



Diverse Audiologic Outcomes in the Pediatric Oncology Population

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Learning Objectives

Learn the auditory physiological impacts of cisplatin vs carboplatin chemotherapies

Learn about the significance of genetic contributions to acquired sensorineural hearing loss in the pediatric oncology population.

Understand the research supporting differences in peripheral auditory functioning based on region of anatomical insult and implications for future directions investigating prognosis of hearing health during cancer survivorship.



St. Jude History

**“No child should die in the dawn of life”
– Danny Thomas (Founder)**



St. Jude Children's Research Hospital

Hospital dedicated to treating children with cancer and catastrophic diseases

Pediatric Cancer Statistics:

- Estimated 400,000 children and adolescents (aged 0-19 years old) are diagnosed with cancer each year
- In the US, 15,000 children & adolescents (aged 0-19 years old) are diagnosed with cancer each year
- The five-year survival rate for all pediatric cancers combined has increased from 63% in mid-1970 to 87% between 2015-2021 (AACR *Pediatric Cancer Progress Report 2025*)
- Approximately 60-70% of pediatric cancer patients treated with platinum-based chemotherapies experience some degree of hearing loss (Oh H, Park MK. *Assessment and Management of Chemotherapy-Induced Ototoxicity in Children. J Audiol Otol. 2025 Apr;29(2):79-85. doi: 10.7874/jao.2025.00073. Epub 2025 Apr 18. PMID: 40296470; PMCID: PMC12046201.*)





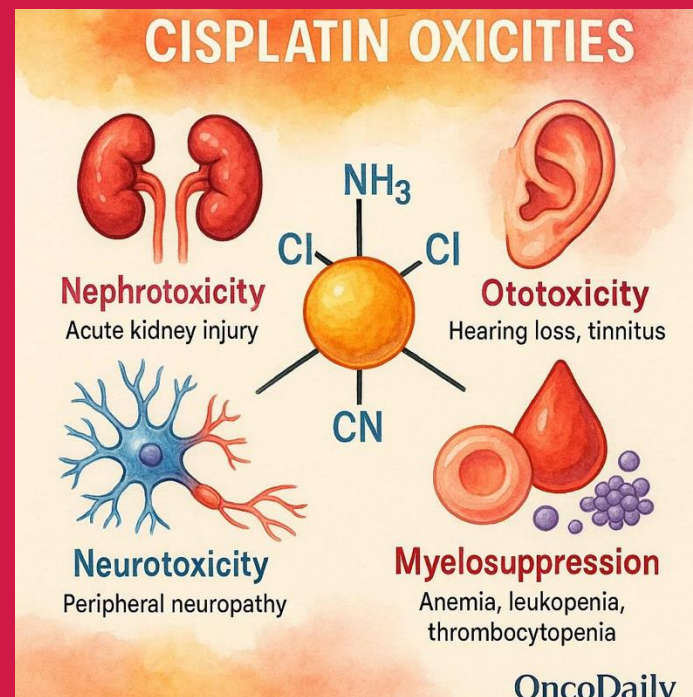
Audiology @ St. Jude

Ototoxicity
Monitoring

Amplification
During and After
Treatment

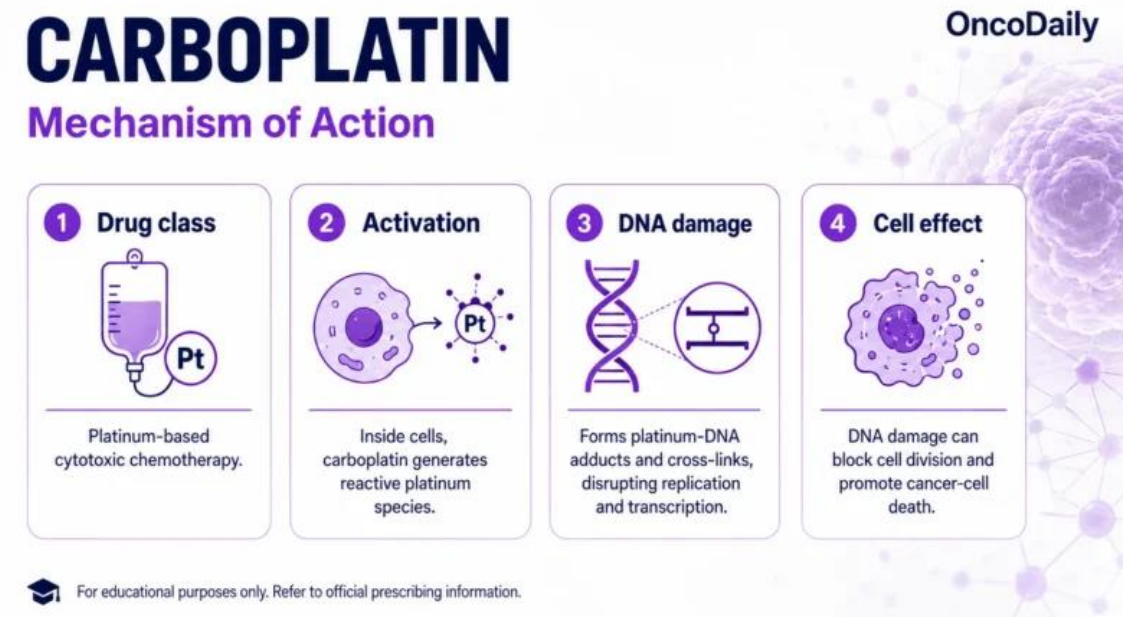
Long-Term
Survivorship
Studies

Cancer-Treatment related Hearing Loss stems from:



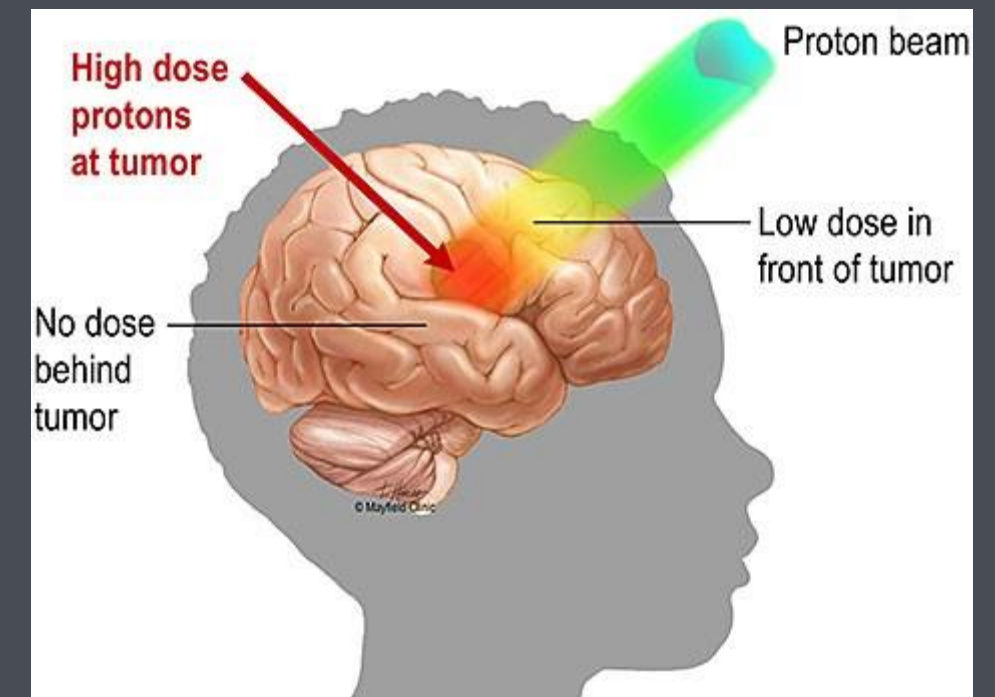
Cisplatin Chemotherapy

Primarily effects outer hair cell integrity



Carboplatin Chemotherapy

Primarily effects inner hair cell integrity

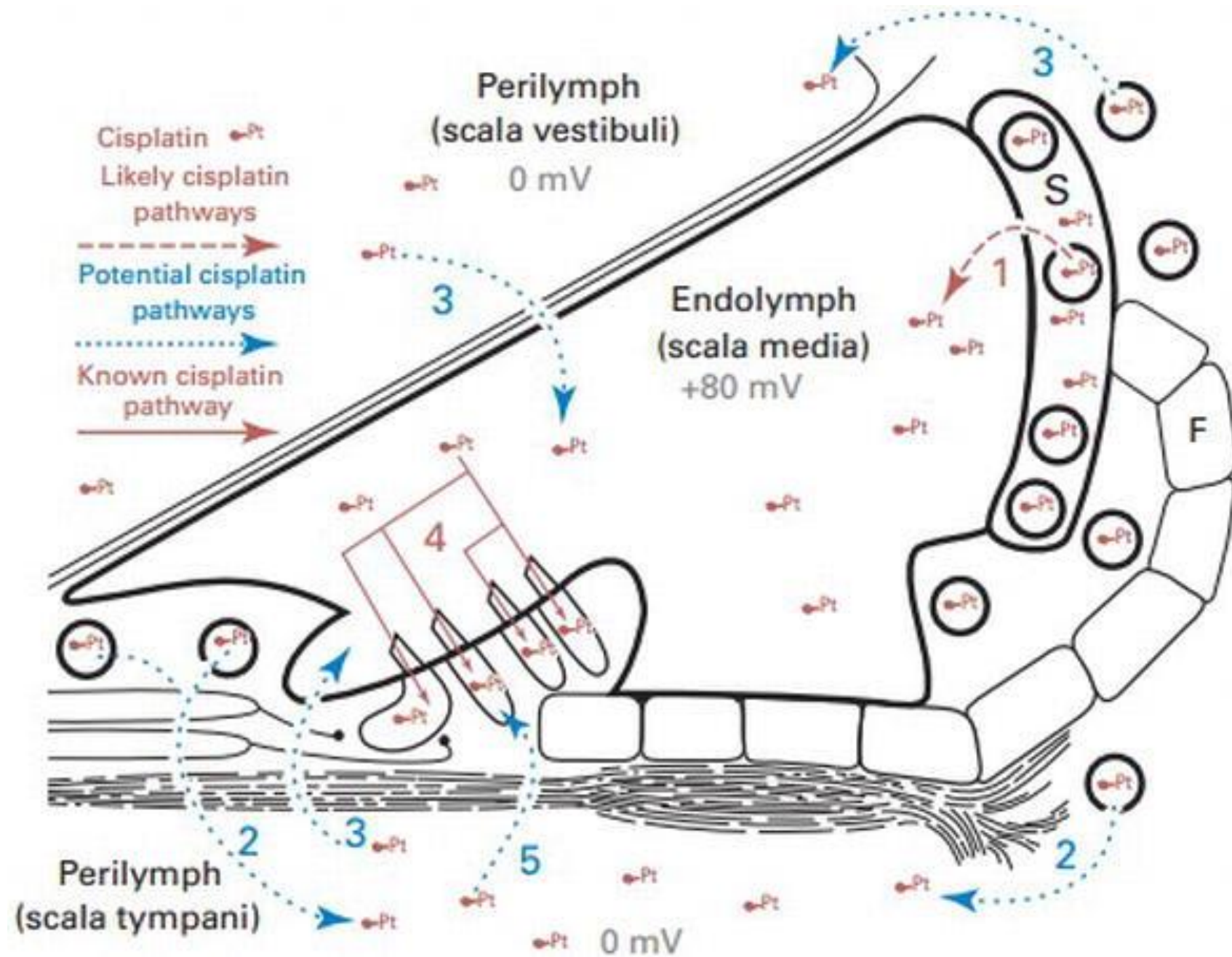
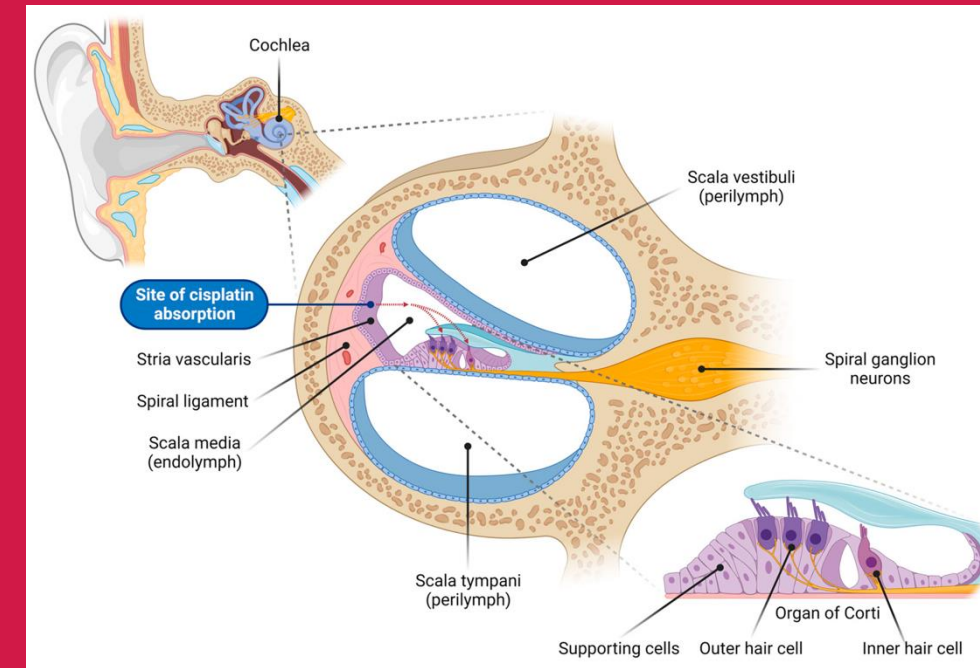


Proton Beam Radiation

Can have effects on outer/inner hair cells (cochlear effects) as well as middle ear pathology

Image from Cincinnati Children's

Pathophysiology: Cisplatin



Enters the cochlea
through the stria
vascularis

- Permeates the endolymph and spreads to the sensory cells
- Becomes trapped in the stria vascularis and inner/outer hair cells

Prevalence & Risk of Cisplatin-Induced Hearing Loss (CIHL)

Moke, D. J., Luo, C., Millstein, J., Knight, K. R., Rassekh, S. R., Brooks, B., ... & Orgel, E. (2021). Prevalence and risk factors for cisplatin-induced hearing loss in children, adolescents, and young adults: a multi-institutional North American cohort study. *The Lancet Child & Adolescent Health*, 5(4), 274-283.

- Determined prevalence of SIOP Grade 2 hearing loss at most recent audiologic follow-up post treatment (& immediately at end of therapy – no baseline data)
 - SIOP Grade 2 = >20 dB HL SNHL at 4000 Hz and above
- Hearing loss is more prevalent/severe for individuals receiving cisplatin who are 5 years old and younger
- Some diagnoses require a heavier treatment regime, which lends to a more severe hearing loss than would be experienced with other diagnoses (e.g., CNS tumors, Hepatoblastoma, Neuroblastoma)

These results help inform dose reduction strategies for oncology teams and identify which diagnoses require a more aggressive hearing loss prevention approach

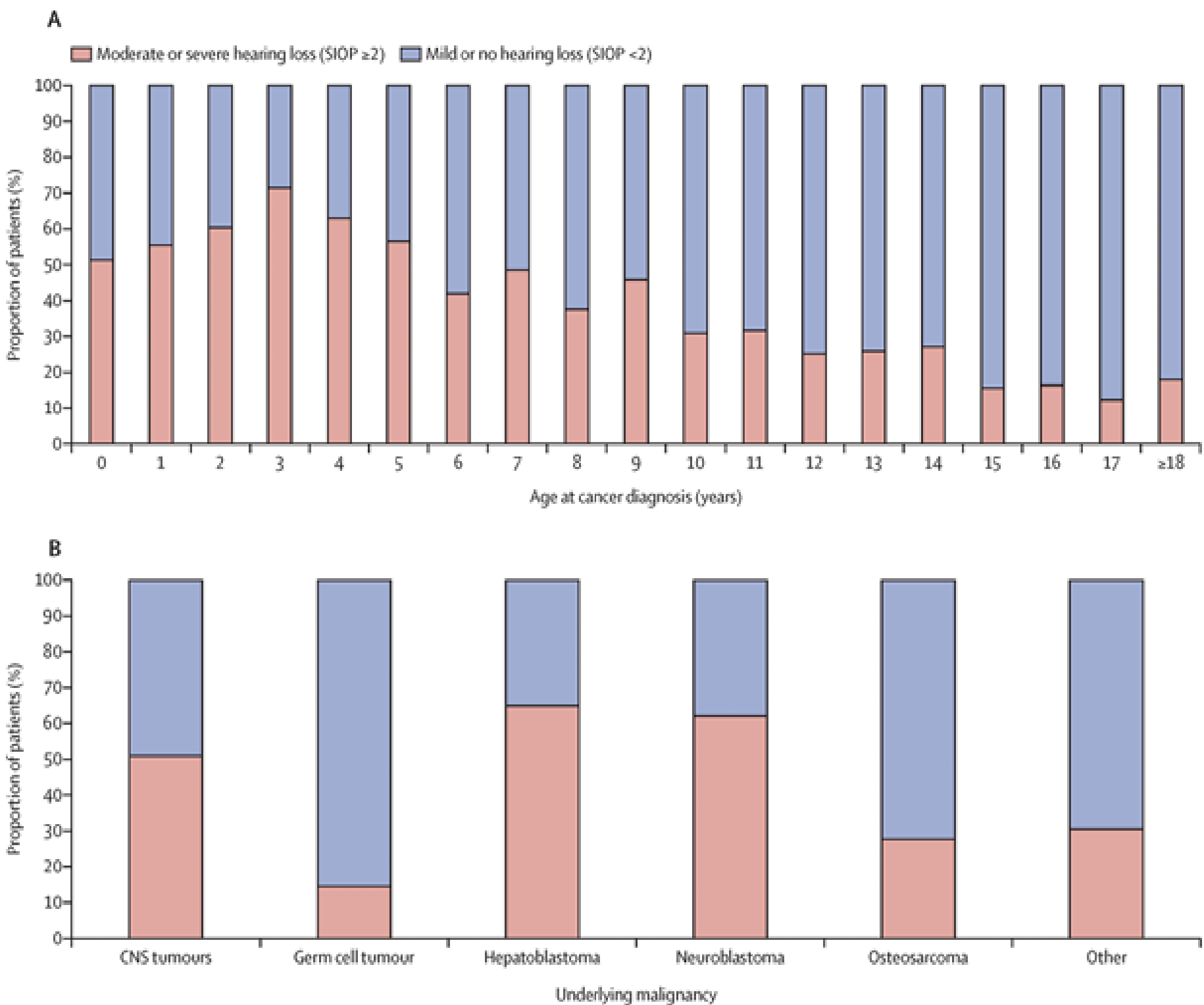


Figure 1: Prevalence of moderate or severe cisplatin-induced hearing loss by age and underlying malignancy
 Prevalence of hearing loss at latest audiometry by age at cancer diagnosis in years (A) and underlying malignancy (B). χ^2 tested for differences by age in part A and by category in part B; p<0.001 in both. SIOP=International Society of Pediatric Oncology Ototoxicity Grade (0–4).

Cisplatin & Late-Onset Hearing Loss

- Hearing loss has been observed to occur as late as 136 months post-treatment for some patients
- 51% of patients were shown to have LOHL, with those having received higher cumulative doses of cisplatin showing more prevalence
- Also prevalent in those having received cranial radiation and a combination of cisplatin/carboplatin
- Of note, 88% of the patients diagnosed with medulloblastoma at a younger age in this study showed LOHL (8/9 patients)
- Posterior fossa radiation was also a significant risk factor for LOHL

Kolinsky, D. C., Hayashi, S. S., Karzon, R., Mao, J., & Hayashi, R. J. (2010). Late onset hearing loss: a significant complication of cancer survivors treated with Cisplatin containing chemotherapy regimens. *Journal of pediatric hematology/oncology*, 32(2), 119-123.

TABLE 3. Treatment Characteristics

	No LOHL	LOHL	Total	P
No. patients	29 (49%)	30 (51%)	59	
Cisplatin cumulative dose average (mg/m ²)	374.7 (± 124.8)	453.5 (± 182.1)	414.8 (± 160.2)	0.071
Chemotherapy				
Carboplatin and cisplatin	11 (38%)	13 (43%)	24	
Cisplatin only	18 (62%)	17 (57%)	35	
Head radiation	7 (24%)	15 (50%)	22	0.044
Posterior fossa radiation	1 (3%)	9 (30%)	10	0.023
Nonhead radiation	6 (21%)	7 (23%)	13	
No radiation	16 (55%)	8 (27%)	24	0.029

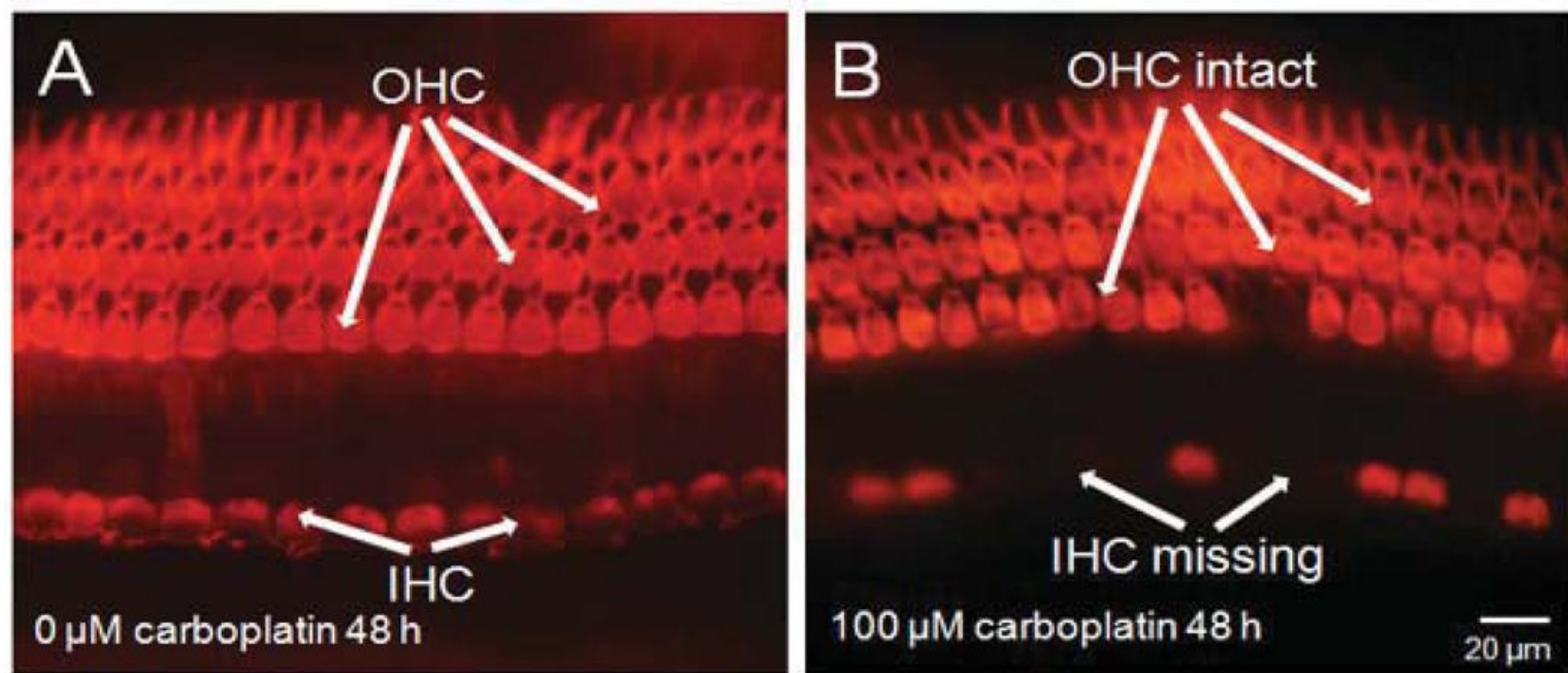
LOHL indicates late onset hearing loss.

TABLE 2. Patient Characteristics

	No LOHL	LOHL	Total	P
No. patients	29 (49%)	30 (51%)	59	
Sex				
Males	17 (59%)	21 (70%)	38	0.36
Females	12 (41%)	9 (30%)	21	
Age range at diagnosis (mo)	2–197	3–195	2–197	
Mean age at diagnosis (mo)	100 (± 66)	64 (± 57)	81 (± 63)	0.031
Time range between last cisplatin to detection of LOHL (mo)		12–98		
Diagnosis				
Solid tumors				
Osteosarcoma	6 (21%)	3 (10%)	9	
Hepatoblastoma	5 (17%)	1 (3%)	6	
Neuroblastoma	7 (24%)	9 (30%)	16	0.69
Germ cell tumor	4 (14%)	2 (7%)	6	
Other solid tumors	0 (0%)	2 (7%)	2	
Brain tumors				
Medulloblastoma	1 (3%)	8 (27%)	9	0.035
Other brain tumors	6 (21%)	5 (17%)	11	
Hearing aids				
Yes	1 (3%)	11 (37%)	12	0.010
No	28 (97%)	19 (63%)	47	

LOHL indicates late onset hearing loss.

Pathophysiology: Carboplatin



Dalian D, Haiyan J, Yong F, Salvi R, Someya S, Tanokura M. OTOTOXIC EFFECTS OF CARBOPLATIN IN ORGANOTYPIC CULTURES IN CHINCHILLAS AND RATS. J Otol. 2012 Dec;7(2):92-101. doi: 10.1016/S1672-2930(12)50023-1. PMID: 25593588; PMCID: PMC4291553.

- Moderate doses of carboplatin selectively damage Type I spiral ganglion neurons and inner hair cells
- With more severe, serial doses and with younger patient age, carboplatin can begin to affect outer hair cells as well
- Research has been largely conducted using animal models (chinchilla)



Incidence & Severity of Carboplatin Induced Hearing Loss

Chawla, A., Carter, S., Wood, A., Staffieri, S., Dodgshun, A., Eisenstat, D. D., & Sullivan, M. (2026). Incidence and Severity of Carboplatin-Associated Hearing Loss in Children With Cancer Assessed by the SIOP Boston 2012 Ototoxicity Criteria. *Pediatric Blood & Cancer*, e70494.

- Only 4.5% of patients were diagnosed with clinically significant hearing loss (SIOP Grade 2 or poorer; 9/200 patients)
- Younger age at first exposure was the only significant predictor of hearing loss following carboplatin treatment (≤ 28 months)
- No baseline hearing evaluations so not entirely confident in saying 9/200 attributable solely to carboplatin exposure

% Hearing loss re: SIOP grade

TABLE 3 | Hearing loss outcomes.

SIOP grade	Definitions	n	% HL	% Total
0	≤ 20 dB HL at all frequencies	185	N/A	92.5
1	> 20 dB HL (i.e., 25 dB HL or greater) SNHL above 4000 Hz (i.e., 6 or 8 kHz)	6	40.0	3.0
2	> 20 dB HL at 4000 Hz and above	2	13.3	1.0
3	> 20 dB HL at 2000 Hz or 3000 Hz and above	6	40.0	3.0
4	> 40 dB HL (i.e., 45 dB HL or more) at 2000 Hz and above	1	6.7	0.5

Abbreviation: HL, hearing loss.

Contributors: Age & Carboplatin dosage

TABLE 6 | Effect of dichotomised continuous variables on hearing outcomes.

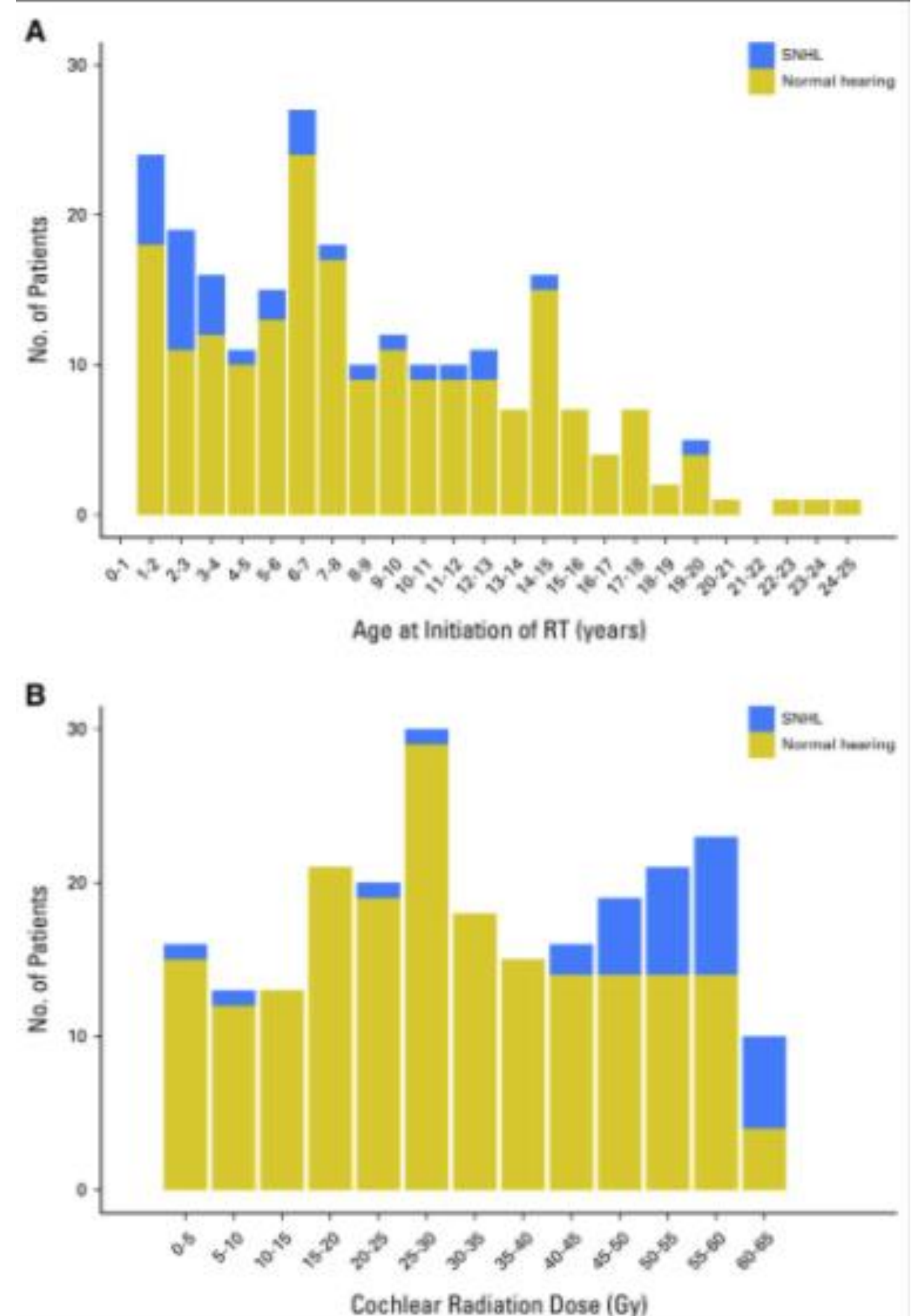
	p value	Odds ratio (95% CI)
Age ≤ 28 months	0.0042*	12.37 (1.822–138.4)
Cumulative carboplatin > 3984 mg/m ²	0.1245	0.3527 (0.09486–1.348)
No. of carboplatin doses < 10	0.0787	5.287 (0.7813–59.41)

*indicates p-value < 0.05 .

