Neuromonics Tinnitus Treatment – Summary of Clinical Efficacy Data
April, 2012

Published Papers in Peer-Reviewed Medical Journals

Initial demonstration of Neuromonics' clinical efficacy is evident in four published papers in peer-reviewed medical journals. In summary, three clinical trials involving 555 patients demonstrated a remarkably consistent clinical benefit that persisted to 12 months in suitable patients. All papers are available on Medline.

1) **Davis PB, Wilde RA, Steed LG, Hanley PJ. Treatment of tinnitus with a customized acoustic neural stimulus: A controlled clinical study. *Ear Nose & Throat Journal,* 2008; 87:330-9.**

   This paper describes the results of a randomized, controlled study in which the Neuromonics treatment was randomized against two control groups. The study is referred to as a "second clinical trial," as it followed a small feasibility trial that has not been published.

   The study showed that after six months of treatment, 86 percent of the Neuromonics patients met the minimum criterion for clinical success, defined as an alleviation of tinnitus disturbance of at least 40 percent (as determined by the Tinnitus Reaction Questionnaire score). By contrast, only 47 percent and 23 percent of the patients in the two control groups reported a successful result according to this criterion. Mean improvement in tinnitus disturbance scores in the Neuromonics Tinnitus Treatment group was 66 percent, compared to 22 percent and 15 percent in the control groups. The differences between the Neuromonics group and the control groups were statistically significant. Significant differences were observed in other clinical outcomes as well.

   Neuromonics proposes that this study is a well-designed and well-conducted investigation showing measurable improvement in the disease condition compared to other available treatments. Not only is the risk for harmful effects extremely low, but patient reports of user acceptability were more consistently positive in the Neuromonics group. This shows that the treatment is not more efficacious and more tolerable.

2) **Davis PB, Paki B, Hanley PJ. The neuromonics tinnitus treatment: third clinical trial. *Ear and Hearing,* 2007; 28:242-59.**

   This paper presents the results of a clinical trial comparing an abbreviated version of the Neuromonics Tinnitus Treatment protocol to the standard protocol that the second clinical trial (referenced in (1) above) studied. This third clinical trial concluded that the abbreviated treatment protocol was not statistically superior. In fact, the results suggest it was inferior to the standard protocol. However, the study produced a number of extremely important outcomes – particularly the consistency of the benefit compared to the previously described trial.

   At six months, 91 percent of all patients showed a clinically significant benefit (defined as an alleviation of tinnitus disturbance of at least 40 percent), which is consistent with the 86 percent in the previous trial. In addition, the benefit persisted in following the patients to 12 months, with 86 percent showing a clinically significant benefit at that time point. The mean improvement in TRQ at six months was 65 percent as compared to 66 percent in the previous trial, showing a remarkably consistent benefit.

3) **Hanley PJ, Davis PB, Paki B, Quinn SA, Bellekom SR. Treatment of tinnitus with a customized, dynamic acoustic neural stimulus: clinical outcomes in general private practice.** ***Annals of Otology, Rhinology, and Laryngology,*** **2008; 117:791-9.**

The previous two trials documented the clinical efficacy of the treatment under controlled clinical studies for the most suitable patients. This paper documents results in real-world clinics across a diverse patient population with a very large patient base (n=470). The most suitable patients, described as Tier 1 patients (n=237), demonstrated a clinical success rate of 92 percent with a mean improvement of 72 percent – values that are extremely consistent with prior studies. Even less-suitable Tier 2 patients (n=223) demonstrated a clinical success rate of 60 percent with a mean improvement of 49 percent.

