Hearing health in patients treated for H&N cancer

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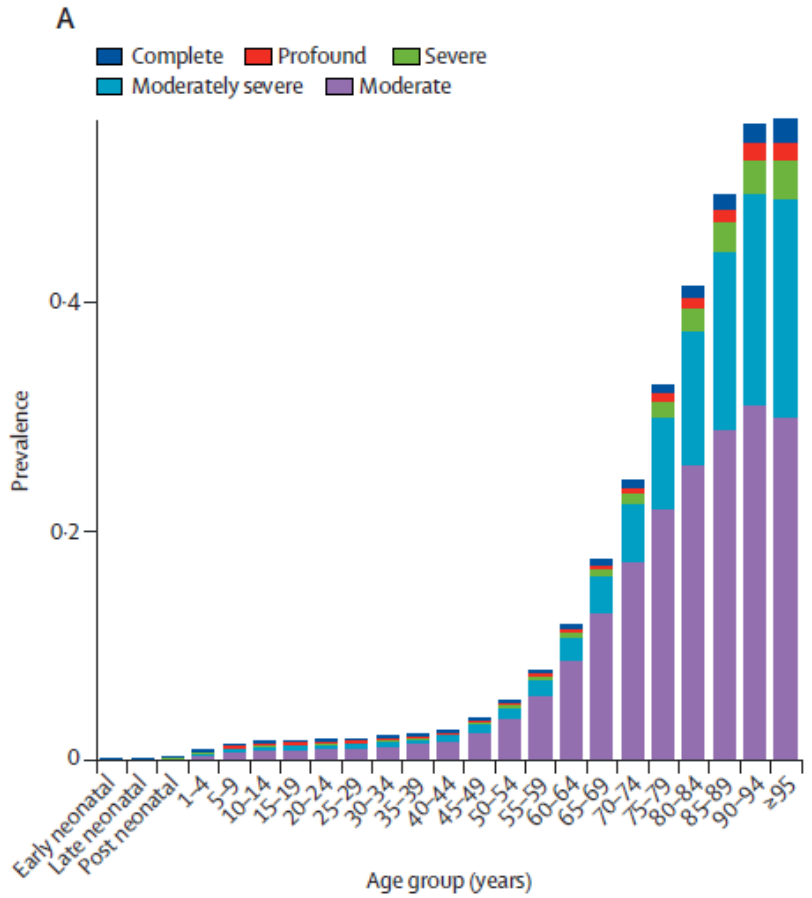
Head and Neck Symposium

4th November 2022

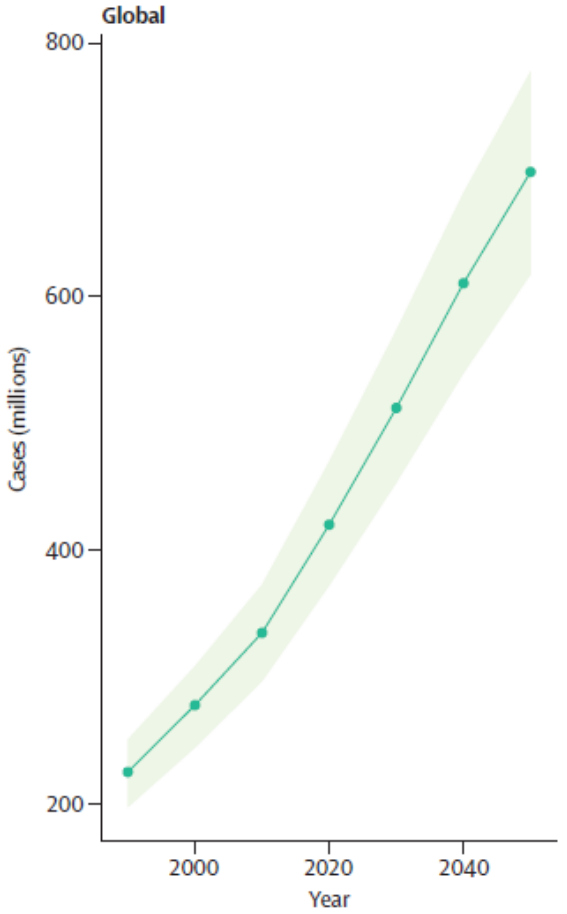
Global Burden of Disease Study 2019
(Lancet 2021; 397: 996-1009)

- 1.5 billion with hearing loss (HL)
- 403 million moderate-to-complete HL (698 million by 2050)
- 40 million Years Lived with Disability (YLD; sum of years with weighting for disability)
  - third globally; first for sensory disorders; first for those over 70 years
- Clear association with age
  - If live long enough, >50% moderate-to-complete HL requiring intervention

Risk factors: age and noise exposure



Prevalence of HL ≥35 dB by age & severity (2019)



Prevalence of HL 35 ≥dB

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Negative consequences on health and wellbeing

- Communication, social interactions and QoL
- Co-morbidities e.g., CVD, diabetes, MH, accelerated cog decline & dementia

Cost

- UK economy (£25 billion/yr.)
- NHS (£450 million/yr.)

