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Extended high-frequency audiometry in research and clinical practice

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Audiometric testing in research and in clinical settings rarely considers frequencies above 8 kHz. However, the sensitivity of young healthy ears extends to 20 kHz, and there is increasing evidence that testing in the extended high-frequency (EHF) region, above 8 kHz, might provide valuable additional information. Basal (EHF) cochlear regions are especially sensitive to the effects of aging, disease, ototoxic drugs, and possibly noise exposure. Hence, EHF loss may be an early warning of damage, useful for diagnosis and for monitoring hearing health. In certain environments, speech perception may rely on EHF information, and there is evidence for an association between EHF loss and speech perception difficulties, although this may not be causal: EHF loss may instead be a marker for sub-clinical damage at lower frequencies. If there is a causal relation, then amplification in the EHF range may be beneficial if the technical difficulties can be overcome. EHF audiometry in the clinic presents with no particular difficulty, the biggest obstacle being lack of specialist equipment. Currently EHF audiometry has limited but increasing clinical application. With the development of international guidelines and standards, it is likely that EHF testing will become widespread in future.

I. INTRODUCTION

Pure-tone audiometry (PTA), the basis of clinical hearing testing, involves measurements of hearing thresholds for pure tones over a range of test frequencies, although frequencies above 8 kHz are rarely included. For example, the British Society of Audiology (2018) recommends testing between 250 Hz and 8 kHz. Standard PTA has a wide range of practical uses, including clinical diagnosis, hearing aid fitting, and occupational hearing health monitoring. Standard PTA is also used extensively in hearing research, for assessment of hearing loss and as a screening tool for participants. However, for young people with normal hearing, sensitivity extends up to 20 kHz, and there is increasing interest in examining sensitivity at frequencies above 8 kHz: the "extended high-frequency" (EHF) range (Hunter *et al.*, 2020).

Even among listeners with normal hearing in the standard PTA frequency range, the variability in EHF thresholds can be substantial (Lee *et al.*, 2012). The filled circles in Fig. 1 show mean hearing thresholds for a group of young listeners, measured using circum-aural headphones specialized for EHF testing. The error bars (standard deviations) plotted in the figure show that there is much more between-listener variability at EHFs compared to lower frequencies. Also shown are thresholds for two listeners with similar thresholds in the standard clinical range, but with wildly different thresholds in the EHF range, particularly at 16 kHz. Both these listeners would be regarded as having "normal hearing" if they were tested in an audiology clinic, but it is obvious that their hearing sensitivities differ greatly in the EHF region. What are the causes of this variability, and what do their EHF thresholds have to tell us about the real-world hearing abilities of these individuals?

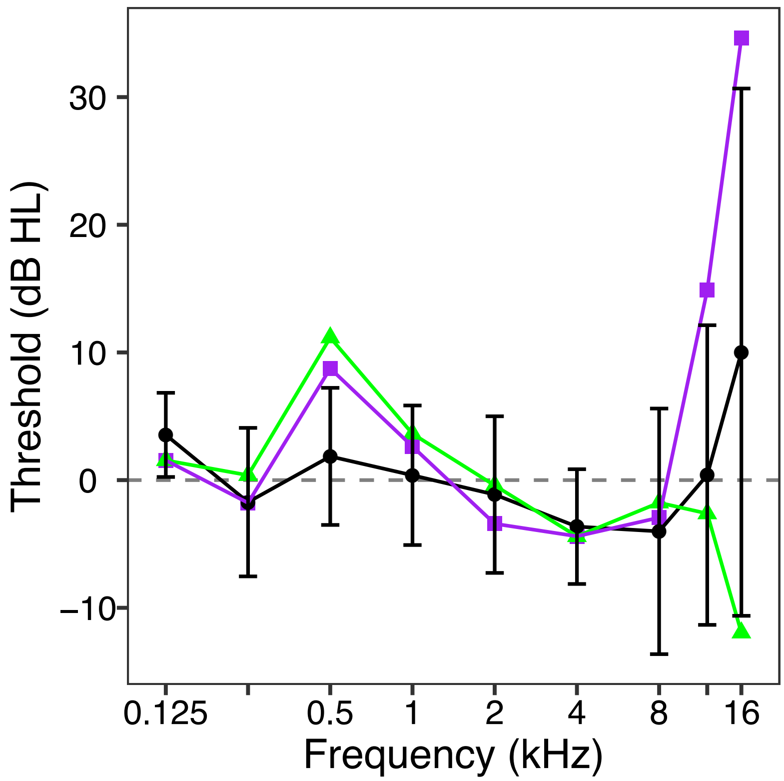

FIG. 1. (Colour online). Mean hearing threshold as a function of frequency for a group of normal-hearing listeners, aged 19-39 yrs (black circles). Error bars show +/- 1 standard deviation. The purple squares and green triangles show the results for two listeners with very similar thresholds up to 8 kHz, but markedly different thresholds above 8 kHz (in the EHF range). Data from Carcagno and Plack (2020).

II. MEASURING EHF THRESHOLDS

A problem with measuring EHF thresholds accurately is that standing wave interference patterns in the ear canal, which are particularly prominent in the EHF region, lead to frequency-dependent variations in the sound pressure level at the eardrum for a given nominal input level (Souza *et al.*, 2014; Bharadwaj *et al.*, 2019). Hence, some of the variability in EHF thresholds seen in Fig. 1 may result from problems of calibration in the EHF range, due in part to individual differences in ear canal anatomy. This is particularly an issue for insert earphones, as compared to circum-aural headphones which theoretically should be less affected by the properties of the ear canal due to their lower impedance (Bharadwaj *et al.*, 2019). Thresholds for insert earphones at frequencies above 3 kHz can also be affected by insertion depth (Souza *et al.*, 2014). However, even in the case of insert earphones, calibration issues probably don't account for more than about 20 dB of the variance in thresholds (Souza *et al.*, 2014; Bharadwaj *et al.*, 2019). When using a depth-compensated calibration technique for insert earphones, Lee *et al.* (2012) found much more variability in thresholds at EHFs compared to lower frequencies, even among young listeners.

The standing wave confound can be avoided by using "forward pressure level (FPL)" calibration, which is based on an accurate estimation of sound level at the eardrum (Souza *et al.*, 2014; Lapsley Miller *et al.*, 2018; Bharadwaj *et al.*, 2019). However, currently this requires expensive specialist equipment, such as the Etymotic ER10X system. Test-retest reliability for circum-aural high-frequency headphones, such as Sennheiser HDA 200s, is good (Frank, 2001; Hunter *et al.*, 2020), and at present it is not clear that the clinical benefits of FPL calibration outweigh the expense and technical difficulties.

In some studies, bands of noise, rather than pure tones, have been used to measure EHF thresholds with circum-aural headphones (Guest *et al.*, 2017; Prendergast *et al.*, 2017). This approach is based on the assumption that thresholds for noise bands, being dependent on the response to a broad frequency range, will be less affected by variations in the frequency response of the ear canal compared to thresholds measured using pure tones.

III. CAUSES OF EHF HEARING LOSS

A. Age

Hearing deteriorates as we age, from early adulthood onwards. A "ski-slope" loss in the audiogram is characteristic of the effects of aging, with high frequencies affected much more than low frequencies. Histopathological data from human temporal bones show substantial age-related loss of inner and outer hair cells, particularly in the cochlear base (Wu *et al.*, 2021). EHF thresholds are particularly sensitive to the early effects of aging, and age-related EHF threshold elevations are seen even in young populations (Stelmachowicz *et al.*, 1989; Jilek *et al.*, 2014). For example, Stelmachowicz *et al.* (1989) reported thresholds above 14 kHz to be about 10-20 dB higher for listeners aged 20-29 years compared to listeners aged 10-19 years, even though thresholds at 8 kHz were almost identical for these groups. Fig. 2 shows typical patterns of hearing thresholds as a function of age and frequency.

Age-related hearing loss is due in part to the age-related reduction in the endocochlear potential, which degrades hair cell function. However, the effects of age *per se* are compounded by the cumulative effects of other insults over time, which may include lifetime noise exposure and the effects of ototoxic drugs (Dubno *et al.*, 2013). These two causes tend to affect the cochlear base, and hence increase the loss at EHFs compared to lower frequencies.