Proton Beam Radiation (Bass et al., 2016)

- Most patients with SNHL post-radiation experience hearing decline within the first 3 years
- Hearing is affected more for children with median age of 3.6 years
- Higher cochlear radiation dose is associated with SNHL

Bass JK, Hua CH, Huang J, Onar-Thomas A, Ness KK, Jones S, White S, Bhagat SP, Chang KW, Merchant TE. Hearing Loss in Patients Who Received Cranial Radiation Therapy for Childhood Cancer. J Clin Oncol. 2016 Apr 10;34(11):1248-55. doi: 10.1200/JCO.2015.63.6738. Epub 2016 Jan 25. PMID: 26811531; PMCID: PMC4933129.



Chang and SIOP Grading Scales



Standardization of measurement and reporting of hearing loss caused by ototoxic therapies/drugs

Brock PR, Knight KR, Freyer DR, Campbell KC, Steyger PS, Blakley BW, Rassekh SR, Chang KW, Fligor BJ, Rajput K, Sullivan M, Neuwelt EA. Platinum-induced ototoxicity in children: a consensus review on mechanisms, predisposition, and protection, including a new International Society of Pediatric Oncology Boston ototoxicity scale. J Clin Oncol. 2012 Jul 1;30(19):2408-17. doi: 10.1200/JCO.2011.39.1110. Epub 2012 Apr 30. PMID: 22547603; PMCID: PMC3675696.

Chang Grading Scale

	Chang	
Grade 0	≤20 dB at 1, 2, and 4 kHz	Normal
Grade 1a	≥40 dB at any freq 6–12 kHz	Normal
Grade 1b	>20 and <40 dB at 4 kHz	Normal
Grade 2a	≥ 40 dB at 4 kHz and above	Normal
Grade 2b	>20 and <40 dB at any freq below 4 kHz	Hearing loss
Grade 3	≥40 dB at 2 or 3 kHz and above	Hearing loss
Grade 4	≥40 dB at 1 kHz and above	Hearing loss

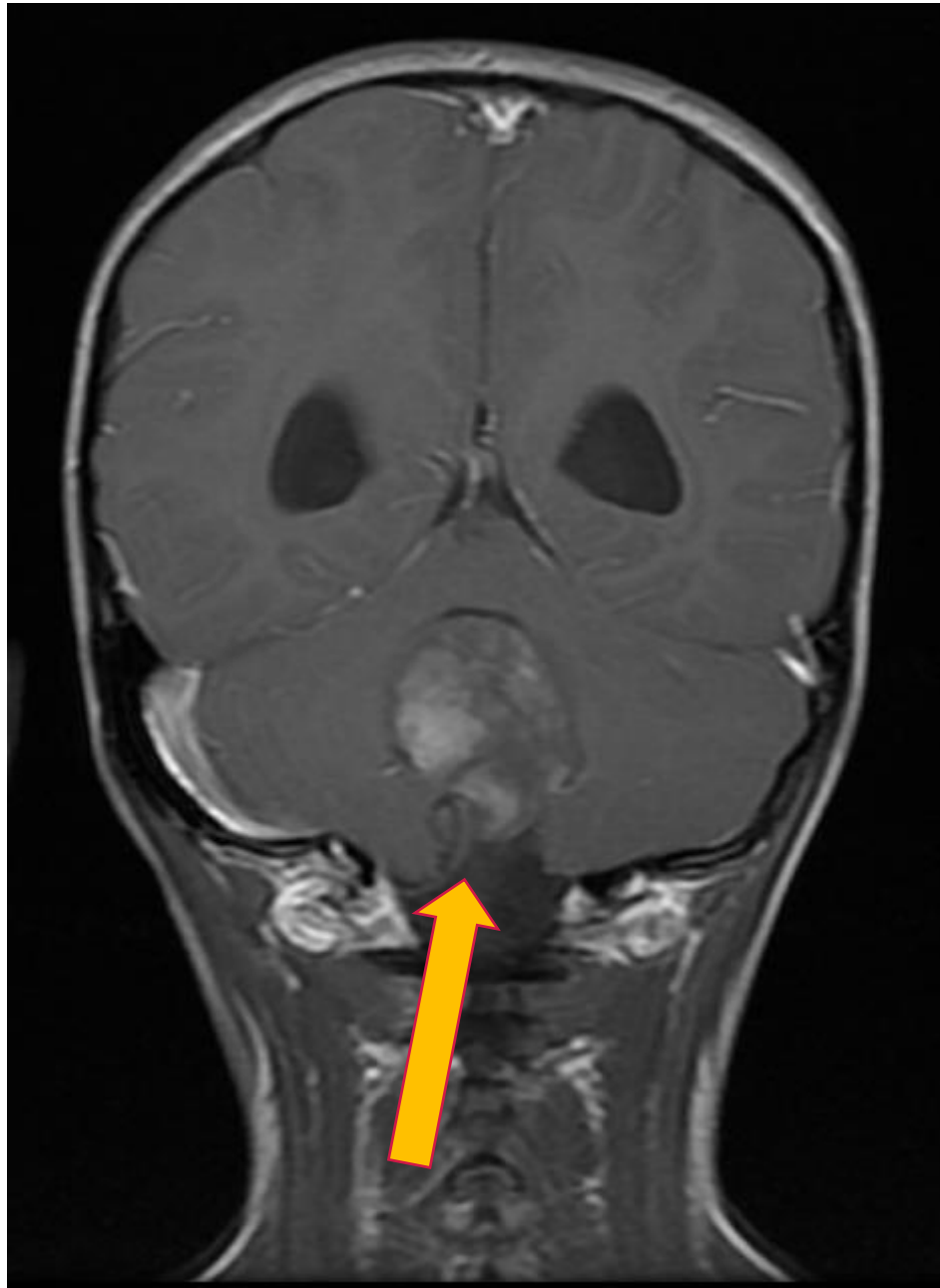
SIOP Grading Scale

Grade	Parameters
0	≤ 20 dB HL at all frequencies
1	> 20 dB HL (ie, 25 dB HL or greater) SNHL above 4,000 Hz (ie, 6 or 8 kHz)
2	> 20 dB HL SNHL at 4,000 Hz and above
3	> 20 dB HL SNHL at 2,000 Hz or 3,000 Hz and above
4	> 40 dB HL (ie, 45 dB HL or more) SNHL at 2,000 Hz and above



Case Studies

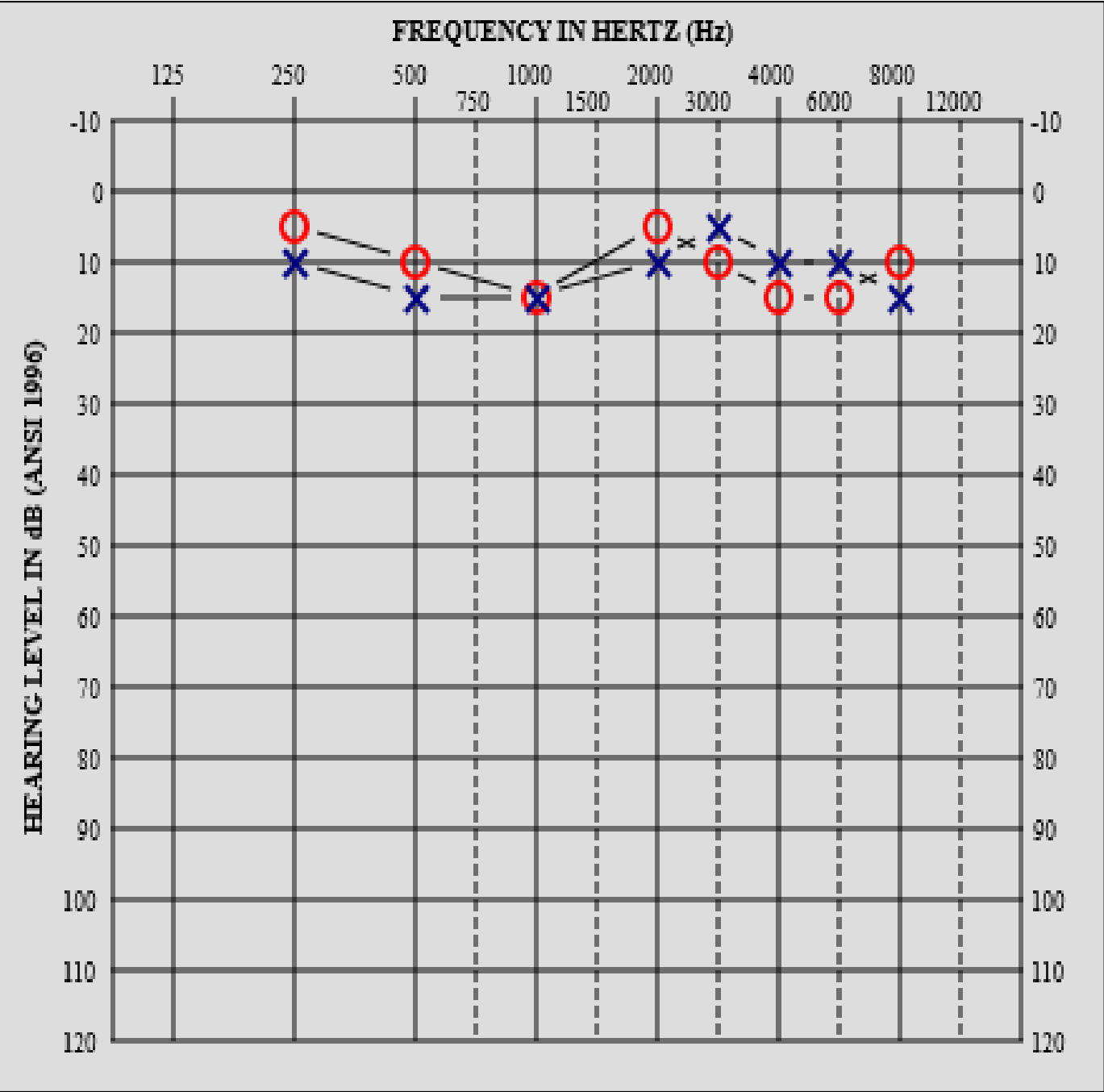
Case Study: Synergistic Effect of Combined Therapies



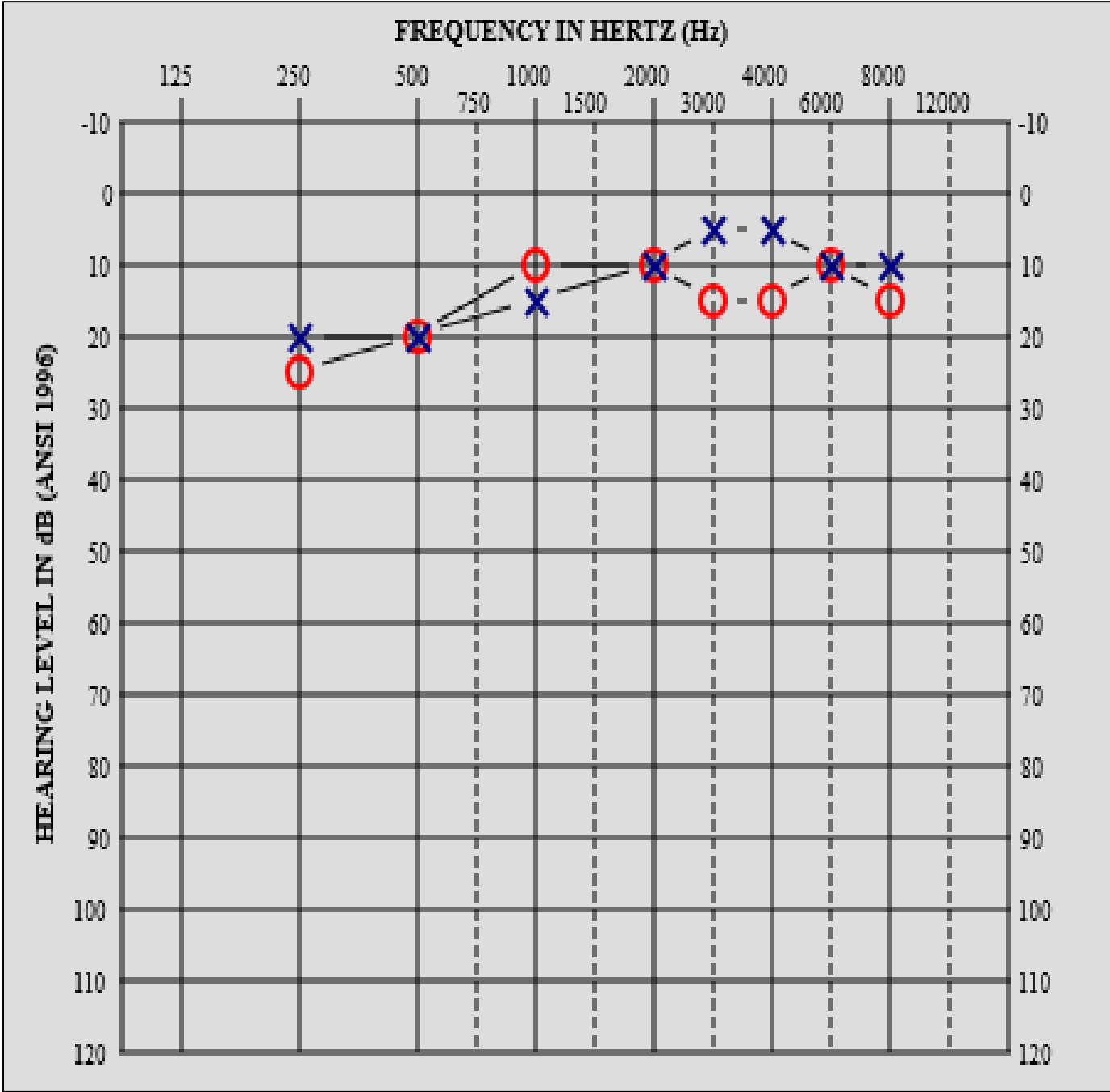
Patient diagnosed with medulloblastoma at 7 years



Case Study: Additive Effect of Combined Therapies

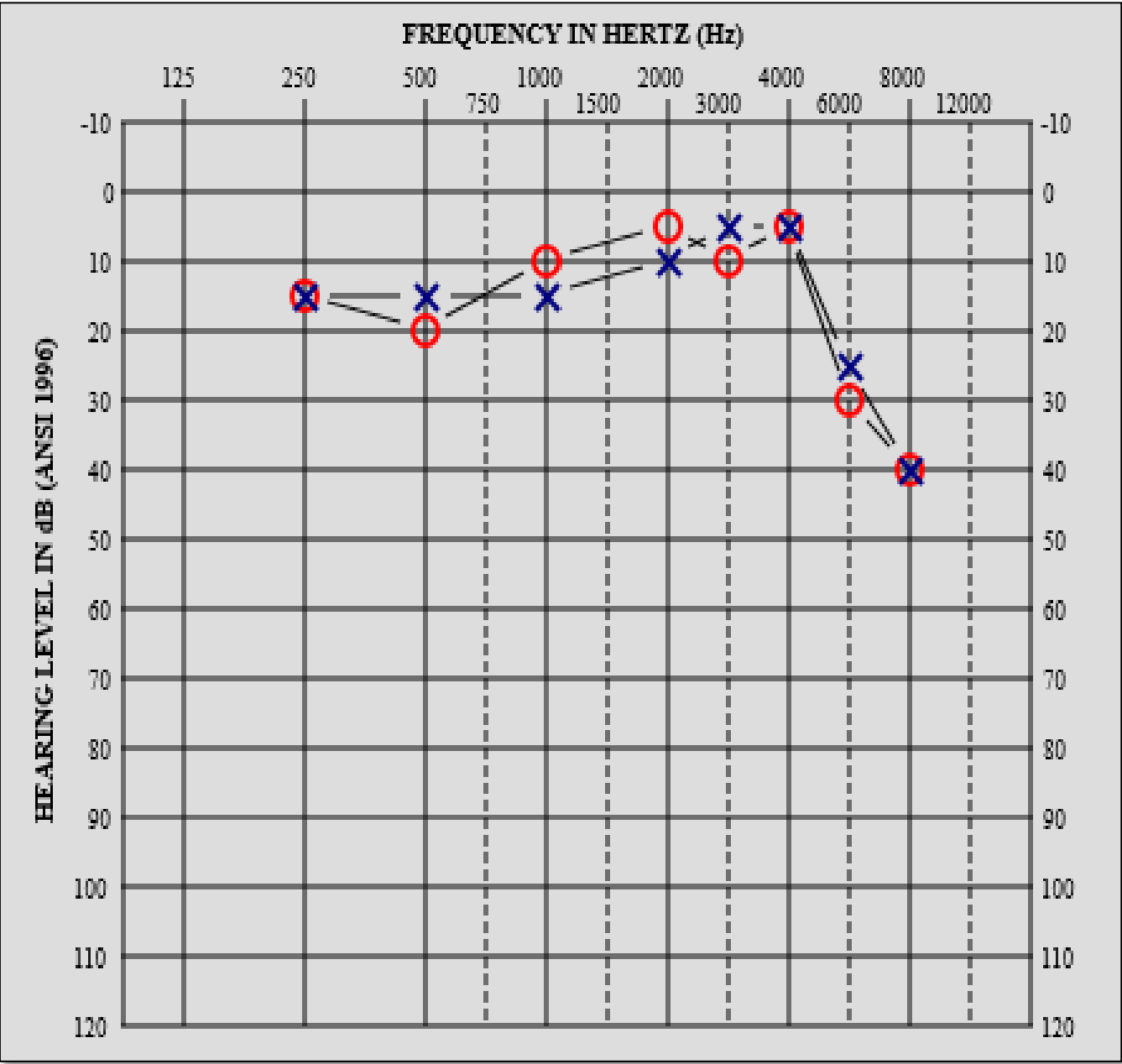


Baseline

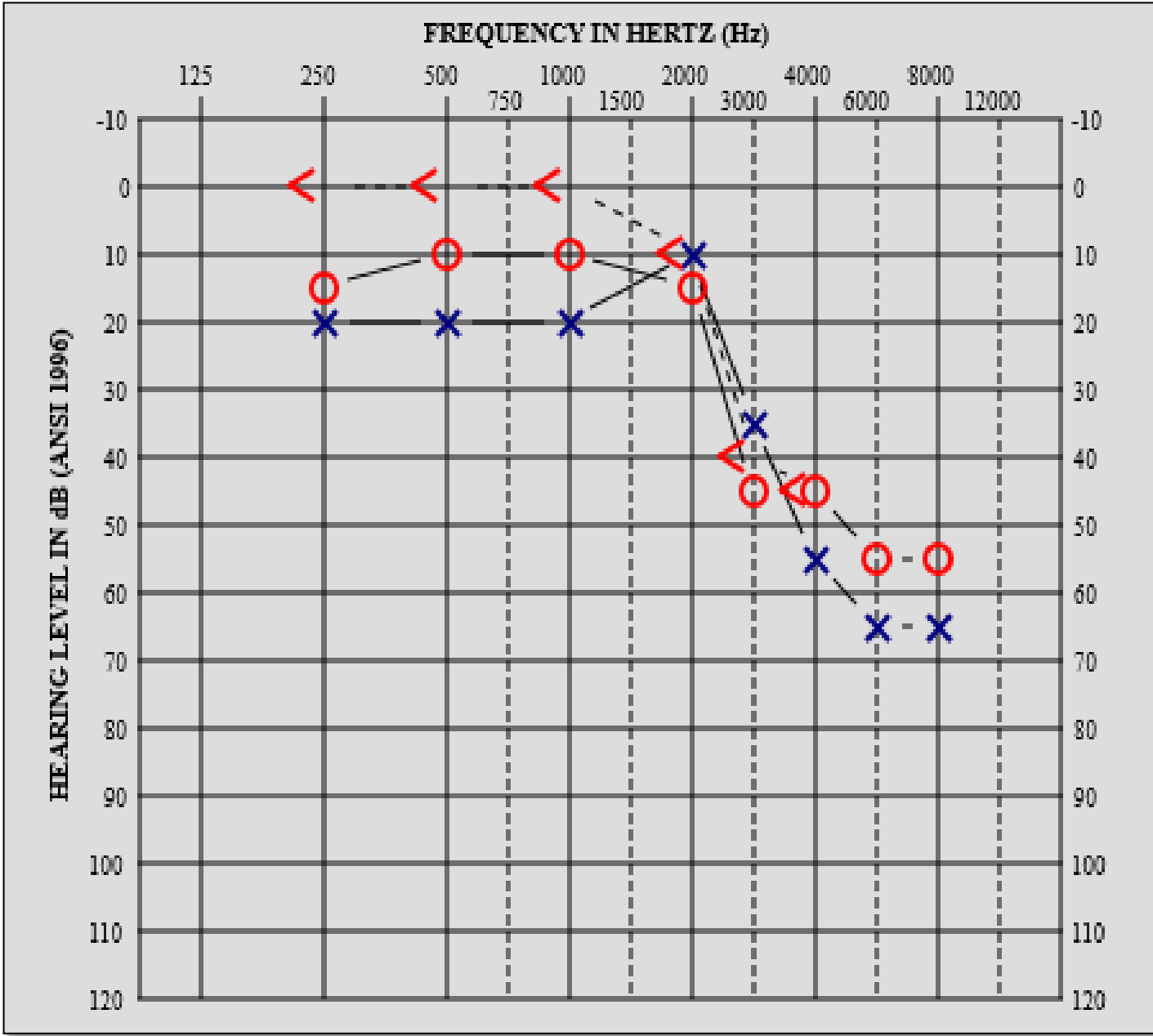


Post radiation therapy

Case Study: Additive Effect of Combined Therapies



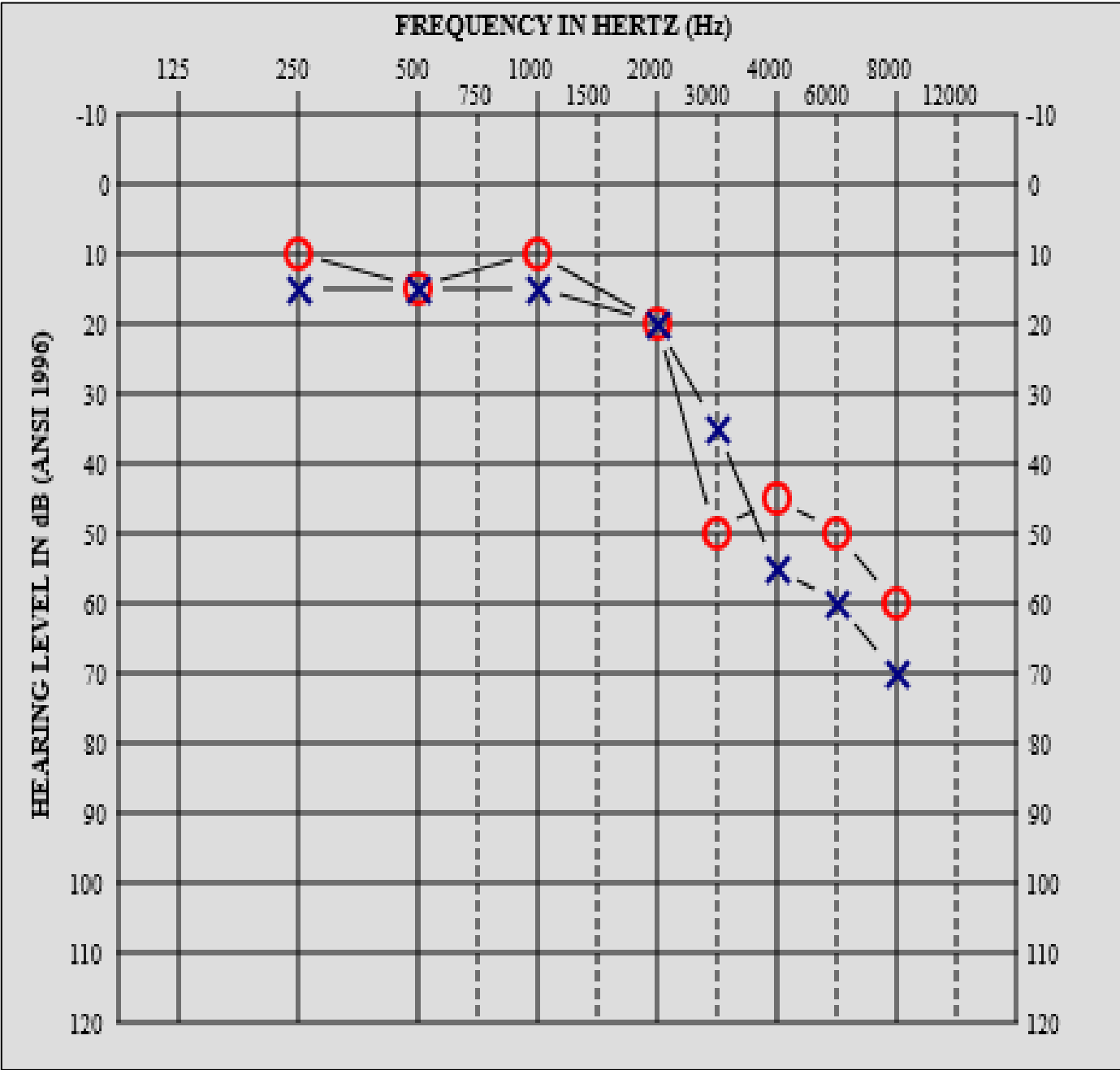
Post 1 cycle of cisplatin therapy



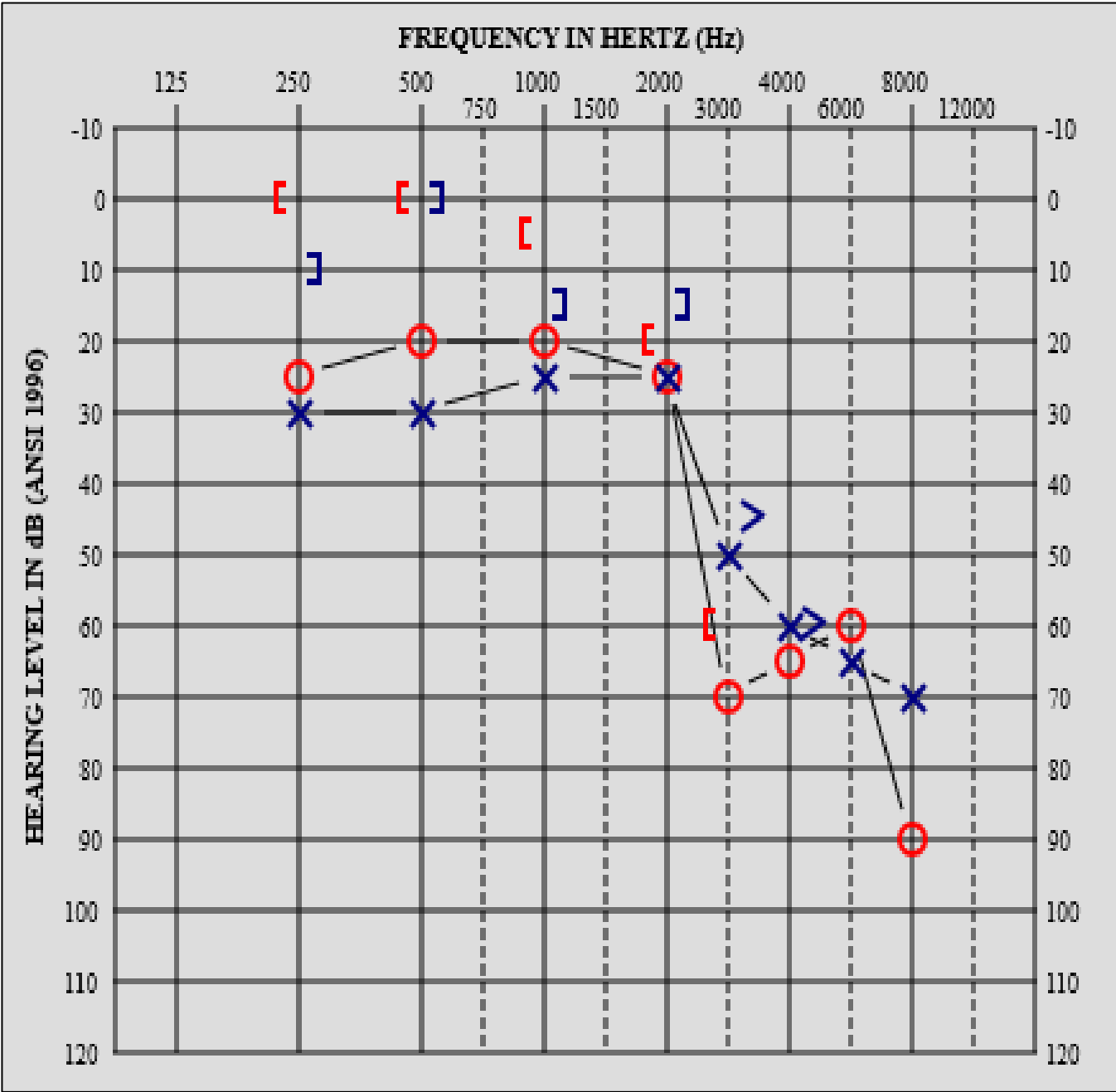
Post 2 cycles of cisplatin therapy



Case Study: Additive Effect of Combined Therapies



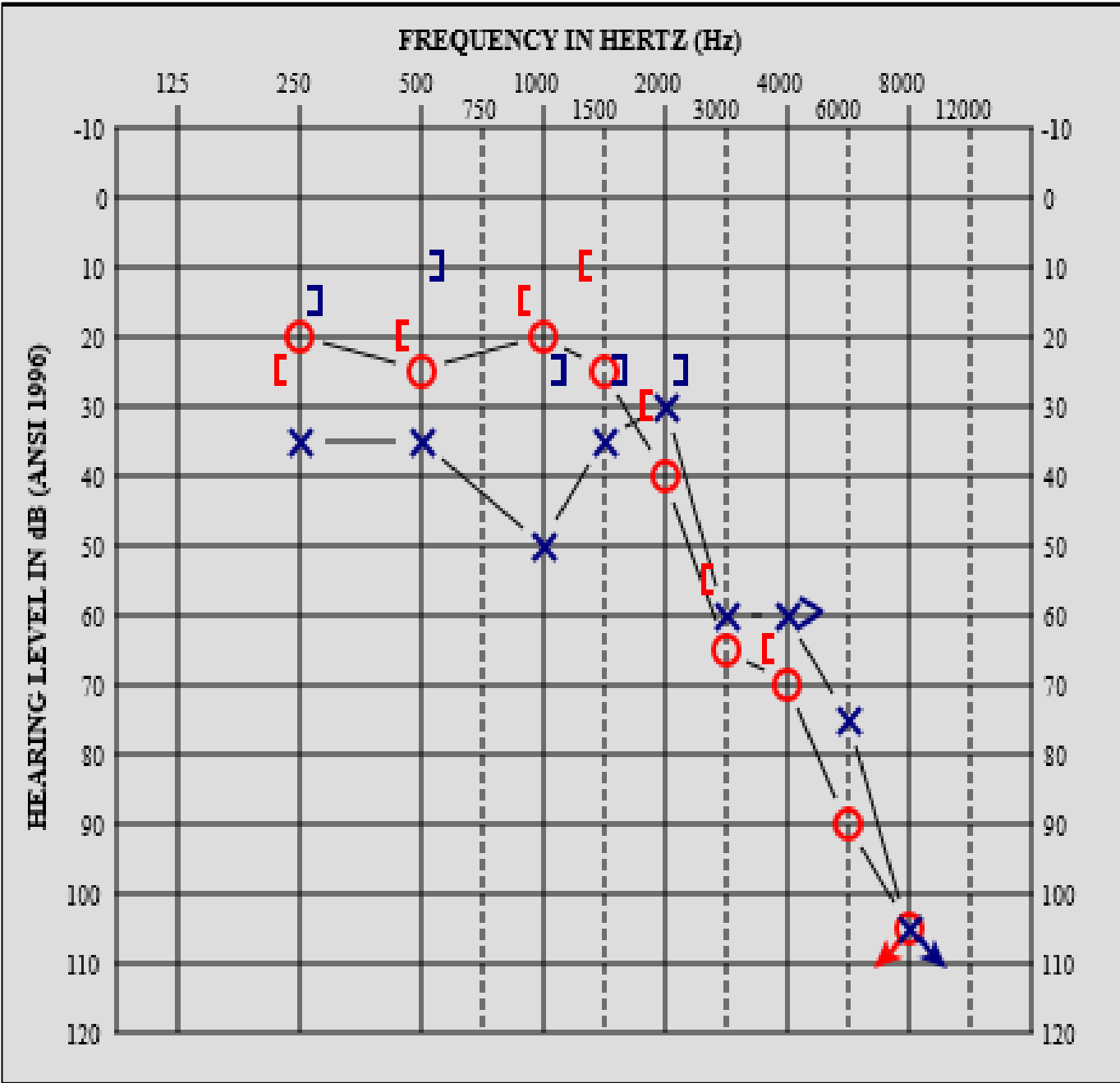
Post 3 cycles of cisplatin therapy
*Cycle 3 dose reduced by 50%



