Cochlear Implant Strategies and Biomaterials from Past to Future

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The cochlear implant (C.I.) is a neurobionic prosthesis, being one of the greatest achievements of auditory neuroscience. Although C.I. represents the gold standard in the treatment of deafness in both the child and the adult, some problems like perception of speech in noise (atmosphere, environment), perception of music, binaural hearing remain, aspect to which improvements are expected. The article (this review) revises the road from the first attempts to cochlear implantation to today's modern and reliable cochlear implant. Continuous improvement of existing technology both in terms of biomaterials used and in terms of speech processing and simultaneous stimulation strategies, promise with certainty the introduction of C.I. with superior performance. A look in the future is through new ideas and techniques, which await the transition from the experimental to the clinical stage in the emergence of a new generation of implants.

Keywords: cochlear implant, severe hipoacusis, strategies deafness therapy, biomaterials

We present a brief history of treatment of deafness, current treatment options, what improvements can be made and what techniques are expected in the future in the treatment of deafness.

Brief history of treatment of deafness

Decreasing to hearing loss has always been a problem for society. Recognition of this disability leads to compassion, in the Mosaic law it is said *Do not curse the deaf*. Since ancient times there has been hope for a person's hearing. The Prophet Isaiah says, *There shall come a time when the eyes of the blind and the ears of the deaf shall be opened* [5].

Deafness, especially when it was congenital and led to deaf-mutilation, was a serious disability in the Middle Ages, which led to consequences. Thus, in France, deaf children were not entitled to inheritance or noble rank.

To help this troubled community in France, l'Epee, develops a sign language (gestural language) that continually improves and remains up to the present day enabling the deaf people to communicate. In Germany, Heineke develops another lip reading system (labiolecture), which is also used up to now (oral system).

The discovery of electricity causes attempts to use it to stimulate the auditory nerve to rehabilitate hearing. In 1790, A. Volta (the inventor of the battery) experimented with the stimulation of the auditory nerve. For this purpose, he inserts two plaques, one silver, and one zinc in one ear and connects them to a battery. At the moment of connection, he feels a shiver in his head, and after a while in which the stream continues to pass he declares that he begins to feel a sound that resembles the sound of boiling water. The feeling is disappointing, after several attempts, Volta does not repeat the experiment again.

This was the first attempt to stimulate the auditory nerve with electric current.

This experiment will inspire Djourno and Eyries in 1957 [34,42,45].

In a patient left deaf after a bilateral cholecystectomy, placed on the auditory nerve boss an electrode with which the nerve intermittently stimulates the 100 Hz signal 15-20 times per minute. Postoperatively the patient can distinguish simple words such as *hello, mom, dad*, but he

does not recognize speech. The experiment only lasts for a few days due to the mobilization of the electrode, which falls into the temporal muscles and can not be reconnected to the nerve.

In 1961, House searches for new ways to stimulate the auditory nerve, and implants a single rubber coated electrode in the tympanic scale to a deaf patient. After a period of 3 weeks, the electrode had to be extracted due to local irritation. The results were not conclusive. The patient could hear sounds, but he was not able to understand the spoken voice.

The experiment has demonstrated that internal ear hearing receptors can be electrically stimulated, and the produced impulse is transported by the auditory nerve to the hearing centers and from there to the central analyzer that can analyze and perceive it as auditory information.

There were researchers' objections to the possibility that the implanted person could understand speech by arguing that the 20,000 internal ear canal cells and their connections were too complex to replace by the simple electrical stimulation of the auditory nerve. There is also the supposition that the auditory nerve and the auditory pathway could be injured by electrical stimulation.

Between 1972-1978, House implanted 33 patients with a monopolar electrode in the tympanum scale, but the benefits were more anecdotal-without patients being able to grasp speech without reading on their lips. The information was transmitted through a single electrode without knowing the relationship between the electrical stimulus and the auditory receptors.

Experimental research between the years 1960-1973, made on animals, has highlighted the limits in which electrical stimulation and the time-space coding of the sound signal can be used in order to be received by the auditory nerve.

Internal ear earphones and CNS cells and fibers are arranged anatomically so as to respond to only a limited number of frequencies on a scale from low tones to high tones. So to reproduce a 5000Hz, artificially stimulated electrical tone, the fibers that normally correspond to these frequencies need to be stimulated. This can be done surgically only by placing multipolar electrodes near the nerve fibers of the auditory nerve in order to supplement Corti's organ.

On August 1, 1978 in Melbourne, Professor Clark postlingual implanted a deaf volunteer, using an C.I. with multichannel superior system in terms of performance [5]. After implantation, the patient was able to incriminate speech. Also in 1978 in Vienna, Kurt Burian implanted the first patient with a multichannel system. Between 1979 and 1980, Hockmaier, in Vienna, developed a 4-channel voice processing system [20].

The achieved success has led to the rapid development of the cochlear implantation process in most countries, USA, Australia, Austria, Germany, France and England.

