

Hearing Restoration with Auditory Brainstem Implant

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Abstract

Auditory brainstem implant (ABI) technology attempts to restore hearing in deaf patients caused by bilateral cochlear nerve injury through the direct stimulation of the brainstem, but many aspects of the related mechanisms remain unknown. The unresolved issues can be grouped into three topics: which patients are the best candidates; which type of electrode should be used; and how to improve restored hearing. We evaluated our experience with 11 cases of ABI placement. We found that if at least seven of eleven electrodes of the MED-EL ABI are effectively placed in a patient with no deformation of the fourth ventricle, open set sentence recognition of approximately 20% and closed set word recognition of approximately 65% can be achieved only with the ABI. Appropriate selection of patients for ABI placement can lead to good outcomes. Further investigation is required regarding patient selection criteria and methods of surgery for effective ABI placement.

Key words: auditory brainstem implant, hearing restoration, brain-machine interface

Introduction

The field of regenerative medicine in the central nervous system is currently developing in two broad directions: biological methods that attempt to repair neural pathways damaged by stroke or spinal cord injury using induced pluripotent stem, embryonic stem, or neural stem cells; and brain-machine interface technology, such as cochlear implants, using microprocessor technology. Cochlear implants convert sound to electrical signals, which are used to directly stimulate the cochlear nerve, thus bypassing the patient's cochlear deficiency. Cochlear implants have already demonstrated excellent outcomes, with hearing improving in nearly 80% of patients; many patients have also gained the ability to communicate via the telephone.

Auditory brainstem implant (ABI) is an extension of the principle of cochlear implants. Cochlear implant replaces the function of the inner ear (cochlea) to stimulate the cochlear nerve (primary neurons). In contrast, ABI involves direct stimulation of the secondary neurons of the relay nucleus (cochlear nucleus) in the brainstem. ABI was first introduced in the United States in 1979,^{1,2)} and considerable improvements have since been made. Currently, ABIs have been provided to more than 700 individuals worldwide. ABIs were first reported in Japan in 2000,³⁾

with later evaluation of the speech recognition of ABIs.⁴⁾ Implementation of this technology has been considerably delayed in Japan compared to Western countries, with only 13 individuals receiving ABIs from 1998 to 2016. Of these, 11 were our patients.

ABI technology is intended to improve hearing ability by direct stimulation of the brainstem, and many aspects of the related mechanisms remain unknown. The unresolved issues can be grouped into three topics: which patients are the best candidates; which type of electrode should be used; and how to improve restored hearing. We investigated our 11 cases of ABI in an attempt to answer these questions.

Structure of ABI

The basic structure of an ABI is the same as that of a cochlear implant except for the electrodes (Fig. 1). Sounds that reach the ear are picked up by a microphone affixed to the ear and the electrical impulses are passed to a speech processor. The sound signals undergo frequency analysis. They are converted to electrical signals and communicated to a conductive coil. The electrical signals also include information data such as stimulation electrode allotment and stimulation intensity of each electrode, which are pre-programmed for individual patients. The conductive coil communicates these electrical signals through the skin via electromagnetic induction to a

