The Analysis of Audiometric Measurements before and after Low-Level Laser Therapy of Spanish Patients with Hyperacusis.

Joaquín Prósper
Otoclínica
Centro Médico de Terapias Auditivas
Príncipe de Vergara, 57, 1C, 28006 Madrid
email: consulta@otoclinica.es
web: www.otoclinica.es
phone: +34-915648744

and

Jan Graffelman
Department of Statistics and Operations Research
Universitat Politècnica de Catalunya
Av. Diagonal 647, 08028 Barcelona, Spain.
email: jan.graffelman@upc.edu
phone: +34-93-4011739
fax: +34-93-4016575

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1 Introduction

This document describes the analysis of several audiometric measurements, provided by Dr. Joaquín Prósper, made in a group of patients treated for Hyperacusis by Otoclínica in Spain. Otoclínica treats patients with a variety of hearing problems (tinnitus, hyperacusis, hypoacusis, vertigo, Menière's syndrome) by applying Low Level Laser Therapy (LLLT). The database analyzed in this document is a selection of patients from Otoclínica that suffered from Hyperacusis. A patient was classified as suffering from Hyperacusis if his or her uncomfortable level (UCL) was below 95 dB for at least two frequencies of the 22 frequency measurements (11 in each ear). The UCL is the sound level at which patients experience as uncomfortable or painful. The database under study consisted of 57 patients. For each patient, the following variables were registered:

1. Demographic variables: age and sex.

2. Identified pathology: tinnitus, vertigo, hyperacusis or hypoacusis.

3. Standard audiometric measurements for air conduction at 11 frequencies from 125Hz through 8kHz (125Hz, 250Hz, 500Hz, 750Hz, 1kHz, 1.5kHz, 2kHz, 3kHz, 4kHz, 6kHz, 8kHz) for the right and the left ear, before and after treatment with LLLT.

4. Standard audiometric measurements for bone conduction at 10 frequencies (the same frequencies as for air conduction, the lowest frequency, 125Hz, not being measured for bone conduction). These variables are not used in the statistical analysis in the next section.

5. Uncomfortable levels for both ears, before and after treatment, for the same set of 11 frequencies.

6. Several index variables calculated on the basis of the aforementioned audiometric measurements. In particular, in the statistical analysis that is to follow we used:

    - The Pure Tone Average (PTA). The PTA was calculated for each patient as the average of the 11 air conduction measurements, for both ears and before and after treatment.
    - The Articulation Index (AI). The AI is supplied automatically by the computer software used for audiometry, and expressed as a percentage. See Humes (1986) for more information on this index. The AI was also registered for both ears, before and after treatment.

- The Dynamic range (DR). The DR was calculated as the average of the 11 differences between uncomfortable levels and air conduction levels. The DR was calculated separately for both ears, before and after treatment.
- The Percentage of Observations with Hyperacusis (POH). We calculated how many patients suffered from Hyperacusis for each frequency, for both ears and before and after treatment.

In the remainder of this document we give a brief demographic description of the sample of patients in Section 2. The main results of the statistical analysis of the audiometric information are given in Section 3. Some conclusions and final remarks in Section 4 complete this report.

2 Sample description

The data concern individuals that visited Otoclínica for a variety of complaints (tinnitus, vertigo, hearing loss, etc.). The frequency of the different complaints in the sample is shown in Figure 1. Tinnitus and vertigo are the most common complaints. Despite this classification, because patients often suffered several complaints simultaneously, all 57 individuals qualified as suffering from hyperacusis. Patients ranged in age from 18 to 81 years, with an average of 47.4 years and a median of 45 years. The sample consists of 31 males and 26 females.

