Creating the Evidence: Lessons from Cochlear Implants

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Abstract

This paper compares the evidence-based outcomes between cochlear implants and hearing aids during the past several decades. Despite many similarities, there are also some important differences that define the progress for the two disciplines. Perhaps the most significant distinction exists in terms of the difference between the Food and Drug Administration’s treatment of hearing aids as Class I medical devices, while cochlear implants are defined as Class III devices. Another point of divergence has been the number of publications in archival, peer-reviewed journals; implant papers have been steadily increasing during the past decade, while hearing aid papers have declined during the same period. The impact of these differences on the past, present, and future of hearing aid and cochlear implant research, technology, and clinical practice is discussed.

Key Words: Cochlear implant, evidence-based outcome, hearing aid, research

Sumario

Este trabajo compara los resultados basados en evidencia entre los implantes cocleares y los auxiliares auditivos a lo largo de varias décadas. A pesar de muchas similitudes, existen algunas diferencias importantes que definen el progreso de las dos disciplinas. Quizás la distinción más significativa sea la diferencia con la Administración de Drogas y Alimentos y su tratamiento de los auxiliares auditivos como dispositivos médicos Clase I, mientras que los implantes cocleares se definen como dispositivos Clase III. Otro punto de divergencia ha sido el número de publicaciones en archivos y revistas con revisión editorial; los artículos sobre implantes han aumentado establemente durante la última década, a la vez que los artículos sobre auxiliares auditivos han disminuido en el mismo periodo. Se discute el impacto de estas diferencias sobre el pasado, el presente y el futuro de la investigación, tecnología y práctica clínica de los auxiliares auditivos y los implantes cocleares.

Palabras Clave: Implante coclear, resultados basados en evidencia, auxiliar auditivo, investigación

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In 1957, Djourno and Eyries activated the peripheral auditory nerve electrically in a human patient, beginning the modern era of the “cochlear implant.” By most accounts, this occurred around five years after the first transistorized hearing aid was offered commercially in the United States. During the past 50 years, there have been dramatic improvements in technology related to both types of devices, but the mechanisms by which these advances have been applied to patient care have been very different.

Although the majority of hearing aids dispensed in this country are now fully digital, market penetration remains low (at approximately 20% of those with measurable hearing loss) and with no dramatic improvements in user satisfaction and benefit (Kochkin, 2000). By contrast, modern cochlear implants now enable many cochlear implant users to achieve excellent speech recognition in background noise (Freisen et al, 2001), when only a few years ago, there was considerable debate regarding their benefit compared to tactile stimulation (Osberger et al, 1993). In fact, in the 20 years since multiple-channel cochlear implants were first approved for use in the United States, the progress has been nothing short of remarkable, and this has been in no small part due to research and development tied to clinical outcomes. The focus of this paper is to examine the divergent paths of research efforts in hearing aids and cochlear implants, in an effort to determine whether there are lessons to be learned from the differences.

**Lesson 1: Importance of Oversight of Scientific Merit of Research**

The Food and Drug Administration (FDA) oversees the process of assessing new medical devices for the United States market, including cochlear implants. In each case, the objective is to determine the degree to which the risk of using a device offsets the opportunities that are afforded by innovation. Furthermore, the FDA aims to provide a level of assurance regarding the safety and effectiveness of a device, and to further refine the assessment of a new device without impeding progress. Successful outcomes require effective communication between the FDA and device manufacturers, researchers, and medical and institutional review boards (IRBs).

The FDA’s primary responsibility in this process is to oversee clinical studies that are designed to assess safety and effectiveness information. Data are compiled, and a review board determines whether the device will be approved for clinical use. The authority to direct clinical studies was granted to the FDA by the Federal Food, Drug, and Cosmetic Act (ACT) amended by the Medical Device Amendments of 1976, the Safe Medical Device Act of 1990, and the Food and Drug Administration Modernization Act (FDAMA) of 1997.