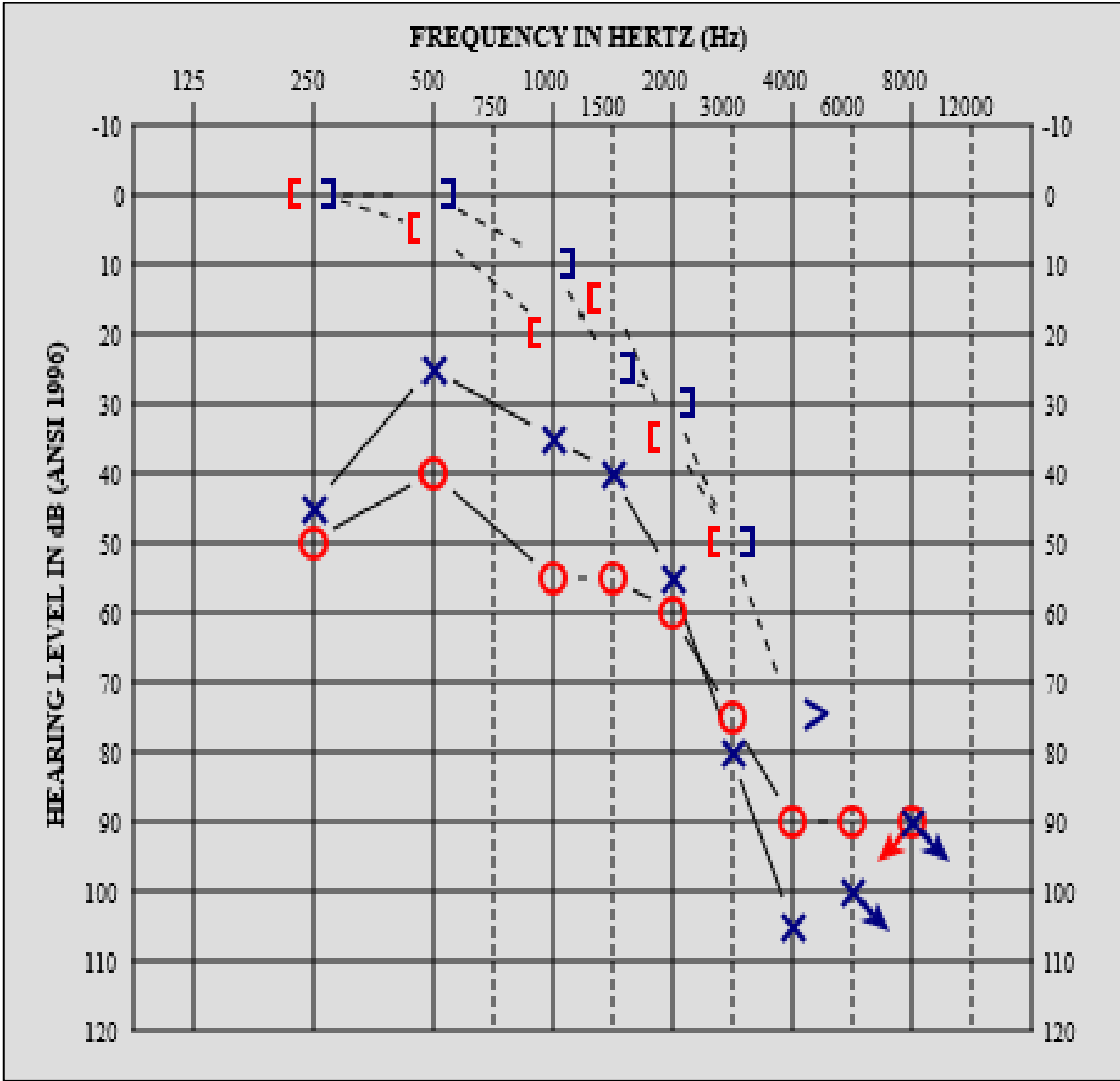
Post 4 cycles of cisplatin therapy
*Cycle 4 dose reduced by 50%



Case Study: Additive Effect of Combined Therapies

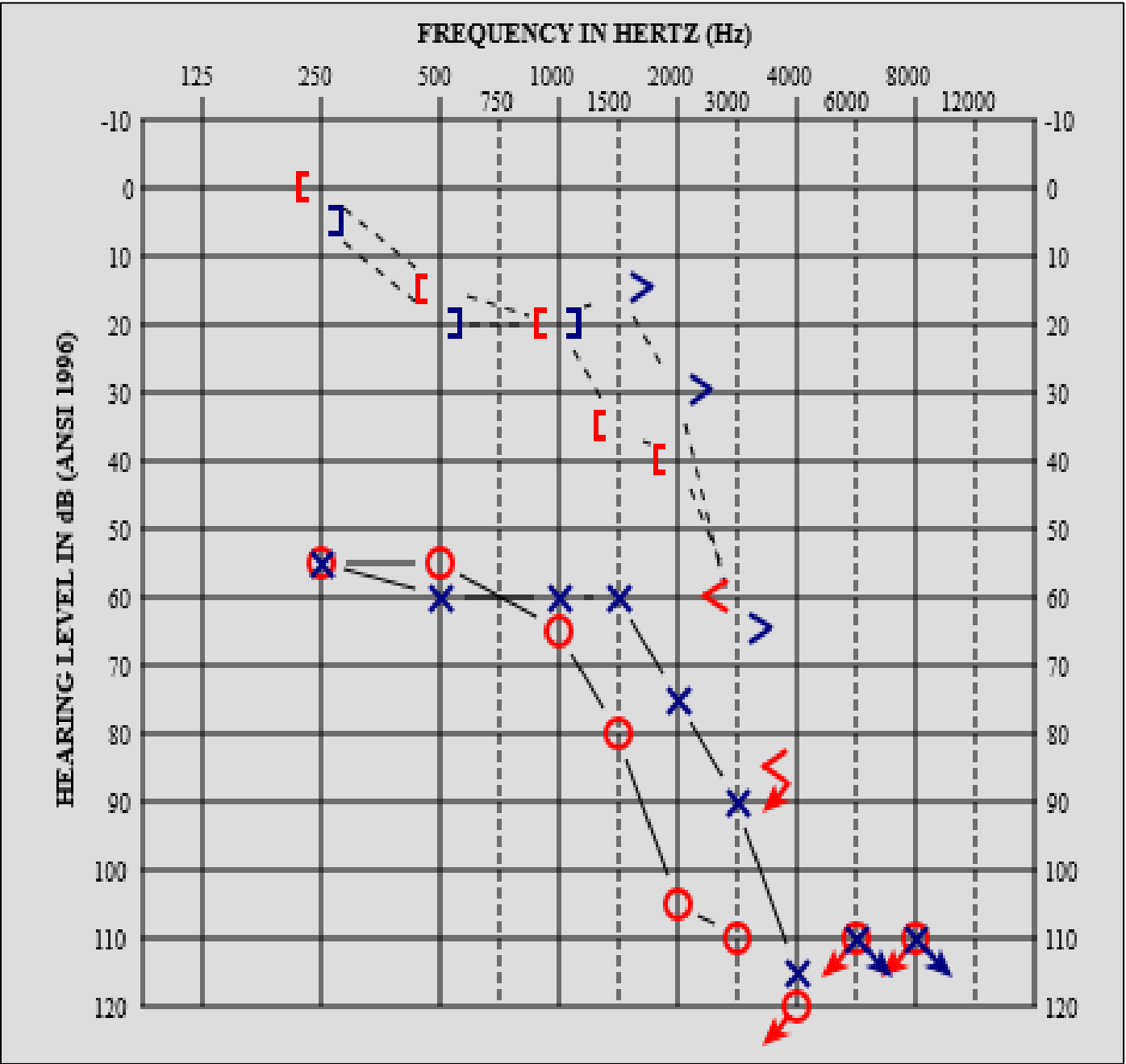


1 year post treatment

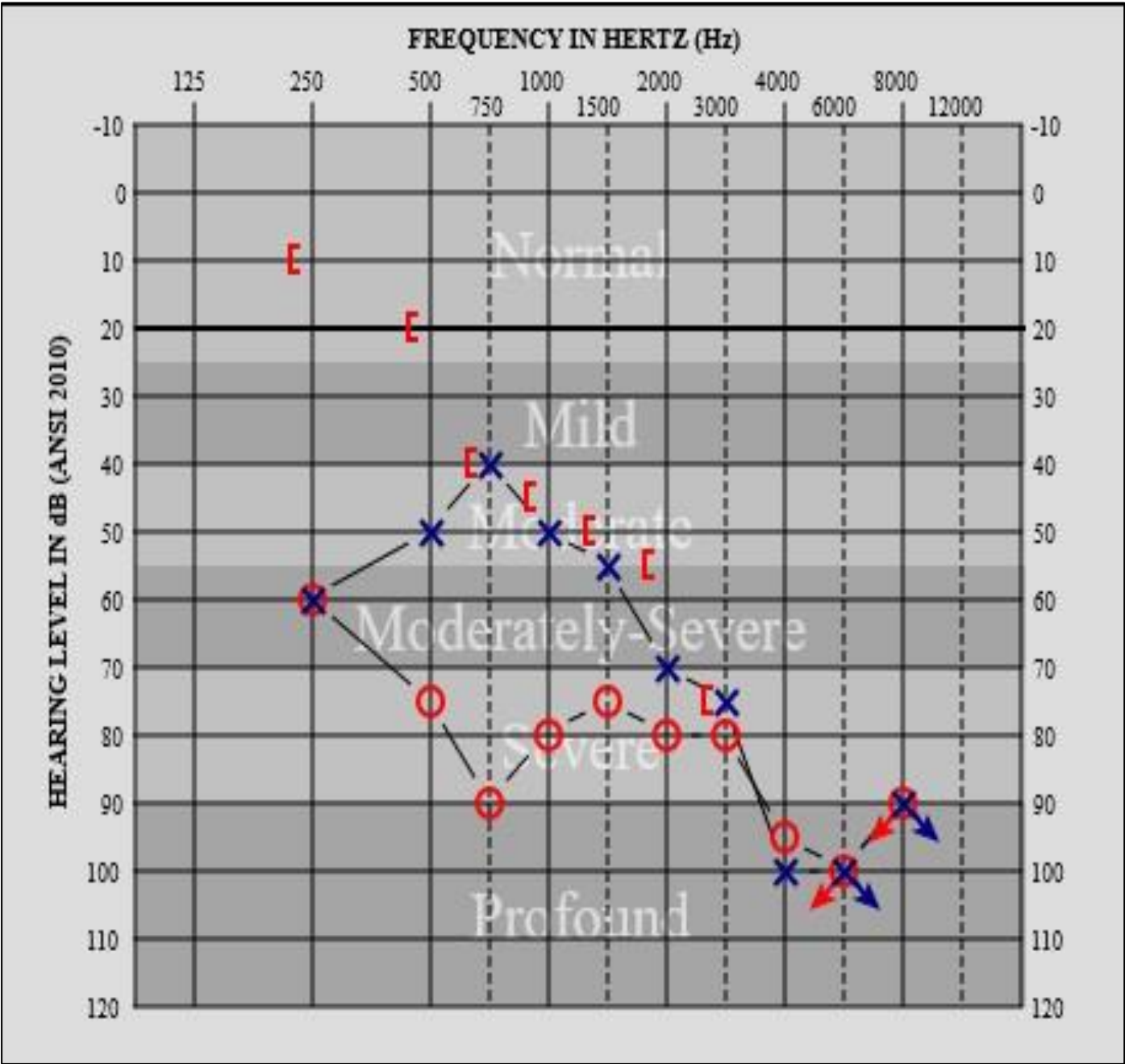


3 years post treatment

Case Study: Additive Effect of Combined Therapies



4 years post treatment



8 years post treatment



CHEMOTHERAPY DRUG

Carboplatin

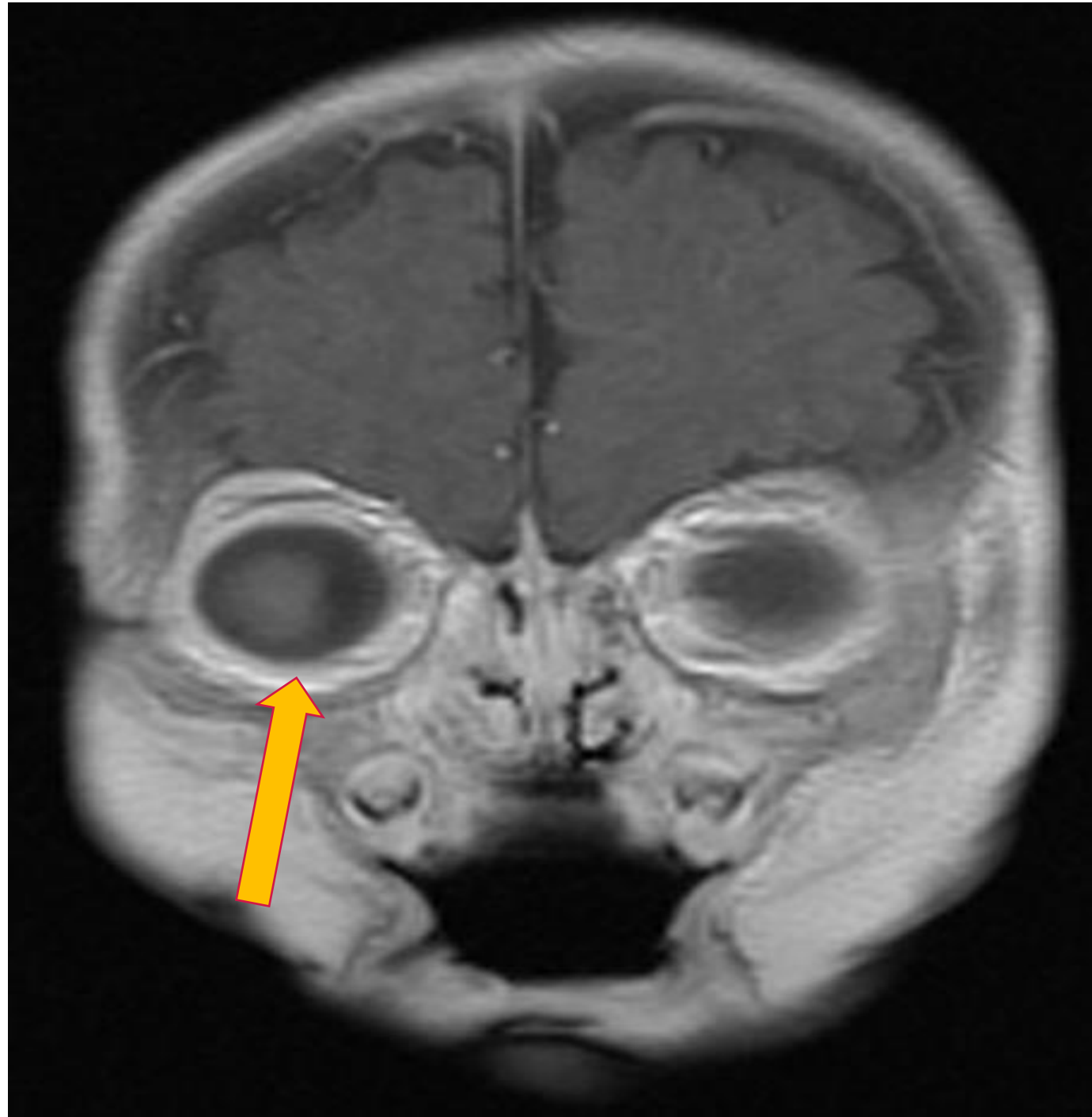
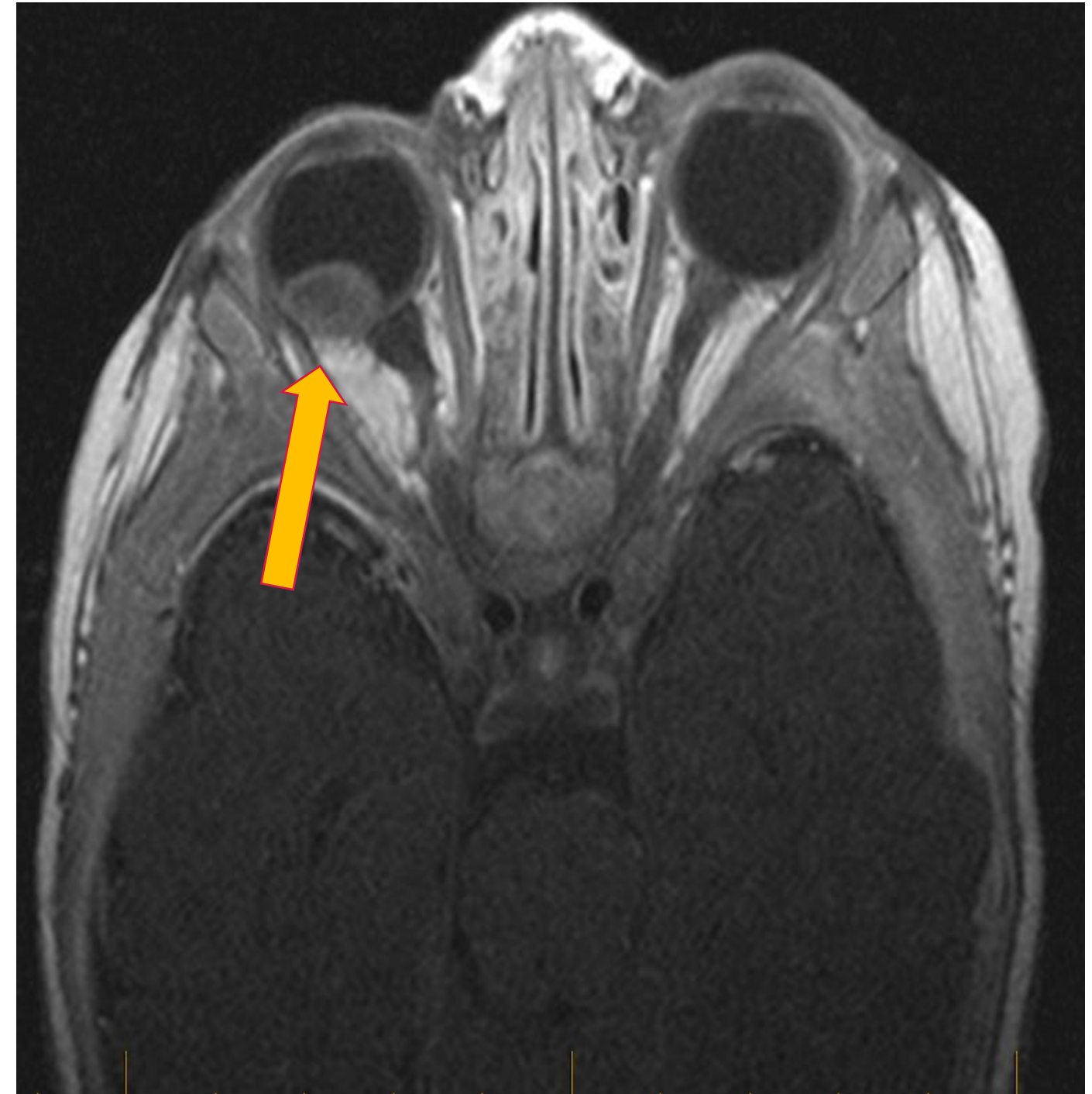
Risk Factors/Types of Cancer: Carboplatin

Risk Factors: Age,
high cumulative
dose, concurrent
administration, prior
radiation, Noise
Exposure, Genetic
tendency

Ex: Wilms' Tumor,
Retinoblastoma,
Low Grade Glioma

*Primarily targets
spiral ganglion
cells/inner hair
cells*

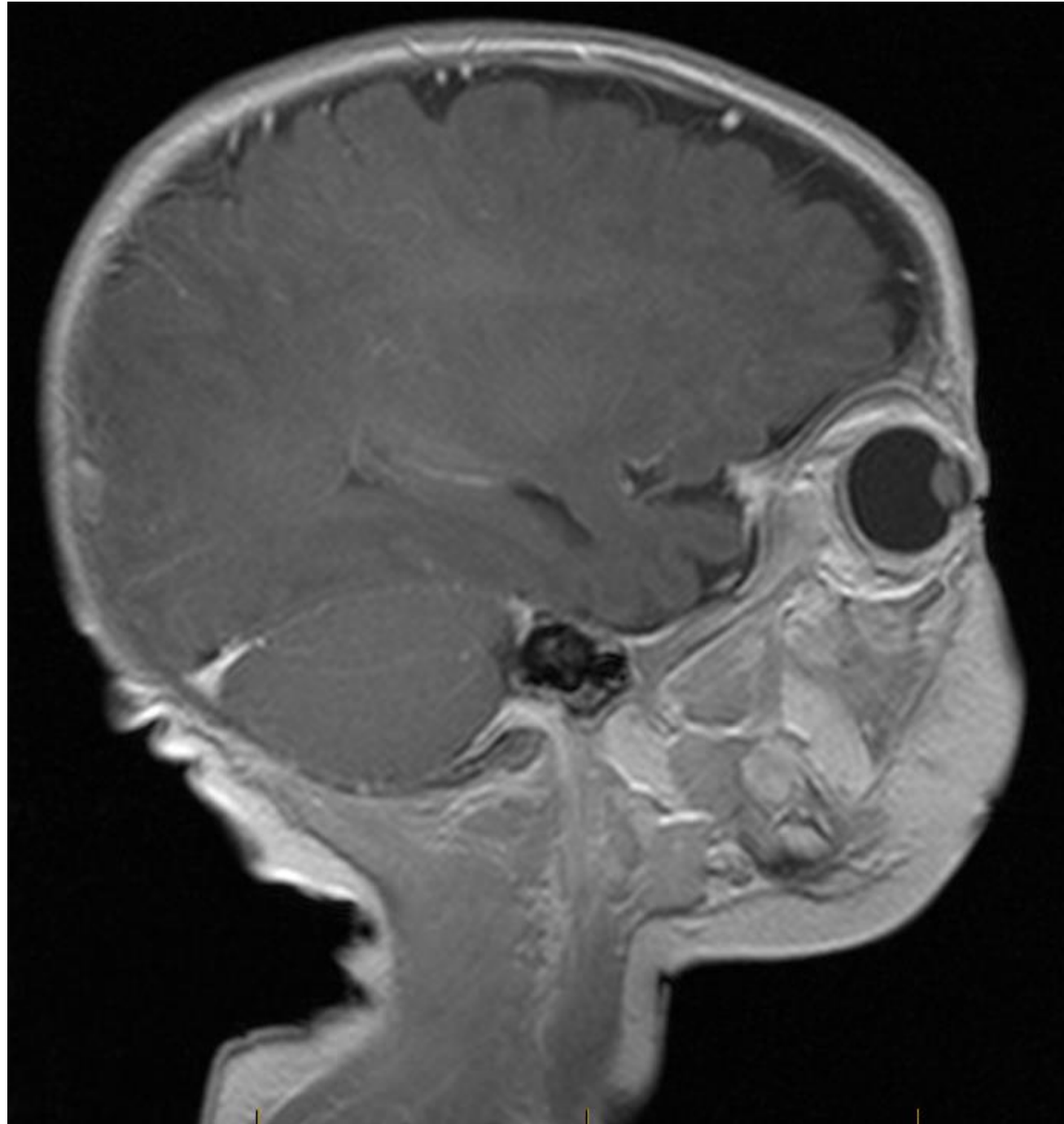
Case Study: Carboplatin-Induced Hearing Loss



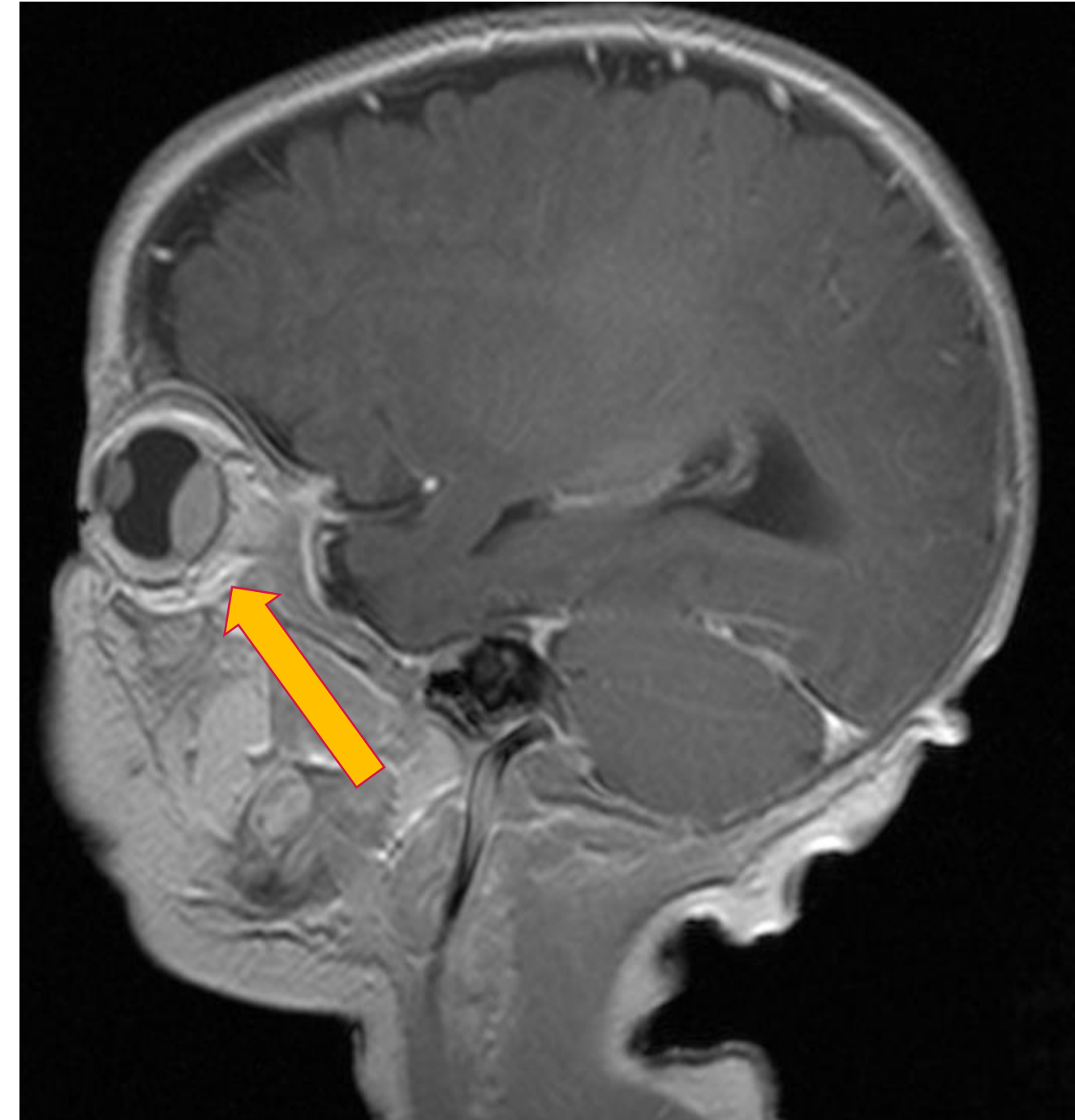
Patient diagnosed with retinoblastoma of the left eye at 3 months



