

AUDIOLOGY

Effect of loading of the central part of the tympanic membrane on pure tone audiometry

Applicazione di pesi a livello della parte centrale della membrana timpanica: effetti sull'audiometria tonale

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SUMMARY

This study was conducted to determine the effects of loading of the central part of the tympanic membrane by different weights on pure tone audiometry of healthy ears. Sixty patients with normal otoscopic view, normal pure tone audiometry and wide external auditory canal to allow direct and endoscopic visualization of TM, but without any history of ear surgeries, were selected and divided equally and randomly into two groups. Loading of the central part of the TM was carried out using weights ranging from [(1 λ) 13.6 mg] to [(40 λ) 544 mg]; (λ) is a symbol for the weight of 1 microliter of mercury. The study was carried out in two steps assisted by direct oto-endoscopy, and pure tone audiometry was used to measure the effects of loading on both air and bone conduction hearing. Air conduction hearing thresholds increased in a statistically significant pattern at low frequencies, 500 Hz, 1000 Hz and 2000 Hz, when the TM was loaded by 340 mg (25 λ). The maximal effect was recorded at 544 mg (40 λ), which affected air conduction hearing at all tested frequencies (500 Hz, 1000 Hz, 2000 Hz and 4000 Hz). However, no statistically significant effect was detected on bone conduction hearing thresholds throughout the study. In conclusion, loading of the tympanic membrane by different masses affects the air conduction hearing threshold by only 340 mg (25 λ), which is very large in comparison to the mass of ossicles, without any significant effects on bone conduction hearing.

KEY WORDS: Loading • The central part of the Tympanic Membrane • Compressed aluminum pellets • Pure tone audiometry • Hearing threshold

RIASSUNTO

Questo studio è stato condotto al fine di determinare gli effetti sull'audiometria tonale dell'applicazione di masse di peso differente a livello della porzione centrale della membrana timpanica di un orecchio sano. Sono stati selezionati sessanta pazienti con anamnesi negativa per pregressa chirurgia dell'orecchio, aventi otoscopia nella norma, soglia audiometrica tonale nella norma, e un canale uditivo esterno sufficientemente ampio da permettere la visione endoscopica diretta della membrana timpanica. I pazienti sono stati equamente suddivisi in maniera randomizzata in due gruppi, Gruppo I e Gruppo II. Sono state utilizzate masse di differente peso, da 13,6 mg (1 λ) a 544 mg (40 λ); λ è pari al peso di un microlitro di mercurio. Lo studio è stato condotto in due steps, sotto visione otoendoscopica; l'audiometria tonale è stata utilizzata per valutare l'effetto dell'applicazioni dei pesi, sia sulla via aerea sia sulla via ossea. Con l'applicazione di un peso pari a 340 mg (25 λ), la soglia per via aerea è aumentata in maniera statisticamente significativa alle frequenze di 500, 1000 e 2000 Hz. Il massimo risultato è stato ottenuto con un peso pari a 544 mg (40 λ), che ha avuto effetto su tutte le frequenze testate (500, 1000, 2000 e 4000 Hz). Tuttavia, non è stato registrato alcun effetto statisticamente significativo sulla conduzione per via ossea. In conclusione, l'applicazione di pesi a livello della membrana timpanica, utilizzando però masse di peso notevole (340 mg), modifica la conduzione e la soglia per via aerea, ma non ha alcun effetto statisticamente significativo sulla conduzione per via ossea.

PAROLE CHIAVE: *Porzione centrale della membrana timpanica • Audiometria tonale • Soglia audiometrica*

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Introduction

Despite its clinical and surgical importance, mass loading of the central part of the tympanic membrane (TM), particularly point wise version, is a rarely discussed topic in the literature.

Basically, a stroboscopic holographic interferometer, which is used to measure vibration of the human TM, reveals that when it is stimulated by 500 Hz and 1000 Hz, its entire surface moves in points with the major indications occurring in posterior half. However, at 2000 and 4000 kHz, the TM vibrates with multiple (4 to 10) lo-

cal maxima, dispersed throughout the surface of the TM. Many of these maxima occur at the same phase of stimulation, while some occur at the opposite phase, and others show signs of graded phase with position (maxima means the point of maximal vibration) ^{1 2}.

