Electric-Acoustic Stimulation Clinical Trial Outcomes

Allison Racey – Audiology Online
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Learning Objectives

- After this course learners will be able to describe candidacy criteria and study design from the US clinical trial on EAS.
- After this course learners will be able to explain important speech perception outcomes for subjects in the US clinical trial.
- After this course learners will be able to describe outcomes for hearing sensitivity post-operatively from the clinical trial.

MED-EL

EAS Clinical Trial Results

- EAS Study Review
  - Clinical trial sites
  - Study Design
  - Surgical protocol
- EAS Results
- MED-EL EAS v. Cochlear Hybrid

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EAS Study Review

Electric-Acoustic Stimulation Clinical Trial

- **Purpose: to determine the safety and effectiveness of MED-EL Electric-Acoustic Stimulation Cochlear Implant System**
- FDA-regulated, multicenter clinical trial
- Conducted in the US at 14 experienced CI centers

Clinical Trial Sites

- Boys Town National Research Hospital
- Duke University
- Indiana University
- Kansas University Medical Center
- Medical College of Wisconsin
- New York Eye & Ear
- Oregon Health & Science University
- Stanford University
- Swedish Neuroscience Institute
- University of Miami
- University of Michigan
- University of North Carolina
- University of Pennsylvania
- University of Texas Southwestern

Candidacy Criteria

- Inclusion criteria:
  - 18-70 years of age
  - Normal hearing to moderate hearing loss in the low frequencies

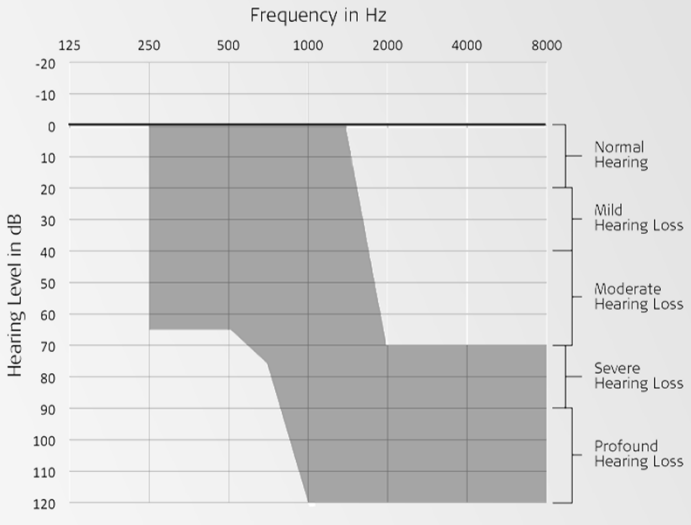
Frequency (Hz)	250	500	750	1000	1500	2000	4000	8000
Lower Limit:	0	0	0	0	0	70	70	70
Upper Limit:	65	65	75	110+	110+	110+	110+	110+

  - Severe to profound hearing loss in the high frequencies
  - 60% or less in the best aided condition on CNC words in quiet
  - Hearing aid experience
  - English as primary language

Candidacy Criteria

- Exclusion criteria:
  - Conductive/retrocochlear hearing loss
  - Asymmetric hearing loss (>20 dB difference)
  - Fluctuating hearing loss (>10 dB at 2 or more frequencies) within the last two years
  - Developmental delays
  - Physical or geographical limitations precluding ability to follow protocol

Candidacy Criteria



0-60% on CNC words in the best aided condition

Clinical Trial Devices

- PULSAR or SONATA implant
- FLEX^{EAS} (equivalent to FLEX^{24})
- DUET Audio Processor
  - Digitally programmable
  - Earmold
- CI Studio programming software

- FDA approved devices:
  - SONATA, CONCERT, SYNCHRONY, FLEX^{24}, DUET2, SONNET^{EAS}

Study Design

- Sentences in noise: CUNY
  - Signal-to-noise ratio based on decision tree at 3 months
  - 0, +5, or +10 dB SNR held constant for each subject after 3 months
- Words in quiet: CNC
- Condition tested:
  - Hearing aids pre-operatively
  - Electric and acoustic stimulation (EAS)
  - Electric stimulation only
- Subjective questionnaires: APHAB, HDSS
- Followed through 12-months post EAS activation

Study Design

- Three primary questions:

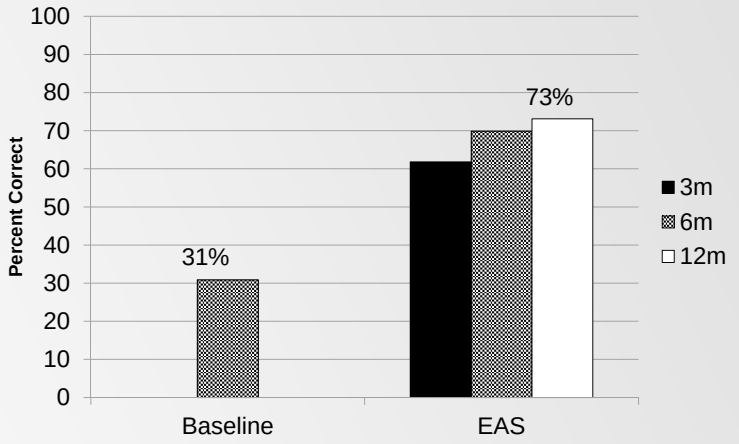
1. Do subjects perform better with EAS than they did with hearing aids pre-operatively?
2. If a subject were to lose hearing, would they perform better with electric stimulation only than they did with hearing aids pre-operatively?
3. Do subjects perform better with combined electric and acoustic stimulation (EAS) than they do with electric stimulation only?

EAS Results

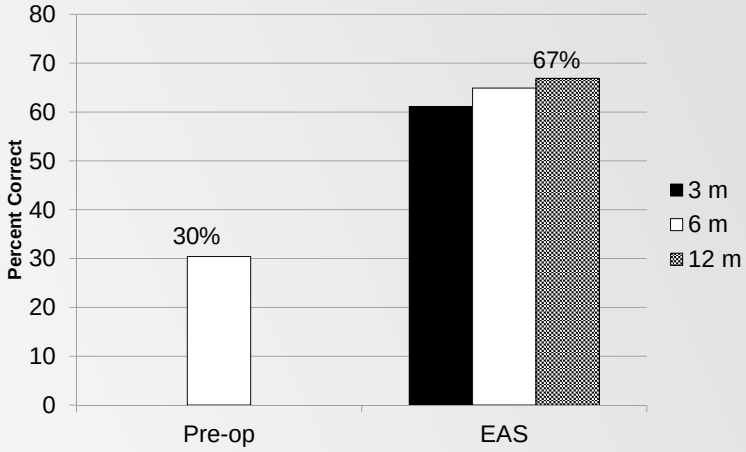
Results

- 73 total subjects implanted
  - 67 subjects followed to 12 months
  - 3 withdrawals, 2 lost to follow-up
  - 1 subject still undergoing testing
- Average age at implantation: 53.7 years
- Male 42.5%, female 57.5%

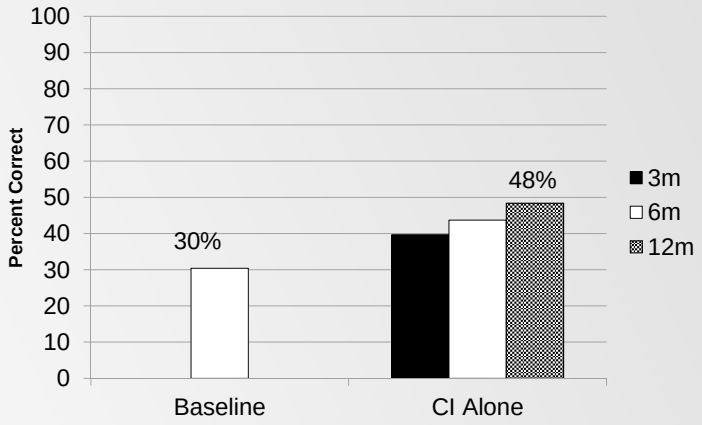
Results – Sentences in Noise (EAS)



Results – Words in Quiet (EAS)



Results – Words in Quiet (Electric Only)



Data from Dillon (2016)

- Full frequency (unfamiliar) map v. truncated electric only (familiar) map v. combined EAS

Figure 1. Percent correct scores on CNC words in quiet ($n = 11$) for each listening condition. Individual subject performance is designated by the symbols provided in Table 1. Brackets indicate significant difference between listening conditions.