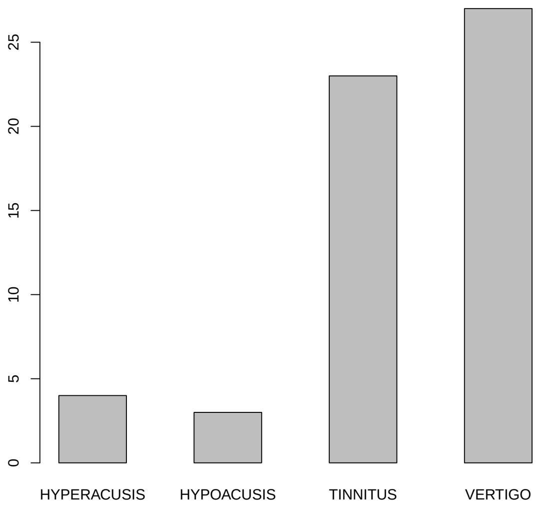

Figure 1: Bar plot with the frequency of hearing complaints in a sample of 57 patients.

3 Analysis of audiometric information

In this section we present some results of the statistical analysis of the audiometric information. Graphics and descriptive statistics of most of the variables involved (air conduction, PTA, AI, uncomfortable levels, DR, POH) are present, usually stratified by ear and frequency. Statistical tests are used to assess the significance of differences in level observed for all variables before and after LLLT.

3.1 Air conduction and the Pure Tone Average (PTA)

Figure 2 shows boxplots of the PTA before and after treatment for both ears. Figure 2 shows the median of the PTA is in the range 10-20 dB, with

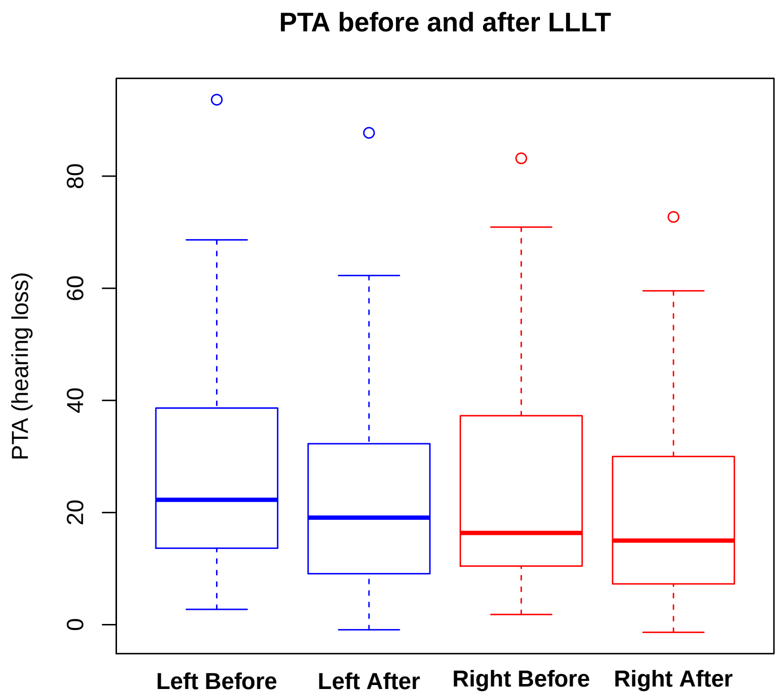

Figure 2: Boxplots of PTA before and after LLLT for both ears.

lower values after treatment in both ears. The distribution of PTA is non-symmetric, skewed to the right, with outliers in the right tail due to the existence of patients with notable hearing loss. The outliers correspond to patient 19 with extreme hearing loss in the left ear, and to patient 12 with extreme hearing loss in the right ear. Table 1 shows descriptive statistics (sample size N, mean, standard deviation, median, first and third quartile, minimum and maximum) for the four PTA measurements.

