# Controlling the Progression of Age-related Macular Degeneration Using the Image Quality Index and the Reference Image

Janusz P. Kowalski[1], Jakub Peksinski[2], Grzegorz Mikolajczak[2]
[1]*Faculty of Medicine, Biotechnology and Laboratory Medicine, Pomeranian Medical University, Rybacka St. 1, 70-204 Szczecin, Poland*
[2]*Faculty of Electrical Engineering, West Pomeranian University of Technology, 26 Kwietnia St. 10, 71-126 Szczecin, Poland*
*jpeksinski@zut.edu.pl*

***Abstract*—This paper presented a possible application of a digital image quality measure, called the Universal Quality Image Index Q, for the diagnostics of the eye fundus. The proposed method supports examination of the progression of macular degeneration allowing to reduce the number of errors during a subjective examination by an ophthalmologist. This occurs mostly when changes are small between successive examinations. This paper proposes an effective algorithm to eliminate the errors during the subjective assessment caused by inaccurate synchronization of examined images.**

***Index Terms*—Digital image, data matching, quality measures.**

## I. INTRODUCTION

Eye fundus examination is one of the basic examinations in ophthalmology. It can provide a lot of information about the condition of health and allows to evaluate, inter alia:

– Condition of blood vessels;
– Condition of retina;
– Condition of optic nerve;
– Macula lutea.

Cone cells present in the macula are responsible for central vision, recognition of details and colours. As the populations are ageing, particularly in developed countries, Age-related Macular Degeneration (AMD) becomes a problem [1], [2] – leading to the loss of central vision.

There are two types of degeneration:

– Dry (atrophic, nonexudative) form which develops slowly and in most cases does not cause the eyesight loss;
– Exudative (wet, neovascular) form leading to an irrevocable eyesight loss.

Early detection of the disease can increase the therapeutic success. The easiest and the most important method of macula examination is the subjective assessment by an ophthalmologist of digital images taken with special cameras, so-called Fundus Camera [3], equipped with a set of filters for eye analysis. Owing to the fact that digital cameras are used, the eye images can be saved, stored, documented for further analysis which will allow to observe the changes occurring in the eye over time.

Manuscript received April 5, 2015; accepted September 12, 2015.

There are many methods to assess the changes in the eye caused by AMD progression. A popular and most often used method is the subjective assessment by an ophthalmologist who analyses a digital image of retina and uses his/her experience to estimate the changes caused by the disease.

Other methods which can support the examination comprise objective assessments performed by means of techniques and methods used in digital processing and analysis of images.

The objective methods include methods which involve assessment of examined photographs with the use of popular algorithms for quality evaluation of digital images.

In our research we applied a popular and widely used measure called the Universal Quality Image Index Q [4] described by equation

$$Q = \frac{4 \times \pm_{xy} \times \overline{x} \times \overline{y}}{\left(\pm_x^2 + \pm_y^2\right) \times \left(\overline{x}^2 + \overline{y}^2\right)}, \tag{1}$$

where:

$$\overline{x} = \frac{1}{N}\sum_{i=1}^{N} x_i , \tag{2}$$

$$\overline{y} = \frac{1}{N}\sum_{i=1}^{N} y_i , \tag{3}$$

$$\pm_x^2 = \frac{1}{N-1}\sum_{i=1}^{N}\left(x_i - \overline{x}\right)^2, \tag{4}$$

$$\pm_y^2 = \frac{1}{N-1}\sum_{i=1}^{N}\left(y_i - \overline{y}\right)^2, \tag{5}$$

$$\pm_{xy} = \frac{1}{N-1}\sum_{i=1}^{N}\left(x_i - \overline{x}\right) \times \left(y_i - \overline{y}\right). \tag{6}$$

This quality measure is only one of many comparison criteria used to evaluate the quality of digital images. However, one can note that the numerical value of the "*Q*" indices depends on loss of correlation, luminance distortion, and contrast distortion. This is very important because thanks to it the index can be used to compare successive images with the reference image selected by the diagnostician.

