H．知的財産権の出願・登録状況

（予定を含む。）

1. 特許取得

なし

2. 実用新案登録

なし

3.その他

なし

残存聴力活用型人工内耳6症例の経験

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研究要旨

低音部に残存聴力を有する高音急墜型感音難聴患者６例に対し、残存聴力活用型人工内耳埋込術(EAS)を施行した。全例で蝸牛窓アプローチと、基底回転内電極挿入により低音部の残存聴力の温存が可能であった。残存聴力活用型人工内耳(EAS)専用のスピーチプロセッサを用い、低音部は音響刺激、高音部は電気刺激により音情報を送り込んだ。語音弁別能は、人工内耳単独使用時よりも良い傾向があり、良好な感想を得ている。

A．研究目的

感音性難聴の中には蝸牛の低音域の音感が保存されているが高音域の音感が障害されている、いわゆる高音急墜型感音難聴例が少ながらず存在する。補聴器装用で言葉の理解が不十分な症例においては人工内耳の適応が考慮されるが、従来の人工内耳では電極の挿入によって低音域の聴力（残存聴力）を失うことが多い。このような症例に対し、低音域を補聴器で活用した上で高音域を人工内耳で補完する残存聴力活用型人工内耳（EAS）が開発されている。

メドエル社が製造している残存聴力活用型人工内耳（スピーチプロセッサー商品名：DUET）は日本では未承認であるが、すでに欧州ではCE Markの許可を得ている。従来の人工内耳との相違点は以下のとおりである。

① インプラントの電極が従来の人工内耳よりも蝸牛内部を痛めることが少ない構造となっている。

② 体外部のスピーチプロセッサーには補聴器が付属しており、高音の聞き取りに対しては人工内耳の電極からの刺激を、低音の聞き取りに対しては補聴器を活用することにより、低音域聴力が保たれた高度感音難聴者に対して従来の人工内耳よりも聞き取りを改善することが期待される。

今回、宇佐美班の分担研究として、メドエル社より残存聴力活用型人工内耳および

器具一式の提供を受け、高音障害型を呈する高度難聴者の聴覚リハビリテーションの向上を図る目的で、当施設で6名の対象患者に、残存聴力活用型人工内耳埋込術ならびに術後訓練を行い、その安全性と有効性につき評価を行った。

B．研究方法

宇佐美班の共同研究として、同班のプロトコールに則って施行した。EAS 適応条件を満たす高音障害型を呈する高度難聴成人患者で、本人ならびに家族に対し所定の説明同意書を使って説明を行い、十分な理解と同意が得られた６名（男性３名、女性3名、年齢 21～51 歳、平均 41 歳）を対象とした。

今年度は３４歳男性（症例５）、５１歳女性（症例６）の2名に施行した。

低音域保存の目的で、より低侵襲とされる正円窓アプローチにより専用の24㎜長電極を全電極（症例1のみ３１．５㎜の標準電極を約２０㎜）挿入した。また、人工内耳電極挿入による聴力低下に関しては、直接的な障害の他、炎症性サイトカインによる遅発的な障害が推測されており、その予防に関しては、ステロイドの使用が有効であることが動物実験で実証（Viveroら、2008）されているため、術後にデキサメサゾン６．６ｍｇから（症例1のみメチルプレドニゾロン１２５ｍｇから）漸減投与した。

（倫理面への配慮）

臨床研究の倫理指針にある、倫理審査委員会の運営に関して定められた細則を遵守し、運営している（承認年月日：平成２３年２月１８日）。

C．研究結果

症例１は４１歳男性で左に施術した。３ヵ月後の評価で、術前裸耳で１０％であった語音弁別能がＥＡＳ装用により７５％にまで改善した。症例２は４７歳女性で、左に施術した。術後３ヵ月の成績は、語音弁別能が術前の裸耳４０％からＥＡＳ装用下の９０％に改善した。症例３は２１歳男性で右に、症例４は５３歳女性で左に、症例５は３４歳男性で右に、症例６は５１歳女性で右に、それぞれ症例２と同様の方法で施行した。各症例における現在までの語音聴取成績を表１に示す。何れの症例でも骨導の残存聴力の悪化は20ｄB以内に温存できた。

