*Otology & Neurotology*
**39**:177–183 © 2017, Otology & Neurotology, Inc.

# What Is the Sensitive Period to Initiate Auditory Stimulation for the Second Ear in Sequential Cochlear Implantation?

*Hong Ju Park, *Jee Yeon Lee, †Chan Joo Yang, *Jun Woo Park, *Byung Chul Kang, *Woo Seok Kang, *Joong Ho Ahn, and *Jong Woo Chung

**Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine; and †Department of Otolaryngology, Hanil General Hospital, Seoul, South Korea*

**Objectives:** Bilateral cochlear implants (CI) are the standard treatment for bilaterally deaf children, but it is unclear how much the second CI can be delayed in sequential bilateral CI. We investigated the performances of sequential CI to answer this question.
**Study Design:** Retrospective case series review.
**Setting:** Tertiary referral center.
**Methods:** We studied a cohort of congenitally deaf children ($n = 73$) who underwent sequential CI without any inner ear anomaly or combined disabilities. Hearing threshold levels and speech perception were evaluated by aided pure tone audiometry and Asan-Samsung Korean word recognition test. The scores were analyzed by the ages at surgery and compared among the different age groups.
**Results:** When the second CI was performed before 3.5 years (the optimal period for the first CI), the second CI scores (96.9%) were comparable to the first CI scores. Although the first CI scores were more than or equal to 80% when the first CI was implanted before the age of 7 years, the second CI scores were more than or equal to 80% when the second CI was implanted before the age of 12 to 13 years. The hearing threshold levels were not different regardless of the ages and between the first and second CIs.
**Conclusion:** Our cohort demonstrated that the second CI showed comparable results to the first CI when implanted before 3.5 years, suggesting that optimal periods for the first CI and the second CI are same. However, the sensitive period (12–13 yr) for the second CI with good scores ($\geq$80%) was much longer than that (7 yr) of the first CI, suggesting that the first CI prolongs the sensitive period for the second CI. The second CI should be implanted early, but considered even at a later age. **Key Words:** Brain—Cochlear implant—Deaf—Hearing loss—Plasticity—Sequential—Speech—Surgery.

*Otol Neurotol* **39:**177–183, 2018.

Cochlear implants (CI) have become the standard treatment for children with bilateral deafness (1,2). Children who are deprived of sufficient amounts and/or quality of language input in their earliest years are at risk of poor outcomes in both language and academic endeavors in later childhood (3). A study showed that the bursts of growth were not observed for consonant-production accuracy in children who were more than 7 years of age at the time of CI, and for vocabulary in children who were more than 3.5 years of age at the time of CI (4). A study on the development of the central auditory system through an electrophysiological test revealed that there is a period of 3.5 years during which the central auditory system remains maximally plastic, and that plasticity remains in some but not all children until 7 years of age (5). Thus, it is generally accepted that the optimal period for CI is within the first 3.5 years of life and that CI placement after the sensitive period (7 yr of age) may result in abnormalities in synaptic plasticity, involving abnormal connectivity, functional disintegration and immaturity of the auditory cortex, and the smearing of feature representations in the auditory system (6,7).

Bilateral early implantation has recently been pursued to expand the benefits obtained with unilateral CI and is beneficial for sound localization, hearing sensitivity improvement, and speech comprehension in a noisy environment (8–10). However, most deaf children underwent CI in only one ear for more than 20 years following the FDA approval of multichannel CI for children in 1990, since bilateral CI implantation only recently became the standard of care. Furthermore, some candidates for bilateral CI might decide not to obtain bilateral CI due to their parents' reluctance, perceived difficulty managing two implants, or a healthcare

Address correspondence and reprint requests to Hong Ju Park, M.D., Ph.D., Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, 86 Asanbyeongwon-gil, Songpa-gu, Seoul 138-736, South Korea; E-mail: dzness@amc.seoul.kr
Sponsorships: None.
Funding Source: None.
The authors disclose no conflicts of interest.
**DOI: 10.1097/MAO.0000000000001640**

