Intracochlear electrical stimulation to suppress tinnitus

Valorization addendum

Although the results obtained in these feasibility studies are promising, one could doubt whether patients would accept such an invasive and expensive procedure to treat their tinnitus.

Treatment acceptance
To reduce tinnitus completely, 38% of the 197 tinnitus sufferers who attended a meeting of the Australian Tinnitus Society would accept (i.e., they indicated an acceptance of 91-100%) a CI as treatment option while 25% would accept a CI in case of reduced tinnitus loudness and annoyance by half. This acceptance rate is comparible to noninvasive wearable devices (42% and 30%, respectively) [Tyler, 2012]. In contrast, based on a Dutch online survey on 415 tinnitus sufferers and member of the Dutch society for the hearing impaired, 29% of the population express a large interest in CI (i.e., they scored their acceptance 8-10 on a visual analogue scale from 0 to 10) in case there is a 100% chance of full tinnitus suppression while 22% is very interested in case there is a 50% chance of full tinnitus suppression. A decrease in treatment acceptability was observed compared to the noninvasive conventional hearing aids, with an acceptance rate of 53% and 51% respectively (unpublished data). The difference in CI-acceptance in relation to noninvasive wearable devices between both studies can probably be explained by selection bias. Nevertheless, both studies have shown that the acceptance of cochlear implantation as a treatment option for tinnitus is considerable which is consistent with the results obtained in an American internet survey with 439 responders. Here, almost three-fourths of the patients would be willing to have a device implanted in their body for a therapy that could eliminate or reduce their tinnitus perception by half [Engineer et al., 2013].

Economic considerations
As mentioned in the introduction of this thesis, tinnitus affects about 50 million people in the United States and an estimated 70 million in the European Union [Cederroth et al., 2013] which is about 10-15% of the general population [Langguth et al., 2013]. The estimated tinnitus prevalence in the Netherlands is 2 million of whom about 60.000 severely suffer from their tinnitus [Cima et al. 2009]. Furthermore, Maes and colleagues [2013] concluded that the economic burden of tinnitus to society is substantial with an on average annual tinnitus related societal cost per patient of €5,315 in the Netherlands. Most of these costs were associated with production losses; on average €3,702. Overall, the annual costs of tinnitus in the Netherlands examined from a societal perspective is about €6.8 billion (95% confidence interval: €3.9 billion - €10.8 billion). The annual health care costs were €1.9 billion (95% confidence interval: €1.4 billion - €2.5 billion) which amounts to 2.3% of the total Dutch health care expenditure [Maes et al., 2013].

Based on these results it is striking that within the National Institute on Deafness and other Communication Disorders, tinnitus funding accounts for only 2% (about $5 million per year from 2009 to 2011) of total hearing research funds [Cederroth et al., 2013]. Private donors like for example the founder of the Tinnitus Research Initiative; Matteo de Nora, the fundraising efforts of for example the American Tinnitus Association and investments from the industry are therefore essential for the knowledge about and treatment options for tinnitus.

Moreover, Tyler [2012] reported about the willingness to pay for tinnitus treatments and asked 197 tinnitus sufferers to indicate how much money they would be willing to pay for effective treatments. Most of these patients indicated to pay at least $5000 and 20.3% were willing to pay as much as $25,000 for complete tinnitus reduction. Furthermore, Engineer and colleagues [2013] reported about an online survey with 439 responders of which 94% reported that they had health insurence. Here, almost 40% had already spent between $500 and $10,000 on tinnitus therapies. Therefore, from an economical point of view, the tinnitus population is an interesting market for the industry with in particular the industry of medical devices as novel drugs take a long time and hundreds of millions of dollars to develop. For purposes of illustration, Auris Medical recently invested $51 million for a phase 3 trial in tinnitus for the pharmacotherapy using AM-101 [Cederroth et al., 2013]. In contrast, the average implantable medical device takes about $10 million and five years to develop [Engineer et al., 2013].

This research project is funded by one of our CI industry partners. They are interested in the long-term effects of electrical stimulation independent of environmental sounds on tinnitus as they see new opportunities to expand their market. Although the highly sophisticated CI shows promising results concerning the tinnitus suppression, the considerable costs (about €25,000 for the device [Broersen, 2010]) have hampered the clinical application. With the promising long-term effects of electrical stimulation independent of environmental sounds on tinnitus, a "Tinnitus Implant" (TI) should by viable. This relatively simple neurostimulator could be produced considerably cheaper because it does not require a strategy to encode environmental sounds. This thesis includes feasibility studies (Chapter 3-7) which open new possibilities for the development of this treatment option.

Possible effects on the standard clinical CI
The results obtained on tinnitus suppression may indirectly lead to future research in order to expand the inclusion criteria for CI, especially regarding residual hearing. To date, there is a considerable risk of damaged residual hearing due to the implantation itself, which is the main reason why only subjects who were deaf in the ear to be implanted were included. Changes in both the device and the surgical procedure could reduce this risk. If this risk can be neglected, this treatment option could possibly be suitable for the tinnitus population with significant residual hearing. This thesis can contribute to the interest to develop an atraumatic procedure for electrode insertion. Although Chapter 2 of this thesis seems to suggest that deterioration of residual hearing as a result of the implantation itself does not cause postoperative chronic tinnitus, hearing loss as a side effect of the electrode insertion for tinnitus treatment is undesirable.

For safety as well as methodological reasons the long-term effects of intracochlear electrical stimulation independent of environmental sounds were investigated using the standard clinical CI which was reprogrammed to function as a tinnitus specific neurostimulator. This gave us the opportunity to additionally investigate the audiological effects of the standard CI in the SSD population (Chapter 7). The positive effects of CI obtained can contribute to the broadening of the indication for the standard clinical CI. For example, in Belgium and Germany the indication for CI is expanded already to SSD associated with tinnitus (the CI system is CE-Market for SSD in both children and adults), because in these countries the value of CI in SSD has been proven [Van de Heyning et al., 2008; Kleinjung et al., 2009; Vermeire et al., 2009; Arndt et al., 2010; Buechner et al., 2010; Arndt et al., 2011; Jacob et al., 2011; Stelzig et al., 2011; Hassepass et al., 2012; Mertens et al., 2013]. It is plausible that the Dutch policy makers (College voor Zorgverzekeringen) will follow after research in the Netherlands has reproduced these findings.

Knowledge valorization
The findings and ideas have been communicated to and shared with fellow researchers around the world at (inter)national congresses and in scientific journals. Furthermore, a huge appreciation for our work is observed in the tinnitus population. The Maastricht UMC+ organizes for example every six months a tinnitus symposium in collaboration with the Dutch society for the hearing impaired (Nederlandse Vereniging Voor Slechthorenden). These symposia were always fully booked. Here, background

information was given about tinnitus and hearing loss and recent findings from research projects were shared. Frequent interest of national media resulted in a generally better understanding of tinnitus. As tinnitus remains refractory to current medical treatment, sufferers are regularly disappointed after consulting a physician and do often not feel taken seriously. This clinical research contributes to the patient's awareness of global developments in this field of research.

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