The reference image in this case is the patient's eye photograph with the earliest date. Only very rarely does the diagnostician have a control image of the correct eye fundus taken during some other examinations. The reality is different, usually the eye photographs of healthy individuals are not taken, the first photograph is the photograph with some degenerative changes already present and noticed during the fundus eye examination. The patient gets the ophthalmological care; the examinations are made at certain time intervals for current control of the eye condition to apply a suitable therapy. It is the time when an objective appraisal of the changes occurring between successive visits to the ophthalmologist becomes very important.

## II. Measurement Using the Q Index and Its Correlation with the Subjective Assessment

Possibility of application of the "*Q*", to evaluate changes in the eye, presented on the example AMD eye images, shown on Fig. 1(a)–Fig. 1(c).

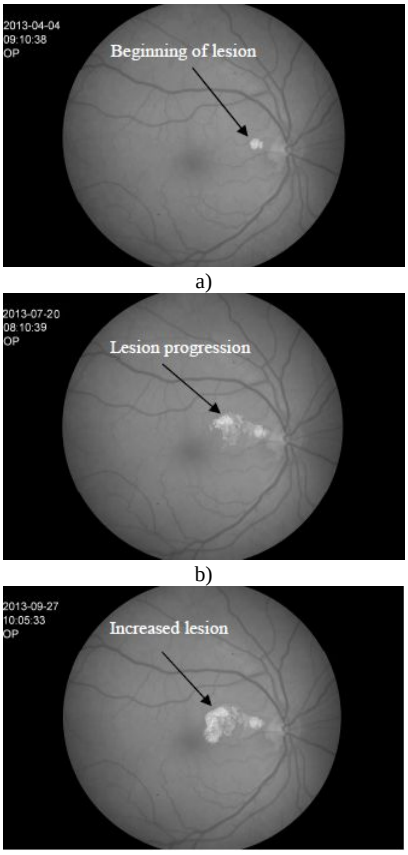



Fig. 1. The first image of the eye taken on 2013.04.04 (a); The second image of the eye taken after 116 days (2013.07.20) (b); The third image of the eye taken after 173 days from the first (2013.09.27) (c).

Figure 1(a) to Fig. 1(c) presents three eye photographs of the same patient with dry AMD [5], [6], taken at a few months' intervals:

– Fig. 1(a) – The first image of the eye taken on 2013.04.04;

– Fig. 1(b) – The second image of the eye taken after 116 days (2013.07.20);

– Fig. 1(c) – The third image of the eye taken after 173 days from the first (2013.09.27).

As we can see Fig. 1(a) shows the eye in which the disease was just diagnosed, and the successive image Fig. 1(b) and Fig. 1(c) show the bad eye with a significant change caused by the disease.

Performing the subjective analysis of images from Fig. 1(a) to Fig. 1(c) the ophthalmologist found a distinct change caused by the progressing eye disease.

The measure *"Q"* described by (1) was used to perform the objective analysis. The result was the *"Q"* values presented in Table I which were compared with the subjective assessment by the ophthalmologist – and the ophthalmologist uses only the following statements:

– "no change" – meaning that no change in the eye occurred,

– "change" – meaning that a change occurred but it is relatively insignificant,

– "significant change" – meaning that a significant change occurred as a result of the disease.

TABLE I. SUBJECTIVE ASSESSMENT AND THE Q VALUES BETWEEN THE PHOTOGRAPHS FROM FIG. 1(A) TO FIG. 1(C).

| | **Q between images 1(a) and 1(a)** | **Q between images 1(a) and 1(b)** | **Q between images 1(b) and 1(c)** | **Q between images 1(a) and 1(c)** |
|---|---|---|---|---|
| **Objective indication Q** | 1.00 | 0.67 | 0.79 | 0.56 |
| **Subjective assessment by the ophthalmologist** | No change | Significant change | Change | Significant change |

The analysis of the *"Q"* values and the assessment by the ophthalmologist clearly indicates the correlation between the objective and subjective assessment.