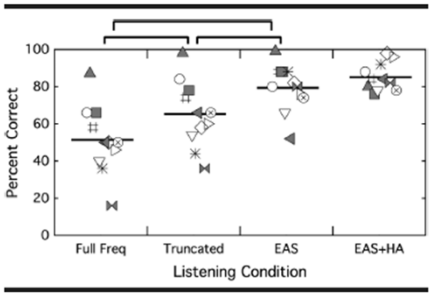
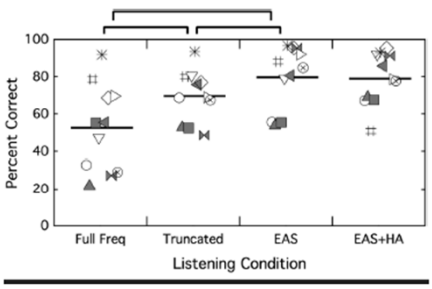
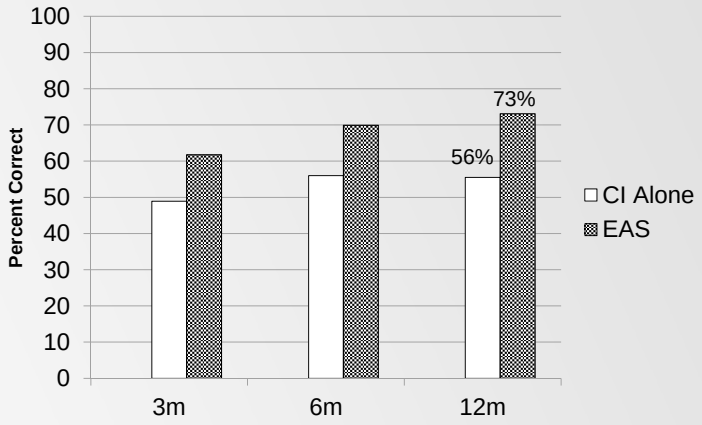


Figure 2. Percent correct scores on CUNY sentences in steady noise (0 dB SNR; $n = 11$) for each listening condition. Plotting conventions are the same as Figure 1.



Results –Sentences in Noise (Electric v. EAS)



Results – APHAB & HDSS

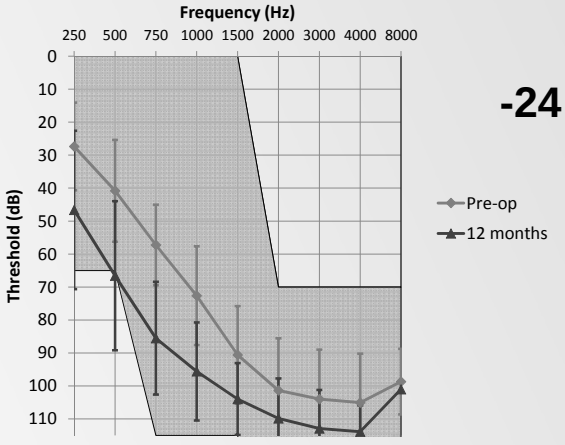
- APHAB
  - 90% of subjects report benefit from EAS
  - 92% of subjects reported improvement in hearing in background noise
  - Significant improvement of 30+ percentage points
- HDSS
  - 86% of subjects reported increased satisfaction with EAS

Results – Hearing Sensitivity

- Subjects able to be fit with the acoustic unit
  - Low-frequency threshold better than 80 dB
  - 97% of subjects able to be fit with acoustic component
- Low-frequency pure-tone average (250, 500, 750, 1000 Hz)
  - Average PTA shift
  - Proportion of subjects experiencing degrees of PTA shift
  - Post-operative degree of low-frequency residual hearing

Results – Hearing Sensitivity

- Group average LF-PTA shift at 12 months (n=67)



-24 dB

Results – Hearing Sensitivity

- 79% of subjects experienced less than 30 dB of low-frequency PTA shift at 12 months

Time Point	< 10 dB	10-20 dB	20-30 dB	> 30 dB
3 Month	10/71 (14%)	30/71 (42%)	18/71 (26%)	13/71 (18%)
6 Month	11/69 (16%)	23/69 (33%)	20/69 (29%)	15/69 (22%)
12 Month	8/67 (12%)	25/67 (37%)	20/67 (30%)	14/67 (21%)

Results – Hearing Sensitivity

- 88% of subjects experienced residual hearing better than a profound degree

Time Point	Mild to Moderate	Moderately-Severe to Severe	Profound
3 Month	9/71 (13%)	58/71 (82%)	4/71 (6%)
6 Month	11/69 (16%)	52/69 (75%)	6/69 (9%)
12 Month	7/67 (10%)	52/67 (78%)	8/67 (12%)

Results – Loss of Hearing

- Two subjects could not use the acoustic unit

	Pre-op	12 months
CNC	28	46
CUNY (0 dB SNR)	0	63

	Pre-op	12 months
CNC	26	74
CUNY (0 dB SNR)	19	97

MED-EL EAS v. Cochlear Hybrid

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MED-EL EAS v. Cochlear Hybrid

MED-EL EAS

- 73 subjects
  - 56 SONATA, 17 PULSAR
- Round Window (77%) & Cochleostomy (23%)
- 18 – 20 mm insertion depth
- 12-month endpoint
- Words in quiet, sentences in noise

Cochlear Hybrid

- 50 subjects
- Hybrid L24
- Cochleostomy
- Up to 16 mm insertion depth
- 6-month endpoint
- Words in quiet, sentences in noise

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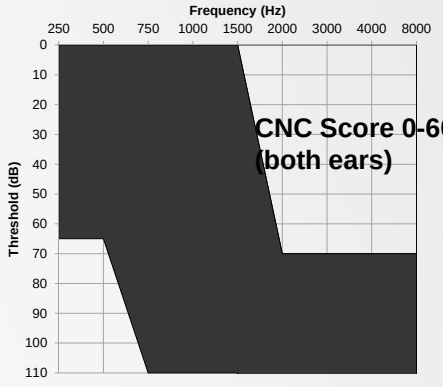
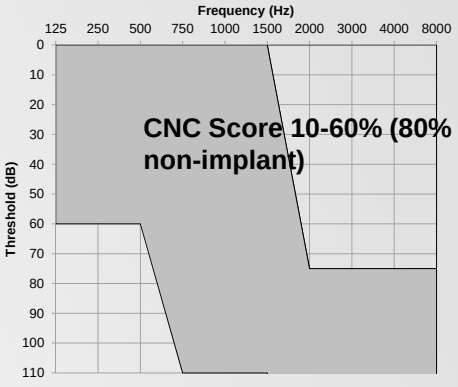
MED-EL EAS v. Cochlear Hybrid – Clinical Trial Candidacy

MED-EL EAS

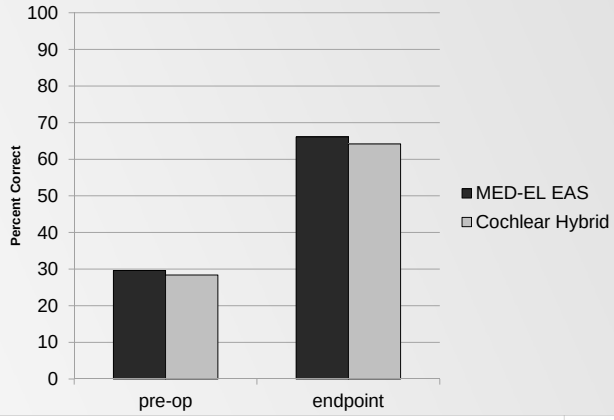


Cochlear Hybrid



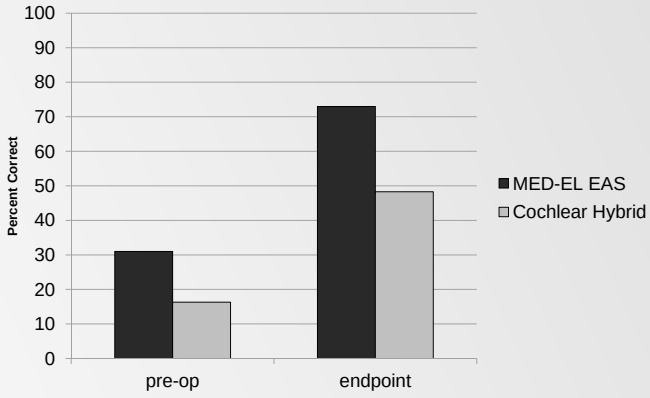
MED-EL EAS v. Cochlear Hybrid – CNC Words (EAS/Hybrid v. pre-op)

