Comparison of High-Frequency TEOAEs and DPOAEs for Monitoring Ototoxicity in Pediatric Cancer Patients
Overview

- Ototoxicity Monitoring
- Technical Issues with High-Frequency OAEs
- Solutions and Progress
- TEOAEs or DPOAEs?
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Cisplatin Ototoxicity

Binds to DNA to prevent cells from reproducing.

Ototoxicity Mechanism not fully understood.
(reactive oxygen species in cochlea?)

Causes permanent cochlear hearing loss, primarily OHC damage.

Damages higher frequencies first, then lower frequencies.
Cisplatin Ototoxicity

Prevalence & degree of ototoxicity inversely related to age of the patient.

Up to 60% of pediatric patients incur significant hearing loss.

Timing and extent of cochlear damage highly variable across individuals.
Ototoxicity Monitoring

Allows physicians to consider altering treatment.

Early identification of hearing loss and intervention reduces negative impact.

Critical for children, who are still developing speech and language.
Ototoxicity Monitoring

Gold standard: pure-tone behavioral thresholds at standard frequencies (0.25-8 kHz).
(ASHA, 1994)

Extended high frequency audiogram (10-20 kHz) more effective, but sometimes impractical.

OAEs: efficient, objective, sensitive indicators of ototoxic hair cell damage

High-Frequency OAEs: more effective? Practical?
Summary

Ototoxicity Monitoring

- Cancer a leading cause of death in children.
- Children susceptible to platinum-based ototoxicity.
- High-frequency monitoring may allow early identification and reduction of negative impact.
- Behavioral testing difficult in children.
- High-frequency OAEs an attractive alternative.
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Accurate and Precise Measurement

- **Accuracy**: The difference between the measured value and the true value.
- **Precision**: The spread of the measured values.

Diagram:
- Vertical axis: Probability Density
- Horizontal axis: True Value vs. Measured Value
OAE Accuracy and Precision

Low Frequencies

High Frequencies
OAE Accuracy and Precision

**Good Test**

- Normal
- Hearing Loss

**Poor Test**

- Normal
- Hearing Loss

**Probability Density**

- OAE Magnitude

**Low Frequencies**

**High Frequencies**
What is the problem with high frequencies?
What is the problem with high frequencies?

- Output Limitations
- Non-flat response
- Insertion Depth
- Ear Canal Diameter
- Probe Tip Type
- Poorer SNR
- Higher intrinsic variability?

Accuracy

Precision
What is the problem with high frequencies?

Output Limitations
Non-flat response

Accurancy

loudest speaker
microphone
loudest speaker
High Frequency Accuracy

Commercially available OAE microphones not designed to measure high frequencies.
Output Limitations

ER2 Loudspeaker Response

Magnitude (dB SPL)

Frequency (kHz)
Output Limitations

ER-3A RESPONSE IN THREE COUPLERS

[Graph showing relative response in dB against frequency (Hz) for different couplers]
Non-Flat Response

ER10B+ Microphone Sensitivity

Frequency Response

Etymotic Research

07/06/06 11:48:41

84dB SPL Sound Field (0.316 Pascal)

ER-10B+ #742  Tested By: D.P.K.
What is the problem with high frequencies?

- Insertion Depth
- Ear Canal Diameter
- Probe Tip Type

Accuracy
Precision
In closed cavities, combination of forward and reverse pressure waves result in standing waves, causing in calibration errors.

Insertion Depth

Actual pressure at eardrum

Measured pressure at OAE microphone
Insertion Depth

Small changes in insertion depth cause notches to shift.
Ear Canal Diameter

Small differences in ear canal diameter relative to the calibration cavity increase error.
Probe Tip Type

Different probe tips result in differing amounts of error.
What is the problem with high frequencies?

- Poorer SNR
- Higher intrinsic variability?
- Insertion Depth
- Ear Canal Diameter
- Output Limitations
- Non-flat response
- Probe Tip Type
Poorer SNR

Middle ear transfer function reduces OAE amplitudes.

![Graph showing pressure gain (dB) vs. frequency (Hz)]
Summary

Technical Issues

- Loudspeaker output limitations
- Non-flat microphone response
- Insertion depth and standing waves
- Variable ear canal diameters
- Probe tip types
- Middle-ear related SNR issues
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**SOLUTIONS: Output Limitations**

Cut the sound tube short to increase high-frequency output.

Correct for resulting changes at other frequencies.
Cut the sound tube short to increase high-frequency output.

Correct for resulting changes at other frequencies.
SOLUTIONS: Non-Flat Response

Use two reference microphones to find correction values. Apply these to measured OAEs.

\[
\text{True ER10B+} = \left( \frac{\text{ER10B+}}{\text{Ref}} \right) \times \left( \frac{\text{Probe}_{\text{Ref}}}{\text{Probe}_{\text{ER10B+}}} \right)
\]

Siegel (2002)
SOLUTIONS: Non-Flat Response

Use two reference microphones to find correction values. Apply these to measured OAEs.
SOLUTIONS: Non-Flat Response

Use two reference microphones to find correction values. Apply these to measured OAEs.
Solutions: Insertion Depth

Mathematically separate forward and reverse pressure waves.

