OBTAINING AND ANALYSIS OF MULTIFOCAL ELECTRORETINOGRAM

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Abstract: The subject matter of this paper concerns the electrophysiological examinations on the vision organ, obtaining and analysis of electroretinogram (ERG), in particular. The specialized equipment and software allowing to obtain a multifocal electroretinogram by means of a simultaneous examination of response to luminance modulations of several areas of retina were used during discussed studies. The results presented and sample analyses refer to the actual multifocal ERG waveforms obtained during patient examinations in clinical conditions. The mathematical model was proposed, which reflects the ERG curve of a healthy retina. Such model may be useful in making a measuring reference database.

Introduction

The eye functions as the converter of the optical signal into an electric one and contains two mutually cooperating systems: sensor and optical. The sensor system converts the photons into electric signals then transmitted to the brain leaving information there on the image formed by the optical system elements. The vision line goes through the central retinal fovea and the central nodular point of the refracting media in the eyeball. In the retinal macula only adherent cones occur that transmit the induction to the brain by means of one nervous fiber – this provides both detection of light of various colors and visual acuity.

The examination methods applied in ophthalmology usually just allow determining the general retinal response to a defined luminance modulation, which frequently appears insufficient in several dysfunctions. Between the outer and inner retinal layer there is a constant static electric potential difference which, under a single short luminous impulse, changes its value. The ERG is a mass potential from the whole retina, to be recorded from the corneal surface of the eye. The thorough examinations of the retina allow precise diagnosing of eye dysfunctions, however, they require individual measurements of the reactions taking place in each particular retinal area. Such measurements are burdened with significant errors as their duration is long enough for the measuring conditions to vary. The application of multifocal electroretinogram allows reducing such errors. The multifocal electroretinogram is a signal reflecting the reactions of several retinal areas evoked by a defined luminance modulation. The signal is an instrument for the objective evaluation of the correctness of retinal actions as the responses of several retinal areas are measured simultaneously, in a respectively short time.

The signal obtained by means of special electrodes is presented in a graphic form. Its parameters reflect the condition of the particular retinal areas. The ERG examination is used in diagnosing retinal diseases, including but not limited to the following: organic retinal lesions caused by such diseases as e.g. pigmentary retinal degeneration, toxic injuries of the retina, degenerative and vascular diseases of the retina.

During the examinations the results whereof are presented herein, a specialized RETIscan device was used to generate the luminance modulating signal and to obtain the multifocal electroretinogram. The program operation consists of menu of appropriate command.

Materials and Methods

The electrophysiological examinations [1, 2, 3] consist in the observation of changes in the action potentials arising within the eyeball, the eye muscles and the cerebral cortex area. Most of the examinations are based on non-invasive measurement of the said potentials by means of electrodes appropriately distributed. Such measurement allows fast, accurate and non-invasive or minimally invasive diagnosing of the lesions occurring in the optic nerve or in the retina. Depending on the manner of electrode distribution and the type of electric potentials measured, the following types of electrophysiological examinations used in ophthalmology are distinguished: electromyography (EMG), visual evoked potentials (VEP), electrooculography (EOG), and electroretinography (ERG). ERG is an examination allowing the measurement of changes of basic potential induced by light wave. The change caused by the appearance of action electric potential is illustrated by a diagram called electroretinogram (ERG waveform). The detailed electrophysiological examinations of the retina require the use of complex measuring apparatus. The traditional examination methods allow to establish the general

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retinal response to a defined modulation only, which appeared insufficient with numerous eye dysfunctions. In some dysfunctions the curve of a general electroretinogram may not differ from the normal. As mentioned, the multifocal examination allows the simultaneous local assessment of the actions of numerous small areas of the retina, in a relatively short time [4, 5]. It is also possible to reduce the errors related to the changing measuring conditions, which take place during the conventional ERG examination, subsequently from each part of the retina.

The basic method of recording the bioelectrical signals in ERG is by stimulating the eye with a flickering image. For such purpose, there are several stimulation methods and special measuring electrodes are applied. The active electrodes are often made with golden foil or wires incorporated in the contact lenses put on the eyeball (Figure 1).