**TABLE 1.** *Characteristics of children by the age at the second CI operation (n = 73)*[a]

| Groups (Age at the Second CI Operation) | 1.4–3.5 yr | 3.6–7 yr | 7–13 yr | 13.1–19 yr |
|---|---|---|---|---|
| n | 15 | 26 | 20 | 12 |
| Ages at the first CI (yr) | 1.6 ± 0.5 | 2.0 ± 0.8 | 2.5 ± 1.3 | 4.8 ± 2.3 |
| Ages at the second CI (yr) | 2.6 ± 0.3 | 5.3 ± 1.1 | 9.6 ± 1.5 | 16.0 ± 2.1 |
| Ages at latest evaluation (yr) | 6.3 ± 1.1 | 9.4 ± 1.9 | 12.7 ± 2.1 | 18.5 ± 2.0 |
| Duration of the second CI use (mo) | 42.9 ± 17.5 | 42.0 ± 20.0 | 32.1 ± 21.2 | 22.9 ± 10.3 |
| Pure-tone averages (dB HL) | | | | |
| The first CI | 29.4 ± 4.8 | 26.9 ± 7.5 | 24.0 ± 5.9 | 27.0 ± 6.8 |
| The second CI | 29.5 ± 4.0 | 25.7 ± 5.9 | 29.1 ± 7.4 | 29.8 ± 6.4 |
| Asan-Samsung Korean monosyllabic word recognition scores (%) | | | | |
| The first CI | 96.9 ± 4.8 | 99.2 ± 2.8 | 96.5 ± 6.1 | 89.1 ± 13.0 |
| The second CI | 96.9 ± 4.8 | 94.6 ± 8.3 | 91.2 ± 8.6 | 67.3 ± 25.3[b] |

[a]Plus–minus values are mean ± SD.
[b]$p < 0.001$ by the Mann–Whitney *U* test.
CI indicates cochlear implants.

reimbursement policy for only one CI (11). In those congenitally deaf children who previously underwent the first CI, it is not clear whether there may be the optimal and sensitive periods for the second CI and whether the periods for the second CI differs from those for the first CI.

Here, we systematically investigated the correlation between word recognition ability after the second CI and the age at the second CI operation. We wanted to determine the optimal period for the second CI, during which the performance of the second CI was similar to that of the first CI implanted during the optimal period (3.5 yr) for the first CI. We also wanted to determine the sensitive period for the second CI, during which the speech performance for the second CI is more than or equal to 80%, which is the estimated value for the first CI when implanted before the age of 7 years (the sensitive period for the first CI).

## PATIENTS AND METHODS

### Patients

We studied a cohort of congenitally deaf children (n = 73) who underwent sequential CI identified among 1,439 patients who underwent CI surgeries in our institute between March 1995 and January 2016. In 2009, Korean National Health Insurance Service started to reimburse for bilateral simultaneous CI for prelingually deaf children; since then, bilateral simultaneous CI was recommended for bilaterally deaf children and sequential CI were implanted in children who previously underwent unilateral CI. Children who received sequential CI with the first CI more than 3 years previous and the second CI more than 1 year previous were eligible for study participation because such a duration of CI use was needed to obtain a plateau on monosyllabic word recognition tests for children (unpublished data). All of the children were more than 5 years of age at the latest follow-up. The study was approved by the institutional review board. There was no commercial involvement in the trial.

We excluded children with any inner-ear anomaly identified on computed tomography and magnetic resonance imaging, syndromes, or combined disabilities, such as developmental disability, cognitive disability, mental retardation, and autism, which may have affected their ability to hear the sound and learn language. To identify inner-ear anomalies, radiological evaluation of the temporal bone was done with high-resolution computed tomography scans and magnetic resonance imaging. Inner-ear anomalies were classified in accordance with a reported classification system (12). All children were also evaluated by a pediatrician and psychologist for other combined disabilities that may have affected their ability to hear the sound and learn language before the CI operation, and additional consultations were obtained when necessary during the postoperative auditory rehabilitation process.