Interventions

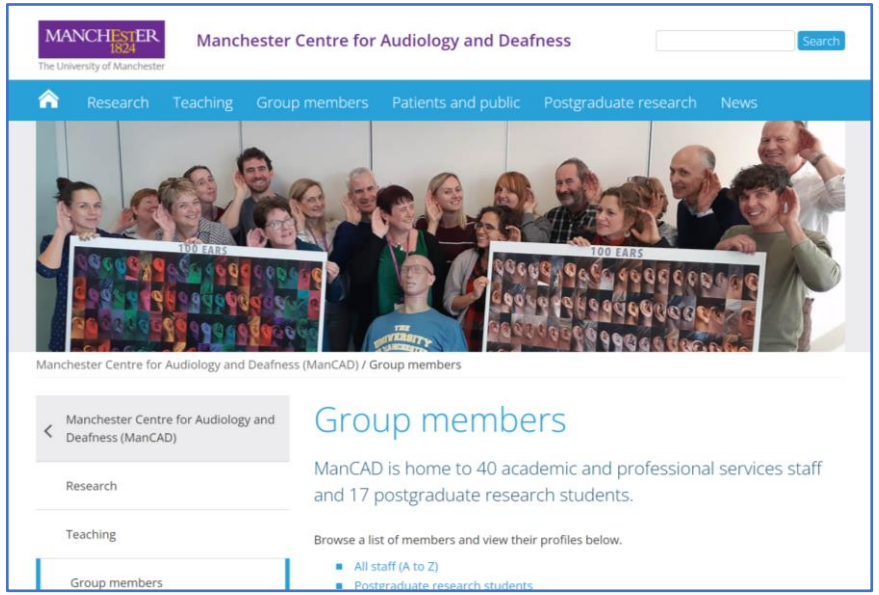
- Hearing assisted technology: NHS largest purchaser, improves QoL but low & slow uptake
- Hearing therapeutics in relative infancy (Isherwood et al, 2021)

Limited medical research income

- <1% of £2 billion UK medical research funding (2014)
- Research spend per person affected is low (e.g., CVD=£20, Sight loss=£11, Hearing loss=£1)