	N	Mean	Stdev	Median	Q1	Q3	Min	Max
Left before LLLT	57	28.37	19.48	22.27	13.64	38.64	2.73	93.64
Left after LLLT	57	23.84	19.03	19.09	9.09	32.27	-0.91	87.73
Right before LLLT	57	24.99	19.29	16.36	10.46	37.27	1.82	83.18
Right after LLLT	57	19.97	17.60	15.00	7.27	30.00	-1.36	72.73

Table 1: Descriptive statistics for PTA for both ears, before and after LLLT

Table 1 shows a difference in PTA level (as measured by the mean) of about 5 dB, PTA being lower after LLLT for both ears. PTA has a standard deviation of about 20 dB for both ears. We note that negative values of the minimum of the PTA occur. This is due to patients that have an air conduction profile of 0 dB, with occasionally one or two negative air conduction measurements (-5 dB). The differences in PTA before and after treatment were statistically significant at the 5% level for both ears, as judged by a Student t test (T = -9.771, p = 1.05e-13 and T = -7.872, p = 1.25e-10 for left and right ear respectively). Similar results were obtained by a non-parametric Wilcoxon test (left ear, p = 2.95e-10, right ear, p = 6.94e-10).

PTA is a global indicator of hearing loss and averages hearing loss over all frequencies. We also studied hearing loss (AC, air conduction) as a function of frequency, and plotted mean AC as a function of frequency for both ears in Figure 3.

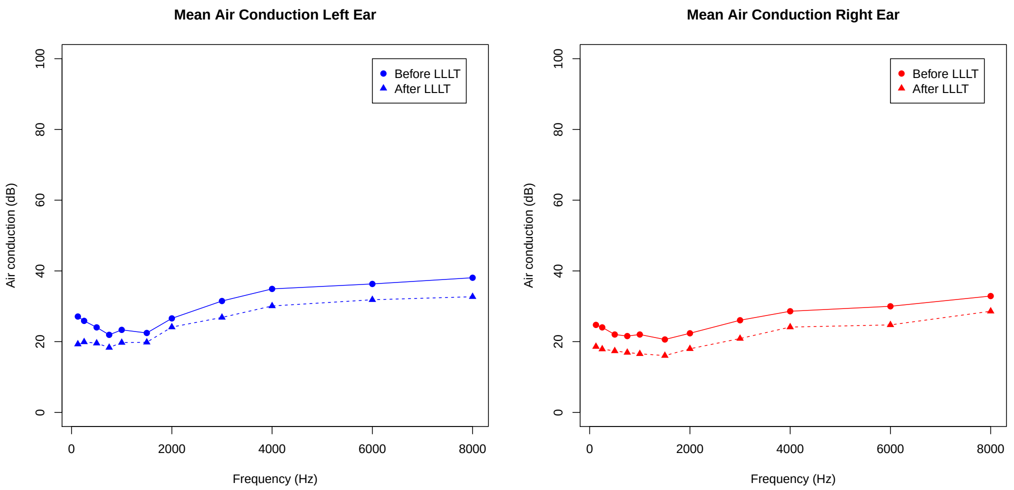

Figure 3: Air Conduction (in dB) as a function of frequency.

This graph shows that:

- The difference of 5 dB is observed for almost all frequencies in both ears.
- There is more hearing loss for higher frequencies (>2kHz.)

We also studied the variability in hearing loss (air conduction) as a function of frequency. The resulting plots are shown in Figure 4.

