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# Frequency discrimination in ears with and without contralateral cochlear dead regions

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**Key words**:

Cochlear dead regions, frequency discrimination.

**Abbreviations**:

DR: Dead region, TEN-HL: Threshold equalizing noise – Hearing level, DLF: Difference limen for frequency, $f_{cut\text{-}off}$ : Audiogram cut-off frequency.

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## ABSTRACT

**Objective:** The purpose of this study was to test the ability to discriminate low-frequency pure-tone stimuli for ears with and without contralateral dead regions, in subjects with bilateral high-frequency hearing loss; we examined associations between hearing loss characteristics and frequency discrimination of low-frequency stimuli in subjects with high-frequency hearing loss. **Design:** Cochlear dead regions were diagnosed using the TEN-HL test. A frequency discrimination test utilizing an adaptive three-alternative forced choice method provided difference limens for reference frequencies 0.25 kHz and 0.5 kHz. **Study sample:** Among 105 subjects with bilateral high-frequency hearing loss, unilateral dead regions were found in 15 subjects. These, and an additional 15 matched control subjects without dead regions, were included in the study. **Results:** Ears with dead regions performed best at the frequency discrimination test. Ears with a contralateral dead region performed significantly better than ears without a contralateral dead region at 0.5 kHz, the reference frequency closest to the mean audiogram cut-off, while the opposite result was obtained at 0.25 kHz. **Conclusions:** Results may be seen as sign of a contralateral effect of unilateral dead regions on the discrimination of stimuli with frequencies well below the audiogram cut-off in adult subjects with bilateral high-frequency hearing loss.

## INTRODUCTION

In some cases of cochlear hearing loss the function of inner hair cells and/or neurons at some regions along the basilar membrane is degraded to such a degree that little, if any, information regarding basilar membrane movement is communicated to the cochlear nucleus or to higher structures of the central auditory nervous system (CANS), including the primary auditory cortex (A1). Such regions are named “cochlear dead regions” (DR) (Moore et al, 2000; Moore, 2001). Previous studies report an enhanced ability to discriminate pure-tone stimuli with frequencies close to the edge frequency of cochlear dead regions in subjects with high-frequency hearing loss (McDermott et al, 1998; Thai-Van et al, 2002; Thai-Van et al, 2003; Kluk & Moore, 2006; Moore & Vinay, 2009). The present study investigates whether frequency discrimination of low-frequency stimuli differed between ears with and without contralateral high-frequency DRs in subjects with bilateral high-frequency hearing loss. It also examines associations between hearing loss characteristics and frequency discrimination of low-frequency stimuli in subjects with high-frequency hearing loss.

A tonotopic organization originating from the properties of the basiliar membrane is seen throughout the CANS including A1. Changes in the tonotopic organization of A1, and also some subcortical structures, have been found in animals following cochlear lesions (Irvine et al, 2003; Kamka et al, 2003). Areas of the auditory cortex that are deprived of input do not go silent, but respond to input from cochlear regions close to the site of the lesion (Huttunen et al, 2007). This causes an overrepresentation at certain frequencies in the cortex, where the area in which frequencies perceived in cochlear regions close to the damaged part of the cochlea are represented becomes larger than before the lesion occurred. Consistent with the assumption that an overrepresentation of certain frequencies in the cortex will lead to an enhanced ability to discriminate these frequencies, previous studies have shown that subjects with cochlear hearing loss have lower difference limens for frequencies close to the edge frequency of DRs (McDermott et al, 1998; Thai-Van et al, 2002; Thai-Van et al, 2003; Kluk & Moore, 2006; Moore & Vinay, 2007). Less uniform findings have been obtained in cases of unilateral hearing loss / DRs; it is not clear whether the increased ability to discriminate certain frequency in certain regions also occurs for the better ear. While Kluk & Moore (2006) found an enhanced ability to discriminate frequencies close to the $f_{cut\text{-}off}$ in the better ear in a subject with a unilateral DR, Moore & Vinay (2009) did not see this contralateral effect for three subjects with unilateral DRs, as they found enhanced DLF near $f_{cut\text{-}off}$ only for the ear with the DR. In the present study we use the definition of $f_{cut\text{-}off}$ of Thai-Van et al (2003) which defines the $f_{cut\text{-}off}$ as the highest test frequency above the audiogram edge (defined by visual inspection) at which the measured absolute threshold was within 5 dB of the best absolute threshold.