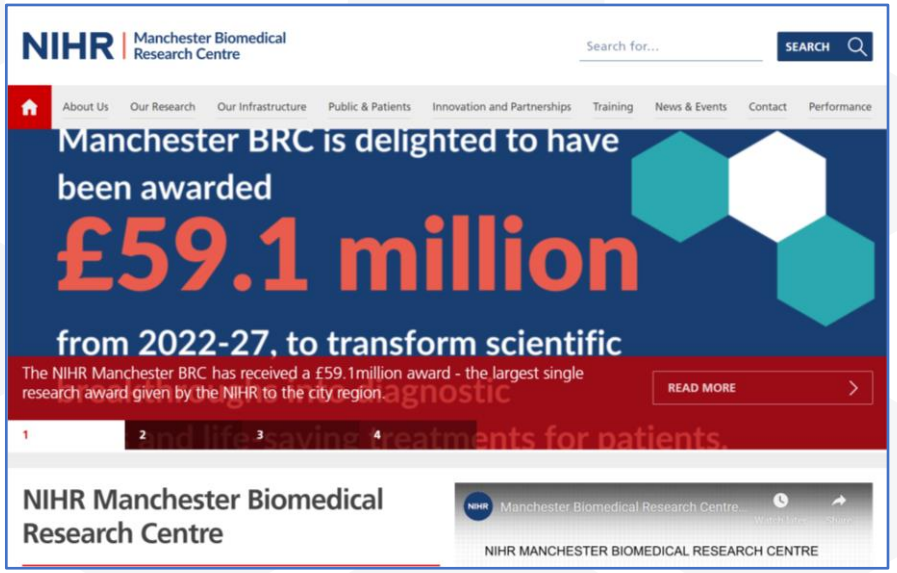
GM hearing health research ecosystem

ManCAD

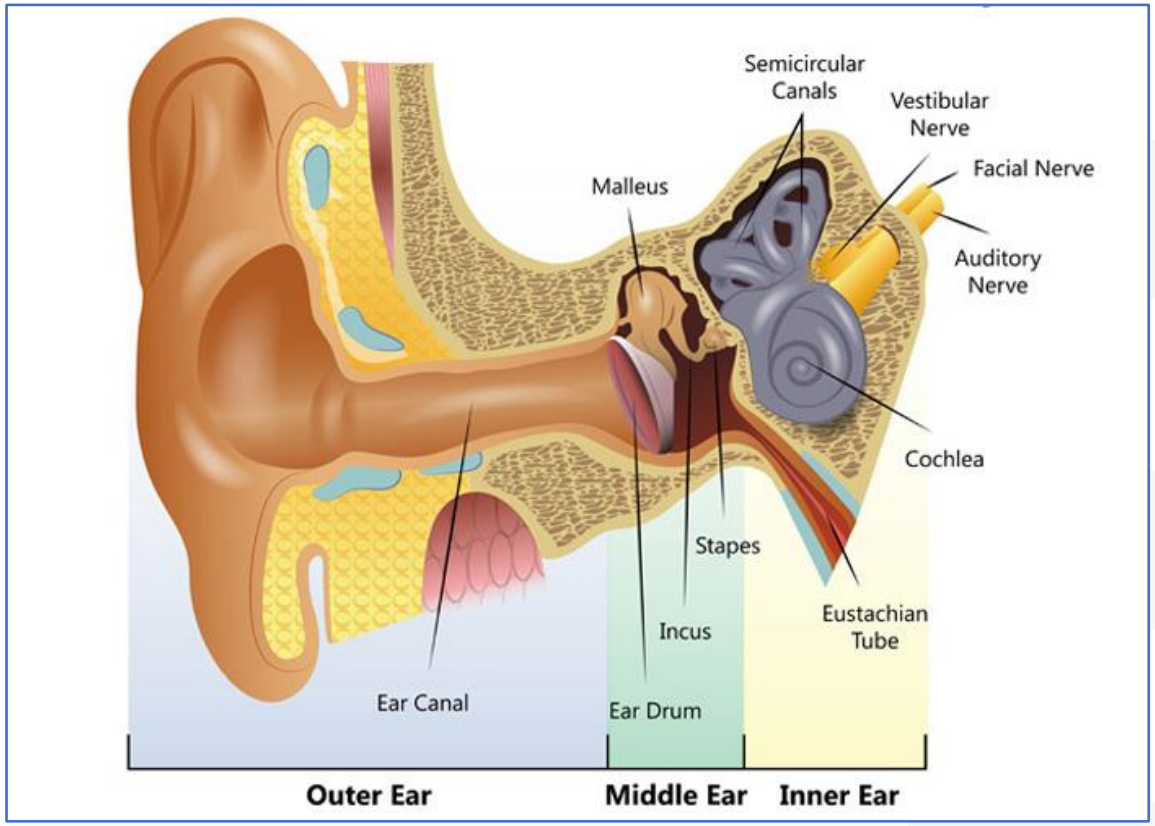


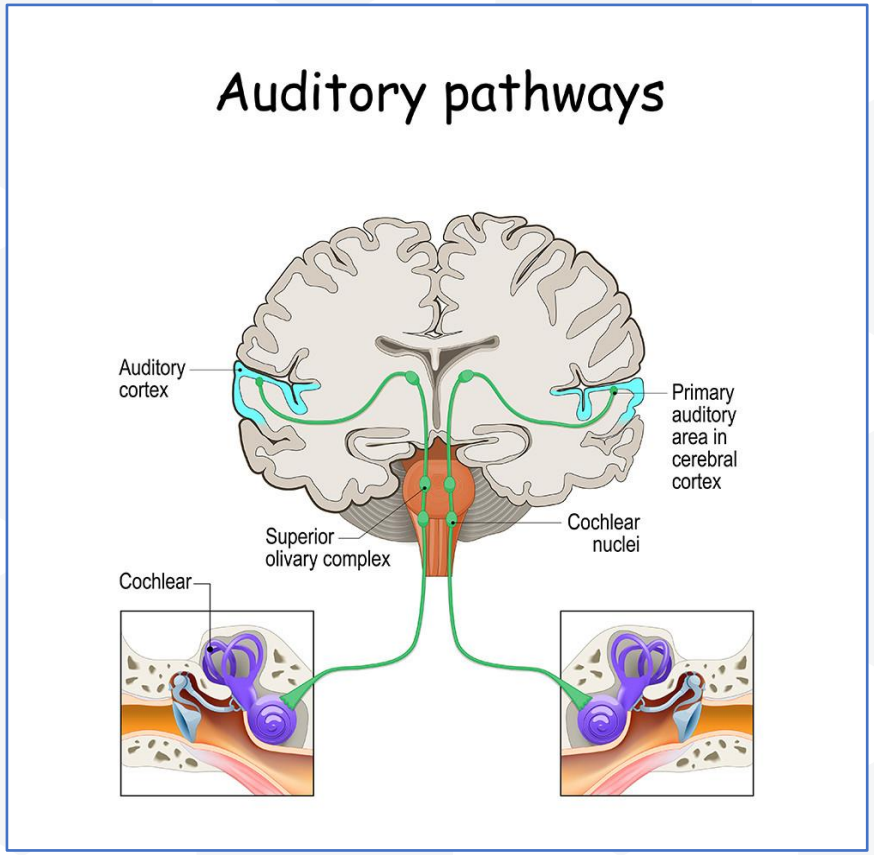
@ManCAD_UoM

BRC (UoM/NHS Trusts)