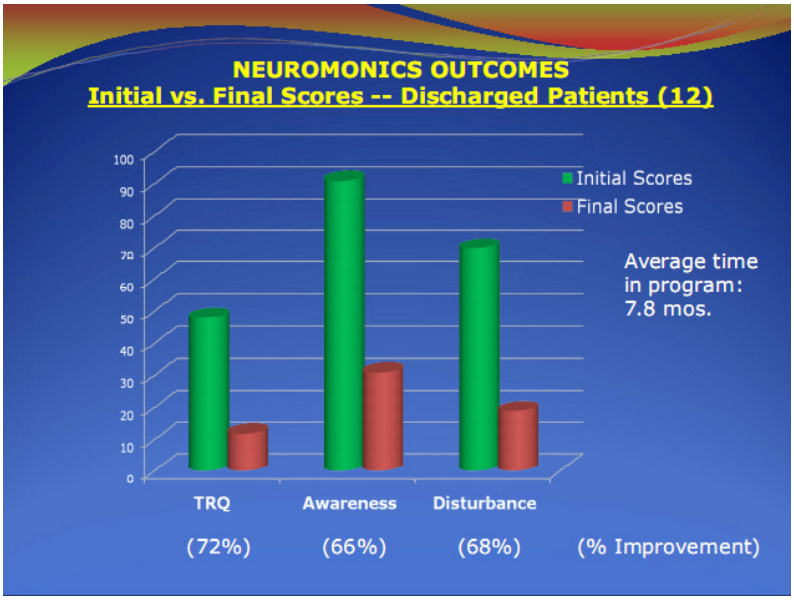
4) **Hanley PJ, Davis PB. Treatment of tinnitus with a customized, dynamic acoustic neural stimulus: underlying principles and clinical efficacy.** ***Trends in Amplification*****, 2008; 12:210-22.**

This paper describes the essential underlying scientific principles behind the Neuromonics Tinnitus Treatment as supported by the medical literature. It also summarizes evidence for clinical efficacy from the previous controlled clinical studies and the private-practice clinical setting, which provides consistently positive outcomes, particularly among those patients meeting specific criteria. This supports the rationale for the consistent and significant clinical benefit of the treatment.

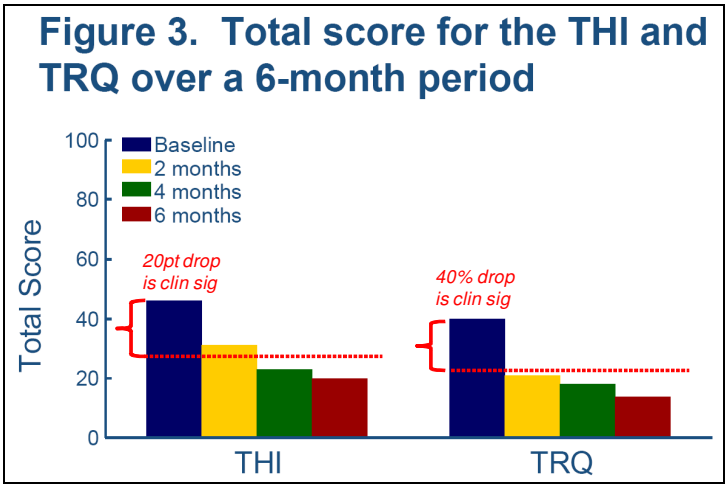
Additional Studies

In addition to the papers available on Medline, are additional studies that have been presented at recent medical meetings. Each provides additional evidence of clinical efficacy. A summary of results follows; additional data available if needed.