- EAS: 37% improvement
- Hybrid: 36% improvement

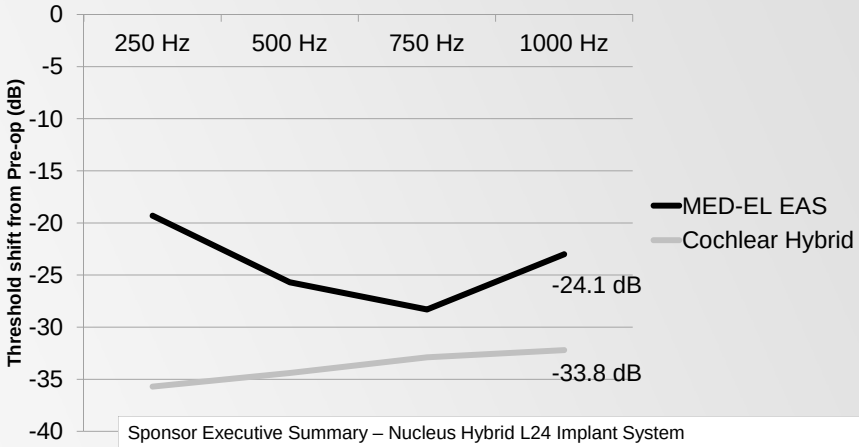


MED-EL EAS v. Cochlear Hybrid – Sentences in Noise (EAS/Hybrid v. Pre-op)

- EAS: 42% improvement (CUNY, variable SNR, 73% at 0 dB)
- Hybrid: 32% improvement (AzBio, +5 dB SNR)

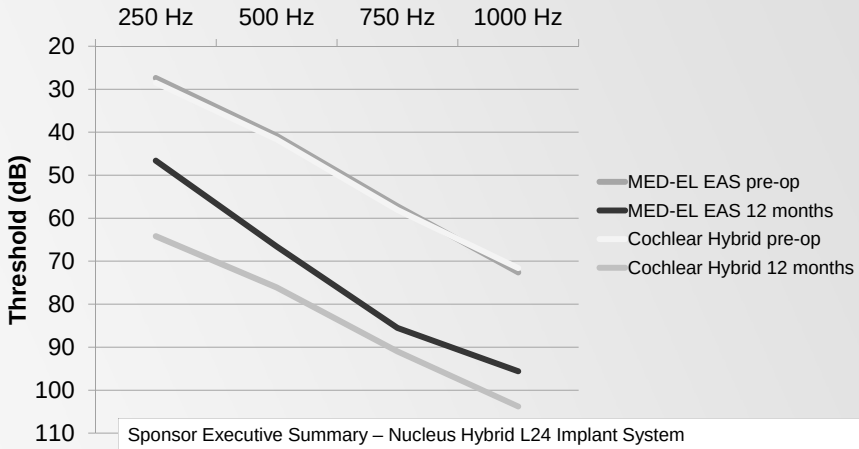


MED-EL EAS v. Cochlear Hybrid – Low-Frequency Shift at 12 Months



Sponsor Executive Summary – Nucleus Hybrid L24 Implant System
http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/EarNoseandThroatDevicesPanel/UCM373793.pdf

MED-EL EAS v. Cochlear Hybrid – Low-Frequency Shift



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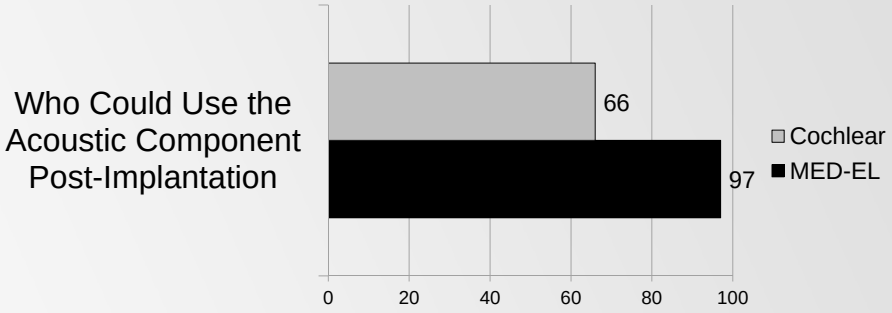
MED-EL EAS v. Cochlear Hybrid – Percentage of Subjects….



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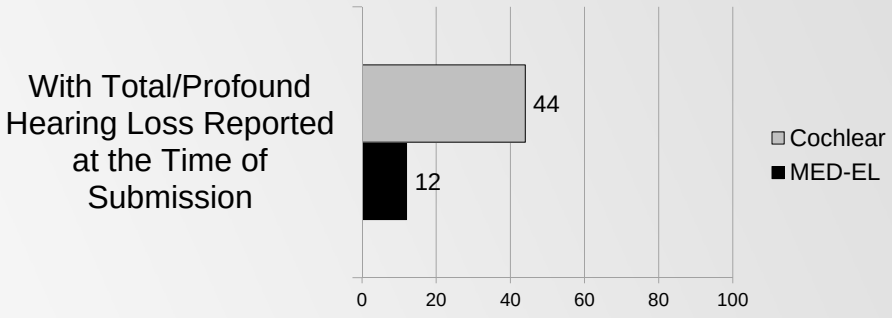
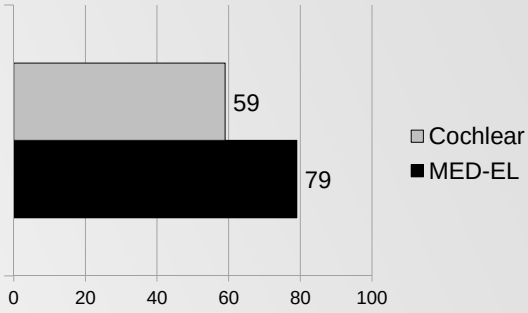
MED-EL EAS v. Cochlear Hybrid – Percentage of Subjects…



Summary of Safety and Effectiveness Data (SSED)
http://www.accessdata.fda.gov/cdrh_docs/pdf13/P130016B.pdf

MED-EL EAS v. Cochlear Hybrid – Percentage of Subjects…

With <30 dB LF-PTA Shift at 12 Months Post-op



Summary of Safety and Effectiveness Data (SSED)
http://www.accessdata.fda.gov/cdrh_docs/pdf13/P130016B.pdf

MED-EL EAS v. Cochlear Hybrid – Adverse Events

Number of…	EAS	Hybrid
Adverse events	35	65
Subjects experiencing adverse events	29 (40%)	34 (68%)
Events reported as “profound/total loss of hearing”	8	22
Months hearing loss data collected	104	48
Revision surgeries due to poor performance	0	6

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Resources

- Dillon, M.T., Buss, E., Adunka, O.F., Buchman, C.A., Pillsbury, H.C. (2015), Influence of Test Condition on Speech Perception with Electric-Acoustic Stimulation. American Journal of Audiology, 24(4):520-8.
- FDA Panel Meeting, October 2013
  - http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/EarNoseandThroatDevicesPanel/UCM375000.pdf
- FDA Summary of Safety and Effectiveness Data, March 2014
  - http://www.accessdata.fda.gov/cdrh_docs/pdf13/P130016B.pdf
- Roland, J. T., Gantz, B. J., Waltzman, S. B., Parkinson, A. J. and The Multicenter Clinical Trial Group (2016), United States multicenter clinical trial of the cochlear nucleus hybrid implant system. The Laryngoscope, 126: 175–181.

