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Long-term results of Provox ActiValve, solving the problem of frequent
Candida- and ‘underpressure’-related voice prosthesis replacements

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Abstract

Objectives: To assess long-term results of a prosthesis for voice rehabilitation after total laryngectomy (Provox ActiValve) aiming at solution of frequent Candida- and “underpressure”-related replacements.

Patients and methods: Retrospective assessment of device lifetime, indications for replacement, voice quality, and maintenance issues, measured by a structured trial specific questionnaire, in a cohort of 42 laryngectomized patients, experiencing a short Provox2 device lifetime (median 21 days).

Results: Median device-related lifetime of Provox ActiValve, replaced for leakage through the device and those still in situ at the date of data collection (N=32), was 337 days (mean 376 days): a statistically significant 16-fold increase compared to Provox2 ($P<0.001$). In 10 patients replacement was fistula-related (median after 86 days): esophageal pouch (N=4), fistula granulation (N=3), extrusion of the device (N=2), and periprosthetic leakage (N=1). 86% of patients used a special lubricant to diminish ‘stickiness’ of the valve. Provox ActiValve was preferred by 90% of the patients completing the trial specific questionnaire.

Conclusions: For patients requiring frequent device-related replacements, Provox ActiValve, also long-term, provides a true solution and thereby is a valuable addition to prosthetic voice rehabilitation.

Key words: active magnetic valve, Candida resistance, prosthetic voice rehabilitation, Provox, total laryngectomy.

Introduction

Prosthetic voice rehabilitation after total laryngectomy has proven to be successful in restoring proper speech function in over 90% of patients and is nowadays the method of choice in most developed countries.^{1, 2}

Many different types of prostheses have been designed in the last decades, being either indwelling,³⁻⁶ or non-indwelling devices.^{7, 8}

A voice prosthesis is a semi-permanent implant requiring occasional replacement. The lifetime of indwelling devices such as the Provox and Groningen prostheses varies from a few weeks to a couple of years, but on average is reported to be several months.⁹ In a retrospective clinical analysis carried out in our institute (N=318), the prosthesis mostly used, the Provox2 prosthesis, turns out to have a mean device lifetime of 163 days, with a median life span of 89 days.¹ Incompetence of the valve, causing leakage of fluids through the prosthesis, is the most frequent indication for replacement of any indwelling voice prosthesis.^{4, 5} Biofilm formation with *Candida* deposits on the esophageal surface of the prosthesis is the main cause of this malfunctioning of the valve.¹⁰ It is noteworthy that there is a significant correlation between radiotherapy and device lifetime in this respect.^{1, 11} This is probably caused by the fact that radiation induced xerostomia leads to a decrease of antibacterial and antifungal salivary peptides, which increases the chance of Biofilm formation.¹² In some patients, leakage through the prosthesis can also occur when the valve opens inadvertently or closes insufficiently because of 'underpressure' in the esophagus due to a negative intra-thoracic and intra-esophageal pressure during deep inhalation or by swallowing as such.¹³

There is a subgroup of patients needing very frequent replacements (in the order of every few weeks), and several methods have been used and advocated in the past to diminish this problem, i.e. to prolong the device life in these patients. Antifungal drugs have been a popular treatment modality in this respect, but their efficacy is doubtful.¹⁰ Therefore, and because of possible overmedication and chances of side effects, some caution in treating these patients with antifungal drugs is justified. Another option could be the use of probiotics (certain types of yoghurts),¹⁴ but beneficial effects of such measures have not been proven yet by randomized trials.

The Provox ActiValve was specially developed to overcome the problems of *Candida* and underpressure-related early prosthesis leakage.¹³ This prosthesis contains a valve made of *Candida*-resistant Teflon-like fluoroplastic and magnets that allow the valve to actively close (see figure 1). These magnets can prevent to a greater or lesser extent (depending on the

magnet force chosen) the valve from inadvertent opening in case of underpressure in the esophagus. In the initial developmental and prospective clinical trial, the device lifetime of the Provox ActiValve turned out to be very favorable with a median of 360 days, leading to a fourteen fold increase of the device-related lifetime in a patient group with a median device life of their Provox2 prosthesis of 25 days.¹³

Since the two years the Provox ActiValve is commercially available (since early 2005) it is regularly used in our clinic for patients with a short device lifetime, which makes it possible now to retrospectively study the long-term (2 years) results in daily clinical practice. In this study, the medical indication, the device lifetime and other clinical parameters such as patient satisfaction and perceived voice quality are investigated in a cohort of patients, who have used or currently are using the Provox ActiValve.

