Doc Ophthalmol (2013) 126:117–123
DOI 10.1007/s10633-012-9364-8

ORIGINAL RESEARCH ARTICLE

The effect of filtering on the two-global-flash mfERG: identifying the optimal range of frequency for detecting glaucomatous retinal dysfunction

Anna A. Ledolter · Sophie A. Kramer · Margarita G. Todorova · Andreas Schötzau · Anja M. Palmowski-Wolfe

Received: 11 June 2012 / Accepted: 26 November 2012 / Published online: 8 December 2012

Abstract
Purpose To study the effects of filtering bandwidth on the two-global-flash multifocal electroretinogram (mfERG) responses in primary open-angle glaucoma (POAG) compared with control subjects.
Methods A two-global-flash mfERG (VERIS 6.06^{TM}, FMS III) was recorded in 20 healthy subjects and 22 POAG patients with a band-pass filter (BPF) of 1–300 Hz (103 Hexagons, M-sequence stimulus: Lmax 100 cd/m^2, Lmin < 1 cd/m^2, global flash: 200 cd/m^2). The root-mean-square average of the central 10° was calculated. Three response epochs were analysed: the response to the focal flash, at 15–45 ms (DC), and the following two components induced by the effects of the preceding focal flash on the response to the global flashes at 45–75 ms (IC1) and at 75–105 ms (IC2). The following BPF settings were analysed: 1–300 Hz, 3–300 Hz, 10–300 Hz, 100–300 Hz, 200–300 Hz, 1–10 Hz, 1–100 Hz and 1–200 Hz.
Results Filtering at 1–300 Hz showed significantly lower responses in POAG than in control subjects ($p < 0.001$) for all epochs analysed. At 1–100 Hz, this also held true even though the difference between the groups became smaller. At 1–10 Hz, responses were extremely small and did not differ between POAG and control ($p > 0.5$). This would suggest a filter setting of 10–300 Hz for mfERG recordings in POAG. However, when a filter setting of 10–300 Hz was compared to 1–300 Hz, with a filter setting of 10–300 Hz, the DC in POAG differed more ($p < 0.0001$) from normal than with 1–300 Hz ($p = 0.0002$). For IC1 and IC2, the stronger difference between POAG and control was found with 1–300 Hz ($p < 0.0001$) rather than with 10–300 Hz ($p < 0.0001$ and $p = 0.0005$, respectively). For the 'oscillatory potentials' at 100–300 Hz, POAG and control differed significantly in IC1 and IC2 ($p < 0.05$), but not in DC ($p = 0.8$). However, filtering at 200–300 Hz did not show a difference between POAG and control ($p > 0.5$). Thus, we applied a filter setting of 1–200 Hz, which seemed to be most sensitive in detecting glaucomatous retinal dysfunction ($p < 0.0001$).
Conclusions A filter setting of 1–200 Hz appears most sensitive to detect glaucomatous damage if using a two-global-flash mfERG: using a band-pass filter a with lower low-frequency cut-off, containing the 10 Hz component, may be especially important in the small induced components that show glaucomatous damage most sensitively. High frequencies of 100–300 Hz also contain information that differentiates glaucoma from normal and thus should be included in the analysis.

The results of this manuscript have been partly presented as poster presentations at the ARVO Annual Meetings in 2011 and 2012.

A. A. Ledolter (✉) · S. A. Kramer · M. G. Todorova · A. Schötzau · A. M. Palmowski-Wolfe
Department of Ophthalmology, University of Basel, Mittlere Strasse 91, 4031 Basel, Switzerland
e-mail: PoluninaA@uhbs.ch

Keywords Multifocal ERG · Filter setting · Glaucoma

Introduction

In electroretinography, signal filtering is crucial to eliminate biological and environmental noise that can contaminate the responses. This is especially important when studying the multifocal electroretinogram (mfERG) recorded from small retinal areas [1]. In order to obtain a high-quality mfERG without losing any useful information, it is important to choose appropriate band-pass frequencies [1]. A major effect on the waveform shape is observed through use of a high-pass filter, that is, in order to reduce amplifier saturation from blinking or slow eye movements [2].

