Management of Severe Cochlear Implant Infections – 35 Years Clinical Experience

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Short running head: Management of Severe Cochlear Implant Infections

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Abstract

Objective. Infectious complications occurring in cochlear implant (CI) recipients is of potentially major impact. A better understanding of severe infections in this cohort is necessary.

Design. Single-centre, retrospective cohort study. Level of Evidence 2B.

Setting. Single-centre, retrospective cohort study at a tertiary referral hospital.

Participants and interventions. We included all patients who received a CI at our institution between 1983 and end of 2018 (4622 implantations).

Main Outcomes. Prevalence, incidence, risk factors and functional outcomes in severe implant infections.

Results. There was an overall prevalence of 0.65% of severe CI infections. The cumulative incidence decreased after the year 2000, with lower infection rates with newer implant models. Patients with local risk factors were more susceptible to implant infection. In most patients, delayed re-implantation was successful. Speech-perception after re-implantation was comparable to pre-revision performance.

Conclusions: Modified implant design and improved surgical technique has led to a decrease in the prevalence and incidence of infected implants. In severe implant infections, active surgical and antimicrobial management is required, in order to achieve good long-term results.

Keywords: cochlear implants, infection, explantation

Introduction

Severe infection complications in cochlear implant (CI) recipients are rare; however, the consequences may be drastic. Infection involving the device may necessitate removal of the implant. This involves considerable morbidity and potential loss of the hearing benefit previously achieved with the implant. If the infection involves the labyrinth, the electrode array also has to be removed, making re-implantation potentially impossible.

Acute infectious complications usually resolve completely with appropriate antibiotic therapy. Rarely, additional surgery is required; if an acute mastoiditis is present, pressure equalizing tubes with abscess drainage is warranted [1]. Infection can spread via the cochlear aqueduct intracranially leading to meningitis [2]. Even in these severe acute infections, explantation of the device is rarely necessary [3].

Chronic infectious complications on the other hand can lead to wound breakdown and device exposure. A subdivision into dry and suppurative cases can be made (Fig. 1). Dry device exposure can be caused by pressure necrosis caused by the magnet or thin and poorly vascularized skin. In these instances, revision surgery can be successful with preservation of the exposed implant by covering it with healthy tissue. In contrast, patients with chronic suppurative infections may have otorrhoea, fluctuant granulation around the device, purulent wound breakdown, and or fistula formation. Here, the implant is usually not salvageable as the infection is often associated with biofilm formation [4]. Extracellular polymeric secretions on the device surface render bacteria relatively invulnerable to the host immune response and antibiotic therapy [5-7]. Conservative therapy and surgical drainage is not successful and device removal is required [8].

The aim of this study was to investigate the epidemiological key figures, underlying risk factors, management, and outcomes in severe CI infections requiring explantation of

the device. Only with a better understanding of these cases, can we optimize the outcome in individual patients and develop new strategies to reduce further the risk of severe infections.

Methods

All CI surgeries between 1983 and December 2018 at our institution were reviewed to identify explantations due to infection. Detailed data from these patients was obtained from clinic charts and hospital records. Variables included age, gender, cause of hearing loss, predisposing risk factors, location of the infection, implant type, identified pathogens, treatment course and hearing outcomes after re-implantation. For hearing outcomes, we examined speech perception scores for the CVC word and phoneme test. The most recent result prior to the occurrence of infection was compared to the latest available value.

The study was conducted with approval of the local ethical committee as a quality assurance activity study (Human Research Ethics Committee, Royal Victorian Eye and Ear Hospital, Melbourne, Australia) and followed the guidelines of the Declaration of Helsinki [9].

Results

Epidemiology

Until 2018 4622 patients underwent CI surgery (adults = 3036, children = 1586). During this period, in 30 cases device removal due to infection was recommended. In one case (tab. 1; ID38), explantation was not performed due to the patient having a terminal medical condition. Explantations occurred in all age groups (8 paediatric and 21 adult

patients). Median age at explanation was 55.7 years (interquartile range, IQR, 13.0 – 65.4 years).

