Electric-Acoustic Stimulation Clinical Trial Outcomes

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December 2, 2016

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.
EAS Clinical Trial Results

- EAS Study Review
  - Clinical trial sites
  - Study Design
  - Surgical protocol
- EAS Results
- MED-EL EAS v. Cochlear Hybrid
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
Inclusion criteria:
- 18-70 years of age
- Normal hearing to moderate hearing loss in the low frequencies
- 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

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

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

- FDA approved devices:
  - SONATA, CONCERT, SYNCHRONY, FLEX\textsuperscript{24}, DUET2, SONNET\textsuperscript{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)

Baseline EAS: 31%
EAS: 73%

Results – Words in Quiet (EAS)

Pre-op EAS: 30%
EAS: 67%
Results – Words in Quiet (Electric Only)

- Baseline CI Alone
- 30% 48%
- 3m 6m 12m

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 (6 dB SNR, n = 11) for each listening condition. Plotting conventions are the same as Figure 1.
Results – Sentences in Noise (Electric v. EAS)

- CI Alone
- 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
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)
Results – Hearing Sensitivity

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

<table>
<thead>
<tr>
<th>Time Point</th>
<th>&lt; 10 dB</th>
<th>10-20 dB</th>
<th>20-30 dB</th>
<th>&gt; 30 dB</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Month</td>
<td>10/71 (14%)</td>
<td>30/71 (42%)</td>
<td>18/71 (26%)</td>
<td>13/71 (18%)</td>
</tr>
<tr>
<td>6 Month</td>
<td>11/69 (16%)</td>
<td>23/69 (33%)</td>
<td>20/69 (29%)</td>
<td>15/69 (22%)</td>
</tr>
<tr>
<td>12 Month</td>
<td>8/67 (12%)</td>
<td>25/67 (37%)</td>
<td>20/67 (30%)</td>
<td>14/67 (21%)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Mild to Moderate</th>
<th>Moderately-Severe to Severe</th>
<th>Profound</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Month</td>
<td>9/71 (13%)</td>
<td>58/71 (82%)</td>
<td>4/71 (6%)</td>
</tr>
<tr>
<td>6 Month</td>
<td>11/69 (16%)</td>
<td>52/69 (75%)</td>
<td>6/69 (9%)</td>
</tr>
<tr>
<td>12 Month</td>
<td>7/67 (10%)</td>
<td>52/67 (78%)</td>
<td>8/67 (12%)</td>
</tr>
</tbody>
</table>
Results – Loss of Hearing

- Two subjects could not use the acoustic unit

<table>
<thead>
<tr>
<th></th>
<th>Pre-op</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNC</td>
<td>28</td>
<td>46</td>
</tr>
<tr>
<td>CUNY (0 dB SNR)</td>
<td>0</td>
<td>63</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Pre-op</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNC</td>
<td>26</td>
<td>74</td>
</tr>
<tr>
<td>CUNY (0 dB SNR)</td>
<td>19</td>
<td>97</td>
</tr>
</tbody>
</table>

MED-EL EAS v. Cochlear Hybrid
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 L.24
- Cochleostomy
- Up to 16 mm insertion depth
- 6-month endpoint
- Words in quiet, sentences in noise

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

**MED-EL EAS**

**Cochlear Hybrid**

CNC Score 0-60% (both ears)

CNC Score 10-60% (80% non-implant)
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

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

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

**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

<table>
<thead>
<tr>
<th>Number of...</th>
<th>EAS</th>
<th>Hybrid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td>35</td>
<td>65</td>
</tr>
<tr>
<td>Subjects experiencing adverse events</td>
<td>29 (40%)</td>
<td>34 (68%)</td>
</tr>
<tr>
<td>Events reported as “profound/total loss of hearing”</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>Months hearing loss data collected</td>
<td>104</td>
<td>48</td>
</tr>
<tr>
<td>Revision surgeries due to poor performance</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>
Resources

- FDA Panel Meeting, October 2013
- FDA Summary of Safety and Effectiveness Data, March 2014
  - http://www.accessdata.fda.gov/cdrh_docs/pdf13/P130016B.pdf
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
  » Annette 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

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
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

<table>
<thead>
<tr>
<th>dB HL</th>
<th>Min</th>
<th>Max</th>
<th>Avg</th>
<th>Avg change from previous interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>15.0</td>
<td>66.7</td>
<td>42.2</td>
<td>NA</td>
</tr>
<tr>
<td>Initial CI activation</td>
<td>35.0</td>
<td>115.0</td>
<td>60.9</td>
<td>-18.7</td>
</tr>
<tr>
<td>6 month</td>
<td>26.7</td>
<td>120.0</td>
<td>60.4</td>
<td>0.5</td>
</tr>
<tr>
<td>12 month</td>
<td>26.7</td>
<td>120.0</td>
<td>63.3</td>
<td>-2.9</td>
</tr>
<tr>
<td>2 year</td>
<td>23.3</td>
<td>120.0</td>
<td>65.3</td>
<td>-2</td>
</tr>
</tbody>
</table>

No Response assigned a value of 120 dB

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# Speech Perception

![Speech Perception graph](image)

**Figure 3**  
Adunke et al (2013)
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

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**

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**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?

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

Methods

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

Methods

• Low-frequency BC PTA

• Charge

\[
\text{charge (nC)} = \frac{\text{MCL (cu)} \times \text{pw (\mu s)}}{1000}
\]

» Mapping completed with CI Studio clinical programming software
  • MCL reported in current units (cu)
  • 1 cu \approx 1 \mu A
» CIS coding strategy


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

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


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

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
Test Conditions

Figure 1: CNC words in quiet


Figure 2: CUNY sentences in steady noise

Test Conditions

Figure 3: BKB-SIN


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

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.

<table>
<thead>
<tr>
<th></th>
<th>CI Alone</th>
<th>EAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNC</td>
<td>56%</td>
<td>88%</td>
</tr>
<tr>
<td>CUNY (0 dB SNR)</td>
<td>59%</td>
<td>74%</td>
</tr>
</tbody>
</table>
Case B: Long-term Stability

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

![Cochlear implantation diagram]

- **Cochlear implantation**
  - LEFT ear

- **Initial activation** scheduled approximately 4 weeks later

![Cochlear implantation diagram]
Case B: Long-term Stability

PreOperative

12-Month Follow-Up

CNC CUNY (0 dB SNR)
26% 23%

CNC CUNY (0 dB SNR)
82% 81%

Case B: Long-term Stability

PreOperative

2 Year Follow-Up

CNC CUNY (0 dB SNR)
26% 23%

CNC CUNY (0 dB SNR)
90% 99%
Case B: Long-term Stability

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!

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