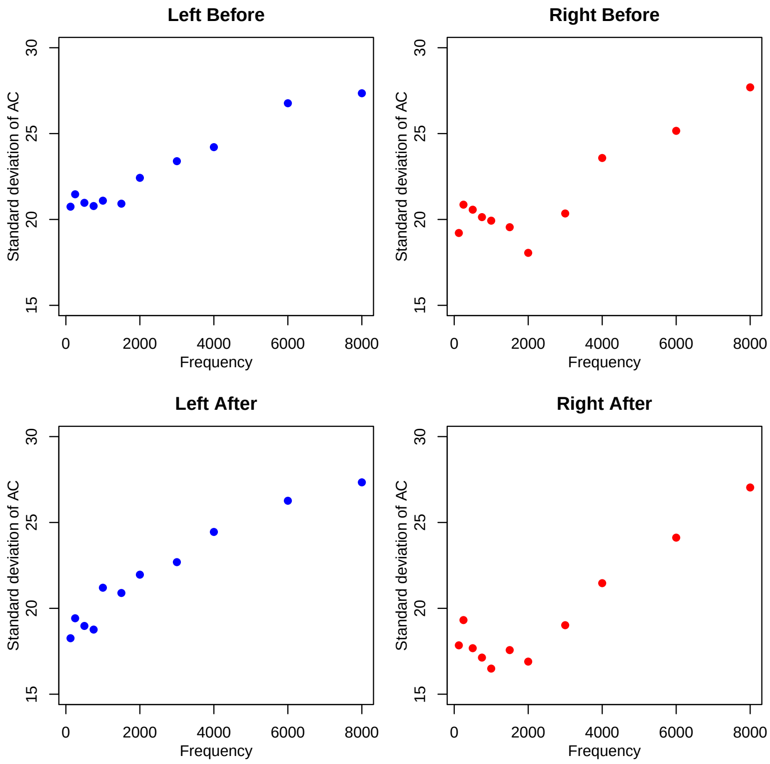

Figure 4: Standard deviation of Air Conduction as a function of frequency.

These plots show that the standard deviation rises as a function of the frequency. It means that patients show larger variability in their ability to hear high frequency tones than low frequency tones.

In Figure 5 we show a multivariate plot of all air conduction measurements prior to LLLT (22 variables for all 57 patients) simultaneously, obtained by a principal component analysis of the air conduction measurements. This analysis reveals the following aspects of the air conduction measurements: air conduction measurements for different frequencies in the same ear are all highly correlated. Air conduction measurements for the left ear are largely uncorrelated to air conduction measurement for the the right ear. Patients 12 and 19 stand out as having the worst AC measurements for right and left ear respectively. Patients 27 and 2 stand out as having bad AC measurements for both ears. A cluster of patients in the second quadrant that have relatively better hearing.

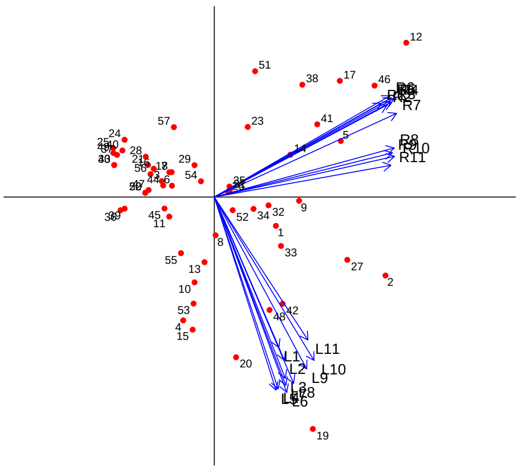

Figure 5: Summary graph of all air conduction measurements prior to LLLT obtained by principal component analysis. R1 through R11 air conduction variables for 11 frequencies in the right ear, L1 through L11 correspondingly for the left ear.

3.2 The Articulation Index (AI)

Figure 6 shows boxplots of the AI before and after treatment for both ears.

