

Validation of a new fiber electrode prototype for clinical electroretinography

Validação de protótipo de um novo eletrodo de fibra para eletroretinografia clínica

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ABSTRACT

Purpose: To validate a new fiber electrode prototype for clinical electroretinography (ERG). **Methods:** A recently developed prototype of a disposable reference-coupled fiber electrode (patent pending Brazilian Institute of Industrial Property # PI0602186-7), including one fiber for corneal signals and a second fiber acting as reference was tested in a group of 20 healthy volunteers (17-31 years; mean 22.7 ± 4.5 ; 8 males). Standard electroretinography rod and cone responses were recorded from a fully dilated pupil simultaneously in both eyes with a reference-coupled fiber electrode prototype in one randomly assigned eye and a DTL[®] electrode in the other eye after 30 min of dark-adaptation. After presenting dark- and light-adapted stimuli, each response was analyzed for a- and b-wave amplitude and implicit time. The VERIS 5.1.9 system was used for electroretinography data acquisition and analysis. Electroretinography outcomes were analyzed by Mann-Whitney test. Slit-lamp examination was performed in both eyes right after electroretinography session to evaluate possible adverse effects. **Results:** Responses recorded with reference-coupled fiber electrode prototypes were comparable to commercially available DTL[®] fiber electrodes. On a qualitative analysis, reference-coupled fiber electrodes provided recordings with less amount of noise. On average, scotopic electroretinography amplitude and b-wave implicit time recorded using DTL[®] were, respectively, 287.6 μV and 36.3 ms with similar findings for the reference-coupled fiber electrode prototype (287.9 μV and 36.3 ms). Under photopic conditions DTL[®] mean amplitude and implicit time were, respectively 108.9 μV and 24.5 ms with similar results for the reference-coupled fiber electrodes prototypes (116.4 μV and 24.5 ms). No corneal abrasions or any other significant adverse effects were found after electroretinography recording with both electrodes. **Conclusions:** The reference-coupled fiber electrode prototype provided stable and safe recordings of corneal electroretinograms compared to the commercially available DTL[®] electrode in healthy human subjects. The prototype is a feasible alternative instrument for clinical electroretinography recording to assess retinal function, however further analysis is recommended to validate its clinical usefulness in patients with retinal disorders.

Keywords: Electrodes; Electroretinography/instrumentation; Retina/physiology; Retinal diseases; Validation studies

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INTRODUCTION

Full-field electroretinography is widely used in the diagnosis and clinical monitoring of several retinal conditions including inherited eye diseases, retinotoxic effects of systemic drugs and to evaluate treatment protocols. The full-field electroretinogram (ERG) represents the summed activity of the distal retina in response to light flashes and this electrical response is recorded by several types of electrodes⁽¹⁻⁴⁾.

Since recording the first human ERG over a century ago, numerous electrodes have been developed in search of an ideal electrode that would accurately record the ERG and still be comfortable for the patient⁽⁵⁾. Corneal contact lens electrodes are considered optimal for recording human full-field flash ERGs since they yield large amplitude and high signal-to-noise ratio⁽⁶⁾. Unfortunately these electrodes have unwanted side effects. The most usual side effects frequently seen by ERG specialists are corneal abrasions, inability to fit small palpebral fissures (pediatric ERGs) and the need of cooperation from the subjects⁽⁶⁾. Besides these disadvantages are the rising cost of these electrodes and the increasing difficulty in getting a regular supply, especially on short notice (usually they are handmade) in developing countries. Finally, the deterioration of the optical quality of the eye, caused by contact lens, prevents its use for pattern ERG studies⁽⁶⁻⁷⁾.

For such reasons, some investigators have chosen electrodes such as the DTL[®] fiber electrode⁽⁷⁾, which is less invasive, does not require anesthesia of the eye, and can be used for lengthy recording periods⁽⁸⁾. The stability and reproducibility of ERG responses recorded by DTL[®] electrodes have been tested and the results were favorable in both aspects⁽⁸⁾.

Bipolar contact lens electrodes are recommended by the International Society for Clinical Electrophysiology of Vision (ISCEV) since they promote more stable and noiseless ERG recordings. However, commercially available fiber electrodes are monopolar, requiring a second electrode placed in the external canthus to act as a reference pole. A fiber electrode with the reference terminal coupled would be highly useful since it would have both terminals attached to the same place.

