The Journal of International Advanced Otology

J Int Adv Otol 2024; 20(4): 289–300 • DOI: 10.5152/iao.2024.231457

Original Article

Cochlear Implantation in Single-Sided Deafness and Asymmetric Hearing Loss: 12 Months Follow-up Results of a European Multicenter Evaluation

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Cite this article as: Wesarg T, Aschendorff A, Baumgaertel R, et al. Cochlear implantation in single-sided deafness and asymmetric hearing loss: 12 months follow-up results of a European multicenter evaluation. *J Int Adv Otol.* 2024;20(4):289-300.

BACKGROUND: People with single-sided deafness (SSD) or asymmetric hearing loss (AHL) have particular difficulty understanding speech in noisy listening situations and in sound localization. The objective of this multicenter study is to evaluate the effect of a cochlear implant (CI) in adults with single-sided deafness (SSD) or asymmetric hearing loss (AHL), particularly regarding sound localization and speech intelligibility with additional interest in electric-acoustic pitch matching.

METHODS: A prospective longitudinal study at 7 European tertiary referral centers was conducted including 19 SSD and 16 AHL subjects undergoing cochlear implantation. Sound localization accuracy was investigated in terms of root mean square error and signed bias before and after implantation. Speech recognition in quiet and speech reception thresholds in noise for several spatial configurations were assessed preoperatively and at several post-activation time points. Pitch perception with CI was tracked using pitch matching. Data up to 12 months post activation were collected.

RESULTS: In both SSD and AHL subjects, CI significantly improved sound localization for sound sources on the implant side, and thus overall sound localization. Speech recognition in quiet with the implant ear improved significantly. In noise, a significant head shadow effect was found for SSD subjects only. However, the evaluation of AHL subjects was limited by the small sample size. No uniform development of pitch perception with the implant ear was observed.

CONCLUSION: The benefits shown in this study confirm and expand the existing body of evidence for the effectiveness of CI in SSD and AHL. Particularly, improved localization was shown to result from increased localization accuracy on the implant side.

KEYWORDS: Cochlear implant, single-sided deafness, asymmetric hearing loss, sound localization, speech intelligibility

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Received: December 09, 2023 • **Accepted:** April 14, 2024 • **Publication Date:** July 29, 2024
Available online at www.advancedotology.org

INTRODUCTION

Binaural hearing enables human normal-hearing (NH) listeners to localize sound sources with high accuracy and provides speech intelligibility advantages in noisy environments.[1,2] These benefits are less pronounced or even unavailable in subjects with one ear inflicted by severe-to-profound hearing loss and normal hearing[3,4] or a slight-to-moderate hearing loss[5-7] in the contralateral ear. Such unilateral or asymmetric bilateral hearing losses with a pure-tone average (PTA) of ≥70 dB HL in the poorer ear and a PTA of ≤30 dB HL or a PTA of >30 and ≤55 dB HL in the better ear are referred to as single-sided deafness (SSD) or asymmetric hearing loss (AHL), respectively.[8]

Traditionally, subjects with SSD or AHL were treated using (bilateral) contralateral routing of signal ((Bi)CROS) hearing aids or bone conduction devices (BCDs). Both types of rehabilitation successfully restore some of the benefits gained by hearing with 2 ears. However, they do not intend to (re)habilitate hearing in the poorer ear, and thus binaural hearing.[9]

In recent years, cochlear implantation has become a viable treatment option for SSD and AHL. While initially it was only considered in cases of debilitating tinnitus,[10,11] current indication criteria include adults with postlingual unilateral severe-to-profound hearing loss with and without tinnitus.[5] Unlike (Bi)CROS hearing aids and BCDs, CIs restore hearing in the poorer ear and thus bilateral auditory input allowing for binaural processing and benefits.[9,12]

To date, several studies have investigated the effect of CI in postlingually deafened adult SSD and/or AHL subjects, reporting improved sound localization accuracy[9,13-17] and better speech intelligibility, especially in noise,[6,9,11-14,18-21] confirming partial restoration of binaural hearing in SSD and AHL. Newer aspects of CI in SSD and AHL include pitch matching between the acoustically hearing ear and the implant ear.[22-24]

Sound localization accuracy was mainly addressed in terms of localization error with all studies reporting a significant reduction of localization error with CI, i.e., a significant benefit in localization accuracy.[9,13-17,25] Only a few studies evaluated additional measures of localization accuracy such as bias[13,25] or bias-adjusted deviation.[25] The assessment of speech intelligibility in noise is largely focused on spatial listening, aiming to investigate binaural effects such as (combined) head shadow, summation, and squelch (see Durlach and Colburn[26] for definitions). While a significant benefit of CI based on the restoration of the (combined) head shadow effect was found in most studies,[6,11,12,19-21] only some of them revealed significant summation[12,21] and/or squelch effects.[6,12,19,20] Recent reviews of studies on CI treatment in SSD and AHL can be found in Sampathkumar et al,[27] Thompson et al,[28] and Oh et al.[29]

Here, we present results from a prospective longitudinal European multicenter study on the effect of CI in SSD and AHL conducted in 7 tertiary referral centers. The main focus was to assess the benefit of CI on sound localization accuracy and speech intelligibility in quiet and noise in adult subjects with SSD or AHL up to 12 months post activation. Furthermore, following implantation, pitch perception for electric stimulation at single electrodes was evaluated.

MAIN POINTS

- Cochlear implantation in adults with single-sided deafness (SSD) or asymmetric hearing loss (AHL) improves the accuracy of sound localization for sound sources on the implant side, and thus overall sound localization.
- Improvement in sound localization accuracy affects both measures, root mean square error, and signed bias.
- Cochlear implantation in adults with SSD also improves speech intelligibility in noise for presentation of speech from the front and noise from the side of the contralateral acoustically hearing ear, i.e., restores head shadow benefit.

MATERIAL AND METHODS

Subjects

At inclusion, the ear to be implanted had to meet the following criteria: unaided pure-tone air-conduction thresholds of ≥50 dB HL at 500 Hz, ≥60 dB HL at 1000 Hz, ≥70 dB HL at 2000, 4000 and 8000 Hz, and marginal hearing aid benefit, defined as word recognition in quiet at 65 dB SPL of ≤50% in best-aided condition (unaided or with hearing aid). Furthermore, postlingual onset of severe-to-profound hearing loss and duration of hearing loss of more than 3 months was required. Depending on the hearing status of the contralateral ear, subjects were included in 1 of 2 subgroups: SSD subjects with normal hearing to slight hearing loss defined as unaided PTA air-conduction threshold at 0.5, 1, 2, and 4 kHz of ≤25 dB HL, and AHL subjects with a PTA of >25 dB HL as well as speech recognition in quiet at 65 dB SPL of ≥70% in best-aided condition. In total, 35 adults, 19 SSD and 16 AHL subjects were included, 5 each from European Institute for ORL, Ghent University Hospital, University Hospitals Leuven and University Clinic St. Pölten, 8 from Unfallkrankenhaus Berlin, 4 from Düsseldorf University Hospital, and 3 from Medical Center – University of Freiburg. Two AHL subjects withdrew from the study after 3 months citing personal reasons. Detailed demographic information is presented in Table 1, and summarized information is shown in Table 2.