The *"Q"* value between Fig. 1(a) and Fig. 1(a) is 1.00 which was expected because these are exactly the same images. This is confirmed by subjective assessment. Similar results are obtained from the analysis of the remaining results, the biggest difference is between the image Fig. 1(a) (beginning of the disease) and Fig. 1(c) (advanced AMD) which is confirmed by both the ophthalmologist and the *"Q"* indication (which is greatest in this case).

Contrary to the subjective comparison by the ophthalmologist, the *"Q"* – based objective comparison gives a clearer picture of changes occurring in the eye as a result of advancing disease. The changes can be evaluated by means of a "quantitative index" and not a purely subjective one. This is evident when analysing images Fig. 1(b) and Fig. 1(c) where changes are relatively small. The *"Q"* – based assessment shows clearly the quantitative change which occurred, unlike the objective assessment which informs only about the change itself which cannot be expressed.

Table II presents the results of experiments confirming the *"Q"* measure effectiveness and its correlation with the subjective assessment by the ophthalmologist.

TABLE II. EXAMPLES OF THE RESULTS OF EXPERIMENTS.

| | ***Q* values between pairs of images** | | | | |
|---|---|---|---|---|---|
| | **1a and 1b** | **2a and 2b** | **3a and 3b** | **4a and 4b** | **5a and 1b** |
| **Objective indication Q** | 0.54 | 0.78 | 0.46 | 0.84 | 0.68 |
| **Subjective assessment by the ophthalmologist** | Significant change | Change | Significant change | Change | Change |

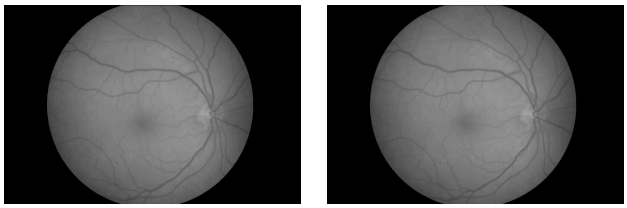
*Note: a – the first eye images, a so-called reference images; b – eye images taken some time after the reference images.*

## III. PROBLEM WITH ASSESSMENT USING THE QUALITY MEASURE "*Q*"

There is a significant problem during the assessment using the *"Q"* index which has a considerable impact on the results. Namely, the results of the *"Q"* – based objective assessment will be credible and will not contain any distortion only when the input data are correctly prepared, the input data in this case being the digital images of the examined eye.

The images must be precisely synchronized with each other. Absence of synchronization will result in a distortion of the Q value caused by the shift between the examined images.

The problem is presented on the example below. Figure 2 shows the images of the same healthy eye. The only difference is that the image Fig. 2(b) is shifted by a few pixels in relation to image Fig. 2(a).



a) b)

Fig. 2. Eye images (a); The same images shifted by a few pixels (b).

When performing the subjective analysis of the photographs from Fig. 2 the ophthalmologist did not notice any changes caused by the disease and concluded that the images are identical (which they are).

However, the *"Q"* index is as follows

$$Q = 0.84. \tag{7}$$

The *"Q"* index clearly indicates that the images Fig. 2(a) and Fig. 2(b) are different and there is a change on them caused by the advancing disease. This is not true because this the same photograph, only shifted by a few pixels in Fig. 2(b). The shift is not visible to the naked eye and as such does not affect the structure of the whole image, but it does affect the *"Q"* measure. The size of the shift is shown in Fig. 3 which presents the difference between the two images.

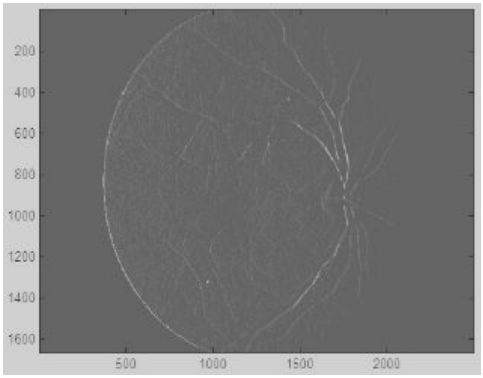



Fig. 3. Difference showing the shift between images Fig. 2(a) and Fig. 2(b).