Vibrations of TM are affected by its mass; when it increases, volume velocity generated by the acoustic stimulus is expected to decrease ³. Moreover, suppression of such vibration leads to variable degrees of hearing loss, if they are suppressed in a selective and focused way (pointwise), which will produce degrees of hearing loss that are essentially different from hearing loss produced from surface loading (covering), in turn inhibiting all TM vibration ⁴. The main two studies in this field revealed that a 0.13 cm³ mercury drop, which weighs about 176 mg, causes a loss of almost 20 to 40 dB, while a water drop of volume 0.2 cm³ produces a loss of only about 3-27 dB, while oil occupies an intermediate position ^{1 3}; both studies investigated the surface covering effect. This means that mass loading on a specific part of the TM has not been tested on humans. In this study, the 'pointwise' method was used not only because it is not studied previously, but also because if the effect is known clearly it will provide practical, scientific and non-statistical evidence why heavy and light grafts such as cartilage and fascia respectively have similar hearing results as is well known in the current literature ⁵.

Materials and methods

The study involved 60 patients who attended the outpatient clinic of the Otolaryngology-Head and Neck Surgery Department, Alexandria Main University Hospital seeking treatment for non-otological conditions. They were prospectively recruited to participate in the study which was approved and conducted by the guidelines of the local institutional review board. Moreover, all participants signed informed detailed consent prior to the study.

All participants had normal otoscopic view, normal pure tone audiometry and wide external auditory canal to allow direct and otoscopic visualization of the TM; they did not have any history of ear surgeries.

The 60 participants were divided randomly and equally in two groups, Group I and Group II, each with 30 participants.

The study was done in two steps:

The first step was a preliminary study to detect the load that might affect hearing; it was conducted for group 'I' (60 TMs) according to the following steps:

1. Full audiological assessment of all participants in the form of air and bone conduction pure tone audiometer to

make sure that they had normal air and bone conduction hearing thresholds, and immittance audiometer, including tympanometry and static immittance to ensure a normal middle ear condition.

2. Loading of the tympanic membrane:

I. Preparation of loads:

A) Weight of loads:

The basic weight was 13.6 and its multiples because Tonndorf, J. (1964) used a one microliter mercury drop, which weighs 13.6 mg (λ), as the smallest load to measure the effect of mass loading in animals and five multiples of this weight to measure further effects ⁶; it is also the weight of the tympanic membrane. Thus, this weight and 10 multiples were used to improve the accuracy of the results:

[(1 λ) 13.6 mg], [(2 λ) 27.2 mg], [(5 λ) 68 mg], [(10 λ) 136 mg], [(15 λ) 205 mg], [(20 λ) 272 mg], [(25 λ) 340 mg], [(30 λ) 408 mg], [(35 λ) 476 mg] and [(40 λ) 544 mg]

B) Shape and surface area:

Because it was extremely difficult to reach the heavy weights in a small surface area to ensure pointwise loading principle and all loads are expected to have standard measures, square shaped aluminum plates with a surface area of 16 mm² (Fig. 1) were also used because it is the resting surface area of a mercury drop (13 ± 3.58 mm²) used by prior researchers.

C) Composition of load:

We selected aluminum loads because it was easy to shape it and easy to reach the target weight with the standardised surface area. The smaller loads, up to 340 mg, were prepared from aluminum foil that was folded to give the

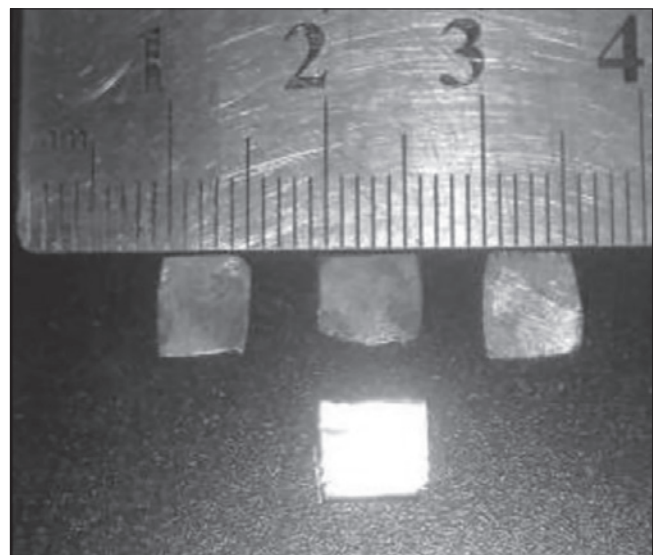


Fig. 1. Different weights with different thicknesses and surface area.

target weight and surface area. However, the larger loads were prepared from thick aluminum pellets that were compressed to the standard measures because it was difficult to reach the target weight using the thin aluminum foil (Fig. 1).