Ethical Considerations

This prospective study was approved by the Ethics Committee of the site of the coordinating investigator, the Ethics Committee of the University of Freiburg, Germany (Approval Number 440/14, Date January 8, 2015), and by the Ethics Committees of all other study sites. All procedures were performed in accordance with the Declaration of Helsinki (2013). Written informed consent was collected from all subjects prior to inclusion.

Study Schedule

Subjects were implanted unilaterally with a HiRes 90K Advantage implant with a HiFocus™ 1J or HiFocus™ Mid-Scala electrode (Advanced Bionics LLC, Valencia, CA, USA). Device activation was performed within 4 weeks after surgery, using a Naída CI Q Series sound processor. Follow-up visits were scheduled at 1, 3, 6, and 12 months following CI activation.

Measurements

Pure-Tone Thresholds

Pure-tone air-conduction thresholds of each ear were measured according to DIN EN 8253-1. When testing the ear to be implanted

Table 1. Subject Demographics. Shaded Rows Indicate Subjects Who Withdrew After the 3 Months Appointment

Subgroup	ID	Gender	Age at Implantation (Years)	Implant Side	Etiology Ipsilateral	PTA Ipsilateral (dB HL)[1]	Duration of Severe-to-Profound HL Ipsilateral (Years)[2]	HA Use Contralateral	Etiology Contralateral	PTA Contralateral (dB HL)[1]	Word Score Contralateral (%)[3]
AHL	AHL1	F	61	R	Acute hearing loss	100	2	Yes	Unknown	35	70
AHL	AHL2	M	71	L	Ménière's disease	94	10	Yes	Unknown	31	100
AHL	AHL3	M	70	R	Acute hearing loss	93	8	Yes	Acute hearing loss	42	70
AHL	AHL4	M	77	R	Acute hearing loss	130	7	Yes	Presbycusis	46	80
AHL	AHL5	M	59	R	Vestibular schwannoma	130	1	Yes	Acute hearing loss	29	95
AHL	AHL6	M	46	R	Ototoxicity	130	5	No	Unknown	26	85
AHL	AHL7	M	45	L	Acute hearing loss	84	2	Yes	Unknown	33	100
AHL	AHL8	F	63	R	Acute hearing loss	130	15	No	Acute hearing loss	38	100
AHL	AHL9	F	42	L	Meningitis (childhood)	130	34	Yes	Unknown	48	100
AHL	AHL10	M	81	R	Unknown	130	1	Yes	Unknown	45	100
AHL	AHL11	M	66	L	Unknown	81	19	No	Unknown	34	80
AHL	AHL12	F	38	R	Unknown	108	5	No	Unknown	36	80
AHL	AHL13	M	18	L	Unknown	119	1.5	Yes	Unknown	51	85
AHL	AHL14	M	75	L	Unknown	105	5	Yes	Unknown	55	88
AHL	AHL15	M	47	L	Ménière's disease	99	7	Yes	Ménière's disease	63	74.5
AHL	AHL16	F	58	L	Unknown	90	3	No	Unknown	36	90.5
SSD	SSD1	M	51	L	Temporal bone fracture	120	1	No	N/A	10	90
SSD	SSD2	F	57	R	Acute hearing loss	130	0.5	No	N/A	15	100
SSD	SSD3	F	35	R	Failed VSB surgery	130	5	No	N/A	5	100
SSD	SSD4	F	55	R	Middle ear pathologies (adolescence)	130	3	No	N/A	15	100
SSD	SSD5	F	66	L	Acute hearing loss	130	2	No	N/A	9	100
SSD	SSD6	M	57	R	Ménière's disease	99	16	No	N/A	19	90
SSD	SSD7	F	68	R	Acute hearing loss	75	10	No	N/A	16	95[4]
SSD	SSD8	M	42	R	Unknown	130	20	Yes (BiCROS)	N/A	16	95[4]
SSD	SSD9	F	30	L	Unknown	130	3	No	N/A	18	95[4]
SSD	SSD10	M	48	R	Unknown	130	1	No	N/A	10	100
SSD	SSD11	M	62	R	Unknown	81	4	No	N/A	9	100
SSD	SSD12	M	36	L	Middle ear surgery	124	3.5	No	N/A	20	100
SSD	SSD13	M	43	R	Temporal bone fracture	106	3	No	N/A	14	100
SSD	SSD14	M	47	L	Hereditary	115	5	Yes	N/A	16	100
SSD	SSD15	M	68	L	Unknown	91	5	Yes (BiCROS)	N/A	13	98[4]
SSD	SSD16	M	55	R	Ménière's disease	89	11	Yes (BiCROS)	N/A	10	100
SSD	SSD17	M	56	L	Unknown	84	1	No	N/A	4	100
SSD	SSD18	F	37	L	Autoimmune disease	130	0.5	No	N/A	18	90.5
SSD	SSD19	F	47	R	Unknown	98	5	No	N/A	13	98.5

AHL, asymmetric hearing loss; F, female; HA, hearing aid; HL, hearing loss; L, left; M, male; PTA, pure-tone average; R, right; SSD, single-sided deafness; VSB, Vibrant Soundbridge.

[1]Average across 0.5, 1, 2, and 4 kHz, rounded to the nearest dB.

[2]Prior implantation.

[3]At baseline, at 65 dB SPL, aided score for HA users, unaided for non-users.

[4]Scores at pre-baseline appointment.

Table 2. Summarized Subject Demographics. Subjects Who Withdrew After the 3 Months Appointment Were Removed from the Statistics

		Age at Implantation (Years)	Duration of Severe to Profound HL Ipsilateral (Years)[2]	PTA Contralateral (dB HL)[1]	Word Score Contralateral (%)[3]
SSD subjects	Min	30	0.5	4	90
	Median	51	3.5	14	100
	Max	68	20	20	100
AHL subjects	Min	18	1	29	70
	Median	60	5	39	86.5
	Max	81	34	63	100
All subjects	Min	18	0.5	4	70
	Median	55	4	18	98
	Max	81	34	63	100

AHL, asymmetric hearing loss; HL, hearing loss; PTA, pure-tone average; SSD, single-sided deafness.
[1]Average across 0.5, 1, 2, and 4 kHz, rounded to the nearest dB.
[2]Prior implantation.
[3]At baseline, at 65 dB SPL, aided score for HA users, unaided for non-users

at baseline and post activation, the contralateral ear was masked. Ipsilateral thresholds were assessed at baseline and contralateral thresholds at baseline and each follow-up visit.