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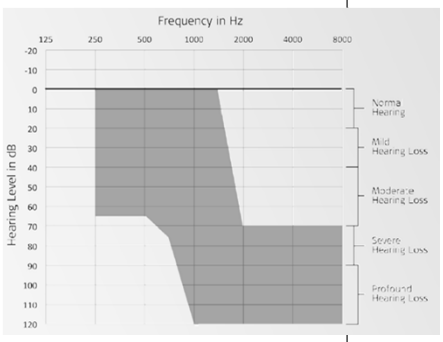
Ten Years of Electric-Acoustic Stimulation Experience: What We Know Now

Margaret Dillon, AuD
Assistant Professor
Director, Cochlear Implant Clinical Research
Department of Otolaryngology/Head and Neck Surgery

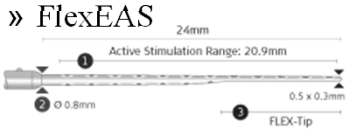
UNC Cochlear Implant Team

- Physicians
  - » Harold Pillsbury III, MD
  - » Kevin Brown, MD, PhD
  - » Carlton Zdanski, MD
  - » Lauren Kilpatrick, MD
- Research
  - » Meredith Anderson, AuD
  - » Emily Buss, PhD
  - » Margaret Dillon, AuD
  - » Douglas Fitzpatrick, PhD
  - » John Grose, PhD
- Adult Audiologists
  - » English King, AuD
  - » Andrea Bucker, AuD
  - » Ellen Deres, AuD
  - » Sarah McCarthy, AuD
  - » Annelle Hodges, PhD
- Pediatric Audiologists
  - » Holly Teagle, AuD
  - » Erika Gagnon, AuD
  - » Lisa Park, AuD
  - » Jennifer Woodard, AuD

Multi-center EAS clinical trial



- Internal
  - » FlexEAS



- External
  - » DUET

MED-EL Corporation

Multi-center EAS clinical trial

- Protocol
  - » Assessment of residual hearing
  - » Aided speech perception performance
    - Quiet (CNC words)
    - Noise (CUNY sentences)
  - » Quality of life
- Intervals
  - » Preoperative
  - » Initial CI activation
    - Electric stimulation only
  - » Initial EAS activation
    - Electric + Acoustic stimulation
  - » 3, 6, and 12 months post-initial EAS activation

Ten Years of EAS Experience: What we know now

SINGLE-SITE FINDINGS

UNC Cohort

- N=33
  - » Age at Implantation
    - **Min:** 20.2 yrs
    - **Max:** 76.6 yrs*
    - **Avg:** 55.8 yrs

*Compassionate Use from FDA prior to cochlear implantation.

Residual Hearing: Low-Frequency PTA

Subjects: n=26 LFPTA: 250, 500, 750 Hz

dB HL	Min	Max	**Avg**	**Avg change from previous interval**
Preoperative	15.0	66.7	**42.2**	**NA**
Initial CI activation	35.0	115.0	**60.9**	**-18.7**
6 month	26.7	120.0	**60.4**	**0.5**
12 month	26.7	120.0	**63.3**	**-2.9**
2 year	23.3	120.0	**65.3**	**-2**

No Response assigned a value of 120 dB

Speech Perception

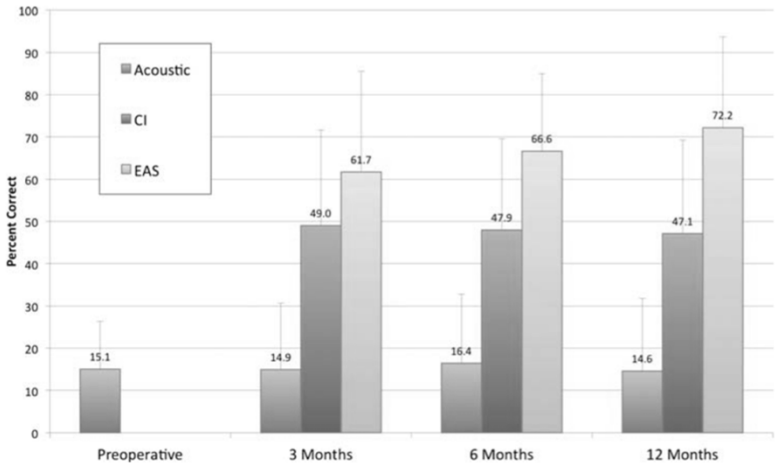
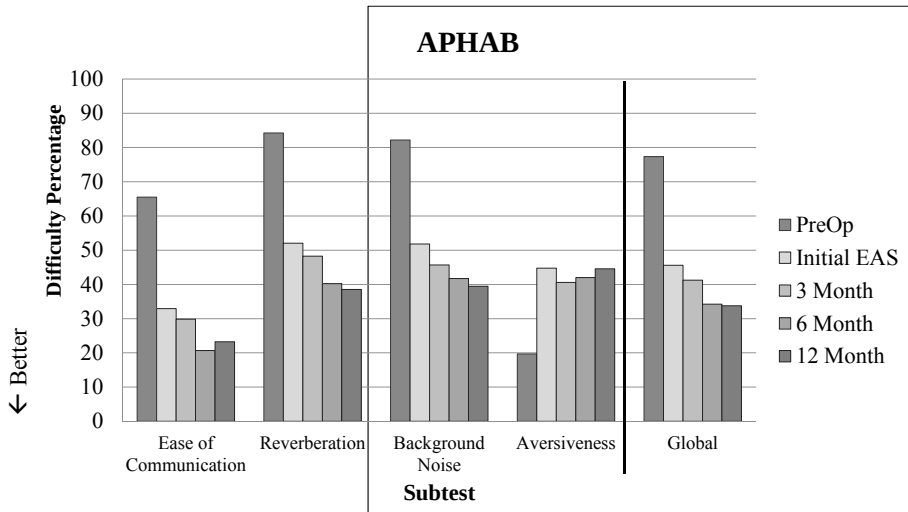


Figure 3

Adunka et al (2013)

Quality of Life



Ten Years of EAS Experience: What we know now

BEYOND THE CLINICAL TRIAL

Beyond the Clinical Trial

- Electric stimulation and residual hearing
- Test Conditions
  - » Test Battery
  - » Listening Conditions
- Case Studies

Ten Years of EAS Experience: What we know now

CHARGE AND RESIDUAL HEARING

Residual Hearing

- EAS recipients experience improved speech perception
- Postoperative benefits rely on the preservation of residual hearing

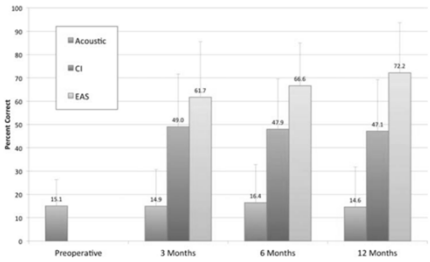
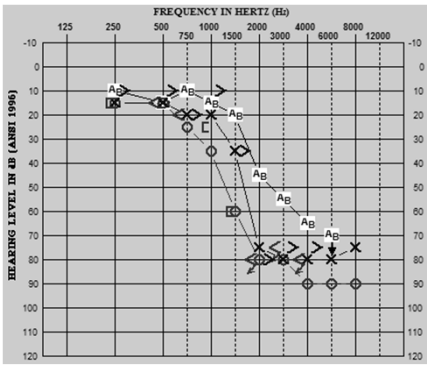


Figure 3 Adunka et al (2013)