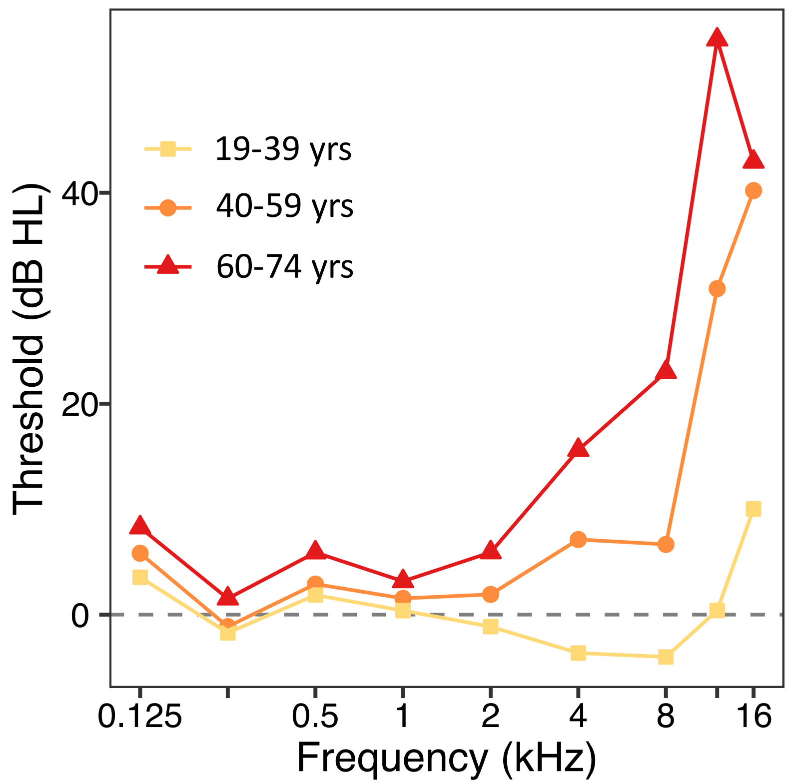

FIG. 2. (Colour online). Mean hearing threshold as a function of frequency for groups of young, middle-aged, and older listeners. Data from Carcagno and Plack (2020).

B. Middle ear disease, dysfunction, and surgery

Otitis media is a disease of the middle ear that most commonly affects children. It can be infective (suppurative) or non-infective (non-suppurative), acute or chronic; however, these categories are interrelated (World Health Organization, 2021b). All forms of otitis media have been shown to cause EHF hearing loss that persists beyond recovery of the disease (Hunter *et al.*, 1996; Margolis *et al.*, 2000; Ryding *et al.*, 2002). This can occur despite negligible effects on hearing thresholds between 250 Hz and 8 kHz. EHF hearing tends to be worse in people with more severe disease histories, as defined by the number of acute otitis media (AOM) episodes, for example (Laitila *et al.*, 1997), but even a single episode of AOM can cause lasting damage to

EHF hearing (Cordeiro *et al.*, 2018). Because the hearing loss worsens with increasing frequency and appears to be unrelated to middle ear impedance and reflectance measurements up to about 10 kHz, it is speculated to be sensorineural in origin, and attributed to toxins entering the inner ear via the round window membrane (Margolis *et al.*, 2000). However, this is not unequivocal and, particularly whilst the disease is still active, other mechanisms may well contribute to the EHF hearing loss.

Indeed, because middle ear impedance is mass-dominated above 4 kHz (and possibly from slightly lower; Withnell and Gowdy, 2013), any structural changes as a result of disease or injury that increase the mass of the middle ear system could theoretically cause conductive hearing loss in the EHF region. The formation of scars or crusts on the eardrum subsequent to pressure equalization tube operations or traumatic eardrum perforations have been associated with poorer EHF hearing thresholds (Hunter *et al.*, 1996; Hallmo, 1997).

Some EHF hearing losses are iatrogenic, meaning they are inadvertently caused by medical procedures/treatment. Middle ear surgery can lead to temporary or permanent EHF hearing loss. Hunter *et al.* (1996) showed that total number of pressure equalization tube operations can predict EHF hearing thresholds, and whereas stapes surgery may lead to improvements in median air conduction thresholds ≤8 kHz, the opposite has been recorded above 8 kHz, with only partial recovery (i.e., to pre-operative levels) observed at three months (Babbage *et al.*, 2017).

C. Ototoxicity

Several widely used drug treatments are ototoxic. In particular, aminoglycoside antibiotics and the chemotherapy medication cisplatin can cause loss of outer hair cells, in part through the generation of reactive oxygen species (Chen *et al.*, 2007; Rybak and Ramkumar, 2007; Jiang *et al.*, 2017). Cisplatin also causes damage to spiral ganglion cells and the stria vascularis (Rybak *et al.*, 2007). Outer hair cell damage progresses from the basal turn of the cochlea to the apex, and hence these drugs particularly affect EHF thresholds (Konrad-Martin *et al.*, 2010; Garinis *et al.*, 2017). EHF threshold monitoring is a valuable tool for early identification of hearing loss due to these drugs, at least for patients with measurable thresholds in this range (Campbell and Le Prell, 2018; Konrad-Martin *et al.*, 2018).

Patients receiving radiotherapy for head and neck cancer are also at risk of developing permanent hearing loss. The risk appears to be dose-dependent, with increased incidence of ototoxicity with cochlear radiation doses upwards of 45-60 Gy (Mujica–Mota *et al.*, 2013). A limited number of studies report EHF audiometry findings in affected patients, and fewer present data exclusively for radiotherapy (as distinct from chemoradiotherapy). However, those that do indicate that radiation-induced hearing loss is more severe, and occurs sooner, at higher frequencies (Schot *et al.*, 1992; Mujica–Mota *et al.*, 2013; Bass *et al.*, 2018), although onset can still be delayed by months or years after completion of treatment (Jereczek-Fossa *et al.*, 2003). The loss is also likely to be asymmetric (Cheraghi *et al.*, 2015).

D. Noise exposure

Overexposure to noise can damage the hair cells in the cochlea. Noise-induced hearing loss (NIHL) is traditionally associated with an audiometric “notch” between 3 and 6 kHz (McBride and Williams, 2001). This corresponds to the region of the cochlea that is maximally stimulated by broadband stimuli after filtering by the middle ear. However, a number of studies have found an association between noise exposure and EHF threshold elevation, even for young people with normal hearing in the standard clinical range (Le Prell *et al.*, 2013; Sulaiman *et al.*, 2014; Liberman *et al.*, 2016; Prendergast *et al.*, 2017). In other words, an EHF loss may precede the notch at lower frequencies. In particular, several studies have reported an association between EHF thresholds and personal listening device use (Peng *et al.*, 2007; Le Prell *et al.*, 2013; Sulaiman *et al.*, 2014). For example, Sulaiman *et al.* (2014) reported about 10 dB worse thresholds at 16 kHz for young users of personal listening devices compared to controls who never or rarely used these devices, despite little between-group threshold differences for frequencies up to 8 kHz. With respect to occupational noise exposure, Ahmed *et al.* (2001) reported that, for participants with normal thresholds up to 8 kHz, EHF thresholds were higher for those exposed to industrial noise compared to non-exposed controls.

However, the findings are mixed and other studies show little relation between recreational noise exposure and EHF thresholds. For example, despite reporting a relation between EHF thresholds and long-term personal listening device use, Le Prell *et al.* (2013) found little relation between EHF thresholds and noise exposure due to other activities, such as bar or club attendance, or attendance at loud sporting events. Wei *et al.* (2017) found no associations between total leisure noise exposure (including use of personal listening devices) and EHF thresholds, and Mishra *et al.* (2021) found no relation between earphone or headphone use and EHF thresholds after controlling for age.

A possible reason for the negative findings is the difficulty of estimating lifetime noise exposure reliably (Wei *et al.*, 2017), since the estimates are largely based on self-report and depend on what events are included and how noise levels are calculated (Guest *et al.*, 2018). It is particularly important to determine if EHF threshold elevation is a useful predictor of future NIHL in the standard clinical range. If so, this would make EHF thresholds a valuable tool for monitoring hearing health, for example, in occupational settings, and EHF testing could be used to screen for individuals at risk of losing hearing ability due to recreational activities.

E. Systemic disease

Systemic disease, as the name suggests, affects multiple body parts or the whole body. Patients with systemic autoimmune rheumatic diseases, such as rheumatoid arthritis, primary Sjögren syndrome, and systemic lupus erythematosus have significantly worse EHF hearing thresholds when compared to age- and sex-matched controls (Lasso de la Vega *et al.*, 2017; Galarza-Delgado, 2018). Hearing loss in patients with these diseases is also far more likely to be picked up by EHF audiometry than by conventional PTA (Lasso de la Vega *et al.*, 2017; Galarza-Delgado, 2018). Similar audiometric findings are reported for patients with polycystic ovarian syndrome, an endocrine disorder that is described as a 'chronic proinflammatory state' (Kucur *et al.*, 2013).

In all of the aforementioned diseases, the pathogenesis of EHF hearing loss is not well understood, although animal models and temporal bone studies report inner ear degeneration consistent with either inflammatory or ischemic mechanisms (Ruckenstein, 2004).

IV. RELEVANCE OF EHF HEARING LOSS FOR PERCEPTION

A. Sound localization

EHF components provide important cues for sound localization. In particular, EHF information is important for determination of sound elevation and for resolving front/back confusions. Peaks and notches in the EHF spectrum are introduced by the filtering effects of the pinna, and these patterns are dependent on the elevation angle of the sound source relative to the listener. The patterns also vary due to individual differences in pinna morphology (Otte *et al.*, 2013). Low-pass filtering stimuli at 8 kHz, removing EHF components, leads to poorer elevation judgements and in more front/back confusions. This applies to both non-speech sounds (Brungart and Simpson, 2009) and speech sounds (Best *et al.*, 2005). Consistent with these findings, older adults with an EHF hearing loss are worse than younger adults at determining sound elevation (Otte *et al.*, 2013).