D) Total loads: all 10 selected weights had six further loads each, for a total of 60 loads.

II. Application of loads:

Each ear in group I was loaded by one of the prepared loads as the following:

An otoendoscope of 2.0 mm diameter, 58 mm length and 0° angles, was used to help good visualisation of all circumferences of the TM (umbo, malleus, annulus anterior and posterior malleolar folds), under this clear vision 0.05 ml of greasy and high viscosity petroleum jelly was applied to the umbo to prevent fall of the load.

Then, a plate of unknown weight, for both the patient and audiologist, was adjusted to the TM at the region of the umbo without any contact with the walls of the external auditory canal (Fig. 2).

3) Audiological assessment.

This step was double-blinded as neither the audiologist nor patient had any information about the weight of the plates.

Pure tone audiometry was done immediately after application of the loads to assess the effect of each load on air and bone conduction hearing thresholds at frequencies of (500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz).

4) Plates were removed a few hours after they fell from the TM with oto-endoscopic assistance.

After the results of this stage had been calculated, the second stage was conducted to confirm them, and included the same steps but with some differences:

1. Five weights were selected from the weights of the first step, [(10 λ) 136 mg], [(20 λ) 272 mg], [(25 λ) 340 mg], [(30 λ) 408 mg], [(40 λ) 544 m], to confirm positive and negative results of the first step.

2. Number of loads:

Twelve plates for each of the five selected weights were prepared; 60 loads of above mentioned measures and compositions were prepared. Each ear in group II was loaded by one of the prepared loads using the same method in the first step.

Statistical analysis of loading effects

At the beginning, we calculated the means and standard deviations of pre- and post-loading air and bone conduction hearing thresholds for each load at 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz. Subsequently, the mean differences between pre- and post-loading means were calculated.

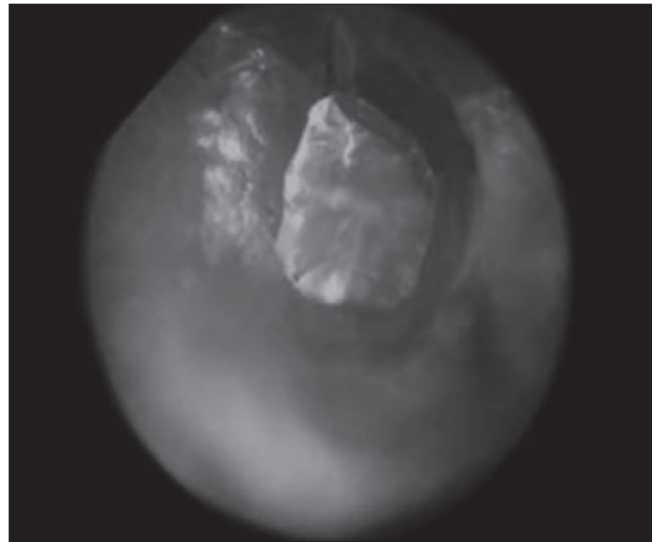


Fig. 2. The weight loaded on the TM.

After that, a t-test was used to compare the mean of the preloading air and bone conduction with post-loading counterparts for every load at 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz. A two-tailed p-value was used to measure the statistical significance of measured differences.

Lastly, 95% confidence interval and standard error of difference was used to improve the accuracy of results for step two results.

Results

The study included 48 males and 12 females, with an age ranging from 20-58 years and a mean of 33.9 ± 10.04 years. The mean weight of the ointment pieces used to hold the plate in place was 3 ± 0.58 mg in vitro. This weight was neglected not only because it was impossible to measure the real weight of the ointment on the TM (in vivo) due to the wasted amount on the tip of the cotton applicator, but also because the same volume (0.05 ml) was used in all cases.

Results of the first step

Small loads (13.6 mg, 27.2 mg, 68 mg, 136 mg, 205 mg, and 272 mg) did not have any significant effect on either type of hearing. The two-tailed p-value was ≥ 0.05 .