（表１）各例の現在までの語音聴取成績（%）

		67式 (55dBHL)				CI2004 単音節				CI2004 単語(SN10)				CI2004 会話文(SN10)			
		1	3	6	12	1	3	6	12	1	3	6	12	1	3	6	12 (カ月)
症例1	EAS	50	75	65	70				53				68				73
	ES				70				46				72				65
	AS				5				6				4				0
症例2	EAS	65	80		90				76				88				95
	ES		75		80				31				68				78
	AS		45		55				33				56				83
症例3	EAS	40	45	60		20	30	55		28	44	60		32	63	71	
	ES	10	25	45		15	31	40		8	20	44		5	25	55	
	AS	35	45	35		19	23	38		16	28	32		20	45	65	
症例4	EAS		65	75	70		53	68	60	16	68	80	80	11	76	96	95
	ES		40	65	50		35	60	55	4	36	72	56	50	70	75	85
	AS		25	25	15		8	23	6	8	20	36	12	21	38	85	41
症例5	EAS	70	90	65		40	19	53		16	12	88		80	70	90	
	ES	75	50	60		25	13	46		13	12	68		20	53	93	
	AS	0	35	15		15	8	25		5	0	36		18	38	41	
症例6	EAS	15				18				44				33			
	ES	10				8				32				26			
	AS	25				23				36				53			

D．考察

全例で蝸牛窓アプローチと、EAS 専用電極挿入、周術期のステロイドの使用により、

低音部の残存聴力の温存が可能であった。語音弁別能は、人工内耳単独使用時よりも（殊に騒音下において）良い傾向があり、全例から良好な感想を得ている。

E．結論

残存聴力活用型人工内耳埋込術を、当施設で6症例に行い、全例に安全かつ有効に施行できた。

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10 月 11-12 日，京都府

H．知的財産権の出願・登録状況
（予定を含む。）
1. 特許取得

2. 実用新案登録

3. その他

高度医療 残存聴力活用型人工内耳挿入術の適応症および有効性、安全性に関する調査研究

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研究要旨

低音域に残聴をもつ症例の補聴効果、EASの術後聴力温存率、聴取成績を検討した。当科の経験症例を比較すると、術前の低音域の残存聴力が良いものほど、術後聴力温存、聴取能が良い結果となった。

A．研究目的

低音域に残聴をもつ症例の補聴効果、EASの術後聴取成績、従来型人工内耳の術後聴取成績を比較し、本邦での基準を提唱する。また聴力温存を意図した手術の成績に影響する因子（手術方法、難聴原因、使用電極など）を明らかにする。

B．研究方法

1）補聴器を装用する高音急墜型高度感音難聴症例において聴取能を調べた。

2）EAS手術患者の難聴原因、聴力温存率、術後成績を検討した。

（倫理面への配慮）

研究対象者の人権の擁護のため、研究前、手術前に予測される危険性または不利益の排除、説明、同意を得た上で、個人のプライバシーを尊重し、個人情報の開示は行わないこととした。

C．研究結果

症例1：43歳女性。音入れ後12か月以上経過したが、聴力低下はみられず、EAS装用閾値、最高語音明瞭度検査でも良好な結果を維持している。

症例2：音入れ後12か月経過。純音聴力検査では、低音域の聴力が20dB閾値上昇を認め、装用閾値でも高音域は40dBHLまで聴力改善を認めた一方、低音域で術前と変化がない結果となった。最高語音明瞭度検査では、単音節・文章で術前10%未満であったが、術後12か月時で45%程度に改善を認め、日常会話が可能な状態となっている。

D．考察

低音域の残存聴力が良い、或いは若年の対象者の方が、術後の聴力や装用閾値の結果が良いといわれる報告があり、当科での結果もその報告を支持するものと考えられた。

E．結論

低音部の残存聴力が良いほど、術後の良好な聴取能を得る一因ではないかと考えられた。

Ｆ．健康危険情報

（分担研究報告書には記入せずに、総括研究報告書にまとめて記入）

Ｇ．研究発表

1. 論文発表

なし

2. 学会発表

なし

Ｈ．知的財産権の出願・登録状況

（予定を含む。）

1. 特許取得

なし

2. 実用新案登録

なし

3. その他

なし

Ⅳ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

書籍

[1] 宇佐美真一、西尾信哉　診療科別先進医療　耳鼻科　先進医療 NAVIGTOR 日本医学出版 東京 2013 pp72-75

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IV.　研究成果の刊行物・別刷

Acta Oto-Laryngologica. 2014; Early Online, 1–11

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ORIGINAL ARTICLE

Hearing preservation and clinical outcome of 32 consecutive electric acoustic stimulation (EAS) surgeries