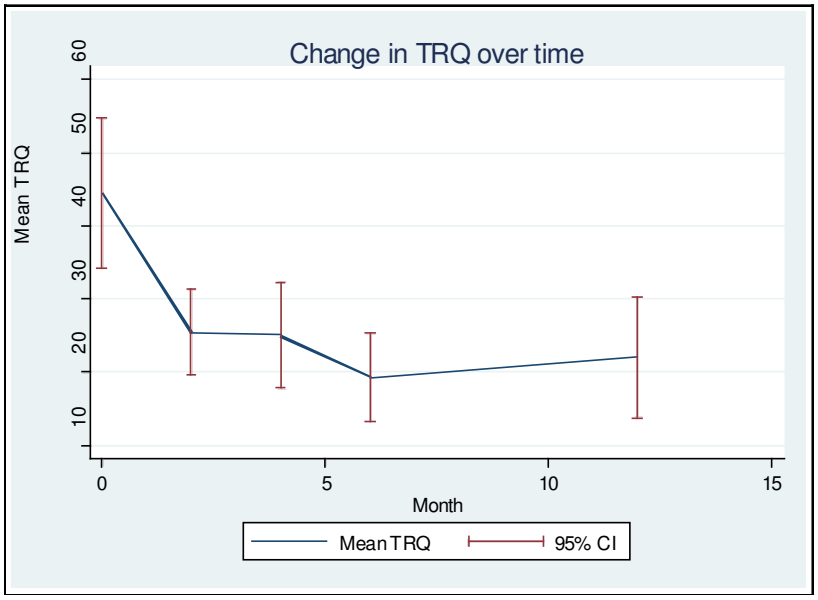
1) **Podium Presentation: March 2009, Joint Defense/Veterans Audiology Conference, Phoenix, AZ**
   Title: Prevalence and Management of Tinnitus
   www.afaslp.org/AVAA%20conferences/White2009_Prev_and_mgmt_tinnitus.pdf
   Presenter: Emily White, Miami Veterans Administration Outpatient Clinic, Hollywood, FL
   Summary: This was an interim presentation of data from an independent efficacy study of the Neuromonics Tinnitus Treatment program. At the time of the presentation, 35 patients were enrolled, 12 had completed treatment and 23 were ongoing.
   Results: For the group of patients who have been in treatment at least four months, 22 of 23 (96 percent) have 40 percent or more improvement in at least 1 of 3 criteria (TRQ, Percent Awareness, or Percent Disturbed). For the 12 patients who have completed the treatment, mean improvement in TRQ is 72 percent (see chart below).



2) **Poster Presentation: April 2009, American Academy of Audiology Annual Meeting, Dallas, TX**
   Title: Long-Term Benefits of Neuromonics Treatment: Preliminary Findings
   Presenters: Sharon Sandridge, Ph.D. and Craig Newman, Ph.D. – Cleveland Clinic
   Summary: The purposes of this study (CALM trial) were to demonstrate changes in perceived tinnitus distress and activity limitation/participation over selected time intervals – up to three years following the initiation of the Neuromonics Tinnitus Treatement for up to 50 patients. The current data set represents preliminary findings at six months of the longitudinal study.
   Results: This study used both the TRQ and the THI (Tinnitus Handicap Questionnaire). Interim results showed significant benefit at six months as illustrated in the figure below (from the poster).