Sound Localization

Sound localization accuracy was tested using a 7-loudspeaker setup with loudspeakers located in a frontal semicircle at 0°, ±30°, ±60°, and ±90° at the listener's ear level at a distance of 1 meter from the subject's head. Stimuli were presented from one of the loudspeakers in random order across speakers and levels. Presentation levels were roved between 59 and 71 dB SPL (mean level 65 dB SPL). Stimuli were sentences from the Oldenburg sentence test (OLSA)[30] (German-speaking centers) or the Leuven Intelligibility Sentence Test (LIST)[31] (Belgian centers).

For display and analysis of the results, data were normalized so that negative angles correspond to the CI side and positive angles correspond to the acoustically hearing side for all subjects. Localization accuracy was quantified in terms of overall root mean square (RMS) error and overall signed bias, calculated as

$$RMS_{err} = \alpha\sqrt{\frac{1}{K}\sum_{k=1}^{K}\frac{1}{M}\sum_{m=1}^{M}\left(r_{k,m}-k\right)^2}$$

and

$$Signed\ bias = \alpha\frac{1}{K}\sum_{k=1}^{K}\frac{1}{M}\sum_{m=1}^{M}\left(r_{k,m}-k\right).$$

where K represents the number of target loudspeakers used in the setup (7), M the number of trials performed per loudspeaker (10), α the angular separation between loudspeakers in degrees (30°), $r_{k,m}$ the subject's response about the perceived loudspeaker location (numbers 1 through 7) on the m^{th} trial for loudspeaker k.

For target azimuth specific analysis, calculation of RMS error and signed bias was reduced to

$$RMS_{err,k} = \alpha\sqrt{\frac{1}{M}\sum_{m=1}^{M}\left(r_{k,m}-k\right)^2}$$

and

$$Signed\ bias_k = \alpha\frac{1}{M}\sum_{m=1}^{M}\left(r_{k,m}-k\right).$$

Localization accuracy was obtained in bilateral best-aided condition at baseline and 12 months post activation.

Speech Intelligibility

Speech recognition in quiet, assessed in percent correct, was tested in the unaided and aided listening condition for each ear using Freiburg monosyllables[32] in German-speaking centers or Flemish monosyllables[33] in Belgian centers. Speech was presented via headphones in the unaided condition and in free-field in the aided condition each at 65 dB SPL. If applicable, the contralateral ear was masked. Unaided ipsilateral word scores were obtained at baseline. Unaided contralateral, as well as aided ipsilateral and contralateral word scores, were recorded at baseline and at 3, 6, and 12 months post activation, as well as aided speech recognition in quiet at 65 dB SPL for each ear using the OLSA or LIST.

At baseline and each follow-up visit, speech intelligibility in noise was assessed as speech reception threshold (SRT) for OLSA or LIST sentences in stationary speech-weighted noise (OLnoise or LIST noise). For each SRT measurement, the noise level was fixed at 65 dB SPL while the speech level was varied adaptively starting at 65 dB SPL, to yield the signal-to-noise ratio, at which 50% of the speech material was intelligible. Using 3 loudspeakers at −90°, 0°, and 90°, SRTs were assessed in 3 spatial configurations: presentation of speech and noise from the front (S_0N_0) as well as speech from the front and noise either from the side of the CI ear (S_0N_{CI}) or the contralateral acoustically hearing ear (S_0N_{AC}). For S_0N_0, SRTs were measured for each ear separately as well as binaurally, and for S_0N_{AC} and S_0N_{CI} for the contralateral ear and binaurally, each in the best-aided condition.

If applicable, the contralateral ear was masked using OLnoise or LIST noise at 65 dB SPL. Speech intelligibility in noise was only assessed if speech intelligibility in quiet at 65 dB SPL in the listening modality to be tested was ≥80%.

Pitch Perception

At each follow-up visit, pitch perception with CI was evaluated for single-electrode stimulation by performing pitch matching, i.e., pitch comparisons between the implant ear and the contralateral ear according to Carlyon et al.[22]

For electrical stimulation, electrodes 1 and 4 were used. If one or both was deactivated, electrodes 2 and 5 were used instead. For each electrode, stimuli were sets of pulses repeating at a rate of 12.5 Hz, achieved by presenting a train of short tone pips at 12.5 Hz and with a carrier frequency equal to the center frequency of the channel corresponding to the electrode (333 and 642 Hz for electrodes 1 and 4, respectively) to the sound processor via direct audio input. Activation of all other electrodes was avoided by use of a customized CI program with T and M levels of those electrodes set to 0.

The acoustically hearing ear was stimulated via headphones using filtered pulse trains with a repetition rate of 12.5 Hz and varying center frequency (f_c). For each electrode, 2 blocks of acoustic stimuli were created, each consisting of 5 different values of f_c, 1 block representing lower frequencies (348-1055 Hz or 459-1392 Hz for electrodes 1 (or 2) and 4 (or 5), respectively), and the other block representing higher frequencies (606-1837 Hz or 799-2423 Hz, respectively). Acoustic stimuli were set to a "soft but comfortable" level, and single-electrode electric stimulation was matched in loudness.

Subjects were presented with 1 electric and 1 acoustic stimulus in random order and were asked to indicate which of these stimuli had higher pitch. For each electrode, each of both stimulus blocks per electrode, and each f_c of the acoustic stimuli, 20 repetitions of electric-acoustic stimulus pairs were administered. Measurement tracks for the 2 electrodes and the 2 respective stimulus blocks were applied in an interleaved fashion, and 4 psychometric curves were obtained. For each curve, the point of subjective equality was determined, which is the frequency of the acoustic stimulus that is judged higher in pitch than the electric stimulus on 50% of the trials.

Statistical Analysis

Statistical analysis was performed using R version 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria).[34] Due to the small sample size of both subgroups, SSD and AHL, and Shapiro–Wilk tests revealing non-normal distribution of data ($P \geq .05$), non-parametric tests were used. Time effects for outcome measures were analyzed using Friedman's analysis of variance (ANOVA). Pairwise comparisons were performed using Wilcoxon signed-rank tests. Bonferroni–Holm corrections for multiple comparisons were applied where necessary.

Outcome measures were first tested for differences between the SSD and AHL subgroups using Mann–Whitney *U*-tests. If no significant differences were found for any time point, SSD and AHL data were pooled. If significant differences were found at any time point, separate analyses were conducted for each subgroup. No further division into German- and Flemish-speaking subjects was applied to avoid further reduction of sample sizes. Since within-subject comparisons were applied, language-specific effects were minimized, justifying the pooling of all subjects. Differences in between-subject measures and within-subject measures were expressed as median differences (*md*) or median improvements (*mi*), which were calculated as medians of the individual differences or improvements.

RESULTS

Sound Localization

Sound localization accuracy was determined binaurally in the best-aided condition at baseline and 12 months after device activation. Sound localization was not investigated at St. Pölten and Ghent, and data from Antwerp were not included in the analysis due to a differing test setup used in this center. Therefore, data could be analyzed from 13 AHL and 7 SSD subjects at baseline. At 12 months follow-up, 2 AHL subjects had withdrawn and, for 1 additional AHL subject, localization tests were not performed due to time constraints, resulting in 17 complete datasets which are presented in the following.

