of the effects by a physician and/or patient (patient satisfaction survey). The four-point IGA (Investigator Global Assessment) erythema reduction assessment scale is often used, where 3 means an improvement rate of 75–100% (severe improvement), 2 means an improvement rate of 50–74% (moderate improvement), 1 means an improvement rate of 25–49% (mild improvement) and 0 means an improvement rate of 0–24% (clean skin). The effects are usually assessed by a group of independent specialists [34]. Semi-quantitative scales are used less frequently (including the rosacea severity score and erythema index) [15,34–36]. The rosacea severity score is a scale based on automatic analysis of photo documentation and measurement of biomechanical properties of the skin, such as transepidermal water loss (TEWL) and hydration of the stratum corneum. Then, using algorithms, the degree of change in the intensity of vascular lesions is calculated [35]. Kim et al. [35] showed that the applied scale can be successfully used to assess the therapy of severe and moderate rosacea. The erythema index score can be based on mexametry or chromatometric measurements. Chromatometers analyze the amount of radiation reflected from the measured object. The degree of erythema reduction can also be assessed by analyzing images recorded using RGB color values (R—red; G—green; B—blue) [30].

The Mexameter is a well-known device mainly used to assess the degree of skin pigmentation (melanin content) and the degree of skin redness (hemoglobin content) [37–39]. The aim of this measurements was to show that the measurement of the degree of redness using a mexameter is not a very precise method and while the tool works well in assessing the degree of reduction of hyperpigmentation, it should not be the only tool for assessing the degree of skin redness. In this case, it should be mentioned that the mexameter allows to determine the melanin/hemoglobin content in the area of about 1 mm². This causes huge variability in the results, depending on the place where the mexameter is applied. The proposed methods of image analysis and processing, which identify the advancement of changes on any large area of the skin, do not have a similar disadvantage.

The proposed methods of image analysis and processing have not been used to assess vascular lesions so far. Thus, it is a completely new approach to the problem, which has not yet received a method allowing for an objective assessment. It should also be emphasized that, in further stages of the work, the results obtained from the biometric (quantitative) research will be correlated with qualitative and semi-quantitative research. The main advantage of the proposed method is repeatability and objectivity. Most of the analyses of the influence of various physical stimuli on the condition of skin affected by erythema and/or rosacea are based on subjective scales. The assessment performed by a specialist is always associated with a subjective verdict based on experience. In addition, the assessment performed by a specialist is more dependent on the type of light in which the observations are carried out (color temperature, angle of incidence, polarization, uniformity of illumination). The proposed method enables the skin to be illuminated under repeatable conditions. However, the proposed method also has its limitations. First of all, these are the limitations associated with a relatively large number of factors that may affect the obtained effect, e.g., skin pigmentation disorders. The proposed methodology of initial image processing minimized the influence of other factors on the obtained image analysis and processing coefficients, but it could not be completely eliminated.

5. Conclusions

Analyzing the measurements performed in this research, the following conclusions can be drawn:

- Image recording in cross-polarized light enables effective visualization of vascular lesions of the facial skin.

- A series of three treatments using an IPL light source seems to be sufficient to reduce vascular lesions in the face.
- GLCM contrast and homogeneity analysis can be an effective method of identifying skin vascular lesions.
- Identification of GLCM contrast and homogeneity for each image channel enables the separation of vascular lesions from other lesions affecting the examined image parameters.
- Quadtree decomposition allows for the quantitative identification of skin vascular lesions to a limited extent.
- The brightness analysis of the images does not allow quantification of the vascular features of the skin.
- Mexametric measurements do not allow for a quantitative assessment of the skin's blood vessel response to high-energy light.

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