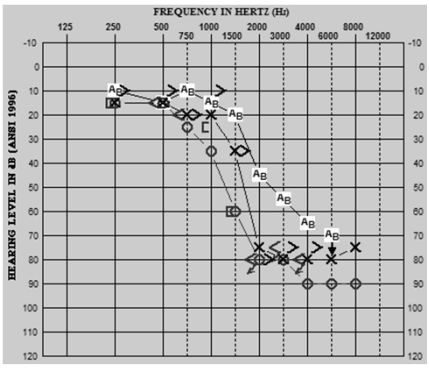
Residual Hearing

Preoperative

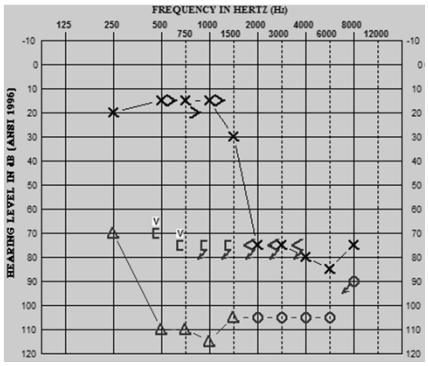


Residual Hearing

Preoperative

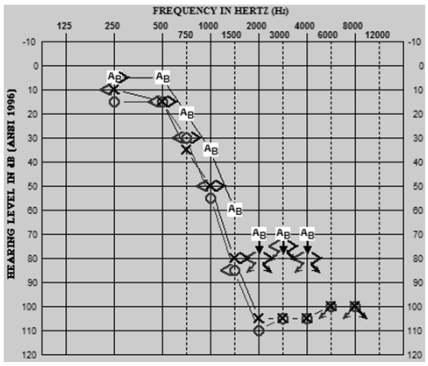


Postoperative: 1 month



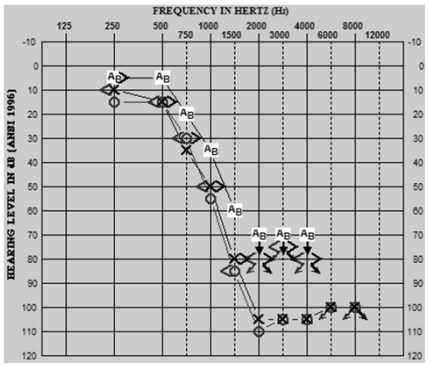
Residual Hearing: progressive loss

Preoperative

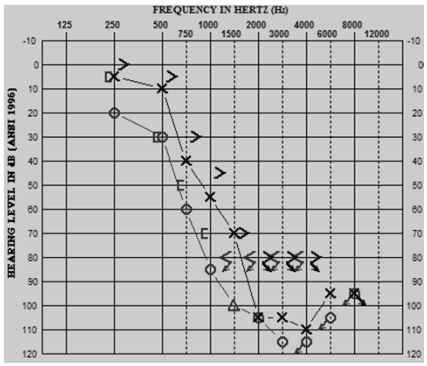


Residual Hearing: progressive loss

Preoperative

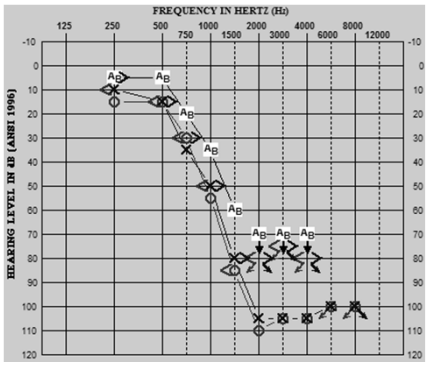


Postoperative: 1 month

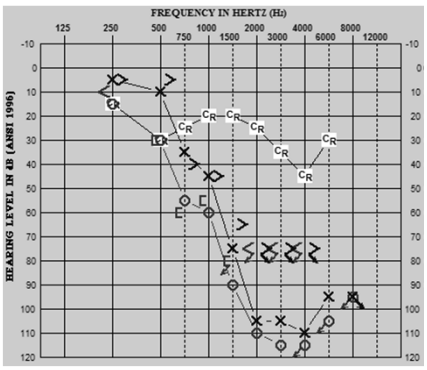


Residual Hearing: progressive loss

Preoperative

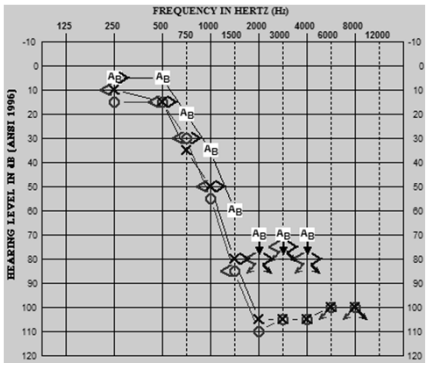


Postoperative: 2 month

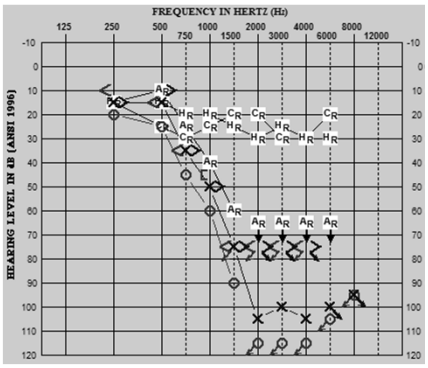


Residual Hearing: progressive loss

Preoperative

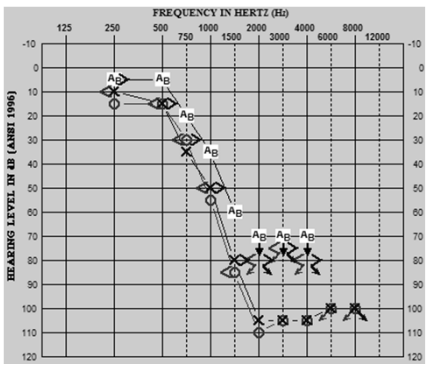


Postoperative: 5 month

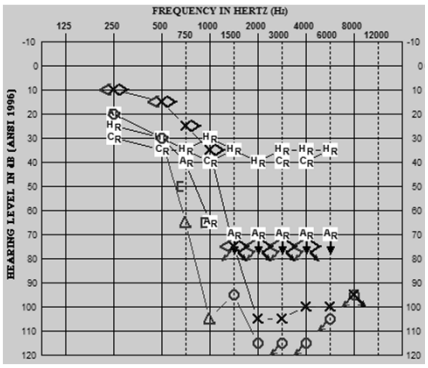


Residual Hearing: progressive loss

Preoperative

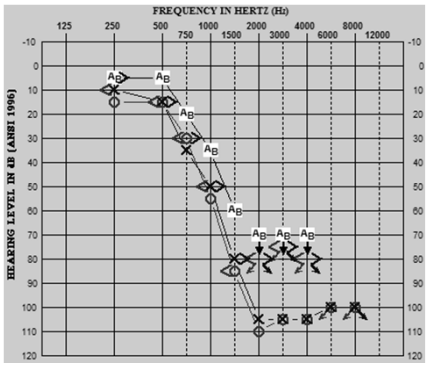


Postoperative: 7 month

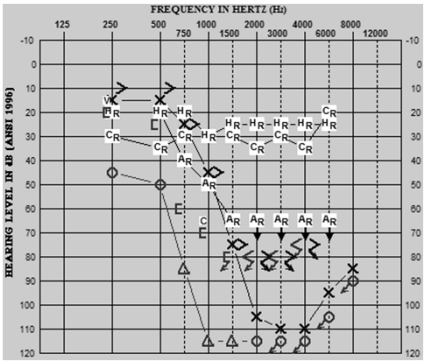


Residual Hearing: progressive loss

Preoperative

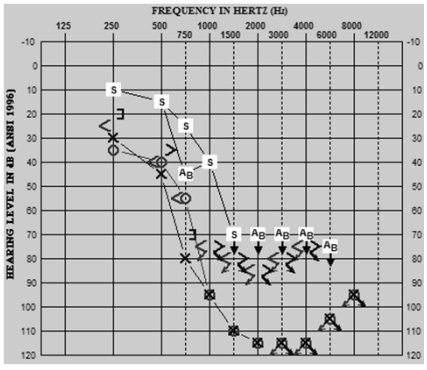


Postoperative: 1 year



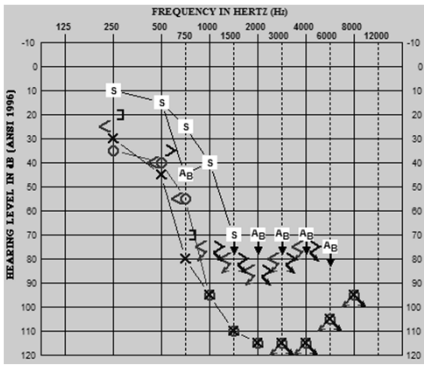
Residual Hearing: stable

Preoperative