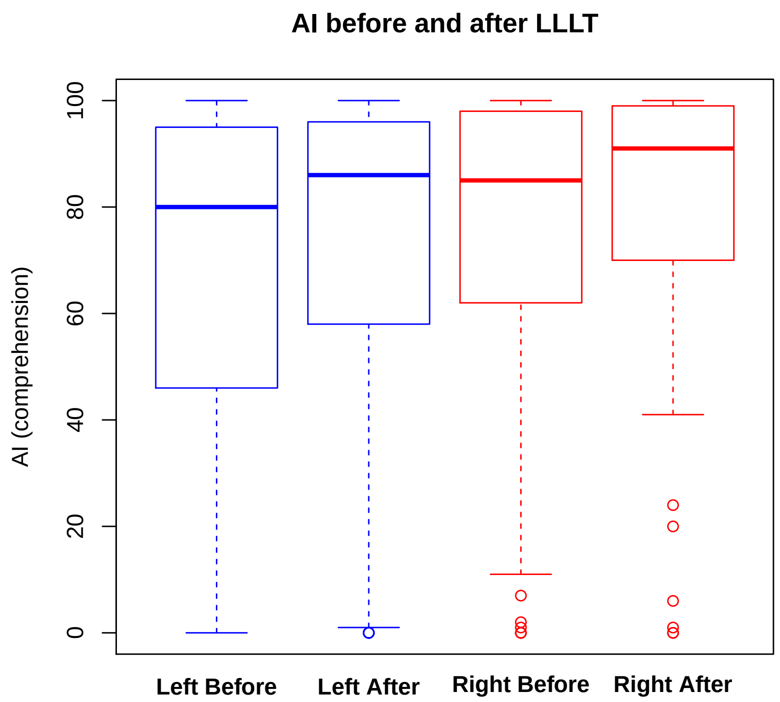

Figure 6: Boxplots of AI before and after LLLT for both ears.

These boxplots show a increase in the AI after LLLT for both ears. The distribution of the AI is skewed to the left due to the existence of patients with very low values for the AI. Descriptive statistics for the AI before and after LLLT and for both ears are given in Table 2.

	N	Mean	Stdev	Median	Q1	Q3	Min	Max
Left before LLLT	57	66.70	33.18	80.00	46.00	95.00	0	100
Left after LLLT	57	71.77	32.48	86.00	58.00	96.00	0	100
Right before LLLT	57	71.93	33.87	85.00	62.00	98.00	0	100
Right after LLLT	57	78.23	29.26	91.00	70.00	99.00	0	100

Table 2: Descriptive statistics for AI for both ears, before and after LLLT

The results in this table show a 5-6% increase in the AI after LLLT. The variability of the AI is large, as AI has a standard deviation of about 30%.

Differences in the AI before and after treatment were statistically significant for both ears, as judged by a Student t test (T = -5.307, p = 1.98e-06 and T = -4.582, p = 2.62e-05 for left and right ear respectively). A non-parametric Wilcoxon test (p = 2.9e-07 and p = 2.13e-07 for left and right ear respectively) leads to the same conclusions.

The index variables AI and PTA are closely related. Scatterplots for AI and PTA for the corresponding ears and before and after treatment correspondingly are shown in Figure 7.

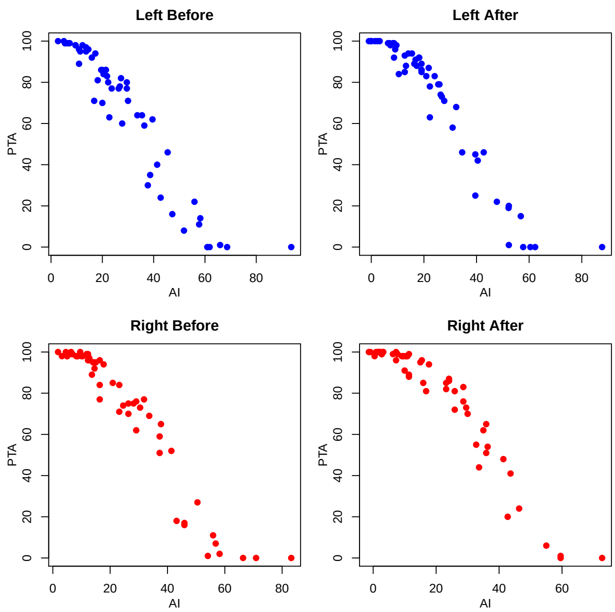

Figure 7: The PTA plotted against the AI, for both ears and before and after LLLT

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These figures show that PTA and AI are inversely related and that they measure largely the same thing. The relationship PTA versus AI seems S-shaped and non-linear.