Success in treating deafness in adults required the introduction of the cochlear implant in children. On April 15, 1986, the first baby, deaf after a meningitis, was implanted at the age of 3 years. The implant is a success for the child when it comes to understanding and then developing speech, so that baby implants continue [7].

After evaluating the results of a multicentre trial conducted in the coming years, which included 142 participants, the FDA approved safe and effective implantation in children between 2-17 years of age on June 27, 1990 [40].

The results, as of 2000, obtained in children implanted for congenital deafness made lower the minimum implantation age from 18 to 12 months. Thereafter, it is recommended to implant at 9 months and even at a younger age, in the idea that, according to the studies, performed, the implantation was performed at a younger age, the better the performance in terms of speech development and social integration are better [1,12,51,52].

The experience gained allows the indication of the treatment of hearing loss with conventional prostheses or with a cochlear implant [31].

The cochlear implant

C.I. is a device that restores hearing to people with severe or profound hearing loss when the hearing organ in the inner ear has not developed or has been destroyed by illness or trauma. He avoids the inner ear and gives information to the hearing centers by direct stimulation of the auditory nerve.

C.I. has the following components:

- a directional microphone that turns the sounds into an electrical signal - which is sent in a small sound processor that is worn by the ear.

- the processor converts the received sound into encoded instructions in the form of modulations that are transmitted by radio frequency using an antenna and a cable to the stimulator receptor that is implanted into the ear and fixed to the bone.

The instructions are decoded by the stimulating, rectified and filtered receiver being transmitted through a cable to the portelectrod on which the electrodes are attached. The electrode port along with the electrodes is inserted through the cochleostoma into the tympanum ramp.

According to statistics, 5% of the world's population, ie 360 million people, presents hearing disorders. Loss or even significant decrease in hearing causes social isolation depression, decreased occupational capacity. In December 2012 there are 330,000 implanting patients worldwide, which is only about 1% of 360 million people with hearing disorder [32].

Current possibilities of the cochlear implant presuppose understanding of speech without labiolecture, the ability to speak on the phone, but there is difficulty in understanding the noise in speech, and perceiving the sound source in the unilateral implant.[33]

By bilateral implantation these last inconveniences improve [13,16,37].

The advances made in the cochlear implantation are continuous and these refer to the indications of implantation, to improvements in the stimulation and coding strategy, to the operative technique and to the construction of the device itself.

Improvements in implantation indications

Regarding the indications of implantation, especially when discussing children with congenital hearing loss, it is necessary to know what binaural and bilateral hearing means.

In a patient with normal hearing we are talking about a binaural hearing. This implies that each ear sends the auditory sound signal to the hearing centers of the CNS. The brain analyzes and combines both auditory signals, making it possible to locate the audible source horizontally at a 1-2° difference. This ability to discriminate exactly the location of the sound source is due to the difference in sound perception that is about 10µs in terms of sound location and 0.5-1db in terms of sound intensity.

Binaural hearing avoids the *shadow* effect of the head and allows the speech to be filtered out of ambient sound which allows it to be understood. The existence of binaural hearing from birth allows the stimulation of auditory pathways and auditory nervous centers during neural plasticity.

The newborn receives 10 h a day of sonic information, reaching 3650 h and 6 years. The older child hears 12 h a day, totalling 4380 h / year. The child with the same age wears prosthetics for only 2.75 h / day, 9 years to reach 4380 h.

The older the child grows, the neural plasticity diminishes so that after 6-7 weeks, the auditory pathways are atrophied and the nervous centers are occupied by other sensory functions. The center of speech at the level of the cerebral cortex can no longer develop and obviously cannot have functional links with other centers of the cerebral cortex such as the center of speech, and thus the deafness is established. It is evident the need to provide auditory ways and nervous centers in the first months of life with auditory stimuli, which can be accomplished through precocious C.I. The earlier it is, the better results will be because neural plasticity is maximal in the first years of life and then decreases with age [24,35,53,54].

The bilateral hearing also implies the existence of the signal from both ears. It happens when there is a difference between the two ears when it comes to the sound signal. It is the case when one who hears with one ear and has a deep hearing to the other. If it gets implanted - after implantation it has an auditory signal from both ears.

In this situation (bilateral hearing) the brain has the ability to use the sound from the better ear. The *shadow* effect of the head is attenuated by the noise on the opposite side of the sound source and it is possible to orient the sound source [26].

The bilateral hearing allows the perception of speech in the noise, but with some difficulty [10].

In the case of children born with a deep bilateral hearing is recommended a bilateral C.I. simultaneously. The optimal situation is to be implanted until 1 year of age or even earlier. These children will have binaural hearing as well as those born with normal hearing. They will also have binaural hearing and if implantation is done sequentially but in the range of up to 2 years of age.

Deafness may occur before the age at which the language - prelingual deafness or after this age develops and develops - postlingual deafness. In the case of post-

lingual deafness the more implantation becomes later the results will be worse. Therefore, it is considered that after the age of 5-7 years implantation is no longer recommended.