Case Study A: Carboplatin-Induced Hearing Loss



Right eye

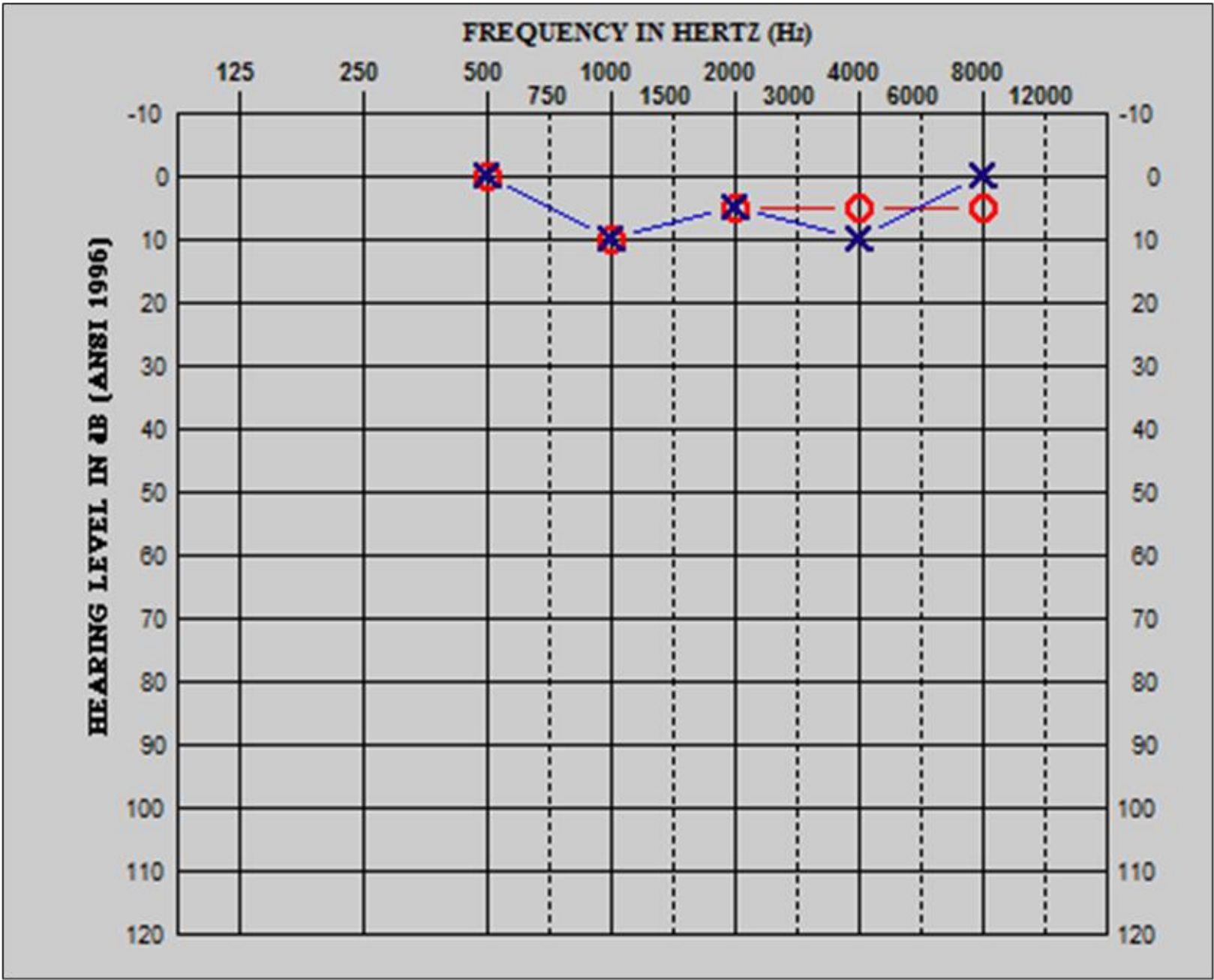


Left eye

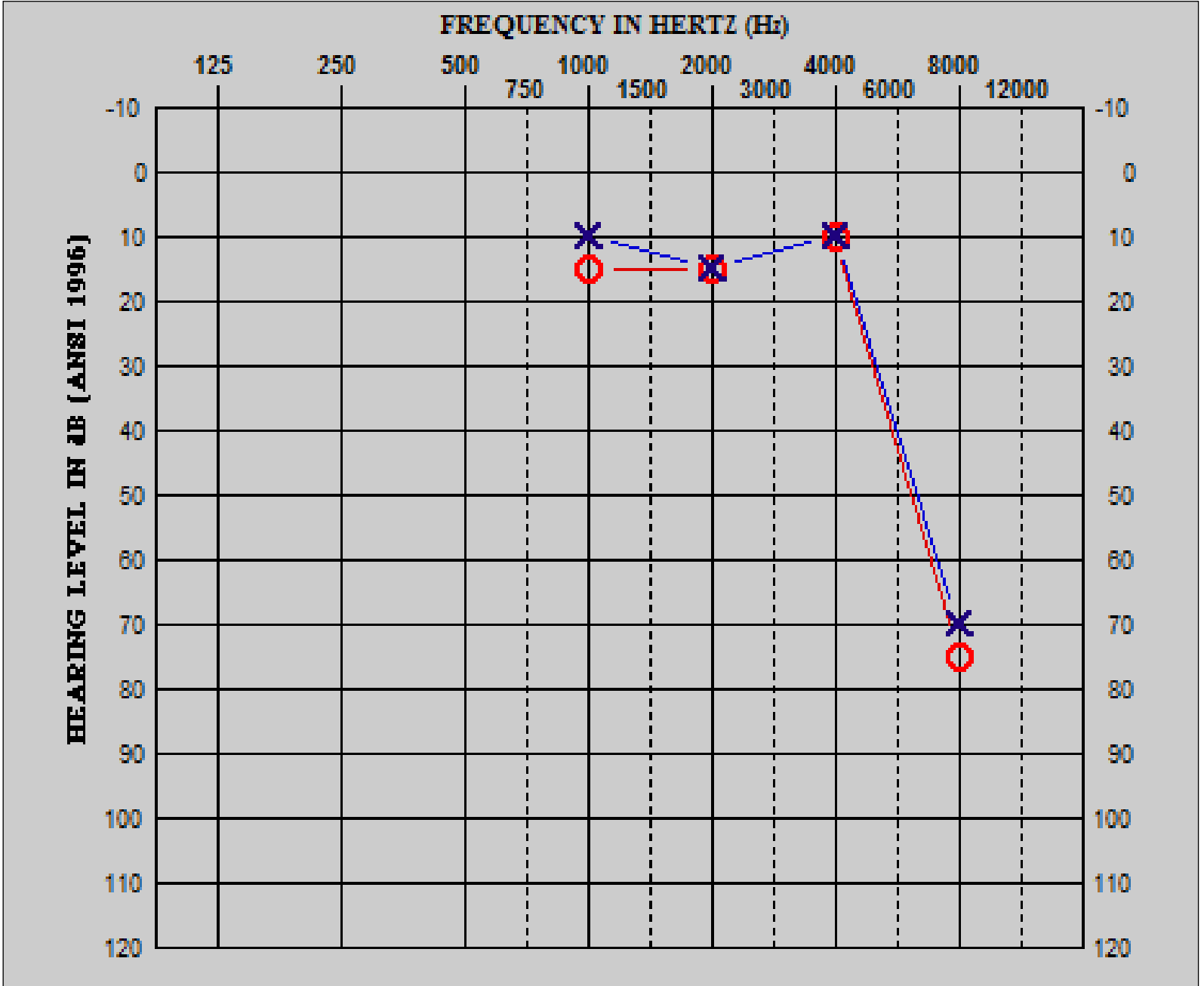
Patient diagnosed with retinoblastoma of the left eye at 3 months



Case Study A: Carboplatin-Induced Hearing Loss

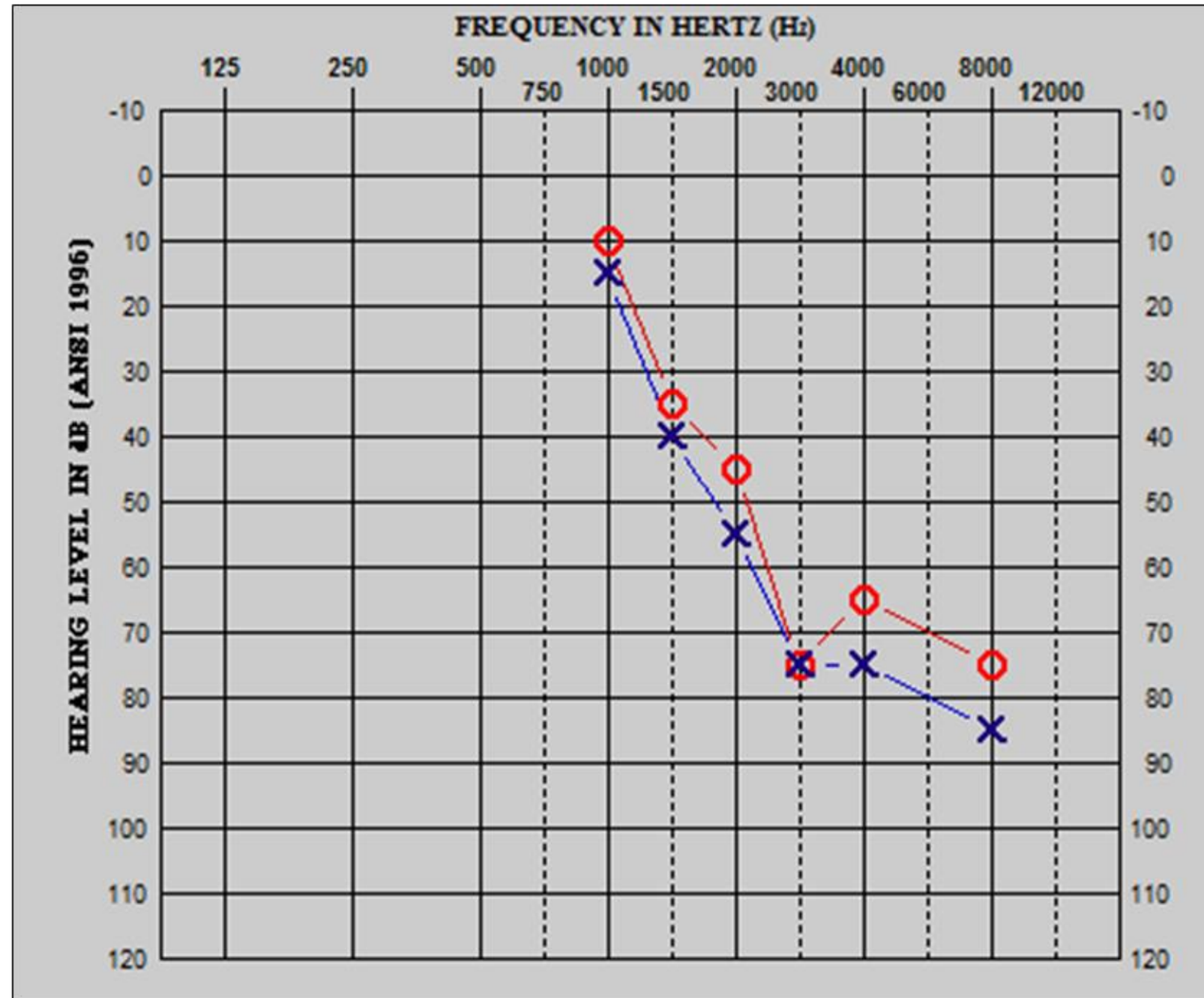


Baseline ABR (eHL)

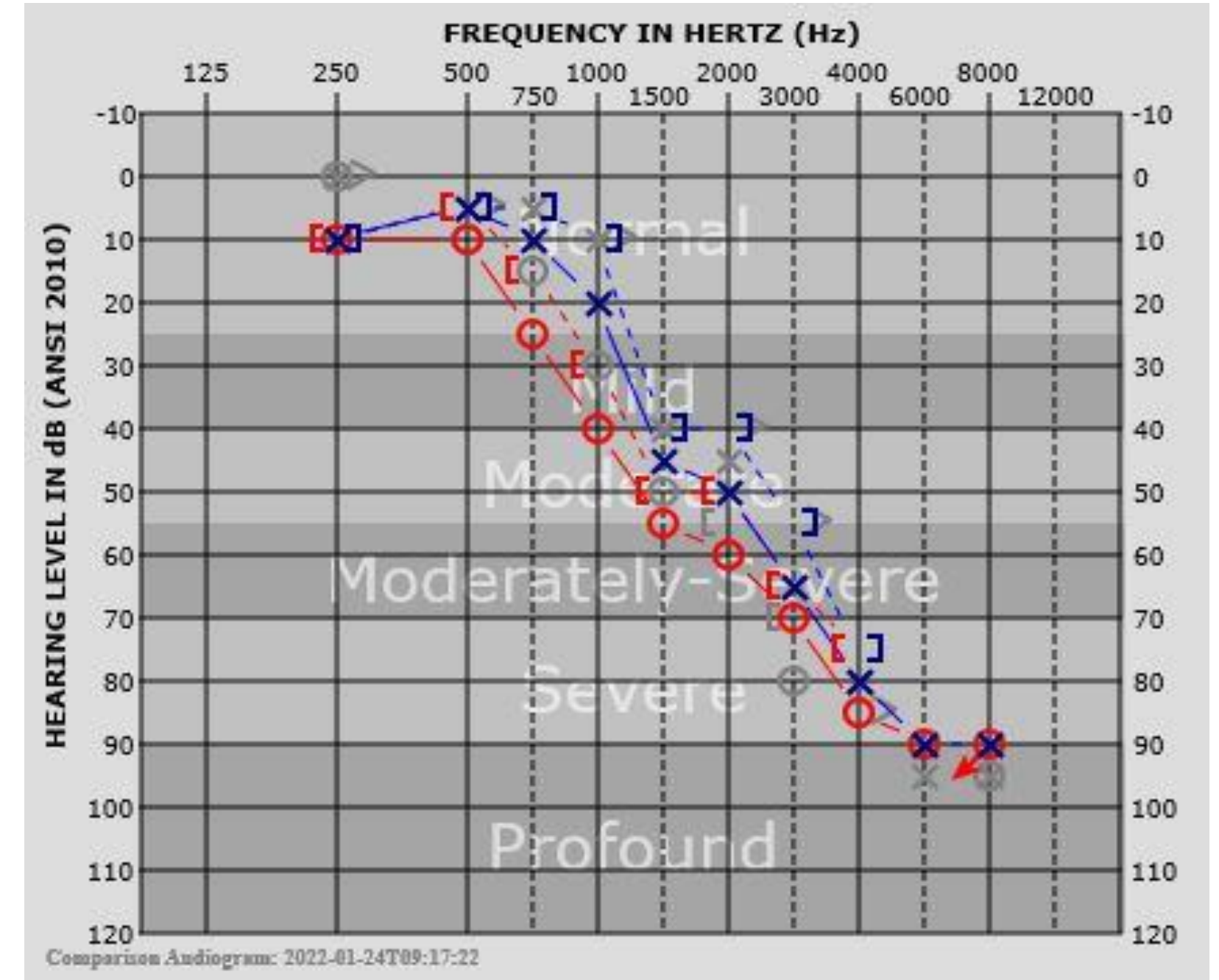


Post 6 cycles of carboplatin chemotherapy (eHL)

Case Study A: Carboplatin-Induced Hearing Loss



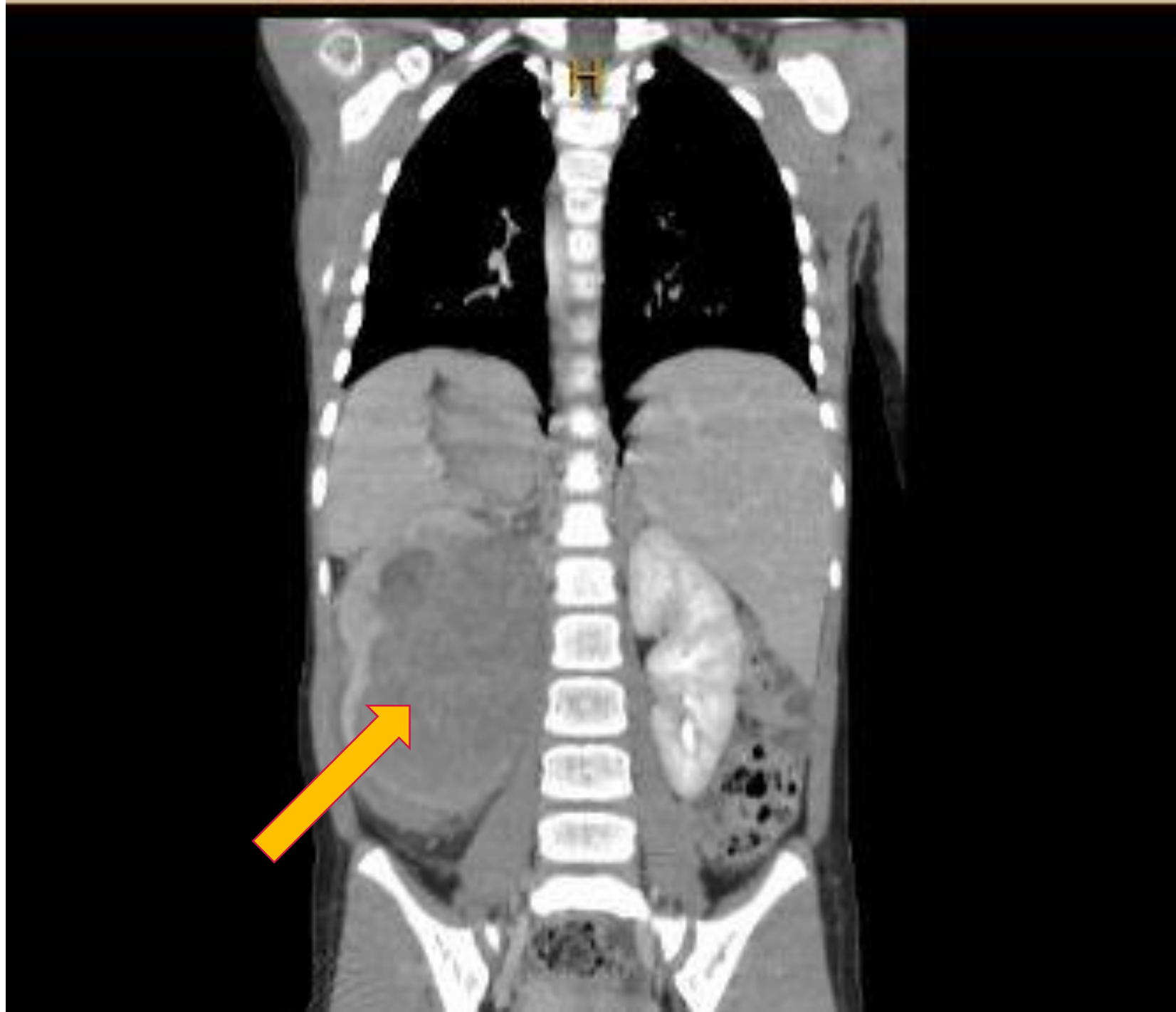
2 years post carboplatin chemotherapy



18 years post carboplatin chemotherapy



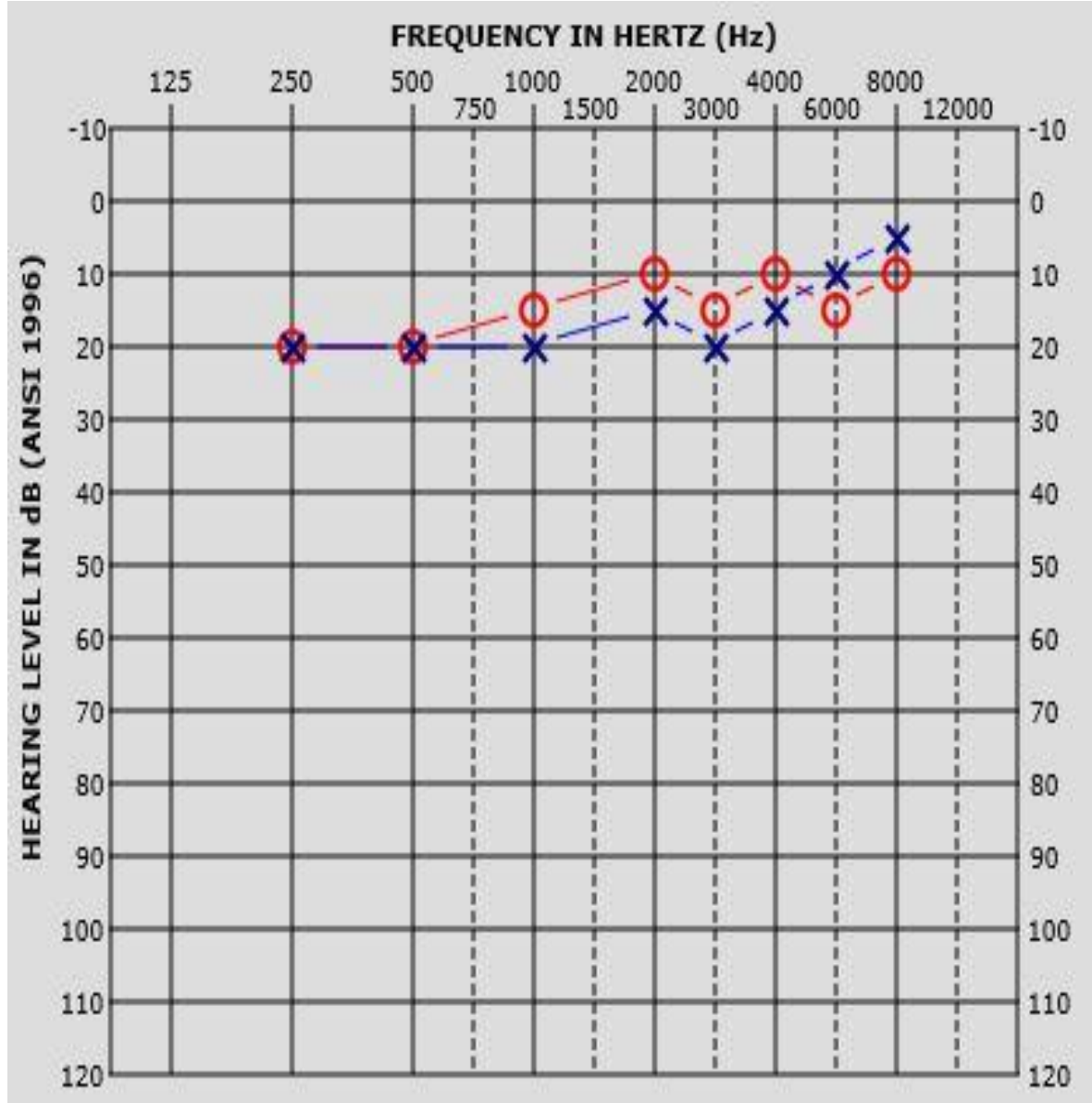
Case Study B: Carboplatin Ototoxic Monitoring



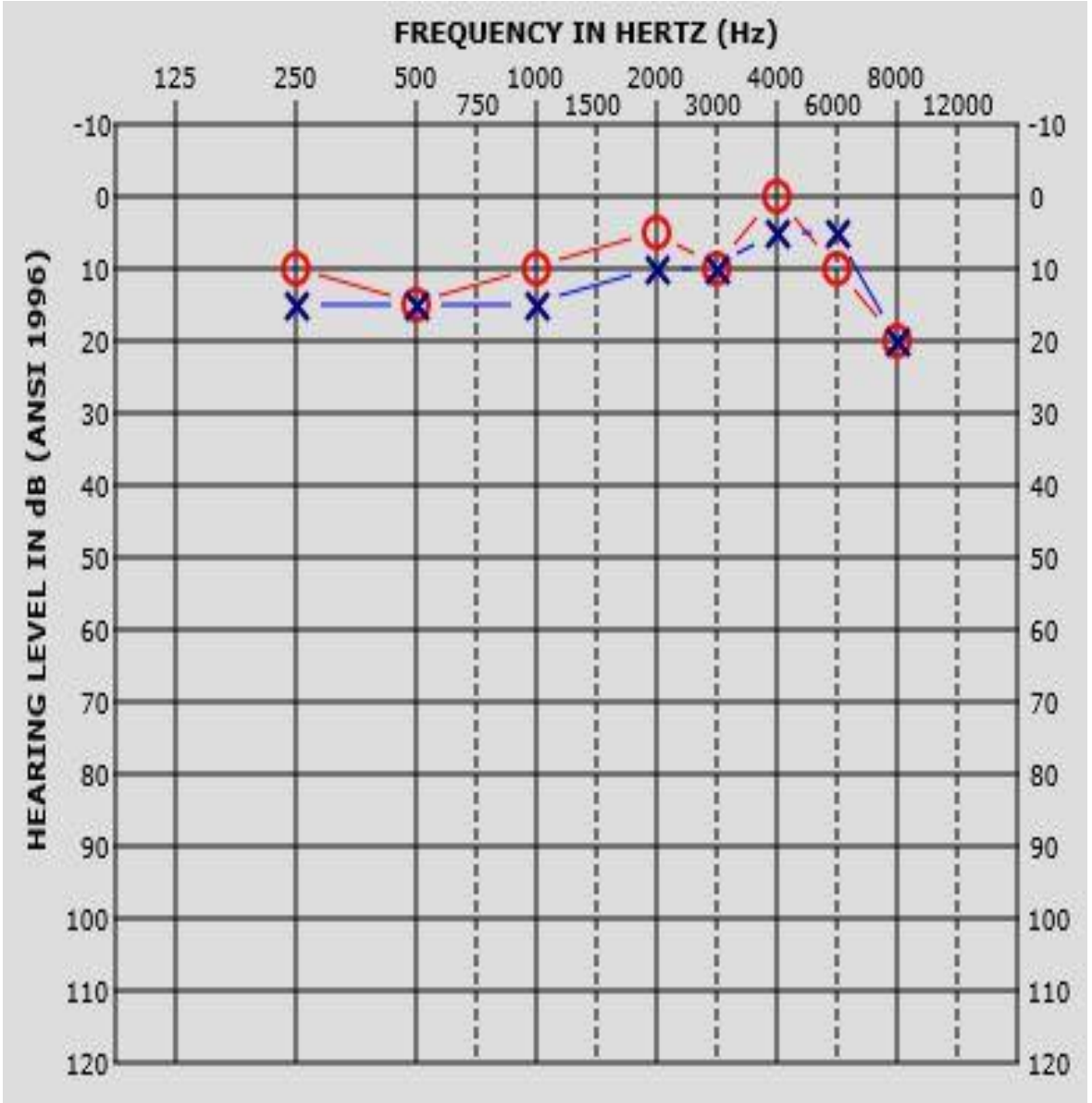
Patient diagnosed with Wilms tumor of the left kidney at 6 years



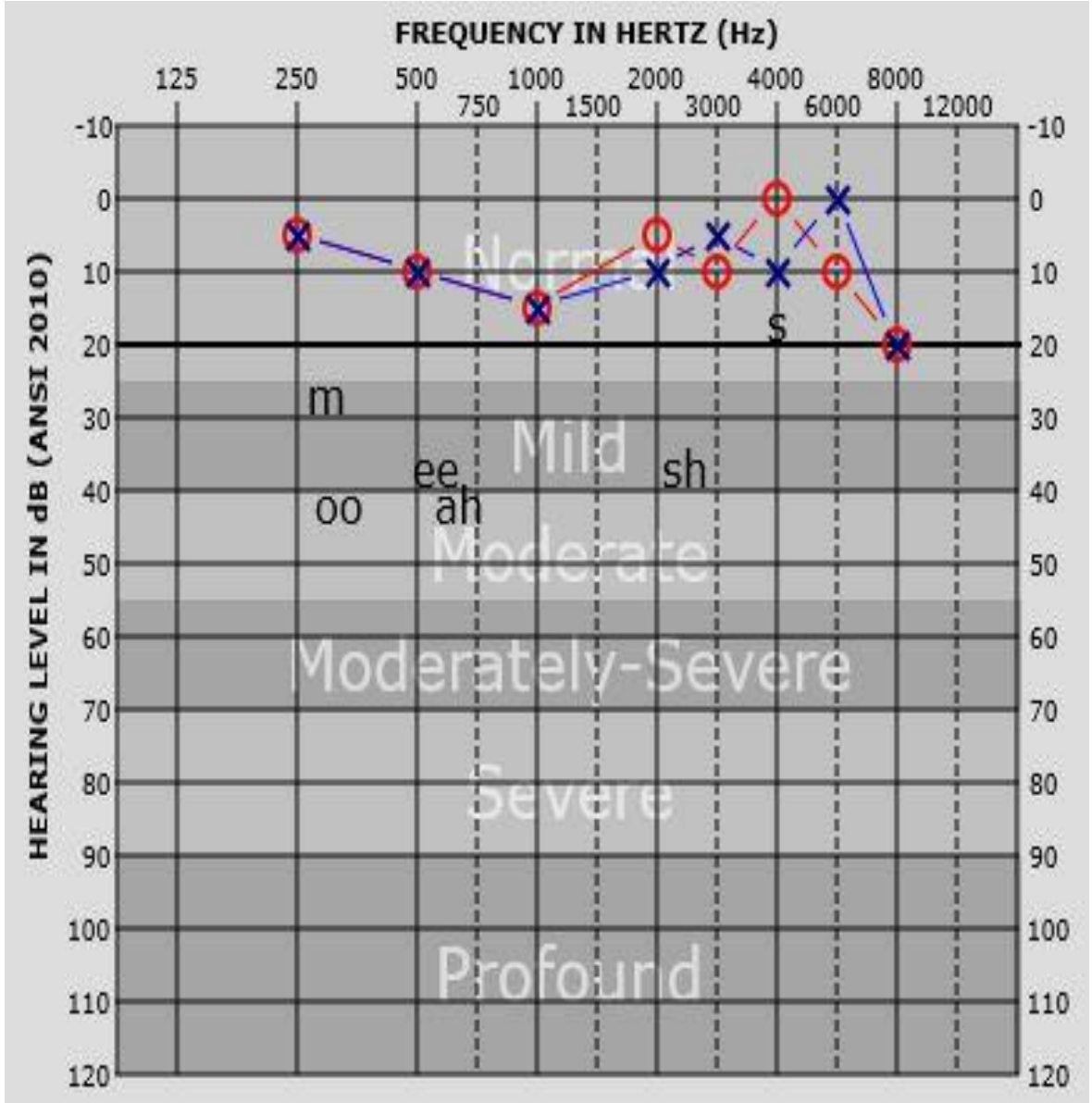
Case Study B: Carboplatin Ototoxic Monitoring