The ACT of 1976 established three regulatory categories for all medical devices. The three classes are based on the degree of control necessary to ensure that the various types of devices are safe and effective. The most regulated devices, including cochlear implants, are in Class III. A Class III device is defined as one that supports or sustains human life, or is of substantial importance in preventing impairment of human health, or presents a potential, unreasonable risk of illness or injury. The lowest level of regulation reported is for Class I devices, which includes hearing aids.

The requirements for Class III devices include an extended premarket approval process, detailed below, while those for Class I comprise general instrument controls, including manufacturer registration, product listing, serialization, maintenance of specified records and reports, and good manufacturing practices. Class II devices include certain implantable devices, such as transcutaneous air-conduction hearing aid systems (TACHAS) and partial or total ossicular replacement prostheses (PORP or TORP, respectively). Class II devices are those that require special controls, including postmarket surveillance, performance standards, and patient registries that go beyond the general controls required of Class I devices. Both Class I and Class II devices are, however, exempt from the premarket approval process required of Class III devices. Therein lies one of the major differences between cochlear implants and hearing aids in terms of requiring the generation of evidence-based outcomes.

**Premarket Approval Process**

The ACT of 1976 provided a mechanism
for conducting clinical studies of cochlear implants and other Class III medical devices to ensure that they are safe and effective for use in human patients. The investigational device exemption (IDE) regulation (21 CFR Part 812) defines the procedures and requirements under which clinical studies of medical devices are conducted.

FDA sets strict requirements for the conduct of IDE studies; an investigation involving a Class III device with “significant risk” (implants that are used to sustain life, are of substantial importance in diagnosing, curing, initiating or treating disease, or otherwise present a potential for serious risk to the health, safety, or welfare of the patient) must be approved by the FDA and an IRB prior to the onset of data collection. Typically, the application process requires that a detailed investigational plan be completed, including a literature review, a complete description of the device and its intended use, the patient informed consent, signed investigator agreement, and identification of all of the participating investigational sites where data will be collected.

The IDE process ensures that the approved clinical protocol uses a properly designed and well-controlled study that will provide scientific evidence regarding the safety and efficacy of the experimental device. In addition, FDA oversight ensures that the IDE studies use sound design principles—including the use of multiple independent locations, appropriate monitoring, and oversight of adverse events—and uphold patient privacy and HIPAA (Health Insurance Portability and Accountability Act of 1996) statutes. Statistical consultants ensure that adequate sample size, randomization, and single- or double-blind controls are used to minimize experimenter and/or subject bias.

The IRB of participating research facilities acts as a liaison for the FDA, which delegates the authority and responsibility to evaluate patient risks and oversee the conduct of an investigational study. IRBs are responsible for the ethical, legal, and safety issues of human subjects engaged in clinical studies, and it is granted the authority by the FDA to terminate or suspend a study that is not being conducted in accordance with IDE requirements, and is responsible to communicate this information directly to the FDA.

Increasingly, many peer-reviewed journals are requiring IRB approval numbers for publication in archival journals. In summary, the FDA’s IDE process ensures that studies incorporating Class III medical devices, including cochlear implants, protect the best interest of the patient and provide valid evidence.

The FDAMA Modernization Act of 1997 enabled additional, earlier collaboration between the FDA and study sponsors for Class III medical devices. These interactions, in the form of meetings prior to the IDE submission, provided an improved mechanism for sponsors to facilitate development of clinical protocols that meet FDA criteria in advance, rather than after their completion. Specifically, this has led to improvements regarding the development of candidacy criteria for cochlear implantation of children and adults.