B. Speech perception

EHFs between 8 and 10 kHz improve the quality of speech (Moore and Tan, 2003) and provide useful information for speech recognition, particularly for consonants (Monson *et al.*, 2014; Levy *et al.*, 2015). However, although speech is characterized by occasional bursts of EHF energy, such as during production of voiceless fricatives (i.e., /s/, /f/, and /v/), most speech energy occurs in the standard clinical frequency range (Byrne *et al.*, 1994; Monson *et al.* 2012b). Although several studies have reported a relation between EHF loss and impaired performance on speech-in-noise tasks (Badri *et al.*, 2011; Motlagh Zadeh *et al.*, 2019; Yeend *et al.*, 2019), it was thought that the EHF region has little direct importance for speech understanding. Recent studies question this assumption (Hunter *et al.*, 2020).

Motlagh Zadeh *et al.* (2019) reported that performance on the popular "digits in noise" test improved (3.2 dB lower speech reception threshold) when the masking noise was low-pass filtered at 8 kHz compared to when the noise was broadband, suggesting that cochlear regions tuned above 8 kHz provide useful information. Until recently, tests of speech intelligibility in a multi-talker environment have used a target talker (who the listener is required to understand) and competing talkers directing speech towards the listener. This is a very unusual situation. Normally, competing talkers would be facing away from the listener, and directing their speech to someone else. When the competing talkers are facing away, the high frequencies from the competing speech are reduced in level, because high frequencies are produced with high directivity from the mouth and diffract less (Monson *et al.*, 2012a). This means that the high frequencies in the target speech may be more audible relative to the low frequencies (which may be obscured by the low frequencies in the competing speech). Monson *et al.* (2019) found that when the interfering speech was directed away from the listener, people performed better (about 2.5 dB improvement in signal-to-noise ratio at threshold) when frequencies above 8 kHz were present than when they were removed by filtering. This implies that these EHFs were contributing important information. Furthermore, Monson *et al.* found that EHF energy helped listeners to judge the orientation of the speaker, which is important when determining who is talking to you. In follow-up articles, Monson and colleagues reported that both temporal and spectral information may contribute to the EHF benefit in these masking situations (Trine and Monson, 2020), and that the benefit of having a masker orientation away from the listener decreases for people with a threshold elevation at 16 kHz (Braza *et al.*, 2022).

C. EHF loss as a marker for damage in lower frequency regions

In the previous section, it was noted that EHF hearing loss has been shown in some studies to be related to deficits in speech-in-noise perception. However, this does not imply causation. In addition to having direct effects on perception, EHF loss may be a marker for sub-clinical deficits (i.e. deficits that are not revealed by standard PTA) in the standard frequency range (Hunter *et al.*, 2020). If so, then EHF audiometry might have broad diagnostic utility.

Over the past decade, there has been considerable interest in cochlear synaptopathy; a loss of synapses between inner hair cells and auditory nerve fibers that is caused by noise exposure or aging in animal models (Kujawa and Liberman, 2009), and has been inferred from nerve fiber loss in human histopathological studies (Wu *et al.*, 2018; Wu *et al.*, 2021). In animal models synaptopathy can occur in the absence of any elevation in hearing threshold (i.e., the loss would be sub-clinical in humans). However, it is possible that an EHF loss is a marker for synaptopathy in a lower frequency region (Liberman *et al.*, 2016; Bharadwaj *et al.*, 2019). In other words, insults that cause synaptopathy, such as noise exposure, may also cause an EHF hearing loss, even when standard PTA is normal. If so, then EHF testing might have utility for the diagnosis of synaptopathy.

Similarly, EHF hearing loss may be a marker for sub-clinical hair cell loss in the standard frequency range. In animal models, up to 80% of inner hair cells can be lost without affecting threshold sensitivity (Lobarinas *et al.*, 2013), and noise exposure can cause 20-40% loss of outer hair cells in the apex of the cochlea without threshold elevation (Bohne and Clark, 1982; Clark *et al.*, 1987). Hence, standard PTA is likely not very sensitive to hair cell loss. It is possible that, since EHF hearing loss often appears to precede threshold elevation in the standard range, EHF thresholds may be providing important information regarding hair cell loss at lower frequencies. This is supported by Mishra *et al.* (2021), who found that listeners with an EHF loss had a greater number of absent distortion-product otoacoustic emissions (DPOAEs) between 2 and 5 kHz compared to controls, and a lower average DPOAE level compared to controls when the emissions were present. Hearing thresholds in the standard frequency range were similar for the two groups. This suggests that EHF thresholds may be an early marker for outer hair cell damage affecting lower frequency regions (Mishra *et al.*, 2021).

V. USE OF EHF AUDIOMETRY IN CLINICAL TRIALS

The World Health Organization (WHO) defines clinical trials as prospective, interventional studies involving human participants that aim to assess the impact of the respective intervention on health outcomes (World Health Organization, 2021a). Therefore, clinical trials involving EHF audiometry may be ones in which: i) the intervention (as a diagnostic test) is EHF audiometry; or ii) EHF audiometry is employed as an outcome measure for studies in which a drug, or other treatment, is the intervention.

A search of the following clinical trial registries, using the search term "extended high frequency audiometry," was conducted: ClinicalTrials.gov; EU Clinical Trials Register; LRSCTN Registry; and the WHO International Clinical Trials Registry Platform (November 2021). The results comprised nine clinical trials. Five of these trials were listed as complete, but the results were only available for one of these. Expanding the search using broader search terms only increased the yield by one after the records (and associated trial protocols) were screened for relevance, completeness and accessibility. The following reasons may explain this apparent lack of registered clinical trials involving EHF audiometry:

i. Such trials have been conducted but were not registered.

ii. A registered clinical trial may include EHF audiometry as a subsidiary part of the protocol, and therefore this test is not listed explicitly. Or, the information on the registry is not detailed enough to be able to determine whether EHF audiometry is included (e.g., "audiometry" is listed but test frequencies are not specified).

iii. In clinical trials involving audiometry, only conventional frequencies are tested. This is particularly plausible given that many clinical trials utilize the Common Terminology Criteria for Adverse Events (CTCAE); EHF hearing loss does not constitute an adverse event, even in the latest version (v.5) of the CTCAE (National Cancer Institute, 2017).

Nevertheless, examples of the use of EHF audiometry in phase I, II and III clinical trials can be found. In phase I and IIa clinical trials, EHF audiometry has been utilized to evaluate the safety, feasibility and potential efficacy of pharmaceutical interventions (Campbell *et al.*, 2003; Peek *et* *al.*, 2020; Duinkerken *et al.*, 2021). In an ongoing phase III trial of intensity-modulated proton beam therapy versus intensity-modulated radiotherapy, the TORPEdO trial (ISRCTNregistry, 2020), EHF audiometry has been included in the trial protocol as a means of monitoring ototoxicity. This will ultimately contribute to our knowledge about multi-toxicity reduction in oropharyngeal cancer and should provide insight into whether EHF audiometry is a more sensitive, or useful, measure (i.e., than conventional PTA) for detecting differences in ototoxic effects between two types of radiotherapy.

VI. CURRENT CLINICAL USE OF EHF AUDIOMETRY

To determine the current clinical use of EHF audiometry across the globe, professional audiology societies from 55 countries (across six continents) were emailed, and asked the following two questions:

1. Is extended high-frequency audiometry performed routinely in [country]?
2. Do you have a standard protocol/procedure for doing extended high-frequency audiometry in [country]?

Contact details for professional audiology societies were obtained from the ASHA website. Contact details were not readily available for all countries, so to broaden the reach of our enquiry the following was also posted on Twitter:

"Is extended high frequency audiometry (testing >8 kHz) performed routinely in your country (excluding research)? For screening / monitoring / other? Are there standard guidelines you follow?"

The responses to question one, along with the anecdotal feedback from other countries via Twitter, are displayed (separately) in Fig. 3.

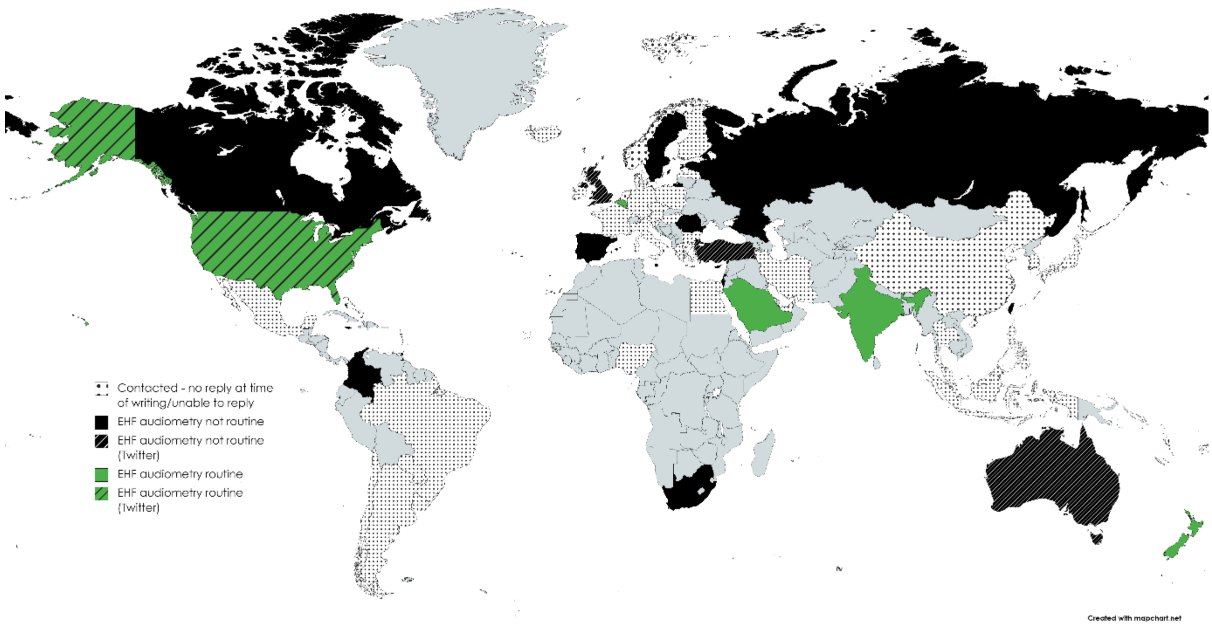

FIG. 3. (Colour online). Map depicting countries in which EHF audiometry is (or is not) routinely performed.