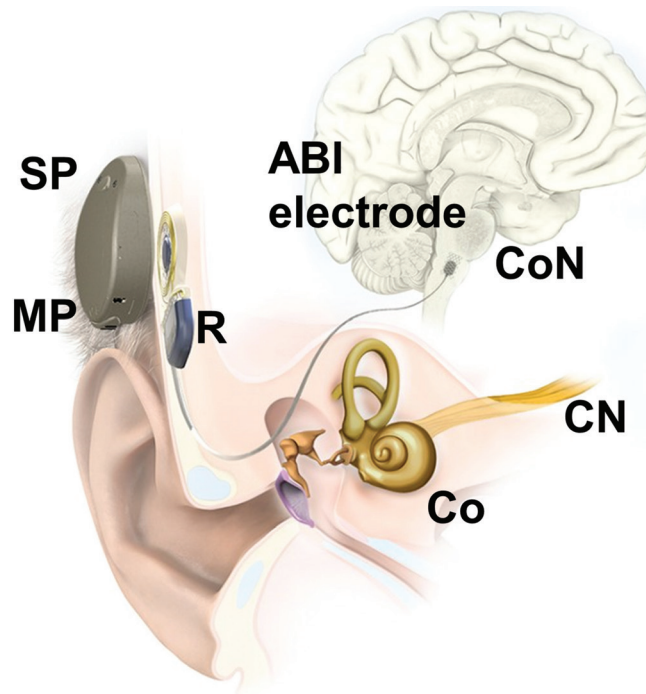


Fig. 1 Schema of the auditory brainstem implant (ABI). Scheme was supplied from MED-EL (Innsbruck, Austria) and partially modified with the permission of Med-EL. CN: cochlear nerve, Co: cochlea, CoN: cochlear nucleus, MP: microphone part, R: receiver, SP: speech processor part.

receiver-stimulator fixed to the skull. Stimulation is then applied to each electrode in accordance with the information communicated to the receiver. An ABI uses plate electrodes (8–21 electrodes) arranged on a 3–5 mm silicone plate fixed to the cochlear nucleus of the brainstem. Both the microphone-speech processor and receiver units offer superior long-term postoperative management, with no internal parts requiring replacement. The speech processor requires batteries, but the internal device operates by electromagnetic induction.

Two types of ABIs are currently available made by the Cochlear Ltd. (Sydney, Australia; 21 electrodes), and the MED-EL (Innsbruck, Austria; 12 electrodes). The Cochlear Ltd. ABI is more comprehensive, and its electrodes are much larger than the dorsal cochlear nucleus. In contrast, MED-EL ABI uses an electrode surface of the same size and shape as the dorsal cochlear nucleus, offering superior stability and adhesion. Currently, speech processors are becoming smaller and lighter, some are now the size of the little finger, so can be worn over the ear with the microphone. In a device recently developed by MED-EL, the secondary coil is integrated with the stimulation device and can be used without taking the magnet off. If a low magnetic field is used,

the patient can even undergo magnetic resonance imaging.⁵⁾ The differences in characteristics of these two devices are important to understand to select the optimal type for individual patients.

Surgical Indications for ABI

ABIs are indicated for deafness caused by bilateral cochlear nerve disorder, assuming no impairment of the central auditory nervous system including the brainstem, where the cochlear nucleus is located. Accordingly, most indicated patients have hereditary neurofibromatosis type 2 (NF2). NF2 affects one in 40,000 of the general population and is characterized by bilateral acoustic tumors.⁶⁾ Hearing loss associated with NF2 is irreversible, so regenerative medicine will be essential in recovering some hearing ability in these patients.

Table 1 shows the eligibility criteria for ABIs in the United States and Europe, as indicated at an international symposium held in 1999 that will be discussed later. The United States criteria state that the side to receive an ABI can be either the side on which the initial surgery was performed or the opposing side; auditory ability at the time is not considered. Thus, patients may be eligible even if some auditory ability is preserved on the contralateral side of initial surgery. Depending on the case, ABIs may ultimately be implanted on both sides so that patients can use the side with better hearing. This point differs from the European criteria, which state that an ABI can only be implanted on one side. Patients who have received gamma knife surgery are excluded by both sets of criteria. Neither set of criteria has established the timing for tumor excision and ABI placement. Simultaneous procedures would reduce the burden of the second surgery on patients. However, ABI placement should be conducted in two stages for large tumors.

Requirements for performing ABI surgery were also outlined at the aforementioned symposium.⁷⁾ Surgeons should have resected >100 cases of auditory tumors and performed cochlear implant surgery on at least 10 patients in the past year and at least 50 patients overall. In addition, neurophysiological intraoperative monitoring and diagnosis should be routinely performed and information on outcomes should be exchanged with other facilities.