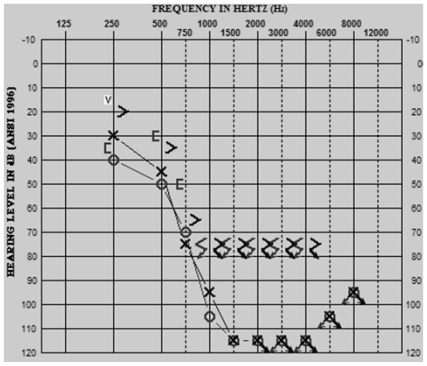


Residual Hearing: stable

Preoperative

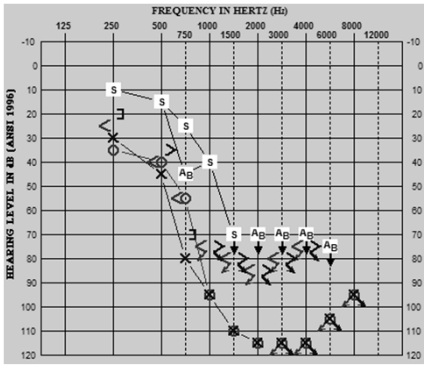


Postoperative: 1 month

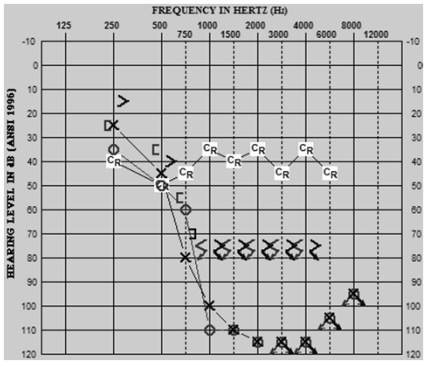


Residual Hearing: stable

Preoperative

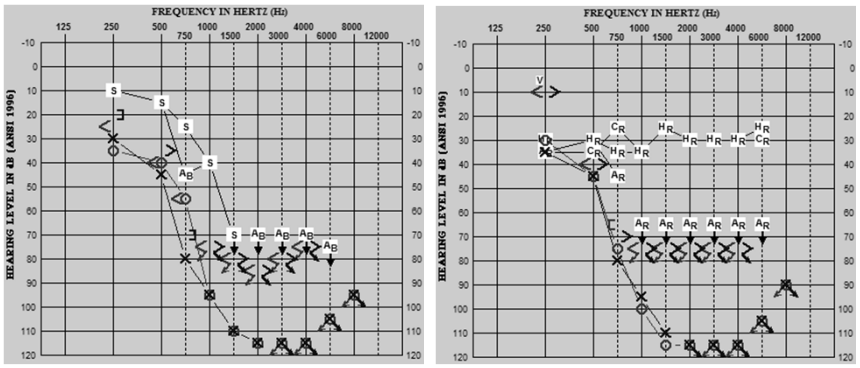


Postoperative: 2 month



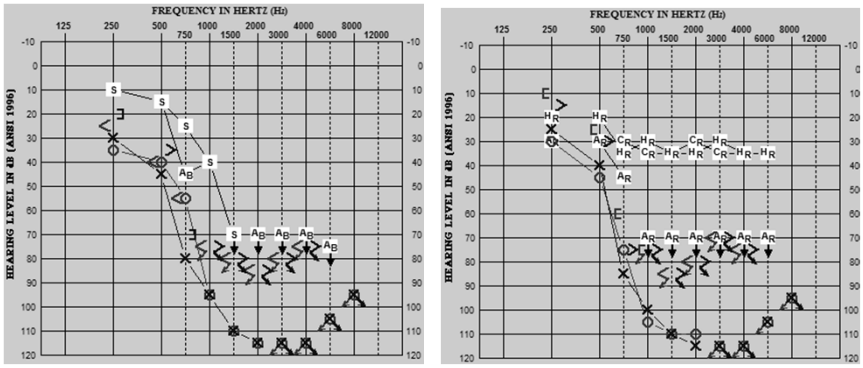
Residual Hearing: stable

Preoperative **Postoperative: 5 month**



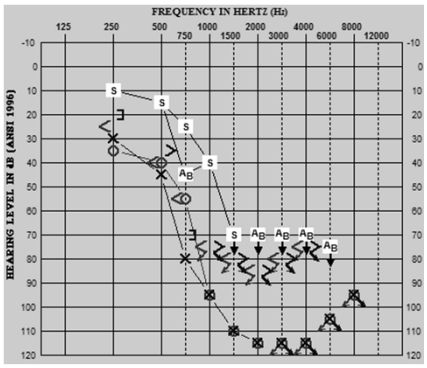
Residual Hearing: stable

Preoperative **Postoperative: 7 month**

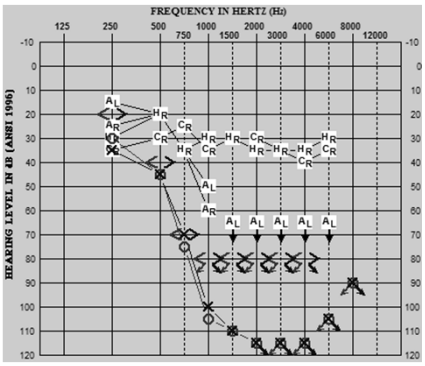


Residual Hearing: stable

Preoperative

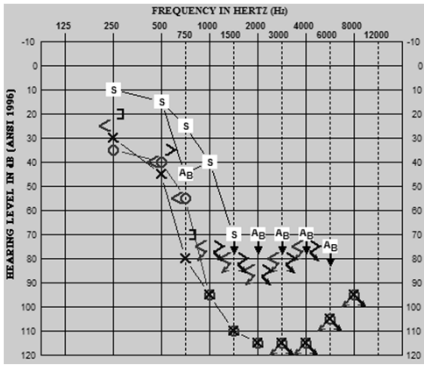


Postoperative: 1 year

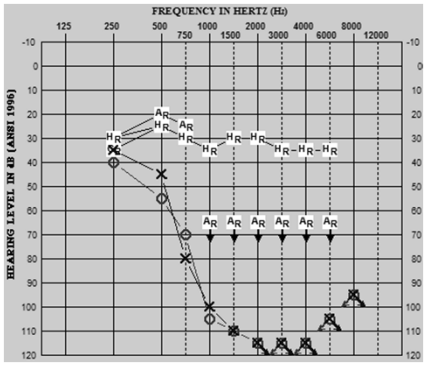


Residual Hearing: stable

Preoperative

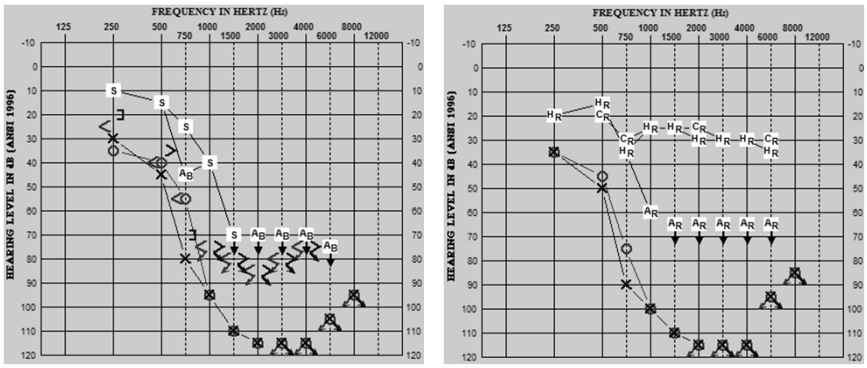


Postoperative: 2 year



Residual Hearing: stable

Preoperative **Postoperative: 3 year**



Residual Hearing

- Potential causes:
  - » Acoustic trauma from drilling the bony portion of the cochlea
  - » Mechanical damage from electrode insertion and associated damage of cochlear structures
  - » Disruption of the cochlear fluid homeostasis
  - » Infection
  - » Cochlear fibrosis
  - » High electric stimulation levels?