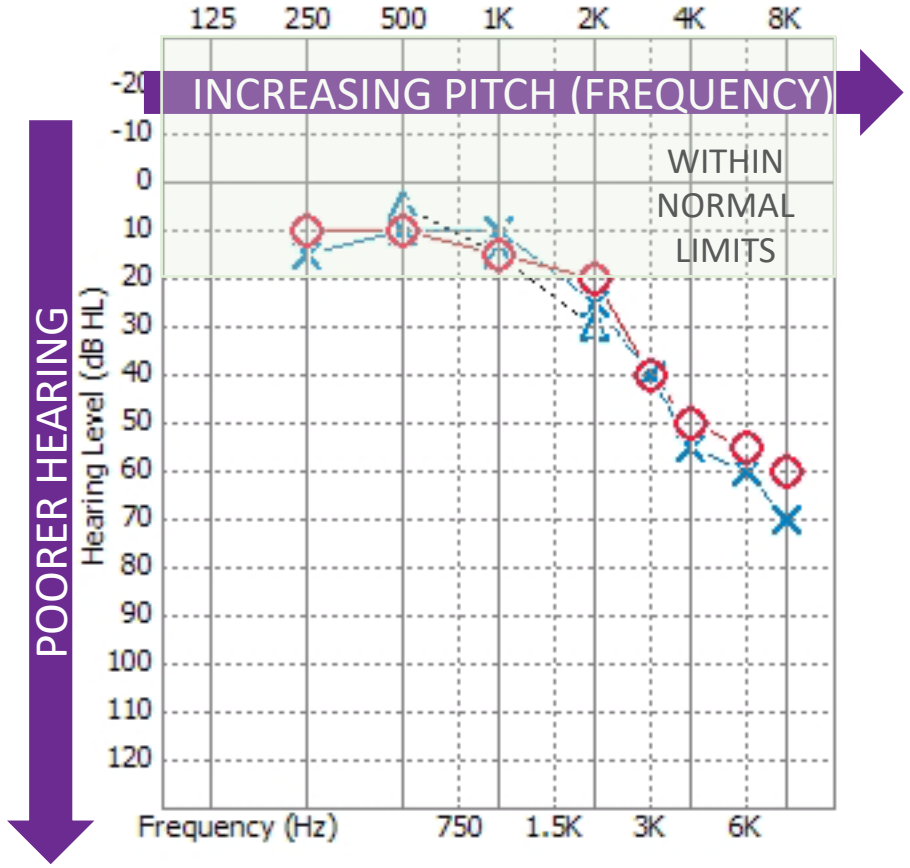
@ManchesterBRC


Semicircular Canals
Vestibular Nerve
Facial Nerve
Malleus
Auditory Nerve
Cochlea
Stapes
Eustachian Tube
Incus
Ear Canal
Ear Drum
Outer Ear
Middle Ear
Inner Ear

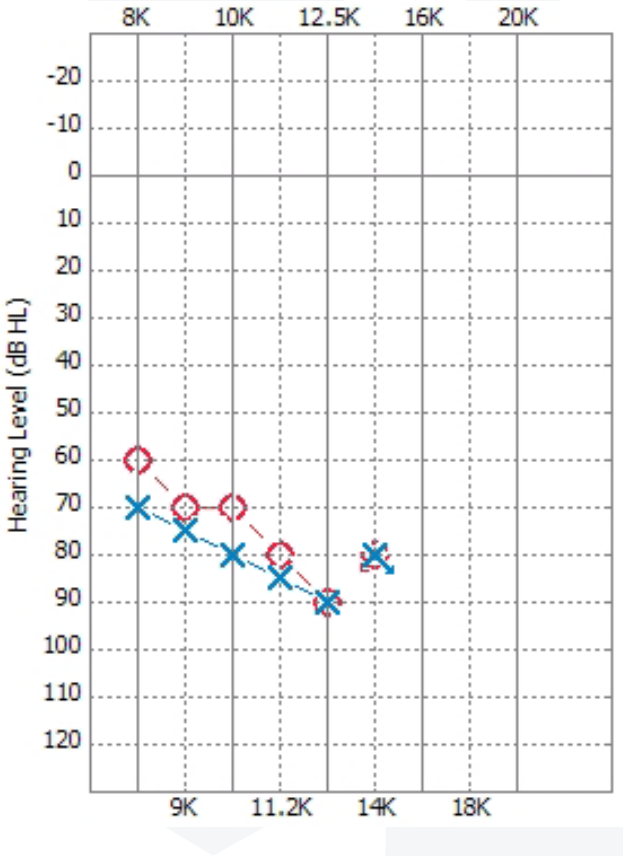

Auditory pathways
Auditory cortex
Primary auditory area in cerebral cortex
Cochlear nuclei
Superior olivary complex
Cochlear