The study cohort consisted of 45 boys and 28 girls. The children were divided into four groups by the ages at the second CI operations: 1 to 3.5, 3.6 to 7, 7.1 to 13, and 13.1 to 19 years old (Table 1). The mean age at the first cochlear implant was 2.5 ± 1.6 years, while that at the second sequential CI was 7.6 ± 4.7 years. The mean device length used at the time of the latest language assessment was 37 ± 19 months for the second CI.

Most (64 of 73) patients were implanted in both ears with devices from Cochlear Corp. (Lane Cove, New South Wales, Australia) with various types of electrodes and speech processors. Devices from Advanced Bionics, Corp. (Sylmar, CA) were implanted in two for the first CI and MED-EL (Innsbruck, Austria) in two for the first CI and in eight for the second CI. After the first CI, hearing aids for the contralateral deaf ears were not used because the contralateral ears were almost deaf and hearing rehabilitation was focused on the first CI. On the second CI side, only five children showed severe hearing loss with threshold averages at four frequencies of 71 to 90 dB without effective discrimination, while the others were deaf.

### Assessment of Speech Perception

Speech perception tests for children have been used routinely to evaluate speech performance in CI recipients at 1 week and 1, 3, 6, and 12 months postactivation and annually thereafter. The children were evaluated with a protocol that included speech perception and production and spoken language skills. Speech perception tests for children consisted of closed-set word recognition, open-set monosyllabic and bisyllabic word recognition tests, sentence perception, and auditory performance. Asan-Samsung Korean (ASK) word recognition test was intended for use with young children and consist of 10 monosyllabic words familiar to younger children who are not familiar with the vocabulary of the word lists for adults. Open-set speech perception tests were administered to each child in an audio-only condition without the presence of visual cues: speech was presented 1 m in front of the child via monitored live voice at an approximate 70 dB sound pressure level. Live voice testing was generally used with the younger children to maintain their attention to the task. Open-set tests are those in which no response alternatives are provided and the listener repeats what is heard; theoretically, there are an unlimited number of response possibilities. We tried to keep the time required to complete the tests short because young children have limited attention spans.

All the children were assessed after more than 36 months of the first CI use and more than 12 months of the second CI use and the most recently collected data for each child were analyzed. Speech perception was tested in three conditions: using the first CI, the second CI, and both the first CI and the second CI.

### Primary Outcome

The ASK word recognition test remained the main outcome of this study because the most direct benefit of CI is improved speech perception and spoken word recognition. Thus, we used the open-set monosyllabic word recognition test scores as the primary outcome because the speech perception materials must be appropriate for the individual's age, developmental level, and linguistic level and the open-set tests simulate natural listening situations.

The ASK monosyllabic word recognition scores of the second CI were analyzed as a function of the ages at the second CI operations to find the optimal period for the second CI, during which the performance of the second CI was similar to that of the first CI implanted during the optimal period (3.5 yr) for the first CI. We also determined the sensitive period for the second CI, during which the speech performance for the second CI is more than or equal to 80%, which is the estimated value for the first CI when implanted before the age of 7 years (the sensitive period for the first CI). The ASK monosyllabic word recognition scores of the second CI were compared among the age groups, because it was suggested that there is a period of about 3.5 years for the first CI during which the central auditory system retains its maximum plasticity, although this could be extended in some children up to 7 years of age, after which it is significantly reduced (5).

### Statistical Analysis

Due to the skewed nature of the data, all of the analyses were nonparametric. The Mann–Whitney *U* test was used to compare the four groups for the ASK word recognition scores. The Wilcoxon signed-ranks test was used to determine whether the scores of the ASK word recognition scores of the first CI were different from those of the second CI in the same group. All reported *p* values were two-sided and declared statistically significant when $<0.05$. The statistical analyses were conducted using SPSS software (version 14.0 for Windows; IBM, Armonk, NY).