Moore & Vinay (2009) reported DLFs for subjects with high frequency hearing loss with and without DR: The subjects with DRs had lower DLFs on average than those without DRs at all frequencies except one (c.f. Tables 2-5 in Moore & Vinay, 2009). The difference in DLF between groups was significant only at the two test frequencies closest to the edge frequency, but this may depend on the sample size used and fact that no within-subject design was used (except in three subjects). Based on this finding, we argue that there is a possibility that DLFs for frequencies farther away from the edge frequency may be improved as well. It is possible that the cortical reorganization encompass areas leading to improved DLFs at frequencies farther separated from the DR edge frequency.

Based on these previous findings, the aim of this study was to investigate whether frequency discrimination of low-frequency stimuli differed between ears with and without contralateral high-frequency DRs in subjects with bilateral high-frequency hearing loss.

## MATERIAL AND METHODS

Subjects were recruited from patients referred for audiological assessment at Haukeland University Hospital. Only men aged 18 to 70 years with bilateral high-frequency hearing loss, and pure tone thresholds 20 dB HL or better at 0.25 and 0.5 kHz, were invited to participate in the study. We chose to include only men in order to decrease the number of variables. Patients with outer- or middle-ear pathology, or with a known retro-cochlear disorder, were not included in the study. Patients who met these primary criteria were tested for DRs using the TEN-HL test (Moore et al, 2004). Subjects who showed bilateral DRs were excluded from the study ($n = 33$). Subjects for whom the criteria for a DR were met for at least one of the test frequencies, and in one ear only, were asked to participate. For each such subject, an additional patient closely matched in age and hearing loss configuration but without DRs was recruited to be part of a control group. Among 105 patients (22-69 yrs., $M = 54$, $SD = 11$) who met the primary criteria for participation and subsequently were tested with the TEN-HL test, 15 (14%) (29-67 yrs., $M = 50$, $SD = 14$) were found to have unilateral DRs. After recruiting subjects to serve as the control group ($n = 15$) (33-66 yrs., $M = 52$, $SD = 14$), the study included 30 subjects (23-67 yrs., $M = 51$, $SD = 13$). All were asked to sign a letter of consent before the frequency discrimination test was carried out. Among the subjects with unilateral DRs ($n = 15$), the DR was in the right ear for seven of the subjects. The criterion for a DR was met at one test frequency for four subjects, at two test frequencies for four subjects, and at three test frequencies for seven subjects. At the test frequencies 0.5 kHz, 0.75 kHz and 1 kHz the criterion for a DR was never met. At 1.5 kHz the criterion was met once, while at 2, 3 and 4 kHz the criterion was met respectively eight, eleven and 15 times. The Norwegian Regional Committees for Medical and Health Research Ethics provided advance approval for the project (Project reference: 2011/494/REK-vest).

## Pure-tone audiometry

Pure-tone hearing thresholds were measured at 0.125, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6 and 8 kHz using an Interacoustics Affinity audiometer and TDH-39P earphones through the AC440 module version 1.8 implemented in the NOAH-software. The equipment was regularly calibrated according to ISO-389-1 (1998). Pure-tone-average hearing thresholds (PTA) were calculated using the mean thresholds for the frequencies 0.5, 1 and 2 kHz. In addition, a high-frequency pure-tone average (HFPTA) was calculated using the mean threshold for the frequencies 2, 4 and 8 kHz. The audiogram $f_{cut-off}$ was defined as the highest test frequency above the audiogram edge (defined by visual inspection) at which the measured absolute threshold was within 5 dB of the best absolute threshold, according to Thai-Van et al (2003). As a measure of audiogram slope, the increase in absolute threshold from $f_{cut-off}$ to one octave above this frequency was calculated. As an additional measure of audiogram slope the change in absolute threshold was calculated between the test frequencies 1 and 2 kHz and 2 and 4 kHz.