3.3 Uncomfortable levels

Uncomfortable levels (UCL) were measured for 11 frequencies in both ears. We created an index, similar to the PTA, that averages the UCL over the 11 frequencies for each ear. Descriptive statistics of these mean UCL's are given in Table 3. Table 3 shows the mean UCL to be about 16 dB higher after

	N	Mean	Stdev	Median	Q1	Q3	Min	Max
Left before LLLT	57	80.70	12.30	80.00	72.27	89.09	52.27	113.18
Left after LLLT	57	96.24	9.94	95.00	88.64	105.45	69.55	114.55
Right before LLLT	57	78.97	12.90	79.55	70.91	88.18	50.00	103.82
Right after LLLT	57	94.94	8.74	95.00	89.09	100.45	69.55	112.91

Table 3: Descriptive statistics for mean UCL for both ears, before and after LLLT

LLLT for both ears. The observed differences are statistically significant, as judged by Student t test (T = -11.862, p = <2e-16 and T = -12.548, p = <2e-16 for left and right ear respectively), and a non-parametric Wilcoxon test (p = 5.13e-11 and p = 5.12e-11 for left and right ear respectively). Figure 8 shows the mean UCL for both ears as a function of frequency.

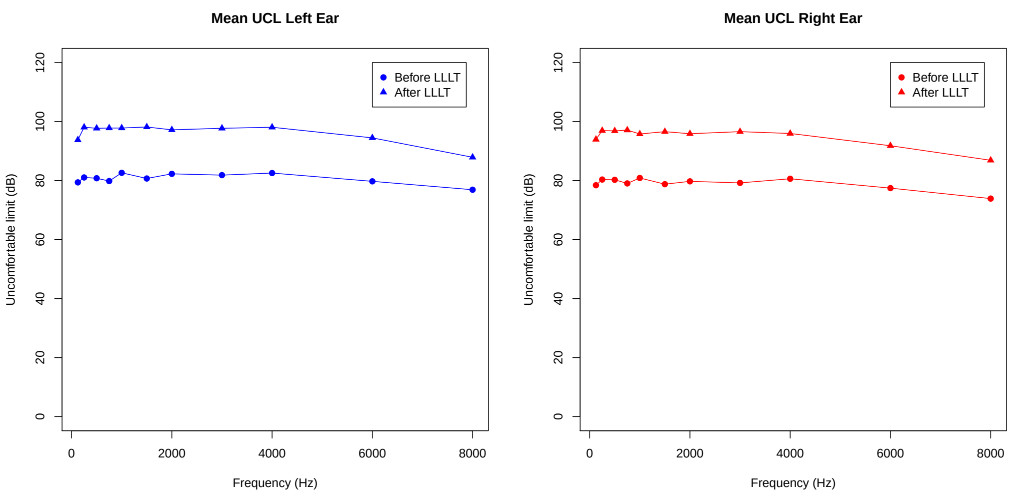

Figure 8: Uncomfortable levels as a function of frequency.

Figure 8 shows that the mean UCL shows little variation as a function of frequency, and a difference of approximately 16 dB is observed for all frequencies.

3.4 The Dynamic Range (DR)

The DR was calculated as the difference between the UCL and the air conduction for all frequencies, and these differences were averaged over the eleven frequencies. Figure 9 shows boxplots of the average DR before and after treatment for both ears.

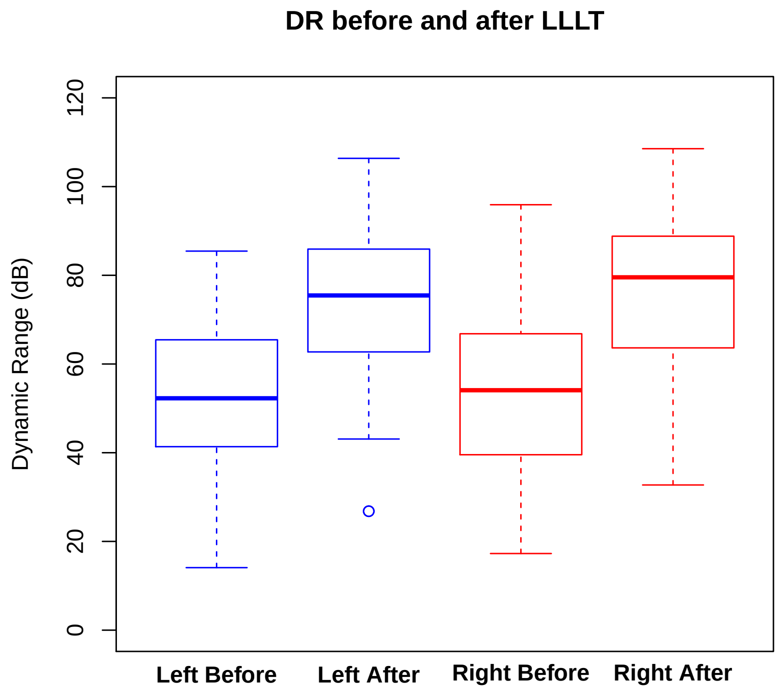

Figure 9: Boxplots of DR before and after LLLT for both ears.