## RESULTS

### Word Recognition Scores of the second CI as a Function of Age at the second CI Operation

The ASK word recognition scores of the second CI showed a negative correlation with age at the second CI operation (Fig. 1A). The lines of best fit and the 95% confidence interval were superimposed on the raw data. We assumed that starting point is vertex since the first order term of quadratic form was not significant. The data were best fit by a growth function based on the quadratic term of age (the second CI scores $= -0.13 \times$ (age at the second CI operation)$^2 + 99.56$) with the *R*-squared value of 0.54. Visual inspection indicated that the second CI scores stayed at more than or equal to 80% until the age of 12 to 13 (12.23) years and then decreased rapidly. If we assume that the second CI scores more than or equal to 80% indicated successful (13), the sensitive period for the second CI to result in a successful word recognition score would be 12 to 13 years of age, while that for the first CI would be around 7 to 8 years of age (Fig. 1A). All six children with poor scores ($\leq$60%) of the second CI underwent the second CI operation after the age of 13 years, although the performances of the first CI were excellent because the first CI was implanted earlier (Fig. 1B).

### Comparison of the Second CI Scores Based on the Ages at the Second CI Operations

The patients were divided into four groups by age at the second CI operation: 1 to 3.5, 3.6 to 7, 7.1 to 13, and 13.1 to 19 years old (Table 1). No significant differences in the performances of the second CI were found among the first young three groups. And the performances of the second CI in the first young three groups were significantly higher than that of the oldest group (the children who received their second CI at an age >13 yr, which is the sensitive period for the second CI with word recognition scores <80%) ($p < 0.001$, Fig. 2A).

Comparison between the first CI and the second CI scores revealed no significant differences only when the second CI was implanted at less than 3.5 years of age, which is similar to the previously reported optimal period for the first CI (Fig. 2B). However, the scores of the second CI in the older three groups were statistically lower than those of the first CI in the older three groups: 3.6 to 7 group ($p = 0.02$), 7.1 to 13 group ($p = 0.013$), and 13.1 to 19 group ($p = 0.003$).

The four-frequency aided threshold levels for sound detection in the ears with the second CI in the oldest group were not different from not only those of the contralateral good-hearing the first CI ears but also those of the second CI ears of the other groups (Table 1 and Fig. 2A).

## DISCUSSION

What are the optimal and sensitive periods for the second CI in children who already developed some word recognition abilities using the first CI in one ear? In a study with 47 children with bilateral sequential CI, children who underwent the second CI up to the age of 13 years could achieve good speech perception (14). However, several reports argued that the second CI should also be implanted early because early unilateral hearing experiences involve the switching of aural preference, leaving the first CI ear preferentially represented in the auditory cortex and explaining the worse outcome of the second CI (14–17).