Localization accuracy presented as response azimuth as a function of target azimuth for SSD subjects, AHL subjects, and all (SSD and AHL) subjects is shown in Figure 1, top row for the baseline appointment and second row for the 12 months follow-up appointment. Group medians (black lines) show localization responses at baseline to be largely focused on the side of the acoustically hearing ear (+90°, AC side) regardless of the target azimuth. Results at 12 months reveal a larger response-azimuth range with responses for targets on the implant side shifting towards −90° (CI side) while responses for targets on the acoustically hearing side remain at +90° (AC side). This change in localization behavior was more apparent in the SSD subgroup than the AHL subgroup.

Localization accuracy was analyzed in terms of RMS error and signed bias. Compared to the location of the target stimulus, positive values of signed bias indicate a tendency to localize sounds more towards the acoustically hearing ear while negative values indicate a tendency to localize sounds more towards the implant ear. Perfect localization performance would result in both RMS error and signed bias of 0°. Both measures are represented in Figure 1, rows 3 and 4, respectively, as a function of target azimuth. Root mean square error and signed bias revealed an improvement in localization accuracy from baseline to 12 months, indicated by lower values for both measures and most pronounced for targets located on the implant side (−90°).

The RMS error differed significantly between the AHL and SSD subgroups at baseline for target azimuths +60° (*md* = 16.5°, $W = 62.0$, $P = .0094$) and +90° (*md* = 22.5°, $W = 57.0$, $P = .0330$); and therefore, both subgroups were analyzed independently. In the SSD subgroup, a significant decrease of RMS error at 12 months compared to baseline was found for targets located at −90° (*mi* = 56.6°, $V = 28.0$, $P = .0156$), −60° (*mi* = 36.0°, $V = 28.0$, $P = .0156$) and −30° (*mi* = 48.0°, $V = 21.0$, $P = .0360$). In the AHL subgroup, compared to baseline, a significant reduction of RMS error at 12 months was found for targets located at −90° (*mi* = 46.3°, $V = 47.0$, $P = .0488$). These significant differences indicate an improvement in localization accuracy.

As the signed bias differed significantly between the AHL and SSD subgroups at baseline for target azimuths +60° (*md* = 31.1°, $W = 9.5$, $P = .0146$) and +90° (*md* = 22.5°, $W = 13.0$, $P = .0330$), both subgroups

were analyzed separately. In the SSD subgroup, significant differences in signed bias between baseline and 12 months were found for targets located at −90° (*mi* = 56.6°, *V* = 21.0, *P* = .0156), −60° (*mi* = 67.3°, *V* = 28.0, *P* = 0.0156), −30° (*mi* = 66.0°, *V* = 21.0, *P* = .0360) and 0° (*mi* = 41.6°, *V* = 21.0, *P* = .0360). In the AHL subgroup, a significant difference in signed bias between baseline and 12 months was found for targets located at −90° (*mi* = 46.3°, *V* = 47.0, *P* = .0488) and −60° (*mi* = 47.3°, *V* = 47.0, *P* = .0488). All significant differences indicate an improvement in performance from baseline to 12 months, i.e., a signed bias score closer to 0°.

Combined across all target azimuths, overall RMS error and overall signed bias are presented for SSD, AHL, and all (SSD and AHL) subjects at baseline and 12 months in Figure 2. Overall RMS error and signed bias did not differ between the AHL and SSD subgroups at baseline and 12 months ($P \geq .05$); therefore, both subgroups were pooled for further analyses. Wilcoxon signed-rank tests revealed a statistically significant improvement in pooled overall RMS error (*mi* = 28.9°, *V* = 143.0, *P* = .0007) and overall signed bias (*mi* = 38.9°, *V* = 136.0, *P* = .0052) from baseline to 12 months.

Speech Intelligibility with Implant Ear

Due to a differing test setup used at St. Pölten, only speech test data from the German and Belgian centers are included in the analysis.

Ipsilateral speech recognition in quiet with the implant ear at baseline was not recorded for numerous subjects, especially those with hearing thresholds outside the measurable range, further limiting the number of complete datasets. Figure 3, left panel shows word recognition in quiet at 65 dB SPL achieved at baseline and with the implant over time for the remaining 12 SSD subjects, 8 AHL subjects, and pooled for all 20 subjects with full datasets available.

No significant difference in word recognition between SSD and AHL subjects was found at any time point ($P \geq .05$); therefore, all subjects were analyzed collectively. Friedman's ANOVA revealed a significant effect of time point ($\chi^2(3) = 35.478$, $P = .0000$). Post hoc comparisons yielded significant differences in word recognition between baseline (group median *m* = 0.0%) and the following post-activation time points: 3 months (*m* = 92.5%, *P* = .0013), 6 months (*m* = 85.0%, *P* = .0013), and 12 months (*m* = 91.0%, *P* = .0006).

Speech reception threshold in noise was only assessed if, at the same time point, the sentence score in quiet at 65 dB SPL with the implant ear was ≥80%. Therefore, complete datasets of SRTs for frontal presentation of speech and noise with CI alone over time could be obtained for 11 SSD subjects and 5 AHL subjects and are presented in Figure 3, right panel. For each time point, SRT did not differ significantly between SSD and AHL subjects ($P \geq .05$), and no significant effect of time point on SRT was observed in the pooled group ($\chi^2(2) = 1.4098$, $P = .4941$).

Benefit of Implant Ear for Speech Intelligibility in Noise

Aided sentence reception in noise was only assessed if, at the same time point, the aided sentence score in quiet at 65 dB SPL in the listening modality to be tested was ≥80%, resulting in full datasets being available for 11 SSD and 5 AHL subjects.

Speech reception thresholds in noise with the contralateral ear alone and in binaural listening condition in 3 spatial configurations, S_0N_0, S_0N_{CI}, and S_0N_{AC}, are presented in Figure 4, top row for SSD subjects, second row for AHL subjects, and third row for all subjects. Significant differences in SRT between AHL and SSD subjects were found for 4 out of 24 spatial configuration, listening modality, and time point conditions for listening with the contralateral acoustically hearing ear alone as well as binaural listening ($P < .05$); therefore, both subgroups were analyzed individually. For the SSD subgroup, a statistically significant difference in SRT between binaural and contralateral ear listening was found for the S_0N_{AC} configuration at 3 months (*mi* = 4.2 dB, *V* = 2.0, *P* = .0178) and at 12 months (*mi* = 1.3 dB, *V* = 0.0, *P* = .0038). For the AHL subgroup, no significant difference in SRT between binaural and contralateral ear listening was found at any time point in any spatial configuration ($P \geq .05$).