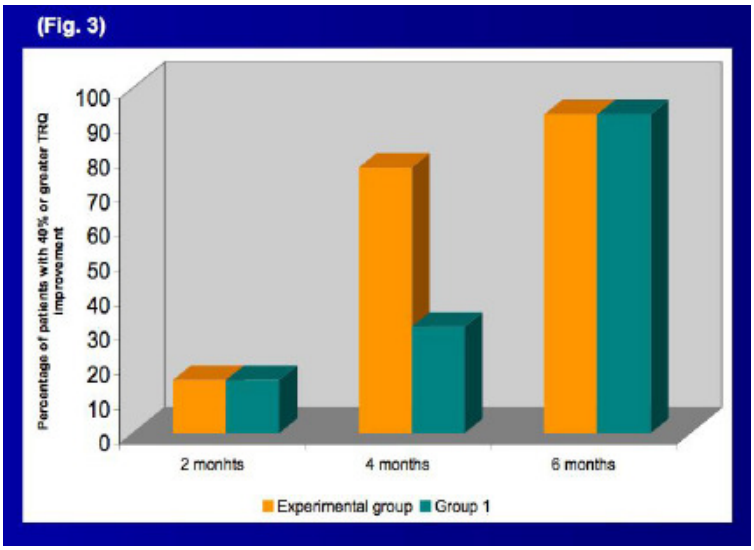


3) **Poster Presentation: June 2009, 9th European Federation of Audiology Societies (EFAS), Tenerife, Canary Islands, Spain**
Title: Long-Term Clinical Outcomes of Tinnitus Treatment Based On Acoustic Stimulation
Presenter: Dayse Tavora-Vieira, Medical Audiology Services, Western Australia, Australia
Summary: This preliminary study intended to determine the long-term tinnitus relief achieved by patients treated with the Neuromonics Tinnitus Treatment, ensuring that the benefits experienced during the first six months are still sustained in the longer term, with the measurement of outcomes to 12 months.
Results: A total of 15 patients were studied. Mean reduction in TRQ was 52 percent at six months and 44 percent at 12 months (see chart below for absolute TRQ results).



4) **Poster Presentation: June 2009, 3rd Tinnitus Research Initiative Meeting (TRI), Stresa, Italy**
Title: Acoustic Stimulation in Tinnitus Treatment for Patients with Significant Levels of Hearting Loss
Presenter: Dayse Tavora-Vieira, Medical Audiology Services, Western Australia, Australia
Summary: To assess the efficacy of a variation of the standard Neuromonics treatment protocol for patients with high levels of hearing loss. Twenty-five patients with high hearing loss randomized to the standard (Group 1) vs. non-standard (experimental) treatment protocol. The non-standard treatment protocol maintained patients in Phase 1 of the treatment for four months instead of the typical two months.

Results: The non-standard protocol demonstrated an improved benefit at four months (mean improvement of 46 percent vs. 29 percent for the standard protocol). But at six months, the results were similar, with a mean improvement in TRQ of 60 percent in the non-standard protocol vs. 52 percent in the standard protocol. This study showed that it may be possible to alter the treatment protocol for patients who fall outside the standard parameters and still achieve a significant clinical benefit.



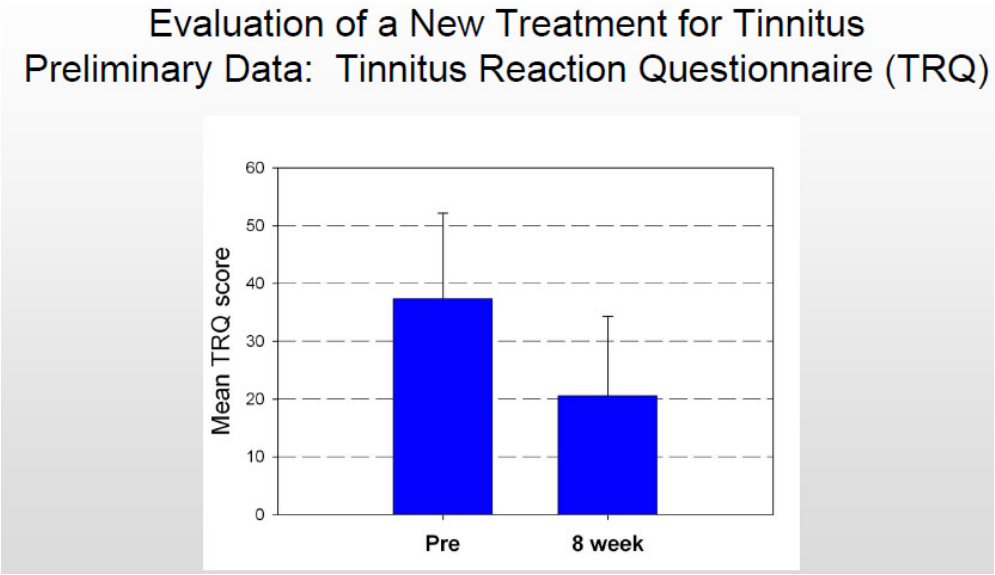
5) Podium Presentation: February 2010, DOD Acoustic Trauma Meeting in San Diego, CA