Contacts in Belgium, India, New Zealand, Saudi Arabia, and the United States (US) confirmed that EHF audiometry is routinely performed in their respective countries. However, a caveat is needed here. In the majority of these countries, EHF audiometry is only routine for certain groups of patients, or within certain sectors. In New Zealand, for example, EHF audiometry is performed routinely on patients receiving ototoxic medical treatment, as well as in some clinics that provide tinnitus counselling and management, but it is rarely done outside of these settings. Similarly, in India, it is a routine procedure in the training institutions, but the situation in the private sector is unknown.

EHF audiometry has not been entirely neglected in other countries, although its application is certainly patchier. The results of a recent web-based survey of pediatric audiology departments in the UK showed that approximately 18% of responding services perform EHF audiometry as part of a pediatric ototoxicity monitoring protocol (Brown *et al.*, 2021). This article also raises an interesting point about inconsistencies in the test procedure employed. Even between the small number of services who reported performing EHF audiometry, there was, "no uniformity of practice or agreement" in terms of number and combination of frequencies tested (Brown *et al.*, 2021). As described previously, in the UK, the scope of the recommended procedure for performing PTA does not extend to testing frequencies above 8 kHz (British Society of Audiology, 2018).

It is possible that the existence of a nationally recognized standard/procedure (as distinct from locally derived guidelines) is a better benchmark of the establishment of EHF audiometry within a country. Only Belgium and the US have so far been identified as having these. However, in the US, the guideline for performing PTA (American Speech-Language-Hearing Association, 2005) only alludes to EHF audiometry once, suggesting that it may be conducted for "special purposes;" further direction on dealing with the unique challenges that come with testing in the EHFs, such as increased inter-subject variability, is not given.

Ototoxicity monitoring is an example of one such "special purpose" and this appears to be the field in which EHF audiometry has gained most traction to date. In 2009, the American Academy of Audiology (AAA) published guidelines, which propounded the incorporation of EHF audiometry within an ototoxicity monitoring test battery (American Academy of Audiology, 2009). The Health Professions Council of South Africa has published similar recommendations (Health Professions Council of South Africa, 2018). A number of the professionals who were contacted by the authors provided additional contextual information; this information hints that when EHF audiometry *is* performed, it is mostly for assessing the effects of ototoxic treatment.

Other current uses of EHF audiometry, according to our international contacts, are displayed in Table I.

TABLE I. Reported uses of EHF audiometry, excluding monitoring ototoxic effects of medical treatment.

Use of EHF audiometry	Country/countries	Further detail provided
During tinnitus assessment and rehabilitation appointments.	Australia India New Zealand Romania Spain Taiwan Trinidad and Tobago Turkey	Used to pitch-match high frequency tinnitus that is outside the conventional testing range [Australia].
In cases of self-reported hearing difficulty, where thresholds in the conventional frequency range are within normal limits.	Australia Romania Turkey	EHF audiometry can form part of the test battery within an auditory processing disorder clinic, or it is performed ad hoc when patients report speech-in-noise hearing difficulties or a sensation of unilateral hearing loss.
To monitor the hearing of patients with certain (unnamed) neurological or urological diagnoses, or cytomegalovirus (CMV).	Australia Jamaica	Only performed on patients with CMV once reliable thresholds at conventional frequencies have been determined [Australia].
Where patients report a history of noise exposure.	India Trinidad and Tobago	
In cases of asymmetric hearing, and vestibular complaints.	Romania	Performed on patients whose symptoms are suggestive of unilateral vestibulopathy.
In cases of sudden hearing loss.	Israel	
When requested by parents.	Australia	Requests reported to be exclusively from parents of children who are being enrolled in a Tomatis sound therapy program.

VII. FUTURE CLINICAL USE OF EHF TESTING

A. Diagnosis

The preceding section shows that some countries/services are already harnessing the diagnostic advantage of EHF audiometry, but to use this test to its full potential requires a more consistent approach. Evidence already exists of the clinical usefulness of EHF audiometry for all patients presenting to an audiologist with hearing difficulties or tinnitus, in the absence of a hearing loss at the conventional PTA test frequencies (Rodríguez Valiente *et al.*, 2016). By comparing test results to age-dependent norms (e.g., Jilek *et al.* (2014) or Rodríguez Valiente *et al.* (2014)), it could help detect premature hearing loss in patients with systemic disease, as well as potentially, those with recreational/occupational noise trauma (see Sections III.D and III.E). EHF audiometry can also uncover cases of sudden hearing loss in patients with acute tinnitus that would otherwise go undetected, and untreated (Abu-Eta *et al.*, 2021). Despite being grey literature, a case report by Colucci (2016) demonstrates how the true extent of a unilateral sudden hearing loss in a 23-year-old male was only realized once EHF hearing was assessed.

Furthermore, from a holistic standpoint, doing a more thorough investigation when the standard tests prove unenlightening can improve the healthcare experience for the patient. Pryce and Wainwright (2008) emphasize the importance of validating a patient's hearing difficulties; they stress that a well-meant "reassurance" that nothing is measurably wrong can have quite the opposite effect.

For patients with pre-existing hearing loss up to 8 kHz, a similar approach to that described above may also prove fruitful. However, the clinical utility of EHF audiometry for these patients will likely decline with increasing hearing loss, unless audiometer output limitations in the EHFs can be overcome.

One (as yet) unexplored area where EHF audiometry could have future clinical utility is in the early detection of vestibular schwannoma (VS), for the following reasons:

i. The most common initial presenting symptom of VS is progressive hearing loss on the ipsilesional side (79.5% of VS patients) (Bento *et al.*, 2012).

ii. Hearing loss is of a sloping configuration (i.e., high-frequency thresholds are worse than low-frequency thresholds) in 51.7% of cases (Lee *et al.*, 2015).

iii. Hearing loss associated with VS can be attributed, *in part*, to a gradual compression of the tonotopically-formed cochlear nerve.

It therefore seems plausible that a certain degree of asymmetry in EHF hearing thresholds could prompt a referral for Magnetic Resonance Imaging (MRI) – the gold standard for VS diagnosis. However, MRI is expensive, and it would be essential, firstly, to develop means of differentiating other causes of EHF asymmetry (e.g., conductive EHF hearing loss) in order to prevent unwarranted medical costs or patient anxiety.

B. Hearing health monitoring

Ototoxicity monitoring programs still appear to be the result of individual service initiatives. However, EHF audiometry is expected to increasingly feature as a key component of future programs, for three reasons:

i. It can detect hearing loss sooner than other tests of auditory function (Knight *et al.*, 2007).

ii. Short-term test-retest variability is generally within 10 dB for HDA 200 earphones and ER-2 insert earphones (Schmuziger *et al.*, 2004; John and Kreisman, 2017), which is smaller than the ASHA criteria for threshold change attributed to cochleotoxicity (1994).

iii. The ASHA cochleotoxicity criteria for threshold change can be applied to the EHFs (Campbell *et al.*, 2003; Knight *et al.*, 2007).

This is at least the case for patients who are, i) capable of giving reliable behavioral responses, and ii) likely to have some measurable hearing thresholds in the EHFs. It is already recommended as part of a comprehensive baseline assessment (prior to the administration of ototoxic treatment), as well as at multiple follow-up appointments (American Academy of Audiology, 2009). Opinions differ as to whether frequencies up to and including 14 kHz (Schmuziger *et al.*, 2004), or 20 kHz (Konrad-Martin *et al.*, 2005), should be tested. Conversely, there appears to be current consensus that the EHF audiometry procedure can be truncated after baseline assessment - as described by Fausti et al. (1999) – unless a change in thresholds is recorded.