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Abstract

Conclusions: Our results indicated that electric acoustic stimulation (EAS) is beneficial for Japanese-speaking patients, including those with less residual hearing at lower frequencies. Comparable outcomes for the patients with less residual hearing indicated that current audiological criteria for EAS could be expanded. Successful hearing preservation results, together with the progressive nature of loss of residual hearing in these patients, mean that minimally invasive full insertion of medium/long electrodes in cochlear implantation (CI) surgery is a desirable solution. The minimally invasive concepts that have been obtained through EAS surgery are, in fact, crucial for all CI patients. *Objectives:* This study was conducted to evaluate hearing preservation results and speech discrimination outcomes of hearing preservation surgeries using medium/long electrodes. *Methods:* A total of 32 consecutive minimally invasive hearing preservation CIs (using a round window approach with deep insertion of a flexible electrode) were performed in 30 Japanese patients (two were bilateral cases), including patients with less residual hearing. Hearing preservation rates as well as speech discrimination/perception scores were investigated on a multicenter basis. *Results:* Postoperative evaluation after full insertion of the flexible electrodes (24 mm, 31.5 mm) showed that residual hearing was well preserved in all 32 ears. In all patients, speech discrimination and perception scores were improved postoperatively.

Keywords: *Deep insertion, residual hearing, high-frequency hearing loss*

Introduction

Hearing preservation with electric acoustic stimulation (EAS) is a new trend for patients with residual hearing at the lower frequencies. Recent techniques, including round window insertion [1], use of minimally invasive electrodes [2,3], and postoperative steroid administration [4], enable hearing preservation rates of around 90–100% [5–11]. We demonstrated in our previous report that hearing preservation can be achieved even in the presence of a long electrode covering the residual hearing region [12]. This is an extremely important observation not only for EAS, but also because of the advantage of the electrode being in place to cover future hearing deterioration, which is very likely to happen as hearing loss in almost all the candidates is more or less progressive. A recent series of studies in different centers further confirmed that hearing

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preservation could be possible with full insertion of a longer electrode [4,6,8,9,12–15].

When performing the hearing preservation surgery, together with the natural course of progressive hearing loss, the surgeon should keep in mind that hearing threshold shift is unavoidable in the majority of cases after insertion of an electrode. To choose the optimal electrode for each individual, detailed data of hearing threshold shifts on a multicenter basis are crucial.

We have previously published a report on short-term hearing preservation results of five cases included in the current paper [12]. The present study expanded the duration of observation, the number of patients, and the number of the centers.

In this study, based on the minimally invasive concepts and using a round window insertion, we evaluated (1) hearing preservation results in 32 consecutive surgeries in 30 patients (including 2 bilateral cases), (2) the postoperative threshold shift of air conduction and bone conduction, (3) whether or not EAS is beneficial for Japanese-speaking patients, and (4) whether or not EAS is beneficial even for patients who do not meet the current audiological EAS criteria.

Material and methods

We performed 32 consecutive hearing preservation surgeries in 30 patients with residual hearing (Table I) who all had late or post-lingual onset, high-frequency involved sensorineural hearing loss. The subjects were divided into two groups according to the length of the electrode used. Group 1 consisted of 29 ears in 27 patients who received MEDEL PULSAR® with a 24 mm FLEX24® device. Among them were 24 patients (case nos. 1–24) who participated in a multicenter clinical trial in Japan and fulfilled the audiological criteria for EAS, slightly modified from that of a multicenter trial in the EU. (The criteria were: pure-tone hearing levels bilaterally at 65 dBHL for 125 Hz, 250 Hz, and 500 Hz; 80 dBHL at 2000 Hz; and 85 dBHL at 4000 and 8000 Hz; as well as minimal benefit from conventional hearing aids, i.e. monosyllable scores in quiet under 60% in the best aided condition.) The remaining three patients (case nos. 25–27; two of which were bilateral cases) had hearing levels only partially fulfilling the above EAS criteria, therefore were not included in the clinical trial. Group 2 comprised three ears in three patients who had less residual hearing and received longer (31.5 mm length) electrodes. One patient (no. 28) received a MEDEL COMBI40+® with a 31.5 mm Standard electrode. Two patients (nos. 29 and 30) received MEDEL PULSAR® with a 31.5 mm FLEXSOFT® electrode. A round window approach was used and full insertion of the electrode was achieved in all 32 surgeries.

The ages of the patients at time of surgery ranged from 21 to 71 years and all had late or post-lingual onset hearing loss at higher frequencies that was slowly progressive, starting at age 3–52 years (Table I).

The round window approach was applied to reduce the insertion damage of the cochlea. The surgeries were performed by four surgeons (Table I). Intraoperative and postoperative systemic dexamethasone treatment was given according to our protocol [12], i.e. intraoperative infusion of dexamethasone sodium phosphate (8 mg) applied before drilling of the bony edge of the round window niche and postoperative dexamethasone treatment administered for 6 days (8 mg, 8 mg, 4 mg, 4 mg, 2 mg, and 2 mg, respectively). The insertion depth of the electrode and the corresponding frequencies were estimated using postoperative X-ray (X-ray digital linear tomosynthesis).