At our institution, the number of implantations has increased steeply since the late 1990's. Fig. 2A) shows the number of implants as well as the explantations performed per year since 1983. The prevalence of CI infection requiring explantation of the device at the end of 2018 was 0.65% (adult population 0.72%; paediatric population 0.5%). Whereas the cumulative incidence of severe implant infections reached nearly 1% in 1990, this number dropped after the year 2000 and has been stable thereafter at around 0.06% (mean value; Fig. 2B).

In our cohort, the most common implant model used was the CI 24RE (CA) with nearly 1500 implantations (infection rate 0.5%; Fig. 2C). The second most common device was the CI512 (n=1183, IR 0.1%). The majority of infections occurred in earlier model implants (i.e. CI22M, IR 4.1%, and CI24M, IR 3.7%). For the newer models (i.e. CI 24RE(ST), CI522 and CI532) no infections necessitating explantation have occurred so far. It must be taken into account however, that the observation time for these models has been shorter compared to older devices.

In the 29 explanted cases, the time interval between implantation and removal of the implant varied widely (Fig. 2D; median 6.6 years, IQR 1.1 - 12 years). 4 patients presented with symptoms within the first 3 months after implantation. In one case, we have to assume a contamination during surgery as the patient presented with postoperative wound infection only days after initial implantation (ID 20). The longest time interval between implantation and explantation was 34.9 years (ID11). This patient suffered from retroauricular fistula formation, extending from the posterior external ear canal.

Pathogens, site of infection

In 23 patients, microbiology results identified at least one pathogen (Fig. 3; tab. 1). In 4 cases two concomitant bacteria could be detected. Most commonly, implant infections were caused by methicillin-susceptible Staphylococcus aureus (MSSA, n=12). A methicillin-resistant Staphylococcus aureus (MRSA) was detected in one case. In 6 cases Pseudomonas or coagulase negative Staphylococci were incubated.

On average (median), antibiotic treatment was given for 18 days post revision surgery (IQR 7- 44 days). In patient ID27, antibiotic treatment was prescribed indefinitely. In all cases, except patient ID27, infection could be controlled by revision surgery and concomitant antibiotic treatment.

Regarding the site of infection, two predominant subtypes were present. The first with device exposure where secondary, confined infection occured. The second, where the device became primarily infected, leading to a wider spread of the infection (tab 2). In latter case, the receiver-stimulator package (RSP), mastoid, and middle ear were often affected and/or there was a postauricular skin breakdown. Intracochlear extension of infection was noted in 4 patients.

In 13 patients, parts of the implant were extruding and visible to inspection. Either the electrode cable (n=6) or a dacron mesh (n=1) protruded into the external ear canal or through the tympanic membrane. Post-auricularly, in 4 patients the RSP, the antenna (n=2) or the ground electrode (n=1) were exposed through the skin breakdown.

Risk factors

Following systemic risk factors were present: one patient had rheumatoid arthritis and one patient chronic eczema and bronchial asthma requiring immunosuppression (tab.

1; ID03 and ID28). Two patients suffered type 2 diabetes (ID04 and 27). The final patient had metastatic melanoma and very poor general health.

Of greater significance was the incidence of local risk factors: 50% of our cohort had chronic ear problems other than hearing loss prior to CI surgery; four patients (13%) had been treated for chronic middle ear effusion, 7 patients (23%) for chronic suppurative otitis media without cholesteatoma (CSOM), and 4 patients (13%) for cholesteatoma.

Speech-perception outcomes

In 17 cases, the electrode cable was cut at the facial recess and left in place. In one patient the electrode lead was replaced by a dummy (ID15). In all 18 cases, re-implantation was subsequently performed. Median time to re-implantation in two-stage procedures was 6 months (IQR 4 – 8 months). In 4 cases re-implantation was done as a single stage procedure at the time of explanting the device (patients with either dry device exposure or cholesteatoma without involvement of the implantation site). Eight patients were not re-implanted on the infected side: in 3 cases, re-implantation was not possible as the infection had spread into the cochlea with subsequent obliteration of the cochlear lumen. One patient (ID29) suffered from an extensive cholesteatoma with multiple infected sites. In 3 cases re-implantation was not performed on patient's preference (in all of them, speech perception was below-average with the initial implant). Finally, one patient was not explanted for the medical reasons given above.

