


Frequency-Following Response with Speech Stimulus: Comparison between Two Methods of Stimulation

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Abstract

Introduction Frequency-following response with speech stimulus (FFR-speech) is a subcortical potential that satisfactorily evaluates the processing of verbal information. However, there still are differences in the literature regarding its analysis and stimulation protocol.

Objective To compare two stimulation protocols for the capture of FFR-speech, to identify the percentage of occurrence of the waves among them and to compare it with the specialized literature, as well as to describe the interpeaks of its waves.

Method Considering the eligibility criteria, the sample consisted of 30 normal-hearing adults, with no complaints of speech comprehension. All of them were submitted to a basic audiological evaluation, to brainstem auditory evoked potential with click stimulus, and to FFR-speech. In the latter, 2 types of stimulation were performed, 3 series of 1,000 sweeps, and 2 series of 3,000 sweeps, for subsequent analysis of the resulting wave, in which we tried to mark the peak V followed by valleys A, C, D, E, F, and O.

Results Differences in latency and interpeaks were not found between the protocols. In general, a higher occurrence of waves in the stimulation of 2 series of 3,000 sweeps was observed, but only the A valley presented a significant difference. When the values of the waves were compared with the literature, the V and A waves showed fewer occurrences in the present study.

Conclusion The protocol of 2 series of 3,000 sweeps was better for FFR-speech in the studied equipment, considering the higher occurrence of waves, even though it is inferior to the specialized literature. Furthermore, it was possible to describe interpeak values and to observe no difference between the studied protocols

Keywords

- ▶ hearing
- ▶ electrophysiology
- ▶ auditory evoked potentials
- ▶ adult

Introduction

Brainstem auditory evoked potential (BAEP) is considered a short-latency examination, since its response is rapidly captured and can be visualized up to 10 milliseconds after stimulation.^{1,2} The most commonly used acoustic stimulus

for this potential is the click, due to the fact that it reaches a wide spectrum of frequency, quickly stimulating a greater amount of fibers.^{3–7} However, it is considered simple when compared with verbal stimulation. Therefore, a speech stimulus arose to better evaluate the structures involved in the processing of complex information.⁸

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Therefore, the frequency-following response with speech stimulus (FFR-speech) is a subcortical potential that has its response generated through a verbal stimulation, represented by a complex stroke, which usually begins before 10 milliseconds and extends until 50 milliseconds.^{8,9} This fact allows us to infer that FFR-speech begins where the BAEP click ends its stimulation; therefore, one exam is not able to replace the other, but to complement it. The trajectory elicited by this stimulus consists of peaks and valleys, which are: V, A, C, D, E, F, and O;¹⁰ with the V wave being analogous to the V wave of the click BAEP.²

Researches have reported the importance of using a complex stimulus to have reliable answers regarding the processing of verbal information, be they in the field of speech, of language, or of auditory abilities. Others bring the click BAEP as a stimulation of insufficient regions, to the point of presenting normal functionality, since it is a less complex stimulus for coding.¹¹⁻¹³

There is in the literature a divergence of protocols regarding the stimulation of FFR-speech in different devices. A renowned study,¹⁴ used today as a reference, infers that the protocol of 2 series of 3,000 sweeps would be more adequate because it provides greater stimulation to the auditory pathway, picking up more reliable responses. However, research has recently been performed using the protocol of 3 series of 1,000 sweeps.^{15,16} Due to this divergence, the importance of the present study is centered in the definition of a protocol that is more suitable for the Smart EP (Intelligent Hearing Systems, Miami, Florida, Estados Unidos) equipment.

Due to the fact that it is still considered a recent exam, its generating sites are not well-defined, as it happens in most of the potentials, its answers do not have reference values materialized in the literature, as well as the verbal stimulus elicited for its abstraction from one device to another. Added to these facts, the divergence in the protocol contributes to its limited use in clinical practice. And because they are electrophysiological responses, it is believed that the number of stimuli can modify the trace of the peaks and valleys, as well as the percentage of occurrence of the waves. Considering that research with FFR-speech in the Smart EP equipment is beginning in the national reality, it is believed that the definition of a protocol would outline future studies.

Thus, the present study aims to compare two stimulation protocols for FFR-speech capture, to identify the percentage of wave occurrence between them, and to compare it with a reference study that uses as stimulation 2 series of 3,000 sweeps, as well as to describe FFR-speech wave interpeak variables.