Basic hearing test: pure tone audiogram

Standard



Extended



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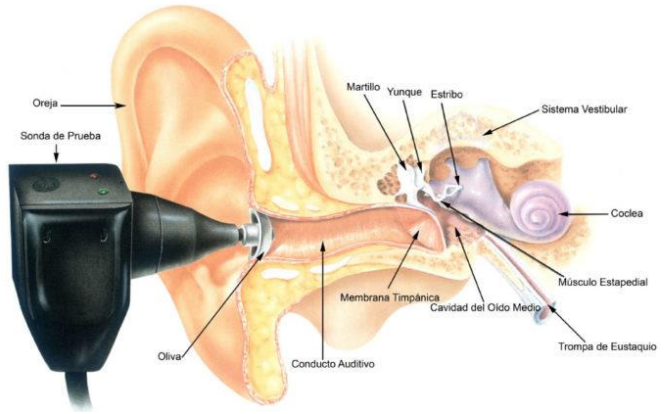
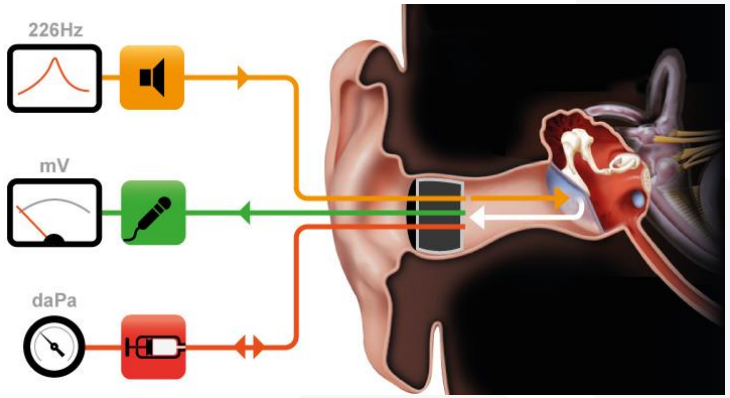
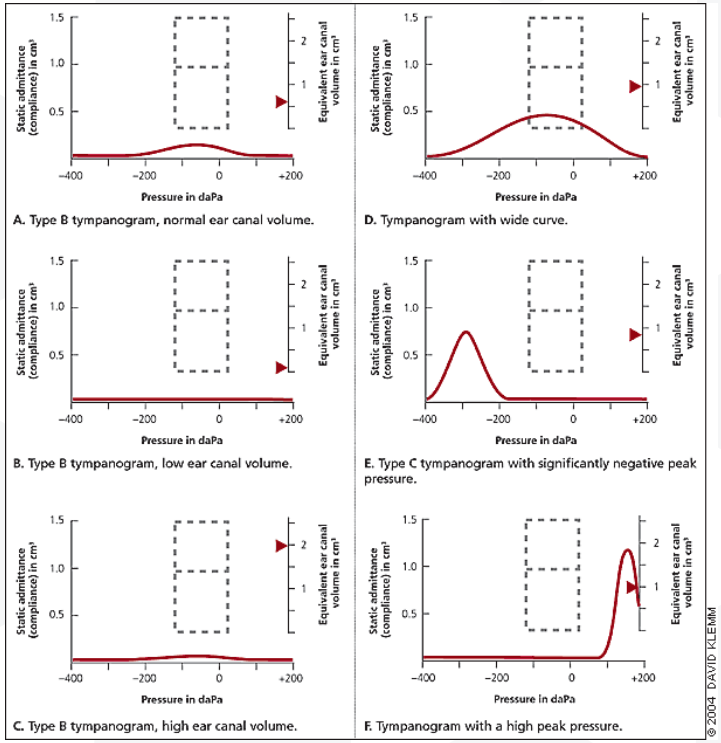
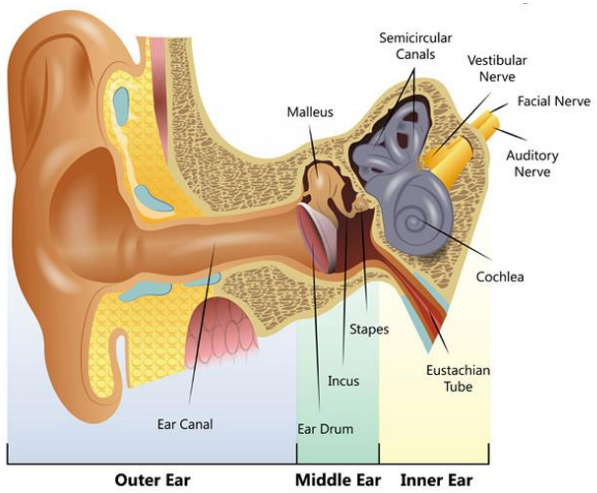
Middle ear function: Tympanometry