Out of the 22 re-implantations, full insertion was achieved in 20 cases. In patient ID15, due to fibrotic tissue within the inner ear, only 17 out of 22 electrodes were introduced. In patient ID14, re-implantation was abandoned as the previously cut electrode had slipped out of the cochlea with complete fibrosis of the lumen. Following re-implantation

speech perception scores were similar to pre-infection performance in the majority of patients (Fig. 4): median understanding of CVC words and phonemes increased after re-implantation slightly but non-significantly (words pre 34%, words post 36%; phonemes pre 60.5%, words post 63%). Two patients (ID13 & 24) had decreased thresholds for CVC words and phonemes (-62%/ -42% and -28%/-33% respectively). No obvious reasons could be ascertained when reviewing their medical files.

Discussion

At our institution, until the end of 2018, 4622 implantations were performed. We are the only medical centre in our state that treats CI patients (population 7 million). All surgeries and follow-up are conducted through our clinic. Hence, all severe complications are directly referred to our institution for evaluation. Furthermore, all devices used have been from the same manufacturer.

Epidemiology

Since 1983, 30 cases of severe infective complications occurred in our cohort, necessitating the explanation of the implant device. This corresponds to an overall prevalence of 0.65%. Smaller studies have reported prevalence rates of 0.74% and 1.5% of patients requiring explantation of the device [8,10]. In our cohort, 8 out of 30 patients were children or adolescents. Reported rates of severe CI infections for paediatric and adult patients has been variable. Some authors reported lower rates in paediatric compared to adult cohorts [10,11] others the reverse [8].

Notably, in our cohort, the cumulative incidence reached nearly 1% in the 1990s. This decreased after the late 1990's and has stabilized since. Beside improvements in surgical practice, one explanation of lower infection rate is the introduction of

modifications to the implant. Older devices (CI22M and CI24M) had higher infection rates compared to newer models. A study by C. Whitchurch and R. Leigh with an in vitro model showed that devices with deep and narrow recesses and steep sides were more prone to bacterial attachment and biofilms (manuscript in preparation). This finding was also confirmed when examining explanted devices under the electron microscope; biofilms were thicker in depressed areas of implants [4,12]. Celerier, Rouillon, Blanchard, Parodi, Denoyelle, Loundon [13] found biofilm staining either on the magnet, on the silicone magnet pocket, at the emergence of the electrode array from the RSP or on the extra-cochlear electrode plate. Reefhuis et al. (2003) demonstrated further evidence that implant design plays a major role in infection rates; her group showed that an electrode positioner led to increased rate of meningitis. These findings have been incorporated into newer implants with wider recesses and smooth transitions of the external package (Cochlear CI 500 model). In a worldwide comparison between CI 500 and former CI24RE implant models, over an observation period of 8 years, there was an infection rate of 0.35% and 0.68%, respectively (courtesy of Cochlear Limited, Australia). Presumably, this lower rate of infection relates to the change in design rather than any changes in surgical approach.

Infections may occur at any stage after surgery [14]. In our findings, median time between implantation and explantation was 6.6 years. In at least one case, we have to assume a contamination during surgery. Most patients however, had delayed infection of their implant. The longest time was nearly 35 years after implantation. There are various possible causes of delayed device infection: haematogenous spread (e.g. dental work), pressure necrosis with device exposure, or ascending infection from the middle ear or mastoid cavity. It is now recognized that biofilm formation plays an important role in delayed infections not responding to conservative interventions. Certain bacteria build

slime-encased communities with elevated resistance to antibiotic and immune defence, making eradication of infection from the device very difficult without explantation. The timing of initial device contamination is still not well understood. Presumably in some cases it occurs at surgery however may not manifest until months or years later.