In the case of bilateral C.I., if it is done sequentially the time between the first and the second C.I. is important. The results are all the better as this interval is lower. In the case of sequential implantation, the ear implanted with prelingual deafness with a long auditory deprivation time will result in poor results after implantation [41].

Progress has also been made with regard to the minimal age of implantation that has dropped below 1 year but also with respect to age of 3, where implantation, if not contraindicated with regard to the intervention, makes virtually no age threshold to counter it [38].

Studies in groups of people with auditory problems at age of 3 point to substantial improvement through C.I. the quality of life of people of the same age with uninfected

hearing problems.

Although the cochlear implant is the only way to restore hearing to prelingual children or adult and children with post-lingual deafness, it has been noticed that post-implantation results are not similar. There are patients with very good results but also patients with poor (less good) results. A number of predictive factors have been studied and identified in order to improve postimplantation results [9,28,46].

Investigating gene mutations responsible for deafness in terms of their prevalence in the population and studying the results obtained after their implantation is also a major concern [28,29,39].

The emergence of new objective techniques to evaluate postimplantation results contributes to the improvement of the results obtained in implanted persons [1,6,52].

Indications of implantation have spread to cochlear malformations - such as the single cochlea and vestibular cavity, incomplete partition, cochlear hypoplasia - situations where special electrodes are used [9,11,17,40].

Ossified cochlear (usually after meningitis) to which a double electrode can be used may also be implanted in certain conditions

Individuals with auditory debris can benefit from electroacoustic stimulation, which involves the double stimulation of the cochlea - by C.I. - electric and acoustic by hearing aid.

In recent years, implantation has been extended to people with severe hearing loss, and even unilateral deafness - to give them the possibility of bilateral hearing.

Some people with tinnitus can benefit from C.I

Improvements in stimulus and coding strategies

Another chapter where improvements have been made is that of stimulation and coding strategies. Electrodes may be straight - which are more flexible - but where the larger gap between the electrode and the electrode leads to higher current consumption, so a shorter battery life. Possible interaction between electrodes causes less electrophoresis for these electrodes. Another type of electrode is the modiolar one that is molded on the modiol. They have the advantage of lower energy consumption, with better stimulation results, avoiding channel interaction.

Stimulation may be monopolar when there is a potential difference between an intracochlear and an extracochlear electrode; bipolar when there is potential difference between 2 intracochlear electrodes in pairs and *common ground* when potential differences exist between an intracochlear electrode and all extracochlear electrodes.

Monopolar stimulation consumes less energy compared to bipolar, sound is more natural, sound threshold is more uniform and strong sound is heard more comfortable instead, it focuses sounds less well than the bipolar. In the encoding process the sound is picked up and then diffused to a particular electrode [36].

The first implants were mono-channel, the picking signal being sent directly to the auditory nerve using an analogous strategy. As a result, the frequency resolution was low and there was no intelligibility. In 1991, Black Wilson introduced the CIS (Continous Interlevel Sampling) strategy - a coding strategy that is still used today in most implants.

It picks up the audio signal, breaks it down into frequency bands and, depending on the energy of each band, stimulates the electrodes sequentially, avoiding the stimulation of the neighboring electrode.

There are a number of different electrodes depending on the implant company and the characteristics of the implanted patient [50,52].

All electrodes can be stimulated individually, but with the condition of there being breaks between stimuli.

If they are stimulated on rapid sequences simultaneously, as is the case when an implanted person participates in a conversation, the electrodes being in a liquid medium (endolimph) there is an overlap of the electric fields between the neighbouring electrodes. This makes it necessary to cancel some electrodes, so practically up to 4 to 8 channels perceive the sound signal. [52]

Consideration should also be given to the refractory period of the nerve as to the effect of summation, which also creates difficulties in stimulating neurons by electrical signals.

The limited number of channels of perception is one of the problems of the cochlear implant that researchers are looking for solutions.

Paradoxically, though, there is such a limited number of channels of perception, the intelligibility of speech is good. The same thing does not happen when the implanted person listens to the music.

Improvements in the actual implant.

These were continuous and refer both to its miniaturization, in terms of its antero-posterior diameter as well as its transversal.

The materials from which it is made are biocompatible, resistant to shockproof liquids, securing the electronics inside the casing. The materials used are ceramics, titanium, silicon, platinum, teflon. All of this has resulted in prolonging the life of the implant.

The current implant can be connected to other systems, Bluetooth, wireless, multidirectional microphones, creating facilities for the wearer.

The Syncrony Med-El model is compatible with 3Tesla MRI, making it possible to perform MRI in implant patients without the need for extracting the magnet.

Improvements in the operatory technique.

As far as the operatory technique is concerned - we discuss the best way of inserting the electrode, discussing the cohleostoma - a hole that is cut in the first spiral of the nucleus and the access to the tympanic ramp through the oval window.

In the case of the cohleostoma, it is recommended that the opening of the peritoneum to be at least of 1.2 mm and to avoid the introduction of the bone by repeated washing during milling. The round window is a natural hole - the difficulty of insertion may be due to the existence of a *eyebrow* - a bone crest - which is sometimes more prominent and requires milling.