In developing countries as Brazil, both contact lens and disposable fiber electrodes for ERG recording are not locally manufactured, requiring importation at high cost. The purpose of this study is to validate a recently developed reference-coupled fiber electrode prototype for clinical electroretinography. Its validation includes investigation of its efficacy compared to commercially available monopolar DTL[®] electrodes for each parameter of the ERG.

METHODS

Subjects

This study has been approved by the Committee of Ethics in Research of the Federal University of São Paulo and has followed the tenets of the Declaration of Helsinki. A group of

20 healthy volunteers (17-31 years; mean 22.7 ± 4.5 ; 8 males) was recruited for the study. The inclusion criteria were: best corrected visual acuity for distance equal or better than 0.0 logMAR (20/20), absence of visual complaints, normal fundus, and compliance with the informed consent form. Exclusion criteria were: history of hereditary eye diseases, history of previous ocular surgeries or high ametropia (myopia = -5.00 spherical equivalent, hyperopia = +5.00 spherical equivalent).

Reference-coupled disposable fiber electrodes

Full-field ERG was recorded through a recently developed disposable reference-coupled fiber electrode prototype (patent pending Brazilian Institute of Industrial Property # PI0602186-7). The prototype is composed of nylon monofilament 6 cm long 100 μm thick impregnated with metallic silver (for corneal signals) and a second fiber with the same parameters serving as reference. At both ends small sponges (1.0 cm x 1.0 cm) are secured to internal and external canthi by means of double-sided adhesive tape and conductive adhesive. The active electrode was positioned in the lower conjunctival sac and at the same time the reference was positioned beside the external canthus (Figure 1).

Full field electroretinography

ERG was simultaneously recorded from both eyes: one randomly assigned eye with the reference-coupled fiber electrode prototype and the fellow eye with monopolar DTL[®] (Diagnosys LLC, Lowell, MA, USA). All ISCEV rod and cone responses were obtained from a fully dilated pupil after 30 min of dark-adaptation⁽²⁾. The VERIS 5.1.9 (Electro-Diagnostic Imaging, San Mateo, California, USA) system was used for ERG data acquisition and analysis. Stimulus and recording parameters are defined in table 1. After 30 minutes of dark adaptation, ERG responses were recorded in the following order: (a) a maximal intensity white light attenuated by a 2.4 log neutral density filter to elicit a dark-adapted rod response; (b) a maximal intensity white light to elicit a mixed dark-adapted rod and cone response; (c) the maximal intensity white light with a 100-Hz low-cut and 1-KHz high-cut filter to elicit oscillatory potentials; and the maximal intensity white light on a 30 cd/m^2 background presented; at (d) 1 Hz and (e) 30 Hz to elicit cone responses. A period of 10 min was allowed to adapt to the background light when collecting the cone responses. Twenty responses were computer-averaged for each step of the standard protocol, except for the 30-Hz flicker for which 50 responses were averaged. After presenting standard dark- and light-adapted stimuli, each response was analyzed for a- and b-wave amplitude and implicit time. Slit-lamp examination was performed in both eyes right after ERG session to evaluate possible adverse effects.

Statistical analysis

Data from ERG parameters (peak-to-peak amplitude and implicit time) from each step of the ISCEV standard protocol were compared between the reference coupled fiber electrode