Surgical Procedure

During surgery, the dorsal cochlear nucleus must be confirmed anatomically from the fourth ventricular lateral recess (Fig. 2). To appropriately place the ABI electrodes on the cochlear nucleus, dummy electrodes for the ABI are specially produced by

Table 1 Indications for auditory brainstem implant

U.S.	1	Neurofibromatosis type 2
	2	Age ≥ 12 years
	3	Implantation on one or both sides
	4	Mentally stable, with no other serious illnesses
	5	Intent to participate proactively in subsequent follow-up
	6	Hearing ability at the time of surgery is irrelevant
	7	Excluded gamma knife-treated patients
Europe	1	Life-threatening bilateral cerebellopontine angle tumors such as neurofibromatosis type 2 or other cranial injury
	2	Age ≥ 18 years
	3	Simultaneously performed with various types of tumor excision or as a two-staged surgery
	4	Excluded patients who have undergone stereotaxic radiotherapy such as gamma knife treatment
	5	Implantation on one side only
	6	Mentally stable, with no other serious illnesses
Our study	1	Neurofibromatosis type 2, bilateral cochlear nerve injury due to various pathology
	2	Age ≥ 12 years
	3	Implantation on one or both sides
	4	Mentally stable, with no other serious illnesses
	5	Intent to participate proactively in subsequent follow-up
	6	Hearing ability at the time of surgery is irrelevant
	7	Excluded gamma knife-treated patients

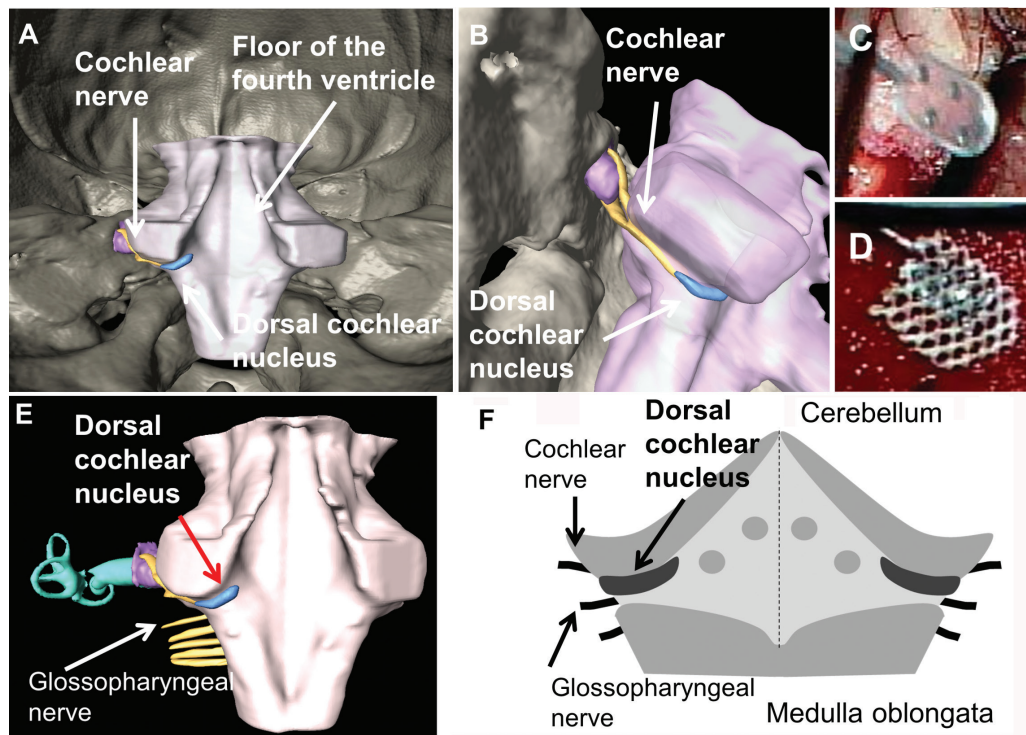


Fig. 2 Three-dimensional anatomy of the dorsal cochlear nucleus. (A, B) Schema of the three-dimensional anatomy of the dorsal cochlear nucleus. (C) Auditory brainstem implant placed at the dorsal cochlear nucleus. (D) Electrode fixation performed using Dacron mesh attached to the dorsal surface. (E) Schema of the three-dimensional anatomy of the dorsal cochlear nucleus and the hypoglossal nerve. (F) Topographic anatomy of the dorsal cochlear nucleus region at the floor of the fourth ventricle.¹³⁾