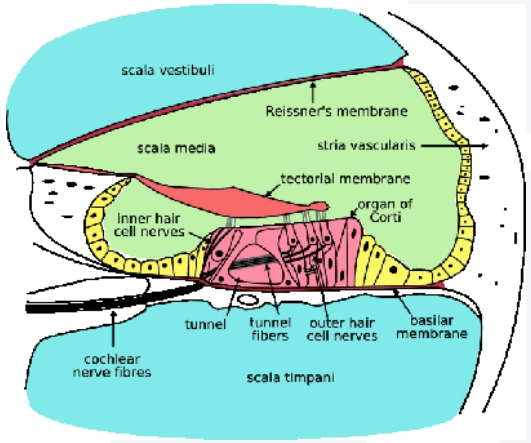




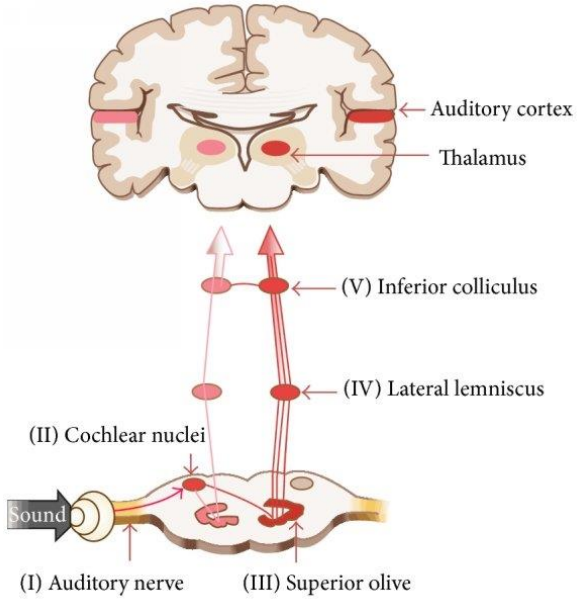


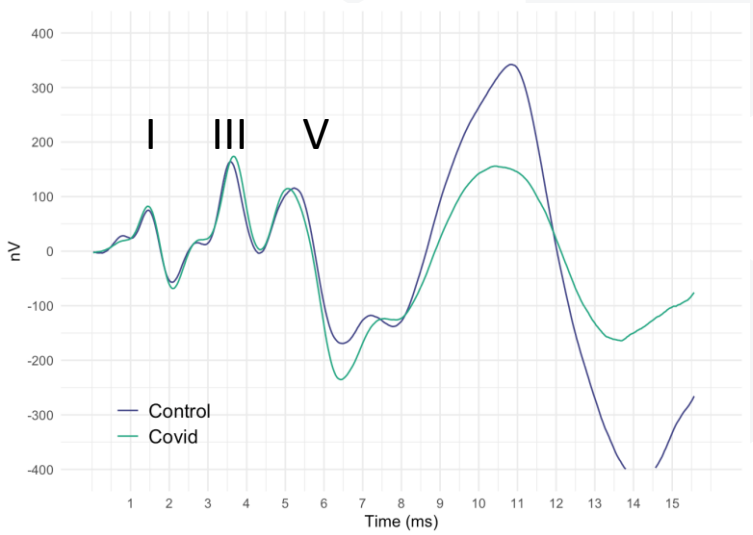
Cochlear function: Otoacoustic emission (OAE)





Neural function:
Auditory brainstem response (ABR)





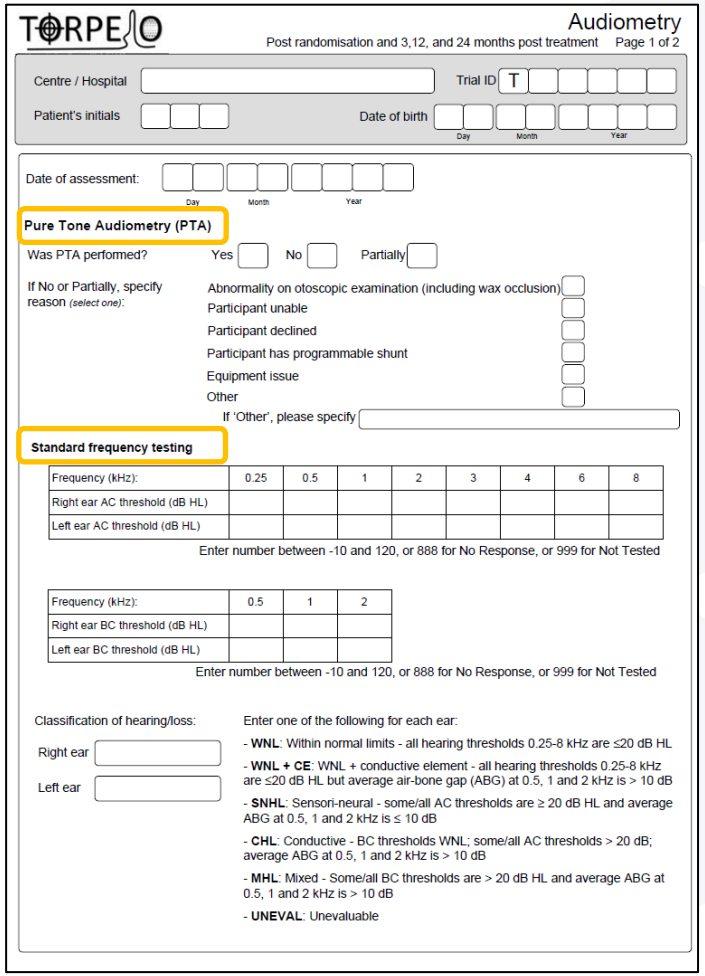
Auditory perception 1: Real world hearing difficulties

- Speech listening in background noise
- Self-reported hearing difficult questionnaires

Auditory perception 2: Tinnitus

- Self-report of tinnitus
- Early warning of potential damage

Phase III trial to improve QoL and reduce treatment side effects in oropharyngeal cancer



TORPEDO

Audiometry

Post randomisation and 3,12, and 24 months post treatment Page 1 of 2

Centre / Hospital | Trial ID T

Patient's initials | Date of birth (Day / Month / Year)

Date of assessment: (Day / Month / Year)

Pure Tone Audiometry (PTA)

Was PTA performed? Yes ☐ No ☐ Partially ☐

If No or Partially, specify reason *(select one)*:

- Abnormality on otoscopic examination (including wax occlusion) ☐
- Participant unable ☐
- Participant declined ☐
- Participant has programmable shunt ☐
- Equipment issue ☐
- Other ☐

If 'Other', please specify

Standard frequency testing

Frequency (kHz):	0.25	0.5	1	2	3	4	6	8
Right ear AC threshold (dB HL)								
Left ear AC threshold (dB HL)								

Enter number between -10 and 120, or 888 for No Response, or 999 for Not Tested

Frequency (kHz):	0.5	1	2
Right ear BC threshold (dB HL)			
Left ear BC threshold (dB HL)			

Enter number between -10 and 120, or 888 for No Response, or 999 for Not Tested

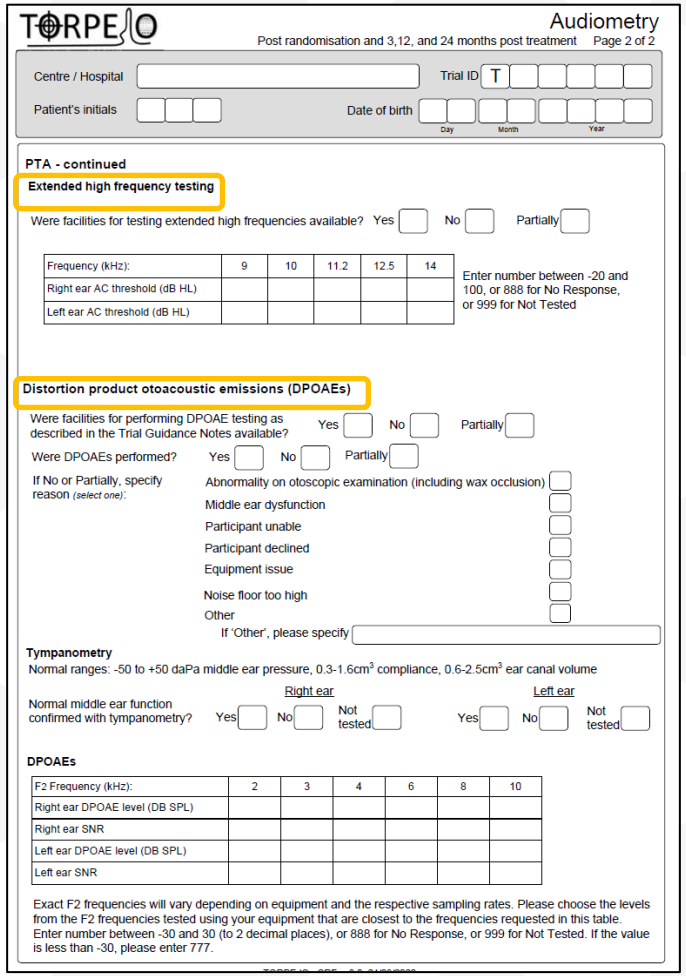
Classification of hearing/loss:

Right ear

Left ear

Enter one of the following for each ear:

- **WNL**: Within normal limits - all hearing thresholds 0.25-8 kHz are ≤20 dB HL
- **WNL + CE**: WNL + conductive element - all hearing thresholds 0.25-8 kHz are ≤20 dB HL but average air-bone gap (ABG) at 0.5, 1 and 2 kHz is > 10 dB
- **SNHL**: Sensori-neural - some/all AC thresholds are ≥ 20 dB HL and average ABG at 0.5, 1 and 2 kHz is ≤ 10 dB
- **CHL**: Conductive - BC thresholds WNL; some/all AC thresholds > 20 dB; average ABG at 0.5, 1 and 2 kHz is > 10 dB
- **MHL**: Mixed - Some/all BC thresholds are > 20 dB HL and average ABG at 0.5, 1 and 2 kHz is > 10 dB
- **UNEVAL**: Unevaluable



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Audiometry

Post randomisation and 3,12, and 24 months post treatment Page 2 of 2

Centre / Hospital | Trial ID T

Patient's initials | Date of birth (Day / Month / Year)

PTA - continued

Extended high frequency testing

Were facilities for testing extended high frequencies available? Yes ☐ No ☐ Partially ☐

Frequency (kHz):	9	10	11.2	12.5	14
Right ear AC threshold (dB HL)					
Left ear AC threshold (dB HL)					

Enter number between -20 and 100, or 888 for No Response, or 999 for Not Tested

Distortion product otoacoustic emissions (DPOAEs)

Were facilities for performing DPOAE testing as described in the Trial Guidance Notes available? Yes ☐ No ☐ Partially ☐

Were DPOAEs performed? Yes ☐ No ☐ Partially ☐

If No or Partially, specify reason *(select one)*:

- Abnormality on otoscopic examination (including wax occlusion) ☐
- Middle ear dysfunction ☐
- Participant unable ☐
- Participant declined ☐
- Equipment issue ☐
- Noise floor too high ☐
- Other ☐

If 'Other', please specify

Tympanometry

Normal ranges: -50 to +50 daPa middle ear pressure, 0.3-1.6cm³ compliance, 0.6-2.5cm³ ear canal volume

Normal middle ear function confirmed with tympanometry?	Right ear			Left ear		
	Yes ☐	No ☐	Not tested ☐	Yes ☐	No ☐	Not tested ☐

DPOAEs

F2 Frequency (kHz):	2	3	4	6	8	10
Right ear DPOAE level (DB SPL)						
Right ear SNR						
Left ear DPOAE level (DB SPL)						
Left ear SNR						

Exact F2 frequencies will vary depending on equipment and the respective sampling rates. Please choose the levels from the F2 frequencies tested using your equipment that are closest to the frequencies requested in this table. Enter number between -30 and 30 (to 2 decimal places), or 888 for No Response, or 999 for Not Tested. If the value is less than -30, please enter 777.