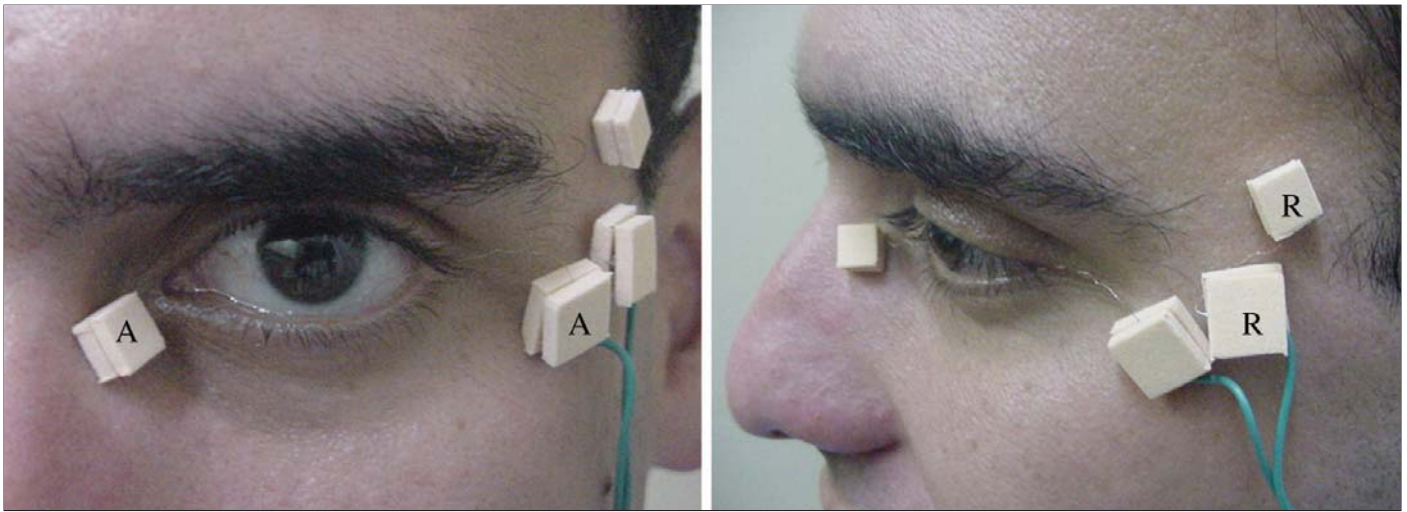


Figure 1 - Fitting of the fiber electrodes with reference coupled prototype for ERG recording. Active electrode is secured to both canthi and placed at the lower conjunctival sac, while the reference electrode is secured at the side. (A) active electrode. (R) reference electrode.

Table 1. Stimulus and recording parameters used for ISCEV ERG standard protocol

Response N (number of trials)	Retinal illuminance (cd.s/m ²)	Frequency of presentation (Hz)	Background (cd./m ²)	Low-cut (Hz)	Hi-cut (KHz)
Rod-isolated 20	0.0084	1	none	1	1
Maximal 10	2.5067	1	none	1	1
Oscillatory potentials 20	2.5067	1	none	100	1
Single-flash cone 20	2.4851	1	30.06	1	1
Flicker 50	2.5021	30	30.82	10	1

prototype and the DTL[®] electrode by the Mann-Whitney rank sum test.

RESULTS

Responses recorded with reference-coupled fiber electrode prototypes were comparable to DTL[®] electrodes. On a qualitative analysis, the fiber electrodes with reference-coupled showed less amount of electrical noise (Figure 2).

Mean b amplitudes (measured peak-to-peak from a wave to b wave) and respective standard deviations for rod, maximal response, cone, flicker responses (average of sinusoidal peak-to-peak responses) and oscillatory potentials (OP2) obtained from both electrodes are plotted in figure 3 and shown in table 2. Mean b implicit times and respective standard deviations for rod, maximal response, cone, flicker responses obtained from both Groups are plotted in figure 4 and shown in table 2.

On average, scotopic ERG amplitude and b-wave implicit time recorded using DTL[®] were, respectively, 287.6 μ V and

36.3 ms while with reference-coupled fiber electrode prototype the same parameters were, respectively, 287.9 μ V and 36.3 ms. Under photopic conditions DTL[®] mean amplitude and implicit time were, respectively 108.9 μ V and 24.5 ms while with reference-coupled fiber electrode prototype they were respectively 116.4 μ V and 24.5 ms. No corneal abrasions were found after ERG recording with both types of electrodes. Rod, maximal, and cone 30-Hz flicker responses showed similar waveforms and parameters for both electrodes.

DISCUSSION

In the present study, the recently developed reference-coupled fiber electrode prototype provided ERG responses similar to those recorded with the commercially available DTL[®] electrode. No statistical differences were found in ERGs obtained by the two electrodes for all parameters studied. The prototype is more affordable locally and provides stable and safe recordings of corneal electroretinograms compared to the gold standard DTL[®] electrode.