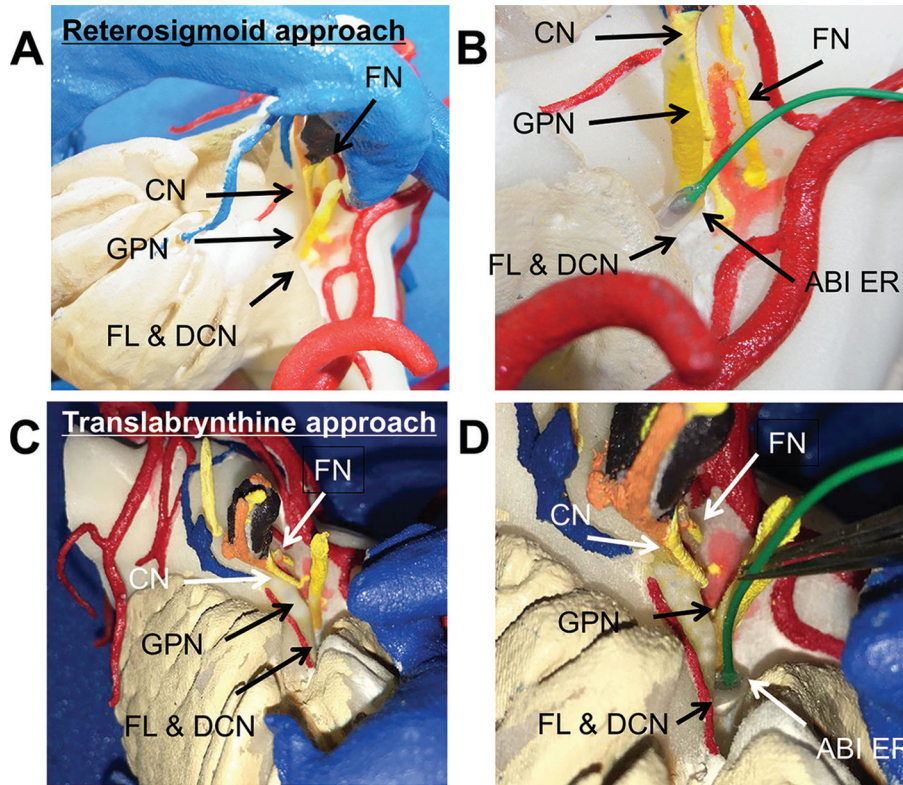


Fig. 3 Surgical landmarks for auditory brainstem implant (ABI) placement in each surgical approach. (A, B) Surgical anatomy via retrosigmoid approach. (C, D) Surgical anatomy via translabyrinthine approach. ABI ER indicates auditory brainstem implant electrode, CN; cochlear nerve, DCN; dorsal cochlear nucleus, FL; Foramen of Luschka, FN; facial nerve, GPN; glossopharyngeal nerve.

MED-EL. Temporary stimulation is applied through these dummy electrodes (four electrodes) to confirm that good electrically evoked auditory brainstem response (eABR) is achieved from all four electrodes. Fine adjustments can be made to the dummy electrode position until a good response is achieved from all four electrodes. The best electrode position was marked upon the brainstem surface with the pyoktanin blue dye. The ABI electrodes, which are exactly the same size as the dummy electrodes, are adhered with fibrin glue and surgical at the sites with the best responses from all four electrodes. Correct implementation of this process is the most critical point of ABI surgery. Electrode fixation is performed using the Dacron mesh attached to the dorsal surface.

Surgical Approach

Most ABIs have been implanted via the translabyrinthine or posterior cranial fossa (retrosigmoid) approaches. In the United States, the translabyrinthine approach accounts for the overwhelming majority of cases. However, in Europe in 1999, the posterior cranial fossa approach was used in approximately

one-third of patients (21 of 58).⁷⁾ Anatomically, the more anterior translabyrinthine approach is thought to be superior for opening the fourth ventricular lateral recess in the anterolateral direction. However, either approach may be used in cases involving large tumors because the lateral recess is deformed. To appropriately place the ABI electrode on the cochlear nucleus after tumor excision, temporary stimulation is applied through the electrodes to confirm that good eABR reproducibility is achieved.