## TEN-HL TEST

The TEN-HL test was carried out according to Moore et al (2004) using the same Interacoustics Affinity audiometer and TDH-39P earphones as used for the pure-tone audiometry. The CD containing pure tones for test frequencies 0.5, 0.75, 1, 1.5, 2, 3 and 4 kHz and the TEN-HL masking noise was played using the internal DVD-ROM (HP GH60L) in a desktop Windows-computer. The pure tones and the TEN-HL noise were fed into two separate channels of the audiometer and played back monaurally allowing the levels of the pure tones and the TEN-HL noise to be adjusted separately. Using the calibration tone provided on the TEN-HL CD, the level in both channels was adjusted to give 0 dB HL on the VU meters, and levels were also confirmed in a Larson-Davis laboratories AEC-100 artificial ear. Absolute hearing thresholds from pure-tone audiometry were used to determine the level of the TEN-HL noise. An initial masking level of 70 dB HL was used for test frequencies where the absolute threshold was found to be 60 dB HL or better. At test frequencies where the absolute thresholds were worse than 60 dB HL, the level of the masking noise was set to be 10 dB HL higher than the absolute threshold. In cases where this would cause the masking level to exceed 90 dB HL the masking level was limited to 90 dB HL. The subject was asked to ignore the masking noise, and respond to the pure tones, as done in pure-tone audiometry. The test tone was first presented at a level corresponding to the unmasked threshold. If the subject responded, the level of the test tone was decreased by 10 dB and then increased in 5-dB steps until a response was given. This was repeated until the subject had responded two times at the same test tone level. Then, the level of the test tone was decreased by 10 dB and increased in 2-dB steps until a response was given. The test tone level was then decreased in 2-dB steps until the subject no longer responded and increased in 2-dB steps until a response was obtained. These two final steps involving increasing and decreasing the test tone level in 2 dB-steps were repeated until the subject gave two responses at the same test tone level. The right ear was tested first. Masked thresholds 10 dB higher than unmasked thresholds *and* 10 dB higher than the level of the masking noise were chosen as criteria for the presence of a DR (Moore et al, 2000; Moore, 2001; Moore et al, 2004; Moore, 2007).

## Frequency discrimination

Frequency discrimination of pure tones was tested using a three-alternative forced choice procedure. The custom-made software “SMAPH-lab” (created in MatLab by Jan Grenner, Skåne University Hospital in Lund/Lund University) was used for this purpose. Stimuli were generated with a sampling rate of 44.1 kHz by a 24-bit M-Audio JamLab external sound card and presented via Sennheiser HDA-200 circumaural earphones. Levels were confirmed using a Larson-Davis laboratories AEC-100 artificial ear. The rise and fall times of the pure-tone stimuli were 0.02 seconds with a plateau of 0.65 seconds. The levels of the tones were set to 30 dB SL to ensure sufficient audibility. In each trial, three pure tones separated by 0.3 second long pauses were presented. Two tones were set to the reference frequency ($f_{ref}$ 0.25 or 0.5 kHz), while one tone was set to the test frequency, which was higher. The position of the tone with the test frequency was selected at random. The subject was instructed to press key 1, 2 or 3 on a numerical keyboard to indicate the odd one out. The subject had to make a choice before the next trial was presented. The instructions were given both orally and in writing on the computer monitor prior to the test. Initially the difference between $f_{ref}$ and the test frequency was 20 %. This difference was reduced after a correct response and increased if the wrong tone was selected. Each response from the subject caused Δf to change by a factor of 10^0.25 in the 11 first trials, and then the amount of change in the test frequency was reduced by 50%. At each reference frequency a maximum of 30 trials or 18 reversals was carried out. The program then calculated the geometrical mean using values at reversal points, after removing the highest and the lowest value. This provided the relative difference limen (DLF) reflecting the smallest deviation from the reference frequency in per cent the subject could perceive. For subjects with DRs the ear with a DR was tested first, while for subjects without DRs the ear with the worse HFPTA was tested first.