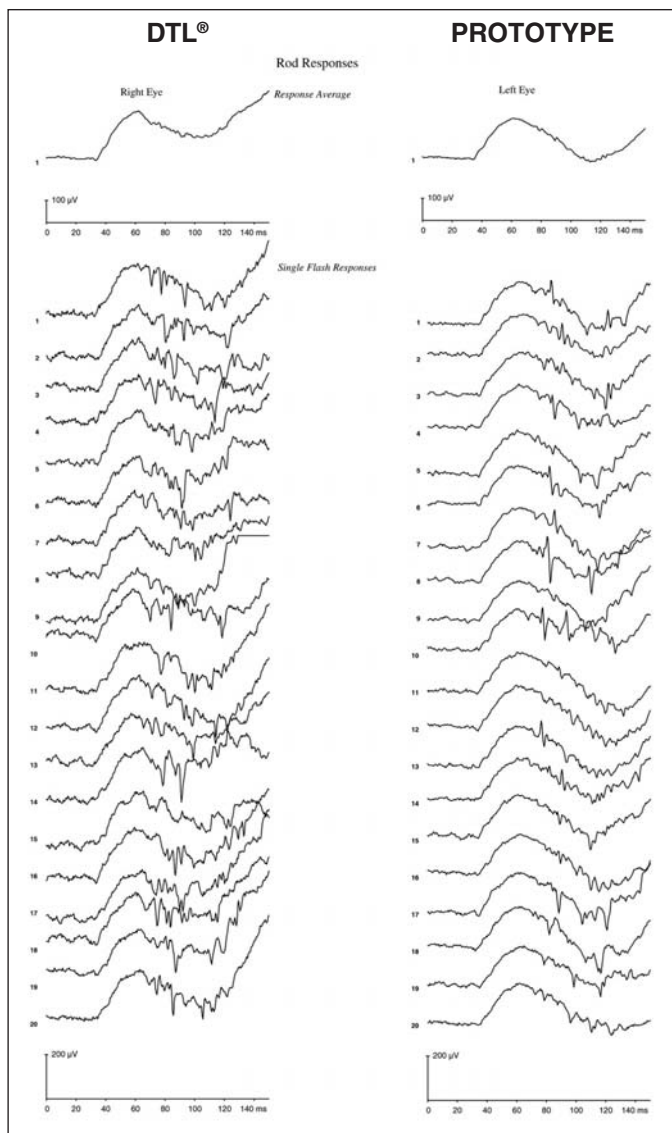


Figure 2 - Representative rod responses from a healthy volunteer. In the left panel ERG recording obtained with DTL® electrode; in the right panel ERG recorded with the new reference-coupled fiber electrode prototype.

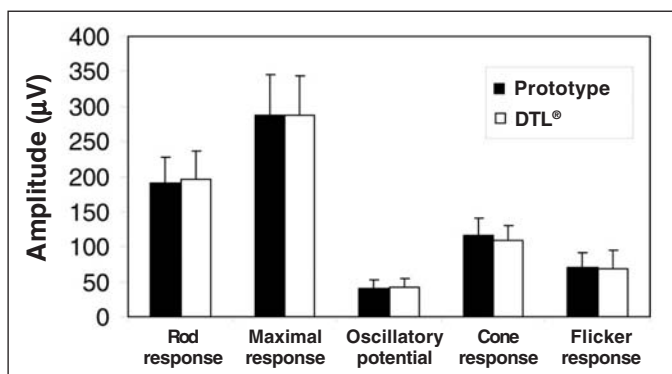


Figure 3 - Mean b-wave ERG amplitudes (measured peak-to-peak from a-wave to b-wave) and respective standard deviation for rod response, maximal response, oscillatory potentials, cone response and 30-Hz flicker from the new reference-coupled fiber electrode prototypes and DTL® electrodes

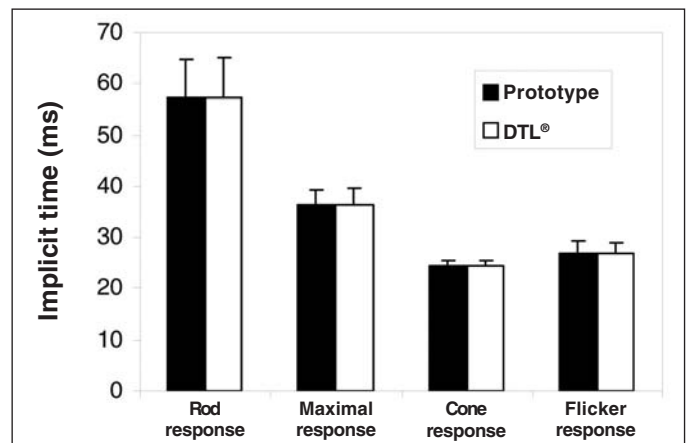


Figure 4 - Mean b-wave ERG implicit time and respective standard deviation for rod response, maximal response, cone response and 30-Hz flicker from the new reference-coupled fiber electrode prototype and DTL® electrodes

Table 2. Peak-to-peak amplitudes (a,b) and b-wave implicit times of the standardized ERG recorded with the new reference-coupled fiber electrode prototype and DTL® electrodes