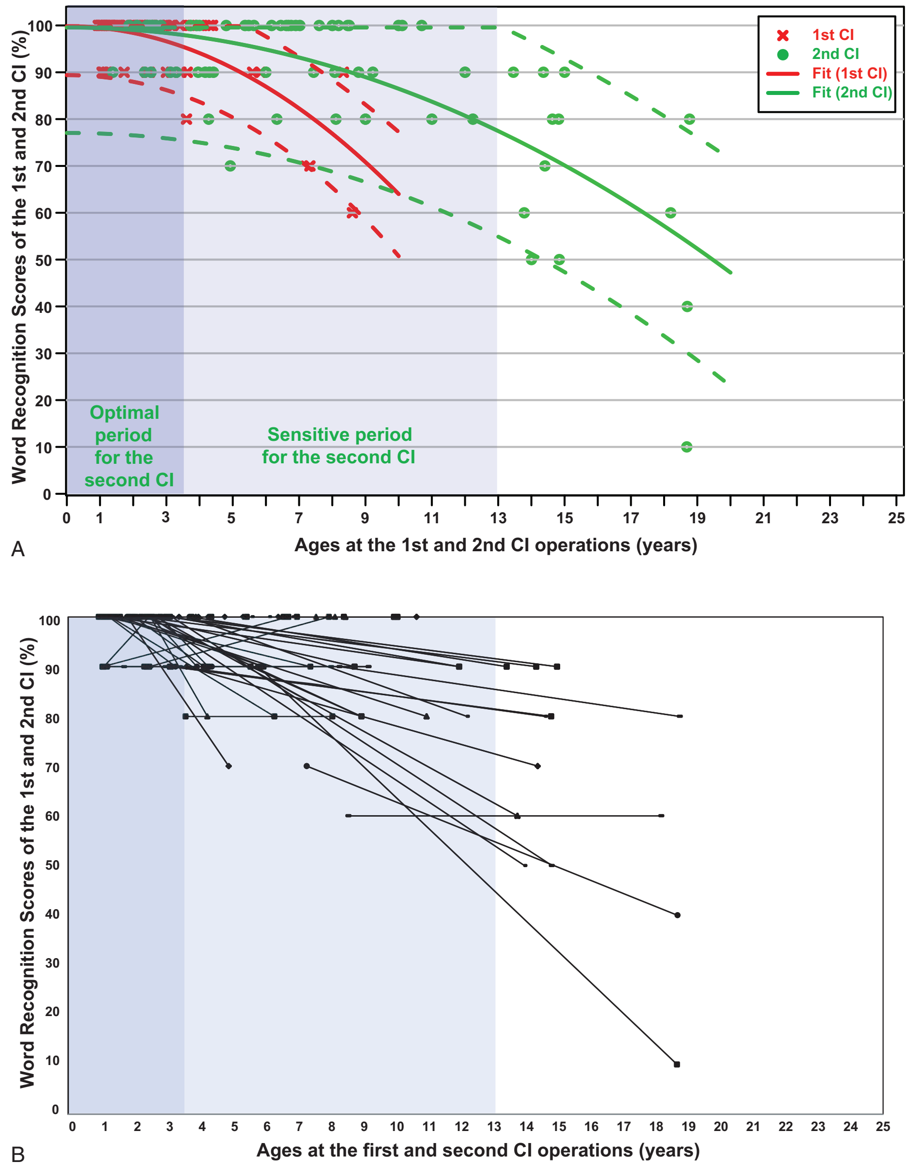


**FIG. 1.** The word recognition scores of the first and second CIs (Panel *A*) and individual plots of word recognition scores (Panel *B*) as a function of age at CI operation. Panel A shows the changes of word recognition scores as a function of age of implantation for bilateral CI subjects; for the first CI in dark gray cross and for the second CI in light gray circle. Word recognition performance decreases with increasing age of implantation. The first CI has a positive effect on the sensitive period (word recognition scores ≥80%) of the second CI and it increases the sensitive period of the second CI up to 12 to 13 years. Panel B shows individual and interaural differences in word recognition scores of the first and second CI as a function of age at CI operation. CI indicates cochlear implants.

In children of our study, the second CI scores of the youngest age subgroup (the second CI operation at 1–3.5 yr of age) were comparable to the first CI scores and the highest in all age groups, suggesting that the optimal period (3.5 yr of age) for the second CI is similar to that for the first CI.

Although the first CI scores were more than or equal to 80% when the first CI was implanted before the age of 7 to 8 years (the sensitive period for the first CI), the second CI scores were more than or equal to 80% when the second CI was implanted before the age of 12 to 13 years. When the second CI was implanted at 3.6 to 13 years of age, the second CI scores were comparable to those of the youngest age subgroup (Fig. 2A), but the oldest group (children who received the second CI at >13 yr of age) achieved the lowest the second CI scores. Thus, the sensitive period (12–13 yr of age) for the second CI, during which the second CI could result in word recognition score more than or equal to 80% and decline thereafter, seemed to be much longer than the sensitive period (7 yr of age) for the first CI (Figs. 1 and 2).