Method

The present study was quantitative, cross-sectional and retrospective, using data from an audiology outpatient clinic of a public network institution. The individuals who agreed to participate in the present study were informed about the procedures, the risks, the benefits, and about the confidentiality of the data, and signed the free and informed consent form, following all ethical precepts, according to the Resolution 466/12 of the National Health Council. The present study

was approved by the Research Ethics Committee under the number 50165115.2.0000.534.

The following eligibility criteria were considered: subjects aged between 18 and 30 years old, auditory thresholds within the limits of normality, that is, up to 25 dBHL in the frequencies between 250 and 8000 Hz, tympanometric curve type "A," ipsi- and contralateral acoustic reflexes present bilaterally, absence of communication or speech comprehension complaints, as well as of diagnosed neurological and/or psychic alterations, and presence of waves I, III and V and interpeak intervals I-III, III-V and IV within click on normal. Thus, the casuistry consisted of 30 subjects, 3 of them male (10%) and 27 female (90%), with ages ranging from 18 to 29 years old, with a mean age of 23.4 years old.

All of the subjects underwent an audiological anamnesis, aiming to collect information about previous diseases, issues related to communication, and family history of hearing diseases. The basic audiological evaluation was performed in a cabin with acoustic treatment. For the visual inspection of the external auditory meatus, the Otoscópio Mikatos Led Mini 1000 (Mikatos, Embu das Artes, SP, Brazil) was used, the tonal limit audiometry and the logoaudiometry were performed on the FONIX Hearing Evaluator FA 12 type I (Frye Electronics, Inc., Beaverton, OR, USA), using supra-aural TDH 39 headphones (Frye Electronics, Inc., Beaverton, OR, USA). The acoustic immittance measurements were performed on the AT235 impedance audiometer (Interacoustics, Middelfart, Denmark) and the electrophysiological evaluations were performed on the Smart EP evoked potentials system (Intelligent Hearing Systems, Miami, FL, USA).

To perform the click BAEP and FFR-speech, the subject was accommodated in a reclining chair. The skin was cleaned with Nuprep (Weaver and Company, Aurora, CO, USA) abrasive paste, the surface electrodes were fixed with Maxxifix (Neurovirtual, Barueri, São Paulo, Brasil) brand electrolytic paste and glued with microporous type tape. The reference electrodes were placed in the left (M1) and right (M2) mastoids, the active electrode (Fz) in the central and upper portion of the forehead and, finally, the ground electrode (Fpz) in the central and lower portion of the forehead. The stimulus was presented through insertion headphones (EAR-TONE 3, Vitasons, Porto Alegre, Rio Grande do Sul, Brasil). It is important to emphasize that the impedance values were kept ≤ 3 KOhms and that the number of artifacts did not exceed 10% of the number of stimuli, emphasizing the reliability of the exams.

For the BAEP click, the stimulus was presented at the intensity of 80 dBnHL, with a record window of 12 milliseconds, a minimum of 2,048 sweeps, rate of 27.7/second, low-pass filter of 100 HZ and high-pass filter of 3,000 Hz, repetition rate gain of 100.0 K, duration of 100 μ sec, rarefied polarity. The click BAEP was considered normal when the absolute latencies of waves I, III and V and the interpeak intervals I-III, III-V and IV presented values within the expected for the equipment: I = 1.67 / standard deviation [SD] = 0.11 ; III = 3.86 / SD = 0.14; V = 5.66 / SD = 0.18; I-III = 2.18 / SD = 0.11; III-V = 1.81 / SD = 0.14; I-V = 3.99 / SD = 0.18¹⁷. The waves were scored when there was reproducibility, to a reliable analysis of auditory pathway responses at the brainstem level.

Frequency-following response with speech stimulus was performed using the syllable /da/ for 40 milliseconds provided by the equipment manufacturer, monaurally (right ear),¹⁴ at an intensity of 80 dBnHL. The recording window used was of 60 milliseconds, low-pass filter of 100Hz and high-pass filter of 3000Hz, speed of 125 μ s, rate 11.10/second, alternating polarity. In the log window itself, a filter was activated in the toolbar by clicking on “process,” “filter-type,” selecting F/R 19 pnt and bandpass 100 Hz–2000 Hz, which was applied only on the resulting wave for an easier and reliable analysis, which is performed through the sum of the stimulations.