For the reasons outlined in Section III.D, EHF audiometry might also be of use in monitoring the hearing of populations at risk of noise- or music-induced hearing loss. The AAA already recommends performing EHF audiometry, where time and equipment allow, on all musicians/music industry personnel attending audiological services (American Academy of Audiology, 2020). The benefit of being able to alert individuals about the onset of early hearing damage is that they may be encouraged to adopt more protective behaviours, such as using ear defenders. However, such subtle EHF threshold changes as those reported by Liberman *et al.* (2016) and Maccà *et al.* (2015), will be difficult to detect clinically until inter-subject variability can be better controlled for. The benefit may also be reduced for people over 30 years of age (Maccà *et al.*, 2015).

C. Fitting hearing aids

Articles that demonstrate how EHF audiometry can be utilised to fit hearing aids have largely been limited to the Earlens system (Arbogast *et al.*, 2019). The Earlens system comprises a behind-the-ear sound processor, a signal delivery tip (which encodes the processed sound signal into a pulsed light signal), and a custom-made lens that is positioned on the eardrum (which receives the light signal and directly vibrates the eardrum). The system is marketed as having a relatively wide bandwidth (125 Hz – 10 kHz), an attribute that is associated with better sound quality ratings by people with normal hearing and - in terms of clarity - mild-to-moderate hearing loss (Füllgrabe *et al.*, 2010), as well as by Earlens wearers comparing full-bandwidth and low-pass-filtered speech and music (Vaisberg *et al.*, 2021). As such, EHF audiometry is necessary for generating the prescription target to which the Earlens sound processor is set. The Earlens system can currently be regarded as a niche product, although it is anticipated to become more universally available over time.

The datasheets of many contemporary conventional hearing aids list bandwidth upper frequencies of 9-10 kHz. Although these values, which have been calculated using American National Standards Institute (ANSI) methods, may not have direct clinical applicability, Kimlinger *et al.* (2015) showed that seven of eight hearing aids they tested had a maximum audible frequency of more than 8 kHz when programed for a flat mild sensorineural hearing loss. It is relevant that in this study, the test hearing aids were selected to have a variety of ANSI bandwidth upper frequencies (i.e., not just the greatest bandwidth upper frequencies). The CAM2 prescription already gives gain recommendations for center frequencies up to 10 kHz (Moore *et al.*, 2010). Thus, in future, EHF audiometry may be clinically useful for i) determining suitability for wide bandwidth amplification, or ii) programming hearing aids with such a capacity.

D. Obstacles to implementation

It appears that the biggest obstacle to clinical implementation of EHF audiometry is a lack of necessary equipment. This point is highlighted by Brown *et al.* (2021), who report that 25% of audited services in the UK cite lack of suitable equipment as a reason for not performing EHF testing as part of an ototoxicity monitoring protocol. Information provided by UK-based participant identification sites, prior to the start of the aforementioned TORPEdO trial, gives a similar picture, with 39% of services stating they did not have the equipment to test beyond 8 kHz. It should be borne in mind, however, that research-active departments may not be representative of all services, and these figures are likely optimistic. Our contacts in Australia, Jamaica, New Zealand, South Africa and Trinidad and Tobago all mentioned lack of necessary equipment as an obstacle to the clinical implementation of EHF audiometry, implying that this barrier is not confined to the UK. Analogous to this, is an account from the Colombian Association of Audiology that EHF audiometry is starting to boom in Columbia *because* of an increased availability of audiometers with EHF testing functionality (personal communication, Saúl Triviño Torres).

A lack of necessary equipment for performing EHF audiometry may be purely due to financial constraints or the result of a lack of perceived need for the equipment in the first place. For example, just because the preferential effects of platinum-based chemotherapy on the EHFs are well known, does not mean that audiologists (or oncologists) deem EHF audiometry necessary; this was corroborated by 16% of respondents to Brown *et al.* (2021). One reason why this view may be held, is that unless hearing loss occurs in the "speech frequencies," the chemotherapy regimen is unlikely to be altered; none of the four most widely used cochleotoxicity classification systems specifically describe how to grade EHF hearing loss (Crundwell *et al.*, 2016). Thus, the utility of EHF audiometry in monitoring chemotherapy patients is restricted to counselling them on the likelihood of, "practical speech frequency hearing loss" (Dasgupta *et al.*, 2021). Whilst this is undoubtedly realistic, the role EHF testing can play in forewarning patients should not be underestimated, as counselling about the ototoxic effects in the early stages of treatment has been shown to be particularly important for young cancer patients (Khan *et al.*, 2020). As maintained by the AAA (2009), "…that the patient may suffer a serious and possibly life-threatening illness does not diminish the importance of these [quality of life] issues".

Even where motivation exists, some hesitancy about the test procedure and interpretation can prevent the translation of EHF audiometry into routine practice. For instance, concerns about normative data for hearing thresholds in the EHF range (Brown *et al.*, 2021), as well as uncertainty about how best to control for the relative variability in the EHF range, may deter services from implementing this test. The development of national/international guidelines (beyond Belgium and the US) that answer clinicians' specific concerns, would help to provide reassurance that EHF audiometry can be performed reliably.

VIII. CONCLUSIONS AND GAPS IN KNOWLEDGE

The most basal region of the cochlea is the most vulnerable to injury, and hence hearing loss in the EHF range is an important "early warning" of cochlear damage; for example, damage caused by ototoxic drugs, disease, and possibly noise exposure. Furthermore, EHF loss impacts sound localization, and may also have direct effects on speech perception in noisy environments. For these reasons, EHF audiometry has great potential for diagnosis and hearing health monitoring, and for fitting hearing aids. Currently, however, EHF audiometry has only limited application internationally, and there is a lack of clinical guidelines and standards. There are also several gaps in knowledge that limit the application of EHF audiometry.

First, it is unclear the extent to which noise exposure affects EHF thresholds before causing threshold elevation at lower frequencies. Reaching a firm conclusion may depend on longitudinal studies where individuals are tracked over a number of years, with more reliable estimates of noise exposure dose than are currently provided by retrospective self-report.

The mechanism (or mechanisms) for the relation between EHF hearing loss and speech perception difficulties has not yet been established clearly. In particular, it is unclear the extent to which EHF hearing loss may have a direct effect on speech perception in noise, or is a marker for sub-clinical deficits at lower frequencies. This is important for determining the potential benefits of amplification in the EHF range, and for understanding what EHF audiometry may tell us about cochlear health.

For the most commonly available EHF headphones, there is a lack of international standard reference equivalent threshold sound pressure levels (RETSPLs), pediatric calibration correction factors, expected test-retest values, and interaural attenuation values. A good explanation of these issues and potential resolutions are provided by Kevin Munro in Hunter *et al.* (2020). Additionally, uncomfortable loudness levels (ULLs) in the EHF range do not appear to have been reported in the literature to date. Knowing what ULLs are typical for a population is important for ensuring patient comfort during testing (Aazh and Moore, 2017), and will have implications for the recommended amplitude of any familiarization tone, as well as whether masking in the EHFs is feasible. Questions concerning the interpretation of EHF hearing thresholds also remain. What degree of asymmetry in the EHFs can be expected normally, and what would warrant concern? How can conductive hearing losses be adequately detected in the EHFs?

Although it is important that these issues are resolved, it is clear that EHF audiometry has clinical utility, and the development of clinical guidelines and standards should not be delayed. These should be founded on the current evidence-base, and supplemented with consensus of expert opinion until such gaps in the knowledge are addressed.

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REFERENCES (BIBLIOGRAPHIC)

Aazh, H., and Moore, B. C. J. (**2017**). "Incidence of Discomfort During Pure-Tone Audiometry and Measurement of Uncomfortable Loudness Levels Among People Seeking Help for Tinnitus and/or Hyperacusis," Am J Audiol **26**, 226-232.

Abu-Eta, R., Gavriel, H., and Pitaro, J. (**2021**). "Extended High Frequency Audiometry for Revealing Sudden Sensory Neural Hearing Loss in Acute Tinnitus Patients," Int Arch Otorhinolaryngol **25**, e413-e415.

Ahmed, H. O., Dennis, J. H., Badran, O., Ismail, M., Ballal, S. G., Ashoor, A., and Jerwood, D. (**2001**). "High-frequency (10-18 kHz) hearing thresholds: reliability, and effects of age and occupational noise exposure," Occup Med (Lond) **51**, 245-258.

American Academy of Audiology (**2009**). "American Academy of Audiology Position Statement and Clinical Practice Guidelines: Ototoxicity Monitoring." Available: https://www.audiology.org/wp-content/uploads/2021/05/OtoMonGuidelines.pdf_539974c40999c1.58842217.pdf. Retrieved November 15, 2021.

American Academy of Audiology (**2020**). "Clinical Consensus Document. Audiological Services for Musicians and Music Industry Personnel," (American Academy of Audiology). Available: https://www.audiology.org/wp-content/uploads/legacy/publications/resources/Musicians%20Consensus%20Doc_Final_1.23.20.pdf. Retrieved February 5, 2022.

American Speech-Language-Hearing Association (**1994**). "Audiologic Management of Individuals Receiving Cochleotoxic Drug Therapy." Available: https://www.asha.org/policy/GL1994-00003/. Retrieved November 15, 2021.

American Speech-Language-Hearing Association (**2005**). "Guidelines for Manual Pure-Tone Threshold Audiometry." Available: https://www.asha.org/policy/GL2005-00014/#:~:text=Testing%20Issues%20%20%20%20%20%20,to%20%20...%20%208%20more%20rows%20. Retrieved November 15, 2021.