Pathogens

In our cohort, the most common bacterium identified was MSSA. In one case, there was resistance to methicillin (MRSA). Coagulase negative Staphylococcus and Pseudomonas aeruginosa were also often observed.

From literature we know that staphylococci cause most infections not only in CI but in in surgical implants in general [15]. The bacteria may be introduced as skin contaminant at the time of surgery with subsequent colonialization of the implant. Staphylococcus and Pseudomonas are known to be able to develop biofilms in the presence of foreign material [16]. The absence of microcirculation at the surface of foreign bodies leads to an insufficient host defence and delivery of antibiotics [17]. However, it must be emphasized that not every colonialization and biofilm formation on implants results in clinical infection [18,19]. Antonelli, Lee, Burne [4] found electron-microscopic evidence of biofilm formation in CI cases, which had been explanted for non-infection reasons. It is only the complex interaction between the host, the implant, and pathogen, which finally causes an active infection [17]. Nonetheless, a colonialization of the implant is a prelude to any subsequent infection.

Risk factors

In the case of severe CI infections, local risk factors seem to play a more important role than systemic ones. In our cohort, 13% had systemic immunodeficiency, whereas 50%

showed local risk factors prior to implantation. Most patients of the latter group suffered from CSOM (23%), chronic middle ear effusion (14%) or cholesteatoma (13%). This accords with previous literature; Cunningham III, Slattery III, Luxford [8] identified a history of ear disease in 52%. Luntz, Teszler, Shpak [20] found that patients who are preoperatively susceptible to otitis media also have more episodes of infections postoperatively. Good control of otitis media before implantation reduces the risk of subsequent infection [14].

Outcomes

In our cohort, two patients demonstrated a deterioration in speech recognition. Rivas, Marlowe, Chinnici, Niparko, Francis [21] reported that out of 6 cases, which were explanted due to infective reasons, 1 had a deterioration of post-revision speech scores.

It is reassuring that in the majority of patients, after re-implantation, speech perception scores were comparable to pre-revision. Also, that none developed intra-cochlear spread or delayed recurrence of infection.

Infective complications managed without explantation

A limitation of this database review is that only cases of infection where implant removal was performed are identified. As noted in the introduction, the occurrence of acute otitis media is not uncommon in children with cochlear implants[1,14]. Fortunately, complete resolution usually occurs with routine treatment without progression to chronic device infection[20]. In severe ear infections, including affections of the mastoid space and skin flap, preservation of the implant is possible in selected cases. In our series, four children had acute otitis media associated with mastoiditis (1 perioperative, 3 delayed).

We performed post-auricular incision and abscess drainage with concurrent initiation of antibiotic therapy. In all these cases, the responsible organism was Streptococcus pneumonia. Complete resolution of infection occurred despite clear evidence of implant contamination, presumably because there was no biofilm formation. In our adult cohort, there were two situations were explantation was avoided in a small number of cases: i) wound breakdown with dry device exposure and ii) cholesteatoma formation, where the chronic infection was separated from the implant. In the first subgroup, a patient showed a partial necrosis of the skin flap with dry device exposure. We repositioned the RSP after antiseptic decontamination and repaired the rotation flap. After three months of additional antibiotic treatment, completely healed skin conditions showed no signs of a persistent infection. In the subgroup with cholesteatoma formation, we successfully performed revision surgery in 2 cases. Preservation of the implant was possible as we could completely separate the cholesteatoma matrix from the implant without further evidence of chronic infection around it. The follow-ups showed no recurrence after 20 and 25 years, respectively.

In severe ear infections, although implant-preserving revisions are possible in selected cases, other patients show that this approach is insufficient. In our cohort, one or more revisions were performed in 6 cases, before finally deciding to remove the implant. In patients ID01 and ID10 skin flaps revisions were performed (in ID01 twice), in patients ID05 and ID23 we evacuated an infected seroma and haematoma, in patient ID09 an infected radical cavity with abscess formation was revised and, finally, patient ID21 showed recurrence of otits media, where a tympanic drainage was tried. In all these cases, implant removal was ultimately unavoidable. If the infection persists despite revision and long-term antibiotic administration, we assume formation of biofilm.