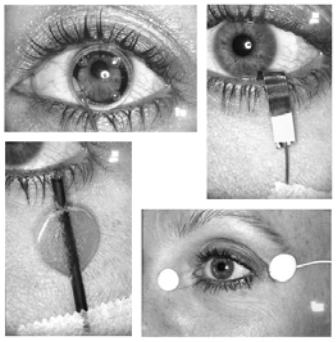

Figure 1: Examples of corneal electrodes used for obtaining ERG signals [6]

A device allowing the acquisition of the said information and the analysis thereof is the RETIscan/RETIport computer supported set [7]. Such set is composed of two mutually complemented devices: RETIscan allowing the multifocal ERG and RETIport, making it possible to carry out the other electrophysiological examinations: ERG, EOG, VEP, and PERG (Figure 2). The set is furnished with specialized RETIsystem software, consisting of two sub-programs: RETIscan and RETIport.

The RETIscan device is composed of several linked subassemblies, including but not limited to two computers: 1) the so-called stimulating computer with the luminous stimulator, and 2) the controlling computer – its task being the examination operation and the analysis of its results. The RETIsystem software, like Windows operating system was built on the basis of Windows. During the starting procedure, RETIsystem carries out test on the devices connected to the steering computer, simultaneously displaying information on program and license version. Upon starting the program a selection window appears where a defined type of examination should be selected by means of appropriate keys.

Figure 2: RETIsystem set used during the reported multifocal ERG examinations

The examination performance requires the generation of a flickering image composed of numerous elements. A shining image on the stimulating computer screen is composed of numerous hexagons – 'honeycombs' (Figure 3). It is possible to select the hexagon resolution, i.e. 19, 37, 61, 103, 241 elements respectively. Each is steered by a binary function appropriately attributed to it, where 0 causes display of a black hexagon and 1 – of a white hexagon. The functions determine the cycle of the hexagon flickering, the size thereof is adapted to the retinal sensitivity distribution (the hexagons in the center are small and increase the further they appear from the center). At each examination stage a different combination of elements is adjusted 'bright'. The size of the image elements must be adapted to the retinal sensitivity distribution – the closer to the center, the smaller is the hexagon surface. The patient observes a flickering image, concentrating on its center.

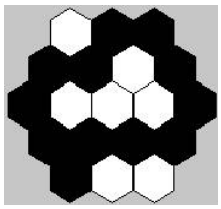

Figure 3: Stimulating flickering image composed of 19 hexagons

The signals being the effect of the examined eye response to the luminous stimuli are received by means of the mentioned electrodes. The resultant signal obtained is a sum of all the stimulated surface responses. The combinations of shining hexagons appropriately steered are used for eye stimulation during the examination.

The luminous signals evoke reactions of stimulated retinal areas, acquired by means of electrodes (Figure 4a). The active electrode, connected to input +, was put on the cornea, the reference electrode was adhered to the temple, while the grounding electrode – on the forehead (between the eyes). During the examinations

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the active electrode of type presented in Figure 4b was used.

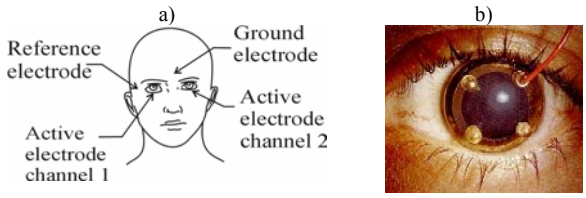

Figure 4: Points of ERG application in multifocal examination (a), and the type of active electrode used during multifocal ERG examinations made with RETIscan device (b)

The ERG signals acquired and processed are displayed on the computer screen. The set of results obtained in the graphic form reflects the condition of the particular retinal areas.

Results

The RETIscan program allows the exportation of a determined examination result from the existing database to a selected directory. The data transmitted were saved in the form of a file of values divided by commas and may be read by means of Microsoft Excel. The time diagrams obtained represent numerical data sets. The examination results were divided into two groups, of which the first determines the values of the latencies and extremes of all the areas examined, while the second allows creating the total ERG curve as well as one for each area separately.