Surgical landmarks for ABI placement in each surgical approach are shown in Fig. 3. Glossopharyngeal nerve is the key anatomical landmark leading into foramen of Luschka and dorsal cochlear nucleus (Fig. 2E, F). Note that retrosigmoid approach is superior to translabyrinthine approach with direct visualization of the dorsal cochlear nucleus behind the glossopharyngeal nerve (Fig. 3A, B). Through a translabyrinthine approach, we can only see the entrance of the foramen of Luschka. Thus, we place the electrode without direct confirmation of the dorsal cochlear nucleus (Fig. 3C, D).

Surgical procedures for auditory brainstem implant placement via the retrosigmoid approach are shown in Fig. 4.

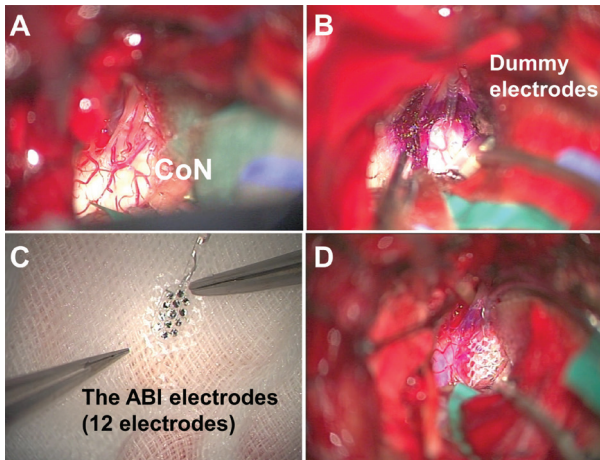


Fig. 4 Surgical procedure for auditory brainstem implant (ABI) placement. (A) Exposure of the cochlear nucleus (CoN). To appropriately place the ABI electrodes on the CoN, dummy electrodes for the ABI are prepared. (B) Temporary stimulation is applied through these dummy electrodes (four electrodes) to confirm that good electrically evoked auditory brainstem response (eABR) reproducibility is achieved. Fine adjustments can be made to the dummy electrode positions until a good response is achieved from all four electrodes. The best electrode position was marked upon brainstem surface with the pyoktanin blue dye. (C) The ABI electrodes (12 electrodes). (D) The ABI electrodes are adhered with fibrin glue and surgical at the sites with the best responses from all four electrodes. Electrode fixation is performed using the Dacron mesh attached to the dorsal surface.

Surgical Outcomes in Europe and the United States

Beginning in 1994, a clinical trial involving a total of 144 patients (92 patients in the United States and 52 patients in Europe) using eight-electrode ABIs in the United States and 21-electrode ABIs in Europe (mainly Germany) was conducted over 5 years, and the results were reported in Germany in 1999.^{7,8)} Outcomes in the United States indicated that some hearing ability was achieved in 85.2% of patients, 93% of whom experienced clear improvements in communication ability when the ABI was used in combination with lip reading. A small number of patients also gained the ability to communicate via telephone, but none of the outcomes rivaled those of cochlear implants. Side effects included sensations and movements other than sounds provoked in several electrodes. The most common were numbness and muscle contractions, which mainly (94%) occurred on the stimulation (ABI) side. Although these electrodes cannot be used, future use may be possible after a period of time in some cases. The 21-electrode series in Europe recreated hearing with 9.4 electrodes.⁷⁾ Moreover, ABIs were used for at least 8 hours per day in 65% of cases.⁸⁾

Our 11 Cases of ABI Placement

We performed ABI placement surgery for a total of 11 patients between 1999 and 2011 at The University of Tokyo Hospital and Toranomom Hospital (Table 2).

Table 2 Clinical characteristics of the 11 patients

Case No.	Underlying disease	Type of ABI	Age (years)	Sex	Age at diagnosis (years)	Laterality	Tumor size (mm)	Surgical approach	Duration of hearing loss (months)	Duration from tumor resection to placement of ABI (months)
1	NF2	Cochlea Ltd., 8-channel	25	M	8	Lt	35	TL	7	4
2	NF2	Cochlea Ltd., 21-channel	26	F	24	Rt	15	MSO	0	0
3*	NF2	Med-EL	42	M	38	Rt	35	RS	0.5	0
4	NF2	Med-EL	62	M	56	Rt	20	RS	192	192
5*	NF2	Med-EL	35	M	33	Rt	35	TL	24	0
6	Meningitis	Med-EL	66	M	33	Rt	0	RS	204	non-NF2
7	NF2	Med-EL	59	F	36	Lt	10	RS	0	0
8	NF2	Med-EL	45	F	38	Rt	10	RS	39	0
9	NF2	Med-EL	39	M	30	Rt	3	RS	10	12
10	NF2	Med-EL	64	M	58	Lt	29	RS	21	25
11*	NF2	Med-EL	39	M	25	Lt	35	RS	14	4
Average			46		34		17.5		46.5	21.5