EAS fitting

The frequency at which the audiogram surpassed 65 dBHL hearing loss was determined and the CI low frequency crossover point was set at that frequency point for fitting the EAS.

Audiometric evaluation

Audiometric evaluation from 125 to 8000 Hz was performed preoperatively and at 1, 3, 6, and 12 months after the initial EAS stimulation. Pure-tone hearing was evaluated at 4 weeks postoperatively; at the time of CI and EAS fittings; as well as at 3, 6, and 12 months postoperatively. Proper masking was applied to the contralateral ear and bone-conduction thresholds were used.

To evaluate speech perception outcomes, speech discrimination scores (using the 67S Japanese monosyllable test) and speech perception scores (using the Japanese CI2004 word and sentence test) were used. Subjects sat 1 meter away from the sound source facing 0° azimuth and recorded monosyllable words in quiet were presented in the sound field at 65 dB SPL. Three listening conditions were used: hearing aid alone, CI alone, and combined EAS. Each subject also underwent hearing in noise-testing using a monosyllable, word, and sentences protocol. A 10 dB signal-to-noise ratio (SNR) was used for subsequent testing determined at 1, 3, 6, and 12 months after the initial EAS stimulation.

This study was approved by the Ethics Committee of Shinshu University School of Medicine as well as

Table I. Clinical features of cases undergoing electric acoustic stimulation (EAS).

Case no.	Gender	Age at time of surgery (years)	Operative side	Inheritance mode	Onset age (years)	Responsible gene	Implant	Insertion depth (mm)	Surgeon
1	F	59	R	Sporadic	43	–	PULSAR FLEX24	24	S.U.
2	F	71	R	AD	30	–	PULSAR FLEX24	24	S.U.
3	F	45	R	Sporadic	25	–	PULSAR FLEX24	24	S.U.
4	F	38	L	Sporadic	28	–	PULSAR FLEX24	24	S.U.
5	F	46	R	AD	30	–	PULSAR FLEX24	24	S.U.
6	M	29	R	AD	7	–	PULSAR FLEX24	24	S.U.
7	M	39	L	AD	11	*ACTG1*	PULSAR FLEX24	24	S.U.
8	F	35	L	Sporadic	25	–	PULSAR FLEX24	24	S.U.
9	M	52	R	Mit	3	Mt.1555A>G	PULSAR FLEX24	24	S.U.
10	F	52	L	Sporadic	48	–	PULSAR FLEX24	24	S.U.
11	F	59	L	Sporadic	38	–	PULSAR FLEX24	24	S.U.
12	F	38	R	AD	13	–	PULSAR FLEX24	24	S.U.
13	F	52	L	Sporadic	37	–	PULSAR FLEX24	24	S.U.
14	M	45	L	Sporadic	35	–	PULSAR FLEX24	24	S.U.
15	M	54	R	Sporadic	52	–	PULSAR FLEX24	24	S.U.
16	M	21	R	AD	7	–	PULSAR FLEX24	24	T.T.
17	F	54	L	Sporadic	32	–	PULSAR FLEX24	24	T.T.
18	M	34	R	Sporadic	7	–	PULSAR FLEX24	24	T.T.
19	F	51	R	Sporadic	3	–	PULSAR FLEX24	24	T.T.
20	F	38	L	Sporadic	18	–	PULSAR FLEX24	24	Y.N.
21	F	58	L	Sporadic	35	–	PULSAR FLEX24	24	Y.N.
22	F	43	R	AR	30	–	PULSAR FLEX24	24	Y.N.
23	M	35	L	AD	10	–	PULSAR FLEX24	24	Y.N.
24	F	69	L	Sporadic	20	–	PULSAR FLEX24	24	H.T./Y.K.
25	M	39	R	Sporadic	30	–	PULSAR FLEX24	24	S.U.
26-1	F	45	L	Sporadic	25	–	PULSAR FLEX24	24	S.U.
26-2	F	48	R	Sporadic	25	–	PULSAR FLEX24	24	S.U.
27-1	F	38	L	AR	10	*TMPRSS3*	PULSAR FLEX24	24	S.U.
27-2	F	40	R	AR	10	*TMPRSS3*	PULSAR FLEX24	24	S.U.
28	F	60	R	Sporadic	40	–	Combi 40+ Standard	31.5	S.U.
29	M	68	R	Sporadic	52	–	PULSAR FLEX SOFT	31.5	S.U.
30	F	64	L	Sporadic	42	–	PULSAR FLEX SOFT	31.5	S.U.