Arbogast, T. L., Moore, B. C. J., Puria, S., Dundas, D., Brimacombe, J., Edwards, B., and Carr Levy, S. (**2019**). "Achieved Gain and Subjective Outcomes for a Wide-Bandwidth Contact Hearing Aid Fitted Using CAM2," Ear Hear **40**, 741-756.

Babbage, M. J., O'Beirne, G. A., Bergin, M. J., and Bird, P. A. (**2017**). "Patterns of Extended High-frequency Hearing Loss Following Stapes Surgery," Otol Neurotol **38**, 1405-1410.

Badri, R., Siegel, J. H., and Wright, B. A. (**2011**). "Auditory filter shapes and high-frequency hearing in adults who have impaired speech in noise performance despite clinically normal audiograms," J Acoust Soc Am **129**, 852-863.

Bass, J. K., Huang, J., Hua, C. H., Bhagat, S. P., Mendel, L. L., Onar-Thomas, A., Indelicato, D. J., and Merchant, T. E. (**2018**). "Auditory Outcomes in Patients Who Received Proton Radiotherapy for Craniopharyngioma," Am J Audiol **27**, 306-315.

Bento, R. F., Pinna, M. H., and Brito Neto, R. V. (**2012**). "Vestibular schwannoma: 825 cases from a 25-year experience," Int Arch Otorhinolaryngol **16**, 466-475.

Best, V., Carlile, S., Jin, C., and Van Schalk, A. (**2005**). "The role of high frequencies in speech localization," J. Acoust. Soc. Am. **118**, 353-363.

Bharadwaj, H. M., Mai, A. R., Simpson, J. M., Choi, I., Heinz, M. G., and Shinn-Cunningham, B. G. (**2019**). "Non-Invasive Assays of Cochlear Synaptopathy - Candidates and Considerations," Neuroscience **407**, 53-66.

Bohne, B. A., and Clark, W. W. (**1982**). "Growth of hearing loss and cochlear lesion with increasing duration of noise exposure," in *New Perspectives on Noise-induced Hearing Loss*, edited by R. P. Hamernik, D. Henderson, and R. Salvi (Raven Press, New York), pp. 283-302.

Braza, M. D., Corbin, N. E., Buss, E., and Monson, B. B. (**2022**). "Effect of Masker Head Orientation, Listener Age, and Extended High-Frequency Sensitivity on Speech Recognition in Spatially Separated Speech," Ear Hear **43(1)**, 90-100.

British Society of Audiology (**2018**). "Recommended Procedure. Pure-tone air-conduction and bone-conduction threshold audiometry with and without masking." Available: https://www.thebsa.org.uk/resources/pure-tone-air-bone-conduction-threshold-audiometry-without-masking/. Retrieved November 15, 2021.

Brown, E. C. M., Caimino, C., Benton, C. L., and Baguley, D. M. (**2021**). "An audit of UK audiological practice in specialist paediatric oncology centres regarding hearing assessment of children at risk of ototoxicity due to chemotherapy," J Laryngol Otol **135**, 14-20.

Brungart, D. S., and Simpson, B. D. (**2009**). "Effects of bandwidth on auditory localization with a noise masker," J Acoust Soc Am **126**, 3199-3208.

Byrne, D., Dillon, H., Tran, K., Arlinger, S., Wilbraham, K., Cox, R., Hagerman, B., Hetu, R., Kei, J., Lui, C., Kiessling, J., Kotby, M. N., Nasser, N. H. A., El Kholy, W. A. H., Nakanishi, Y., Oyer, H., Powell, R., Stephens, D., Meredith, R., Sirimanna, T., Tavartkiladze, G., Frolenkov, G. I., Westerman, S., and Ludvigsen, C. (**1994**). "An international comparison of long-term average speech spectra," J. Acoust. Soc. Am. **96**, 2108-2120.

Campbell, K. C., Kelly, E., Targovnik, N., Hughes, L., Van Saders, C., Gottlieb, A. B., Dorr, M. B., and Leighton, A. (**2003**). "Audiologic monitoring for potential ototoxicity in a phase I clinical trial of a new glycopeptide antibiotic," J Am Acad Audiol **14**, 157-168; quiz 170-151.

Campbell, K. C. M., and Le Prell, C. G. (**2018**). "Drug-Induced Ototoxicity: Diagnosis and Monitoring," Drug Saf **41**, 451-464.

Carcagno, S., and Plack, C. J. (**2020**). "Effects of age on electrophysiological measures of cochlear synaptopathy in humans," Hear Res **396**, 108068.

Chen, Y., Huang, W. G., Zha, D. J., Qiu, J. H., Wang, J. L., Sha, S. H., and Schacht, J. (**2007**). "Aspirin attenuates gentamicin ototoxicity: from the laboratory to the clinic," Hear Res **226**, 178-182.

Cheraghi, S., Nikoofar, P., Fadavi, P., Bakhshandeh, M., Khoie, S., Gharehbagh, E. J., Farahani, S., Mohebbi, A., Vasheghani, M., and Zare, M. (**2015**). "Short-term cohort study on sensorineural hearing changes in head and neck radiotherapy," Medical Oncology **32**, 1-7.

Clark, W. W., Bohne, B. A., and Boettcher, F. A. (**1987**). "Effect of periodic rest on hearing loss and cochlear damage following exposure to noise," J Acoust Soc Am **82**, 1253-1264.

Colucci, D. (**2016**). "Ultra-High Frequency Sudden Sensorineural Hearing Loss," The Hearing Journal **69(12)**, **36-38**. doi: 10.1097/01.HJ.0000511131.91864.8e

Cordeiro, F. P., da Costa Monsanto, R., Kasemodel, A. L. P., de Almeida Gondra, L., and de Oliveira Penido, N. (**2018**). "Extended high-frequency hearing loss following the first episode of otitis media," Laryngoscope **128**, 2879-2884.

Crundwell, G., Gomersall, P., and Baguley, D. M. (**2016**). "Ototoxicity (cochleotoxicity) classifications: A review," Int J Audiol **55**, 65-74.

Dasgupta, S., Pizer, B., Ratnayake, S., Hayden, J., and O'Hare, M. (**2021**). "Comments on published article 'An audit of UK audiological practice in specialist paediatric oncology centres regarding hearing assessment of children at risk of ototoxicity due to chemotherapy'by Brown et al," The Journal of Laryngology & Otology **135**, 373-374.

Dubno, J. R., Eckert, M. A., Lee, F. S., Matthews, L. J., and Schmiedt, R. A. (**2013**). "Classifying human audiometric phenotypes of age-related hearing loss from animal models," J Assoc Res Otolaryngol **14**, 687-701.

Duinkerken, C. W., de Weger, V. A., Dreschler, W. A., van der Molen, L., Pluim, D., Rosing, H., Nuijen, B., Hauptmann, M., Beijnen, J. H., Balm, A. J. M., de Boer, J. P., Burgers, J. A., Marchetti, S., Schellens, J. H. M., and Zuur, C. L. (**2021**). "Transtympanic Sodium Thiosulfate for Prevention of Cisplatin-Induced Ototoxicity: A Randomized Clinical Trial," Otol Neurotol **42**, 678-685.

Fausti, S. A., Henry, J. A., Helt, W. J., Phillips, D. S., Frey, R. H., Noffsinger, D., Larson, V. D., and Fowler, C. G. (**1999**). "An individualized, sensitive frequency range for early detection of ototoxicity," Ear Hear **20**, 497-505.

Frank, T. (**2001**). "High-frequency (8 to 16 kHz) reference thresholds and intrasubject threshold variability relative to ototoxicity criteria using a Sennheiser HDA 200 earphone," Ear Hear **22**, 161-168.

Füllgrabe, C., Baer, T., Stone, M. A., and Moore, B. C. (**2010**). "Preliminary evaluation of a method for fitting hearing aids with extended bandwidth," Int J Audiol **49**, 741-753.

Galarza-Delgado, D. A. V. G., M.J. Riega Torres, J. Soto-Galindo, G.A. Mendoza Flores, L. Trevino Gonzalez, J.L. (**2018**). "Early hearing loss detection in rheumatoid arthritis and primary Sjögren syndrome using extended high frequency audiometry," Clinical Rheumatology **37**, 367-373.

Garinis, A. C., Cross, C. P., Srikanth, P., Carroll, K., Feeney, M. P., Keefe, D. H., Hunter, L. L., Putterman, D. B., Cohen, D. M., Gold, J. A., and Steyger, P. S. (**2017**). "The cumulative effects of intravenous antibiotic treatments on hearing in patients with cystic fibrosis," J Cyst Fibros **16**, 401-409.

Guest, H., Dewey, R. S., Plack, C. J., Couth, S., Prendergast, G., Bakay, W., and Hall, D. A. (**2018**). "The Noise Exposure Structured Interview (NESI): An instrument for the comprehensive estimation of lifetime noise exposure," Trends Hear **22**, 2331216518803213.