The benefit in speech intelligibility in noise derived from the implant ear (unaided or aided with HA at baseline, aided with CI at post-activation time points) was assessed over time for each of the 3 spatial configurations and is shown in Figure 4, fourth row. At each time point, it was computed as the difference in SRT between the contralateral acoustically hearing ear alone and binaural listening with positive differences indicating improvements in SRT, i.e., benefits from the implant ear.

Implant ear benefits did not differ significantly between the SSD and AHL subgroups in any spatial configuration at any time point ($P \geq .05$); therefore, SRT benefits were analyzed for the pooled subject group. Friedman's ANOVAs revealed a significant effect of time point on benefit from the implant ear in the pooled group in the S_0N_{AC} configuration ($\chi^2(3) = 17.788$, $P = .0005$). Post hoc analyses using Wilcoxon signed-rank tests revealed a significant increase in implant-ear benefit at 3 months (*mi* = 1.9 dB, *V* = 110.5, *P* = .0225) and 12 months (*mi* = 1.55 dB, *V* = 120.0, *P* = .0043) compared to baseline.

No significant effect of time point was found in the S_0N_0 configuration ($\chi^2(3) = 7.1176$, $P = .0682$) or the S_0N_{CI} configuration ($\chi^2(3) = 6.3228$, $P = .0969$).

Pitch Perception

Consistent with previously published pitch matching procedures,[22] a reliable pitch match could be obtained in about 50% of trials (71 matches for 140 trials across all subjects, electrodes, and time points). Furthermore, as the pitch matching procedure could only be administered at Freiburg, Düsseldorf, Berlin, Ghent, and Antwerp, only 3 subjects remain with data available at 1 month and 12 months and for electrodes 1 and 4. These data are shown in Figure 5. AHL16 exhibited a lowering in perceived pitch from 1 month to 12 months for both electrodes, while AHL2 showed an increase in perceived pitch over time for both electrodes. AHL5 initially (1 month) perceived both electrodes close together in pitch. Over time, the pitch percept for electrode 1 decreased while the pitch percept for electrode 4 increased, resulting in a larger separation between the 2 electrodes in terms of perceived pitch at 12 months.

DISCUSSION

Sound Localization

This study found significantly improved sound localization accuracy following implantation. Results published by Mertens et al[25]

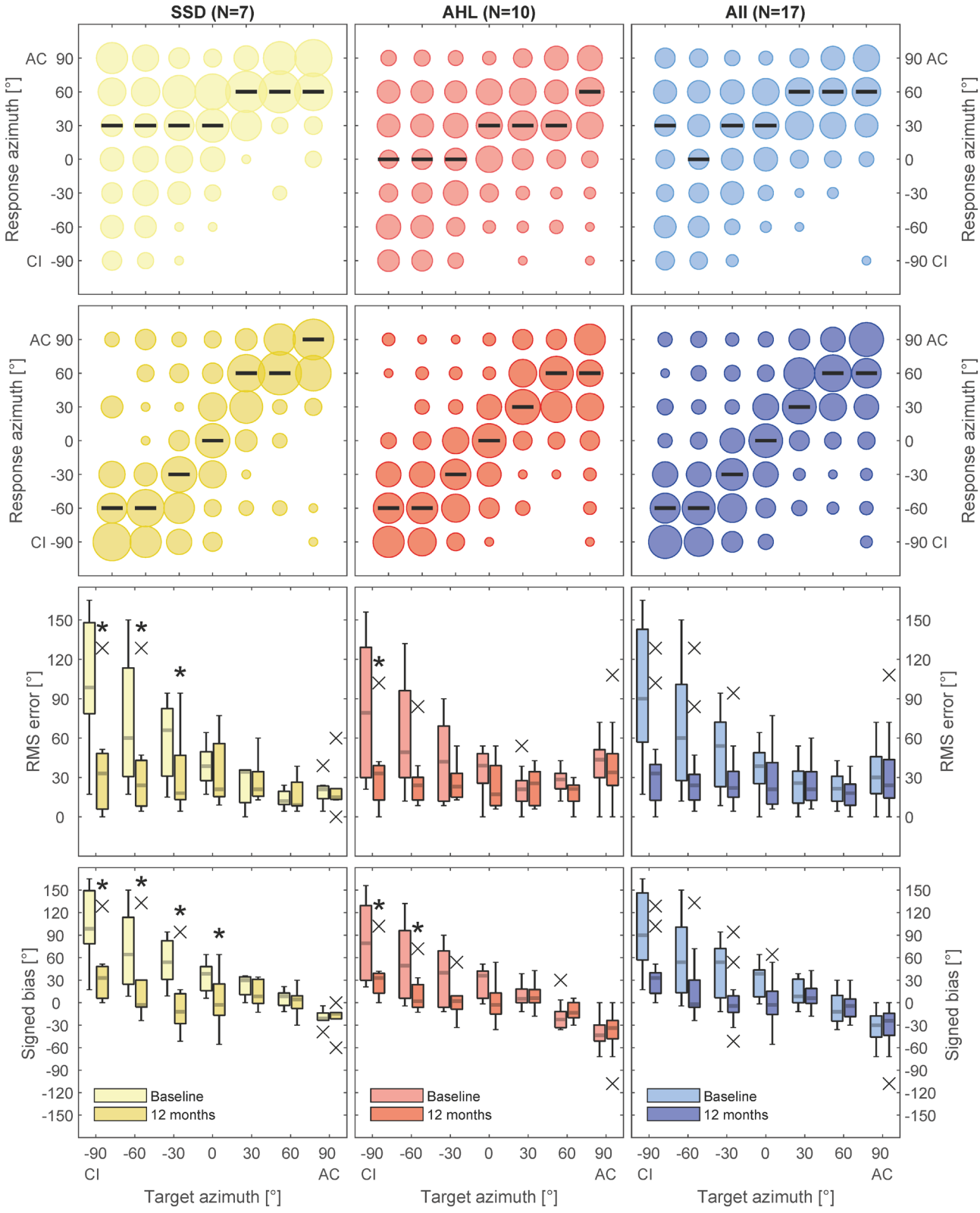

Figure 1. Bubble charts of localization accuracy of SSD subjects (left column), AHL subjects (center column), and all subjects combined (right column) in bilateral best-aided condition. The top row depicts response azimuth at baseline as a function of target azimuth from −90° (CI side) to +90° (AC side). The sizes of the circles represent the number of responses for each target azimuth. Median responses are indicated by black lines. The second row repeats this format for 12 months data. The third row shows the root mean square (RMS) error as a function of target azimuth from −90° (CI side) to +90° (AC side). Data are depicted as box-whisker plots with boxes representing median, lower and upper quartiles, and whiskers showing minimum and maximum. The fourth row repeats this format for the signed bias. AC, contralateral acoustically hearing ear; AHL, asymmetric hearing loss; All, all subjects; CI, cochlear implant; SSD, single-sided deafness; *$P < .05$.