Frequency-following response with speech stimulus was applied in two different ways. First, stimulation was performed with 3 series of 1,000 sweeps (taking ~ 5 minutes to complete the stimulation), followed by 2 series of 3,000 sweeps (totalizing 10 minutes of stimulation), with wave analysis resulting in both. The methodological choice used for the tracing analysis was to unite latency, morphology, and neural representativeness. In this way, the presence of the waves: V (peak), A, C, D, E, F, and O (valleys) was used, using the following latency values of the Bio-logic Navigator Pro (Natus, Pleasanton, CA, USA) equipment: wave V = 6.46 milliseconds; A = 7.37 milliseconds; C = 18.32 milliseconds; D = 22.47 milliseconds; E = 30.64 milliseconds; F = 39.19 milliseconds; O = 48.01 milliseconds.¹⁸

It should be emphasized that, in the present study, the latency, wave, and interpeak analysis of V-A, A-C, C-D, D-E, E-F, F-O, and V-O were performed, but frequency analyzes were not performed, which are usually exposed in other studies in the area, due to the impossibility of performing these analyses on the Smart EP equipment. The interpeaks were calculated by decreasing the latency value from one wave to another (example: V = 6.46, A = 7.37, intercept V-A = 0.91). It should be emphasized that the analysis of the exams was performed jointly by three researchers, and the markings used in the labor statistics were obligatorily agreed by at least two professionals. (►Fig. 1)

For analysis of the data, the analysis of variance (ANOVA) and equality of two proportions tests were used. The first is a fairly usual parametric test, which aims to compare the

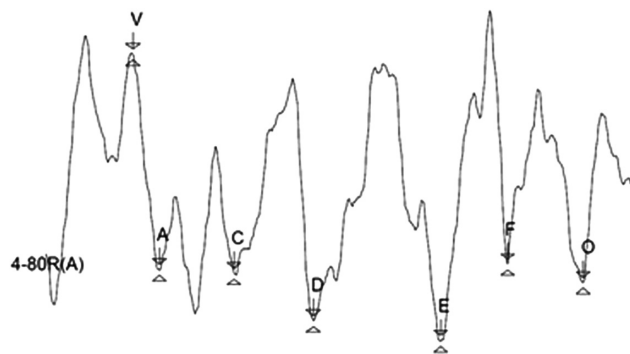


Fig. 1 Exemplification of the wave layout resulting from the Frequency-Following Response potential with speech stimulus. Note: 4-80 R (A) means fourth stimulation at the intensity of 80dBnHL in the right ear, stimulation channel A. Waves V, A, C, D, E, F and O.

means using the variance; the second one compares two variables, aiming to identify the presence or not of statistical significance; and the third analyzes the statistical significance between the means, assuming that the population variances are unknown. A significance level of 5% ($p \leq 0.05$) was considered in all of the analyzes.

Results

In ►Table 1 it is possible to observe that there was no difference in FFR-speech wave latencies when compared with the 3 series of 1,000 sweeps and the two series of 3,000 sweeps.

Regarding the comparison of the occurrence of waves between the stimulations, the peak A presented greater occurrence in the stimulation of 2 series of 3,000 sweeps. It is important to note that this stimulation has a higher occurrence in all of the waves, except in the O wave, but with no statistically significant difference, as shown in ►Table 2.

When comparing the percentage of occurrence of FFR-speech waves in the two stimulations performed in the present study and the occurrences found in the study by Skoe et al,¹⁴ there is a difference in waves V and A, which have a lower occurrence in the present study (►Table 3).

Regarding interpeaks, when compared in both stimuli (►Table 4), they did not present any difference.