Kiefer et al (2004); Kopelovich et al (2014)

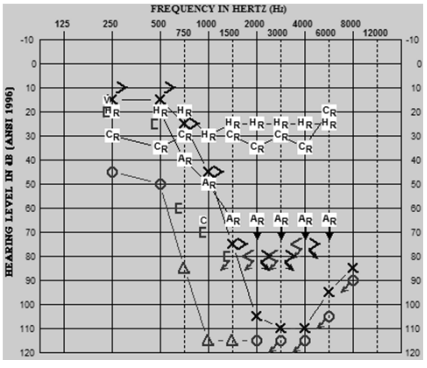
Objective

- Evaluate whether charge levels associated with electric stimulation influence postoperative hearing preservation within the first year of listening experience
  - » Clinical trial study endpoint: 12-month post-initial EAS activation

Dillon et al (2015)

Methods

- Low-frequency BC PTA
  - » 500, 750 and 1000 Hz
  - » Masking presented to the contralateral ear



Dillon et al (2015)

Methods

- Low-frequency BC PTA
- Charge

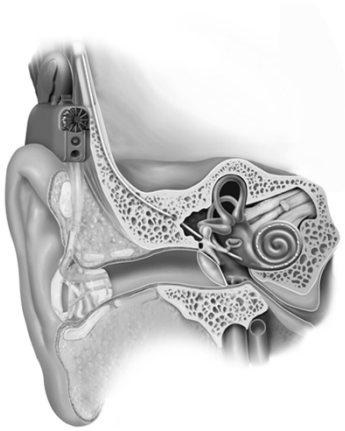
$$\text{charge } (nC) = \frac{\text{MCL } (cu) * \text{ pw } (\mu s)}{1000}$$

  - » Mapping completed with CI Studio clinical programming software
    - MCL reported in current units (*cu*)
    - 1 *cu* ≈ 1 µA
  - » CIS coding strategy

Dillon et al (2015)

Methods

- Low-frequency BC PTA
- Charge
- Electrodes
  - » Apical electrodes
    - E1
    - Apical average
      - » E1, E2, & E3
  - » Mid average
    - E4, E5, & E6
  - » Basal average
    - E7, E8, & E9



Dillon et al (2015)

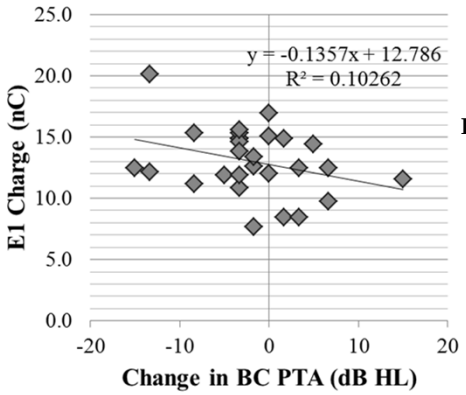
Methods

- Low-frequency BC PTA
- Charge
- Electrodes
  - » E1
  - » Apical average
  - » Mid average
  - » Basal average
- Bivariate Pearson correlation
- Evaluation Intervals:
  - » Initial CI activation
  - » Initial EAS activation
  - » 3-month post-initial EAS activation
  - » 6-month post-initial EAS activation
  - » 12-month post-initial EAS activation

Dillon et al (2015)

Results

- Charge levels had little to no association with the postoperative change in low-frequency bone conduction PTA within the first year of listening experience



E1 Charge at Initial CI activation by Change in low-frequency BC PTA (Initial CI to Initial EAS activation)

Dillon et al (2015)

Ten Years of EAS Experience: What we know now

TEST CONDITIONS

Test Conditions: listening conditions

- Multi-Center EAS Clinical Trial
  - » HA Alone
  - » CI Alone
    - Full-frequency map
  - » Combined (EAS)
    - HA + CI (truncated map)
- Influence of frequency filters on speech perception

Test Conditions: speech perception

- Multi-Center EAS Clinical Trial
  - » CNC words in quiet
  - » CUNY sentences in steady noise
- Minimum Speech Test Battery
  - » CNC words in quiet
  - » AzBio sentences in a 10-talker babble
  - » BKB-SIN
    - 4-talker babble

Test Conditions

- Evaluate the contribution of the HA to EAS in babble conditions
- Performance in the CI Alone condition
  - » Full-frequency (unfamiliar)
  - » Truncated (familiar)
- Evaluate differences between EAS and EAS+HA

Dillon et al (2015)

Test Conditions

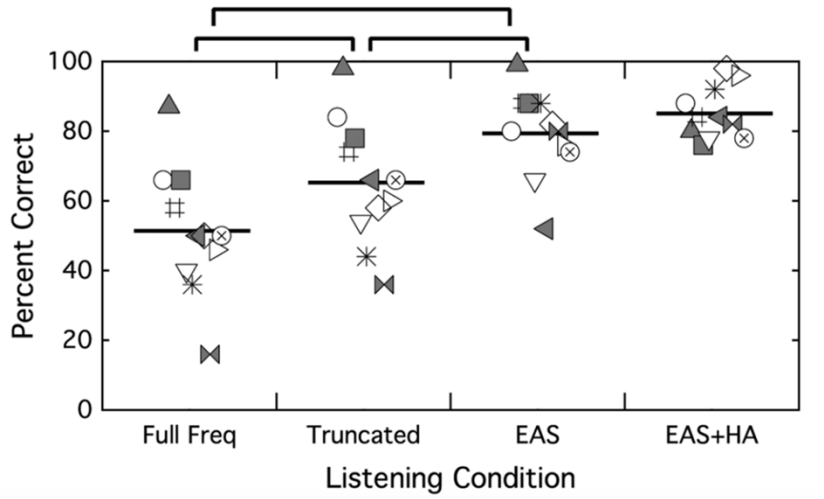


Figure 1: CNC words in quiet Dillon et al (2015)

Test Conditions

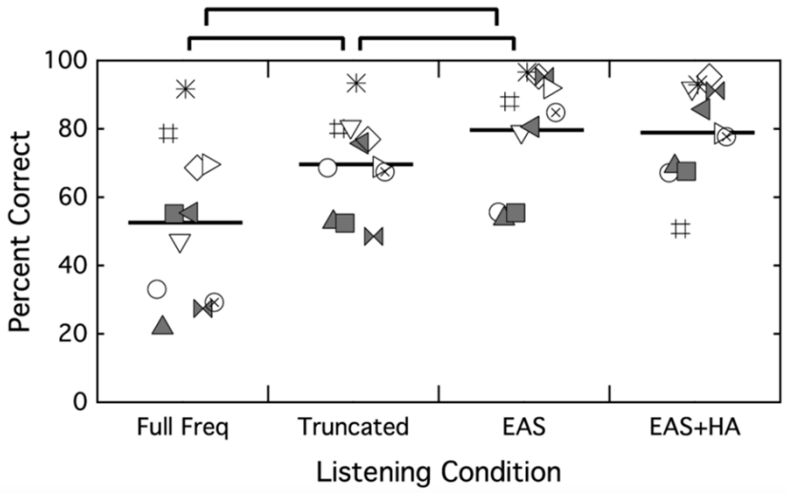


Figure 2: CUNY sentences in steady noise Dillon et al (2015)

Test Conditions

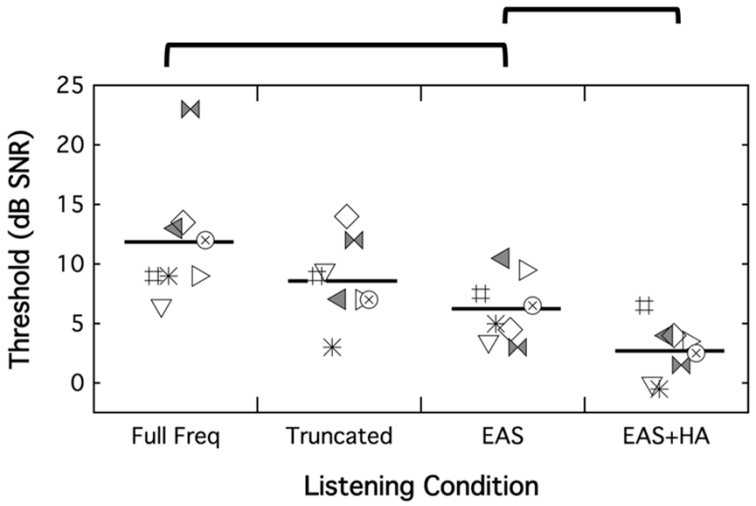


Figure 3: BKB-SIN Dillon et al (2015)