## RESULTS

Since there were 15 subjects with unilateral DRs and 15 subjects without DRs, the study included 60 ears in total. These were categorised in the following groups to allow us to do the necessary comparisons: Ears with DRs ($n$ = 15); ears with contralateral DRs ($n$ = 15); ears with neither ipsi- nor contralateral DRs ($n$ = 30); ears without DRs ($n$ = 45). The significance of differences between groups of ears was tested using Mann-Whitney U-tests, and the alpha-level was set to 0.05. The alpha level was adjusted with a Bonferroni-correction by dividing the alpha level by the number of Mann-Whitney U-tests performed ($n$ = 15), providing a corrected alpha level of 0.003.

## Pure-tone audiometry

Table 1 shows mean PTA, HFPTA and $f_{cut\text{-}off}$ for ears with ipsilateral, contralateral or no DRs. PTA was higher for ears with DRs than for ears without DRs. The difference was not significant when compared to ears with a contralateral DR ($U(29) = 94.50$, $p = 0.45$), or when compared to ears without a contralateral DR ($U(44) = 121.50$, $p = 0.012$). In ears without DRs, PTA did not differ significantly between ears with and without a contralateral DR ($U(44) = 158$, $p = 0.104$). Ears with DR had higher HFPTA than ears without DR, but in comparison to ears without a DR this difference was not significant ($U(44) = 130$, $p = 0.022$). When compared among ears without DR, no significant difference in HFPTA was found between the ears with and without a contralateral DR. When change in absolute threshold from $f_{cut\text{-}off}$ and one octave above was used as a measure of audiogram slope, no significant ($U(59) = 257.50$, $p = 0.169$) difference was seen between ears with and without DR. This was also true for the other two measures of audiogram slope.

## Frequency discrimination

Results from the frequency discrimination test for ears with ipsilateral, contralateral or no DR are shown in table 2 as mean ($M$) DLFs with standard deviations ($SD$). DLF was significantly lower at 0.25 kHz for ears with DR than for both ears with ($U(29)= 1$, $p < 0.001$) and without ($U(44)= 32$, $p < 0.001$) a contralateral DR. DLF was significantly lower at 0.5 kHz for ears with DR than for both ears with ($U(29)= 1$, $p < 0.001$) and without ($U(44)= 0$, $p < 0.001$) a contralateral DR. At 0.25 kHz ears without a contralateral DR had significantly ($U(44)=63$, $p$

< 0.001) lower DLF than ears with a contralateral DR. At 0.5 kHz ears with a contralateral DR showed significantly lower DLF than ears without a contralateral DR ($U(44)= 0$, $p < 0.001$).

Spearman's rank correlation coefficient (rho) showed a weak but significant positive correlation between DLF at 0.25 kHz and 0.5 kHz over all 60 ears ($r_s(58)= 0.524$, $p < 0.001$). For ears with DR, the correlation between these variables was strong and significant ($r_s(13)= 0.998$, $p < 0.001$) and this was also the case for ears with a contralateral ($r_s(13)=0.999$, $p < 0.001$) DR and ears without a contralateral DR ($r_s(28)= 0.999$, $p < 0.001$). Figure 1 shows a scatter plot of individual DLFs at 0.25 and 0.5 kHz for ears with ipsilateral, contralateral or no dead region.

A weak but significant negative correlation was observed between PTA and DLF at both 0.25 kHz ($r_s(58) = -0.296$, $p = 0.038$) and 0.5 kHz ($r_s(58) = -0.439$, $p < 0.001$). Weak but significant correlations were also observed between HFPTA and DLF at 0.25 kHz ($r_s(58) = -0.326$, $p = 0.01$) and 0.5 kHz ($r_s(58) = -0.346$, $p = 0.007$). There was no significant correlation between audiogram slope and DLF at either 0.25 kHz ($r_s(58)= -0.219$, $p = 0.092$) or 0.5 kHz ($r_s(58)= -0.05$, $p = 0.707$).

## DISCUSSION

This study shows that subjects with high-frequency hearing loss and unilateral DRs perform better than those without DRs, when DLF is measured at frequencies well below the audiogram cut-off frequency.

Using the TEN test the number of subjects with DRs among our screened subjects with HF-loss (n=105) was 15 (unilateral DRs) and 33 (bilateral DRs); which is in total 46 %

Differences in study design and subjects make a direct comparison with earlier studies difficult, but the prevalence of DRs seems similar to that reported by Preminger et al (2005) and Cox et al (2011).