Clinical implications

To prevent infectious complications, all patients should be vaccinated at least 2 weeks prior to surgery [22,23]. A stable ventilated middle ear that is free from active infection needs to be achieved prior to surgery. If this is not possible or recurrence of otitis media is likely, then blind sac closure with or without obliteration of the middle ear and mastoid space should be considered [24].

Intravenous antibiotics should be administered within 1 hour prior to implant surgery[25]. Intraoperatively, a meticulous sterile technique must be used during the whole procedure including change of gloves immediately before handling the implant. Optimally the RSP should be in a stable position postero-superior to the mastoidectomy and not crossed by the periosteal or skin incisions. Incisions should be curvilinear in order to avoid disrupting scalp circulation and crossing the implant body [26]. The periosteal flap incision should be performed in an offset fashion. Before opening the inner ear, the entire surgical site must be thoroughly irrigated to remove bone dust and debris. After insertion of the electrode, the insertion site should be sealed carefully with fibrous tissue. This step is particularly important in patients with inner ear malformations [27,28]. The electrode cable within the mastoid cavity should be placed away from the bony ear canal, preferably beneath a cortical bony overhang. The implant body should lie directly on the skull bone and completely be covered by the periosteal layer. Wound closure should be performed in at least two separate layers (periosteal flap and skin).

Any ear infection in implant users must be treated immediately. Depending upon the severity of infection, patients are usually treated with intravenous and/or oral antibiotics for one to three months [29]. Microbiology results taken from a swab should guide in the selection of antibiotic therapy. However, negative culture does not mean absence of

infection. While dry infections with implant exposure and patients with cholesteatoma formation where the infection is clearly separated from the implant can sometimes be managed by revision revision surgery, in chronic suppurative cases, explantation of the device is usually the only choice. When explantation is performed, all inflamed tissue should be debrided thoroughly. If the mesotympanum is free of disease, the electrode cable can be cut at the facial recess [30]. Alternatively, a dummy electrode can also replace the intracochlear array. The intracochlear electrode or dummy array serve as placeholders and permit re-implantation at a second stage procedure. If the infection has spread to the cochleostomy and inner ear, the electrode should be fully removed to allow complete resolution of the infection. However, in these cases successful re-implantation is generally not possible and the hearing on this side lost.

Conclusion

Severe infectious complications in CI recipients are rare but can occur years after implantation. Modified implant design has reduced the tendency to Biofilm adherence and improved surgical procedures have diminished both intraoperative contamination and delayed device exposure. This has led to a decrease in the prevalence and incidence of infected implants.

Figures Captions

Fig. 1. Differentiation of chronic implant infections. Patient A) presents with a dry wound breakdown with device exposure. No granulation tissue is present. Note that the implant was positioned immediately beneath the skin incision (scar). In dry infection cases, revision surgeries might allow to preserve the implant in some cases. Patient B) shows a suppuratives implant infection with profuse granulation tissue and purulent discharge. In latter case, an explantation is usually indicated.