The Hearing Aid Industry and the FDA

As stated above, according to the ACT of 1976, hearing aids were determined to be a Class I medical device and were exempt from the premarket notification process. In April 1993, however, the FDA sent warning letters to five hearing aid companies for unsubstantiated claims of improved performance in background noise, which was determined to be a “new intended use” for hearing aids that required premarket clearance. In August of 1993, the FDA sent warning letters to all hearing aid manufacturers registered in the United States. Subsequently, in August of 1994, the FDA released a document entitled “Guidance to Hearing Aid Manufacturers for Substantiation of Claims” that required the study sponsors to design studies that used a minimum of two research facilities, with the same protocols used at all locations. In addition, it was mandated that norm referenced, standardized materials be used and that data be analyzed using standard statistical treatment that required larger sample sizes than had traditionally been used by many hearing aid studies. Most importantly, the new FDA guidance required that study sponsors must make study data available for FDA review and approval prior to making advertising and marketing claims. Further, the FDA guidance created two tiers of claims, relating to technical performance of hearing aids and to wearer benefits, which
specifically addressed the issue of speech recognition in noise as a “new intended use” for which data were required to substantiate claims. The intervention made an immediate impact, in that better controls and larger sample sizes were used, but little consistency developed in the selection of objective and subjective evaluation materials. In fact, if anything, it spawned the development of numerous test measures, including the HINT (Nilsson et al, 1994), the APHAB (Cox and Alexander, 1995), and the COSI (Dillon et al, 1997), among others. More recently, there has been a concerted effort to develop and use standard measurement tools such as the IOI-HA (Cox et al, 2000) to facilitate easier comparisons between studies. Interestingly, only a handful of advertising benefit claims were approved during the period of time that the regulations were in place. Ultimately, the FDA regulations reduced the number of hearing aid-related publications in peer-reviewed, archival journals (Figure 1), but the development of additional assessment and outcome measures provided an infrastructure for future research studies.

The FDAMA Modernization Act of 1997 also had an impact on the hearing aid industry, by exempting them and 189 other Class I devices from the 510k requirement for preclearance of Type 2 wearer benefit claims for speech recognition in noise. In essence, this change placed the burden on the hearing aid industry to self-regulate the claims and testimonials that had been previously monitored under FDA guidance.

Implications

The primary difference between Class I and Class III medical devices is the amount of FDA oversight regarding the design and completion of clinical protocols. The progress, in terms of meaningful advancement of technology, candidacy requirements, and processing strategies, has been much greater for cochlear implants versus hearing aids during the past decade. There is absolutely no guarantee that direct government involvement contributed in any way to this difference, but it does suggest the need for attention to the scientific merit of research and some level of self-regulation and standardization by the hearing aid industry. Recently (November 26, 2002), the Hearing Industries’ Association (HIA) developed a new document, called Guidelines for Hearing Aid Manufacturers for Substantiation of Performance Claims, that required substantiation for advertising claims, including performance or user-benefit claims with hearing aids. This document, which was adopted by the HIA board as a standard

![Figure 1. Number of publications in peer-reviewed journals for the topic area of cochlear implants and hearing aids, based on MEDLINE review.](image-url)
LESSON 2: FOCUS ON A FEW IMPORTANT QUESTIONS, AND DESIGN WELL-CONTROLLED STUDIES TO ANSWER THEM

During the past two decades, the progress achieved with both hearing aid and cochlear implant technology has been impressive; in the U.S. market, the transition to digital, in-the-ear technology has afforded smaller, more flexible hearing aids than ever, and yet market penetration remains at 20%. Only recently, directional microphones were “rediscovered” by the market, and more recently, miniature behind-the-ear hearing aids have enabled “open fit” hearing instruments to expand the hearing aid market somewhat. There has been no consistent focus, however, throughout this period to combine recent research and clinical efforts to expand our understanding of hearing aid candidacy or outcomes by conducting larger-scale research studies. Instead, the focus has shifted among a variety of topics, often without adequate resolution, and the blame is shared equally by industry and researchers. Too many studies use a small sample size, poor experimental design, or a lack of appropriate control conditions and as a result have failed to provide conclusive results. In part, research funding agencies also contribute to the problem, as many studies have been seen in the past as “too commercial” for government funding, which exacerbates the problem by introducing the possibility of experimenter bias with industry-sponsored research.