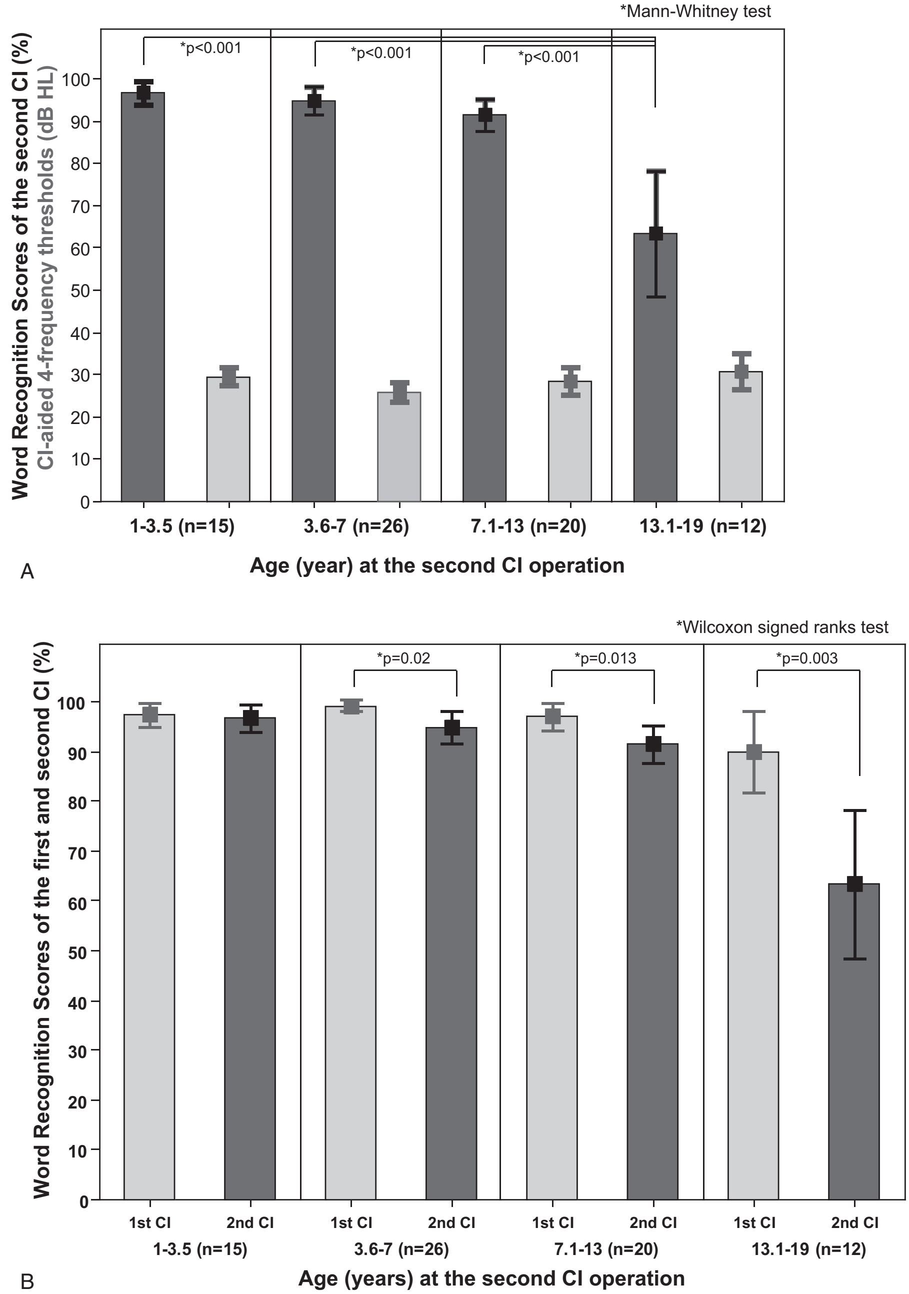


**FIG. 2.** The word recognition scores (95% confidence interval for the mean, dark gray) of the second CI and aided pure-tone thresholds (light gray) by the age at the second CI operation (Panel *A*) and the comparison between the scores of the first and second CIs (Panel *B*). In Panel *A*, the speech performance of the second CI in the first three subgroups (before age of 13 yr) were significantly higher than those from the oldest subgroup who underwent the second CI after the age of 13 years, though the hearing thresholds to the sound was not different from each other. When the second CI was implanted at less than 3.5 years of age (optimal period for the second CI), the performance of the second CI (dark gray) was comparable to that (light gray) of the first CI (Panel *B*), thereafter the scores of the second CI were lower than those of the first CI. CI indicates cochlear implants.