AD, autosomal dominant; AR, autosomal recessive; F, female; L, left; M, male; Mit, mitochondrial mutation; R, right.

the respective ethical committees of the other participating institutions and prior written consent was obtained from each patient after a full explanation of the study.

Results

The current study included five cases (nos. 25, 26, 27, 28, and 29) from our previous report [12] on short-term hearing preservation results, and expanded the duration of observation, the number of patients, and the number of centers involved.

Hearing preservation

Achievement of full insertion was confirmed by combined postoperative imaging with the referential tonotopic map and the corresponding frequencies and the depth of the electrode were evaluated (see Usami et al. [12] for examples).

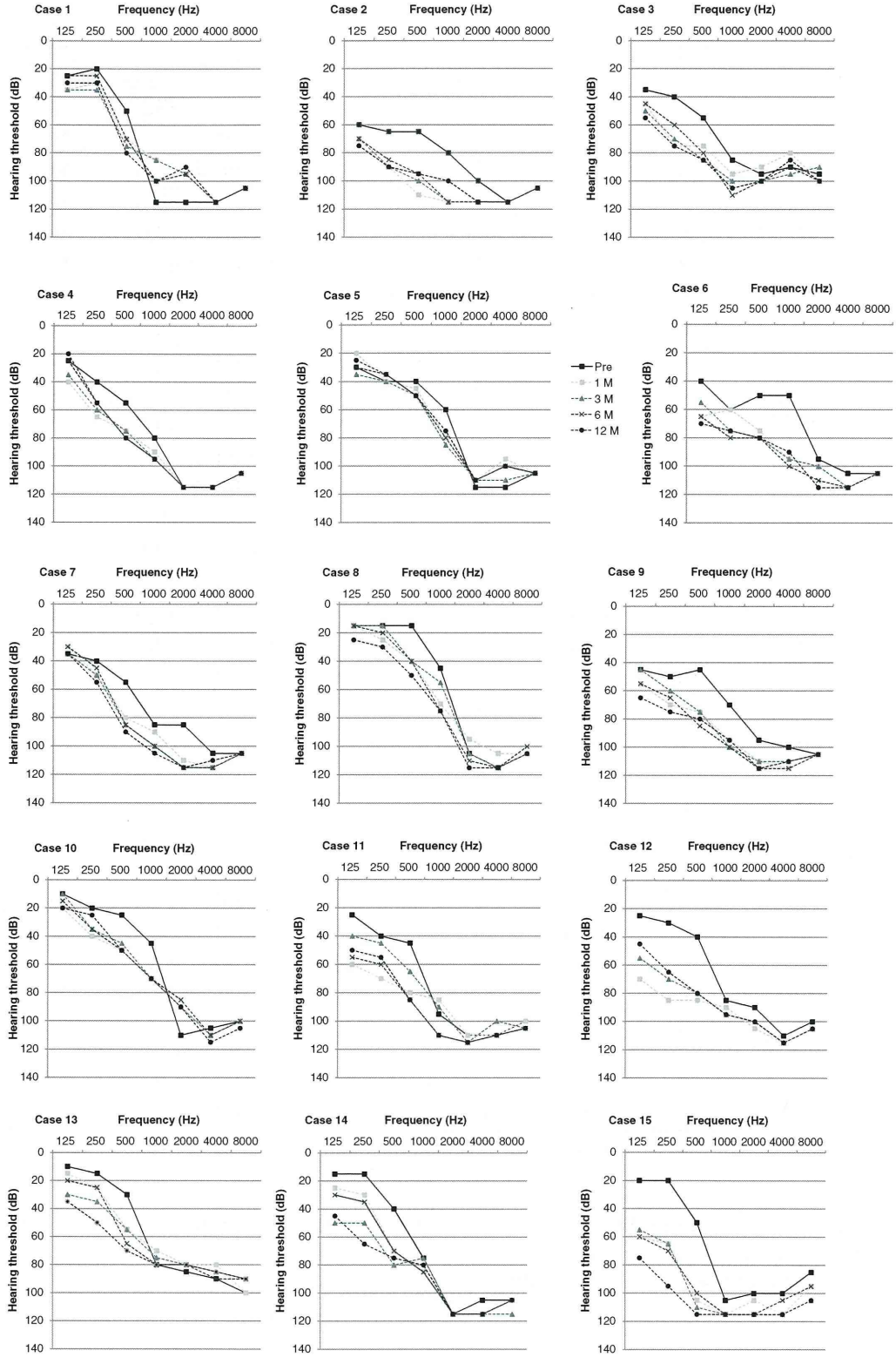

Figure 1. Hearing preservation results of group 1 with FLEX24 electrode. The lines indicate preoperative, and 1, 3, 6, and 12 months postoperative audiograms. Shadow indicates the audiological criteria for electric acoustic stimulation (EAS) clinical trial (patient nos. 1–24 fulfilling the audiological criteria for EAS, nos. 25–27 not fulfilling the criteria for the clinical trial for EAS).