By contrast to the hearing aid industry, the cochlear implant literature has focused more directly on a few major issues, and systematically engaged the support of researchers, clinicians, and industry sponsors. For example, in the 1980s, the major research questions addressed whether cochlear implants provided superior speech recognition than that with vibro-tactile devices. Subsequently, cochlear implants were compared with hearing aids in patients with severe-to-profound hearing loss, followed by question of single- versus multiple-electrode array processors. In addition, as new technologies emerged, the issue of brainstem implants, binaural cochlear implants, and bimodal stimulation were systematically addressed. During the past decade, candidacy requirements for cochlear implants have also been developed, based on pooled data of (relatively) large-scale, controlled studies and meta-analyses (e.g., Cheng and Niparko, 2000). The focus on a few “big” questions, rather than product-specific studies that pervade the hearing aid literature, is certainly a main factor, as is the fact that the FDA acts as a de facto review panel required with Class III medical devices.

In addition, cochlear implant research has received substantial funding by government agencies, whereas hearing aid research has typically been privately sponsored, which places a higher priority on more immediate results for marketing claims. Also, there has been more “collaborative competition” among the three major cochlear implant companies, including joint sponsorship of national and international research congresses, while still providing for competition within the marketplace. Admittedly, the stakes are different than with the hearing aid industry, as there are many fewer companies and potential patients than for the hearing aid industry, leading to fewer claims (at least at the moment). However, the stakes for hearing aid development are enormous in the public health domain, considering the millions of people who need hearing help but do not have it.

Implications

At the present time, the hearing aid market is a much larger commercial industry than the one related to cochlear implants. Furthermore, the fact that cochlear implants must be placed surgically into the ear essentially guarantees that they are perceived by consumers as more “medical,” while hearing aids are seen as more of a “retail” product. As a result, much of the supporting research for hearing aids is related more to competitive “marketing” issues (e.g., product-
related features) than to more basic issues (e.g., signal processing strategies, candidacy) that might impact all hearing aid users. This is not to say that competitive forces have not played a role or that the CI literature has not been bogged down by some problems. The fact remains that the competitive stakes are much higher at the moment with hearing aids than with cochlear implants, but this alone cannot resolve the difference. Is it that the cochlear implant industry has focused better on the “big” questions, or is it that there are more “big” questions to be addressed at the present time?

LESSON 3: PUBLISH IN ARCHIVAL, PEER-REVIEWED JOURNALS

One of the ways that the quality of an academic research program is evaluated is by the number and quality of publications in scholarly, peer-reviewed journals, which serves as perhaps the most objective benchmark for evidence-based outcomes. Ten years ago, the number of articles published in archival journals pertaining to cochlear implants and hearing aids were roughly the same. More recently, however, cochlear implant papers have doubled the number of manuscripts devoted to hearing aid issues (Figure 1).

Several plausible reasons exist for this growing disparity. First of all, the nonarchival “trade” magazine journals, including Hearing Review, Hearing Journal, and other periodicals devoted to the hearing aid industry have improved their quality and often offer shorter publication delays than peer-reviewed journals. As a result, they have provided a mechanism for industry-sponsored marketing studies and other hearing aid related articles to be published in more timely fashion than those that use the traditional editorial review process. That said, the trade journals do not have a mandate or a mechanism for monitoring the scientific merit of studies they publish. Further, they are not listed on MEDLINE and other search engines and, therefore, may not be as widely available to researchers or practitioners practicing evidence-based hearing care.

A review of recent articles indicates that the majority of research publications in the trade journals use evidence Levels 4–6, due to inadequate sample size, lack of double-blind controlled studies, or inconsistent methodology, even when multiple test sites are used. By contrast, review of peer-reviewed, archival journals indicate a much higher percentage of Level 1, 2, or 3 studies.