As we can see the lack of synchronization is a major problem which needs to be eliminated if the objective indication *"Q"* is to be credible and without any distortions.

The results of the experiments on the impact of the shift between photographs of the same eye on the objective assessment and correlation with the subjective assessment are given in Table III. It should be added that for the purposes of the experiment all shifts were artificially forced and the examined eye photographs in individual pairs were the same.

TABLE III. SHIFT IMPACT ON THE C VALUE AND ITS CORRELATION WITH THE SUBJECTIVE ASSESSMENT.

| Eye images | Shift in pixels | | Q index | | Subjective assessment | |
|---|---|---|---|---|---|---|
| | X | Y | Before shift | After shift | Before shift | After shift |
| pair No. 1 | -1 | 0 | 1.00 | 0.93 | The same | The same |
| pair No. 2 | -2 | 0 | 1.00 | 0.86 | The same | The same |
| pair No. 3 | 0 | -1 | 1.00 | 0.9 | The same | The same |
| pair No. 4 | 0 | -2 | 1.00 | 0.79 | The same | The same |
| pair No. 5 | 2 | 2 | 1.00 | 0.56 | The same | The same |

Analysis of the results presented in Table III clearly indicates that absence of synchronization between the examined photographs significantly affects the correlation between the subjective assessment by the ophthalmologist and the objective assessment based on the *"Q"* measure.

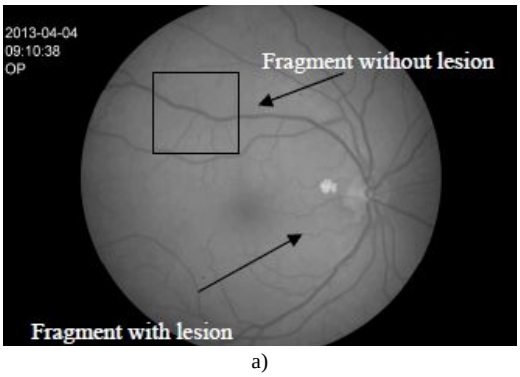
In order to eliminate the errors in the *"Q"* – based assessment of eye images and to correlate with the result of the subjective assessment, the authors proposed a synchronizing algorithm which is based on the analysis of the *"Q"* values.

The above examples show that the *"Q"* value is strongly dependent on the shift between images. Owing to this "negative" property of the *"Q"* measure, it can be successfully used in the image synchronizing algorithm in which this very "negative" property will be applied to synchronize the images.

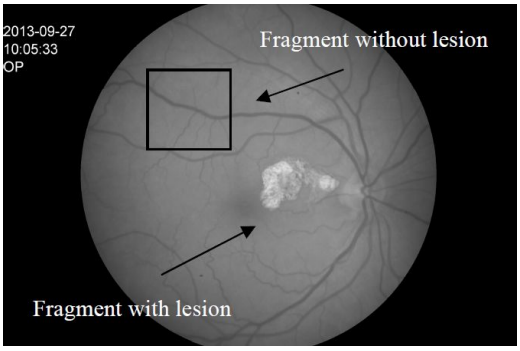
## IV. PRINCIPLE OF OPERATION OF THE SYNCHRONIZING ALGORITHM FOR EYE IMAGES

In order to determine if the synchronization process between the examined images is needed, firstly we need to check if the synchronization of images is required [7].

To do that, on each examined image we select a fragment of the same size and in precisely the same position on the *X – Y* plane in relation to the absolute coordinate system. It is important here that the selected fragment is free of degenerations caused by the disease, as shown in Fig. 4. Otherwise, the distortion of result will occur.




a)




b)

Fig. 4. Eye images with the fragment selected for the analysis: a) eye image taken on 2013.04.04; b) eye image taken on 2013.09.27.