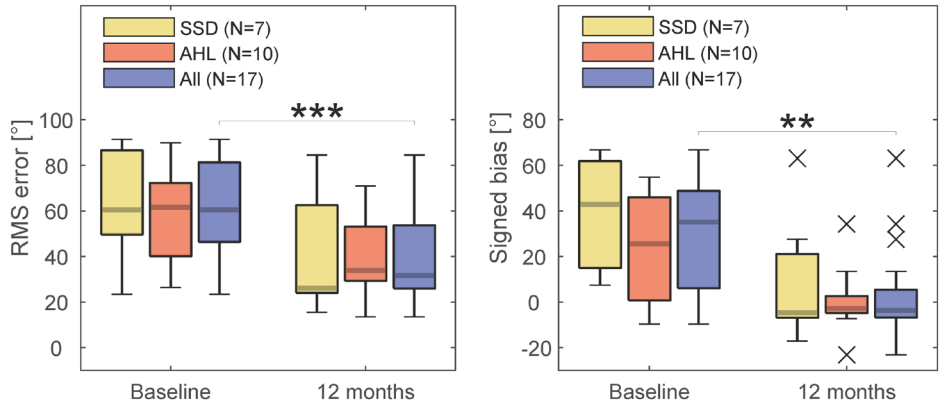

Figure 2. Box-whisker plots of overall RMS error and overall signed bias in bilateral best-aided condition. The left panel shows the overall RMS error at baseline and 12 months for SSD (yellow), AHL (red), and all (blue) subjects. The right panel repeats this format for the overall signed bias. AHL, asymmetric hearing loss; All, all subjects; CI, cochlear implant; SSD, single-sided deafness; $^{**}P < .01$, and $^{***}P < .001$.

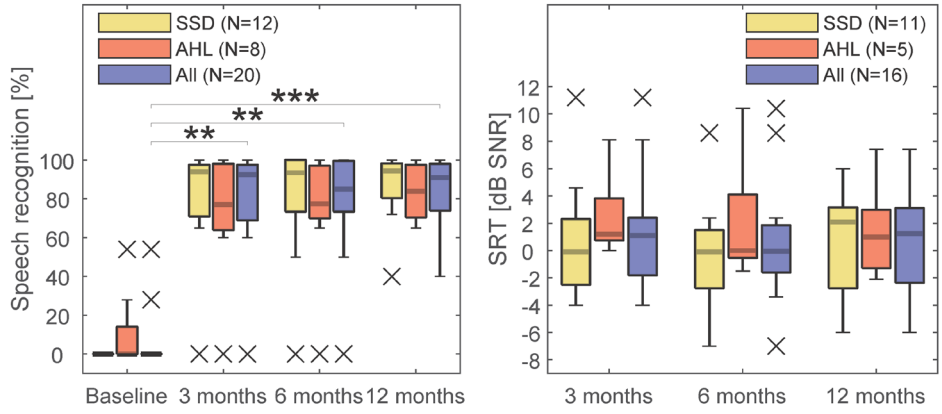

Figure 3. Box-whisker plots of speech intelligibility in quiet and noise with the implant ear alone in best-aided condition at different time points. Data at 3, 6, and 12 months post activation were obtained with CI. Left: speech recognition for monosyllabic words in quiet. Right: speech reception thresholds (SRTs) for frontal presentation of speech and noise. AHL, asymmetric hearing loss; All, all subjects; CI, cochlear implant; SSD, single-sided deafness; $^{**}P < .01$, and $^{***}P < .001$.

revealed that the localization performance of SSD CI users depended strongly on whether the stimulus used was broadband, lowpass-, or highpass-filtered noise. This finding confirms that a fair comparison between localization results can only be drawn if the stimulus type is comparable, in addition to comparability of test setups and outcome measures. Therefore, our discussion is limited to published work addressing localization using speech or speech-shaped noise in the frontal half-plane.

The significant median improvement in overall RMS error of 28.9° with CI at 12 months compared to baseline found here compares well with the improvement of approximately 32° reported by Buss et al.[13] However, Dillon et al[14] reported a larger improvement of around 40°, while Firszt et al[15] showed a smaller improvement of 16.2°. The difference between the sentences used in this study and the speech-shaped noise[13,14] or words[15] used in the comparator studies, in addition to slight differences in test setup, may account for the differences in outcome.

The significant median improvement in overall signed bias of 38.9° with CI at 12 months compared to baseline found in this study is much larger than the improvement of approximately 15° reported by Buss et al.[13] However, Buss et al[13] used speech-shaped noise in an 11-loudspeaker setup compared to speech stimuli in a 7-loudspeaker setup applied in our study.

In addition to the overall RMS error and signed bias of localization, we also present these accuracy measures as functions of the target azimuth. This analysis also allowed for a target-azimuth-specific investigation of the improvements in localization accuracy with CI, to the best of our knowledge, the first target-azimuth-specific analysis of benefits in sound localization for sentences in AHL and SSD subjects with a cochlear implant in the published literature. While for sound sources located on the acoustically hearing side, no improvement in either RMS error or signed bias was found, both measures improved significantly for target sound sources located on the CI side. Therefore, the overall improvement in localization accuracy with CI, seen in both RMS error and signed bias, likely results from enhanced localization accuracy for sound sources on the implant side. As in our study, Ludwig et al[35] also addressed target-azimuth-specific localization accuracy with CI; however, they did not specifically focus on the improvement provided by the CI.

Speech Intelligibility

Speech intelligibility in quiet with the implant ear alone, measured as monosyllabic word recognition, significantly improved following CI activation. At all post-activation time points, word recognition of the pooled AHL/SSD group was significantly better compared to baseline. There was no significant difference in speech intelligibility between any of the post-activation time points comparable to results