A statistically significant effect of mass loading was detected when the TM was loaded by 340 mg (25 λ). The mean air conduction hearing losses were 10 ± 3.55 dB, 10 ± 2.35 dB and 10 ± 3.69 dB at 500, 1000 and 2000 Hz, respectively, with a p-value < 0.05 . However, some differences were measured at 4000 Hz, although these differences were not statistically significant.

The effect increased gradually as the weight of the load was increased; at 476 mg (35 λ) the mean differences between the mean pre- and post-loading air conduction hearing thresholds were -5 ± 5.22 dB, -10 ± 3.98 dB, -15 ± 4.22 dB, and -15 ± 2.35 dB at 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz, respectively, with a two-tailed p-value < 0.05 .

Similarly, at the maximal weight used in this study, 544 mg (40 λ), the mean air conduction hearing loss was 15 ± 4.32 dB at 500 Hz and 10 ± 3.47 dB, 10 ± 4.29 dB and 10 ± 3.22 dB at 1000, 2000 and 4000 Hz, respectively. Lastly, none of the loads had a statistically significant effect on bone conduction hearing thresholds.

Results of the second step

When the TM was loaded by 136 mg (10 λ), the mean of differences between pre- and post-loading air hearing thresholds were 0 ± 0.36 dB at 500 Hz, 1 ± 0.58 dB at 1000 Hz, 0 ± 0.98 dB at 2000 Hz and 1 ± 1.36 dB at 4000 Hz, with no significant differences. However, there were similar differences in bone conduction hearing thresholds (2 ± 0.25 dB at 500 Hz, 0 ± 0.89 dB at 1000 Hz, 1 ± 1.89 dB at 2000 Hz and 1 ± 0.36 dB at 4000 Hz), none of which were statistically significant ($p > 0.05$ for all; Table I).

Similarly, at 272 mg, there were several differences at air and bone conduction hearing, but none with any statistical

significance (Table II). Line graph of pre- and post-loading thresholds were identical without any gaps (Fig. 3).

A statistically significant effect of mass loading was detected when the TM had a central load of 340 mg (25 λ). At this weight, the mean differences at 500 Hz, 1000 Hz and 2000 Hz were statistically significant with paired p-value < 0.05 ; at 500 Hz the mean difference was -10 ± 2.35 dB, at 1000 Hz the ear lost 10 ± 4.45 dB and at 2000 Hz air conduction hearing loss was 10 ± 2.18 dB. However, the effect of this mass was not significant at 4000 Hz (Table III) (Fig. 4), although with no statistically significant effect on bone conduction hearing (Table III).

At 408 mg (30 λ), the mean air conduction hearing losses (mean differences) were 17 ± 3.38 dB at 500 Hz, 16 ± 4.87 dB at 1000 Hz and 10 ± 2.60 dB at 2000 Hz. Nonetheless, this had no significant effect on 4000 Hz (Table IV). There were several differences in bone conduction hearing thresholds, but none with statistical significance ($p > 0.05$ for all; Table IV).

The above-mentioned effect increased in intensity when TM had a load of 544 mg (40 λ). The mean air conduction hearing loss (mean difference) was 20 ± 3.44 dB at 500 Hz, which continued at other frequencies but to a lesser degree, (14 ± 5.67 dB at 1000 Hz, 10 ± 3.58 dB at 2000 Hz and 10 ± 3.98 dB at 4000 Hz; Table V). Larger gaps between pre- and post-loading air conduction hearing threshold depicted this phenomenon (Fig. 5). Similar

Table I. Changes in hearing thresholds at 136 mg.