*Three cases were treated at The University of Tokyo Hospital. Others were treated at Toranomom Hospital. ABI: auditory brainstem implant, MSO: midline suboccipital approach, NF2: neurofibromatosis type 2, RS: retrosigmoid approach, TL: translabyrinthine approach.

Six of the 11 patients in this article have been reported in our previous article.⁹⁾ This study was approved by the Ethics Committee of the Faculty of Medicine, The University of Tokyo (approval number 0332). Written informed consent was obtained from all study participants. Patient selection criteria for ABI placement in our study is listed in Table 1. In brief, in addition to patient selection criteria in the United States, those with deafness from bilateral cochlear nerve dysfunction, for example, a unilateral acoustic schwannoma with contralateral eighth cranial nerve caused by a congenital pathology or head injury, were also candidates for use of the ABI.³⁾

The first two patients received ABIs manufactured by Cochlear Ltd. (Sydney, Australia), and the remaining nine patients received ABIs made by MED-EL. Ten patients had NF2, and one patient had developed loss of hearing as a result of meningitis. This latter patient responded to ABI despite having suffered from hearing loss for more than 16 years. Some patients who underwent tumor excision simultaneously with ABI placement were also responders.

I. Illustrative case (Case 4)

This NF2 male patient underwent bilateral removal of the acoustic tumors at age 56 years. He lost hearing bilaterally after the surgery. He did not have facial palsy (House-Brackmann grade 1). He underwent placement of ABI via the right retrosigmoid approach at age 62 years. The operation was done under intraoperative eABR and facial nerve

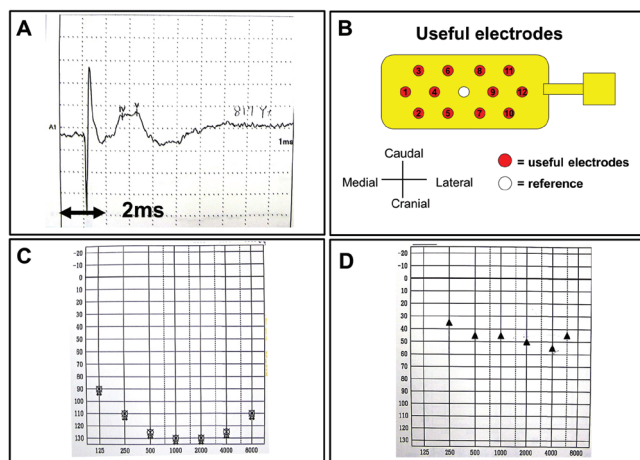


Fig. 5 Perioperative evaluation of Case 4. (A) Intraoperative evoked auditory brainstem response to temporary stimulation through the auditory brainstem implant (ABI) electrode. (B) Useful ABI electrodes after electrode fixation. Eleven electrodes were useful in this case. (C) Preoperative audiogram. Hearing had been lost after surgery for bilateral acoustic tumors. (D) Postoperative audiogram. Hearing significantly restored after ABI placement.

Table 3 Relationship between deformation of the fourth ventricle and number of available electrodes

Case no.	Deformation of fourth ventricle	Total number of electrodes	Number of available electrodes
1	severe	8	5→4
2	none	21	5
3	severe	12	5→2
4	none	12	11
5	mild	12	7
6	none	12	9
7	mild	12	7
8	none	12	8
9	none	12	8
10	none	12	6→3→1
11	none	12	12

electromyography monitoring. The eABR achieved after temporary stimulation through the ABI electrode intraoperatively (Fig. 5A). After placement of the plate electrodes, 11 electrodes were useful (Fig. 5B). His hearing was restored significantly after the surgery. Pre- and postoperative audiograms are shown in Fig. 5C, D. Long-term outcome was evaluated at 82 months after the surgery. His pure tone average was 43 dB. Open set sentence recognition of 31% and closed set sound recognition of approximately 80% were achieved with only the ABI. With lip reading, open set sentence recognition was possible of 78%.