The effect of restricted filter bandwidth on the shape of the ERG waveform is recognized by the International Society for Clinical Electrophysiology of Vision (ISCEV). For the standard multifocal ERG, ISCEV recommends a high-pass cut-off between 3 and 10 Hz and low-pass cut-off between 100 and 300 Hz [3]. As these are large possible margins, we studied the effects of filtering on a special two-global-flash mfERG in glaucoma patients compared with healthy subjects. This stimulus was chosen as it has been shown that the introduction of global flashes to the mfERG increased the sensitivity of the mfERG to detect glaucomatous retinal dysfunction [4–6]. In our most recent study, we applied a two-global-flash mfERG with a focal flash of 100 cd/m^2 Lmax and global flashes of 200 cd/m^2 Lmax, filter setting: 1–300 Hz. Here, glaucoma patients differed significantly from healthy subjects in the central 10° [7]. In the present paper, we report on the effect of digital filter settings on those recordings.

Materials and Methods

Multifocal ERGs obtained in a previous study [7] were analysed.

The study protocol was approved by the Ethics Committee of the University of Basel, and informed consent was obtained from all participants before the examination. Procedures adhered to the tenets of the Declaration of Helsinki.

Twenty healthy subjects were enrolled in the study, 7 males and 13 females with a mean age of 51.8 (SD 14.8) years. The group of primary open-angle glaucoma (POAG) patients consisted of 22 subjects (16 males and 6 females) with a mean age of 64 (SD 6.4) years.

Inclusion criteria

The following criteria were considered for inclusion: visual acuity of 0.8 or better, refractive error less than ±6 dioptres; for glaucoma patients: glaucomatous optic neuropathy and localized thinning of the peripapillary nerve fibre layer as well as abnormal visual fields. On average, patients had a mean defect (MD) of 6.19 (SD 4.11) and a loss variance (LV) of 51.05 (SD 40.18) (Octopus, G2 program).

Exclusion criteria

History of ophthalmic surgical treatment of the tested eye, clinical signs of macular pathology, presence of systemic diseases (such as diabetes mellitus), currently under antidepressants, alcohol or drugs were considered as exclusion criteria.

mfERG recording

The mfERG was recorded using VERIS 6.06^{TM}, FMSIII (Electro-Diagnostic Imaging, San Mateo, CA, USA). The stimulus consisted of 103 hexagons, scaled with eccentricity, which flickered independently according to an m-sequence of 2^{13}-1, where the first frame in the m-sequence (Lmax 100 cd/m^2, Lmin $<$ 1 cd/m^2) was always followed by two global flashes (Lmax 200 cd/m^2) at an interval of 26 ms. The band-pass filter (BPF, Grass filter) was set at 1–300 Hz. Three response epochs were analysed: the response to the focal flash, at 15–45 ms (DC), and the following two response components induced by the effects of the preceding focal flash on the response to the global flashes at 45–75 ms (IC1) and at 75–105 ms (IC2). Under these stimulus parameters, glaucoma patients differed most from control subjects in the response average of the central 10° (for more details, see also Kramer et al. [7]). Therefore, we analysed the response averages from the central 10°.

Filter settings

The recorded data were filtered offline with the high-pass and low-pass filters incorporated in the VERIS

system (VERIS^{TM} scientific 6.2.2 d2). These apply a non-causal filtering: a Fourier transform is performed. All frequencies above or below a certain limit are cut out. Thus, these filters use a sharp cut-off. No cut-off transitions or 'windowing' is performed. [8].

The following BPF settings were analysed: 1–300 Hz, 3–300 Hz, 10–300 Hz, 100–300 Hz, 200–300 Hz, 1–10 Hz, 1–100 Hz and 1–200 Hz. The artefact rejection technique incorporated in the software was applied twice; spatial filtering was not used. The root mean square was calculated for each focal response and then averaged for the central 10°. For each filter setting, the root mean square was analysed for the three response epochs [DC, IC1 and IC2 (see above)].