Baseline

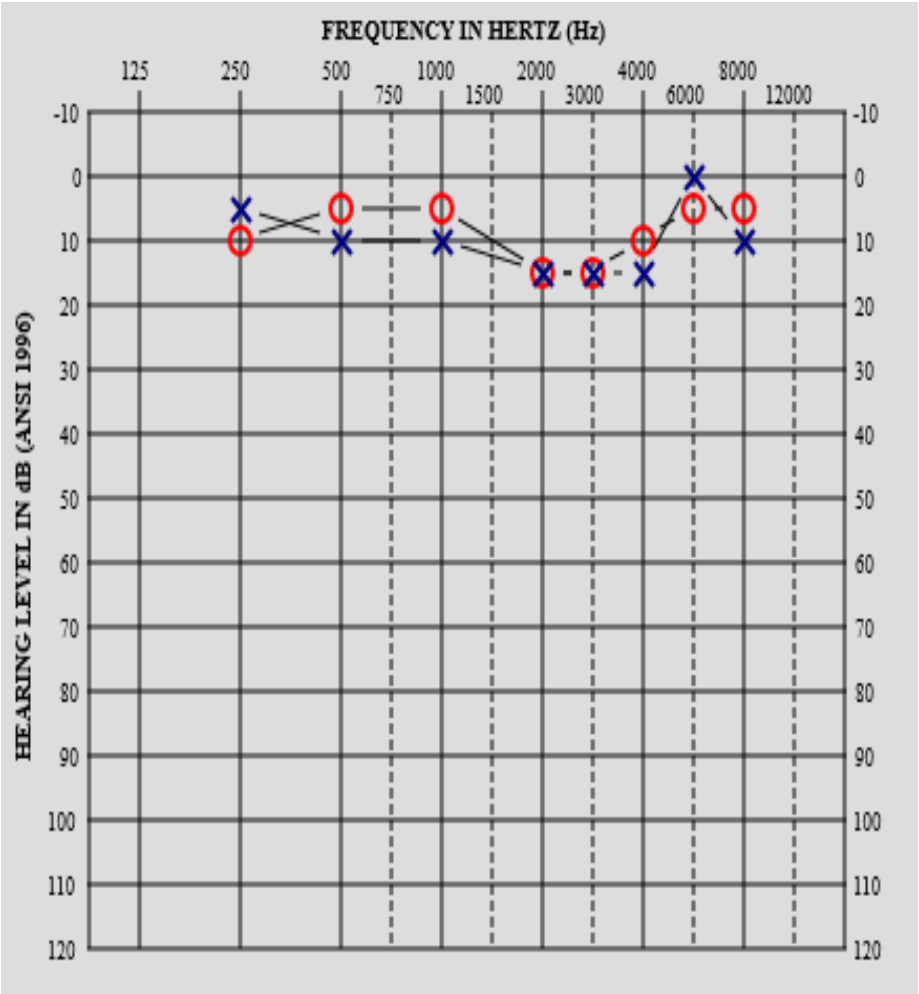


Post 6 cycles of carboplatin chemotherapy

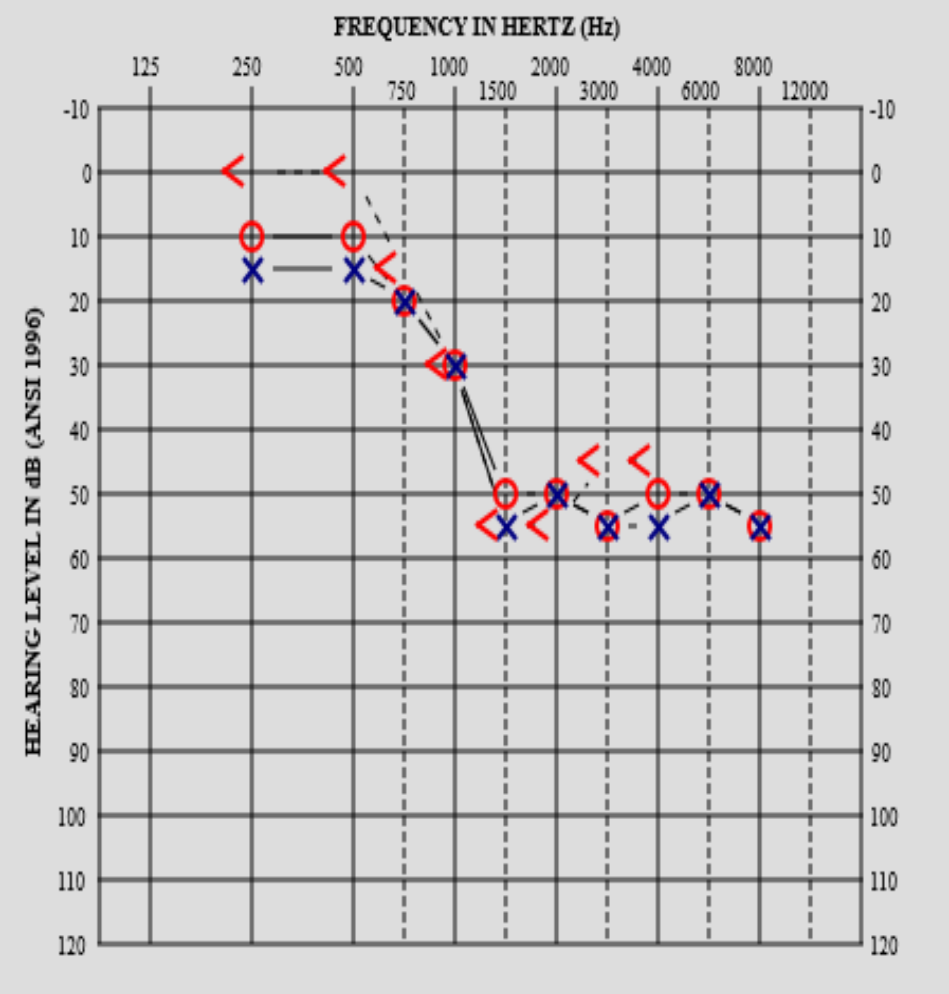


8 years post carboplatin chemotherapy

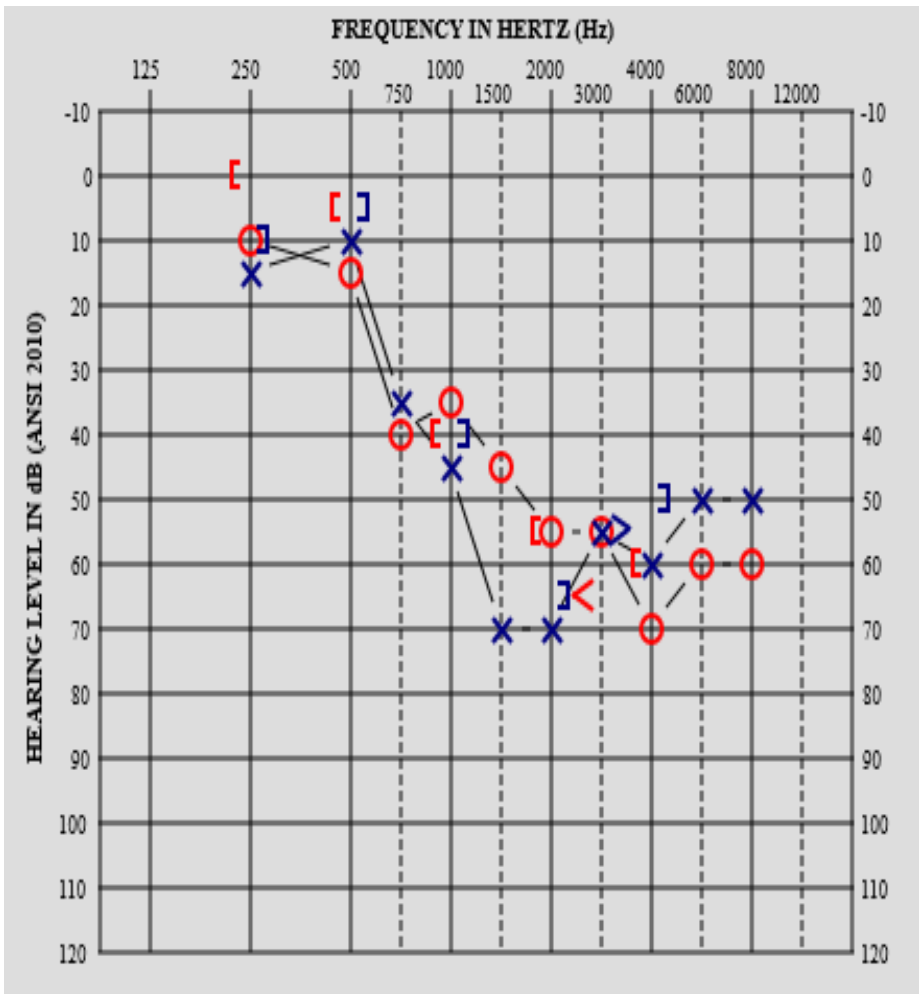
Double Whammy: Cisplatin and Carboplatin-Induced Hearing Loss



Baseline at SJCRH
S/p 8 cycles of carboplatin



S/p 8 cycles of carboplatin
and 1 cycles of cisplatin



S/p 8 cycles of carboplatin
and 2 cycles of cisplatin

Patient diagnosed with neuroblastoma locally at 8 years.
Referred to SJCRH following 1 year of local carboplatin therapy.



CHEMOTHERAPY DRUG

Cisplatin

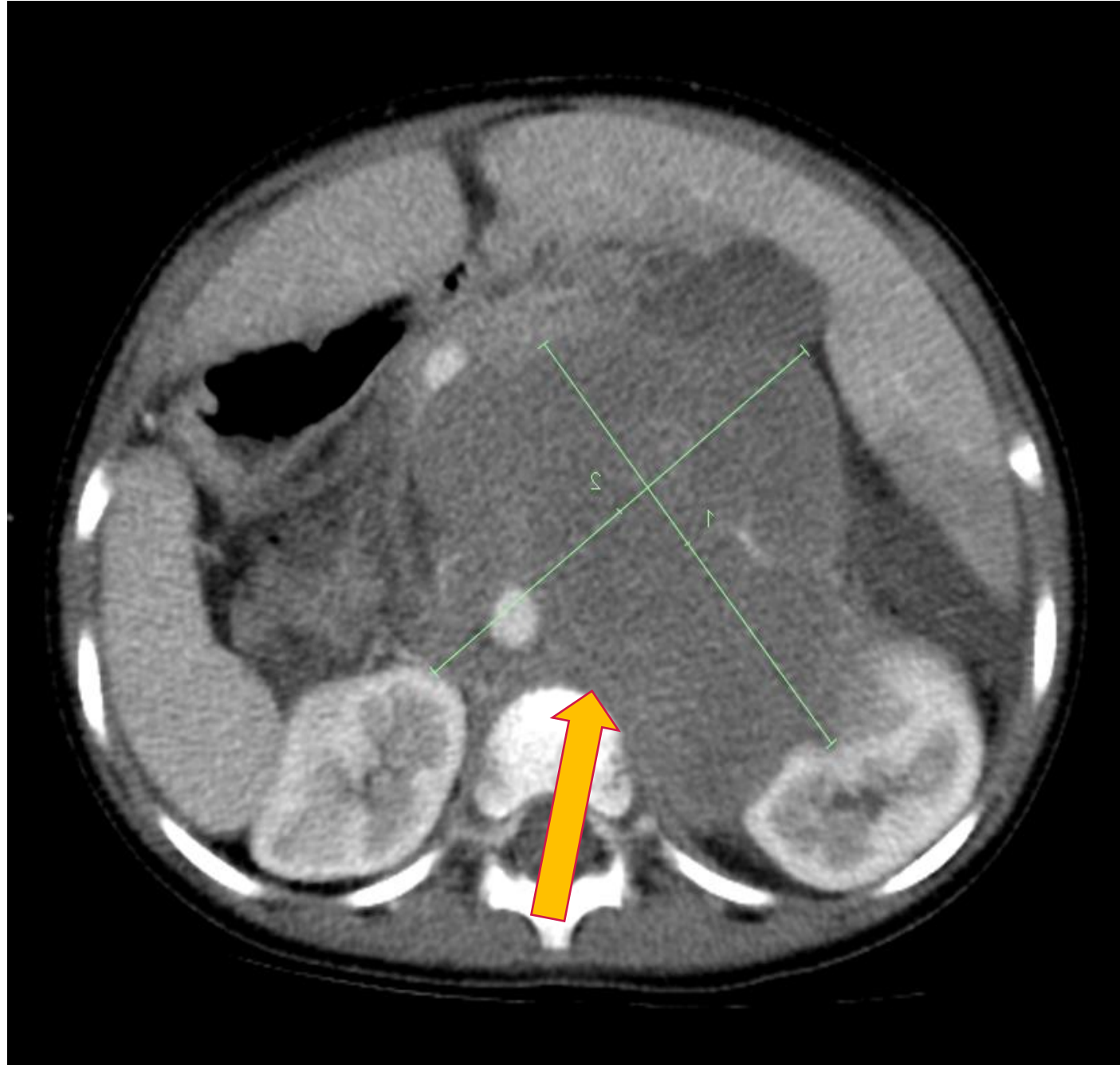
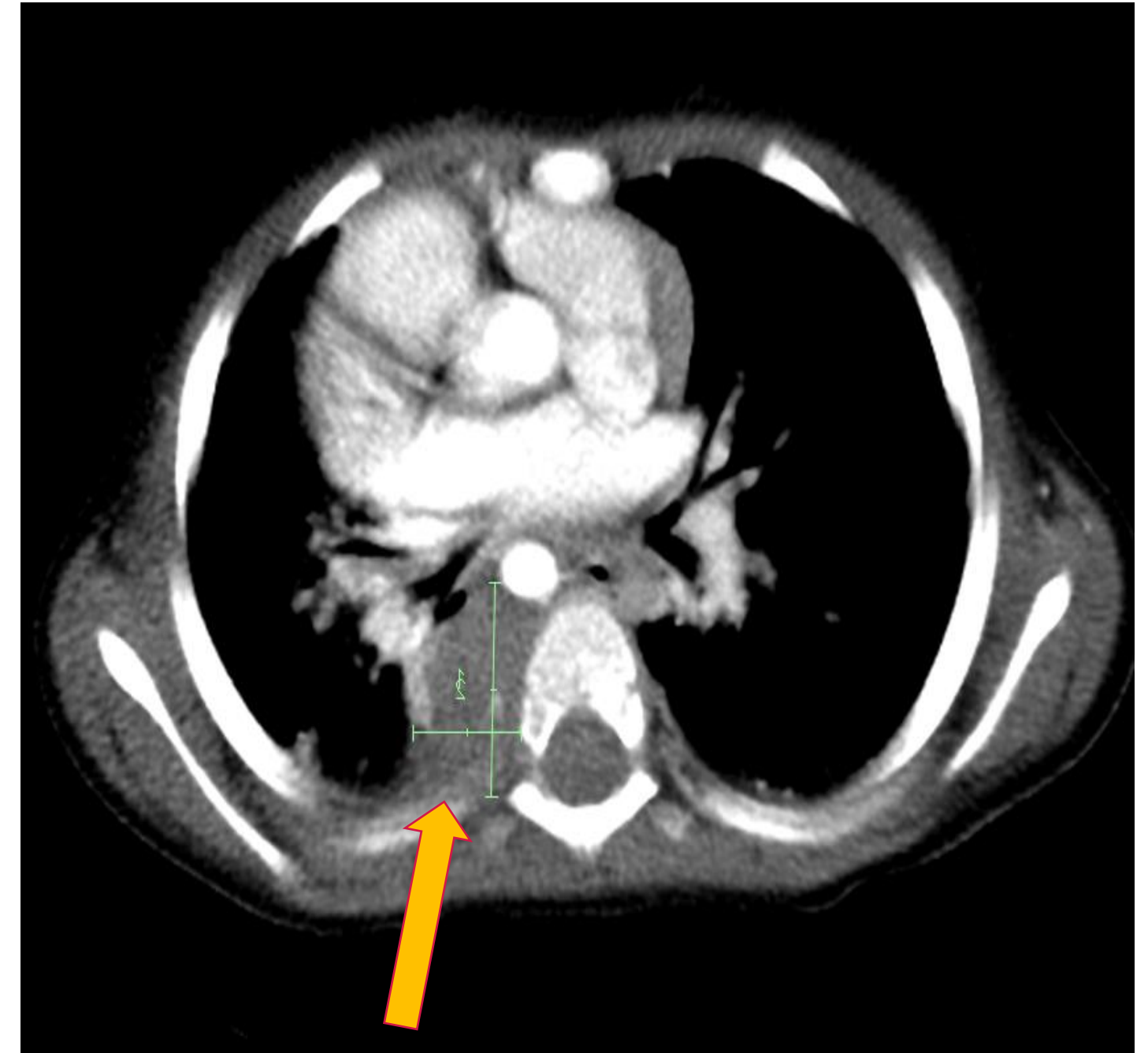
Types of Cancer: Cisplatin

Osteosarcoma
Nasopharyngeal
Carcinoma

Neuroblastoma
Hepatoblastoma

Medulloblastoma

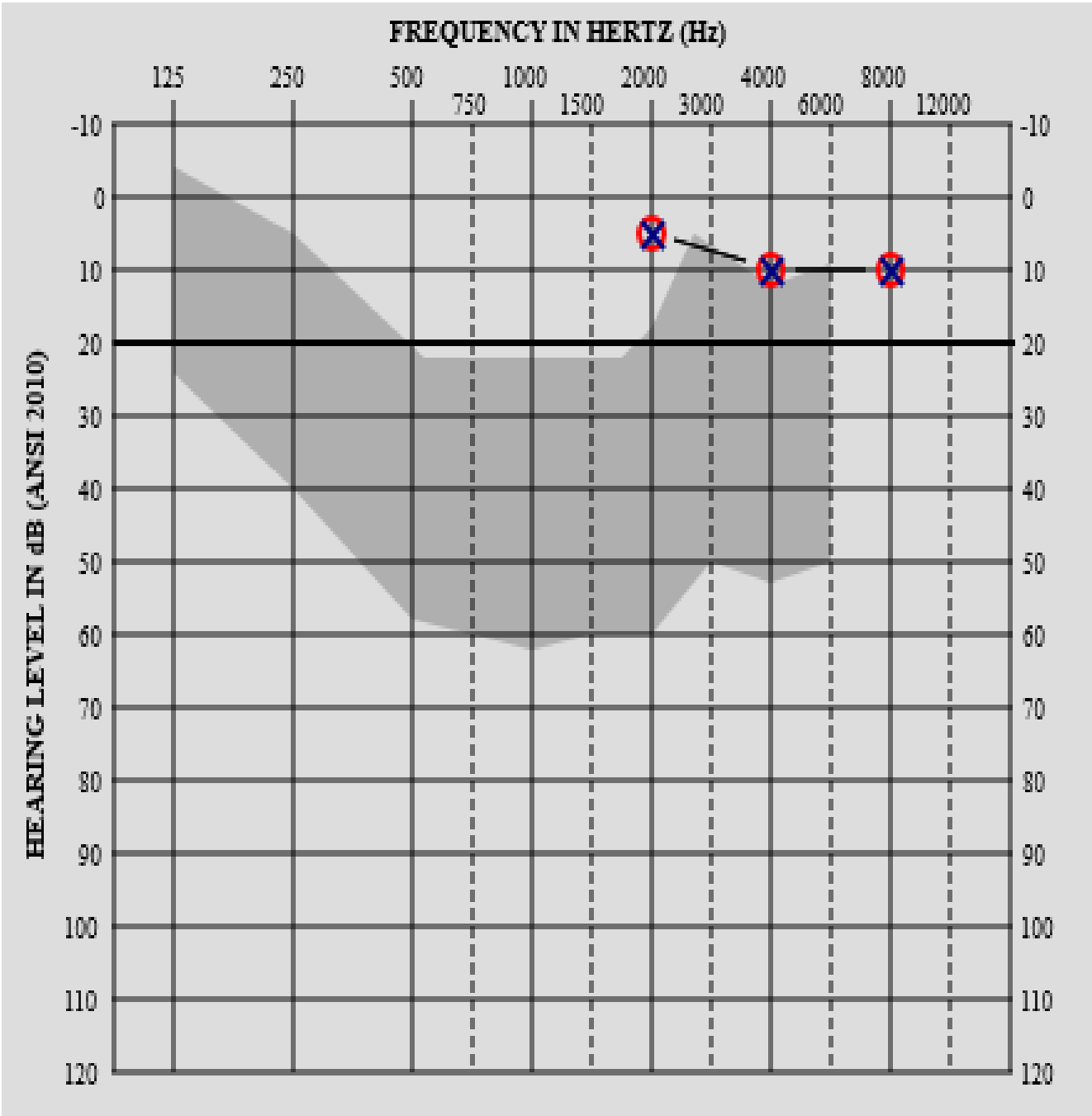
Case Study: Cisplatin-Induced Hearing Loss



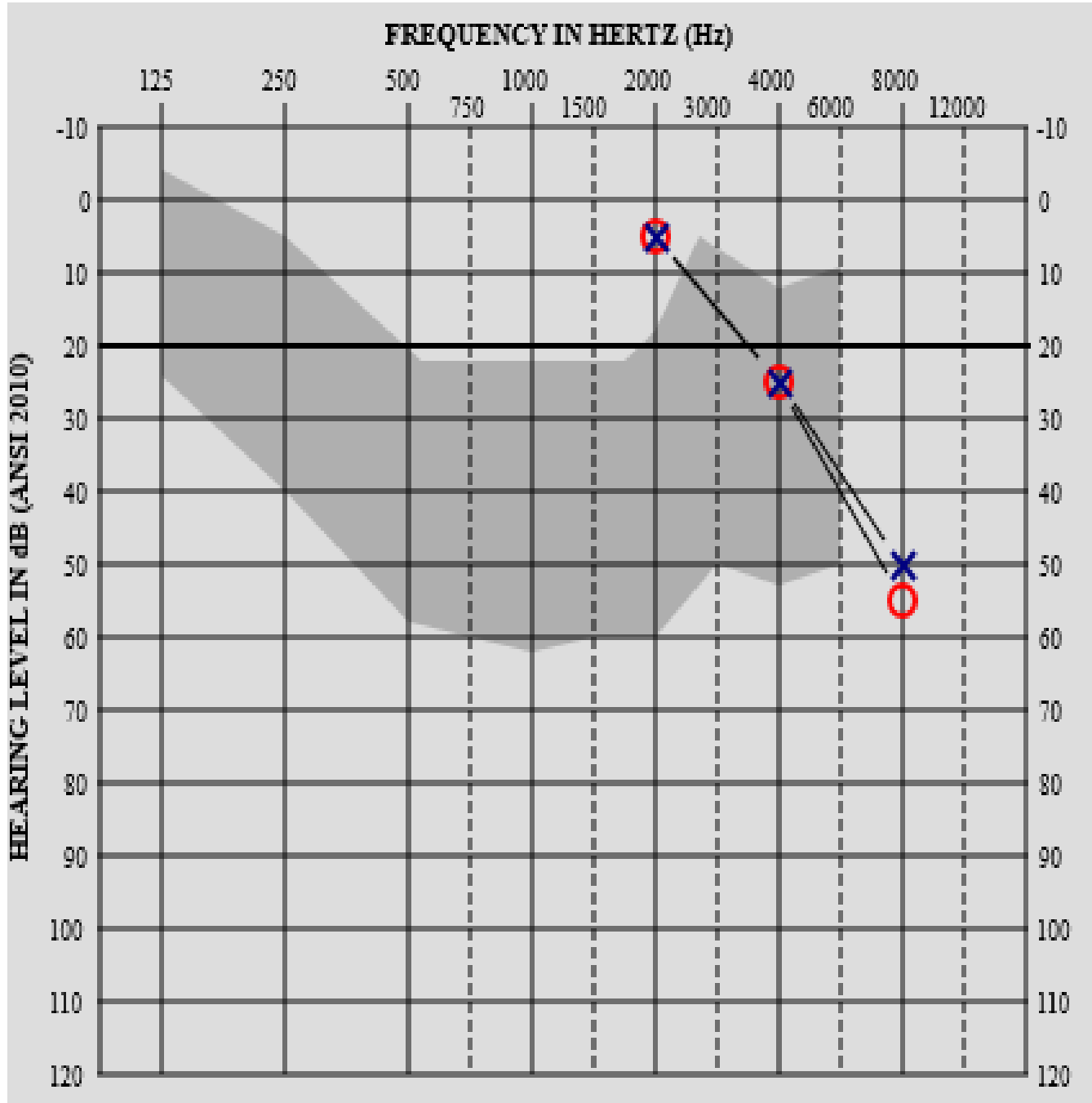
Patient diagnosed with a retroperitoneal neuroblastoma at the age of 2 years