Title: Evaluation of a New Treatment for Tinnitus

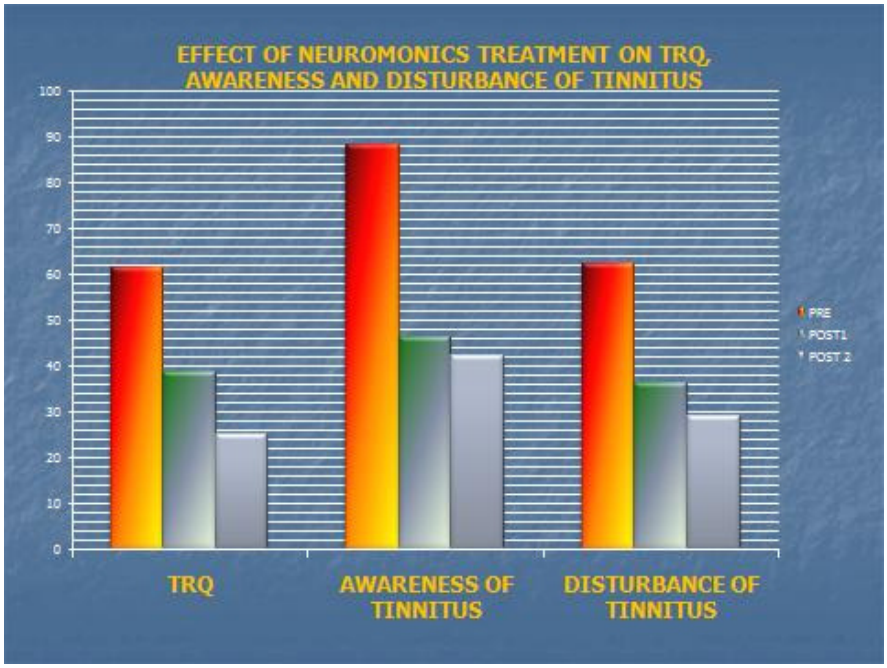
Presenter: Melinda Hill, Au.D., U.S. Army Aeromedical Research Laboratory, Fort Rucker, AL

Summary: The researcher presented interim results of an ongoing independent clinical trial with the stated goal to "provide a treatment recommendation to the Surgeon General of the Army for debilitating tinnitus adversely affecting soldier retention, deployability and operational performance." A total of 40 soldiers are being recruited for the study. Hill presented preliminary results from the Neuromonics cohort.

Results: After just eight weeks, the group showed a mean reduction in TRQ of more than 40 percent.



6) **Podium Presentation: February 2010, Joint VA/DOD Audiology Meeting in Orlando, FL**
Title: Impact of Setting Up a Tinnitus Clinic
Presenter: Margaret Peak and Kathy Duncan, VA Gulf Coast Veterans Health Care System
Summary: The researcher presented results from a review of 2,093 tinnitus patients in FY '09. Of those, 75 (3.6 percent) proceeded to individualized treatment with Neuromonics and 52 completed treatment through to Phase 2.
Results: The results show a reduction in the TRQ score of approximately 60 percent, which is consistent with previous trials. The awareness and disturbance of tinnitus also decreased significantly.



7) **Poster Presentation: April 2010, American Academy of Audiology Meeting in San Diego, CA**
Title: Clinical Experience with Progressive Tinnitus Management (PTM)
Presenter: Steven L. Benton, Au.D., Atlanta VA Medical Center
Summary: Reviewed records of 2,543 subjects referred to the Atlanta VA Audiology Clinic over a 14-month period, comparing characteristics of those referred for tinnitus services with those referred for hearing problems, and identifying and describing differences in the characteristics between subjects referred for tinnitus services who do or do not progress from one PTM level to the next.
Results: Only a small percentage (1.4 percent) progressed to individualized management (PTM Level 5).

Subjects

After exclusion of duplicate referrals, no shows and subjects who provided invalid behavioral test results, **2543** subjects were included in this review, **654** of whom (**25.7%**) were referred for complaint of tinnitus. Subjects were then assigned to one of four groups, presented here in order of increasing need for tinnitus management.