After selecting an appropriate fragment which meets the above-mentioned criterion, we analyse the differences between the selected fragments. If the difference is not equal to zero as shown in Fig. 5 which clearly shows the shift between the images, then the images are not synchronized and a detailed synchronization process is required.

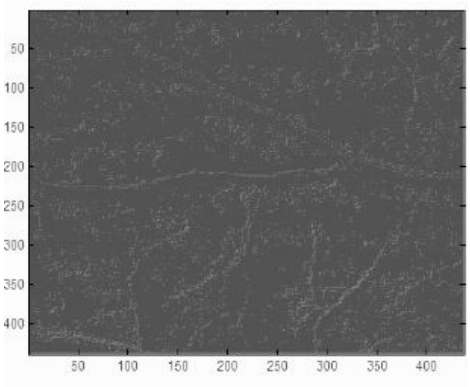



Fig. 5. Difference showing the shift between the fragments of images Fig. 4(a) and Fig. 4(b).

The next step in the algorithm is to find by how many pixels the examined images are shifted in relation to each other on the X – Y plane. We establish the shift using the earlier selected image fragments which were used to determine the differences between the images.

Firstly, we determine the initial *"Q"* value between the selected fragments, this value will be used as a reference. Then, we move one fragment of the image in relation to the other fragment in the direction of axis X and axis Y by one pixel at a time. We check the *"Q"* value in each new position.

The best synchronization between the images is in the position in which the *"Q"* value is the least. Knowing the initial position of the examined fragments on the plane and the number of pixels by which the fragments were shifted as well as the shift direction, we are able to precisely synchronize the examined images.

The distribution map of *"Q"* values for the image fragments from Fig. 4 is shown in Fig. 6.

The analysis of the distribution map obtained by means of the matching algorithm presented above shows that the images are shifted in relation to one another by two pixels in the direction +X (horizontal) and two pixels in the direction +Y (vertical) – as indicated by the arrow in Fig. 6.

Table IV presents the results of determination of the shift between images based on the analysis of the *"Q"* value.

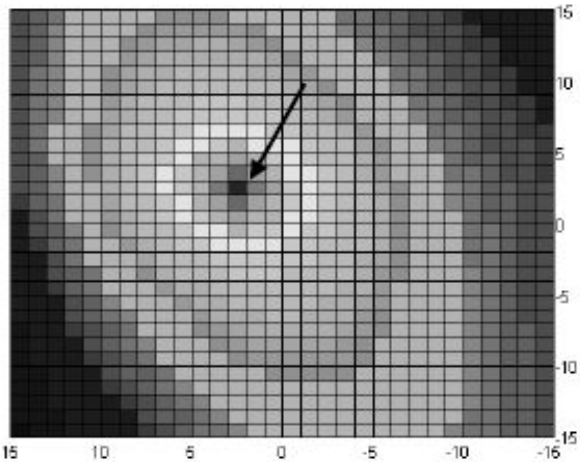



Fig. 6. Distribution map of Q values for the image fragments from Fig. 4.

TABLE IV. EFFECTIVENESS OF THE MATCHING ALGORITHM.

| Eye images | Set shift in pixels | | Initial Q value | Found shift in pixels | | Q value after matching |
|---|---|---|---|---|---|---|
| | X | Y | | X | Y | |
| pair No.1 | -1 | 0 | 0.93 | -1 | 0 | 1.0 |
| pair No.2 | -2 | 0 | 0.86 | -2 | 0 | 1.0 |
| pair No.3 | 0 | -1 | 0.9 | 0 | -1 | 1.0 |
| pair No.4 | 0 | -2 | 0.79 | 0 | -2 | 1.0 |
| pair No.5 | -2 | 2 | 0.56 | -2 | -2 | 1.0 |

The analysis of results given in Table IV clearly indicates the effectiveness of the proposed algorithm. The shift between images was found with 100 % accuracy in each case.