Loads Step 2	Changes of air conduction hearing thresholds				Changes of bone conduction hearing thresholds				
	500 Hz	1000 Hz	2000 Hz	4000 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	
136 mg (10 λ)	Mean pre-loading thresholds ± SD	10 ± 2.2 dB	10 ± 1.52 dB	10 ± 3.5 dB	12 ± 2.5 dB	11 ± 3.85 dB	10 ± 3.98 dB	12 ± 4.96 dB	10 ± 3.58 dB
	Mean post loading threshold ± SD	10 ± 3.58 dB	12 ± 2.15 dB	10 ± 2.56 dB	14 ± 2.36 dB	10 ± 2.86 dB	10 ± 3.58 dB	13 ± 3.5 dB	11 ± 2.52 dB
	Mean difference ± SD	0 ± 0.36 dB	1 ± 0.58 dB	0 ± 0.98 dB	1 ± 1.36 dB	2 ± 0.25 dB	0 ± 0.89 dB	1 ± 1.89 dB	1 ± 0.36 dB
	95% CI	± 2.51561	± 2.57634	± 2.5960	-4.0582 dB to 0.0582 dB	-1.87128 to 3.87128	± 3.20483	-4.63429 to 2.63429	-3.62100 to 1.62100
	Standard error of difference	1.213 dB	0.760 dB	1.252 dB	0.992 dB	1.385 dB	1.545 dB	1.752 dB	1.264 dB
	two-tailed P value	1.0000	0.2018	1.0000	0.0563	0.4777	1.0000	0.5740	0.4372

Table II. Changes in hearing thresholds at 272 mg.

Loads Step 2	Changes of air loads conduction hearing thresholds				Changes of bone conduction hearing thresholds				
	500 Hz	1000 Hz	2000 Hz	4000 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	
272 mg (20 λ)	Pre-loading thresholds ± SD	10 ± 3.65 dB	12 ± 2.36 dB	10 ± 3.78 dB	10 ± 2.87 dB	10 ± 2.36 dB	14 ± 2.69 dB	12 ± 3.5 dB	10 ± 1.25 dB
	Post-loading threshold ± SD	10 ± 3.25 dB	11 ± 3.25 dB	11 ± 2.63 dB	10 ± 4.52 dB	11 ± 3.25 dB	12 ± 3.58 dB	12 ± 2.85 dB	10 ± 2.87 dB
	Mean difference ± SD	0 ± 0.63 dB	1 ± 0.97 dB	1 ± 0.12 dB	0 ± 0.36	1 ± 0.58 dB	2 ± 1.85 dB	0 ± 0.36 dB	0 ± 0.89 dB
	95% CI	± 2.92586	-1.40457 to 3.40457	-3.75685 to 1.75685	± 2.71902	-3.40457 to 1.40457	-0.68087 to 4.68087	± 2.70218	± 1.87409
	Standard error of difference	1.411 dB	1.159 dB	1.329 dB	1.311 dB	1.159	1.293	1.303	0.904
	two-tailed P value	1.0000	0.3977	0.4599	1.0000	0.3977	0.1361	1.0000	1.0000

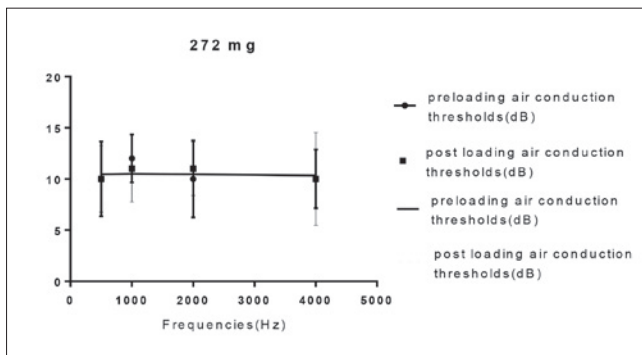


Fig. 3. Changes in air conduction hearing thresholds at 272 mg.

to previous bone conduction results, there was no significant effect.

Discussion

This topic is one of the least discussed issues in the literature despite its great relevance. Its importance can be observed by the fact that the greater the understanding of TM biomechanics, the greater the potential to monitor future advances in medical technology related to its surgical repair (myringoplasty) ⁷.

There are only a very limited number of studies in the literature about this issue, which also involved animal experiments cats, dogs, rats and guinea pig ⁶. Lüscher E. (1945) concluded that pointwise loading of the umbo or the manubrium in cats causes predominantly deafness towards low frequencies, whereas surface loading (covering) of the pars tensa, principally, causes deafness towards high frequencies ⁴.

According to repeated results of our study, the human hearing system is resistant to pointwise mass loading except at very large masses (340 mg; 25 λ). This mass is very large compared to the mean weight of the ossicles and the TM; the mean weights of human ossicles are 23 mg for the malleus, 27 mg for the incus and 4 mg for the stapes; the average weight of the TM is 14 mg ⁸. It is also larger than the mean weight of the cartilage graft, which is 20 ± 4.36 mg according to our experiments ⁵.