Implications

These findings are not intended as an incrimination of the trade journals; rather, they serve a very useful purpose and enjoy higher subscription rates than most archival journals. Nor does it suggest that quantity of publication in peer-reviewed journals implies consistent quality. If, however, the perception exists that it is easier and faster to develop and conduct studies that will be publishable in the trade journals rather than archival journals, then blame for the lack of evidence-based research in the hearing aid literature must be shared equally by industry, funding agencies, and researchers. There have been examples (e.g., Larson et al, 2000) when the government, industry, and researchers have collaborated to provide appropriately designed studies that address important questions related to the positive impact of hearing aids on hearing-impaired people. That said, the challenges presented by large scale, multicenter studies might mean that the technology is obsolete by the time the data are published, particularly in the hearing aid industry.

LESSON 4: MAINTAIN A CENTRAL DATABASE FOR BOTH PUBLISHED AND UNPUBLISHED RESULTS

One of the added benefits of Class III medical device status is that the FDA serves as a data warehouse, among other things, for premarket studies. The benefits of this utility should not be underestimated, as it provides access to larger data sets for meta-analyses that combine published and unpublished results.

One example of utility of this central database dates back to May of 2003, when an adverse event report was filed for a patient who had received a cochlear implant and developed bacterial meningitis. The FDA, which requires and monitors these data carefully, immediately accessed the U.S. and
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A worldwide database of over 50,000 cochlear implant recipients, and isolated 118 cochlear implant users worldwide (55 in the United States, 63 elsewhere) who had suffered from meningitis, with 32 developing meningitis within one year of implantation. In addition, the FDA was able to review 4264 patients in the United States who had received implants at age six or younger, with 26 reported cases of meningitis. This was a higher incidence than in the normal population, including those with severe-to-profound hearing loss, and it prompted the FDA to force an evaluation of the implant positioning device used to surgically place the electrode array. The rapid mobilization was only possible because the FDA had access to a global database of published and unpublished findings, and the full cooperation of the implant manufacturers. Admittedly, Class III devices involve more patient safety issues than for Class I devices, but it is not inconceivable that a correlation could be established between hearing loss, hearing aids users, and cardiovascular disease, multiple sclerosis, or even Alzheimer’s disease, and it would be useful to have a central database to evaluate the impact of treated and untreated hearing loss on these relationships in aging populations.

Implications

The reality is that there is a benefit to the FDA's oversight. The advantages of a data warehouse are undeniable, and yet the proprietary nature of many research questions often complicates this situation. It may be of some benefit to develop an independent repository for unpublished results to provide a tool for meta-analysis of important research questions (e.g., adaptive directionality, feedback cancellation, noise reduction, multiband compression) that are not reported when the data are not favorable. If carefully controlled, there may be a way to protect confidential information while preventing “reinvention of the wheel,” and may also serve to safeguard the patient’s interests in the event that adverse results are reported.

SUMMARY

In summary, federal oversight forces cochlear implant research to conform to good research design and execution. Oversight by the ENT device panel provides review and intervention in the event of adverse events regarding quality of execution and patient safety. Self-governance by the hearing aid industry, researchers, and funding agencies must target the same objectives. There is often a “catch-22” whereby government entities view hearing aid research as too “commercial,” while industry views hearing aid research as too restrictive for marketing purposes. Consideration should be given to the creation of an independent entity to serve as a repository for unpublished data. Furthermore, it suggests the need for more independent funding for patient-based hearing aid research, which has the potential for huge societal impact, given that hearing loss is one of the most common disabilities suffered by the elderly. Periodic publication of review papers and meta-analyses should be considered in the hearing aid archival literature. At issue will be the impact of converging technologies (e.g., hybrid cochlear implant/hearing aid devices [Gantz and Turner, 2003]) that will challenge the current FDA device classification system. Although some contend that hearing aids should be exempt from the classification system entirely, past history seems to suggest that greatest research progress has been made with at least some independent oversight. Whether this should be self-regulatory, the FDA, or some other government agency remains to be seen. The future of hearing aid technology is very promising, but if there is one lesson to be learned from the cochlear implant literature, it is that research efforts must focus on asking “big” questions and on designing and completing large, well-controlled, multicenter studies that provide more valid evidence and fewer testimonials. Further, it is the responsibility of the researchers to “complete the loop” and publish the results in peer-reviewed journals.
REFERENCES