Guest, H., Munro, K. J., Prendergast, G., Howe, S., and Plack, C. J. (**2017**). "Tinnitus with a normal audiogram: Relation to noise exposure but no evidence for cochlear synaptopathy," Hear Res **344**, 265-274.

Hallmo, P. (**1997**). "Extended high-frequency audiometry in traumatic tympanic membrane perforations," Scand Audiol **26**, 53-59.

Health Professions Council of South Africa (2018). "Audiological Management of Patients on Treatment that includes Ototoxic Medications. Guidelines." Available at: https://www.hpcsa.co.za/Uploads/SLH/Guidelines%20for%20Audiological%20Management%20of%20Patients%20on%20Treatment%20that%20includes%20Ototoxic%20Medications.pdf

Hunter, L. L., Margolis, R. H., Rykken, J. R., Le, C. T., Daly, K. A., and Giebink, G. S. (**1996**). "High frequency hearing loss associated with otitis media," Ear Hear **17**, 1-11.

Hunter, L. L., Monson, B. B., Moore, D. R., Dhar, S., Wright, B. A., Munro, K. J., Motlagh Zadeh, L., Blankenship, C. M., Stiepan, S. M., and Siegal, J. H. (**2020**). "Extended high frequency hearing and speech perception implications in adults and children," Hear. Res. **397**, 107922. doi.org/10.1016/j.heares.2020.107922

ISRCTNregistry (2020). "A phase III trial of intensity-modulated proton beam therapy versus intensity-modulated radiotherapy for multi-toxicity reduction in oropharyngeal cancer," Available: https://www.isrctn.com/ISRCTN16424014, (date last viewed: 15-Nov.-2021). doi.org/10.1186/ISRCTN16424014

Jereczek-Fossa, B. A., Zarowski, A., Milani, F., and Orecchia, R. (**2003**). "Radiotherapy-induced ear toxicity," Cancer Treat Rev **29**, 417-430.

Jiang, M., Karasawa, T., and Steyger, P. S. (**2017**). "Aminoglycoside-Induced Cochleotoxicity: A Review," Front Cell Neurosci **11**, 308.

Jilek, M., Suta, D., and Syka, J. (**2014**). "Reference hearing thresholds in an extended frequency range as a function of age," J Acoust Soc Am **136**, 1821-1830.

John, A. B., and Kreisman, B. M. (**2017**). "Equivalence and test-retest reproducibility of conventional and extended-high-frequency audiometric thresholds obtained using pure-tone and narrow-band-noise stimuli," Int J Audiol **56**, 635-642.

Khan, A., Mubdi, N., Budnick, A., Feldman, D. R., Williams, S. W., Patel, S., and Tonorezos, E. S. (**2020**). "The experience of hearing loss in adult survivors of childhood and young adult cancer: A qualitative study," Cancer **126**, 1776-1783.

Kimlinger, C., McCreery, R., and Lewis, D. (**2015**). "High-frequency audibility: the effects of audiometric configuration, stimulus type, and device," J Am Acad Audiol **26**, 128-137.

Knight, K. R., Kraemer, D. F., Winter, C., and Neuwelt, E. A. (**2007**). "Early changes in auditory function as a result of platinum chemotherapy: use of extended high-frequency audiometry and evoked distortion product otoacoustic emissions," J Clin Oncol **25**, 1190-1195.

Konrad-Martin, D., Gordon, J. S., Reavis, K. M., Wilmington, D. J., Helt, W. J., and Fausti, S. A. (**2005**). "Audiological Monitoring of Patients Receiving Ototoxic Drugs," Perspectives on Hearing and Hearing Disorders: Research and Diagnostics **9**, 17-22.

Konrad-Martin, D., James, K. E., Gordon, J. S., Reavis, K. M., Phillips, D. S., Bratt, G. W., and Fausti, S. A. (**2010**). "Evaluation of audiometric threshold shift criteria for ototoxicity monitoring," J Am Acad Audiol **21**, 301-314; quiz 357.

Konrad-Martin, D., Poling, G. L., Garinis, A. C., Ortiz, C. E., Hopper, J., O'Connell Bennett, K., and Dille, M. F. (**2018**). "Applying U.S. national guidelines for ototoxicity monitoring in adult patients: perspectives on patient populations, service gaps, barriers and solutions," Int J Audiol **57**, S3-S18.

Kucur, C., Kucur, S. K., Gozukara, I., Seven, A., Yuksel, K. B., Keskin, N., and Oghan, F. (**2013**). "Extended high frequency audiometry in polycystic ovary syndrome," The Scientific World Journal **2013**.

Kujawa, S. G., and Liberman, M. C. (**2009**). "Adding insult to injury: cochlear nerve degeneration after "temporary" noise-induced hearing loss," J Neurosci **29**, 14077-14085.

Kujawa, S. G., and Liberman, M. C. (**2015**). "Synaptopathy in the noise-exposed and aging cochlea: Primary neural degeneration in acquired sensorineural hearing loss," Hear Res **330**, 191-199.

Laitila, P., Karma, P., Sipila, M., Manninen, M., and Rakho, T. (**1997**). "Extended high frequency hearing and history of acute otitis media in 14-year-old children in Finland," Acta Otolaryngol Suppl **529**, 27-29.

Lapsley Miller, J. A., Reed, C. M., Robinson, S. R., and Perez, Z. D. (**2018**). "Pure-Tone Audiometry With Forward Pressure Level Calibration Leads to Clinically-Relevant Improvements in Test-Retest Reliability," Ear Hear **39**, 946-957.

Lasso de la Vega, M., Villarreal, I. M., López Moya, J., and García-Berrocal, J. R. (**2017**). "Extended high frequency audiometry can diagnose sub-clinic involvement in a seemingly normal hearing systemic lupus erythematosus population," Acta oto-laryngologica **137**, 161-166.

Le Prell, C. G., Spankovich, C., Lobarinas, E., and Griffiths, S. K. (**2013**). "Extended high-frequency thresholds in college students: effects of music player use and other recreational noise," J Am Acad Audiol **24**, 725-739.

Lee, J., Dhar, S., Abel, R., Banakis, R., Grolley, E., Lee, J., Zecker, S., and Siegel, J. (**2012**). "Behavioral hearing thresholds between 0.125 and 20 kHz using depth-compensated ear simulator calibration," Ear Hear **33**, 315-329.

Lee, S. H., Choi, S. K., Lim, Y. J., Chung, H. Y., Yeo, J. H., Na, S. Y., Kim, S. H., and Yeo, S. G. (**2015**). "Otologic manifestations of acoustic neuroma," Acta Oto-Laryngologica **135**, 140-146.

Levy, S. C., Freed, D. J., Nilsson, M., Moore, B. C., and Puria, S. (**2015**). "Extended High-Frequency Bandwidth Improves Speech Reception in the Presence of Spatially Separated Masking Speech," Ear Hear **36**, e214-224.

Liberman, M. C., Epstein, M. J., Cleveland, S. S., Wang, H., and Maison, S. F. (**2016**). "Toward a Differential Diagnosis of Hidden Hearing Loss in Humans," PLoS One **11**, e0162726.

Lobarinas, E., Salvi, R., and Ding, D. (**2013**). "Insensitivity of the audiogram to carboplatin induced inner hair cell loss in chinchillas," Hear Res **302**, 113-120.

Maccà, I., Scapellato, M. L., Carrieri, M., Maso, S., Trevisan, A., and Bartolucci, G. B. (**2015**). "High-frequency hearing thresholds: effects of age, occupational ultrasound and noise exposure," Int Arch Occup Environ Health **88**, 197-211.

Margolis, R. H., Saly, G. L., and Hunter, L. L. (**2000**). "High-frequency hearing loss and wideband middle ear impedance in children with otitis media histories," Ear Hear **21**, 206-211.

McBride, D. I., and Williams, S. (**2001**). "Audiometric notch as a sign of noise induced hearing loss," Occup Environ Med **58**, 46-51.

Mishra, S. K., Saxena, U., and Rodrigo, H. (**2021**). "Extended High-frequency Hearing Impairment Despite a Normal Audiogram: Relation to Early Aging, Speech-in-noise Perception, Cochlear Function, and Routine Earphone Use," Ear Hear. doi: 10.1097/AUD.0000000000001140

Monson, B. B., Hunter, E. J., Lotto, A. J., and Story, B. H. (**2014**). "The perceptual significance of high-frequency energy in the human voice," Front Psychol **5**, 587.

Monson, B. B., Hunter, E. J., and Story, B. H. (**2012a**). "Horizontal directivity of low- and high-frequency energy in speech and singing," J Acoust Soc Am **132**, 433-441.

Monson, B. B., Lotto, A. J., and Story, B. H. (**2012b**). "Analysis of high-frequency energy in long-term average spectra of singing, speech, and voiceless fricatives," J Acoust Soc Am **132**, 1754-1764.

Monson, B. B., Rock, J., Schulz, A., Hoffman, E., and Buss, E. (**2019**). "Ecological cocktail party listening reveals the utility of extended high-frequency hearing," Hear Res **381**, 107773.

Moore, B. C., and Tan, C. T. (**2003**). "Perceived naturalness of spectrally distorted speech and music," J Acoust Soc Am **114**, 408-419.