## V. RESULTS OF THE EXPERIMENTS

A series of experiments was performed to verify the effectiveness of the algorithm synchronizing the digital images to allow to correlate the subjective assessment by an ophthalmologist with the objective assessment using the *"Q"* index.

TABLE V. RESULTS OF EXPERIMENTS FOR EYE IMAGES OF A FEW PATIENTS.

| Patients | Eye image taken on | | Objective assessment before synchronizarion | Subjective assessment before synchronization | Synchronization on axes X and Y | | Objective assessment after synchronization | Subjective assessment after synchronization |
|---|---|---|---|---|---|---|---|---|
| P1 | 02.23 2011 | 09.24 2011 | 0.37 | Change | -3 | -2 | 0.89 | Change |
| P2 | 07.13 2011 | 12.20 2011 | 0.81 | Little change | 1 | 0 | 0.94 | Little change |
| P3 | 05.06 2012 | 11.08 2012 | 0.32 | Significant change | -4 | 3 | 0.55 | Significant change |
| P4 | 02.07 2012 | 10.11 2012 | 0.26 | Significant change | 3 | -5 | 0.61 | Significant change |
| P5 | 01.08 2013 | 05.09 2013 | 0.43 | Little change | 0 | 2 | 0.91 | Little change |

The experiments involved the assessment of the eye photographs containing changes caused by advancing disease. The first assessment was made by the ophthalmologist who subjectively graded the images using the following statements: "no change", "little change", "change", "significant change" and "very significant change". Then, the objective *"Q"* – based assessment was

performed, first without using the synchronizing algorithm, later after the application of the synchronizing algorithm described in the article.

The examples of the results for a five selected patients from 221 surveyed and the photographs of their eyes taken on different dates are presented in Table V.

## VI. SUMMARY AND ANALYSIS OF RESULTS

The analysis of results presented in Table V allows to say that the proposed method of synchronization of eye images is effective. The synchronization algorithm proposed by the authors eliminates the errors of the subjective assessment caused by imprecise matching of the examined eye images. As a result, the process of correlation of the subjective assessment with the *"Q"* – base objective assessment no longer includes errors caused by absence of synchronization between the examined eye images of a patient. This is particularly evident, e.g. during examination of the disease condition in patients P1, P3, P4, P5 where the objective *"Q"* – based assessment before synchronization indicates a very large change caused by the disease, and the subjective assessment by ophthalmologists indicates otherwise. Both evaluations, objective and subjective, were correlated only when the synchronizing algorithm was applied.

Elimination of such errors allows to apply in the AMD examination the measure used to evaluate the image quality. The measure is used as a method supporting the subjective assessment by ophthalmologists. Application of objective methods enables a quantification of the changes in the eye in addition to typically subjective evaluations such as "change", "significant change", *etc*.

It should be mentioned that during a series of experiments the authors estimated the range of *"Q"* values after the synchronization process to which the subjective evaluations can be assigned. The ranges are presented in Table VI.

TABLE VI. Q RANGES AND CORRESPONDING SUBJECTIVE EVALUATIONS.

| **Range of Q index** | | **Subjective assessment** |
|---|---|---|
| 1.00 | 0.99 | No change |
| 0.98 | 0.90 | Little change |
| 0.89 | 0.71 | Change |
| 0.70 | 0.44 | Significant change |
| 0.43 | 0.00 | Very significant change |

Of course, the use of the objective assessment in the form of the *"Q"* measure proposed in the article only supports the decision making process concerning the advance of the disease. However, it will make things easier for the ophthalmologist in case of a large number of analysed images.

It is disputable why the authors used the *"Q"* index for objective assessment, and not another method such as popular Mean Square Error (MSE) [8], [9]. The reason was that the *"Q"* index is a relatively new measure, and its objective indication is well correlated with perception of images by humans. In addition, this measure and its modifications are continuously being developed, and new and more effective modifications are being introduced.

Therefore, in further research on the problem presented in this paper the authors will attempt to implement new modifications of the *"Q"* measure as described in the literature [10], [11].