Descriptive statistics for the DR are given in Table 4. The table shows an increment of 20 dB in DR after LLLT, and a standard deviation of 18 dB. Differences in DR before and after treatment were statistically significant for both ears, as judged by a Wilcoxon test (p = 5.12e-11 and p = 5.13e-11 for left and right ear respectively).

	N	Mean	Stdev	Median	Q1	Q3	Min	Max
Left before LLLT	57	52.33	17.25	52.27	41.36	65.45	14.09	85.45
Left after LLLT	57	72.40	17.81	75.45	62.73	85.91	26.82	106.36
Right before LLLT	57	53.97	19.51	54.09	39.55	66.82	17.27	95.91
Right after LLLT	57	74.96	17.71	79.55	63.64	88.82	32.73	108.55

Table 4: Descriptive statistics for mean DR for both ears, before and after LLLT

3.5 The Percentage of Observations with Hyperacusis

For each frequency, the number of patients with hyperacusis was counted, both before and after LLLT and separately for both ears. Percentages of patients with hyperacusis for a given frequency are plotted in Figure 10.

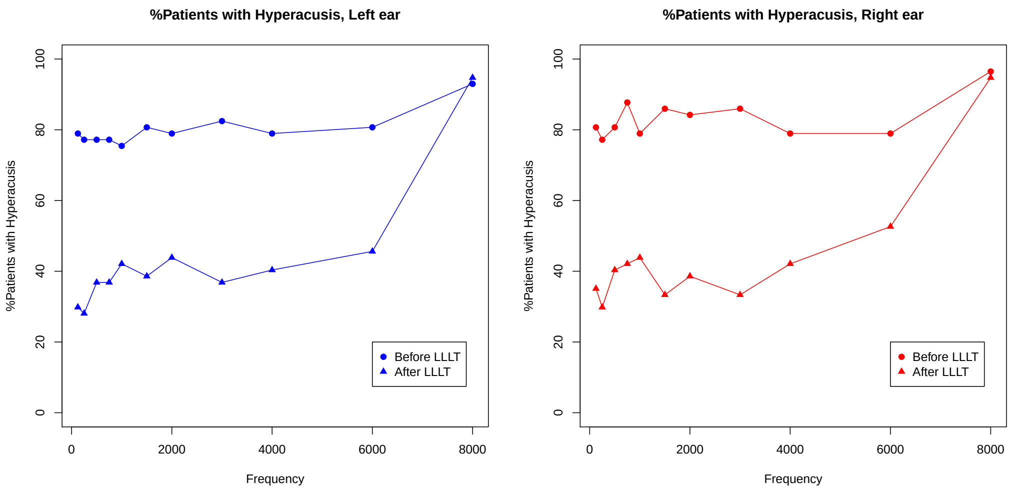

Figure 10: % Patients with hyperacusis as a function of frequency.

Figure 10 shows the percentage of patients with hyperacusis to be lower after LLLT, for all frequencies except 8kHz. At 8kHz, no difference is observed. This is probably due to a physical limitation in the audiometric equipment, which has a maximum of 95 dB at 8kHz, and improvements beyond this limit cannot be measured. Differences in percentages before and after LLLT are given in Tables 5 and 6 for left ear and right ear respectively. We tested the null hypothesis of equal proportions prior and after LLLT for each frequency. Results (chi-square statistics and p-values) are summarized in the same tables.