Moore, B. C. J., Glasberg, B. R., and Stone, M. A. (**2010**). "Development of a new method for deriving initial fittings for hearing aids with multi-channel compression: CAMEQ2-HF," International Journal of Audiology **49**, 216-227.

Motlagh Zadeh, L., Silbert, N. H., Sternasty, K., Swanepoel, W., Hunter, L. L., and Moore, D. R. (**2019**). "Extended high-frequency hearing enhances speech perception in noise," Proc Natl Acad Sci U S A **116**, 23753-23759.

Mujica–Mota, M., Waissbluth, S., and Daniel, S. J. (**2013**). "Characteristics of radiation-induced sensorineural hearing loss in head and neck cancer: A systematic review," Head & neck **35**, 1662-1668.

National Cancer Institute (**2017**). "Common Terminology Criteria for Adverse Events (CTCAE) - Version 5.0." Available: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf, (date last viewed: 15-Nov.-2021).

Otte, R. J., Agterberg, M. J., Van Wanrooij, M. M., Snik, A. F., and Van Opstal, A. J. (**2013**). "Age-related hearing loss and ear morphology affect vertical but not horizontal sound-localization performance," J Assoc Res Otolaryngol **14**, 261-273.

Peek, N. F. A. W., Nell, M. J., Brand, R., Jansen-Werkhoven, T., van Hoogdalem, E. J., Verrijk, R., Vonk, M. J., Wafelman, A. R., Valentijn, A. R. P. M., Frijns, J. H. M., Hiemstra, P. S., Drijfhout, J. W., Nibbering, P. H., and Grote, J. J. (**2020**). "Ototopical drops containing a novel antibacterial synthetic peptide: Safety and efficacy in adults with chronic suppurative otitis media," PLOS ONE **15**, e0231573.

Peng, J. H., Tao, Z. Z., and Huang, Z. W. (**2007**). "Risk of damage to hearing from personal listening devices in young adults," J Otolaryngol **36**, 181-185.

Prendergast, G., Guest, H., Munro, K. J., Kluk, K., Leger, A., Hall, D. A., Heinz, M. G., and Plack, C. J. (**2017**). "Effects of noise exposure on young adults with normal audiograms I: Electrophysiology," Hear Res **344**, 68-81.

Pryce, H., and Wainwright, D. (**2008**). "Help-seeking for medically unexplained hearing difficulties: A qualitative study," International Journal of Therapy and Rehabilitation **15**, 343-349.

Rodríguez Valiente, A., Roldán Fidalgo, A., Villarreal, I. M., and García Berrocal, J. R. (**2016**). "Extended High-frequency Audiometry (9000–20000Hz). Usefulness in Audiological Diagnosis," Acta Otorrinolaringologica (English Edition) **67**, 40-44.

Rodríguez Valiente, A., Trinidad, A., García Berrocal, J. R., Górriz, C., and Ramírez Camacho, R. (**2014**). "Extended high-frequency (9–20 kHz) audiometry reference thresholds in 645 healthy subjects," International Journal of Audiology **53**, 531-545.

Ruckenstein, M. J. (**2004**). "Autoimmune inner ear disease," Curr Opin Otolaryngol Head Neck Surg **12**, 426-430.

Rybak, L. P., and Ramkumar, V. (**2007**). "Ototoxicity," Kidney Int **72**, 931-935.

Rybak, L. P., Whitworth, C. A., Mukherjea, D., and Ramkumar, V. (**2007**). "Mechanisms of cisplatin-induced ototoxicity and prevention," Hear Res **226**, 157-167.

Ryding, M., Konradsson, K., Kalm, O., and Prellner, K. (**2002**). "Auditory consequences of recurrent acute purulent otitis media," Ann Otol Rhinol Laryngol **111**, 261-266.

Schmuziger, N., Probst, R., and Smurzynski, J. (**2004**). "Test-retest reliability of pure-tone thresholds from 0.5 to 16 kHz using Sennheiser HDA 200 and Etymotic Research ER-2 earphones," Ear Hear **25**, 127-132.

Schot, L. J., Hilgers, F. J., Keus, R. B., Schouwenburg, P. F., and Dreschler, W. A. (**1992**). "Late effects of radiotherapy on hearing," Eur Arch Otorhinolaryngol **249**, 305-308.

Souza, N. N., Dhar, S., Neely, S. T., and Siegel, J. H. (**2014**). "Comparison of nine methods to estimate ear-canal stimulus levels," J Acoust Soc Am **136**, 1768-1787.

Stelmachowicz, P. G., Beauchaine, K. A., Kalberer, A., and Jesteadt, W. (**1989**). "Normative thresholds in the 8- to 20-kHz range as a function of age," J Acoust Soc Am **86**, 1384-1391.

Sulaiman, A. H., Husain, R., and Seluakumaran, K. (**2014**). "Evaluation of early hearing damage in personal listening device users using extended high-frequency audiometry and otoacoustic emissions," Eur Arch Otorhinolaryngol **271**, 1463-1470.

Trine, A., and Monson, B. B. (**2020**). "Extended High Frequencies Provide Both Spectral and Temporal Information to Improve Speech-in-Speech Recognition," Trends Hear **24**, 2331216520980299.

Vaisberg, J., Folkeard, P., Levy, S., Dundas, D., Agrawal, S., and Scollie, S. (**2021**). "Sound Quality Ratings of Amplified Speech and Music Using a Direct Drive Hearing Aid: Effects of Bandwidth," Otology & Neurotology **42(2)**, 227-234.

Wei, W., Heinze, S., Gerstner, D. G., Walser, S. M., Twardella, D., Reiter, C., Weilnhammer, V., Perez-Alvarez, C., Steffens, T., and Herr, C. E. W. (**2017**). "Audiometric notch and extended high-frequency hearing threshold shift in relation to total leisure noise exposure: An exploratory analysis," Noise Health **19**, 263-269.

Withnell, R. H., and Gowdy, L. E. (**2013**). "An analysis of the acoustic input impedance of the ear," Journal of the Association for Research in Otolaryngology : JARO **14**, 611-622.

World Health Organization (**2021a**). "International Clinical Trials Registry Platform (ICTRP)," Available: https://www.who.int/clinical-trials-registry-platform. Retrieved November 15 2021.

World Health Organization (**2021b**). "World report on hearing," (World Health Organization, Geneva). Available: file://nask.man.ac.uk/home$/Downloads/9789240020481-eng%20(2).pdf, (date last viewed: 15-Nov.-2021).

Wu, P. Z., Liberman, L. D., Bennett, K., de Gruttola, V., O'Malley, J. T., and Liberman, M. C. (**2018**). "Primary Neural Degeneration in the Human Cochlea: Evidence for Hidden Hearing Loss in the Aging Ear," Neuroscience **407**, 8-20.

Wu, P. Z., O'Malley, J. T., de Gruttola, V., and Liberman, M. C. (**2021**). "Primary Neural Degeneration in Noise-Exposed Human Cochleas: Correlations with Outer Hair Cell Loss and Word-Discrimination Scores," J Neurosci **41**, 4439-4447.

Yeend, I., Beach, E. F., and Sharma, M. (**2019**). "Working Memory and Extended High-Frequency Hearing in Adults: Diagnostic Predictors of Speech-in-Noise Perception," Ear Hear **40**, 458-467.

TABLE I. Reported uses of EHF audiometry, excluding monitoring ototoxic effects of medical treatment.

Use of EHF audiometry	Country/countries	Further detail provided
During tinnitus assessment and rehabilitation appointments.	Australia India New Zealand Romania Spain Taiwan Trinidad and Tobago Turkey	Used to pitch-match high frequency tinnitus that is outside the conventional testing range [Australia].
In cases of self-reported hearing difficulty, where thresholds in the conventional frequency range are within normal limits.	Australia Romania Turkey	EHF audiometry can form part of the test battery within an auditory processing disorder clinic, or it is performed ad hoc when patients report speech-in-noise hearing difficulties or a sensation of unilateral hearing loss.
To monitor the hearing of patients with certain (unnamed) neurological or urological diagnoses, or cytomegalovirus (CMV).	Australia Jamaica	Only performed on patients with CMV once reliable thresholds at conventional frequencies have been determined [Australia].
Where patients report a history of noise exposure.	India Trinidad and Tobago	
In cases of asymmetric hearing, and vestibular complaints.	Romania	Performed on patients whose symptoms are suggestive of unilateral vestibulopathy.
In cases of sudden hearing loss.	Israel	
When requested by parents.	Australia	Requests reported to be exclusively from parents of children who are being enrolled in a Tomatis sound therapy program.

FIG. 1. (Colour online). Mean hearing threshold as a function of frequency for a group of normal-hearing listeners, aged 19-39 yrs (black circles). Error bars show +/- 1 standard deviation. The purple squares and green triangles show the results for two listeners with very similar thresholds up to 8 kHz, but markedly different thresholds above 8 kHz (in the EHF range). Data from Carcagno and Plack (2020).

FIG. 2. (Colour online). Mean hearing threshold as a function of frequency for groups of young, middle-aged, and older listeners. Data from Carcagno and Plack (2020).

FIG. 3. (Colour online). Map depicting countries in which EHF audiometry is (or is not) routinely performed.