Discussion

It is important to emphasize that the Smart EP equipment, in which the present research was performed, is still under study and standardization, and the discussion is mainly elaborated with studies performed on different equipment. In addition, it is possible to observe a divergence in the literature regarding FFR-speech stimulation protocols, mainly using 3 series of 1,000 sweeps,^{8,19–22} 2 series of 2,000 sweeps,^{2,23} 2 series of 1,000 sweeps⁵, and, more recently, the protocol of 2 series of 3,000 sweeps has been found in the literature.^{13,24–27}

In view of this divergence, ►Table 1 shows the latency comparison between the types of stimulation performed in the present study, noting similarity. This data corroborates with some studies that presented similar results even when performed in different equipment and using different forms of stimulation. One of the studies evaluated 40 subjects aged between 7 and 24 years old in the Bio-logic Traveler Portable System (Natus, Pleasanton, CA, USA), distributed in a control group (without auditory processing complaint) and in a study group (with auditory processing complaint), and analyzed the values of latency of the V, A, C, and F waves, using as stimulation 3 series of 1,000 sweeps. The authors found the following values for the control group: 6.54 milliseconds for the V wave, 8 milliseconds for the A wave, 18.27 milliseconds for the C wave, and 40.26 milliseconds for the F2 wave. The second study sought to describe the responses of the V and A waves in 50 adult normal-hearing subjects, using 2 sets of 2,000 sweeps in the GSI Audera (GSI, Eden Prairie, MN, USA) equipment as stimulation. The authors found 7.18

Table 1 Comparison of latencies using as stimulation three series of 1000 sweeps and two series of 3000 sweeps

Stimulations		<i>n</i>	Average (ms)	DP	Min	Max	<i>p-value</i>
Wave V	3 × 1,000	20	6.52	0.43	6.00	7.88	0.344
	2 × 3,000	25	6.68	0.65	5.88	8.63	
Wave A	3 × 1,000	19	7.82	0.62	7.13	9.63	0.447
	2 × 3,000	26	8.01	0.92	7.25	11.50	
Wave C	3 × 1,000	21	17.70	0.95	16.25	19.25	0.581
	2 × 3,000	25	17.55	0.90	16.13	18.88	
Wave D	3 × 1,000	27	23.70	1.22	21.38	26.50	0.286
	2 × 3,000	29	23.37	1.10	21.25	25.75	
Wave E	3 × 1,000	27	31.34	0.87	29.25	33.13	0.837
	2 × 3,000	30	31.29	1.24	27.28	33.13	
Wave F	3 × 1,000	30	39.14	1.18	35.38	41.13	0.693
	2 × 3,000	30	39.27	1.32	35.13	42.50	
Wave O	3 × 1,000	30	47.93	1.19	44.00	52.00	0.583
	2 × 3,000	29	48.06	0.57	47.13	49.38	

Abbreviations: Max, maximum; Min, minimum; ms, milliseconds, *n*, number of subjects.
 Statistical test: ANOVA.

Table 2 Comparison of the occurrence of waves using 3 series of 1,000 sweeps and 2 series of 3,000 sweeps

Occurrence	3 × 1,000		2 × 3,000		<i>p-value</i>
	<i>n</i>	%	N	%	
Wave V	20	66.7%	25	83.3%	0.136
Wave A	19	63.3%	26	86.7%	0.037*
Wave C	21	70.0%	25	83.3%	0.222
Wave D	27	90.0%	29	96.7%	0.301
Wave E	27	90.0%	30	100.0%	0.076
Wave F	30	100.0%	30	100.0%	1.000
Wave O	30	100.0%	29	96.7%	0.313

Abbreviations: %, occurrence percentage; *n*, number of subjects.
 Statistical test: Equality of two proportions.
 *Significant values ($p \leq 0.05$).

Table 3 Comparison of the percentage of wave occurrence using as stimulation 3 series of 1,000 sweeps and 2 series of 3,000 sweeps with the percentages found by Skoe et al¹⁴

Occurrence	Skoe (2 × 3,000 sweeps)	3 × 1,000		2 × 3,000		<i>p-value</i>	
		<i>n</i>	%	<i>n</i>	%	3 × 1,000	2 × 3,000
Wave V	100%	20	66.7%	25	83.3%	< 0.001*	0.020*
Wave A	100%	19	63.3%	26	86.7%	< 0.001*	0.038*
Wave C	- x -	21	70.0%	25	83.3%	- x -	- x -
Wave D	95.8%	27	90.0%	29	96.7%	0.301	1.000
Wave E	100%	27	90.0%	30	100.0%	0.076	1.000
Wave F	99.3%	30	100.0%	30	100.0%	1.000	1.000
Wave O	97.9%	30	100.0%	29	96.7%	0.313	1.000

Abbreviations: %, occurrence percentage; *n*, number of subjects.
 Statistical test: Equality of two proportions.
 *Significant values ($p \leq 0.05$).