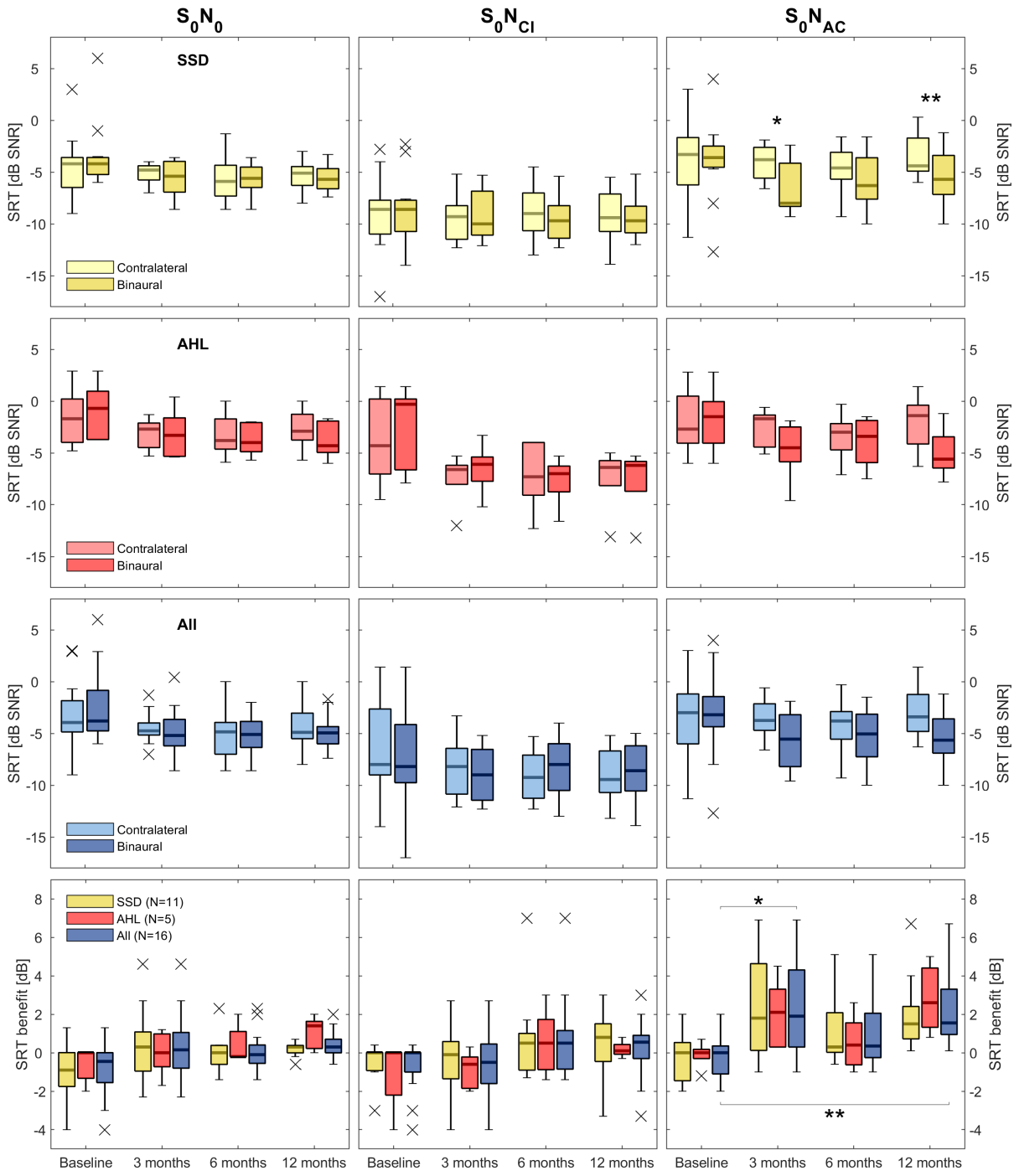

Figure 4. Box-whisker plots of performance and benefits for sentence reception in noise. The top row presents speech reception thresholds (SRTs) over time in the S_0N_0 (left), S_0N_{CI} (center), and S_0N_{AC} (right) configurations for SSD subjects listening with the contralateral ear alone and binaurally. The second row repeats this format for the AHL subjects. The third row repeats this format for all subjects. The fourth row presents benefits in SRT in noise gained with the implant ear in the best-aided condition over time in the S_0N_0 (left), S_0N_{CI} (center), and S_0N_{AC} (right) configurations. Data at 3, 6, and 12 months post activation were obtained with CI. AC, contralateral acoustically hearing ear; AHL, asymmetric hearing loss; All, all subjects; CI, cochlear implant; SSD, single-sided deafness; *$P < .05$, and **$P < .01$.

presented by Galvin et al,[18] i.e., performance remained stable after 3 months indicating fast learning following CI activation.

Speech intelligibility in noise was assessed by measuring the speech reception threshold in noise in 3 spatial configurations. For S_0N_{AC}, a significant median improvement in SRT with CI, i.e., a significant head shadow effect after 3 and 12 months was found for the SSD subgroup but not the AHL subgroup. For S_0N_0 and S_0N_{CI}, no significant benefits in SRT with CI, i.e., no summation or squelch effect, respectively, were obtained in either subgroup, AHL and SSD, at any post-activation time point.

As with localization accuracy, these benefits can only reasonably be compared across studies if stimulus type, spatial configuration, and

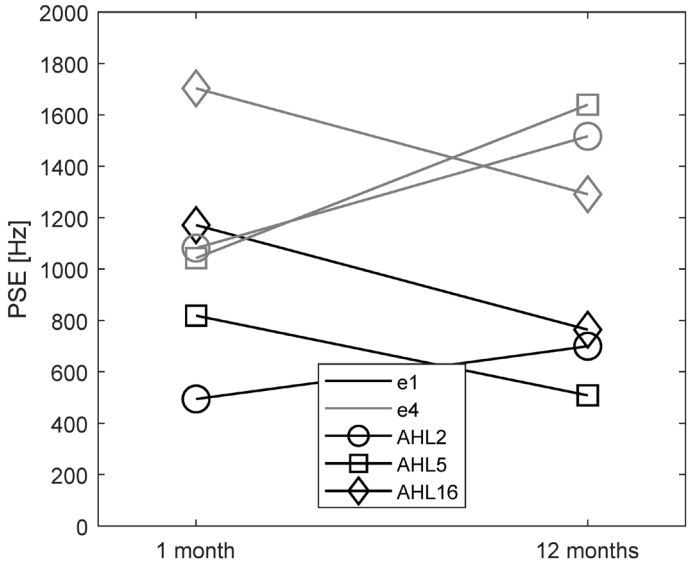

Figure 5. Pitch in terms of the point of subjective equality (PSE) for electrical stimulation at 2 electrodes assessed at 1 month and 12 months post activation. Data for electrode 1 (e1) is indicated by black lines and symbols, and electrode 4 (e4) by gray lines and symbols. Different symbols indicate different subjects.

outcome measures are similar. A list of several studies assessing SRTs for sentences in speech-weighted noise or multitalker babble in S_0N_0, S_0N_{AC}, and S_0N_{CI} and their outcomes, including the present study, is compiled in Table 3.

The significant median head shadow benefit of 2.75 dB on average (4.2 dB and 1.3 dB after 3 and 12 months, respectively) found in the SSD subgroup, is smaller than the benefit of 3.5 dB at 6 months reported by Grossmann et al[19] in a study group corresponding to our pooled group, but compares well to the head shadow benefit of 2.7 dB at 12 months reported by Peter et al[20] for a group corresponding to our SSD subgroup and a benefit of 2.6 dB at 12 months reported by Távora-Vieira et al[21] in a group with a less restrictive range of PTA in the contralateral earcompared to our SSD subgroup. All other studies listed in Table 3 did not investigate the S_0N_{AC} configuration, preventing a direct comparison with the results presented here.