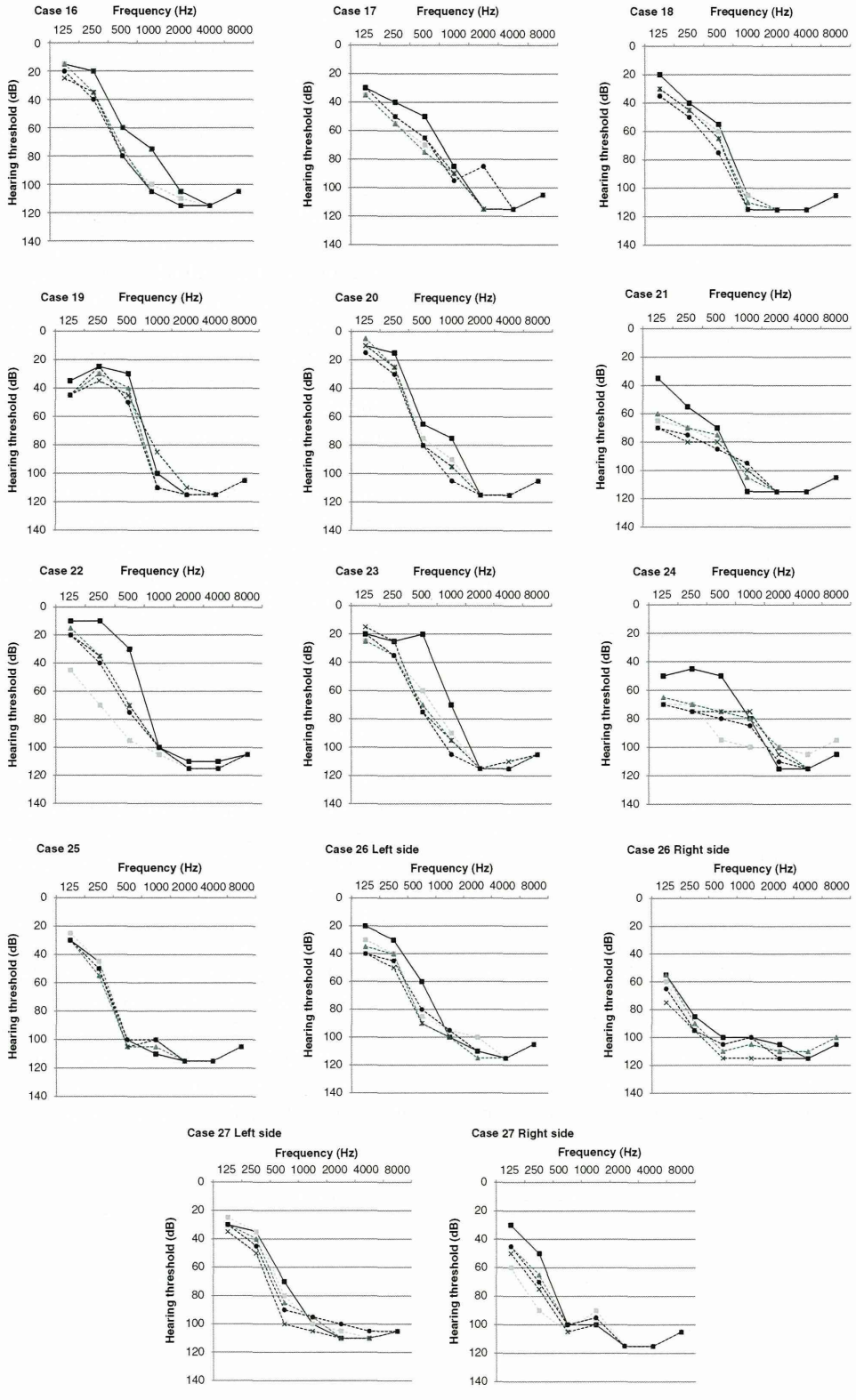

Figure 1. (*Continued*).