It is recommended that in order not to damage the endocochlear fin structures, avoid sudden opening of the cochleostat and aspiration of the intraocular fluid.

The electrode will be lubricated with hyaluronic acid and will be slowly introduced with gentleness, being careful about the possible resistance to its endocochlaric conditioning. Brutal insertion of the electrode may cause intracochlear injuries. Intracochlear injuries caused by electrode insertion can be (Ramos) [40]:

- major - characterized by loss of neural elements - by bony spine bruising or by basilar membrane rupture.

- moderate - when there are partial lesions of the cochlear structures - such as the basal membrane microlensions

- minor injuries that do not alter neural function: these lesions can cause spinal ligament trauma, damage to auditory debris, or trauma to endostasis.

Hazardous areas at the introduction of the electrode are the basal spindle termination - at an insertion of the 8-12 mm or 140°-180° of the electrode. Another area of risk is the insertion at 400° of the insertion of the electrode, being the area where the second shell of the cochlea ends [40].

The insertion of the electrode must be individualized according to the dimensions of the cochlea.

More often the electrode is inserted too deeply than too shallow. The too deep insertion causes the electrode to curl and thus it does not come in contact with the nerve elements.

Researches on optimizing the performance of current implants

The following themes are proposed:

- 1. better copying of processes in terms of the cochlea,
- 2. Increasing the number of effective sensory channels with more focused stimulation in the trunk of the auditory nerve,
- 3. Improving the biological condition of the implanted cochlea for better brain information
- 4. activation of the transmission paths in the auditory brain by new electrodes designs and new processing strategies
- 5. Understand phenomena in the auditory brain and find strategies and methods of training, the brain being a vital part of the prosthesis system.

Optimization of the electrode nerve interface could be achieved by introducing drug substances into the cochlea which could cause the growth of neurites to the electrode [21,22].

The existence of a barrier between the blood and the cochlea prevents the substances from reaching the inside of the cochlea. In order to overcome this obstacle, the electrode introduced into the tympanic ramp can be used as a vector for the introduction of various substances.[37]

Substances that may be introduced may be - antioxidants (trolox, ascorbic acid). In animal experiments, the introduction of antioxidants into the cochlea causes increased electrical thresholds [22].

They are also being discussed for neurotrophic factors (neurotrophins and cytokines). This favors both peripheral neural development and CNS.

Hydrogel electrodes have been proposed that curve in contact with the fluid in the cochlea to make contact with the nerve cells.

The creation of harsh surfaces by electrochemical processes to increase the contact surface of the electrode has also been proposed [49].

Pinyon [36] explores the use of electrodes for the transfer of genes into the cochlear cells. To this end, he experimentally uses the genetic transfer of BDNF neurotrophin into the mesenchymal cells of the cochlea so that they can be used in the future to support the survival and growth of peripheral neuritis and CNS [43,47].

Steroids such as triamcinol decreases impedance after cochlear implantation and also reduces connective tissue growth around the electrode. Dexamethasone is already used to introduce the implant into the cochleostoma. It has been noticed that its use will result in a decrease in the chochlear lesions [8,25,27,45].

Another possibility of optimization is represented by nanoparticles. By nanobiotechnology an anti-inflammatory and antimicrobial layer can be applied to the electrode, protecting the implant from a possible superinfection that is the main cause of explants [49].

For its antimicrobial qualities it is envisaged the use of silver for the manufacture of the electrode port. One of the causes of neurosensory deafness is the degeneration of spinal cord cells that are electrically stimulated in C.I.

The use of nanoparticles to transport neurotrophic or steroid substances [25,27] to restore or prevent degeneration of these cells is a promise in improving implant performance [29,55].

Experimentally, implants were made to which a pump capable of releasing drug substances was attached [49].

Current implants have a number of inconveniences through their external components.

They are exposed to the action of external factors that can lead to their damage. The implanted person can not swim, is prevented from doing some sports, excessive sweating is an inconvenience for the C.I. in order to avoid these incidents and also for aesthetic reasons, the project of the total implantable cochlear implant (TICI).

In 2008, Briggs implanted 3 patients with a device called *invisible hearing* - the microphone being placed subcutaneously. The operation of the device was ensured by a lithium battery. That device was not a time-resistant project.

The difficulties with TICI are represented by the placement of the microphone - which is placed subcutaneously and has low access to the sound environment

It is discussed for avoiding this impediment the use of the tympanic membrane and the osicular chain as a microphone [44].

Another problem is the operation of the device which is activated by a battery – which, once implanted, it rises the problem of the recharging module.

Future projects

Hearing pathways can be stimulated by acoustic signal (hearing aids), by electrical (C.I.) signal, optical or by heat (infrared laser) [50,51].

Optogenetic stimulation (OGS) allows the electrical stimulation to be overcome because, if compared, light has a number of advantages.