Ten Years of EAS Experience: What we know now

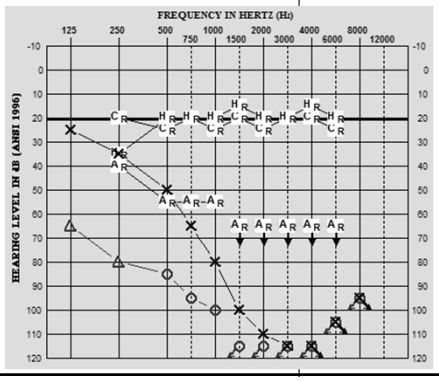
CASE STUDIES

Case A: Low-Frequency Hearing

- Audiology protocol measured unaided thresholds from 250 to 8000 Hz
  - » When hearing 80 dB HL or poorer, use of the acoustic component was discontinued
    - However, the fitting range of the acoustic component is 125 to 1800 Hz

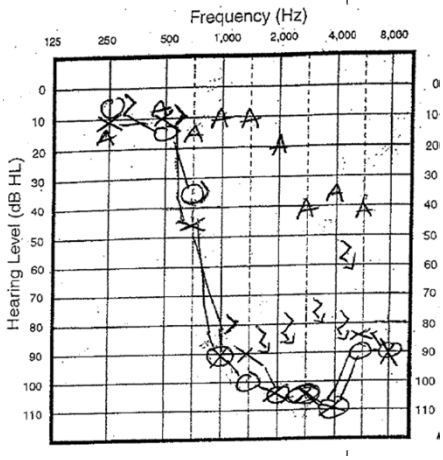
Case A: Low-Frequency Hearing

- Audiology protocol measured unaided thresholds from 250 to 8000 Hz
  - » Some subjects continued to experience an improvement in the EAS condition as compared to the CI alone, potentially due to residual hearing at 125 Hz



	CI Alone	EAS
CNC	56%	**88%**
CUNY (0 dB SNR)	59%	**74%**

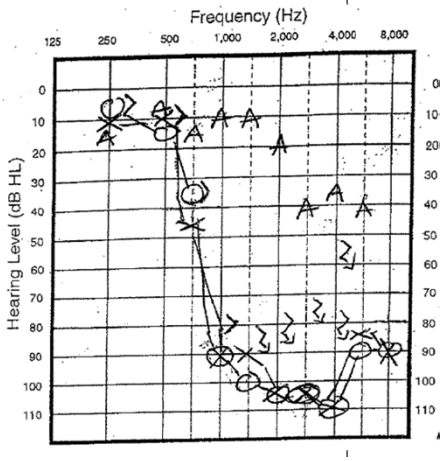
Case B: Long-term Stability



CNC	CUNY(0 dB SNR)
26%	23%

- History
  - » 33 yr old, male
  - » Etiology: reportedly genetic (mother, brother)
  - » Fit with HAs at 24 yrs old
  - » Reports difficulty hearing at home and work

Case B: Long-term Stability

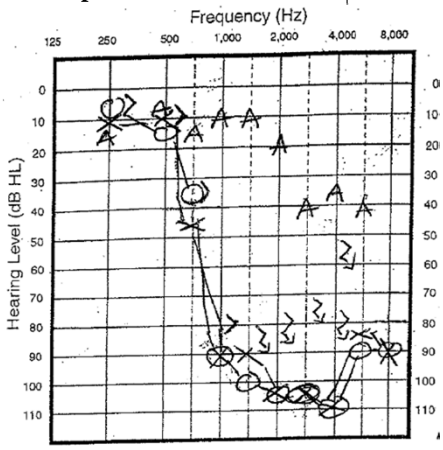


CNC	CUNY(0 dB SNR)
26%	23%

- Cochlear implantation
  - » LEFT ear
- Initial activation scheduled approximately 4 weeks later

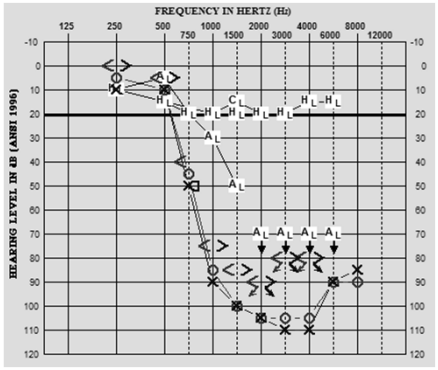
Case B: Long-term Stability

PreOperative



CNC	CUNY(0 dB SNR)
26%	23%

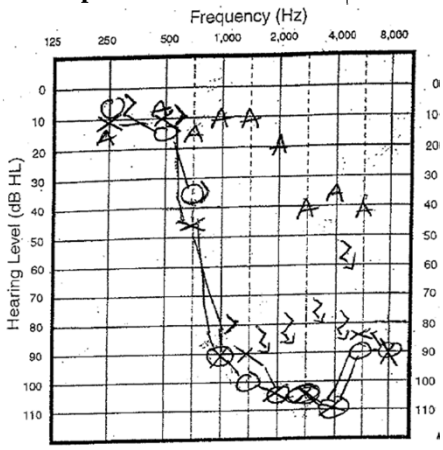
12-Month Follow-Up



CNC	CUNY(0 dB SNR)
82%	81%

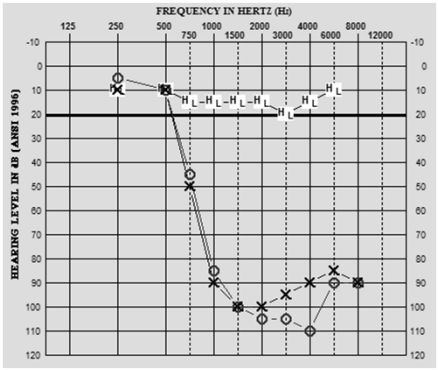
Case B: Long-term Stability

PreOperative



CNC	CUNY(0 dB SNR)
26%	23%

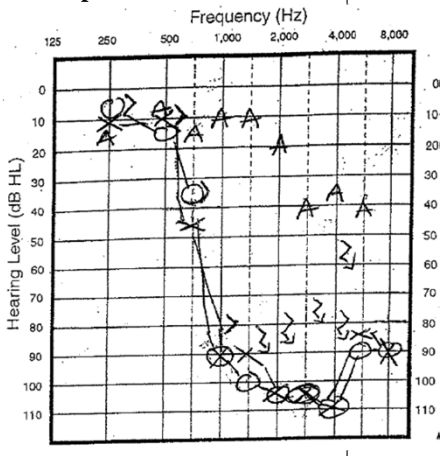
2 Year Follow-Up



CNC	CUNY(0 dB SNR)
90%	99%

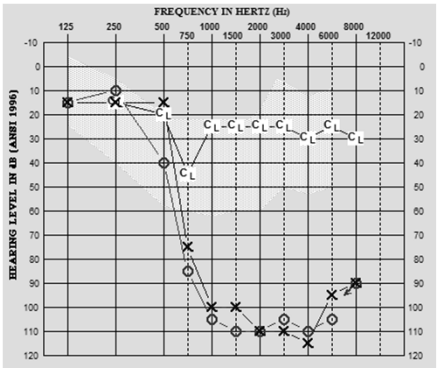
Case B: Long-term Stability

PreOperative



CNC	CUNY(0 dB SNR)
26%	23%

7 Year Follow-Up



CNC	CUNY (0 dB SNR)	AzBio (5 dB SNR)	BKB-SIN
92%	82%	91%	3.5 dB

Summary

- Recipients experienced improvement in speech perception and quality of life with EAS as compared to conventional amplification
- Charge levels were unrelated to change in residual hearing
- Assessment of speech perception in babble as opposed to steady noise may better demonstrate the contribution of the acoustic component
- Listening experience may influence CI alone findings

Summary

- Low-frequency residual hearing can offer improved speech perception
  - » Noise
  - » 125 Hz
- Residual hearing can be maintained with long-term use
  - » Assessment of residual hearing over time

Thank you!

Contact:
Margaret Dillon, AuD: mdillon@med.unc.edu