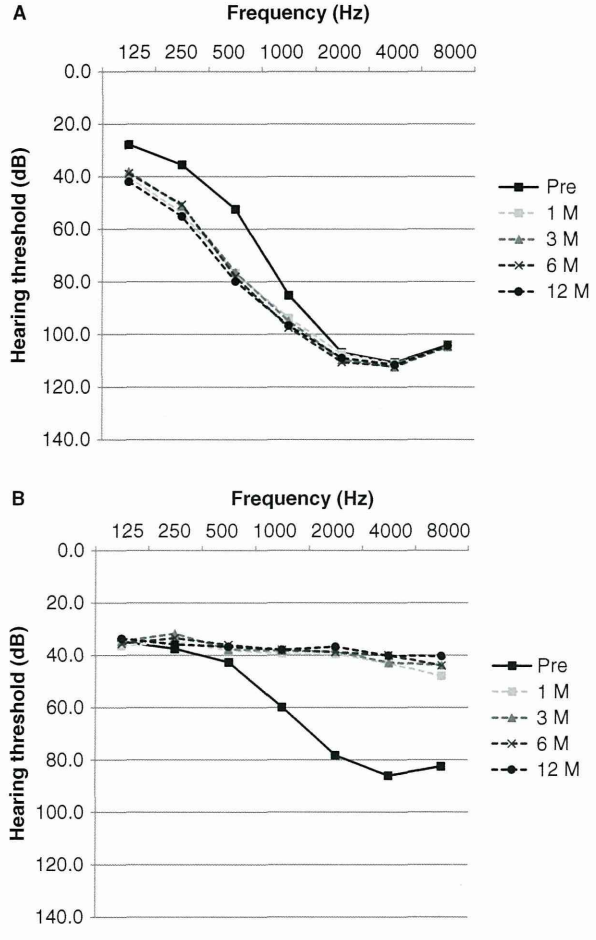

Figure 2. (A) Average audiogram of group 1. The lines indicate preoperative, 1, 3, 6, and 12 months postoperative audiograms. Note that good hearing preservation could be achieved. (B) Hearing level of group 1 with electric acoustic stimulation (EAS).

Overall, postoperative evaluation after deep insertion (24 or 31.5 mm) of the electrodes showed that residual hearing was well preserved in all 32 ears.

Individual preoperative and postoperative audiograms for group 1 are shown in Figure 1. Up to the 12-month follow-up, postoperative evaluation after full insertion of the electrodes showed that hearing in the low frequencies was well preserved in all 24 ears, but 1 patient (case no. 2) lost hearing at more than 6 months following surgery without any episode. The average audiograms for group 1 are shown in Figure 2A. Details of hearing threshold shift are indicated in Table II. Change in air conduction was 14.1 dB in 125 Hz, 19.7 dB in 250 Hz, 27.4 dB in 500 Hz, and 11.6 dB in 1000 Hz. Change in bone conduction was 8.3 dB in 250 Hz, 16.7 dB in 500 Hz, and 5.0 dB in 1000 Hz, respectively.

Low-frequency (250–1000 Hz) pure-tone thresholds dropped at the initial cochlear implant activation at 1 month postoperatively. In particular, hearing deterioration at 500 Hz was evident compared with 250 Hz or 1000 Hz. After initial deterioration, pure-tone thresholds were maintained until the 12-month evaluation.

In group 2, in which there was less residual hearing, it was also well preserved. Individual preoperative and postoperative audiograms are shown in Figure 3 and the average audiogram is shown in Figure 4A. Change in air conduction was 20.0 dB in 125 Hz, 25.0 dB in 500 Hz, and 8.3 dB in 500 Hz. Bone conduction was 10.8 dB in 250 Hz. Details of hearing threshold shift for group 2 are indicated in Table III.

EAS fitting

In two subjects (case nos. 2 and 15), residual hearing was not sufficient to utilize acoustic stimulation. Cochlear implant fitting using a full-frequency map and subsequent bimodal mode of stimulation with a contralateral hearing aid was used. Their cochlear implant alone monosyllable perception scores were 50% and 40% after 1 year, and 75% and 70% in the bimodal setting, respectively. We excluded these two cases from the evaluation of the speech perception outcome. For all other patients, an EAS speech processor (DUET II®) was applied. Postoperative hearing levels of groups 1 and 2 with EAS are shown in Figures 2B and 4B, respectively.

Table II. Average hearing thresholds of electric acoustic stimulation (EAS) patients in group 1.