Interestingly, the loudness levels for sound perception itself (pure-tone averages) in the ears of the second CI in the oldest group were not different from not only those of the contralateral good-hearing CI-aided ears but also those of the ears with the second CI in the other groups (Table 1 and Fig. 2A). This finding suggests that they could hear the sounds well using the second CI regardless of the ages, but could not discriminate speech when the second CI was implanted after the age of 13 years. Our findings showed that the auditory stimulation from one ear prolonged the sensitive period of the contralateral ear for the second CI, possibly by preserving auditory cortical plasticity. Though their earlier implanted first CI could hear and understand the spoken words very well, the contralateral ears with the second CI could hear the words with similar sound detection abilities but not understand them through the second CI by lack of discriminating ability when implanted after the sensitive period. These findings might be related to the decreased plasticity of the auditory and associated cortices.

Although the performance of the second CI decreases rapidly after the sensitive period, there should a caution in limiting patient ages for the second CI because there were large individual variations. For example, the second CI performed in one patient aged 19 years could provide adequate speech perception (Fig. 1A). Variability in word recognition across subjects is also widely recognized and related to not only age at implantation but also inner-ear malformations, combined disabilities, mode of communication, family support, and the duration of deafness (18–23).

Because the primary benefit of CI use for children with prelingual deafness is improved speech perception and we cannot test all the children after they reach adulthood, we compared the results of ASK monosyllabic word recognition test for children, which is familiar to younger children and easy to reach ceiling levels in those children. We also tested the children using a monosyllabic word recognition test for adults and observed similar results. The limitation of this study is that our data did not provide any evidence regarding whether the auditory systems enable processing of binaural cues available through bilateral stimulation when it is performed within the sensitive period. Children who received CI with an inter-implant delay more than 2 years were reported to show mismatched timing of auditory activity in the brainstem and a biased input to the cortex, creating difficulties in perceiving inter-implant timing differences to localize sound and distinguish between sounds separated in space (3,14,17,24,25).

The selection regarding which ear to implant initially was based on surgical, medical, and audiological factors, regarding which ear had more residual hearing as that would usually indicate better preservation of neural pathways and a higher likelihood of a better outcome. Though it is possible for the ear of second CI to have less preserved neural pathways than the ear of the first CI, most of patients were bilaterally deaf, which was similar to each other, and all the patients had no inner ear anomaly. Thus, we assumed that the effect of the preoperative interaural difference would be minimal. The strength of this study is that we studied the largest cohort from a single institute that used the same evaluation protocol during a long follow-up period.

## CONCLUSION

Our cohort of children with bilateral sequential CI demonstrated that the second CI showed comparable word recognition to the first CI when implanted before 3.5, which is also the optimal period for the first CI. However, the sensitive period (13 yr of age) for the second CI, resulting in relatively good word recognition and decline thereafter, was much longer than that (7 yr) of the first CI. Our findings suggest that the second CI should be implanted early, but considered even at a later age because the first CI, which was implanted earlier successfully, prolonged the sensitive period for the second CI.