Case Study: Cisplatin-Induced Hearing Loss

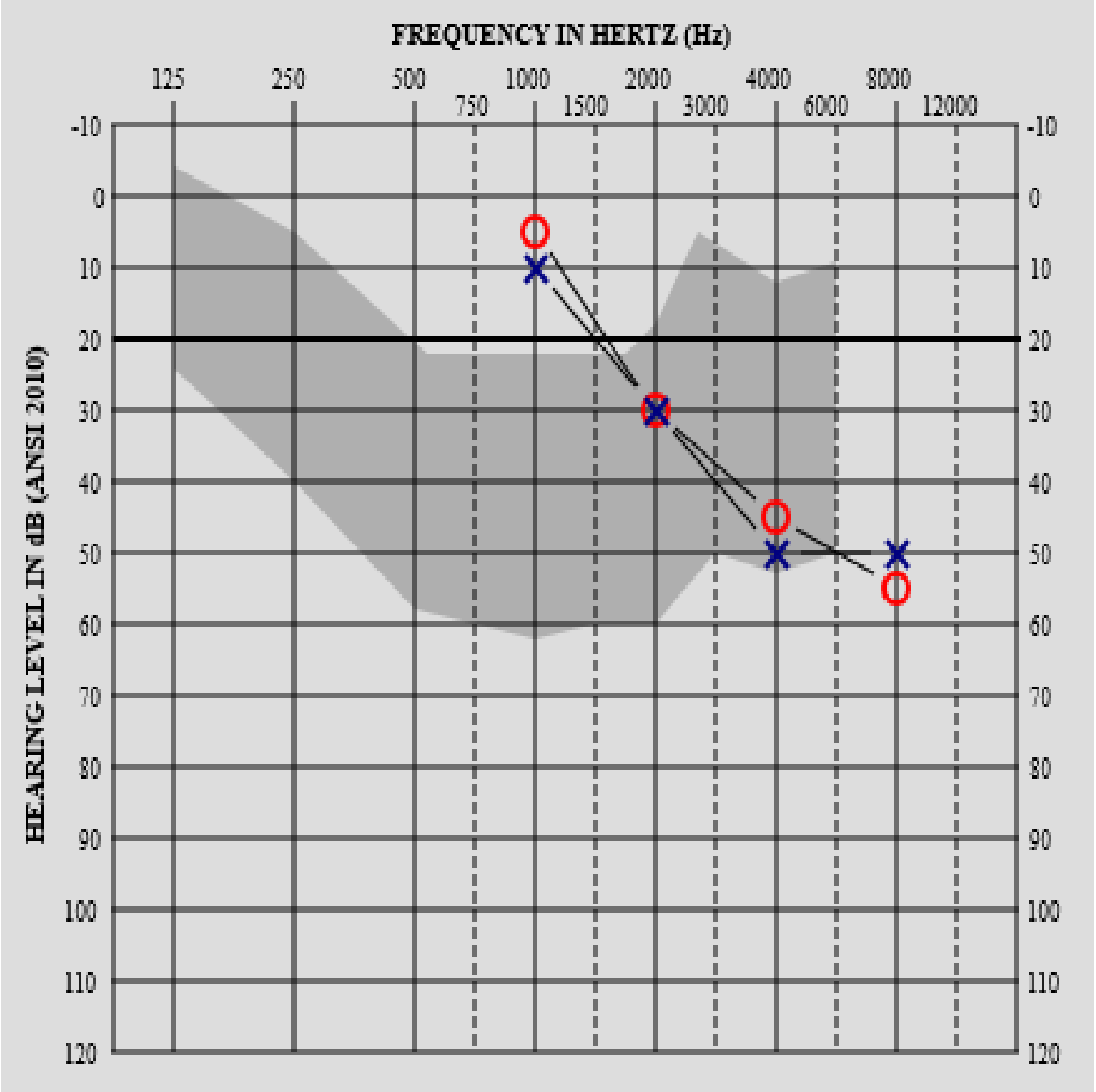


Baseline prior to treatment

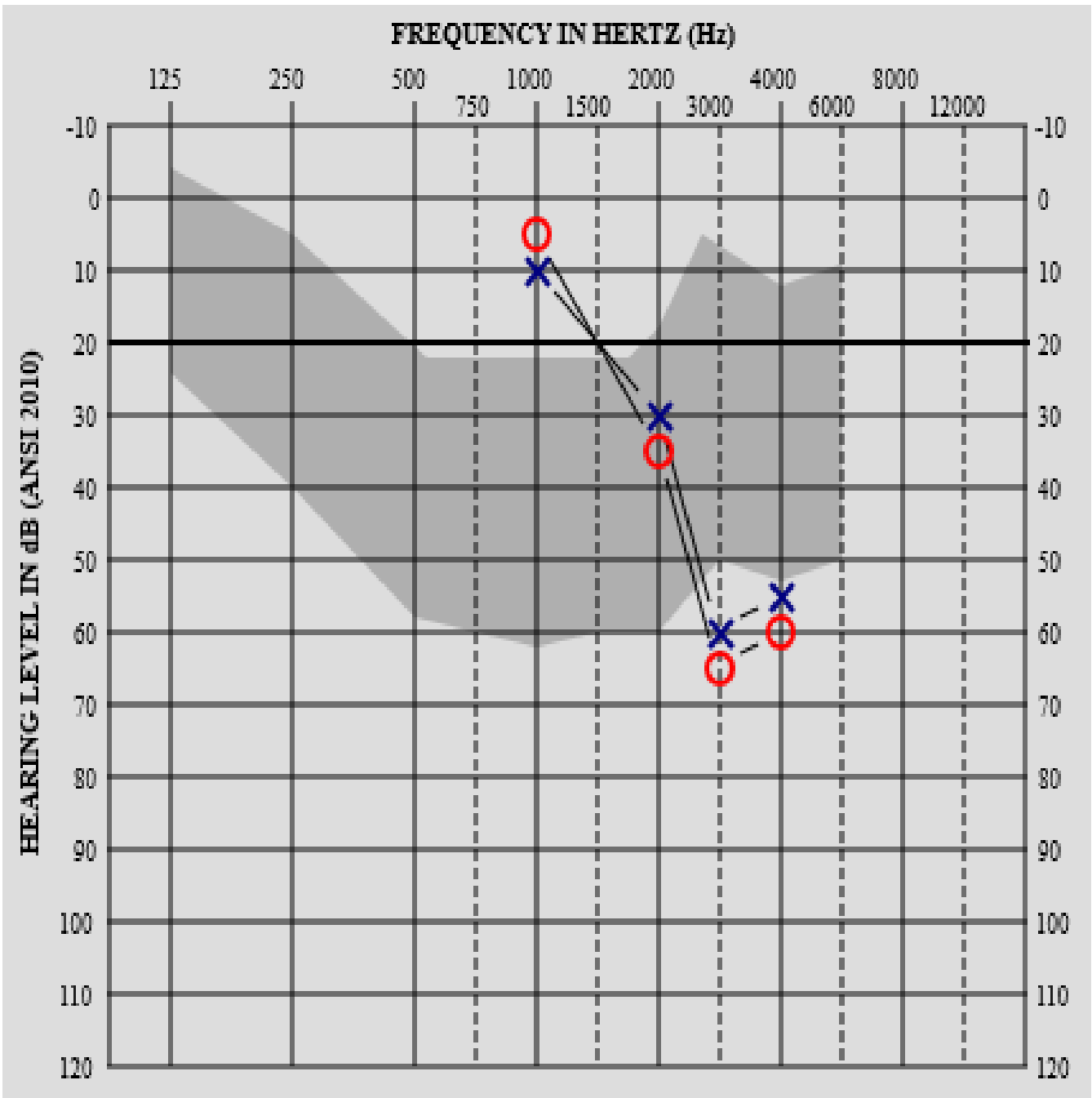


Post 1 cycles of cisplatin therapy

Case Study: Cisplatin-Induced Hearing Loss

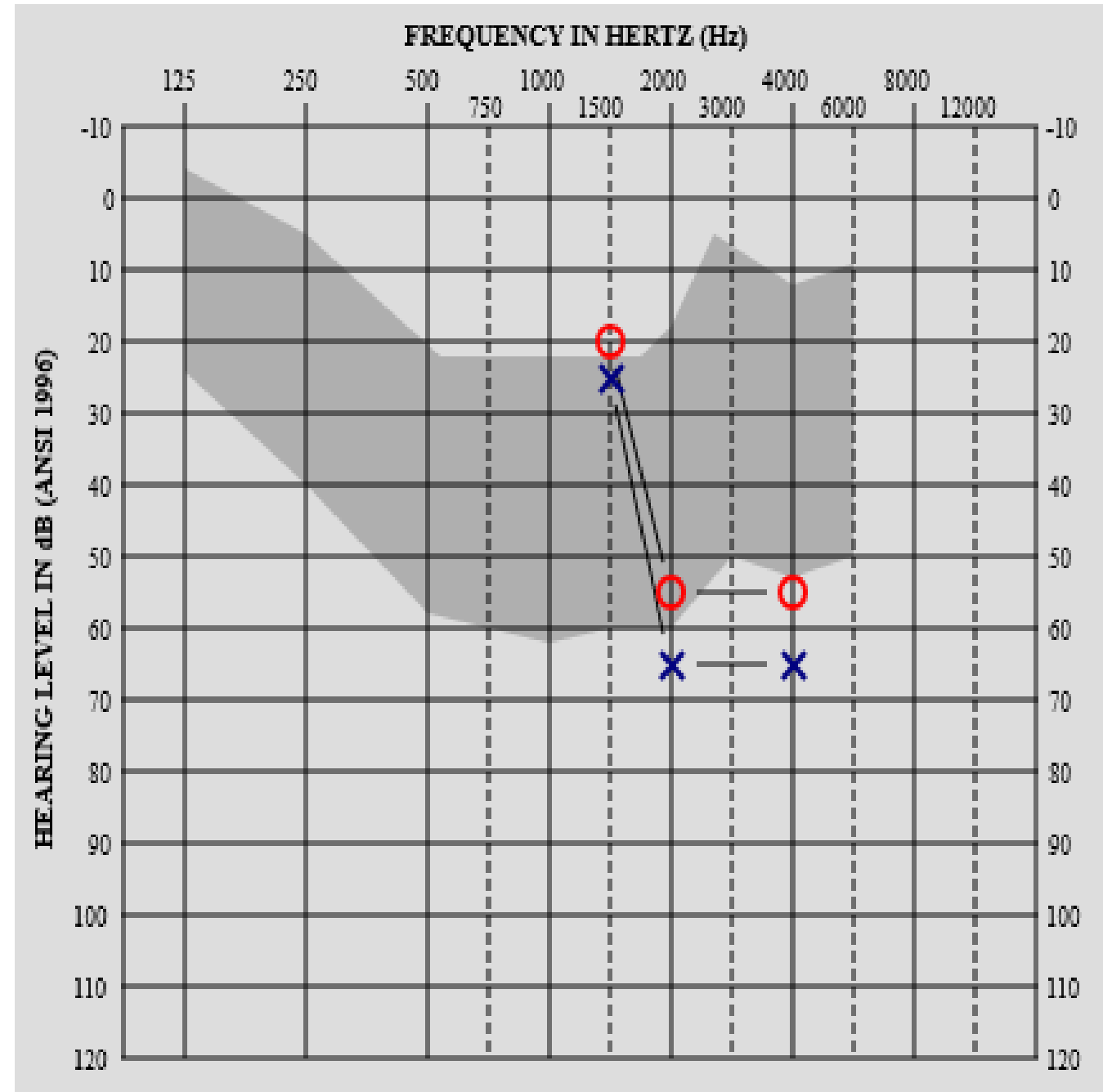


Post 2 cycles of cisplatin therapy

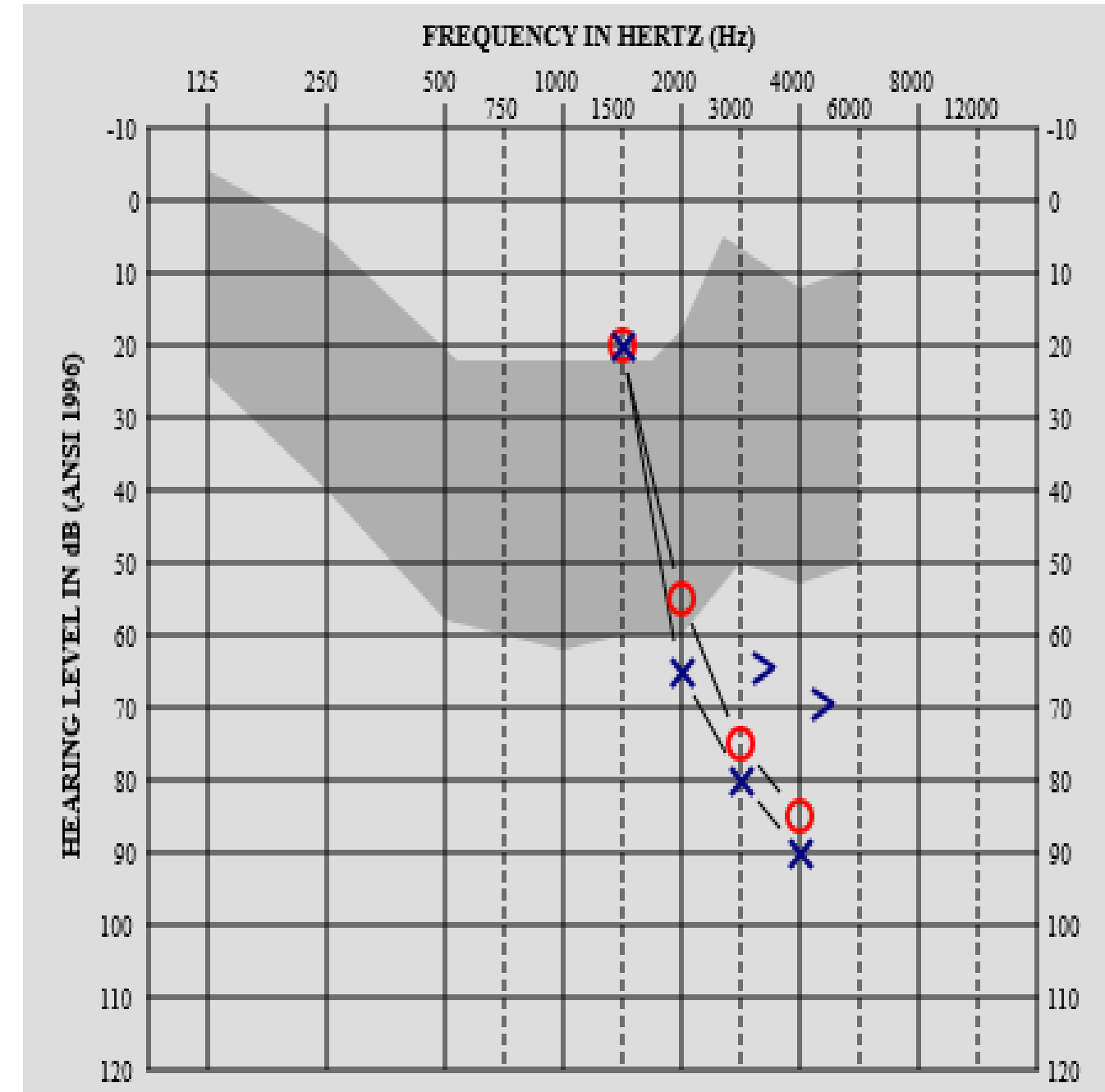


6 months post cisplatin therapy

Case Study: Cisplatin-Induced Hearing Loss



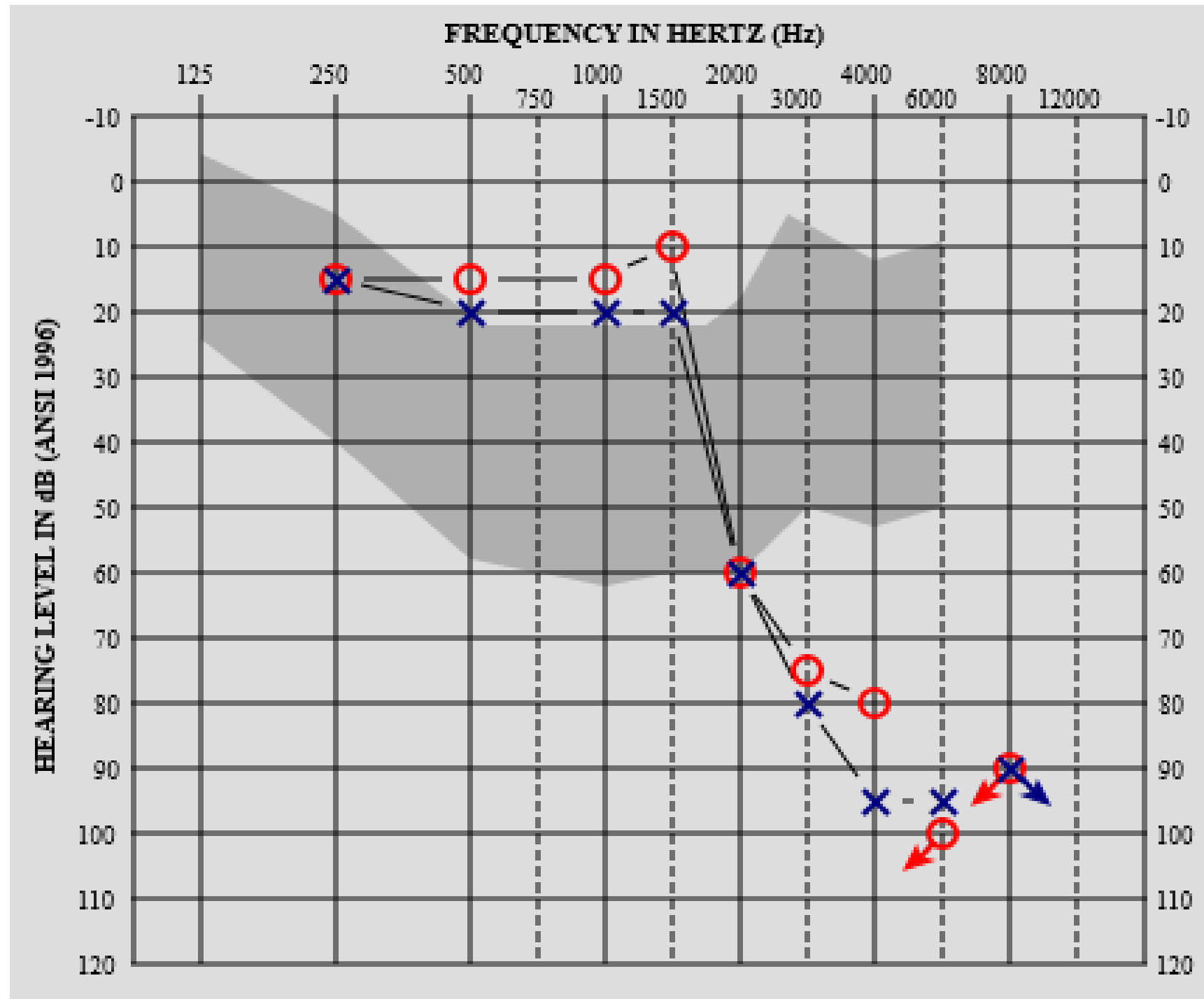
8 months post cisplatin therapy



2 years post cisplatin therapy



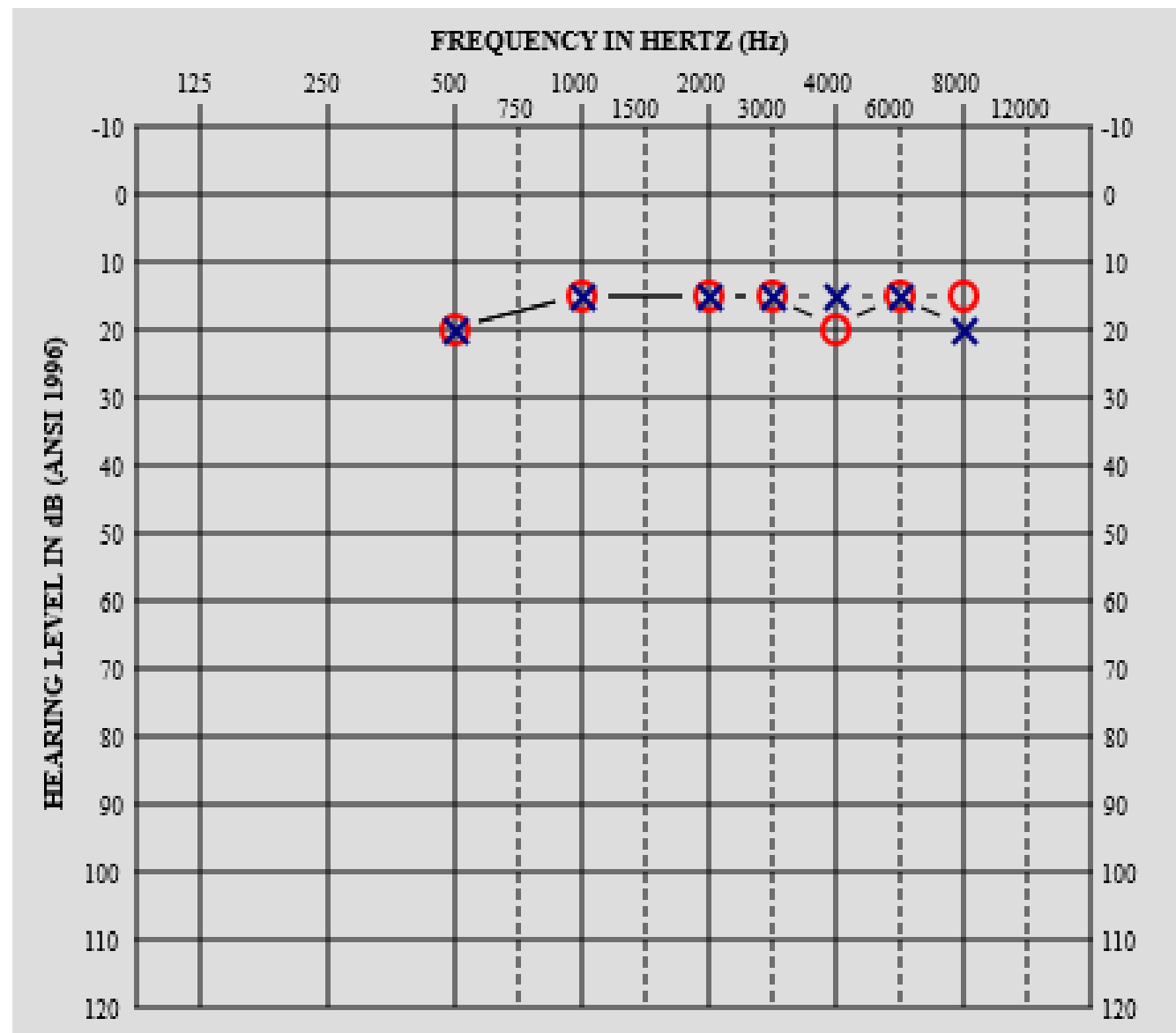
Case Study: Cisplatin-Induced Hearing Loss



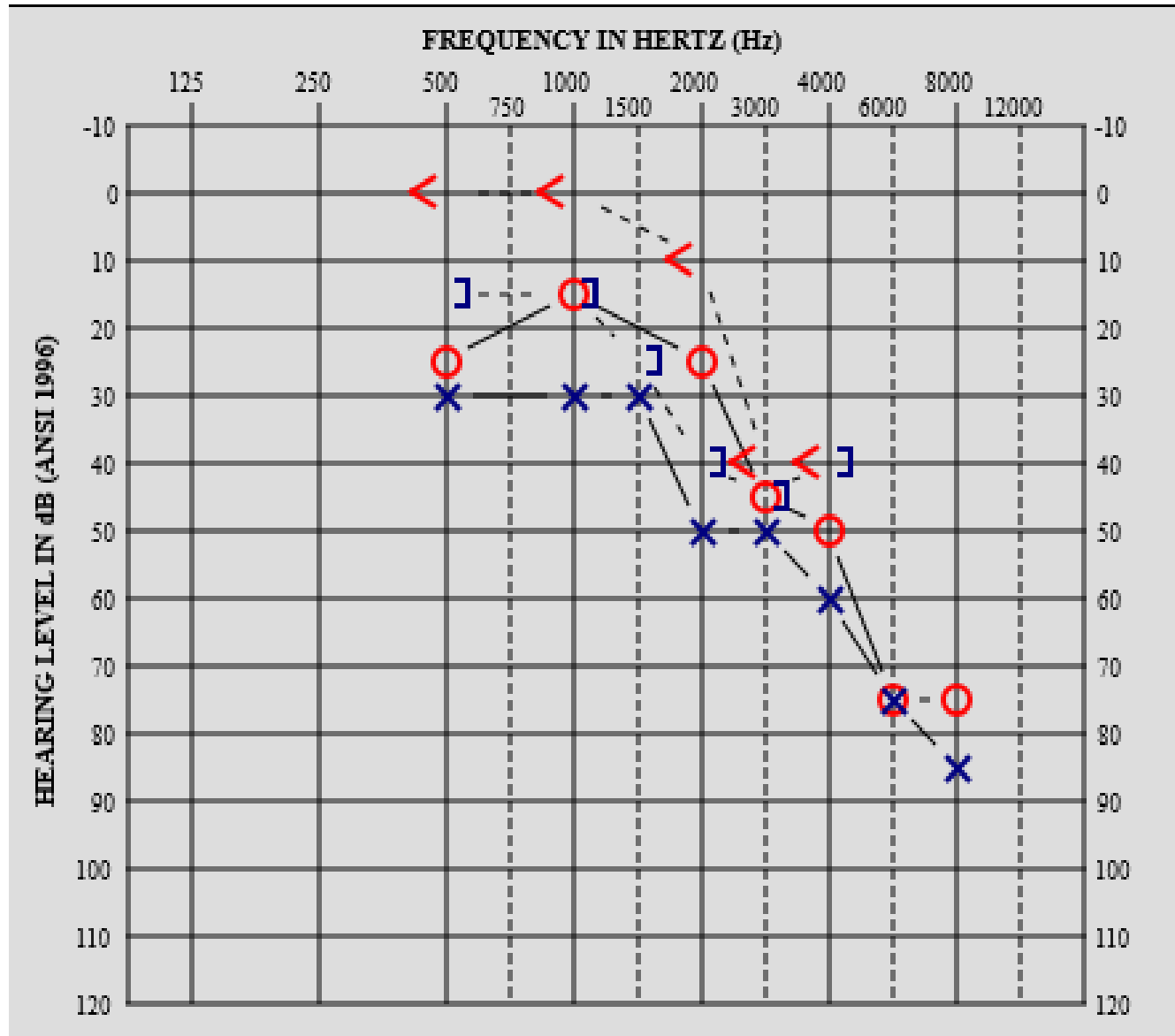
5 years post cisplatin therapy



Another Look: Cisplatin-Induced Hearing Loss



1 year post cisplatin therapy



2 years post cisplatin therapy

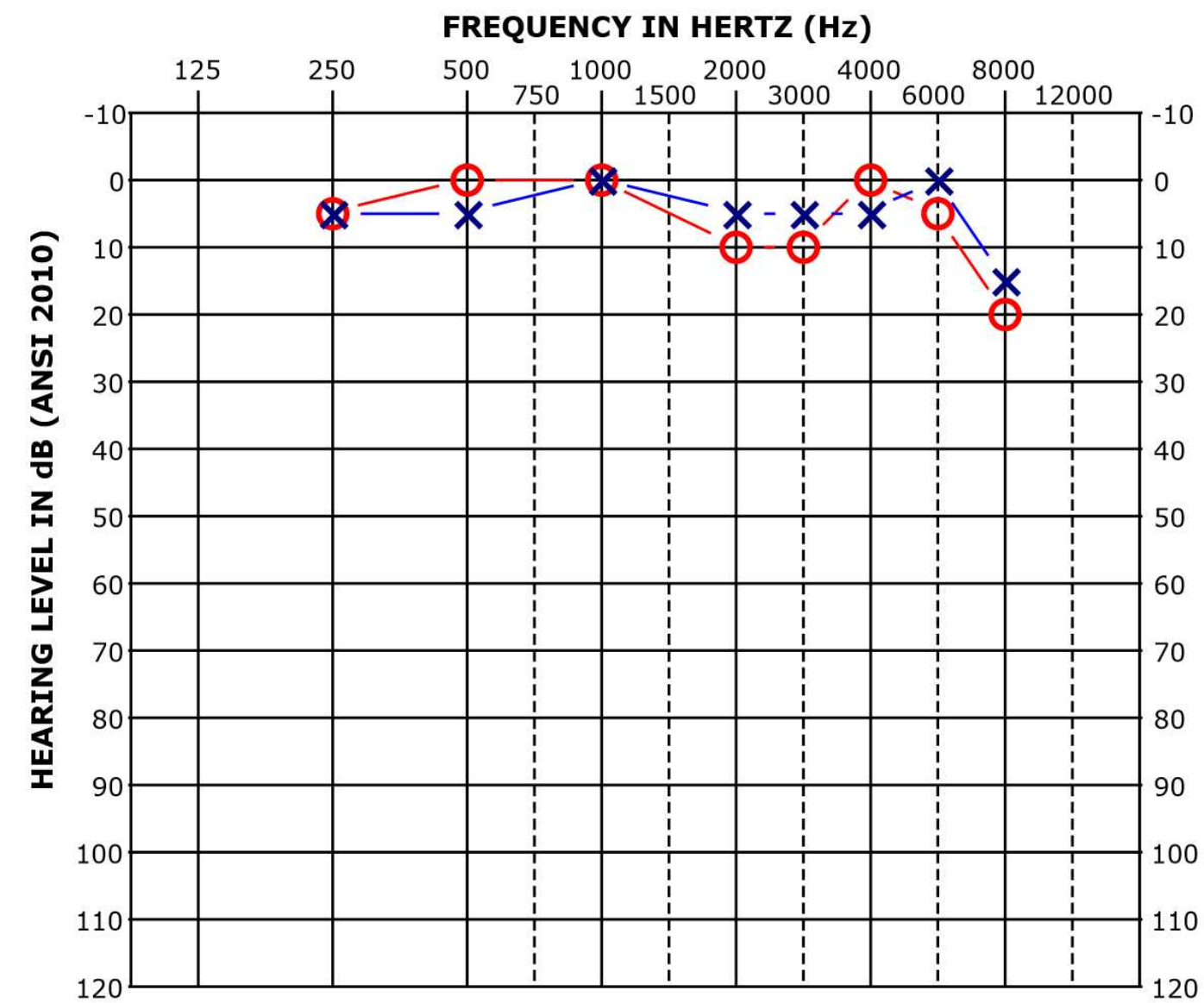
Patient diagnosed with medulloblastoma at 4 years.

Treatment included radiation therapy and 4 high dose cisplatin chemotherapy rounds.