Electricity spreads uniformly in all directions in the liquid (the endolimph in the tympanic box). This leads to the overlapping of the electric fields of neighbouring electrodes, which makes them inefficient, leading to the closure of electrodes, which results in a low number of sensory channels through which the information goes acoustically to the cortex.

Light can be directed, or even more, it can be focused on a precise target. By focusing a better spatial framing is achieved, resulting in increased frequency of resolutions and a resolution of better sound intensity [51].

If in the case of electric stimulation, due to field interference, there can be only 4-6 sensory channels, in the case of stimulation by precisely focused light there can be up to 100 sensing channels when using an electrode of the same dimensions as in classical C.I.

There are 2 optical strategies whereby light can be sent through the auditory neurons: stimulation of infrared

neurons and optogenetic stimulation [3].

Richter first used the infrared light stimulus of neurons and measured the necessary energy, temporal fidelity, spatial stretching of excitation. As reported by the spatial location of excitation through light, it was much better than electrical stimulation, but the energy needed is much higher than that required for classical C.I.

A second possibility is stimulation by optogenetics (OGS) [32]. The OGS combines genetic opsin transfection techniques in SGN with optical techniques for coding auditory information. Opsins are light transmembrane

proteins that can depolar cells [4,14,48].

Opsins are microbial - type I and animal - type II. The microbial ones are divided into 3 classes - bacredhodopsin, halorhodopsin and rhodopsin channel (ChR). ChR may be of type 1 or 2. ChR type 2 is a chlamidomonas reinhardii

gene and is used for SGN manipulation.

This gene can be transferred by adenovirus (viral transfection) into the spinal ganglion neurons (SGN). Adenovirus at a single injection gives a long duration of opsins and does not cause any obvious signs of neural toxicity or destruction of the cells in the cochlea or cochlear nuclei. The ChR2 gene transporter virus can be introduced by postnatal or transurethral injection. The latter has the advantage of offering more animals for the experiment.

In order to avoid the immune response and the compromise or even the death of genetically manipulated cells, transgenic mice are used. OGS of ascending auditory pathways has been demonstrated in animal models (mice) that mimic the human model of neurosensory deafness.

Gene transfer using adenovirus has been shown to be safe and effective in human trials by injection under the

retina (on the human eye) [44].

Optical stimulation through the implant can be active or passive - each using optoelectronic implants to generate light inside the organ, the light guided through an external source. Passive single electrode solutions offer the advantage of good tissue compatibility and stability. This would cause electrical recording artefacts because the light source and the tissue are separate. A problem is also represented by the low coupling efficiency and additional light loss by absorption.

Implantable active solutions require advanced technological innovation in terms of power-efficiency, adjustment and integration. In the development of the OGS is implanted and a maximum stimulus is created that can be applied to SGN. The temporal fidelity of stimulation above the stimulation threshold is influenced by the dynamics of ChR deactivation. In the OGS process the Ca+2 permeation causes an increased rhythm of hyperpolarization which causes acceleration of stimulation

on the auditory nerve [23].

The most promising ChR is the newly discovered Chronos that has the shortest deactivation constant (3is at room temperature). This makes possible a much faster depolarization resulting in a better rate of stimulation. Another advantage of the Chronos besides the rapid kinetics

is its great sensitivity to light. This causes a decrease in energy demand [15].

One possible advantage of OGS is that it produces small electrical artefacts that can be used for electrical recording of neural activity. It is thus possible to establish a loop stimulation system by which to control the stimulation in function of the usual neural activity. This feedback mechanism is a basic principle in regulating and controlling NS activity. The use of this mechanism leads to the improvement of direct stimulation of neural elements, reduces channel interaction and stimulates dispersion.

OGS has to answer a number of questions - one of these is biological risks. What happens after transplanting neurons with new genetic material? It is a problem that is

expected to be answered.

Another question is related to the effect of light energy on tissues, to what extent it can cause injuries. Experiments on animals made with short pulses show minimal lesions. How much energy should the light have in order not to cause lesions and if this energy is enough to cause stimulation in humans, there are questions waiting to be answered. OGS leads to the formation of H+ and Ca2+ ions and these are known to affect neurons. It is a subject of reflection.

Another issue is the energy consumption. If for the electric stimulation there are enough 0.2µJouli, in the case of OGS using ChR2 2ìJouli is needed - so 10x more energy. Closure of ion channels within the OGS is slow - solutions are needed for speeding up this process. To maintain the ionic gradient, important genetic material is required, which is a stress for neurons.

Also, a number of technical issues regarding the optical system itself await resolution. These refer to the way of focusing the beam of light that is diverted, absorbed, reflected by the cochlear and bone fluids. On which surface can be projected and how intense it should be for an optimal stimulation to selectively stimulate neurons is a problem that researchers focus on. Radiant lights in the tympanum ramp require elements to focus on the idea of selective stimulation of neurons.

As well as how the auditory cortex is activated and how the sensory perception generated by the SOG is perceived by the cortex is to be studied. The potential effect of OGS on non-auditory neurons should also be studied.