## REFERENCES

1. Niparko JK, Tobey EA, Thal DJ, et al. Spoken language development in children following cochlear implantation. *JAMA* 2010;303:1498–506.
2. O'Donoghue GM, Nikolopoulos TP, Archbold SM. Determinants of speech perception in children after cochlear implantation. *Lancet* 2000;356:466–8.
3. Kral A, Hubka P, Heid S, et al. Single-sided deafness leads to unilateral aural preference within an early sensitive period. *Brain* 2013;136:180–93.
4. Connor CM, Craig HK, Raudenbush SW, et al. The age at which young deaf children receive cochlear implants and their vocabulary and speech-production growth: Is there an added value for early implantation? *Ear Hear* 2006;27:628–44.
5. Sharma A, Dorman MF, Spahr AJ. A sensitive period for the development of the central auditory system in children with cochlear implants: implications for age of implantation. *Ear Hear* 2002;23:532–9.
6. Kral A, Sharma A. Developmental neuroplasticity after cochlear implantation. *Trends Neurosci* 2012;35:111–22.
7. Svirsky MA, Teoh SW, Neuburger H. Development of language and speech perception in congenitally, profoundly deaf children as a function of age at cochlear implantation. *Audiol Neurootol* 2004;9:224–33.
8. van Schoonhoven J, Sparreboom M, van Zanten BG, et al. The effectiveness of bilateral cochlear implants for severe-to-profound deafness in adults: a systematic review. *Otol Neurotol* 2013;34:190–8.
9. Laske RD, Veraguth D, Dillier N, et al. Subjective and objective results after bilateral cochlear implantation in adults. *Otol Neurotol* 2009;30:313–8.
10. Ramsden JD, Gordon K, Aschendorff A, et al. European bilateral pediatric cochlear implant forum consensus statement. *Otol Neurotol* 2012;33:561–5.
11. Ramsden JD, Papaioannou V, Gordon KA, et al. Parental and program's decision making in paediatric simultaneous bilateral cochlear implantation: who says no and why? *Int J Pediatr Otorhinolaryngol* 2009;73:1325–8.
12. Sennaroglu L. Cochlear implantation in inner ear malformations—a review article. *Cochlear Implants Int* 2010;11:4–41.
13. Thornton AR, Raffin MJ. Speech-discrimination scores modeled as a binomial variable. *J Speech Hear Res* 1978;21:507–18.
14. Graham J, Vickers D, Eyles J, et al. Bilateral sequential cochlear implantation in the congenitally deaf child: evidence to support the concept of a 'critical age' after which the second ear is less likely to provide an adequate level of speech perception on its own. *Cochlear Implants Int* 2009;10:119–41.
15. Gordon K, Henkin Y, Kral A. Asymmetric hearing during development: the aural preference syndrome and treatment options. *Pediatrics* 2015;136:141–53.
16. Peters BR, Litovsky R, Parkinson A, et al. Importance of age and postimplantation experience on speech perception measures in children with sequential bilateral cochlear implants. *Otol Neurotol* 2007;28:649–57.
17. Gordon KA, Jiwani S, Papsin BC. What is the optimal timing for bilateral cochlear implantation in children? *Cochlear Implants Int* 2011;12 (Suppl):S8–14.

18. Brackett D, Zara CV. Communication outcomes related to early implantation. *Am J Otol* 1998;19:453–60.
19. Waltzman SB, Cohen NL, Gomolin RH, et al. Long-term results of early cochlear implantation in congenitally and prelingually deafened children. *Am J Otol* 1994;15 (Suppl):9–13.
20. Wang NY, Eisenberg LS, Johnson KC, et al. Tracking development of speech recognition: longitudinal data from hierarchical assessments in the Childhood Development after Cochlear Implantation Study. *Otol Neurotol* 2008;29:240–5.
21. Fryauf-Bertschy H, Tyler RS, Kelsay DM, et al. Cochlear implant use by prelingually deafened children: the influences of age at implant and length of device use. *J Speech Lang Hear Res* 1997;40:183–99.
22. Wiley S, Meinzen-Derr J, Choo D. Auditory skills development among children with developmental delays and cochlear implants. *Ann Oto Rhinol Laryngol* 2008;117:711–8.
23. Beer J, Harris MS, Kronenberger WG, et al. Auditory skills, language development, and adaptive behavior of children with cochlear implants and additional disabilities. *Int J Audiol* 2012; 51:491–8.
24. Gordon KA, Valero J, Papsin BC. Auditory brainstem activity in children with 9–30 months of bilateral cochlear implant use. *Hear Res* 2007;233:97–107.
25. Gordon KA, Wong DD, Papsin BC. Cortical function in children receiving bilateral cochlear implants simultaneously or after a period of interimplant delay. *Otol Neurotol* 2010;31:1293–9.