Statistical analysis

Statistical analysis was performed using a linear mixed-effects model in the statistical package R, version 2.13.0. [9], where disease status, location, epoch and age were the fixed factors, while subject was treated as a random factor. Adjustment was made for the difference in age between the controls and the glaucoma patients ($p = 0.014$). Results are expressed as differences of means with corresponding 95 % confidence intervals and p values ($p < 0.05$ were considered significant). Differences between groups were visualized using boxplots showing median values and interquartile ranges.

Results

Changing a high- and low-frequency cut-off of the band-pass filter by digital filtering affects the waveform shape of the ERG. Compared to the waveform obtained at 1–300 Hz, a filter setting of 1–200 Hz shows a preservation of the waveform in both DC and IC. At 1–100 Hz, the original waveform is still present, but smaller in amplitude. In addition, the small induced components appear less clear. With a filter setting of 100–300 Hz, small high-frequency oscillatory potentials are seen, while at 1–10 Hz, a slow low frequency predominates (Fig. 1).

When all epochs per subject were pooled together, the following differences were observed between POAG and control subjects: with a filter setting of 1–300 Hz, responses in POAG were significantly lower than in control subjects ($p < 0.001$). With a filter of 1–100 Hz, this also held true ($p < 0.001$), even though the difference between the groups became smaller. At 100–300 Hz, POAG and control differed even less, but still significantly ($p = 0.032$). With 1–10 Hz, responses were extremely small and did not differ between POAG and control ($p = 0.85$) (Fig. 2).

For each of the three epochs of the mfERG, Table 1 summarizes the numeric calculated data, showing the difference between POAG and control group, for all filter settings analysed. POAG differed most in the IC1 of the mfERG response.

For the DC of the mfERG, significant differences were found with a filter setting of 1–300 Hz and 1–100 Hz ($p < 0.001$). We did not find a significant difference between POAG and control at 100–300 Hz ($p = 0.8$), nor at 1–10 Hz ($p = 0.84$).

For the IC1, the POAG group was significantly lower than the control group at a filter setting of 1–300 Hz, 1–100 Hz and also 100–300 Hz. There was no difference at 1–10 Hz ($p = 0.5$).

For IC2, POAG patients also differed significantly from control at a filter setting of 1–300 Hz, 1–100 Hz and 100–300 Hz, but not at 1–10 Hz ($p = 0.96$).

As we did not find a significant difference with a filter setting of 1–10 Hz in any of the epochs analysed, most of the differences between POAG and control appear to be found in the frequency range above 10 Hz. As a consequence, we then analysed the effect of a band-pass filter set at 10–300 Hz in order to see whether this might increase the sensitivity of the mfERG to detect glaucomatous retinal dysfunction.

With a filter setting of 10–300 Hz, the DC of mfERG in POAG differed more ($p < 0.0001$) from normal than with filter 1–300 Hz ($p = 0.0002$). However, for IC1 of the mfERG, POAG differed more from control at 1–300 Hz [$p < 0.0001$, difference of means (95 % CI) $= -4.1$ (-5.1 to -3.3)] than at 10–300 Hz [$p < 0.0001$, difference of means (95 % CI) $= -3.1$ (-4.2 to -2.0)]. IC2 of the mfERG also differed more at 1–300 Hz ($p < 0.0001$) than at 10–300 Hz ($p = 0.0005$) (Table 1).