Finally, research should answer the question of whether a robust and durable OGS system can be built in time.

Intraneural C.I.

If the OGS proposes to improve the ability to stimulate as directly and accurately the neural elements using techniques that are difficult to achieve and using a signal that still does not know exactly how the cortical centers will react, there is an easier way to stimulate direct nerve, with an electrode inserted directly into the nerve, or stimulation of neural elements of modiol with a special electrode, thus solving the problems that arise concerning the distance between E. and the neural elements and the fact that the electrical implant had to go through a fluid environment - perilimph - and then pass the bone sheath that covers the neural elements.

Looking at the C.I history, we note that Djourno and Eyres's first implantation attempt was to introduce the electrode directly into the trunk of the nerve. This path was subsequently followed by Simmons, which, after studies on public experimental animals since 1964, results in the direct stimulation of the auditory nerve. [41]

The long-term results as well as the anatomopathological studies performed on experimental animals lead him to pass on the implantation of patients. In 1979 a preliminary report with data obtained after implantation of 2 volunteers was published. This demonstrates that chronic intranasal implantation is well tolerated, highlighting the lack of partial SGN loss and trauma resulting from intranasal implantation, and auditory thresholds are stable over the long term. As opposed to classical implantation, direct implantation in the nerve allows the direct interaction with neural tissue to increase the number of sensory channels and stimulate more apical fibers, which would lead to better stimulation for low frequencies [30].

Another advantage relates to situations where the cochlea is ossified and classic implantation is difficult or can not be achieved. In this type of implantation it is also mentioned that the risk of damage to the facial neuron is much diminished, the electrode being at a distance from it

The next type of electrode is the *Michigan* electrode that has been well tolerated in animal experiments. The electrode was used either intracanalicular or intramodiolar.

According to implantation studies in modiol there were fewer neural losses.

On the same idea of diminishing the neural lesions due to the introduction and existence of the electrode in the nerve structure, in 2002 Badi presents a technique of implanting an electrode in the modiolar nerve through the facial recession in order to present in 2007 the insertion technique and the results of implanting an electrode the cochlear nerve. They collected auditory responses following implantation and reported minimal histological trauma to the experimental animal (cat) [2].

Also, studies by Myddlebrooks and Snyder demonstrate that intraneural implantation with the right electrode ports causes neural responses evoked auditively at lower current levels than conventional implants [30].

These studies have also shown that it is possible to stimulate with increased number of independent channels by reducing the number of channel interactions, which is the phenomenon of electrical stimulation [28].

This type of implant, if it proves to be safe and will not be inferior in terms of performances compared to the classic C.I., is a valid option for patients with cochlear malformations or ossuary cochlear.

References

1.ARCHBOLD S, O'DONOGHUE GM. Cochlear implantation în children: current status.Paediatrics and Child Health, 2009, 19(10):457-463.

2.BADI AN, HILLMAN T et al. A technique for implantation of a 3 dimensionat penetrating electrode array in the modiolar nerve of cats and humans. Arch. Otolaryngol. Head Neck Surg. 2002, 128 (9), 1019-2025 [Pabmed 12220205]

3.CALLAWAY E.M., YUSTE R., Stimulating neurons with light. Curr Opin Neurobiol. 2002,12(5):587–592.

4.CARDIN J.A., CARLÉN M., MELETIS K., KNOBLICH U., ZHANG F., DEISSEROTH K., TSAI L-H, MOORE C.I., Targeted optogenetic stimulation and recording of neurons în vivo using cell-type- specific expression of channelrhodopsin-2. Nat Protoc. 2010, 5(2):247-254. 5.CLARK GRAEME, Cochlear implants. Fundamentals and Applications Springer, 2003, ISBN:0-387-95583-6.

6.COZMA S., DASCALU C.G., RADULESCU L., MARTU C., BITERE O., MARTU D., OLARIU R. Audiological clinical validation of new original romanian speech audiometry materials for evaluation of communication abilities in children of primary school age.Revista de Cercetare si Interventie Sociala, 2016, vol. 55, pp. 47-62

7.ESHRAGHI AA, NAZARIAN R, TELISCHI FF, et al. The cochlear implant: historical aspects and future prospects. Anatomical record. 2012; 295(11):1967–1980.

8.ESHRAGHI AA, ROELL J, SHAIKH N et al A novel combination of drug therapy to protect residual hearing post cochlear implant surgery. Acta Otolaryngol,2016, 136:420–424

9.FAULKNER K.F., PISONI D.B., Some observations about cochlear implants: challenges and future directions. Neuroscience Discovery ISSN 2052-6946, 2013, 1-9

10.FRIESEN L.M., SHANNON R.V., BASKENT D., WANG X., Speech recognition în noise as a function of the number of spectral channels: comparison of acoustic hearing and cochlear implants. J Acoust Soc Am., 2001,110(2):1150.