Greater Manchester Cancer

BRC Hearing Health collaboration with Advanced Radiotherapy

1. PREVENTION Lead: Iain Bruce	2. DIAGNOSIS: TOOLKIT Lead: David Moore	3. DAGNOSIS: CLUSTERS Lead: Chris Plack	4. TREATMENT Lead: Gabrielle Saunders & Michael Stone	5. INCLUSION SCIENCE Lead: Chris Armitage
Identification of genetic, environmental and immunological factors causing hearing loss will inform therapies that mitigate risk	Innovative diagnostic tools designed for more sensitised and precise detection will enhance personalised care	Understanding mechanisms that link hearing loss with co-morbidities of dementia and diabetes will improve diagnosis, prevention and management of all three	Personal digital technology, remote care, and person-centred-metrics can be used to optimise hearing health outcomes and monitor general health	Behavioural science approaches will improve identification of disease, uptake and outcomes of treatments

EARAD: The Effects on Auditory Function of RADiotherapy and Chemotherapy Treatments

- Radiotherapy and combined chemotherapy for H&N tumours
- Treatment may result in hearing loss and/or tinnitus with major impact on QoL
  - e.g. HL in 72% patients (Schultz et al., 2010)
- Mechanisms of damage and substructures involved not well understood

Objectives

- Measure treatment effects on various hearing structures
- Compare with individual treatment dose characteristics to identify auditory system most sensitive to effects of radiation
- Prevent or reduce hearing damage by formulating new dose constraints that will limit radiation dose to susceptible substructures

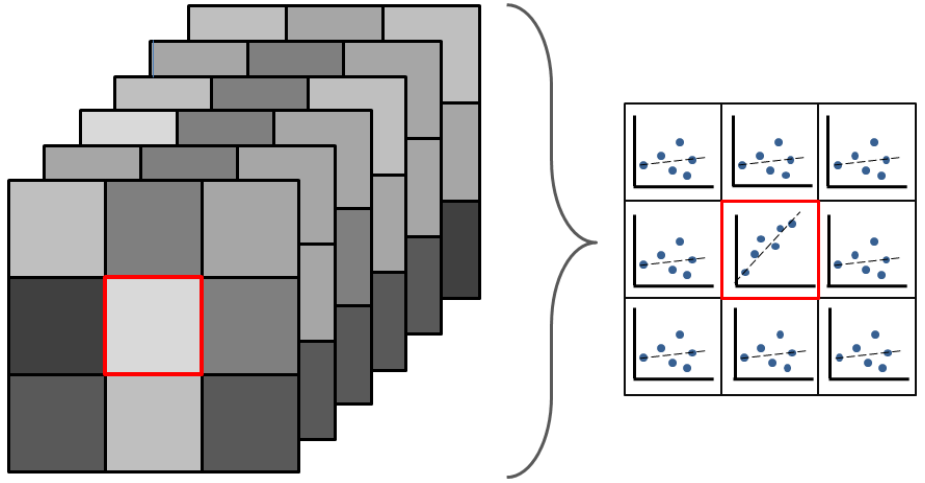
Methods: participants

- Group 1: Radiotherapy alone
- Group 2: Radiotherapy plus cisplatin chemotherapy
- Group 3: Retrospective group with unilateral radiotherapy (comparison with control ear)

Methods: tests

- Battery of auditory tests before and after (12 weeks) treatment
- Basic hearing test: standard and extended high frequencies
- Cochlear function: OAE
- Neural function: ABR
- Real world hearing difficulties: DiN and CRM; self-report SSQ hearing Scale and tinnitus
- QoL: EQ5D

Methods: image based data mining



A B C

A) Spatially normalizing dose distributions

B) Dose at each anatomical point can be correlated with outcome to identify the most sensitive regions.

C) Dose in the red region, in muscles close to the tumour, shows a significant effect on mouth opening ability. In this project we will use the same methodology to investigate hearing loss.

Methods: optional bloods

- Option to donate blood (baseline, during and after treatment)
- Objectives:
  - Monitor changes in blood levels of **prestin** (found in inner ear Outer Hair Cells) may provide a sensitive measure of OHC damage during treatment
  - Future radiogenomics study, identify common genetic variants associated with developing HL post treatment

Take home message

- HL common and consequences not trivial
- Treatment for H&N cancer can damage hearing
- Traditional clinical tests of hearing not the most sensitive to damage
- Early damage associated with tinnitus and HL at extended high frequencies

Thank you