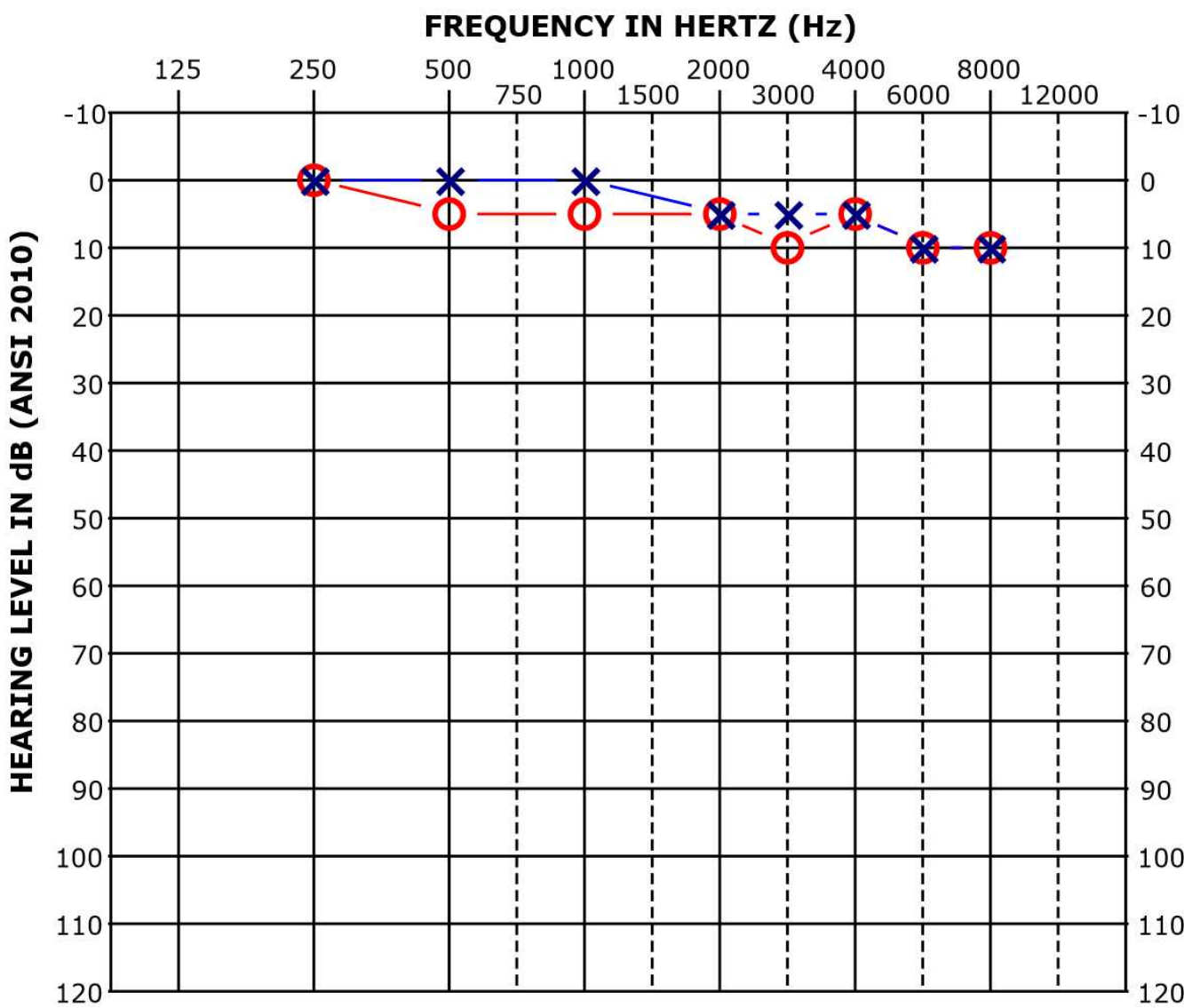


Diverse Audiologic Outcomes

Case Study: Cisplatin w/ No Hearing Loss



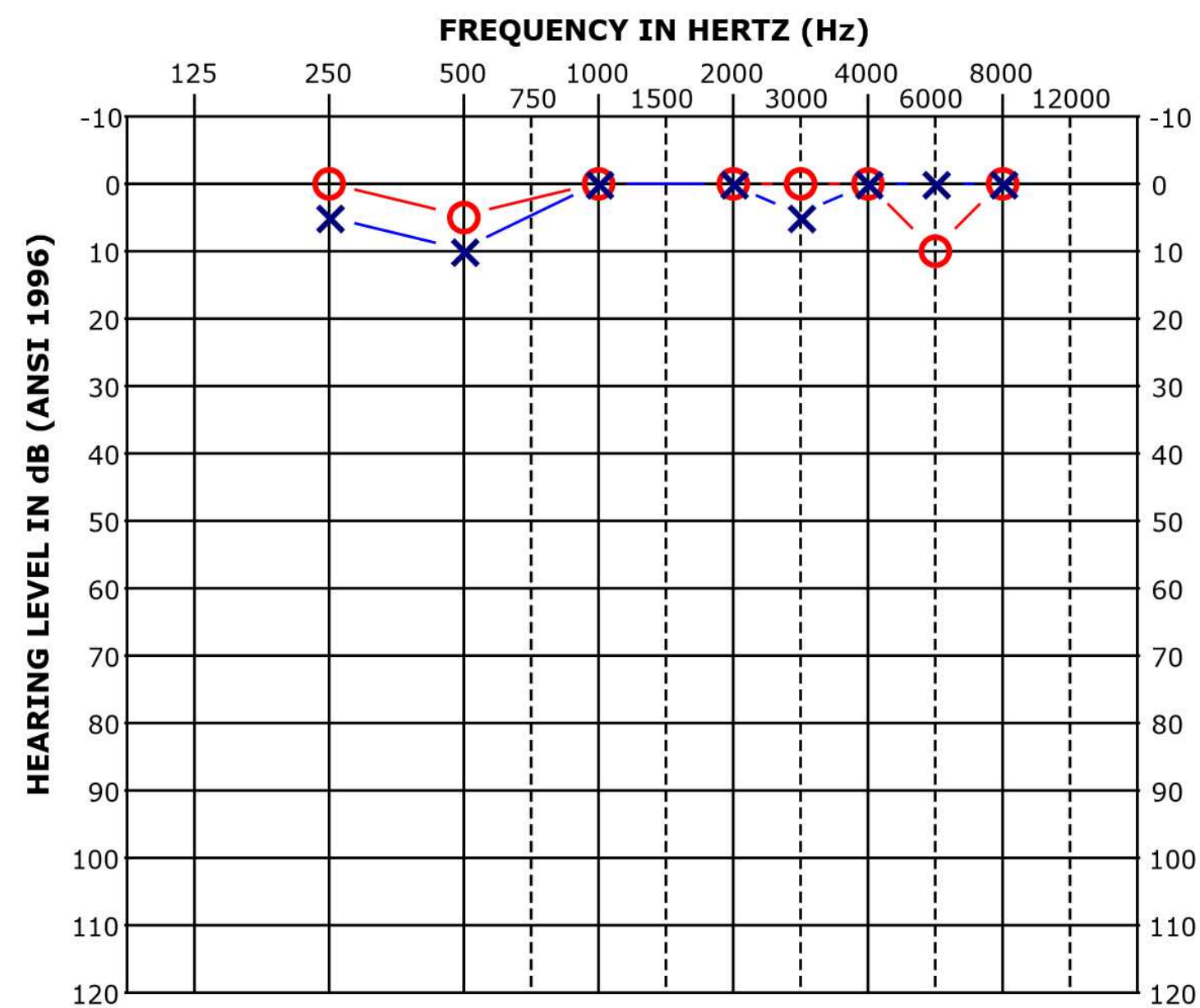
Baseline Evaluation



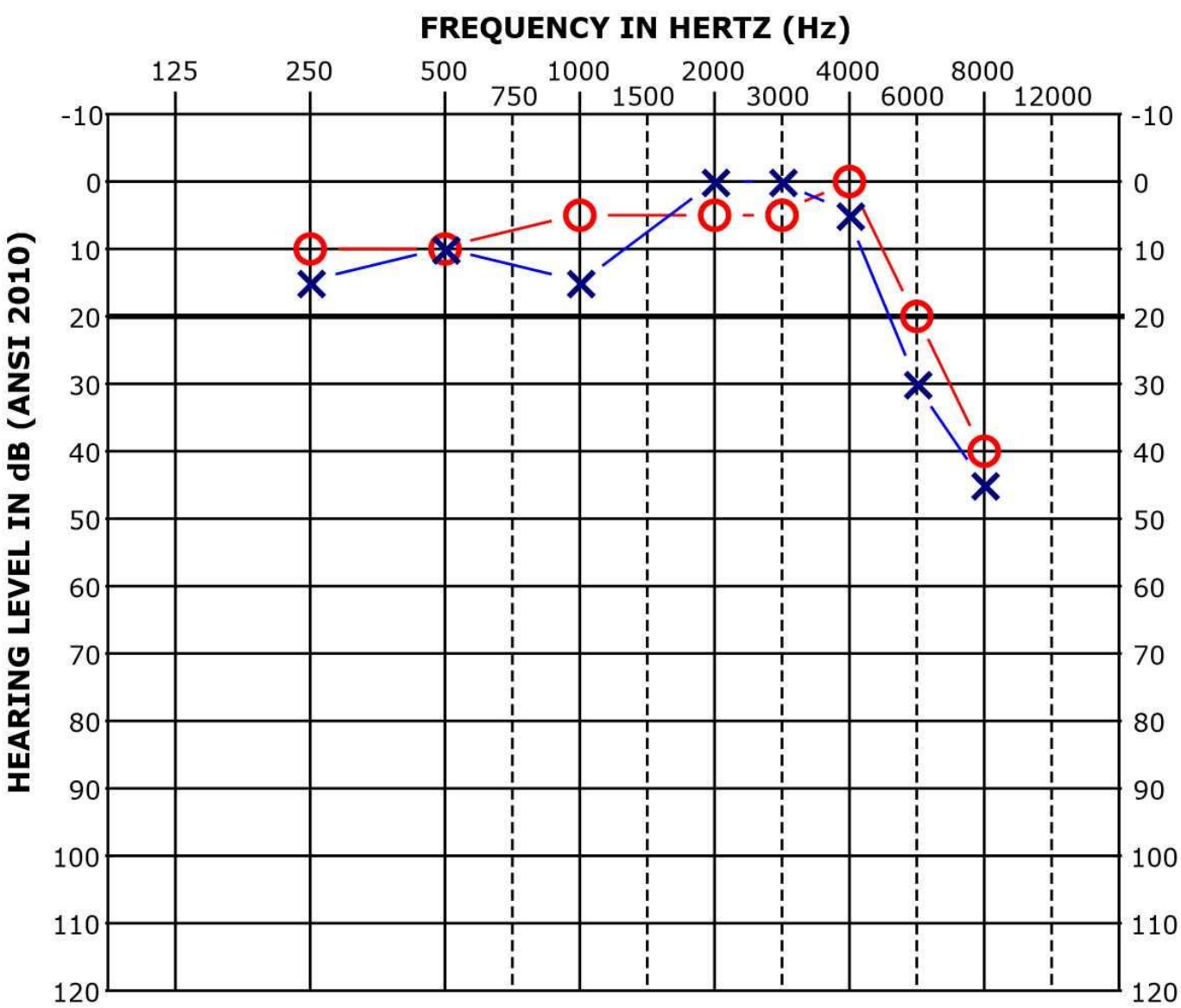
5 years post radiation + cisplatin therapy

Diagnosed Medulloblastoma at 14 y/o

Case Study B: Cisplatin w/ Only High-Frequency Loss



Baseline Evaluation



7 years post radiation + cisplatin therapy

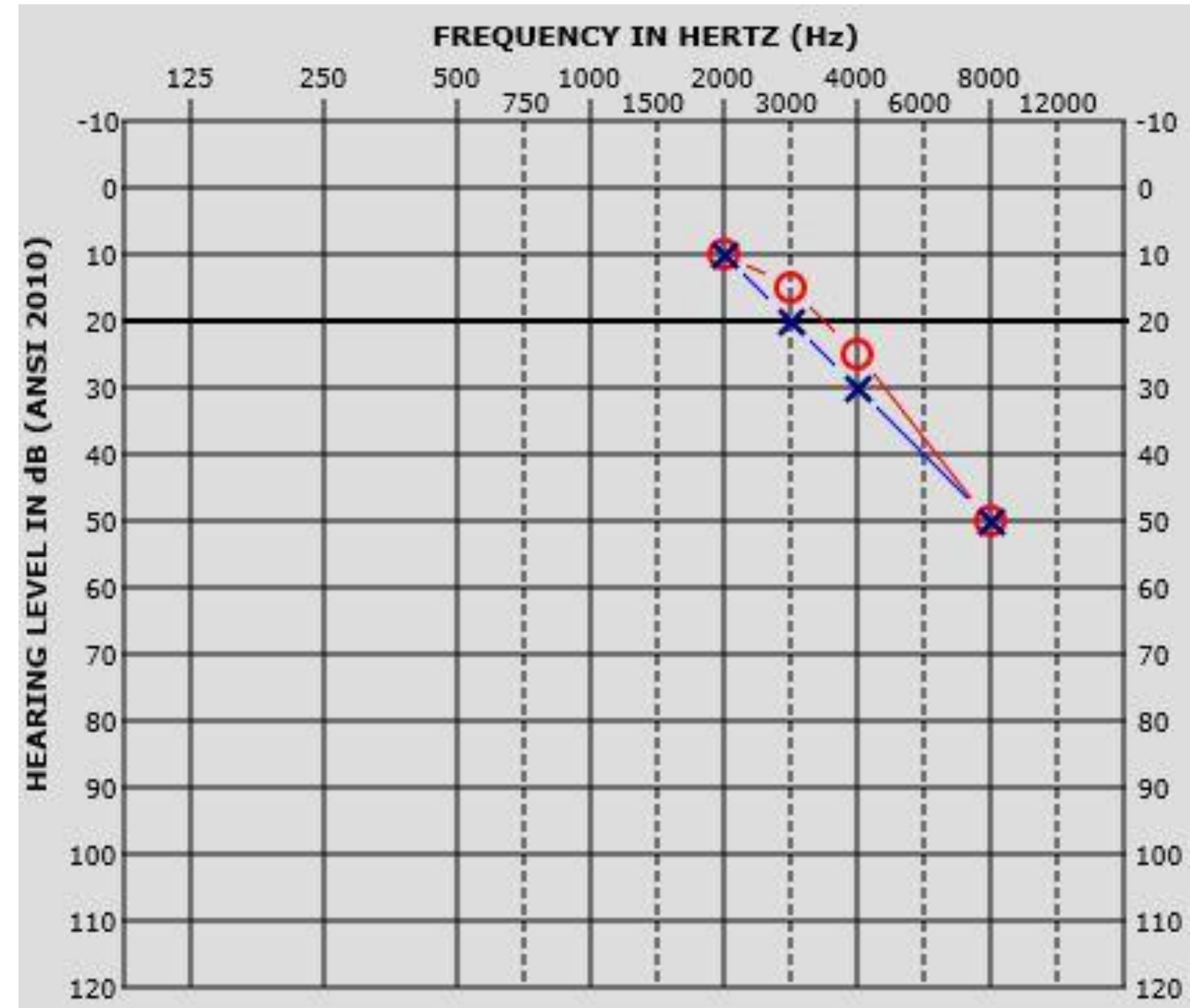
Diagnosed Medulloblastoma at 8 y/o



Case Study 1: Cisplatin w/STS (Heptoblastoma)

Sodium Thiosulfate:

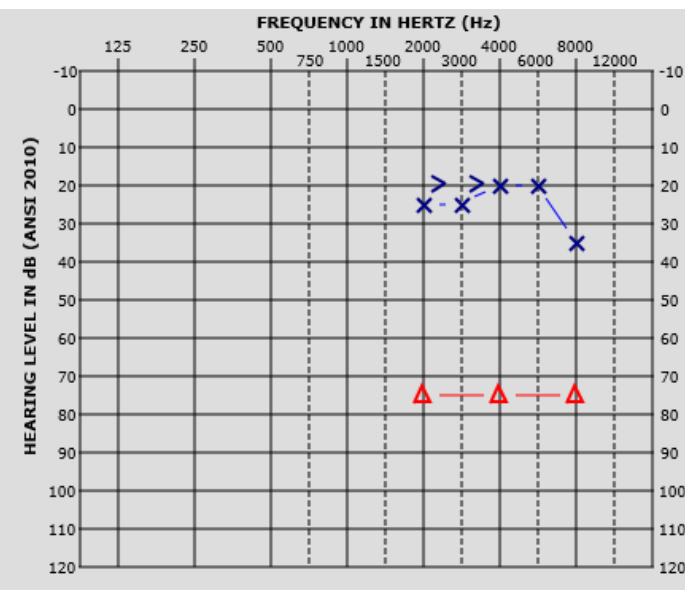
- Reduces cisplatin chemotherapy toxicity
- Administered intravenously
- In 2005, there were two phase III randomized clinical trials approved to study sodium thiosulfate (STS) for protection against cisplatin induced hearing loss in children
- COG Study #1 published in 2017 showing 56% HL in children w/cisplatin only vs. 28.6% HL in children w/cisplatin & STS
- Approved for children with non-metastatic solid tumors



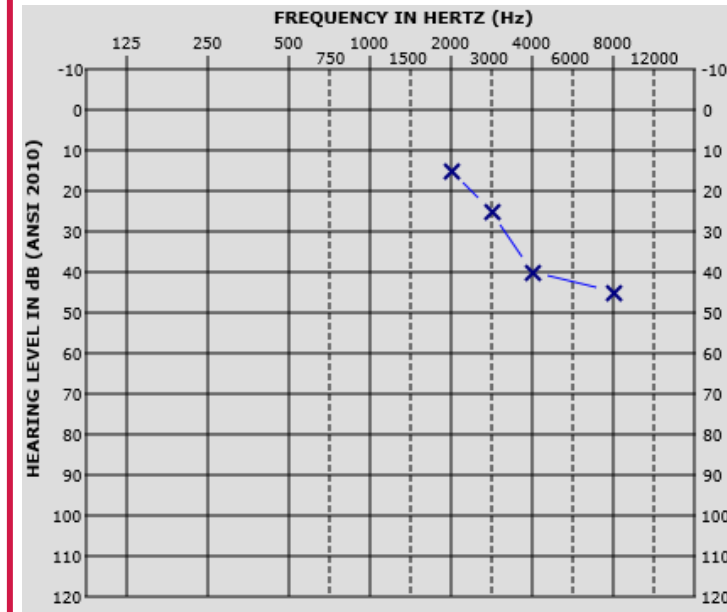
Post 6 cycles of cisplatin + STS

Case Study 2: Cisplatin w/STS (Hepatoblastoma)

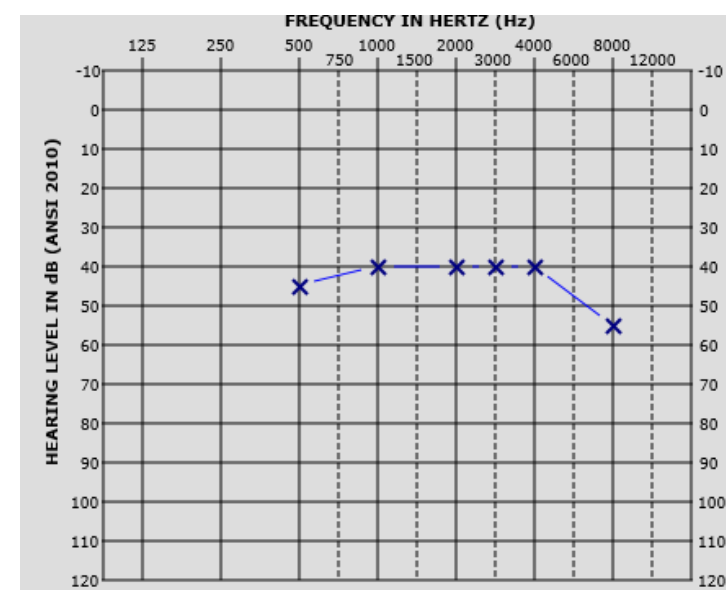
**13-Month-Old Male treated with Cisplatin & Concurrent STS
...then treated with carboplatin chemotherapy**



Baseline: 1/9/2024
Present OAEs, bilaterally



11/26/24 – s/p 5 cycles
cisplatin+STS; aged 23
months



4/29/25 – s/p 5 cycles
cisplatin+STS; aged 2 yrs,
4 mos

- Patient is fit with a BTE device for the left ear
- Monitoring of SNHL is ongoing

STS was not as affective in this case

What are the underlying mechanisms contributing to diverse audiologic outcomes in oncology patients?



Noise Exposure History



**Other Non-Ototoxic Drug
Exposure/Radiation**



Genetic Contributions



Genetic Contributions

Harman et al., 2026

Several studies have investigated the association between SNPs and susceptibility to ototoxic hearing loss

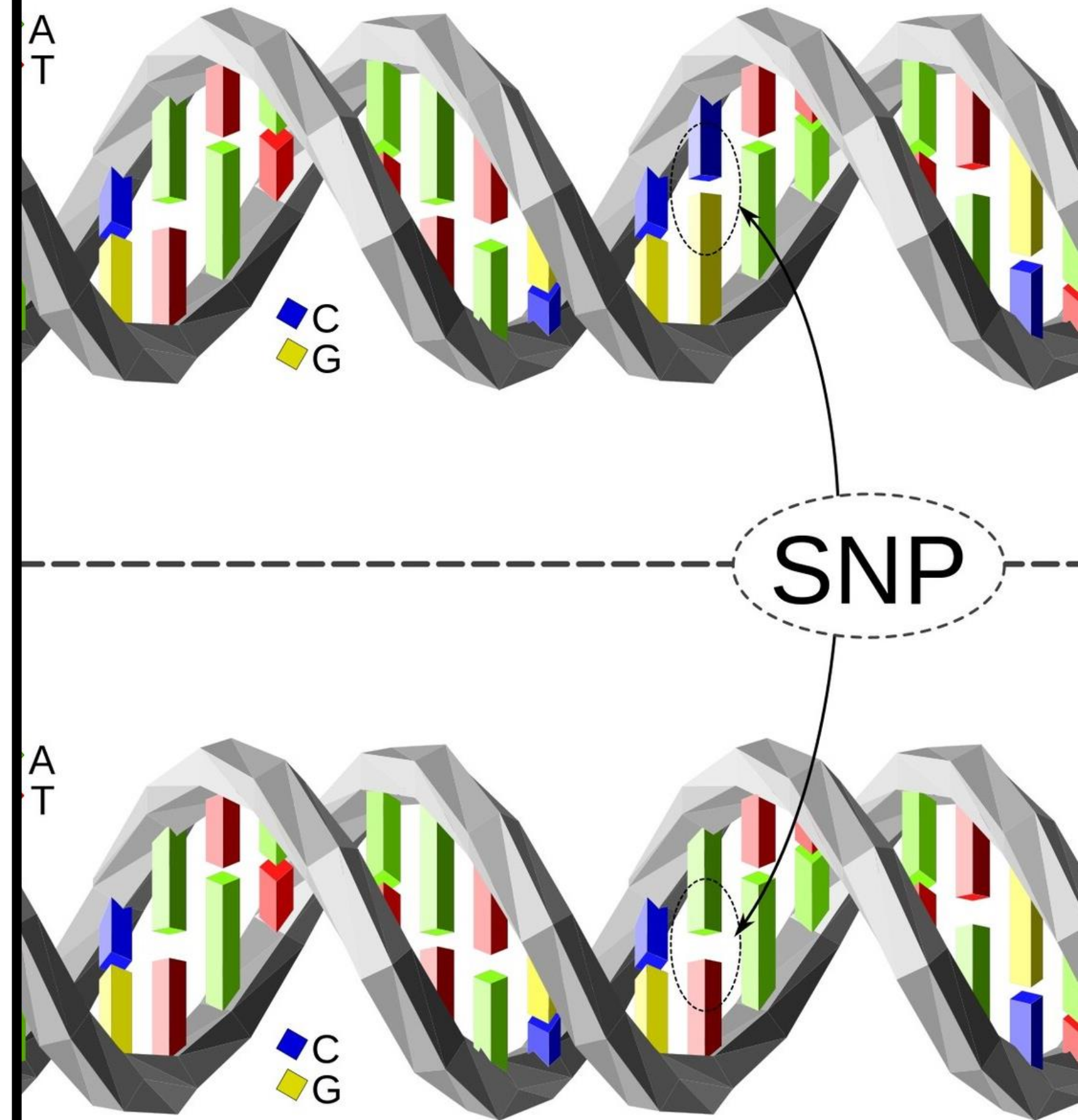
These can cause “variations in drug transport, detoxification, oxidative stress response and DNA damage repair” (Harman et al., 2026)

Reviewed 47 publications investigating genetic susceptibility to cisplatin-induced ototoxicity:

- Significant associations were found in SNPs across 31 unique genes
- Only variants in *ACYP2* (rs1872328), *SLC22A2* (rs316019), and *TLR4* (rs10759932) showed reproducible findings across studies as being associated with ototoxicity independently of other genetic modifiers

For example, SNPs in GSTs (Glutathione S-transferases) affect ability to aid in detoxification and metabolism of cisplatin

Harman, D., Lim, C. X., Kichenadasse, G., Morrison, J., & Suppiah, V. (2026). The Pharmacogenomics of Cisplatin-Induced Ototoxicity. *Life*, 16(10), 1599.
<https://doi.org/10.3390/life16101599>



SNP - Different DNA bases at the same position

Relevant Facts: Genetics & Ototoxicity

Variants can introduce greater oxidative stress or act as otoprotectants...

Variations in some antioxidant pathways (ACYP2, TPMT, and SOD2, for example) can influence whether a patient will experience permanent, high-frequency hearing loss **and/or** tinnitus

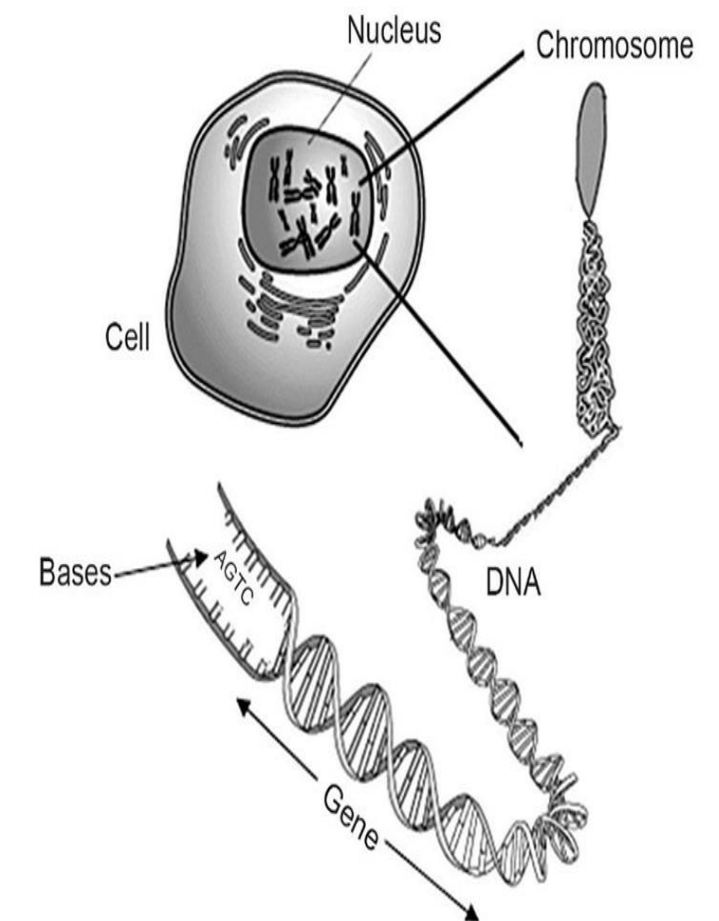
Iațentiuc et al., 2025

Some variants (ABCB5 and EPXH1) provide a degree of natural otoprotection against ototoxic drugs like cisplatin

Iațentiuc A, Iațentiuc IM, Frăsinariu OE, Cozma SR, Bîtere-Popa OR, Olariu R, Rădulescu LM, Ioniuc I, Cuciureanu M, Alecsa M, Guma C, Miron IC. The Role of Genetic and Non-Genetic Factors in the Occurrence of Cisplatin-Associated Ototoxicity. *Int J Mol Sci*. 2025 May 16;26(10):4787. doi: 10.3390/ijms26104787. PMID: 40429930; PMCID: PMC12112311.

Widespread genetic variations in how the body handles oxidative stress can change hair cell sensitivity (in withstanding chemical stress, for example)

Esteves F, Caria H. Genetic and Environmental Factors Shaping Hearing Loss: Xenobiotics, Mechanisms and Translational Perspectives. *J Xenobiot*. 2026 Feb 5;16(1):27. doi: 10.3390/jox16010027. PMID: 41718270; PMCID: PMC12921957.

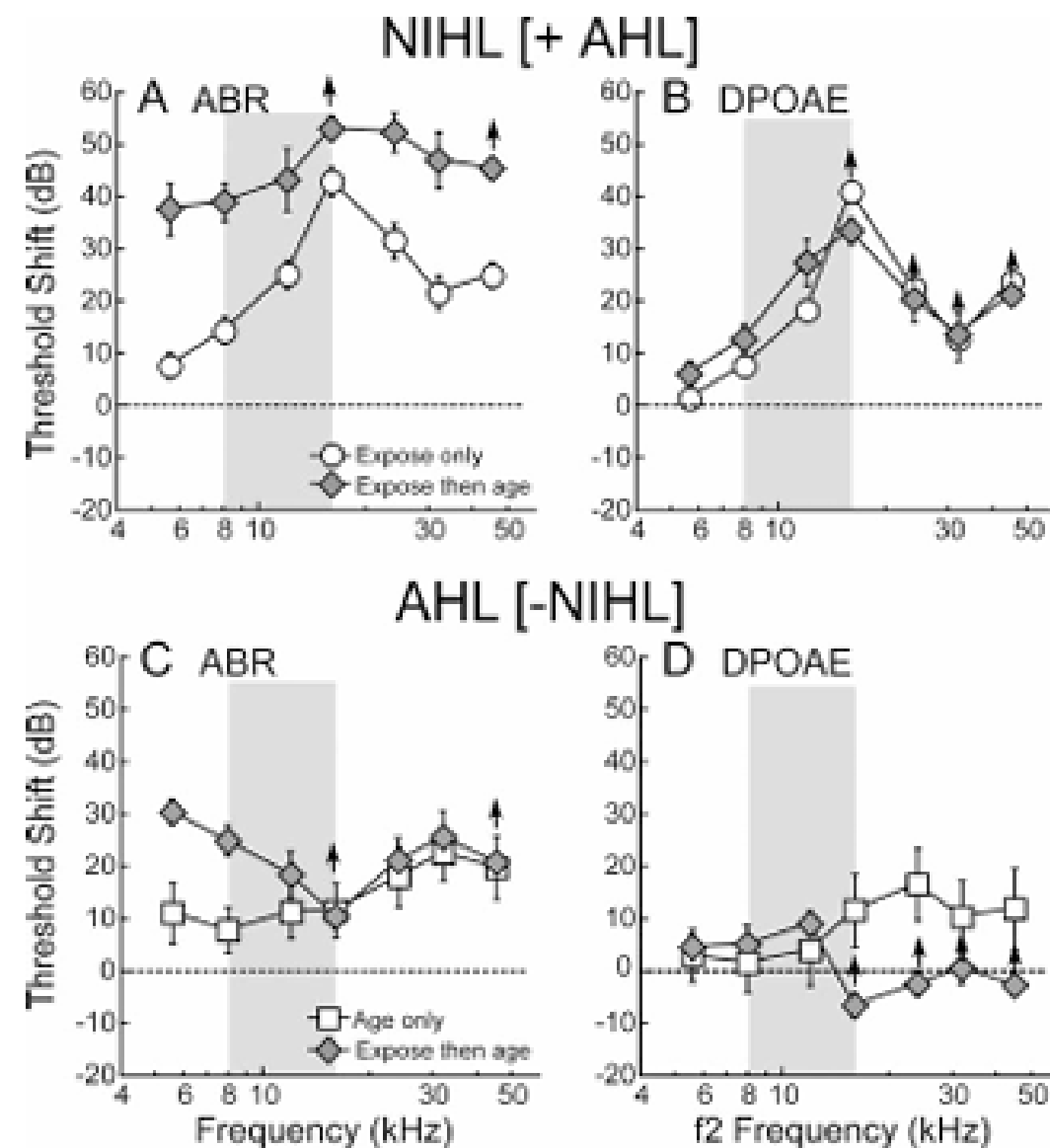
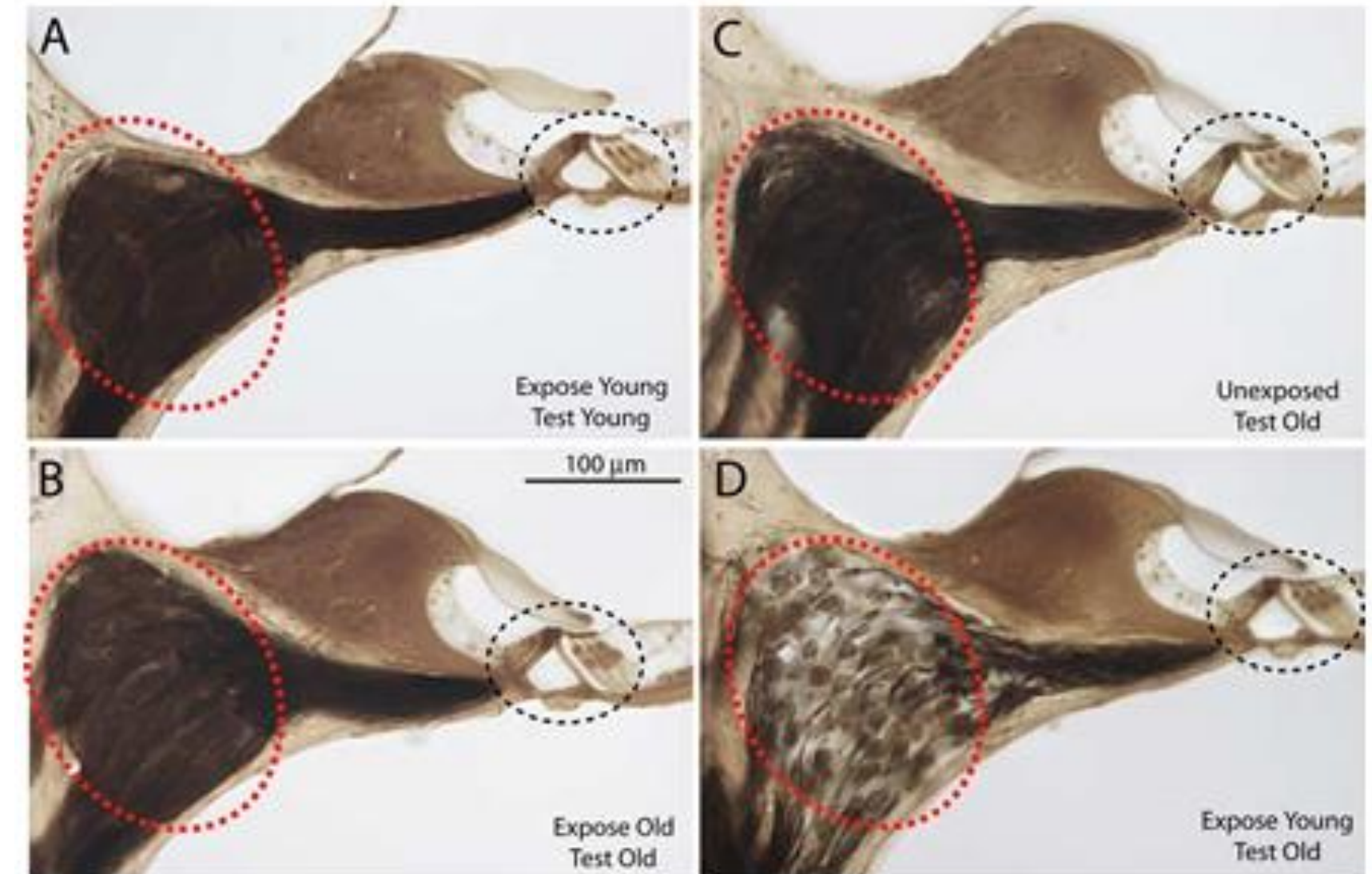


More research is warranted for clinical application

Noise Exposure History

“Evidence of a misspent youth” (Kujawa & Liberman, 2006)

Noise increases susceptibility to the phenotype of age-related hearing loss (to true aging in mice)