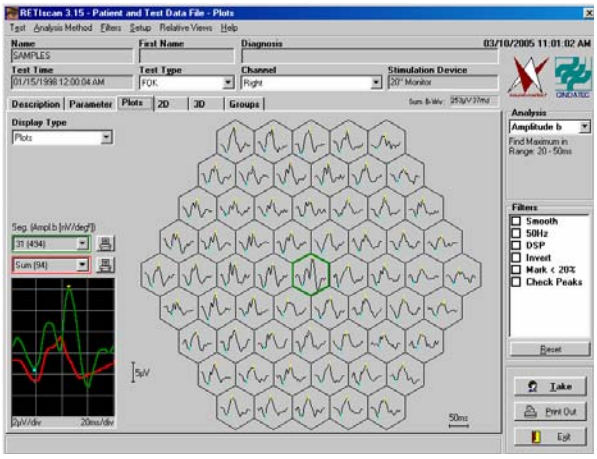

Figure 5: View of the screen with sample examination result obtained from RETIscan for an image composed of 61 hexagons

The example presented in Figure 5 concerns the results obtained for an image composed of 61 hexagons; on the left there is the ERG waveform (green line) for the central hexagon. In Table 1 a fragment of ERG parameters collected with examination results for 61 hexagons is placed. The specific measures of the recorded ERG waveform are the amplitude and latency values for the a- and b-waves, respectively. The a-wave is the first large negative component, followed by the b-wave which is positive and usually larger in amplitude.

Table 1: Fragment of a table with sample examination results obtained for 61 hexagons

	Area [deg^2]	a Latency [s]	a Value [V]	b Latency [s]	b Value [V]	Amplitude b [V/deg^2]	Amplitude a [V/deg^2]	FFT Base Wave [V/deg^2]	Scalar Product [V/deg^2]
Sum	1	0.016891	1.61E-06	0.037162	4.14E-06	4.14E-06	1.61E-06	2.02E-06	1.12E-06
Seg.1	1	0.016891	2.,21E-06	0.037162	6.63E-06	6.63E-06	2.21E-06	2.98E-06	1.54E-06
Seg. 2	1	0.018581	1.88E-06	0.038851	5.59E-06	5.59E-06	1.88E-06	2.47E-06	1.42E-06
.	.	.	.	..	.	.	.	.	.
.	.	.	.	..	.	.	.	.	.
Seg. 61	1	0.018581	2.28E-06	0.035472	4.78E-06	4.78E-06	2.28E-06	1.72E-06	1.12E-06
	Values	**[V]**							
Sum	3.73E-07	3.96E-07	4.05E-07	4.00E-07	2.79E-07	1.95E-08	-3.49E-07	-7.87E-07	.....
Seg. 1	1.18E-07	-2.14E-07	-2.73E-07	-2.53E-07	-5.76E-07	-7.61E-07	-8.88E-07	-1.37E-06	.....
Seg. 2	1.85E-07	2.83E-07	5.46E-07	4.98E-07	1.95E-07	-9.81E-08	-3.42E-07	-7.91E-07	.....
.	.	.	.	.	.	.	.	.	.....
.	.	.	.	.	.	.	.	.	.....
Seg. 61	-5.72E-08	3.33E-07	6.36E-07	5.78E-07	2.65E-07	1.19E-07	5.03E-08	-1.45E-07	.....

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Acquisition of data obtained during examination of numerous healthy eyes allows drawing standard ERG curves that allow the creation of a healthy retina mathematical model. A concept of such a model is considered below.

Discussion

It is known that the a-wave reflects the properties of the outer retina photoreceptors while the b-wave reflects properties of the inner layers of the retina [3]. Figure 6 illustrates an example of differences between the healthy retina and normal ERG waveform and their abnormal attributes caused by retinoschisis [6].

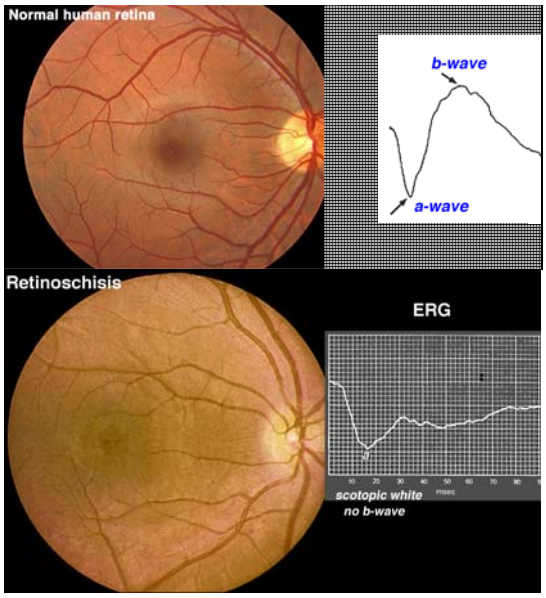

Figure 6: Comparison of ERG waveforms obtained for a normal human retina and retinoschisis, respectively [6]