As the ISCEV standard also allows a low-frequency cut-off of 3 Hz, we analysed the response of the mfERG with a low-frequency cut-off of 3 Hz. The difference between POAG patients and control subjects was significant with this filter in all three epochs analysed ($p < 0.001$). For the DC, this difference was

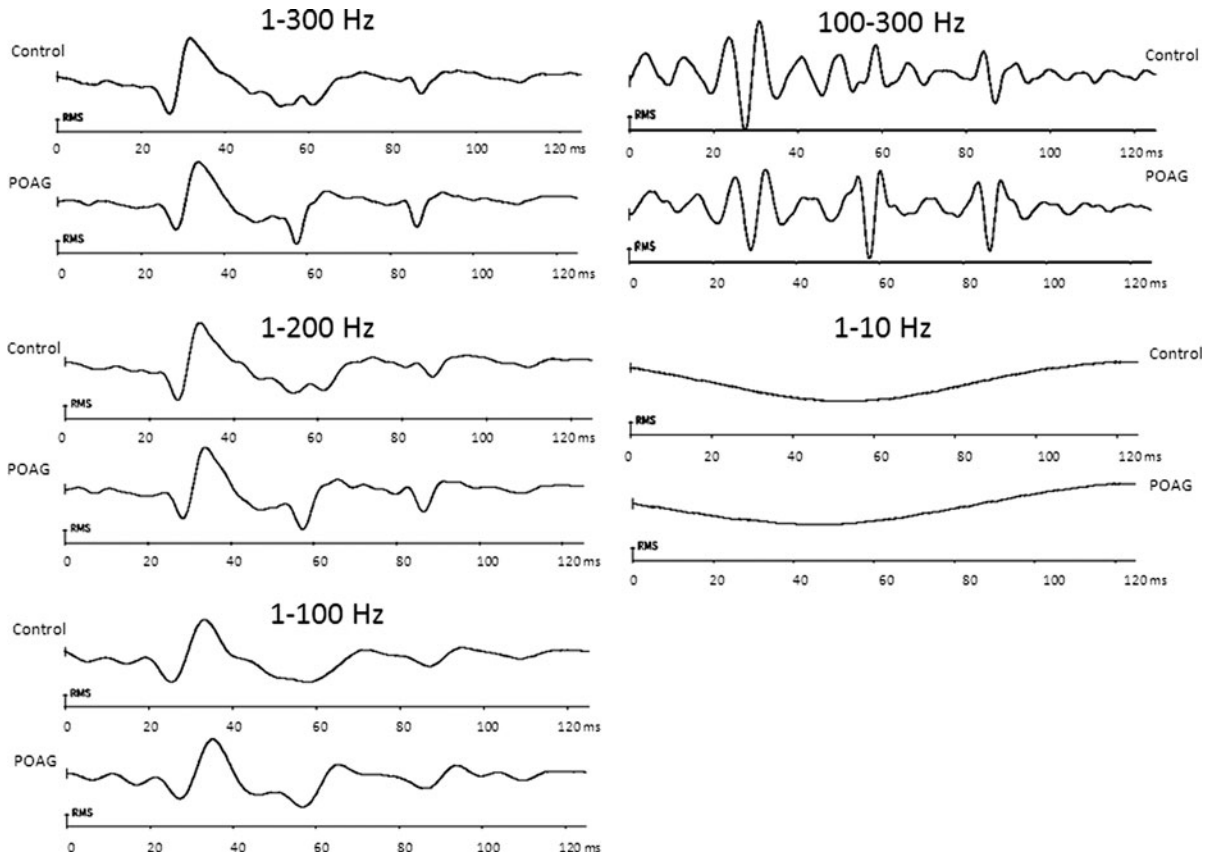

Fig. 1 A representative overall response average from the mfERG for a glaucoma subject and a control subject for some of the different filter settings analysed. Filtering dramatically changes the waveform of the mfERG response

less significant than with the low-frequency cut-off set at 10 Hz, but more significant when compared to a low-frequency cut-off set at 1 Hz. However, for both IC1 and IC2, the most significant difference between POAG and control was seen when the low-frequency cut-off was set at 1 Hz.

In the high-frequency response components, a filter set at 100–300 Hz showed significantly reduced multifocal oscillatory potentials (mfOPs) in POAG in both IC1 and IC2, but not in DC.

A band-pass filter set at 200–300 Hz showed no significant difference between POAG and control ($p > 0.5$) in all three epochs. As this suggested that with our stimulus paradigms, frequencies between 200 and 300 Hz do not contribute significantly to glaucoma, we then filtered our data at 1–200 Hz.