11.GIFFORD RH AND REVIT LJ. Speech perception for adult cochlear implant recipients în a realistic background noise: effectiveness of preprocessing strategies and external options for improving speech recognition în noise. J Am Acad Audiol. 2010; 21:441-51;

12.GORDON KA, JIWANIS AND PAPSIN BC. What is the optimal timing for bilateral cochlear implantation în children? Cochlear Implants Int, 2011; 12 Suppl 2:S8-14.

13.GORDON KA, WONG DD AND PAPSIN BC. Bilateral input protects the cortex from unilaterally-driven reorganization în children who are deaf. Brain., 2013; 136:1609-25.

14.GROSSMAN N., NIKOLIC K., TOUMAZOU C., DEGENAAR P. Modeling study of the light stimulation of a neuron cell with channelrhodopsin-2 mutants. Biomed Eng IEEE Trans. 2011,58(6):1742–1751.

15.GUNAYDIN LA, YIZHAR O, BERNDT A, SOHAL VS, DEISSEROTH K, Hegemann P. 2010. Ultrafast optogenetic control. Nat Neurosci. 13(3):387–392.

16.HANCOCK KE, NOEL V, RYUGO DK AND DELGUTTE B. Neural coding of interaural time differences with bilateral cochlear implants: effects of congenital deafness. J Neurosci. 2010; 30:14068-79.

17.HANCOCK KE, CHUNG Y AND DELGUTTE B. Congenital and prolonged adult- onset deafness cause distinct degradations în neural ITD coding with bilateral cochlear implants. J Assoc Res Otolaryngol. 2013; 14:393-411.

18.HERNANDEZ V.H., GEHRT A., JING Z., HOCH G., JENCHKE M., STRENZKE N., MOSER T., Optogenetic stimulation of the auditory nerve. J.Vis. Exp. 2014 (92):52069;258-

19.HERNANDEZ V.H.,, GEHRT A., REUTER K., JING Z., HOCH G., JENCHKE M., Mendoza Schultz A., Hoch G., Bartels M., Vogt G., Garnham CW.: Optogenetic stimulation of the auditory pathway, J Clin Invest, 2014, 124, 1114-1129.

20.HOCHMAIR INGEBORG, The importance of being flexible. Nature Medicine, 2013, 19(10), 1240-1243

21.HOMSY A, LAUX E, BROSSARD J et al, Fine control of drug delivery for cochlear implant applications. Hearing Balance Commun, 2015,13:153–159

22.IHLER F, PELZ S, COORS M et al, Application of a TNF-alpha-inhibitor into the scala tympany after cochlear electrode insertion trauma în Guinea pigs: preliminary audiologic results. Int J Audiol. 2014, 53:810–816

23.ISERI E. KUZUM D,Implantable optoelectronic probes for în vivo optogenetics, Journal of Neural Engineering, 2017, 14, (3): 695-730 24.KRAL A AND SHARMA A. Developmental neuroplasticity after cochlear implantation. Trends Neurosci. 2012; 35:111-22.

25.KUTHUBUTHEEN J, SMITH L, HWANG E et al, Preoperative steroids for hearing preservation cochlear implantation: a review. Cochlear Implants Int., 2016,17:63–74

26.LITOVSKY RY, PARKINSON A AND ARCAROLI J. Spatial hearing and speech intelligibility în bilateral cochlear implant users. Ear Hear. 2009:30:419-31.

27.LIU Y, JOLLY C, BRAUN S et al. în vitro and în vivo pharmacokinetic study of a dexamethasone- releasing silicone for cochlear implants. Eur Arch Otorhinolaryngol 2016,273:1745–1753

28.MARTU C. Predictors factors for auditory- verbal evolution in patients with cochlear implant, Doctoral Thesis, UMPh, Grigore T. Popa, Iasi, Romania, 2012.

29.MARTU, C., GEORGESCU, M.G., MARTU, I., BUTNARU, C., PORUMB, V., RADULESCU, L., Utility of Drug Loaded Nanoparticles in the

Treatment of Inner Ear Pathology. Mat. Plast., **53**, no.2,2016, p. 321-325

30.MIDDLEBROOKS J.S., SNYDER R.L., Auditory prosthesis with a penetrating nerve array. J. Assoc Res. Otolaryngol, 2007(8): 258-279. 31.MORGON A.H., Supleance instrumentale de la surdite: les aides auditives. 1998, Societe Francaise d'ORL, Paris, ISBN: 2-9511343-2-0 32.MOSER T., Optogenetic approaches to cochlear prosthetics for hearing restoration. în Optogenetics. De Gruiter 2013: 187-192.

33.MOSER T., Optogenetic stimulation of the auditory pathway for research and future prosthetics. Current Opinion în Neurobiology, 2015.34:29-36

34.MUDRY A AND MILLS M. The early history of the cochlear implant: a retrospective. JAMA Otolaryngol Head Neck Surg. 2013; 139:446-53. 35.NIPARKO JK, TOBEY EA, THAL DJ, EISENBERG LS, WANG NY, QUITTNER AL, FINK NE. Spoken language development în children following cochlear implantation. JAMA. 2010; 303:1498-506.