Within the examinations carried out on the analysis of the multifocal electroretinogram, an attempt to define a model for the so-called total ERG waveform was made, assuming that the local extremes of the model should be in line with the extremes of the actual signal examined. Moreover, it was assumed that the model searched for should minimize the mean square error PRD, given by the dependence

$$PRD = \sqrt{\frac{\sum_{t=1}^{N}\left(Y[t]-F[t]\right)^2}{\sum_{t=1}^{N}Y[t]^2}} \qquad (1)$$

where $Y[i]$ mean ERG curve samples, while $F[i]$ are the corresponding values of the model function. During the examinations a similarity between the ERG curve and the second derivative of Gauss function was found, given by the dependence

$$G(t) = 2T_1k_1\left(1-2T_1t^2\right)\exp\left(-T_1t^2\right) \qquad (2)$$

where T_1 and k_1 are the constants determined basing on the location of zero points. The observations made were verified analyzing the location of the characteristic points of the curves examined: local extremes (E1, E2, E3, E4) and zero points (Z1, Z2), and the results obtained that confirm the similarity of both curves were illustrated in Figure 7. The ERG curve was marked with a black line and the second derivative of the Gauss – red.

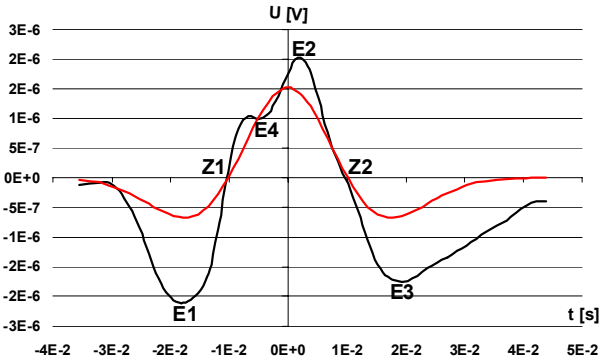

Figure 7: The second derivative of the Gauss function curve (red line) compared to the ERG curve examined (black line)

Considering the similarity of these curves, the possibility of building a model ERG curve was examined using the second derivative of the Gauss function as the basic component and assuming the model structure shall have the form given by the dependence

$$F(t) = G(t)\cdot M(t) + E(t) \qquad (3)$$

where $M(t)$ is the so-called multiplier function, and $E(t)$ the function used for modeling a slight local extreme E_4.

Settling the parameters of the main component of the model required the shift of the examined actual waveform in the time axis direction so that both zero points are spaced symmetrically in relation to the axis of values where the measured electrical voltage was marked. The time-constant T_1 was calculated basing on the zero points location of the actual curve examined, while the reinforcement coefficient k_1 was determined basing on the examined curve value in point $t = 0$.

The local minima values E_1 and E_3 were matched by such selection of the multiplier function parameters $M(t)$, that it should fulfill the set of equations given by the dependence

$$\begin{cases} M(t_1) = \dfrac{Y_1}{G(t_1)} \\ M(0) = 1 \\ M(t_3) = \dfrac{Y_3}{G(t_3)} \end{cases} \qquad (4)$$

where Y_1 and Y_3 are the values of the actual curve local minima. In dependence (4) $M(0) = 1$ was assumed, due to the assumption that the multiplier function should not

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change the value of the local maximum E_2 occurring in point $t = 0$ and on its basis the value of coefficient k_1 was calculated.

Selecting the multiplier function model character, it was considered to apply the exponential function or trinomial square. In the first case the accurate solution of the set of equations (4) was impossible and the possible approximation by means of e.g. curvilinear regression could be practically applied only if the dependence were fulfilled

$$M(t_1) > M(0) > M(t_2) \tag{5}$$

In case of the trinomial square, however, the set of equations (4) always has a solution in practice and the possible relations between the multiplier functions values did not affect the accuracy of determining its parameters.