A band-pass filter of 1–200 Hz resulted in the highest sensitivity to detect glaucomatous retinal damage ($p < 0.0001$).

Discussion

In the present paper, we studied the influence of the filter setting on the two-global-flash mfERG, in order to identify the range of frequency that might detect most glaucomatous retinal dysfunction in the mfERG. With the two-global-flash paradigm used, POAG differed most from control in the central 10° [7]. Therefore, we focused our analysis on the response average of the central 10°.

Low-pass filter

It has been suggested that a high-frequency cut-off of 300 Hz rather than 100 Hz may introduce more noise than signal, which could produce greater random variation of the mfERG waveforms [1]. Han et al. have shown that implicit times and amplitudes of the standard mfERG in normal subjects and also in

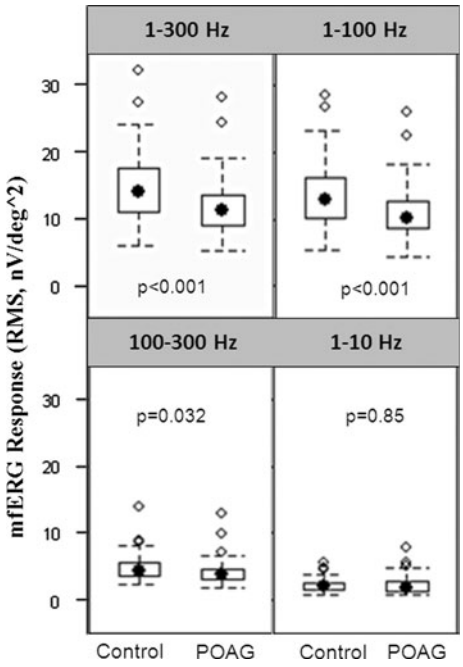

Fig. 2 Root-mean-square (RMS) response averages (three epochs per subject pooled together) from the central 10° of the retina are shown for the following filter settings analysed: 1–300 Hz, 1–100 Hz, 100–300 Hz, 1–10 Hz. *Boxplot*: *black dots* median; *lower* and *upper box edges* 25th and 75th percentile, respectively (the *lower* and *upper* quartiles); *whiskers* the lowest data point still within 1.5 IQR (interquartile range) of the *lower* quartile, and the highest data point still within 1.5 IQR of the *upper* quartile; *open circles* represent the outliers

patients with diabetic retinal dysfunction have less intersubject variability and noise content with a filter setting of 10–100 Hz than with a filter setting of 10–300 Hz. However, the authors also caution that high-frequency response components may be valuable when non-standard mfERG paradigms are used. Indeed, when we compared responses filtered at 1–300 Hz to the responses filtered at 1–100 Hz in the two-global-flash paradigm mfERG, we found that POAG patients differed significantly in both filter settings in all three epochs analysed. However, this difference was more pronounced in the response that included high frequencies, that is, with the filter set at 1–300 Hz (Table 1).

High-frequency component

In order to visualize high-frequency OPs for the standard mfERG (mfOPs), ISCEV recommends a filter setting of 100–300 Hz [3]. In a mfERG that was slowed down by introducing 3 dark frames after each m-sequence stimulus, peaks of the mfOPs in the healthy central retina (1.5–10°) occurred at a mean frequency of 147 Hz [10]. When the stimulus sequence was slowed down further by introducing 14 dark frames, mfOPs occurred at a frequency of 110–224 Hz (peak at 143 Hz) [11]. These mfOPs were reduced in glaucoma [11].