Arndt et al[5] reported a small summation effect of approximately 0.5 dB after 12 months in the SSD, but not the AHL subgroup. However, the absence of a significant summation effect reported here compares well with most of the literature.[6,11,19-21] Mertens et al,[6] who did not report a significant summation effect at 12 months follow-up (see Table 3), did find a significant effect of up to 4.0 dB after 3 years, suggesting longer CI experience to be crucial for a significant summation effect to occur. Further evidence is presented by Távora-Vieira et al,[21] the second study listed in Table 3 to report a summation effect (1.7 dB). Their subject group was tested acutely after an average CI use of 5 years.

In the current study, no significant squelch effect was found, which is in line with some of the published literature.[20] Other studies did find a significant squelch effect in groups including, according to our definitions, AHL and SSD subjects[19] or found this effect only in AHL, but not SSD subjects.[6] Since Grossmann et al[19] for example, did not make the same PTA-based distinction between AHL and SSD as Mertens et al[6] and the investigation presented here, the results are challenging to compare. One reason for not finding a significant squelch effect in our AHL subgroup, as reported by Mertens et al[6] for their (AHL/SSD) subgroup, may be the small sample size of only five subjects.

Vermeire and Van de Heyning[11] found no squelch effect in the pooled (AHL/) subject group but did find a squelch effect (3.8 dB) in the

Table 3. Summary of binaural effects for speech intelligibility in noise found in our study compared to published literature. For each publication, the investigated subgroup according to the definitions applied in our study (SSD, AHL, or all) is specified in parentheses. Unless otherwise noted, 12 months follow-up data are listed.

Reference	Speech Material	Masker	Head Shadow Effect (S_0N_{AC} Unless Otherwise Noted)	Summation Effect (S_0N_0)	Squelch Effect (S_0N_{CI} Unless Otherwise Noted)
This study	OLSA/LIST	Speech-weighted noise	1.3 dB (SSD) n.s. (AHL)	n.s. (SSD) n.s. (AHL)	n.s. (SSD) n.s. (AHL)
Arndt et al (2017)[5]	OLSA	Speech-weighted noise	SCIN0 ~7.1 dB (SSD) ~5.0 dB (AHL)	~0.5 dB (SSD) n.s. (AHL)	SACNCI n.s. (SSD) n.s. (AHL)
Grossmann et al (2016)[19] [a]	OLSA	Male two-talker babble	3.5 dB (all)	n.s. (all)	1.8 dB (all)
Mertens et al (2017)[6]	LIST	Speech-weighted noise	SCINAC 3.0 dB (SSD) 4.3 dB (AHL) 3.3 dB (all)	 n.s. (SSD) n.s. (AHL) n.s. (all)	 n.s. (SSD) 2.7 dB (AHL) n.s. (all)
Peter et al (2019)[20]	OLSA	Speech babble noise	2.7 dB (SSD)	n.s. (SSD)	n.s. (SSD)
Távora-Vieira et al (2019)[21] [b]	LIST/BKB-SIN	Speech-weighted noise / Four-talker babble	2.6 dB (all)	1.7 dB (all)	Not evaluated
Vermeire and Van de Heyning (2009)[11] [c]	LIST	Speech-weighted noise	$S_{CI}N_0$ 1.7 dB (all) 6.5 dB (AHL)	 n.s. (all) n.s. (AHL)	 n.s. (all) 3.8 dB (AHL)

AHL, asymmetric hearing loss; SSD, single-sided deafness.
[a]After 6 months (maximum follow-up duration in this publication).
[b]Acute testing on average 5 years after implantation.
[c]AHL subgroup showed a substantially larger median PTA (66 dB) than the AHL subgroup in our study (39 dB).

AHL subgroup. Compared to the AHL subgroup investigated in the present study, their AHL subgroup had a substantially larger median PTA (see footnote 3, Table 3).

Pitch Perception

The low number of complete data sets of pitch perception with CI did not allow for a comprehensive statistical analysis; instead, individual pitch perception results will be discussed. Similarly to Reiss et al,[24] no uniform pattern of development of pitch over time was apparent in the present study. While Reiss et al[24] only evaluated pitch for 1 electrode, the data presented here further undermine the notion that changes in pitch perception following cochlear implantation are highly individualized, as even within 1 subject (AHL5), different pitch trajectories over time were obtained for the 2 investigated electrodes.

CONCLUSION

In conclusion, this multicenter study confirms the vast potential of CIs to improve speech intelligibility in noise in SSD and AHL, corroborating existing literature. An improvement in sound localization accuracy was shown, again confirming previous research. A more detailed analysis of localization accuracy was able to demonstrate that this well-established increase in performance is due to the enhanced accuracy of localization of sound sources positioned on the implant side.

Ethics Committee Approval: This study was approved by the Ethics Committee of the site of the coordinating investigator, the Ethics Committee of the University of Freiburg, Germany (Approval Number: 440/14; date: January 8, 2015).

Informed Consent: Informed consent was obtained from all subjects who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – T.W., A.A., N.V., A.Z.; Design – T.W., A.A., N.V., A.Z.; Supervision – T.W., A.A., I.D., G.S., N.V.; Materials – T.W., A.A., N.V., A.Z., A.E.; Data Collection and/or Processing – T.W., A.A., J.B., L.D.C, I.D., A.D., T.K., P.S., G.S., F.S., N.V., A.V., S.V., A.Z., A.E.; Analysis and/or Interpretation – T.W., A.A., R.B., I.D., A.D., T.K., P.S., G.S., F.S., N.V., A.Z.; Literature Search – T.W., R.B., A.D., F.S., N.V., A.Z.; Writing – T.W., R.B.; Critical Review – T.W., A.A., I.D., A.D., T.K., P.S., G.S., F.S., N.V., A.Z.

Declaration of Interests: T.W. reports non-financial support from Advanced Bionics AG, during the conduct of the study; grants and non-financial support from Advanced Bionics AG, grants and non-financial support from Cochlear Deutschland GmbH & Co. KG, grants and non-financial support from MED-EL Deutschland GmbH, outside the submitted work. A.A. reports a grant and non-financial support from Advanced Bionics AG, during the conduct of the study; grants and non-financial support from Advanced Bionics AG, grants and non-financial support from Cochlear Ltd, grants and non-financial support from MED-EL Gesellschaft m.b.H., grants and non-financial support from Oticon, Inc., outside the submitted work. R.B. is an employee of Advanced Bionics GmbH. T.K. reports grants and non-financial support from Advanced Bionics AG, during the conduct of the study; grants, personal fees and non-financial support from Cochlear Europe Ltd, grants and non-financial support from MED-EL Deutschland GmbH, outside the submitted work. S.V. reports grants and non-financial support from Advanced Bionics AG, during the conduct of the study. A.Z. is a member of the Editorial Board of The Journal of International Advanced Otology. We declare that A.Z. had no involvement in the peer review of this article and has no access to information regarding its peer review. J.B., L.D.C., I.D., A.D., P.S., G.S., F.S., N.V., A.V., and A.E. have no conflicts of interest relevant to the content of this article to declare.

Funding: This study was funded by a grant provided by Advanced Bionics AG (Stäfa, Switzerland).

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