Patients and methods

Between April 2005 and May 2007, forty-two laryngectomized patients were considered to be appropriate candidates for Provox ActiValve. Thirteen of these 42 patients were especially referred to our institution from other clinics as being ‘problem’ patients because of their frequent replacement needs. The institutions involved in referring these patients are: the Erasmus Medical Center Rotterdam, St. Radboud University Hospital Nijmegen, the Isala Clinic in Zwolle, the Medical Center Haaglanden in The Hague, the University Medical Center Leiden, and the Free University Medical Center in Amsterdam. In our institution, approximately 200 patients with a voice prosthesis are in long-term follow-up, which means that the ActiValve patients form approximately 15% of our laryngectomy patient population. The study group consisted of 35 men (83%) and 7 women (17%). The mean age was 65 years (range 44-84 years). The time since total laryngectomy ranged from 8 months to 21 years, with a median of 7.5 years. Twenty-three patients received radiotherapy before surgery, 15 patients postoperatively. Four patients never had radiotherapy.

In 69% of the patients, the pharynx was closed primarily after total laryngectomy. Eight patients received a pectoralis major flap, four patients a gastric pull-up and one patient a radial forearm flap reconstruction. Eleven patients (26%) were reported to have had a pharyngeal stenosis, for which dilatations have been performed. Four patients were deceased at the time of analysis: 2 patients of intercurrent disease, 1 of recurrent cancer and 1 patient of a secondary malignancy. Patient characteristics are shown in Table 1.

Provox ActiValve is available in three different versions, depending on the magnetic forces in the valve, namely Light (with an opening resistance of approximately 0.7 kPa), Strong (approximately 2 kPa) and XtraStrong (approximately 4 kPa). The choice of the appropriate version is based on whether there is a moderate (Strong) or severe (XtraStrong) underpressure or no visible underpressure at all (Light), i.e. whether an opening or fluttering of the valve of the prosthesis during swallowing and/or deep inhalation can be observed.

The survival times of the ActiValve prosthesis as well as the Provox2 prosthesis were calculated from the date of insertion to the date of replacement of the device. For the device lifetime of the Provox2 prosthesis, we evaluated the data of two replacements (last and second last) preceding the insertion of the first ActiValve prosthesis.

If a prosthesis was replaced because of leakage through the device, the replacement was considered to be device-related. Other reasons for replacement, such as infection, granulation formation, hypertrophic scarring, esophageal pouch formation or extrusion of the device were

considered fistula-related. Finally, a few patients required replacement because of a too long device or a too strong magnet.

As four patients died and one patient suffered from severe Alzheimer (therefore not able to answer the questionnaire properly), the study population for completing the trial specific questionnaire consisted of 37 patients. These 37 patients were interviewed, either during a routine follow-up visit to the outpatient clinic, or by telephone. Thirty patients were using a Provox ActiValve at the moment the questionnaire was completed; the remaining seven patients were at that time using a Provox2 voice prosthesis. The structured trial specific questionnaire contained items about possible resistance (felt) or clicking sounds (heard) during speaking with the new prosthesis, voice quality, the preference of the patient, and general questions concerning the maintenance of the prosthesis by the patient (e.g. the use of a special lubricant to diminish the 'stickiness' of the valve).

Statistics

The 4 voice-related items (intelligibility, loudness, pitch and fluency) of the trial specific structured questionnaire were combined into a more limited set of multiple-item scales according to Likert's method of summated ratings. Statistical analyses primarily included descriptive analyses and tabulations. Statistical associations were calculated by Pearson's correlation coefficient. Survival-type calculations of the life-time of the 2 devices were done by the product-limit method of Kaplan and Meier. A two-tailed P-value of <.05 was taken to indicate statistical significance.

Results

The median and mean time between total laryngectomy and switching from Provox2 to Provox ActiValve was 87.5 and 85.8 months, respectively (range 9-247 months). The main reason for replacement of the Provox2 prosthesis (N=42) was device related, i.e. leakage of fluids through the prosthesis, which obviously was the primary selection criterion. This occurred in 37 cases (88%) of the second last replacement and in 41 cases (98%) of the last replacement. Only these events of leakage through the device were taken into account in calculating the device-related survival time. For both replacement periods this resulted in a median life time of Provox2 device of 21 and 21 days and a mean of 29 and 30 days (range 4-96 days). The remaining replacements of these Provox2 devices were fistula-related, including: periprosthetic leakage (N=3), granulation formation (N=1), formation of an esophageal pouch (N=1) and one replacement was requested by the patient because he went on holiday. The median and mean follow-ups of patients using Provox ActiValve are 527 and 460 days, respectively (range 20-706 days).