Introducing one global flash into the stimulation sequence, Fortune et al. [6] reported the reduction in the mfOPs in IC (i.e. 50–100 ms in their recordings) in glaucoma subjects. A late high-frequency activity that

Table 1 Results obtained with the different filter settings in POAG patients compared with control subjects

Epoch of two-flash mfERG	Filter settings (Hz)	Difference of means (nV/deg^2) (95 % CI)	*p* value
DC	1–300	−2.1 (−3.2 to −1.0)	0.0002
	3–300	−2.6 (−3.7 to −1.5)	<0.0001
	10–300	−2.9 (−4.0 to −1.8)	<0.0001
	100–300	−0.1 (−1.0 to 0.8)	0.8
	200–300	−0.1 (−1.2 to 1.0)	0.9
	1–10	−0.1 (−1.0 to 0.8)	0.8
	1–100	−1.9 (−2.8 to −1.0)	<0.0001
	1–200	−3.1 (−4.2 to −2.0)	<0.0001
IC1	1–300	−4.2 (−5.1 to −3.3)	<0.0001
	3–300	−4.2 (−5.3 to −3.1)	<0.0001
	10–300	−3.1 (−4.2 to −2.0)	<0.0001
	100–300	−1.0 (−1.9 to −0.1)	0.02
	200–300	−0.1 (−1.2 to 1.0)	0.8
	1–10	0.3 (−0.6 to 1.2)	0.5
	1–100	−4.1 (−5.0 to −3.2)	<0.0001
	1–200	−4.7 (−5.8 to −3.6)	<0.0001
IC2	1–300	−3.6 (−4.5 to −2.7)	<0.0001
	3–300	−2.6 (−3.7 to −1.5)	<0.0001
	10–300	−2.0 (−3.1 to −0.9)	0.0005
	100–300	−1.0 (−1.9 to −0.1)	0.02
	200–300	−0.2 (−1.3 to 0.9)	0.7
	1–10	0.03 (−0.9 to 0.9)	0.96
	1–100	−3.1 (−4.0 to −2.2)	<0.0001
	1–200	−3.8 (−4.9 to −2.7)	<0.0001

DC direct component of 15–45 ms of mfERG, *IC1* first indirect component of 45–75 ms of mfERG, *IC2* second indirect component of 75–105 ms of mfERG; difference of means with 95 % confidence intervals (95 % CI)

occurs between 50 and 70 ms has also been described in the retinal component of the mfERG obtained with the introduction of two global flashes. This response component has been reported to be reduced or absent in experimental glaucoma in monkeys [12]. When we analysed our mfERG responses with a filter setting of 100–300 Hz, the mfOPs were significantly reduced in POAG in both IC1 (45–75 ms) and IC2 (75–105 ms), but not in DC (15–45 ms). However, we did not find a significant difference in the high frequencies between 200 and 300 Hz when our glaucoma patients were compared to healthy subjects. This suggests a high-frequency cut-off of 200 Hz to be most sensitive to detect glaucomatous retinal dysfunction in the two-global-flash mfERG.

It is not unexpected that IC1 and IC2 should be primarily affected in glaucoma. Glaucomatous damage affects primarily the inner retina, especially the ganglion cells. Inner retinal contributions in our two-flash paradigm are thought to predominantly contribute to IC1 and IC2. This is supported by recent animal research, where the origin of the mfERG response to a one-global-flash paradigm was studied in the porcine eye: when inner retinal contributions were blocked with isofluoran, tetrodotoxin and *N*-methyl-D-aspartic acid, it could be demonstrated that the DC of the global-flash mfERG contains mainly outer retinal contributions and is only minimally shaped from inner retinal activity in the form of superimposed regular oscillation-like wavelets [13]. The IC, however, contains mainly inner retinal contributions.

Low-frequency component

For the standard multifocal ERG, ISCEV recommends a high-pass cut-off between 3 and 10 Hz [3]. In the clinic, lowering the high-pass filter to capture low-frequency components in the global-flash ERG is problematic, as involuntary eye movements of low frequency may then contribute more to the response recorded. Therefore, a low-frequency cut-off of 10 Hz has frequently been applied. With a band-pass filter setting of 10–300 Hz, significant differences have been observed between glaucoma and control. Indeed, in most cases, a low-frequency cut-off of 10 Hz will not affect the interpretation of the mfERG [14].

However, a band-pass filter with lower low-frequency cut-off results in larger amplitudes, which may be especially important in the small induced components that reflect inner retinal function and are expected to be more sensitive to detect glaucomatous damage [5, 15, 16].