Masses from 13.6 mg (λ) to 272 mg (20 λ) did not have any significant impact on air or bone conduction hearing thresholds. The only significant effect was seen when the TM had a load of 340 mg. The air conduction hearing thresholds at 500 Hz, 1000 Hz and 2000 Hz increased by 10 ± 3.69 dB, 10 ± 2.35 dB, and 10 ± 3.55 dB, respectively, without any evident effect at the frequency of 4000 Hz.

When the TM had a load of 408 mg (30 λ), the air con-

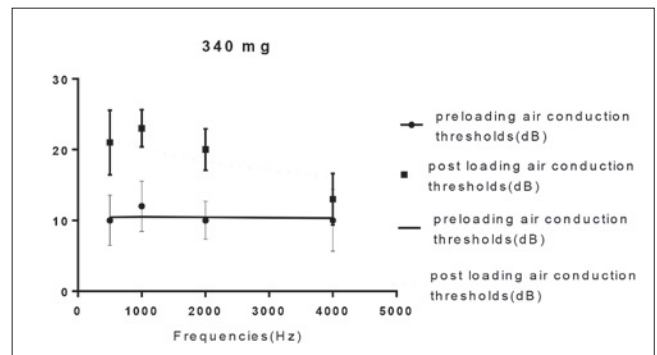


Fig. 4. Changes in air conduction hearing thresholds at 340 mg.

duction hearing threshold was increased by 17 ± 3.38 dB at 500 Hz. This effect decreased towards higher frequencies: at 1000 Hz air conduction hearing threshold increased by 16 ± 4.87 dB and at 2000 Hz it increased by 10 ± 2.60 dB, but there was no effect at 4000 Hz which was affected only when the TM had plates of 476 mg (35 λ) and 544 mg (40 λ). At 544mg (40 λ), the mean air conduction hearing loss was 10 ± 3.98 dB (at 4000 Hz). However, several experiments revealed an increase in bone conduction responses at low frequencies accompanied by a decrease at high frequencies and both of these changes, which is consistent in some proportion to the applied load ⁹. In our study, there was no statistically significant difference in bone conduction hearing thresholds.

These results demonstrates why a heavy and stiff cartilage graft does not affect hearing results and changes some concepts regarding the mechanics of hearing loss in middle ear effusion; it is evident in the literature that the mass of fluid on the TM may reduce middle-ear input admittance ¹⁰; however, the actual effect of the mass of effusion is minor according to our pointwise loading experiments.

Conclusions

The hearing system is very resistant to mass loading except at very large weights (340 mg). Loading of the TM by different masses affects the air conduction hearing thresholds, especially low frequencies, but does not affect bone conduction hearing. Thus, it is now very clear why hearing results of the heavy and light grafts are statistically non-significant. Lastly, there is an obvious practical and experimental demonstration that the mass of the effusion of the middle ear does not have any role in hearing loss.

Table III. Changes in hearing thresholds at 340 mg.

Loads Step 2	Changes in air conduction hearing thresholds				Changes of bone conduction hearing thresholds			
	500 Hz	1000 Hz	2000 Hz	4000 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz
340 mg (25 λ)								
Pre-loading thresholds ± SD	10 ± 3.56 dB	12 ± 3.56dB	10 ± 2.69 dB	10 ± 4.36 dB	13 ± 3.69 dB	10 ± 5.36 dB	14 ± 2.65 dB	12 ± 3.35 dB
Post-loading threshold ± SD	21 ± 4.56 dB	23 ± 2.63dB	20 ± 2.95 dB	13 ± 3.65 dB	14 ± 2.31 dB	12 ± 2.46 dB	13 ± 2.36 dB	12 ± 2.84 dB
Mean difference ± SD	10 ± 2.35 dBHL	10 ± 4.45 dBHL	10 ± 2.18 dBHL	4 ± 2.36 dBHL	0 ± .25 dBHL	2 ± .85 dBHL	1 ± 1.63 dBHL	0 ± 0.21 dBHL
95% CI of difference	-13.36981 to -6.63019	-13.64981 to -8.35019	-12.39010 to -7.60990	-6.40415 to 0.40415	-3.6063 to 1.6063	-5.53072 to 1.53072	-1.12442 to 3.12442	± 2.62928
Standard error of difference	1.625	1.278	1.152	1.641	1.257	1.702	1.024	1.268
two-tailed P value	<0.0001*	<0.0001*	<0.0001*	0.0812	0.4347	0.2527	0.3396	1.0000

Table IV. Changes in hearing thresholds at 408 mg.