Of the first Provox ActiValve devices inserted, 20 prostheses were Light, 20 Strong and 2 XtraStrong. At the date of analysis, the first Provox ActiValve is still in situ in 15 patients (36%) (range 20–665 days), whereas in 27 (64%) it has been replaced (range 4-540 days). Leakage through the device was the indication for replacement in 41% of cases (n=17). In the group of 32 patients thus available for device lifetime analysis (15 still in situ and 17 replaced for leakage through), the median and mean device life of the Provox ActiValve voice prosthesis was 337 and 376 days respectively (range also 20-665 days). This means a 16-fold increase in device life time compared to the last and second Provox2 (median 21 days, range 4-96; $P < 0.001$). In the remaining 10 patients (24%), the replacements were fistula-related: formation of an esophageal pouch (4 patients), granulation formation (3 patients), extrusion of the device (2 patients) and leakage around the prosthesis (1 patient). The median device life time until fistula-related problems occurred was 86 days (range 4-337 days). If all first 42 devices (still in situ, device-related and fistula-related replacements) are taken into account, there is a statistically significant 8.7 and 8.9 fold increase in device life compared to the last and the second last Provox2 median device life (all 2x42 Provox2 indications for replacement included this time; $P < 0.001$).

There is no statistically significant correlation between radiotherapy or pharyngeal stenosis and fistula-related reasons for prosthesis replacement in this small series of patients. There is

a trend towards a correlation between pharyngeal stenosis and pharynx reconstruction with 6/11 patients with a stenosis having had a reconstruction (4 pectoralis flaps and 2 gastric pull-ups) and 7/31 non-stenosis patients (4 pectoralis, 1 radial forearm, and 2 gastric pull-ups; $P = 0.066$).

The prosthesis survival curves for the first replacement group are shown in figure 2.

The subsequent replacements in the 27 patients that have their first Provox ActiValve replaced are either a second Provox ActiValve (22 patients), or in case of a fistula-related replacement a Provox2 prosthesis (5 patients). These subsequent replacements in a decreasing number of patients are not analyzed any further due to the limited numbers, but at the date of analysis, 34 patients still appeared to have a Provox ActiValve in situ and 8 a Provox2 device. Seven of these 8 (most likely temporarily) have a Provox2 because of treatment for fistula-related problems, whereas the eighth patient was unfit for further follow-up because of progressive Alzheimer's disease.

Questionnaires were submitted to 37 patients in total. The results of 30 questionnaires were further evaluated, since these were based on actual experience with Provox ActiValve. The results of the seven patients using a Provox2 prosthesis at the moment they were interviewed, were left out of the analysis, because their answers were based on experiences sometimes way back in the past. All 30 patients maintained their Provox ActiValve device by daily cleaning it with the regular cleaning brush (mean: 2 times per day). None of the patients used anti-mycotics. Only one patient heard the device make a "clicking"-sound during speech, but he did not consider this to be disturbing. Twenty-seven patients (90%) experienced quite some opening resistance of the valve after waking up in the morning. The majority of them (83%) used their brush to open the valve and 7% were able to clear the blockage (by mucous) by 'coughing', much like most of them to a somewhat lesser extent experienced with Provox2. The special lubricant to diminish the 'stickiness' of the valve was used by 25 of the 29 patients (data missing in one patient), responding to this question (86%), with a frequency of 2 times a day (range 1-4). Patients reported no difference between Provox ActiValve and Provox2 with respect to voice quality: based on the four voice quality items (summated Likert scale; Cronbach's alpha: 0.89) 76% found their voice quality to be equal to that with Provox 2, 7% rated it to be much better, 3% better and 14% worse. There is only a moderate correlation between the reported 'onset' and 'ease' of voicing, with 17 patients reporting the

onset of voicing to be heavier (12 somewhat and 5 a lot), while from both categories 3 patients each reported the voicing itself to be somewhat heavier, and no patients a lot heavier. Moreover, when correlated with the type of voice prosthesis used (magnet force Light or (Xtra)Strong), there is no correlation with this subjective judgment, i.e. the magnet force does not seem to play a role in onset and ease of voicing. Overall, 27 of the patients (90%) said they, also long-term, preferred the Provox ActiValve voice prosthesis over the Provox 2 device.

Discussion

The present study results are in line with those of the earlier published developmental and first clinical assessment study: the device lifetime now shows a statistically significant 16-fold increase, which is slightly better than that obtained in the first study, where a 14-fold increase was observed.¹³ Not only is the sample size of the present study larger than that of the earlier one (42 versus 18 patients), but more importantly, the observation time of over 2 years is considerably longer, which make this a realistic outcome.

Despite the fact that prosthetic voice restoration is the primary method of choice in rehabilitating speech function in the laryngectomized patient, there are several common device-related or fistula-related problems that can arise, which decrease their ease of use and therefore remain issues requiring improvement.² Although the reported median and mean device lifetimes on average are in the order of several months, the main device-related problem is the sometimes very short lifetime of any prosthesis in a given patient.^{9, 15} Especially, in the subgroup of patients whose average device lifetime is shorter, i.e. in the order of only a few weeks, the quality of life is more impeded. The study group in the current study is representative in this context, with devices having a median life span of 21 days only, which concerns approximately 15% of the total laryngectomy cohort primarily treated in our institution.