Similarly, the methods based on the coefficient of correlation [12] could have been used during the synchronization process, but the choice of a single measure for two purposes (assessment and synchronization) allows to facilitate and accelerate significantly the operation of the whole algorithm. The problem could be solved by using the Monte Carlo method [13], [14].

## REFERENCES


[1] A. C. Bird, N. M. Bressler, S. B. Bressler, *et al*, "International classification and grading system for age-related maculopathy and age-related degeneration", *Surv. Ophthalmol*, vol. 39, pp. 367–374, 1995. [Online]. Available: http://dx.doi.org/10.1016/S0039-6257(05)80092-X

[2] R. Klein, M. D. Davis, Y. L. Magli, P. Segal, B. E. Klein, L. Hubbard, "The Wisconsin age-related maculopathy grading system", *Ophthalmology*, vol. 98, pp. 1128–1134, 1991. [Online]. Available: http://dx.doi.org/10.1016/S0161-6420(91)32186-9

[3] P. J. Saine, "Fundus photography: What is a Fundus camera?", *Ophthalmic Photographers' Society*, 2006.

[4] W. Zhou, A. C. Bovik, "A Universal image quality index", *IEEE Signal Processing Letters*, vol. 9, no. 3, pp. 81–84, 2002. [Online]. Available: http://dx.doi.org/10.1109/97.995823

[5] C. Rickman, F. Bowes, T. Sina, A. Cynthia, "Dry age-related macular degeneration: mechanisms, therapeutic targets, and imaging", *Investigative Ophthalmology & Visual Science*, vol. 54, no. 14, 2013.

[6] A. D. Kulkarni, B. D. Kuppermann, "Wet age-related macular degeneration", *Advanced Drug Delivery Reviews*, vol. 57, no. 14, pp. 1994–2009, 2005. [Online]. Available: http://dx.doi.org/10.1016/j.addr.2005.09.003

[7] J. Peksinski, G. Mikolajczak, "Using a neural network to generate a FIR filter to improve digital images using a discrete convolution operation", *Lecture Notes in Artificial Intelligence*, vol. 7197, pp. 294–300, 2012.

[8] J. Peksinski, G. Mikolajczak, "Generation of FIR filters by using neural networks to improve digital images", in *Proc. 34th Int. Conf. Telecommunications and Signal Processing (TSP)*, Budapest, 2011, pp. 527–529. [Online]. Available: http://dx.doi.org/10.1109/tsp.2011.6043674

[9] Z. Wang, A. C. Bovik, "Mean squared error: Love it or leave it? A new look at Signal Fidelity Measures", *IEEE Signal Processing Magazine*, vol. 26, no. 1, pp. 98–117, 2009. [Online]. Available: http://dx.doi.org/10.1109/MSP.2008.930649

[10] K. Okarma, "Combined image similarity index", *Optical Review*, vol. 19, no. 5, pp. 349–354, 2012. [Online]. Available: http://dx.doi.org/10.1007/s10043-012-0055-1

[11] K. Okarma, "Colour image quality assessment using structural similarity index and singular value decomposition", *Int. Conf. on Computer Vision and Graphics (ICCVG 2008)*, Warsaw, Poland, 2008.

[12] J. Peksinski, G. Mikolajczak, "The preparation of input data in digital image processing", *Przegląd Elektrotechniczny (Review on Electrical Engineering)*, vol. 89, no. 3b, pp. 282–284, 2013.

[13] P. Lech, "The detection of horizontal lines based on the Monte Carlo reduced resolution images", *Computer Vision and Graphics*, pp. 374–381, 2014. [Online]. Available: http://dx.doi.org/10.1007/978-3-319-11331-9_45

[14] P. Lech, K. Okarma, "Optimization of the fast image binarization method based on the Monte Carlo approach", *Elektronika Ir Elektrotechnika*, vol. 20, no. 4, pp. 63–66, 2014. [Online]. Available: http://dx.doi.org/10.5755/j01.eee.20.4.6887