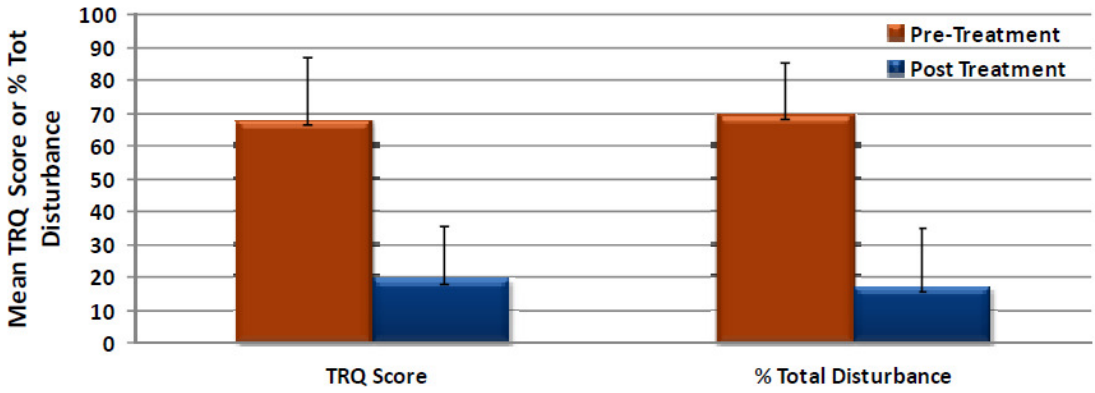
NonT:	Non-tinnitus subjects. N = 1889. 74.3% of all subjects.
T-GrpN:	Tinnitus subjects not referred to Tinnitus Group Education. N = 546. 25.7% of all subjects.
T-GrpY-IndN:	Tinnitus subjects referred to Group Education who did not continue on to Individualized Management. N = 72. 2.8% of all subjects.
T-GrpY-IndY:	Tinnitus patients referred to Group Education who did continue on to Individualized Management. N = 36. 1.4% of all subjects.

The Atlanta VA uses the Neuromonics Tinnitus Treatment for patients who require individualized management. The author presented the results from a total of 61 patients treated with Neuromonics. The mean reduction in the TRQ score was 69 percent – slightly better than previous trials.

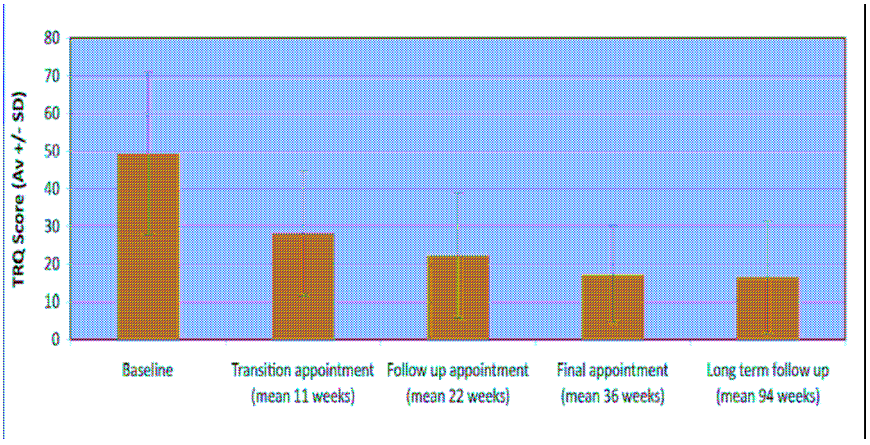
PTM Level 5 – Individualized Management (Cont'd)