Calibrate in Forward Pressure Level (FPL) instead of Sound Pressure Level (SPL).
SOLUTIONS: Insertion Depth

Mathematically separate forward and reverse pressure waves.

Calibrate in Forward Pressure Level (FPL) instead of Sound Pressure Level (SPL).
Mathematically separate forward and reverse pressure waves.

Calibrate in Forward Pressure Level (FPL) instead of Sound Pressure Level (SPL).

Cavity impedances yield overdetermined set of equations to estimate the source impedance.

\[ Z_{\text{load}} = \frac{Z_{\text{source}} P_{\text{Load}}}{P_{\text{source}} - P_{\text{Load}}} \]

\[ FPL = \frac{P_{\text{Load}}}{2} \left( 1 + \frac{Z_0}{Z_{\text{Load}}} \right) \]
**SOLUTIONS**: Insertion Depth

Mathematically separate forward and reverse pressure waves.

Calibrate in Forward Pressure Level (FPL) instead of Sound Pressure Level (SPL).
Solutions: Ear Canal Diameter

Accurate in-situ FPL calibration is dependent upon an appropriate estimate of characteristic impedance ($Z_0$).

Estimate $Z_0$ from load impedance by minimizing the corresponding time-domain reflectance at $t = 0$.

Scheperle, Goodman, & Neely (2011); Rasetshwane and Neely (2011)
**SOLUTIONS:** Probe Tip Type

Use standard foam tip or modified ER10D (rubber) tip.

Scheperle, Goodman, & Neely (2011)
**SOLUTIONS:** Probe Tip Type

Use standard foam tip or modified ER10D (rubber) tip.

*Scheperle, Goodman, & Neely (2011)*
SOLUTIONS: Poorer SNR

Increase high-frequency loudspeaker output to overcome middle ear transfer function in the forward direction.

Frequency (kHz) | Stimulus Level (dB SPL)
--- | ---
0.1 | 70
1 | 70
10 | 80

*shape of behavioral auditory threshold curve*
Solutions: Poorer SNR

Increase high-frequency loudspeaker output to overcome middle ear transfer function in the forward direction.
Summary

Solutions and Progress

- Cut sound tube short.
- Calibrate microphone and apply corrections.
- Use FPL to specify stimulus levels.
- Use new technique to estimate characteristic ear canal impedance.
- Modify the probe tip.
- Give high-frequency emphasis to stimuli.
Overview

- Ototoxicity Monitoring
- Technical Issues with High-Frequency OAEs
- Solutions and Progress
- TEOAEs or DPOAEs?
A stimulus that is infinitely long in time (sinusoid)…

… is infinitely narrow in frequency.

TEOAEs or DPOAEs?
As a stimulus becomes shorter in time… its frequency content becomes more broad.

TEOAEs or DPOAEs?
As a stimulus becomes shorter in time…

… its frequency content becomes more broad.

As a stimulus becomes shorter in time…
An infinitely short stimulus... contains all frequencies.

TEOAEs or DPOAEs?
TEOAEs or DPOAEs?

Continuous versus Discrete OAE spectra

Implications for test time, SNR, variability
TEOAEs or DPOAEs?

446 Ears classified as normal/impaired

Impairment predicted for HL > 20 dB

<table>
<thead>
<tr>
<th>Study</th>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>Current CEOAE (65 dB pSPL)</td>
<td>Current CEOAE (65 dB pSPL)</td>
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<tr>
<td>Current CEOAE (62 dB pSPL)</td>
<td>Current CEOAE (62 dB pSPL)</td>
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f (kHz) ROC Area

Goodman, & Keefe

Perfect test

Random
TEOAEs or DPOAEs?

But if we use continuously swept DPOAE primaries...

Implications for test time, SNR, variability
TEOAES or DPOAEs?

Single versus Multiple Generation Components

Implications for test sensitivity and differential diagnosis
TEOAEs or DPOAEs?

But if we use analyze the TEOAEs appropriately...
TEOAEs or DPOAEs?

But if we use analyze the TEOAEs appropriately…
TEOAEs or DPOAEs?

But if we use analyze the TEOAEs appropriately...

Implications for test sensitivity and differential diagnosis
TEOAEs or DPOAEs?

Multiple Generation Components

Implications for test sensitivity and differential diagnosis
Summary

TEOAEs or DPOAEs?

- Continuous versus Discrete OAE spectra.
- Implications for test-retest variability.
- Multiple components: reflection versus distortion.
- Implications for differential sensitivity.
- Achievable SNR for given test time.
- Achievable high-frequency stimulus levels.
Conclusions

- High-Frequency Ototoxicity Monitoring using OAEs — almost there...

- Have now found viable solutions for known technical issues.

- TEOAEs or DPOAEs? Measure both and determine empirically.
Acknowledgements

- ASH Foundation Grant
- ACS Holden Cancer Center Grant
- Rachel Scheperle
- James Lewis
- Ian Mertes
- Steve Neely