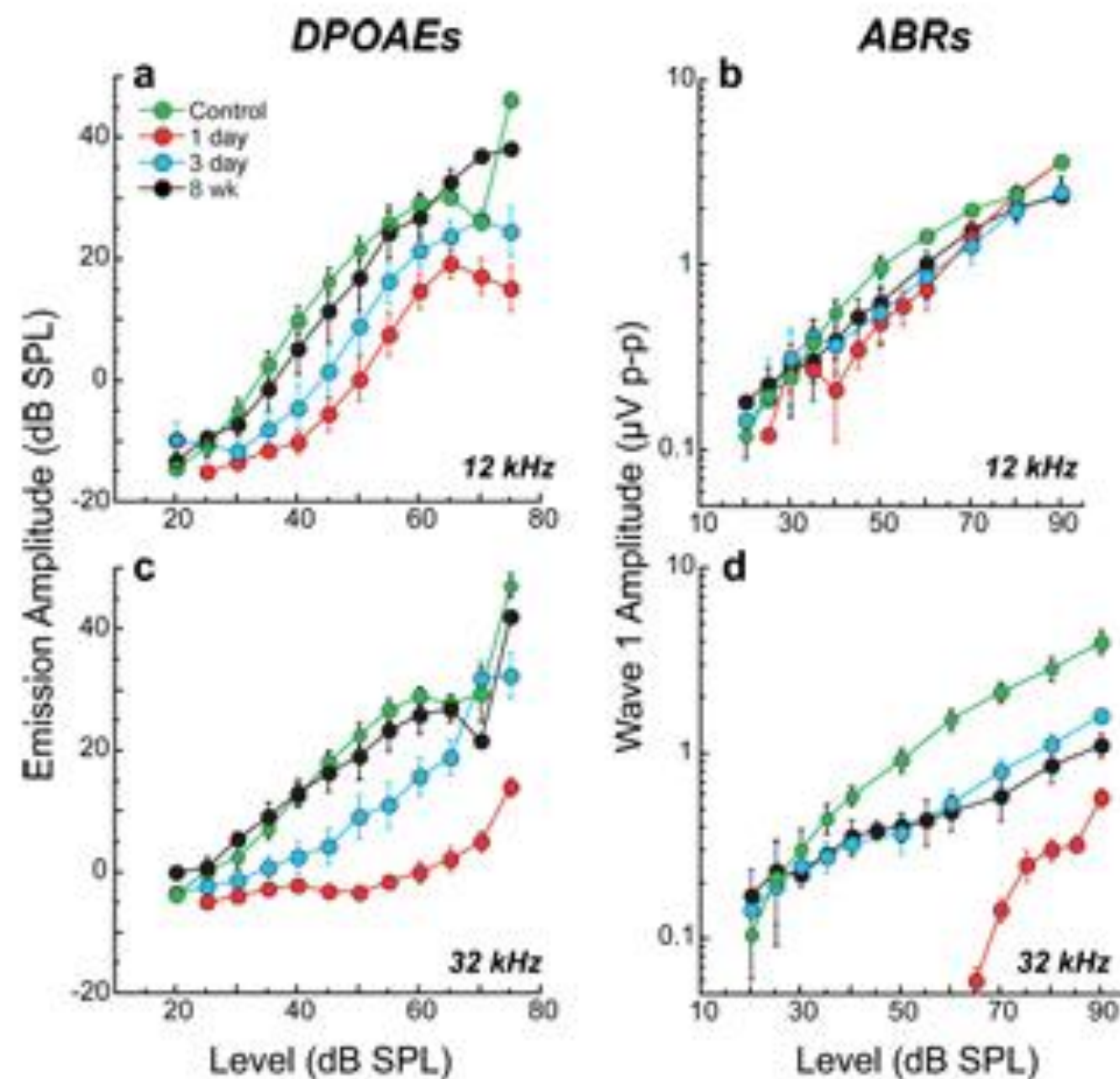
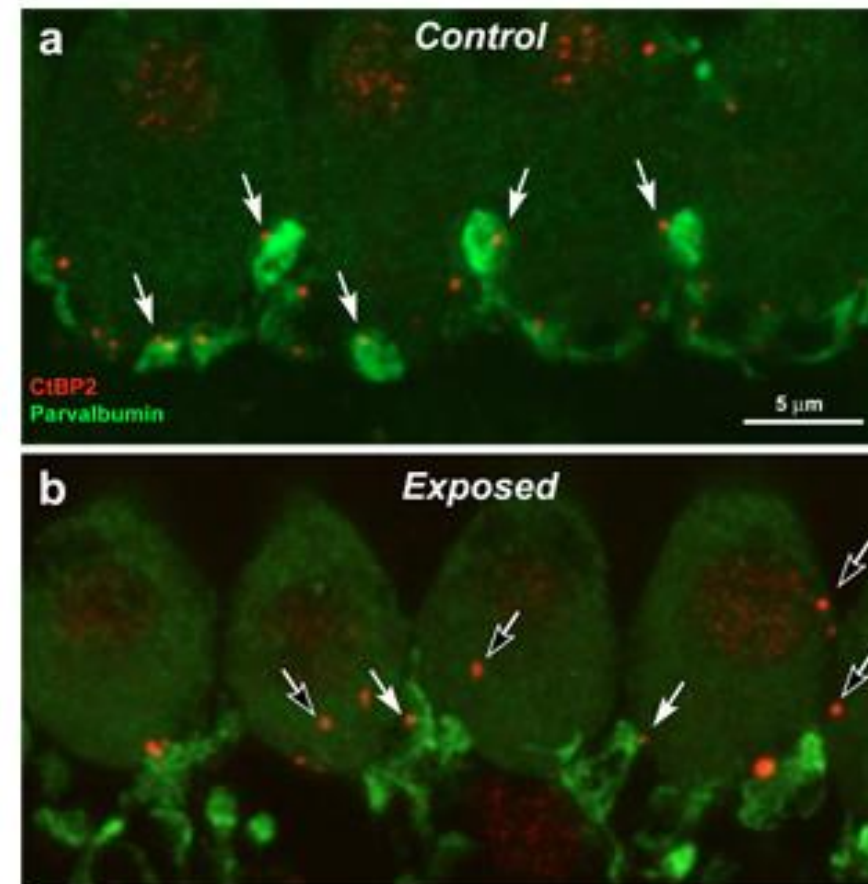
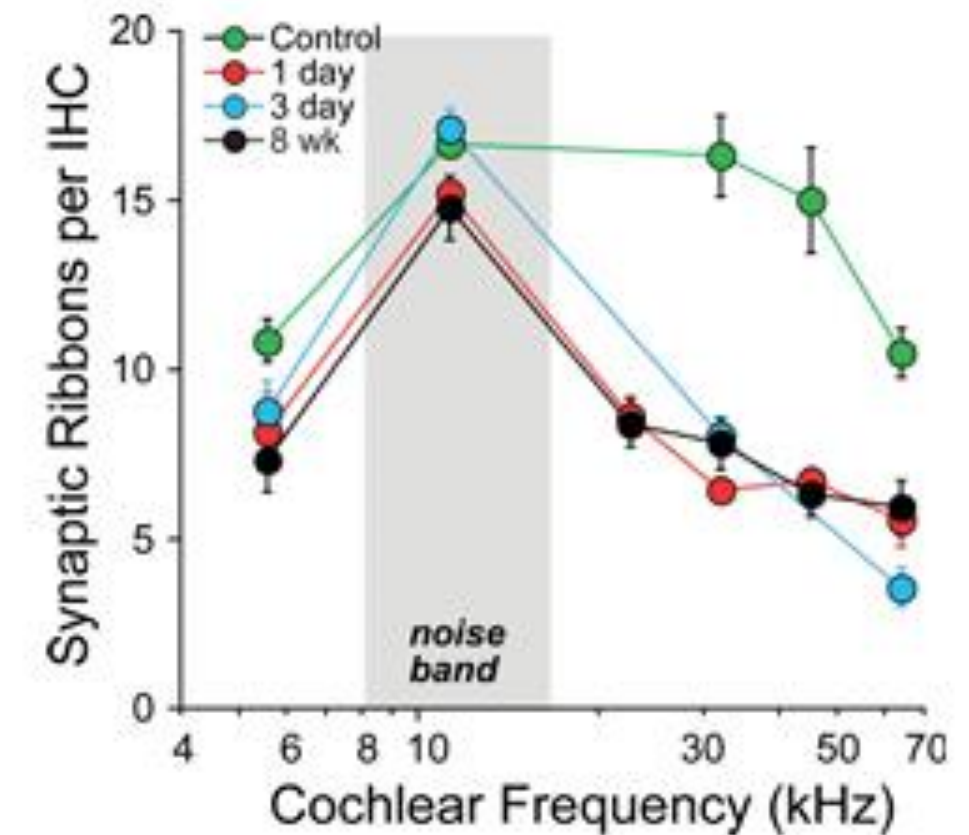


Noise exposure plus aging produces a significant threshold shift

Noted loss of spiral ganglion cells (primary neural degeneration) with exposure at a young age

Historically, noise exposure can cause permanent hearing loss

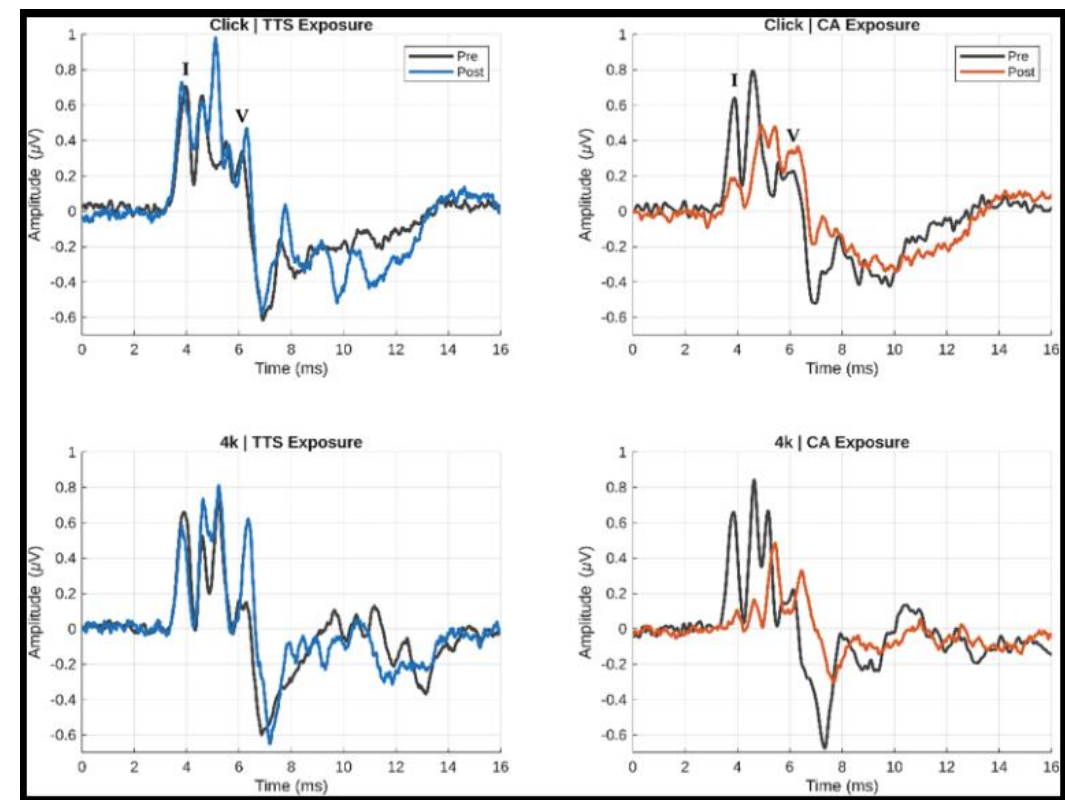
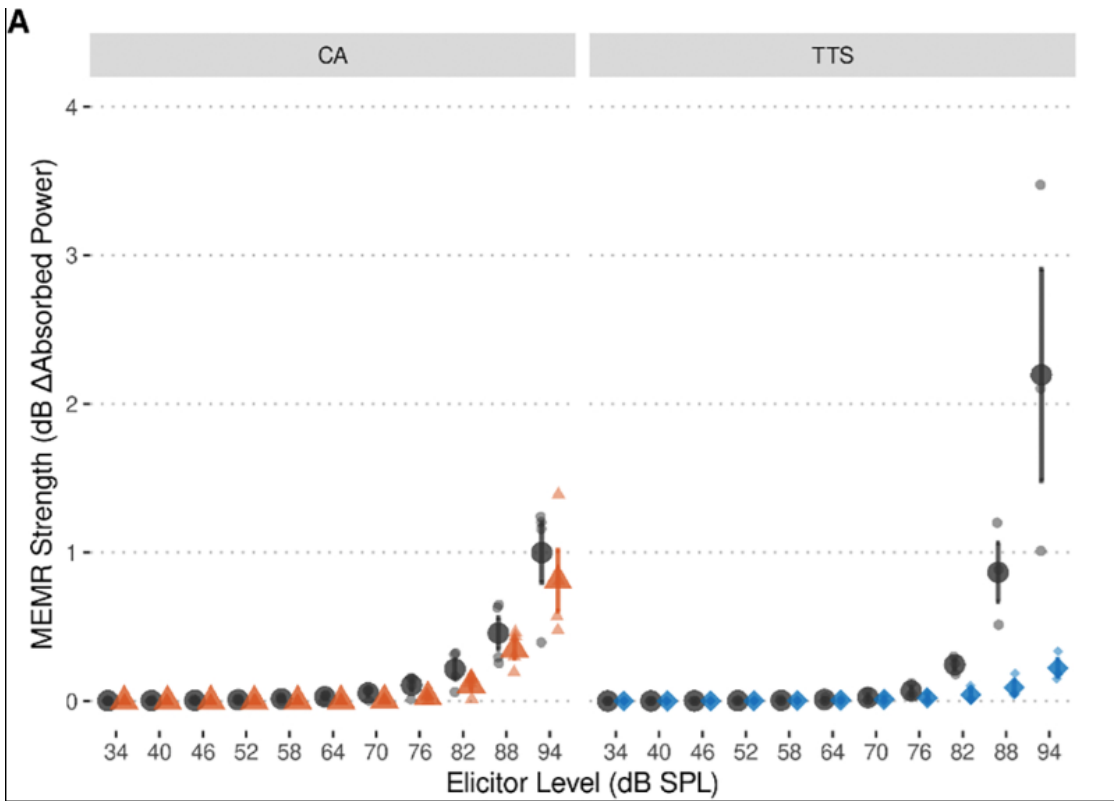
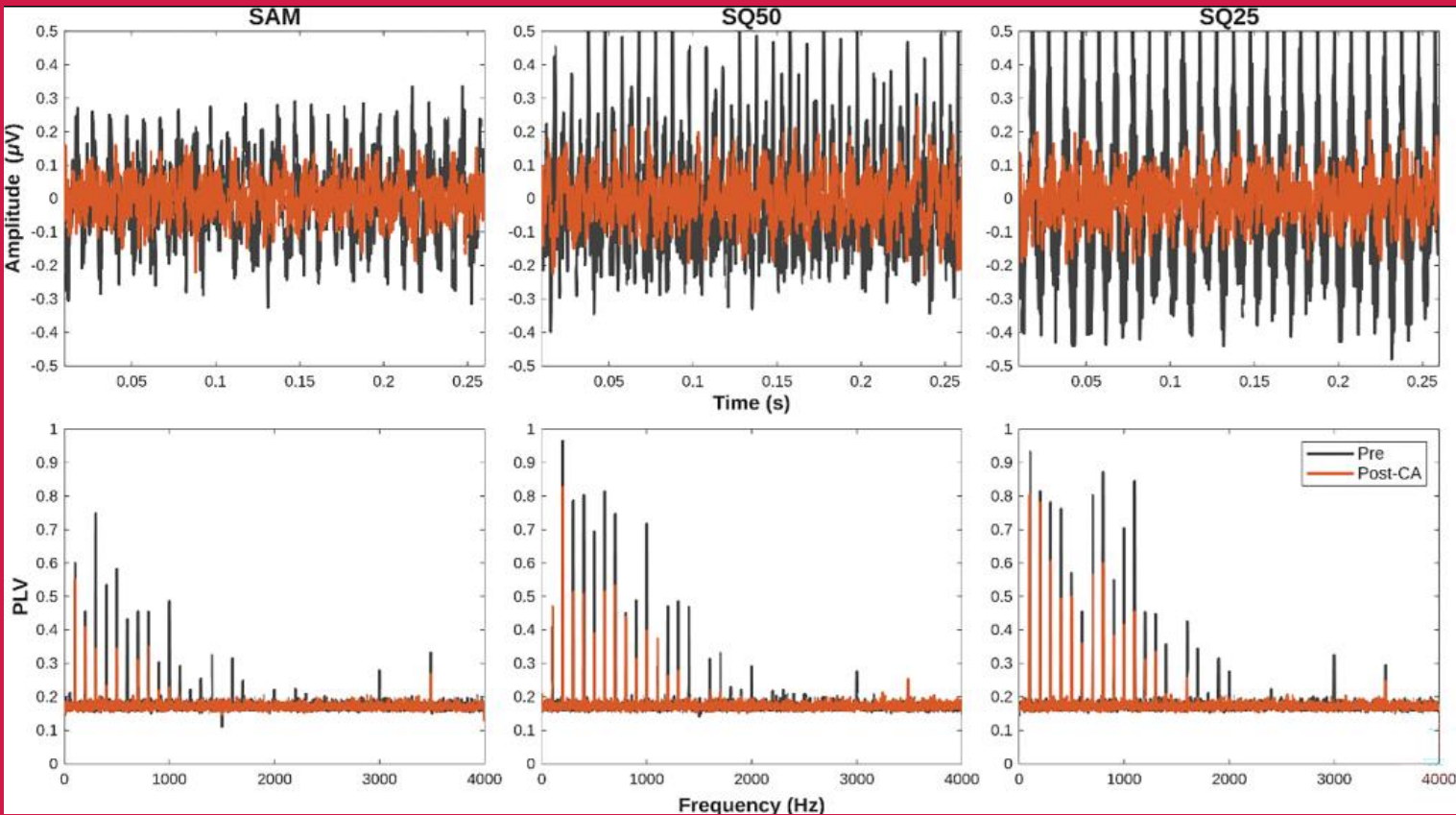
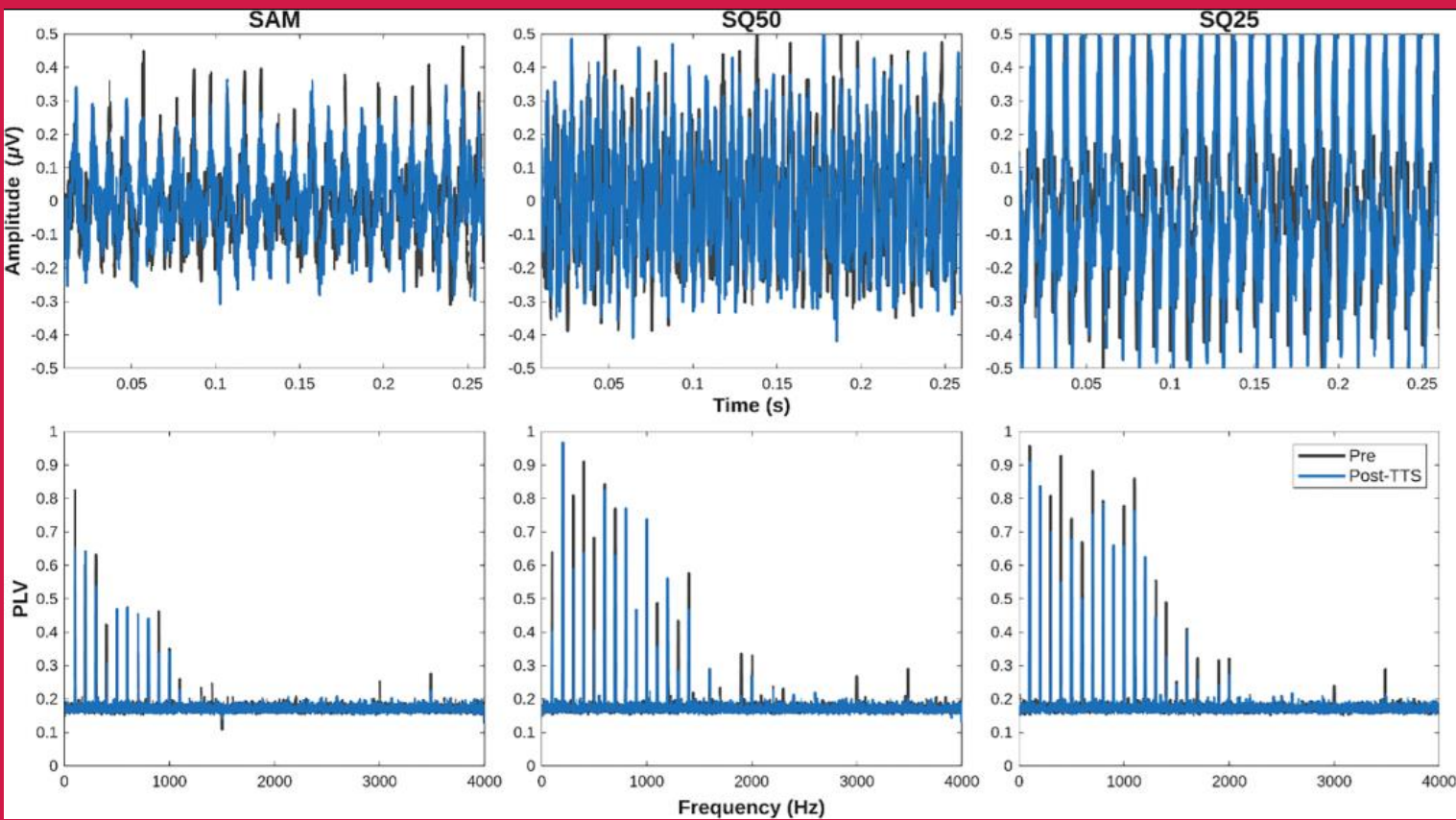
“Adding Insult to Injury: Cochlear Nerve Degeneration After ‘Temporary’ Noise-Induced Hearing Loss” (Kujawa & Liberman, 2009)



- 8-16 kHz octave band noise at 100 dB SPL for 2 hrs
- Threshold recovery with permanent degradation of suprathreshold neural responses
- Severe damage to synaptic ribbon terminals (IHC neural degeneration) – significant decrease in overall percentage of spiral ganglion cells post-exposure

Noise Exposure & Impaired Envelope Coding

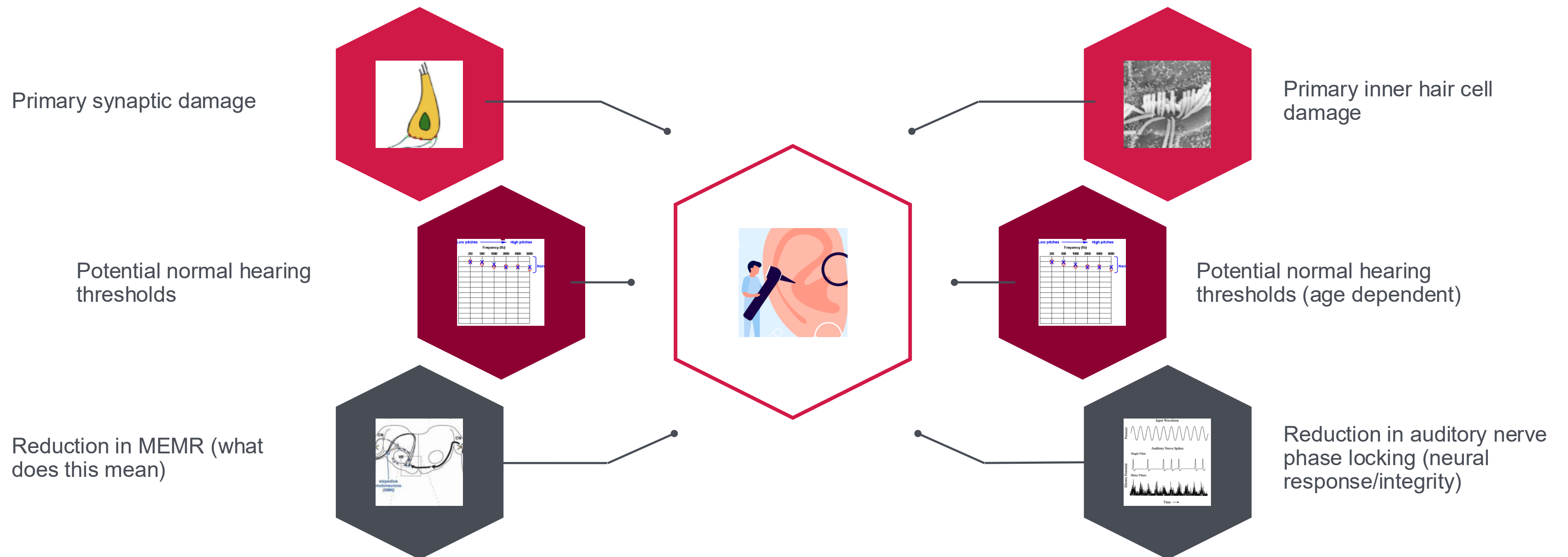
Sivaprakasam, Schweinzger, & Heinz (2026)



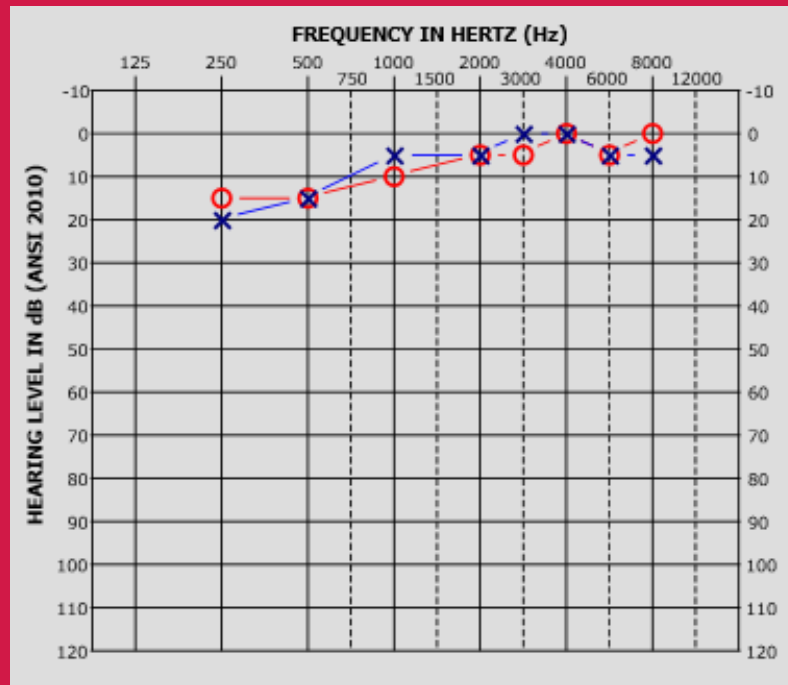
Notable, yet diverse, changes in Wave V/I ratio, MEMR Threshold, and EFR Amplitude/PLV for the TTS-inducing noise group (Auditory neural damage group) and carboplatin exposed group (IHC damage picture)

Difference in auditory physiological functioning w/noise-induced damage vs inner hair cell damage

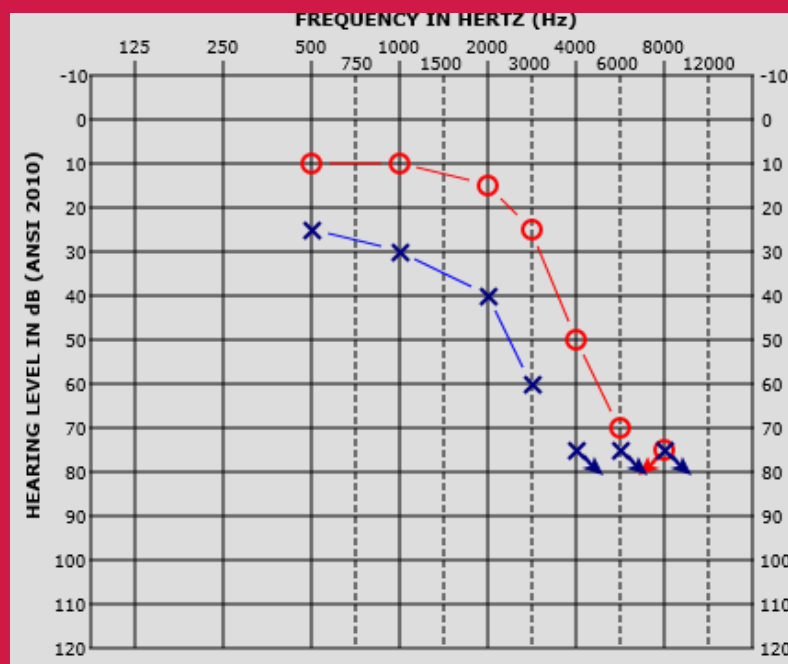
Think significant noise exposure history as an etiology vs (or in conjunction with) carboplatin chemotherapy



Relating these findings to Cancer-Treatment related Hearing Loss



S/P Cranial radiation, 4 cycles cisplatin, 2 cycles carboplatin



S/P Cranial radiation, 4 cycles cisplatin, 1 cycle carboplatin

1

Same Tx/protocol (radiation + 4 cycles of cisplatin chemotherapy)

2

One normal hearing outcome, one significant hearing loss outcome

3

Theory #1: Children exposed to more frequent, high-intensity noise are more susceptible to either cochlear OHC or IHC damage due to increased ROS or neural insult, respectively, as a result of noise exposure, the effect of which is compounded by the chemotherapeutic agents

4

Theory #2: Children with certain genetic predispositions are more susceptible to hearing loss regardless of the type of treatment/exposure

5

What can we do??

Current Research w/ St. Jude Audiology



CSI Memphis: Previously treated medulloblastoma patients

- ✓ Tinnitus Outcomes
- ✓ Audiogram
- ✓ Noise Exposure History
- ✓ Hearing Related QOL

How do these outcomes differ for patients with significant HL/HAs vs normal hearing or only high-frequency HL?

Investigating an Adapted Pediatric HA Fitting Guideline for Oncology Patients

Identifying Prominent Impediments to Hearing Aid Adherence

Implementing A Hearing Aid Counseling & Education Program for Patients with Cancer-Treatment Related Hearing Loss



“

“I really truly felt like admitting to and getting assistance for hearing loss is almost like acknowledging that my cancer treatment is still with me.”

-Quote from a pediatric cancer survivor

Khan A, Mubdi N, Budnick A, Feldman DR, Williams SW, Patel S, Tonorezos ES. The experience of hearing loss in adult survivors of childhood and young adult cancer: A qualitative study. *Cancer*. 2020 Apr 15;126(8):1776-1783. doi: 10.1002/cncr.32698. Epub 2020 Jan 3. PMID: 31899553; PMCID: PMC7424539.



Questions?