Loads Step 2	Changes in air conduction hearing thresholds				Changes of bone conduction hearing thresholds			
	500 Hz	1000 Hz	2000 Hz	4000 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz
408 mg (30 λ)								
Pre-loading thresholds ± SD	10 ± 2.35 dB	12 ± 3.56 dB	14 ± 4.36 dB	14 ± 2.56 dB	10 ± 2.36 dB	10 ± 3.56 dB	12 ± 2.47 dB	11 ± 3.25 dB
Post-loading threshold ± SD	27 ± 2.36 dB	28 ± 3.56 dB	24 ± 2.36 dB	16 ± 2.36 dB	10 ± 3.65 dB	12 ± 3.26 dB	10 ± 4.35 dB	10 ± 3.89dB
Mean difference ± SD	17 ± 3.38 dB HL	16 ± 4.87 dBHL	10 ± 2.60 dBHL	2 ± 1.56 dBHL	0 ± 0.25 dBHL	0 ± .59 dBHL	2 ± 1.36 dBHL	1 ± 0.29 dBHL
95% CI of difference	-18.99388 to -15.00612	-19.0141 to -12.9859	-12.96808 to -7.03192	-4.08449 to 0.08449	± 2.60215	-4.88989 to 0.88989	-0.99478 to 4.99478	-2.03468 to 4.03468
Standard error of difference	0.961	1.453	1.431	1.005	1.255	1.393	1.444	1.463
two-tailed P value	<0.0001*	<0.0001*	<0.0001*	0.0592	1.0000	0.1653	0.1799	0.5015

Table V. Changes in hearing thresholds at 544 mg.

Loads Step 2	Changes in air conduction hearing thresholds				Changes of bone conduction hearing thresholds			
	500 Hz	1000 Hz	2000 Hz	4000 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz
544 mg (40 λ)								
Mean pre-loading thresholds ± SD	10 ± 3.25dB	10 ± 2.89 dB	13 ± 5.85 dB	10 ± 5.85 dB	12 ± 3.36 dB	10 ± 1.56 dB	10 ± 2.47 dB	13 ± 2.25 dB
Mean post-loading threshold ± SD	30 ± 3.25dB	25 ± 3.65 dB	24 ± 3.69 dB	20 ± 2.36 dB	11 ± 3.21 dB	10 ± 3.24 dB	12 ± 4.25 dB	12 ± 2.89 dB
Mean difference ± SD	20 ± 3.44 dBHL	14 ± 5.67 dBHL	10 ± 3.58dBHL	10 ± 3.98 dBHL	1 ± 0.25 dBHL	0 ± .89 dBHL	1 ± 1.36 dBHL	1 ± 0.99 dBHL
95% CI	-22.86821 to -17.13179	-17.78719 to -12.21281	-14.14077 to -5.85923	-13.77650 to -6.22350	-1.78199 to 3.78199	± 2.15284	-4.94287 to 0.94287	-1.19271 to 3.19271
Standard error of difference	1.383	1.344	1.997	1.821	1.341	1.038	1.419	1.057
two-tailed P value	<0.0001*	<0.0001*	<0.0001*	<0.0001*	0.4639	1.0000	0.1727	0.3545

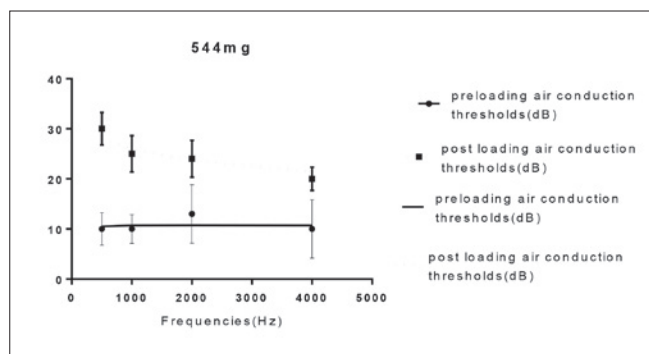


Fig. 5. Changes in air conduction hear at 544 mg.

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only work to produce a positive impact in the literature that could change some concepts in my specialty.

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