II. Analysis and investigation of our 11 cases for appropriate ABI placement

Appropriate ABI placement requires accurate identification of the dorsal cochlear nucleus. We investigated the presence or absence of deformation of the fourth ventricle because we considered this to be an important factor. The results are presented in Table 3. In the most recent eight cases, in which no or only mild deformation of the fourth ventricle occurred, at least seven of the 12 electrodes could be used (except in Case 10, in which an electrode moved position). No significant differences were noted between the translabyrinthine and retrosigmoid approaches.

We also investigated possible correlations between the auditory function following ABI surgery and the number of useful electrodes (Table 4). In five of the seven cases with at least seven effective electrodes, open set sentence recognition of approximately 20% could be achieved using only the ABI. In three cases, closed set word recognition of approximately 65% could be achieved with only the ABI. Through patient

Table 4 Outcomes of hearing ability

Case no.	Postoperative PTA (dB)	Closed set sound recognition		Closed set word recognition		Open set sentence recognition	
		ABI only	ABI + LR	ABI only	ABI + LR	ABI only	ABI + LR
1	40	NA	NA	NA	14%	0%	10%
2	50	NA	NA	NA	NA	NA	NA
3	55	29%	90%	NA	NA	0%	9%
4	43	80%	NA	NA	NA	31%	78%
5	40	88%	100%	28%	60%	23%	93%
6	35	70%	NA	NA	NA	21%	89%
7	45	80%	NA	65%	100%	0%	0%
8	45	75%	NA	72%	NA	8%	98%
9	40	30%	NA	77%	100%	NA	NA
10	55	NA	NA	67%	100%	NA	35%
11	40	75%	100%	4%	68%	12%	60%

ABI: auditory brainstem implant, LR: lip reading, NA: not available, PTA: pure tone average.

satisfaction questionnaires from seven patients, they have felt really useful in the aspect of environmental sound recognition (7/7, 100%), improved lip reading (5/7, 71%) and word understanding (2/7, 28%).¹⁰⁾ If we apply more popular auditory tests such as pure tone average (PTA) and speech discrimination score (SDS) to these patients, they could achieve 40–50 dB on PTA, however, since SDS is the open-set syllable test, their score ended up around 0-10%.

Outcomes for our 11 cases can be summarized as follows. The MED-EL ABIs provided stable electrode placement because both the dummy electrodes and final placement electrodes were approximately the same size as the dorsal cochlear nucleus. If the fourth ventricle is deformed, post-placement electrode movement and the number of electrodes useful for stimulation are likely to be affected, influencing the outcome of hearing restoration. The duration of deafness did not ultimately affect the outcome of hearing restoration. In the presence of deformation of the fourth ventricle, tumor excision and ABI placement were separately performed. Time for recovery of brainstem deformation was important in some cases. Although the eligibility for ABI placement was limited to non-NF2 cases at introduction, better hearing outcome can be achieved in non-tumor cases than in NF2 cases on the basis of the subsequent data. The nerve pathways necessary for understanding speech might have been destroyed by the tumor or by surgery in patients with NF2.¹¹⁾ Recently, ABI surgery with great care to minimize physical and venous trauma was found to improve the outcomes of speech recognition ability even in patients with NF2 and large tumors.¹²⁾ Similarly,

good outcomes were achieved in 20–30% of NF2 cases among our 11 patients.

Based on the present and previous findings, we can now answer the three questions posed at the beginning of this report: which patients are the best candidates; which type of electrode should be used; and how to improve restored hearing. Currently, effective placement of at least seven electrodes in a patient with no deformation of the fourth ventricle will result in discernment of approximately 20% of sentences and approximately 65% of words with only the ABI. A number of issues need to be solved to further improve outcomes, including determination of the optimal timing for ABI placement, whether to perform single- or dual-stage surgery, the optimal approach, and methods for ensuring firm adhesion. We hope to proceed with further analysis to clarify the answers to these questions.