After LLLT, the percentage of patients with hyperacusis was about 30-50% lower for all frequencies except 8kHz. Differences in percentages are seen to be statistically significant for all frequencies except for 8kHz.

	Frequency	Before LLLT (%)	After LLLT (%)	Decrease(%)	Chi-square	p-value
1	125	78.9	29.8	49.10	26.0	3.4e-07
2	250	77.2	28.1	49.10	26.0	3.4e-07
3	500	77.2	36.8	40.40	21.0	4.5e-06
4	750	77.2	36.8	40.40	21.0	4.5e-06
5	1000	75.4	42.1	33.30	17.1	3.6e-05
6	1500	80.7	38.6	42.10	22.0	2.7e-06
7	2000	78.9	43.9	35.10	18.1	2.2e-05
8	3000	82.5	36.8	45.60	24.0	9.4e-07
9	4000	78.9	40.4	38.60	20.0	7.6e-06
10	6000	80.7	45.6	35.10	18.1	2.2e-05
11	8000	93.0	94.7	-1.80	0.0	1

Table 5: Percentages of patients with Hyperacusis for the left ear

	Frequency	Before LLLT (%)	After LLLT (%)	Decrease(%)	Chi-square	p-value
1	125	80.7	35.1	45.60	24.0	9.4e-07
2	250	77.2	29.8	47.40	25.0	5.6e-07
3	500	80.7	40.4	40.40	21.0	4.5e-06
4	750	87.7	42.1	45.60	24.0	9.4e-07
5	1000	78.9	43.9	35.10	16.4	5.1e-05
6	1500	86.0	33.3	52.60	28.0	1.2e-07
7	2000	84.2	38.6	45.60	24.0	9.4e-07
8	3000	86.0	33.3	52.60	28.0	1.2e-07
9	4000	78.9	42.1	36.80	19.0	1.3e-05
10	6000	78.9	52.6	26.30	13.1	3e-04
11	8000	96.5	94.7	1.80	0.0	1e+00

Table 6: Percentages of patients with Hyperacusis for the right ear

4 Conclusions and discussion

The PTA is defined as the average of the air conduction over all 11 frequencies. This implies that the PTA can strongly decrease if a patient has a low value for the air conduction for one or two frequencies only. This (undesirable) situation could be avoided if the PTA would be calculated as the median. The same issue arises in all computations where we average PTA, AC, UCL over patients. In this report we used averages as the summary statistics in all cases.

The DR was calculated as an average over the 11 frequencies, though these frequencies are not uniformly distributed. An alternative measure would be the area between the UCL curve and the air conduction curve. This area can exactly be calculated, and incurs no loss of information due to averaging.

Strong negative correlations were found between PTA and AI whenever these variables referred to the same ear. Though these variables represent differently defined indexes of the air conduction measurements, they apparently measure largely the same thing.

Index variables PTA, AI, mean UCL, mean AC, mean DR and percentage of patients with hyperacusis all showed a difference in level prior and after LLLT. PTA was on average 5 dB lower after LLLT. AI was as on average 5-6% higher after LLLT. Average UCL levels were on average 16 dB higher after LLLT. The DR augmented 20 dB on average, and the POH decreased by 30-50%. Results were similar for both ears, and, with the exception of POH, approximately the same differences were observed over all 11 measured frequencies.

This report shows that all observed changes of the index variables (PTA, AI, DR, mean ACL, mean UCL, POH) after LLLT are statistically significant, implying improvements in certain hearing parameters and symptoms of patients treated by irradiation with laser photo-therapy[1].

[1]Second author's note: However, it should be kept in mind that this study concerns data of *patients only*, and that the data do not correspond to a randomized clinical trial with cases and controls. This means that it cannot be excluded that the observed improvements are due to other factors such as a placebo effect, or curing due to other causes in the course of time.

References

Humes, L. E., D. D. Dirks, T. S. Bell, C. Ahlstrom, and G. E. Kincaid (1986). Application of the articulation index and the speech transmission index to the recognition of speech by normal-hearing and hearing-impaired listeners. *Journal of Speech and Hearing Research 29*, 447–462.