Table 4 Comparison of interpeak latencies found using 3 series of 1,000 sweeps and 2 series of 3,000 sweeps as stimulation

Interpeaks	Average (ms)	Median	Standard Deviation	CV	Min	Max	n	CI	p-value	
V-A	3 × 1000	1.30	1.25	0.50	39%	0.63	2.88	19	0.23	0.718
	2 × 3000	1.36	1.25	0.52	39%	0.75	2.87	25	0.21	
A-C	3 × 1000	10.12	10.13	0.89	9%	8.75	11.37	15	0.45	0.179
	2 × 3000	9.60	9.88	1.25	13%	7.00	11.38	22	0.52	
C-D	3 × 1000	6.09	6.25	1.54	25%	3.38	8.37	19	0.69	0.503
	2 × 3000	5.82	6.07	1.07	18%	3.50	7.24	24	0.43	
D-E	3 × 1000	7.58	7.13	1.39	18%	5.00	10.37	25	0.55	0.480
	2 × 3000	7.88	7.88	1.66	21%	3.28	10.25	29	0.60	
E-F	3 × 1000	7.85	8.00	1.44	18%	3.38	10.50	27	0.54	0.746
	2 × 3000	7.99	7.87	1.66	21%	5.88	11.97	30	0.60	
F-O	3 × 1000	8.77	8.75	2.00	23%	3.87	16.62	30	0.71	0.998
	2 × 3000	8.77	8.75	1.44	16%	6.25	13.99	29	0.53	
V-O	3 × 1000	41.87	41.49	1.91	5%	37.87	47.37	19	0.86	0.248
	2 × 3000	41.37	41.50	0.85	2%	39.13	42.75	25	0.33	

Abbreviations: CI, confiability interval; CV, coefficient of variation; Max, maximum; Min, minimum; n, number of subjects.

Statistical test: ANOVA.

* Significant values ($p \leq 0.05$).

milliseconds for the V wave, and 8.66 milliseconds for the A⁵ wave. Another study analyzed the A and C waves of the FFR-speech in the Navigator Pro, using the MATLAB (MathWorks, Natick, MA, USA) software, in 40 youngsters distributed in a study group (diagnosis of dyslexia) and in a control group (typical development), using as stimulation 2 series of 2,000 sweeps. The study group presented a response of 7.59 milliseconds for A, and of 17.85 milliseconds for C; the control group presented a response of 7.48 milliseconds for A, and of 17.54 milliseconds for C.²³ It is observed that all of the values presented are similar to each other, even with the modification of the protocol of stimulation and of the population.

Thus, according to the above results, it is believed that the latency is not influenced by the number of stimulations; however **Table 2** shows that it can influence the occurrence of waves. It is observed that all waves, except wave O, presented a higher occurrence in the stimulation of 2 series of 3,000 sweeps, but with statistical significance only in valley A. Analyzing the percentage of wave occurrence in this stimulation, it is possible to infer that waves V and C were the least likely to appear. This data partially corroborates 2 studies performed on the Navigator Pro equipment, also using as stimulation 2 series of 3,000 sweeps. The 1st,²⁸ with 48 young normal-hearing adults, analyzed the occurrence of waves while seeking to find the best form of presentation of the FFR-speech stimulus (binaural, only in the right ear, and only in the left ear). The authors observed a lower percentage of occurrences in the C wave, 85.4% in binaural stimulation, 79.2% in the right ear, and 75% in the left ear. The second study²¹ analyzed the occurrence of waves in a sample of 57 children, distributed in groups with typical development, with auditory processing disorder, and with language disorder, and

found that the only wave that did not present 100% occurrence in any of the groups was again the C wave.

It should be noted that other well-known studies,^{14,29} performed on the Navigator Pro equipment, did not consider the C wave in their analyzes, due to the low percentage of occurrence, judging that the absence of this wave could not mean change in FFR-speech. Although large authors affirm this data, it is of great importance to carry out new studies in the Smart EP equipment, to really verify the behavior of the C wave. It is believed that this answer would be of great value to understand how the subject detects the transition of the consonant to the vowel, the task exerted by this wave in the subcortical potential.¹⁰