	Mean and respective standard deviation		
	Bipolar prototype	DTL®	
Amplitude (µV)			
Rod	191.1 (36.2)	195.7 (40.7)	p=0.835
Maximal response	287.9 (58.05)	287.6 (56.4)	p=0.874
Oscillatory potentials	40.4 (11.7)	42.5 (11.4)	p=0.783
Cone response	116.4 (24.9)	108.9 (20.8)	p=0.330
Flicker response	69.8 (22.2)	68.5 (26.2)	p=0.845
Implicit time			
Rod	57.4 (7.5)	57.3 (7.60)	p=0.764
Maximal response	36.3 (3.3)	36.3 (3.11)	p=0.812
Cone response	24.5 (1.0)	24.5 (0.90)	p=0.733
Flicker response	26.7 (2.4)	26.9 (2.40)	p=0.393

Many kinds of electrodes have been patented. When compared with contact lens electrode, the fiber electrode is better tolerated by children because it is less traumatizing and does not require anesthetic eye drops. Several studies showed high stability for DTL® as the conventional contact lens electrodes⁽⁸⁻¹⁰⁾. The present study indicated that a quantitative measurement of fiber electrodes with reference coupled prototype is adequate for diagnostic purposes and for standard ERG recordings. Eye movements and electrode type can affect the quality of ERG recordings. To maximize recording stability, the reference-coupled fiber electrode prototype should be loosely placed in the conjunctival sac. This new fiber electrode minimized the risk of corneal abrasion and seems to be a good alternative for developing countries.

CONCLUSION

In summary, our findings clearly indicate that the reference-coupled fiber electrode prototype is adequate for ERG

recording in healthy humans. It presented lower cost, easiness of use and provided comfort to the subject. Finally, further studies using this new electrode in retinal disease patients are needed to analyze the clinical usefulness and to extend the clinical validation of this new instrument.

RESUMO

Objetivo: Validar um novo protótipo de um eletrodo de fibra para eletrorretinografia clínica (ERG). **Métodos:** Foi testado em um grupo de 20 voluntários saudáveis (17-31 anos; média $22,7 \pm 4,5$; 8 homens), um protótipo de eletrodo de fibra com referência acoplado descartável recentemente desenvolvido (depósito de patente no Instituto Nacional de Propriedade Intelectual # PI0602186-7), constando de uma fibra de sinais corneanos e uma segunda fibra servindo como referência. Após 30 minutos de adaptação ao escuro, as respostas de cones e bastonetes da eletrorretinografia foram registradas simultaneamente com dilatação completa das pupilas em ambos os olhos, com o protótipo de eletrodo de fibra com referência acoplado em um olho escolhido ao acaso e um eletrodo DTL[®] no outro olho. Após a apresentação dos estímulos escotópicos e fotópicos cada resposta foi analisada em amplitude e tempo de culminação das ondas a e b. O sistema VERIS 5.1.9 foi usado para a aquisição e análise dos dados. Os resultados da eletrorretinografia foram analisados pelo teste de Mann-Whitney. Após a sessão da eletrorretinografia foi feito exame em lâmpada de fenda para avaliar possíveis eventos adversos. **Resultados:** As respostas obtidas com o protótipo de eletrodo de fibra com referência acoplado foram comparáveis às do eletrodo DTL[®] comercialmente disponível. Numa análise qualitativa, o eletrodo de fibra com referência acoplado produziu sinais com menos ruído. Na média, a amplitude escotópica da eletrorretinografia e o tempo de culminação da onda-b usando o eletrodo DTL[®] foram respectivamente, 287,6 μ V and 36,3 ms com achados similares para o protótipo (287,9 μ V e 36,3 ms). Sob condições fotópicas, a amplitude média do eletrodo DTL[®] e o tempo de culminação

da onda b foram respectivamente 108,9 μ V e 24,5 ms com resultados similares para o protótipo (116,4 μ V e 24,5 ms). Após os registros da eletrorretinografia com ambos os tipos de eletrodos não houve abrasões corneanas ou outros eventos adversos significantes. **Conclusões:** Em sujeitos humanos saudáveis, o protótipo de eletrodo de fibra com referência acoplado forneceu registros estáveis e seguros de eletrorretinogramas a partir da córnea comparado aos obtidos com o eletrodo DTL[®] comercialmente disponível. O protótipo é um instrumento alternativo viável para registro clínico da eletrorretinografia para avaliar a função retiniana, no entanto, análises adicionais são necessárias para validar sua utilidade clínica em pacientes com distúrbios retinianos.

Descritores: Eletrodos; Eletrorretinografia/instrumentação; Retina/fisiologia; Doenças retinianas; Estudos de validação

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