Earlier studies (McDermott et al, 1998; Thai-Van et al, 2002; Thai-Van et al, 2003; Kluk & Moore, 2006; Moore & Vinay 2009) have shown intrasubject enhancements in DLF at frequencies close to $f_{cut\text{-}off}$ in patients with hearing loss configurations similar to those in our study. Our results show that significant differences in DLF for low frequencies can be seen at group level when comparing ears with and without DRs in subjects with bilateral high-frequency hearing loss. When we compared results among ears without DRs, the ears with contralateral DRs had significantly lower DLF at 0.5 kHz than the ears without contralateral DRs. This is in agreement with Kluk & Moore (2006) who in a study including 13 subjects with a DR in at least one ear found that one subject with a unilateral DR had enhanced DLF in the contralateral ear at frequencies corresponding to $f_{cut\text{-}off}$ in the ear with the DR. However, these findings were not reproduced by Moore & Vinay (2009), who found three subjects with unilateral DRs that showed enhanced DLF only in the ear with the DR. Comparison of these studies and the present one is complicated by the small number of subjects with unilateral DRs and because different frequencies were tested for DLFs. Even though we measured DLF at two test frequencies and further from $f_{cut\text{-}off}$, only our results at 0.5 kHz corroborate those of Kluk & Moore (2006). At 0.25 kHz we found that the average DLF was poorer for the ears with contralateral DRs. The average DLF was even poorer than seen among the ears without contralateral DRs. The cause of this latter finding is unclear. However, the observations at 0.5 kHz suggest the central processing of input from a cochlea with a high-frequency hearing loss can be affected by the presence of a contralateral DR (Thai-Van et al, 2007).

The diagnosis of DRs in our subjects could have been strengthened by the use of psychoacoustic tuning curves (PTCs). PTCs could also have provided more accurate estimates of edge frequencies for the DRs, and future studies should include such measurements. Also, the levels of the tones used in the frequency discrimination test should have been roved to reduce the possible influence of loudness cues (Kluk & Moore, 2006). On the other hand, we performed the frequency discrimination test at frequencies with absolute thresholds 20 dB HL or better, and at frequencies well below the audiogram cut-off frequency. This should reduce influence of loudness cues on the frequency discrimination for our subjects.

The adaptive procedure used in the frequency discrimination test tracks the 50 % correct point. This may be undesirable, as this is not far from the chance score of 33 %. Though, all subjects were tested using the same procedure and thus it should not substantially affect differences between groups.

If the finding of enhanced DLF for certain frequencies is in fact a result of tonotopic reorganization at a cortical level, it might not solely depend on a completely DR, as our results showed that in subjects with high-frequency hearing loss, worse PTA and HFPTA to some extent correlated to a lower DLF. Further, and also depending on the assumption that the difference in DLF between ears with and without DRs is due to cortical reorganization, the presence of a unilateral high-frequency DR seems to significantly improve the ability to discriminate low frequency pure tones. The enhanced DLFs in ears with ipsi- or contralateral DRs seem to be hard to explain solely as a consequence of a cochlear phenomenon. Reversal of DLF enhancement after fitting of hearing aids (Gabriel et al, 2005; Thai-Van et al, 2010) indicates a kind of “secondary” plasticity, but Kluk & Moore (2006) found enhanced DLF in their subjects regardless of hearing aid use. We did not include use of hearing aids as a variable so we do not know if the DLFs have a relationship to use of amplification.

Duration of hearing loss was also not recorded, but as the age distribution in the DR and non-DR groups was similar, we believe that this factor has not influenced the results.

Further studies should measure DLF over a wider range of frequencies for subjects with unilateral DRs.

## Conclusions

A significantly better ability to discriminate pure-tone stimuli at reference frequencies 0.25 kHz and 0.5 kHz was found for ears with DRs than for ears without DRs. The DLF was lower at 0.5 kHz than at 0.25 kHz for ears with either an ipsi- or contralateral DR but not for ears with neither ipsi- nor contralateral DRs. This may indicate that the DR can cause enhanced discrimination of pure-tone stimuli further from the DR than observed in earlier studies, and this may be true also for ears with contralateral DRs.