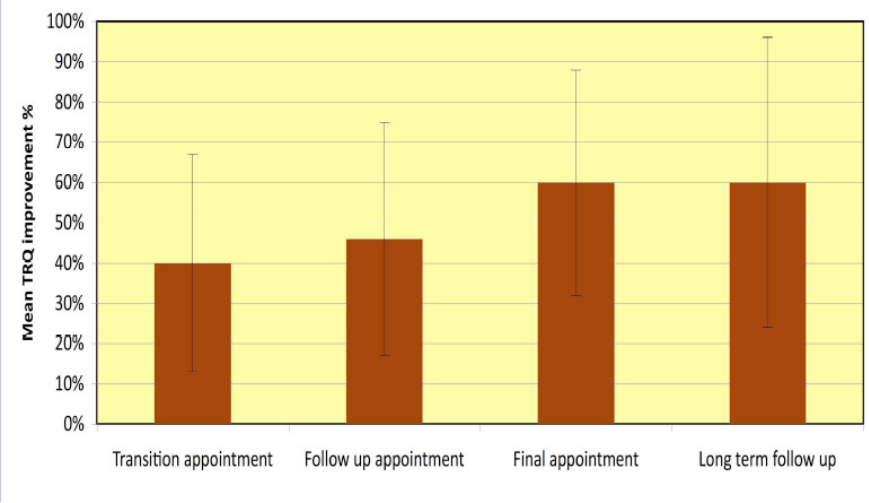
Successful Neuromonics Tinnitus Treatment outcome is defined by a 40% reduction in TRQ score and a reduction in tinnitus awareness and tinnitus disturbance. Figure 5 reveals the mean TRQ scores and total disturbance percentage both before treatment and after 5-8 months of treatment. For the subjects who thus far had reached this point in the treatment, the mean decrease in TRQ scores was **69.0%** (S.D. = 19.7) and the mean reduction in total tinnitus disturbance was **72.4%** (S.D. = 24.1).

Figure 5: Mean Pre- and Post-Treatment TRQ Scores and % Total Disturbance



8) **Poster Presentation: April 2010, American Academy of Audiology Meeting in San Diego, CA**
Title: Long Term Clinical Outcomes of Tinnitus Management Applying Customized Acoustic Stimulation – an Independent Private Practice Study
Presenter: Dayse Tavora-Vieara, Medical Audiology Services, Western Australia, Australia
Summary: This study aimed to review the long-term tinnitus relief achieved by patients treated with the Neuromonics Tinnitus Treatment. The researcher reviewed the records of 70 patients from the United States and Australia who had completed the Neuromonics Tinnitus Treatment at least six months prior.
Results: At the mean long-term follow up point of 94 weeks, the clinical benefit persisted at a level almost identical to the benefit achieved at the final appointment, with a mean reduction in TRQ of 60 percent. This is very consistent with previous trials and shows the longer-term benefit of the treatment.





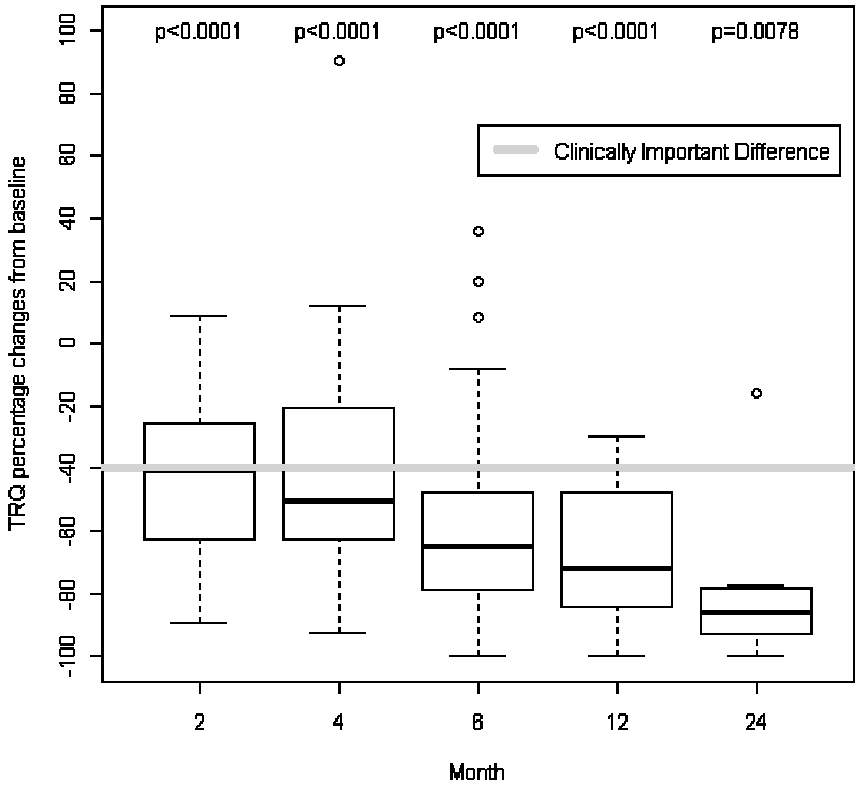
9) Podium Presentation: May 2010, American Otological Society Meeting in Las Vegas, NV