36.PINYON J.L., TADROS S.F., FROUD K.E., WONG Y., TOMPSON A.C., CRAWFORD I.T., KO E.N., MORRIS M., KLUGMANN R., HOUSLEY M.G.D., Close-field electroporation gene delivery using the cochlear implant electrode array enhances the bionic ear. Sci Transl. Med. 2014, 6: 54-

37.PLONTKE S.K., GOTZE G., RAHNE T., LIEBAU A., Intracochlear drug delivery în combination with cochlear implants. HNO, 2017, 65(supl.1):519-528.

38.RADULESCU L., MARTU D., Do we need an ethics committee in order to make decisions regarding the cochlear implant?. Revista Romana de Bioetica, 2007, 5(2):27-32

39. RADULESCU L., MARTU C., BIRKENHAGER R., COZMA S., UNGUREANU L., LASZIG R. Prevalence of mutations located at the DFNB1 locus in a population of cochlear implanted children in eastern Romania. Int J Pediatr. Otorhinolaryngol. 2012, 76 (1):90-94

40.RAMOS-MACIAS A., BORKOSKI-BARREIRO S., FALCON-GONZALEZ J., RAMOS DE MIGUEL A.; Implante coclear. Estado actual y future. Rev. Med. Clin. Condes, 2016, 27(6):798-807.

41.RAMSDEN JD, PAPSIN BC, LEUNG R, JAMES A AND GORDON KA. Bilateral simultaneous cochlear implantation în children: our first 50 cases. Laryngoscope. 2009; 119:2444-8.

42.RAMSDEN RT. History of cochlear implantation. Cochlear implants international. 2013; 14(Suppl 4):S3–5. [PubMed: 24533753]

43.RICHARDSON RT, THOMPSON B, MOULTON S et al, The eûect of polypyrrole with incorporated neurotrophin-3 on the promotion of neurite outgrowth from auditory neurons. Biomaterials, 2007,28:513–523

44.ROCHE JP., HANSEN M.R., CARDIN JA, CARLÉN M, MELETIS K, KNOBLICH U, ZHANG F, DEISSEROTH K, TSAIL-H, MOORE CI, Targeted optogenetic stimulation and recording of neurons în vivo using cell-type-specific expression of channelrhodopsin-2. Nat Protoc., 2010, 5(2):247-254.

45.ROCHE JP, HANSEN MR., On the horizon: cochlear implant technology. Otolaryngol Clin North Am, 2015, 48:1097–1116

46.RUBEN H. M. VAN EIJL, MSC; PATRICK J. BUITENHUIS, BSC; INGE STEGEMAN, SJAAK F. L. KLIS, PHD; WILKO GROLMAN, MD, PhD, Systematic review of compound action potentials as predictors for cochlear implant performance. Laryngoscope, 2017,127:476-487,

47.SAMEER MALLICK A, QUREISHI A, PEARSON R et al, Neurotrophins and cochlear implants: A solution to sensorineural deafness? Cochlear Implants Int. 2013,14:158–164

48.SHIMANO T., FYK-KOLODZIEJ B., MIRZA N., ASAKO M., TOMODA K.,BLEDSOE S., PAN Z.H., MOLITOR S., HOLT A.G.,Assessement of the AAV-mediated expression of channelrhodopsin-2 and halorhodopsin în brainstem neurons mediating auditory signalling. Brain Research,http://dx.doi.org/10.1016/jbrainres.2012.10.030

49.STOVER T., LENARTZ T., Biomaterials în cochlear implants. GMS Current Topics în Otorinolaryngology - Head and Neck Surgery, 2009, vol. 8, pg. 1-22, ISBN 1865-1011.

50.TYLER R.S., OPIE J.M., FRYAUF-BERTSCHY H., GANTZ B., Future directions for cochlear implants. Orientations futures pour les implants cochleaires. JSLPA,1992, 16(2)/Roa,1992,16(2), 151-161

51.WEISS R.S., VOSS A., HEMMERT W., Optogenetic stimulation of the cochlea-A review of mechanisms, measurements, and first models. ISSN: 0954-898X (Print) 1361-6536 (Online), J.homepage:http://www.tandfonline.com/loi/inet20

52.WILSON B.S., DORMAN M.F., Cochlear implants: current designs and future possibilities. J.Rehabil Res.Dev., 2008, 45: 695-730.

53.YOUNG N.M., KIRK I.K., Pediatric cochlear impantation , Springer, 2016, ISBN:978-1-4939-2788-3

54.ZIMMERMAN-PHILLIPS S, ROBBINS AM AND OSBERGER MJ. Assessing cochlear implant benefit în very young children. Ann Otol Rhinol Laryngol Suppl., 2000; 185:42-3.

55.ZOU J., PYYKKO I., HYTTINEN J., Inner ear barriers to nanomedicine-augmented drug delivery and imaging. J of Otology, 2016,11:165-177.

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