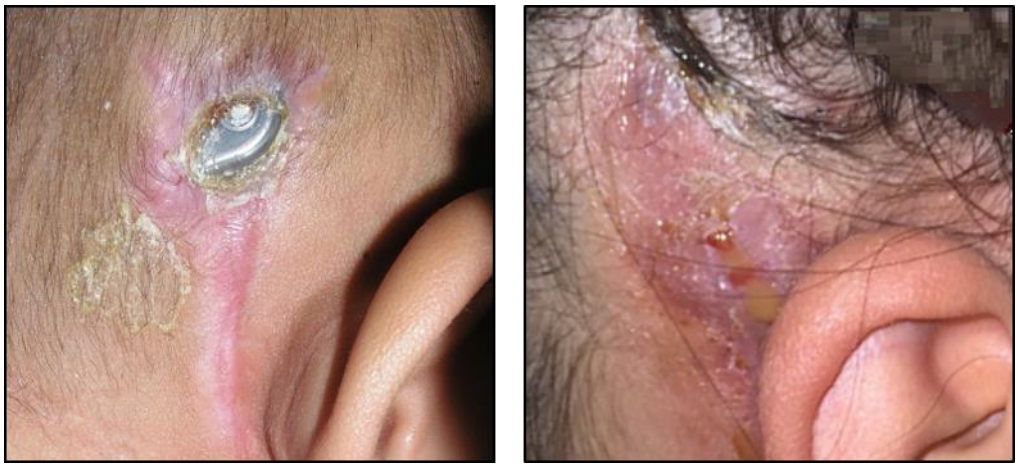
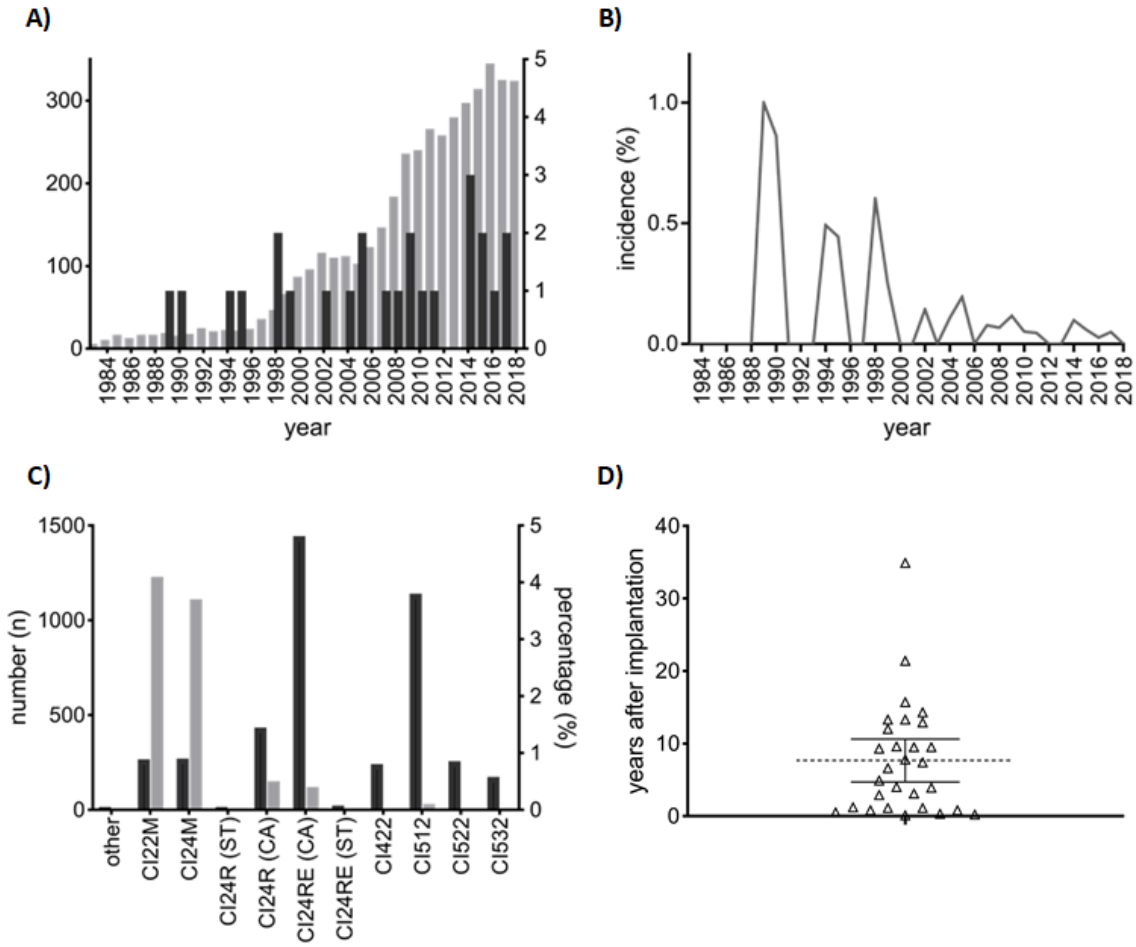


Fig. 2. Epidemiological findings in severe implant infections. A) Implanted devices per annum (grey bars) and explanted devices due to infectious reasons (black bars). B) Cumulative incidence of severe implant infections. Since the beginning of the new century, the incidence has dropped and stabilized at around 0.05%. C) Number of implanted devices since 1983 (y-axis, left side, black bars). Percentage of explanted devices due to infections (y-axis, right side, grey bars). D) Time between initial implantation and explantation (median 6.6 years; interquartile range 1.1 – 12.5 years). The shortest duration was 7 weeks, the longest 35 years.