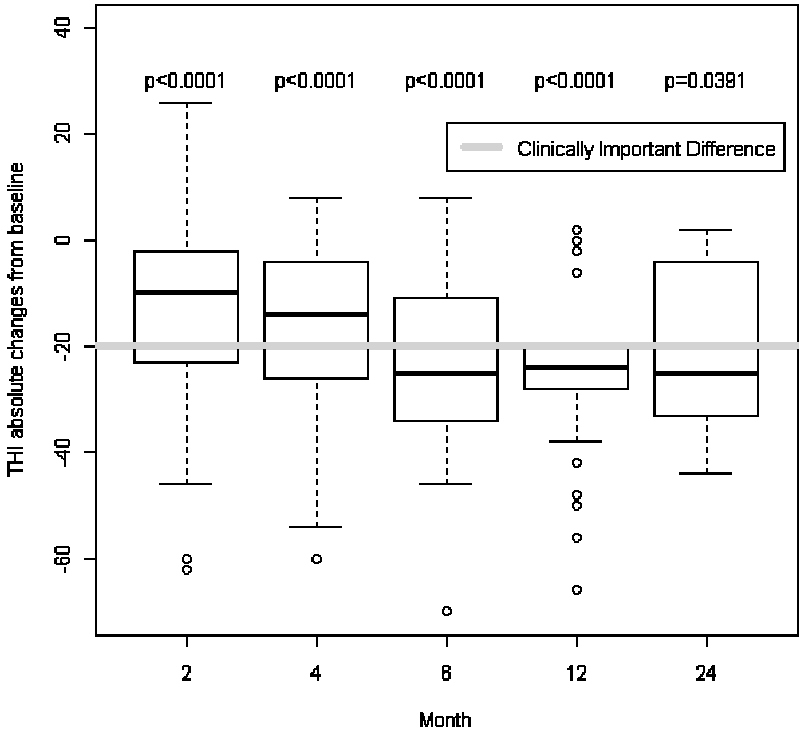
Title: Interim Results from a Long Term Tinnitus Treatment Study

Presenter: Jack Wazen, M.D., Silverstein Institute, Sarasota, FL

Summary: Wazen is the medical PI for the CALM trial, a longer-term clinical study of the Neuromonics Tinnitus Treatment. The CALM trial is an independent assessment of clinical efficacy to 36 months, and has recruited a total of 50 patients. Interim results were presented on patients out to 24 months.

Results: The results showed both a clinically and statistically significant benefit at all time points when measured using either the TRQ or THI questionnaires. The mean reduction in the TRQ at 12 months was 68 percent, and the benefit actually increased at the 24-month time point. The box plots that follow indicate the distribution of continuous data by means of percentiles. The top and bottom edges of the box represent the 25th and 75th percentiles of the data, with whiskers extending from the top and bottom of the box representing the 5th and 95th percentiles. The bold line in the middle of the box represents the median of the data.

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Clinically Important Difference
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