As the function 'responsible' for fulfilling the slight local minimum marked in Figure 7 as E_4, the first derivative of the Gauss function was used given by the dependence

$$E(t) = 2T_2k_2t\exp\left(-T_2t^2\right) \tag{6}$$

The k_2 and T_2 parameters were determined basing on the location and value of the local E_4 and E_2 extremes.

The final form of the model, including the values of its particular parameters are described in the equation

$$F(t) = 2T_1k_1\left(1-2T_1t^2\right)\exp\left(-T_1i^2\right)\cdot \\ \cdot\left(At^2+Bt+1\right)+2T_2k_2i\exp\left(-T_2i^2\right) \tag{7}$$

The results obtained were illustrated in Figure 8. The ERG waveform was marked with a black line, while the model obtained – green. The red and blue lines respectively signified the multiplier function and the function used for modeling the E_4 extreme.

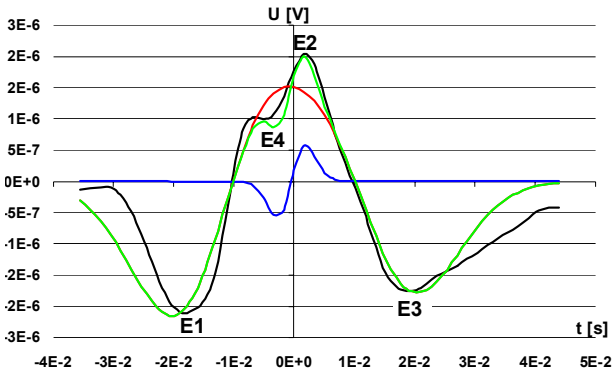

Figure 8: The ERG curve model obtained and the components used for its determination

The assessment of the model obtained was carried out basing on two criteria formulated at first. Analyzing the location of the characteristic points of the actual curve, some slight divergences were noted in the location of the local extremes. The subject of further research shall include, inter alia, the extent the divergences observed may be significant to, from the diagnostic point of view.

Making the general assessment of the adjustment of the waveforms analyzed, in the scope determined by the location of the two local minima E_1 and E_3, it was discovered that the relative mean square error calculated in virtue of dependence (1) did not exceed 15%. The significant divergences in the course of the curves analyzed appear along with approaching the actual course limits only and the direct cause of such phenomenon is the nature of the component functions of the model. It is worth emphasizing, however, that the extreme fragments of the ERG curve have no such significant diagnostic meaning as the location of its extremes.

Analyzing the form of the model obtained, the dependence nature is worth noting, as reflected by the ERG curve. In the description obtained time is not the independent variable, while the time square is, which induces further research aimed at the explanation of the physiological essence of the phenomena modeled. The mathematical model presented herein thus requires a more detailed analysis and determines the preliminary conditions for further numerical processing.

Conclusions

Electroretinography is at present the commonly used method allowing the diagnostics of retinal and optic nerve dysfunctions. It frequently is the only method allowing the accurate, non-invasive and objective diagnosis of the dysfunctions that occur.

The present level of knowledge and technology allows to construct a device making it possible to minimize the errors related to the changing measuring conditions during the ERG examination and the artifacts then occurring. The minimization of such errors is possible thanks to the application of the multifocal electroretinogram and the appropriate data processing algorithms for the data obtained during the examination. The RETIscan device used during examinations described herein makes use of the multifocal ERG. The examination results are displayed on the steering monitor screen in the form of the ERG waveform appropriately scaled. Such results, upon transmission to a specified program enable drawing raw ERG curves. In virtue of the numerical data, acquired during examination of healthy eyes, it is also possible to create a model of a healthy retina.

The healthy retina model may represent referential data in the examinations of various retinal dysfunctions and enable the comparison of the ERG curves obtained during such examination. Moreover, the possibility of analysis of the raw signals from RETIscan should allow a more detailed evaluation of the retinal condition. Such a model, which improvement is the subject of further studies in progress, will act as reference data in

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examination of different diseases of human retina and visual nerve. Furthermore, it could be applied in analyzing raw bioelectrical signals to be obtained from RETIscan device before their final conditioning.

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