Conclusions

Hearing function, which operates through an extremely specialized sensory organ, is very difficult to regenerate using only biological methods. Brain-machine interface technology can be quite successful, similar to cochlear implant technology. Appropriate selection of patients can lead to good outcomes. Further investigation is required regarding patient selection criteria and methods of surgery for effective ABI placement.

Acknowledgment

The authors wish to thank Dr. Akio Morita (Department of Neurological Surgery, Nippon Medical

School, Tokyo), Dr. Kimitaka Kaga (National Institute of Sensory Organs, National Tokyo Medical Center, Tokyo), Dr. Tatsuya Yamasoba (Department of Otolaryngology, Faculty of Medicine, The University of Tokyo), Dr. Masaaki Usui (Department of Neurosurgery, Toranomon Hospital, Tokyo), Dr. Yojiro Seki (Department of Neurosurgery, Tokyo Kyosai Hospital, Tokyo), Dr. Kozo Kumakawa (Department of Otolaryngology, Toranomon Hospital, Tokyo) and Dr. Michihiro Kohno (Department of Neurosurgery, Tokyo Medical University, Tokyo) for clinical support.

Conflicts of Interest Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices in the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

References

- 1) Hitselberger WE, House WF, Edgerton BJ, Whitaker S: Cochlear nucleus implants. *Otolaryngol Head Neck Surg* 92: 52–54, 1984
- 2) House WF, Hitselberger WE: Twenty-year report of the first auditory brain stem nucleus implant. *Ann Otol Rhinol Laryngo* 110: 103–104, 2001
- 3) Seki Y, Umezumi H, Usui M, Kumakawa K, Kumagai F, Komatsuzaki A, Hitselberger WE: Restoration of hearing with an auditory brainstem implant in a patient with neurofibromatosis type 2—case report. *Neurol Med Chir (Tokyo)* 40: 524–527, 2000
- 4) Kumakawa K, Motizuki Y, Takahashi N, Takeda H, Muto N, Yamane M, Seki Y, Takemori S, Komatsuzaki A: [Speech perception ability in a patient with a 8-channel auditory brainstem implant]. *Nihon Jibiinkoka Gakkai Kaiho* 104: 510–513, 2001 (Japanese)
- 5) Jackson KB, Mark G, Helms J, Mueller J, Behr R: An auditory brainstem implant system. *Am J Audiol* 11: 128–133, 2002
- 6) Gutmann DH, Aylsworth A, Carey JC, Korf B, Marks J, Pyeritz RE, Rubenstein A, Viskochil D: The diagnostic evaluation and multidisciplinary management of neurofibromatosis 1 and neurofibromatosis 2. *JAMA* 278: 51–57, 1997
- 7) Ebinger K, Otto S, Arcaroli J, Staller S, Arndt P: Multichannel auditory brainstem implant: US clinical trial results. *J Laryngol Otol Suppl* 27: 50–53, 2000
- 8) Sollmann WP, Laszig R, Marangos N: Surgical experiences in 58 cases using the Nucleus 22 multichannel auditory brainstem implant. *J Laryngol Otol Suppl* 27: 23–26, 2000
- 9) Nakatomi H: Surgical procedure in auditory brain stem implant. *Nihon Jibiinkoka Gakkai Kaiho* 114: 851–854, 2011
- 10) Kato H, Ootawa Y, Takeda H, Kumakawa K: Comparison of cochlear implantation and auditory brainstem implantation in neurofibromatosis type 2 patients at our department. *Otol Jpn* 21: 244–249, 2011
- 11) Colletti V, Shannon RV: Open set speech perception with auditory brainstem implant? *Laryngoscope* 115: 1974–1978, 2005
- 12) Behr R, Colletti V, Matthies C, Morita A, Nakatomi H, Dominique L, Darrouzet V, Brill S, Shehata-Dieler W, Lorenz A, Skarzynski H: New outcomes with auditory brainstem implants in NF2 patients. *Otol Neurotol* 35: 1844–1851, 2014
- 13) Quester R, Schroder R: Topographic anatomy of the cochlear nuclear region at the floor of the fourth ventricle in humans. *J Neurosurg* 91: 466–476, 1999

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