Still in **Table 2**, it can be observed that in the stimulation of 3 series of 1,000 sweeps, the smallest percentage occurred in wave A, and the highest percentage occurred in waves F and O. Again, these data corroborate partially with two studies that used the same stimulation in the Smart EP^{15,16} equipment in adults with hearing loss. The first study also found the wave O as one of the waves with more occurrences, but the wave A also fits in that group. The second study found 100% occurrence only in the O wave. These data demonstrate a certain instability in this type of stimulation and it is not feasible to attribute it to peripheral hearing loss, since it is already verified that hearing losses of moderate to severe degree do not influence in the responses of the FFR-speech.¹⁶

Therefore, these data suggest the use of 2 series of 3,000 sweeps, which is in line with the study by Skoe et al.,¹⁴ in which the occurrence of waves was compared in **Table 3**. This study evaluated a sample of 586 subjects aged between 0 months and 73 years old, distributed in several age groups, aiming to understand the variations that occur in FFR-speech

at different ages. The same was performed in the Navigator Pro equipment, and the stimulation used was 2 series of 3,000 sweeps. The values used to perform the comparisons were those of the subjects aged between 21 and 30 years old, composed of 143 individuals.

► **Table 3** shows that the V and A waves presented a lower occurrence in the present study, a fact that can be attributed to the change of equipment, to the modification of the stimulus, as well as to the number of subjects evaluated in both surveys. The current one was composed by 30 subjects compared with the 143 mentioned above. In addition, it can be inferred that, once again, the stimulation of 2 series of 3,000 sweeps came closer to the results of the specialized literature,¹⁴ which reinforces the importance of using the protocol that best stimulates the auditory pathway to obtain more the exam.

The search for reliable answers has been the main objective for the researchers who use the Smart EP equipment as a tool. Unlike the Navigator Pro device, which describes the largest number of searches, the Smart EP does not have frequency analyzes, which provide important information about pitch (F0), allowing the possibility of identifying a speaker or emotional voice intonations, as well as provide phonetic information (F1 and HF), which allow to distinguish the contrasts of speech sounds.⁹ Due to this deficit, more and more analyzes are needed to better understand the operation of FFR-speech in this equipment.

For this, ► **Table 4** brings the analysis and the comparison of the interpeaks between the stimulations and finds similarity between them. We did not find in the literature a wide range of studies that performed this analysis. However comparing with the need to perform it in the click BAEP and the importance of understanding the time the auditory pathway takes to respond from one generating site to the other, and from the beginning to the end of the decoding of the verbal stimulus, it is considered an improvement in the FFR-speech analysis. In the Navigator Pro device, an analysis of the interpeaks of the sustained portion was performed, with D-E: 8.75 milliseconds for both ears, 8.63 milliseconds for the right ear, and 8.86 milliseconds for the left ear, and for E-F: 8.45 milliseconds for both ears, 8.75 milliseconds for the right ear, and 8.59 milliseconds for the left ear. Therefore, it is observed that the values of the present research are slightly diminished, which differs from the research by Skoe et al.¹⁴ In this study,¹⁴ the interpeaks were not analyzed, but with the latency information provided by the study, it was possible to perform the calculations described in the method and to generate the following values: V-A: 0.96 milliseconds; D-E: 8.52 milliseconds; E-F: 8.49 milliseconds; F-O: 8.72 milliseconds; and V-O: 41.68 milliseconds. It should be noted that the study did not refer to the C-valley, so the interpeaks A-C and C-D were not calculated, but an increase of V-A, D-E, and E-F was observed in the present study. As described, further studies are needed including this analysis, enabling further discussions on the subject.

In general, FFR-speech is a potential that is constantly improving. The renowned study,¹⁴ used for comparison,

described the need to use at least 4,000 sweeps to have reliable answers in the Navigator Pro device. This study is of great importance to the scientific community, noting the best way to stimulate in a different device. In addition, it is of utmost importance to enter more and more into the FFR-speech universe to generate values and analyzes that respond reliably in the examination of the varied and distinct biological processing of speech sounds in the subcortical region.

Conclusion

The comparison of the protocols found that the stimulation of 2 series of 3,000 sweeps is more adequate for the realization of FFR-speech in the Smart EP equipment, since it presented a greater occurrence of waves in relation to the other protocol studied, even though inferior to the specialized literature. It was possible to describe the interpeak values and, due to the limited literature found, it is suggested that these values be studied in future works, given their importance described in the text.

Conflicts of Interests

The authors have no conflicts of interests to declare.

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