	Air conductive hearing level (dB)							Bone conductive hearing level (dB)				
Timing	125 Hz	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz
Preoperative	27.8	35.5	52.4	85.2	106.9	110.7	104.1	29.3	42.6	67.9	73.6	64.5
1 month	40.3	53.8	76.7	93.8	107.4	111.2	104.5	35.2	54.8	72.7	73.8	63.9
3 months	38.1	51.2	76.4	95.0	109.7	112.4	104.8	35.9	55.0	73.3	73.6	63.6
6 months	38.8	50.7	78.0	97.5	110.5	112.1	104.5	33.7	56.4	73.6	74.3	63.9
12 months	41.9	55.2	79.8	96.7	109.0	111.6	104.3	37.6	59.3	73.0	73.9	63.9

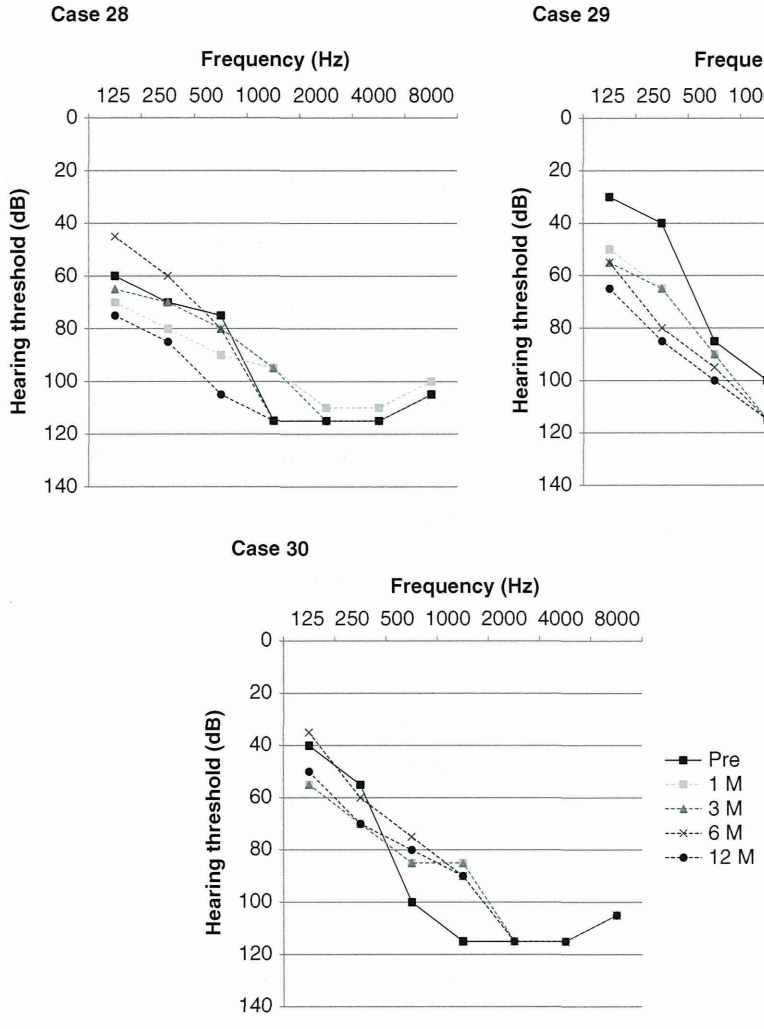

Figure 3. Hearing preservation results of group 2 (cases with less residual hearing and receiving longer electrodes (no. 28 with standard electrode, nos. 29 and 30 with FLEXSOFT electrode). The lines indicate preoperative, and 1, 3, 6, and 12 months postoperative audiograms. Note that good hearing preservation could be achieved.

Speech perception outcome

Improvement of speech discrimination and perception scores was seen in both groups (Figures 5 and 6). In group 1, the average monosyllable discrimination score in quiet (67S 65 dBSPL) was improved from 24.1% preoperatively with hearing aid to 67.4% with EAS 12 months after the first fitting. This postoperative improvement occurred gradually from 48.4% at 1 month to 67.4% at 12 months (Figure 5) and was mainly based on the adaptation of electrical stimulation, because in a comparison of monosyllable discrimination scores in three conditions (acoustic stimulation only (AS only), electric stimulation only (ES only) and EAS), acoustic stimulation scores changed only slightly from 13.8% to 18.1% at 12 months after the first fitting, but electrical stimulation improved from 35.0% to 55.4%. Also, the EAS condition showing the best performance for monosyllable discrimination revealed that acoustic stimulation combined with electrical stimulation increases perception ability (EAS results were significantly better than ES only; $p < 0.001$, paired t test). Similar results were observed in monosyllable, word, and sentence perception tests in noise. The results for monosyllable perception in noise were improved from 21.0% preoperatively with hearing aid to 60.2% with EAS 12 months after the first fitting. This postoperative improvement occurred gradually from 36.9% at 1 month to 60.2% at 12 months. Also, EAS results (60.2% correct) were significantly better than AS only (13.9% correct) and ES only (46.0% correct) results ($p < 0.001$ and $p = 0.009$, paired t test). The average word and sentence perception test score in noise improved from 35.8%, and 51.3% to 77.0%, and 88.2%, respectively. In both word and sentence