There is also evidence that a low-frequency component may be affected in the mfERG in glaucoma. In experimental glaucoma in macaques, a glaucoma-sensitive low-frequency component, the (mf)PhNR, has been recorded using a low-frequency cut-off at 0.1 Hz [17]. In human glaucoma patients, a focal ERG PhNR with a low-frequency cut-off of 5 Hz showed significant reduction in amplitude associated with a local decrease in retinal sensitivity in POAG [18]. Luo et al. [12] reported that the low-frequency band of the two-global-flash mfERG can provide information on retinal dysfunction in experimental glaucoma in monkeys. In their control monkeys, they described a low-frequency component (LFC) that peaked at 12.1 Hz (SD 1.1, reaching half amplitude at about 6.2 Hz and decaying to half amplitude at 18.3 Hz). In experimental glaucoma eyes, this LFC was drastically reduced, making it potentially useful in assessing glaucomatous changes in the global-flash mfERG [12]. This suggests that a filter setting of 1–300 Hz might be more sensitive than a filter setting of 10–300 Hz in POAG. Thus, the mfERG in this study was recorded with a filter setting of 1–300 Hz in an attempt to include these low-frequency components and thus increase the sensitivity of the mfERG to glaucoma. Indeed, in our patient population, the sensitivity of the mfERG to detect glaucomatous dysfunction was highest with a low-frequency cut-off of 1 Hz, followed by a low-frequency cut-off of 3 Hz, while a low-frequency cut-off of 10 Hz seemed least sensitive.

Glaucoma did not differ from normal at 1–10 Hz. Taking with the finding that a filter setting of 1–300 Hz seemed more sensitive to glaucomatous dysfunction than a filter setting of 10–300 Hz supports that a component at 10 Hz may be notably affected in glaucoma.

This is reinforced by observations from Lachapelle and Benoit who found that the major difference between the rabbit ERG response, which is band-pass-filtered at 10–1,000 Hz, and that filtered at 1–1,000 Hz is the presence of a peak at 10 Hz in the latter and a lack thereof in the former [19].

With a low-frequency cut-off of 10 Hz, only the least sensitive epoch, the DC of mfERG response, showed more glaucomatous retinal dysfunction, but not the most sensitive components, the IC1 and IC2. This may be explained as follows:

Keating et al. [2, 20] found a slight reduction in amplitude in the standard mfERG when the high-pass filter was increased to 10 Hz. In the negative ERG, this resulted in dramatic changes, such as an artificial positive component. Thus, increasing the low-frequency cut-off from 1 to 10 Hz may affect a pathologic DC of the mfERGs in glaucoma and controls differently and thus artificially increase the difference between these responses, which may explain our finding that the DC seemed more abnormal at 10–300 Hz than at 1–300 Hz.

In summary, we suggest that mfERG recordings in glaucoma using a two-global-flash paradigm at present be obtained with a filter setting of 1–200 Hz, as this was the most sensitive setting in our patient group. However, a filter setting of 1–300 Hz will allow data to later be filtered digitally at 1–200 Hz, the most sensitive setting in our study, but will also leave the opportunity to evaluate the responses of higher frequencies between 200 and 300 Hz that, according to the literature, may in some instances still contain important information.

Acknowledgments This study was funded by Swiss Government Scholarship for Foreign Students (FCS) 2009.0251; Swiss National Science Foundation (SNSF) 32003B-135219; LHW Stiftung Lichtenstein.

Conflict of interest The author(s) have no proprietary or commercial interest in any materials discussed in the article.