## DECLARATION OF INTEREST

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.


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# TABLES

**Table 1**: PTA, HFPTA and $f_{cut\text{-}off}$ for ears with ipsilateral, contralateral or no dead regions.

| | | | ***PTA(dB)*** | ***HFPTA(dB)*** | ***$f_{cut\text{-}off}$ (Hz)*** |
|---|---|---|---|---|---|
| ***DR*** | Ipsi (*n*= 15) | Mean | 28.3 | 71.2 | 950 |
| | | *SD* | 7.3 | 7.3 | 194 |
| | Contra (*n*=15) | Mean | 26.4 | 63.5 | 933 |
| | | *SD* | 7 | 12.8 | 200 |
| | None (*n*= 30) | Mean | 23 | 64 | 958 |
| | | *SD* | 6.0 | 9 | 175 |
| | Total (*n*= 60) | Mean | 25.3 | 65.7 | 958 |
| | | *SD* | 6.9 | 10 | 167 |

**Table 2:** DLF at 0.25 and 0.5 kHz for ears with ipsilateral, contralateral or no dead regions.

The DLF is presented as per cent deviation from the reference frequency.

| | | | ***DLF0.25kHz*** | ***DLF0.5kHz*** |
|---|---|---|---|---|
| ***DR*** | Ipsi (*n*= 15) | Mean | 1.13 | .55 |
| | | *SD* | .60 | .21 |
| | Contra (*n*=15) | Mean | 3.45 | 1.24 |
| | | *SD* | .48 | .25 |
| | None (*n*= 30) | Mean | 2.39 | 2.44 |
| | | *SD* | .84 | .54 |
| | Total (*n*= 60) | Mean | 2.34 | 1.67 |
| | | *SD* | 1.09 | .91 |

## FIGURES

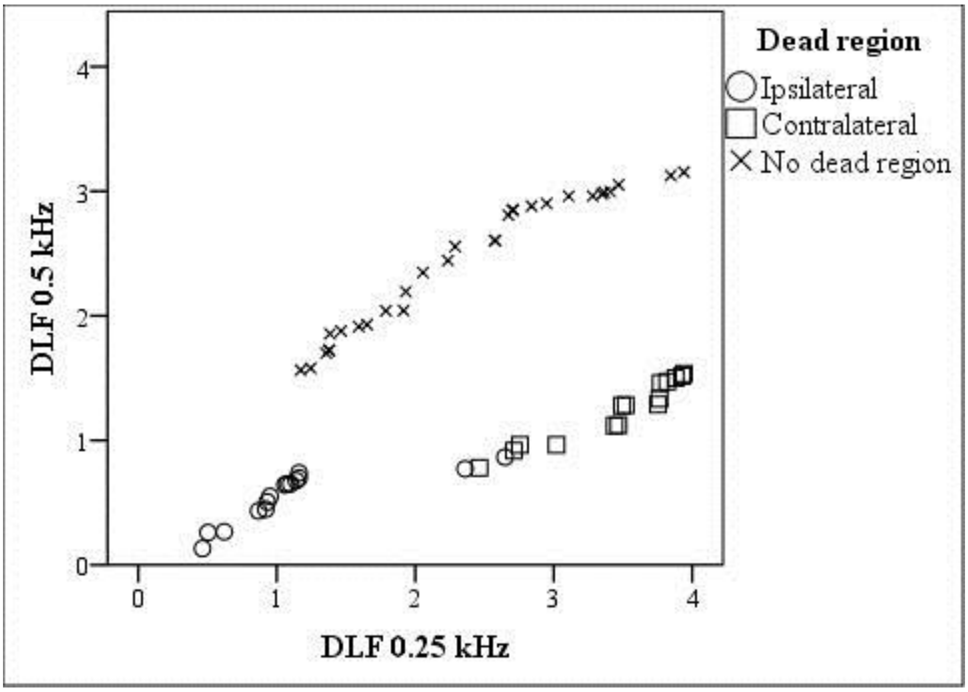


**Figure 1:** Scatter plot of DLF at 0.25 and 0.5 kHz for ears with ipsilateral, contralateral or no dead region. The DLF is presented as per cent deviation from the reference frequency.