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367 Fig. 3. Most commonly, Staphylococcus aureus, coagulase-negative Staphylo-coccus,
368 and Pseudomonas were identified as causative pathogens. In some of the patients,
369 concomitant germs were incubated.

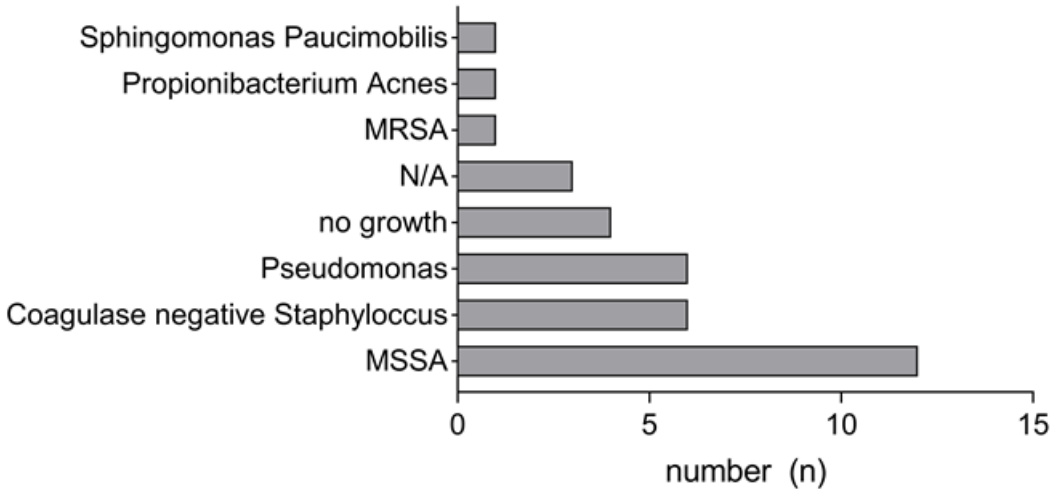

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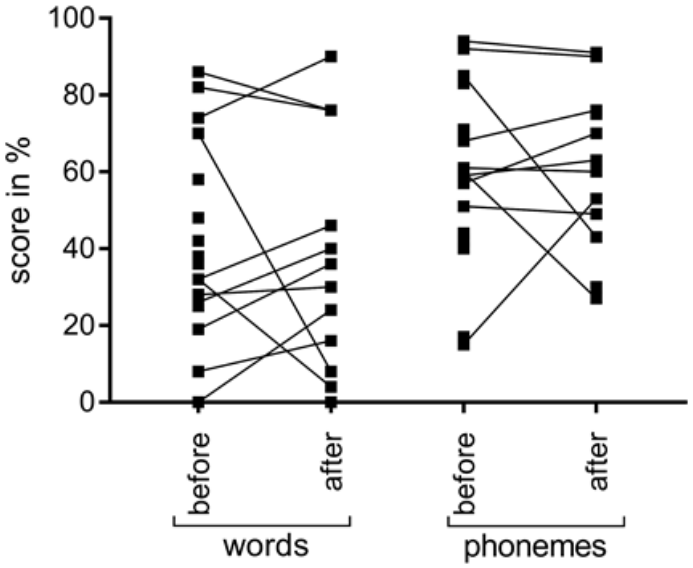
Fig. 4. Speech understanding scores were stable in most patients. Median understanding of CVC words and phonemes increased after re-implantation slightly but non-significantly. In two patients, speech scores decreased after revision surgery.



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