References

1. Han Y, Bearse MA Jr, Schneck ME, Barez S, Jacobsen C, Adams AJ (2004) Towards optimal filtering of "standard" multifocal electroretinogram (mfERG) recordings: findings in normal and diabetic subjects. Br J Ophthalmol 88:543–550
2. Keating D, Parks S, Evans AL, Williamson TH, Elliott AT, Jay JL (1997) The effect of filter bandwidth on the multifocal electroretinogram. Doc Ophthalmol 92:291–300
3. Hood DC, Bach M, Brigell M, Keating D, Kondo M, Lyons JS, Marmor MF, McCulloch DL, Palmowski-Wolfe AM, International Society For Clinical Electrophysiology of Vision (2012) ISCEV standard for clinical multifocal electroretinography (mfERG) (2011 edition). Doc Ophthalmol 124:1–13
4. Palmowski AM, Allgayer R, Heinemann-Vernaleken B, Ruprecht KW (2002) Multifocal electroretinogram with a multiflash stimulation technique in open-angle glaucoma. Ophthalmic Res 34:83–89
5. Palmowski-Wolfe AM, Todorova MG, Orguel S, Flammer J, Brigell M (2007) The 'two global flash' mfERG in high and normal tension primary open-angle glaucoma. Doc Ophthalmol 114:9–19
6. Fortune B, Bearse MA Jr, Cioffi GA, Johnson CA (2002) Selective loss of an oscillatory component from temporal retinal multifocal ERG responses in glaucoma. Invest Ophthalmol Vis Sci 43:2638–2647
7. Kramer SA, Ledolter AA, Todorova MG, Schötzau A, Orgül S, Palmowski-Wolfe AM (2012) The 2-global flash mfERG in glaucoma: attempting to increase sensitivity by reducing the focal flash luminance and changing filter settings. doi:10.1007/s10633-012-9360-z
8. VERIS™ Science 5.1, Reference guide. http://veris-edi.com/pubftp/VERIS%20Documents/VERIS%205.1%20Ref%20Guides/. Accessed 21 Aug 2012
9. R Development Core Team (2009) R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna
10. Bearse MA Jr, Shimada Y, Sutter EE (2000) Distribution of oscillatory components in the central retina. Doc Ophthalmol 100:185–205
11. Rangaswamy NV, Zhou W, Harweth RS, Frishman LJ (2006) Effect of experimental glaucoma in primates on oscillatory potentials of the slow-sequence mfERG. Invest Ophthalmol Vis Sci 47:753–767
12. Luo X, Patel NB, Harwerth RS, Frishman LJ (2011) Loss of the low-frequency component of the global-flash multifocal electroretinogram in primate eyes with experimental glaucoma. Invest Ophthalmol Vis Sci 52:3792–3804
13. Chu PHW, Chan HHL, Ng Y-f, Brown B, Siu AW, Beale BA, Gilger BC, Wongd F (2008) Porcine global flash multifocal electroretinogram: possible mechanisms for the glaucomatous changes in contrast response function. Vision Res 48:1726–1734
14. Hood DC (2000) Assessing retinal function with the multifocal technique. Prog Retin Eye Res 19:607–646
15. Shimada Y, Bearse MA Jr, Sutter EE (2005) Multifocal electroretinograms combined with periodic flashes: direct responses and induced components. Graefes Arch Clin Exp Ophthalmol 243:132–141
16. Chu PH, Chan HH, Brown B (2006) Glaucoma detection is facilitated by luminance modulation of the global flash multifocal electroretinogram. Invest Ophthalmol Vis Sci 47:929–937
17. Viswanathan S, Frishman LJ, Van Alstine AW, Lou X, Swanson WH (2009) Multifocal photopic negative responses (mfPhNR) of macaques and humans. Invest Ophthalmol Vis Sci (E-Abstract 4758, 2009 ARVO)
18. Machida S, Toba Y, Ohtaki A, Gotoh Y, Kaneko M, Kurosaka D (2008) Photopic negative response of focal electoretinograms in glaucomatous eyes. Invest Ophthalmol Vis Sci 49:5636–5644
19. Lachapelle P, Benoit J (1994) Interpretation of the filtered 100- to 1000-Hz electroretinogram. Doc Ophthalmol 86(1):33–46
20. Keating D, Parks S, Evans A (2000) Technical aspects of multifocal ERG recording. Doc Ophthalmol 100:77–98