The most frequent and well known problem in prosthetic speech is leakage through the device, which is mostly due to *Candida* deposits on the valve but can also be provoked by an underpressure of the esophagus.^{10, 13} The present study again shows that both problems in a selected group of patients, proven to require frequent replacements because of these reasons, can be solved with Provox ActiValve, which is especially designed to solve both *Candida* growth because of the Teflon-like material applied, and the underpressure phenomenon, counteracted by the incorporated magnets. The somewhat increased tendency for this valve to become 'sticky' is to a great extent taken care of by the use of a special lubricant, which is used by 86% of the patients 1-4 times per day (mean 2). The fact that they need the valve to get going in the morning is for most patients not uncommon, because they also experienced this with their former valves. Regarding the voice quality as experienced by the patients, it can be said that 17 (out of 30) patients noticed that the onset of speech was heavier, while 6 of

them reported that also voicing in itself took somewhat more effort. However, this appeared not to influence their intelligibility as compared with the Provox 2 voice prosthesis.

With respect to the incidence of fistula-related problems it is interesting to observe, that despite the fact that this patient population is selected on the basis of frequent replacements, it still took a median of 86 days for fistula problems to arise, which is a comparable finding with the more extensive study of Op de Coul et al., who reported a median time of 57 days with Provox2 to develop these problems.¹ Furthermore, only 10 of the 42 patients (24%) developed a fistula problem during the observation time, which seems not worse than found in an earlier study from our institute on Provox and Provox2 prostheses (32% of the patients over a mean observation period of 6 years). This shows that there apparently is no increased risk of fistula-related complications with this problem-solving indwelling device which stays in situ much longer in this specific patient cohort.

The fact that some patients (8) did not use a Provox ActiValve at the date of analysis is mainly based on the decision not to use a considerably more expensive device while the patient is recovering from a fistula problem. For instance, a local infection or an esophageal pouch means that a temporary upsizing of the prosthesis is required. Frequently in these cases, after a few weeks to months a shorter prosthesis has to be placed to avoid or treat periprosthetic leakage due to a subsiding of the swelling of the party wall, which would be a waste to do with an otherwise perfectly functioning, more expensive Provox ActiValve. It is expected that 7 of these 8 patients will return to a Provox ActiValve, as soon as their fistula has stabilized (the eighth patient suffer from progressive Alzheimer's disease and most likely will stay on Provox2). Although some patients needed more than 3 Provox ActiValve prostheses (N=8) during the 2 year follow-up, the device lifetime of the new prosthesis remained much longer than the median device life span of 21 days these patients were used to. These data indicate that this device is a welcome solution for those 15% of patients who require a more durable prosthetic device. This retrospective study was not intended to be a cost-effective assessment, though, because that would require a different approach, but it is fair to assume that the 16-fold increase in device life time already is easily compensating for the increased costs (according to the distributor's information in the Netherlands 7.82 fold,), not even taking into account the decreased travel and hospital costs and the highly increased quality of life for the patient, not needing to rush to the clinic every couple of weeks. Even if all first 42 devices, irrespective of their replacement indication, i.e. those replaced for either a

device-related or a fistula-related reason, and those still in situ, are taken into account, there is still a statistically significant increase in device life compared to the last and the second last Provox2 median device life (8.7 and 8.9 respectively; $P < 0.001$). This means that even if we would assume that all in situ prostheses would have been replaced on the day of analysis, which is obviously not the case, the balance still is very much in favor of Provox ActiValve.

As already mentioned in the introduction, Biofilm formation with Candida deposits on the esophageal surface of the prosthesis is the main cause of malfunctioning of the valve.¹⁰ This problem is effectively solved by the Teflon-material the Provox ActiValve prosthesis is made of. Consequently, there is no need for anti-mycotic drugs anymore, diminishing the financial costs, possible overmedication and side-effects and importantly, the nuisance for the patients. Adjustment of the device to possibly overcome the problem of fungal colonization was also supplied by Leder et al. with the introduction of the Advantage Voice prosthesis.⁶ By incorporating 7% silver oxide in the valve, this indwelling device might diminish the adhesion of Candida deposits. However, this chemical preventive method seems to have limited effect, also because, as already discussed by these authors, not all microbes are susceptible to silver oxide. The increased device lifetime they observed, in the order of 77-82 days, was an improvement in that selected group of patients, which does not exceed the earlier published device lifetime of Provox2 (median and mean 89 and 163 days),¹ and certainly not the present ActiValve results.

The other reason for frequent replacements, 'underpressure' in the esophagus, also seems effectively solved by the active closure by the magnets in the Provox ActiValve. In fact, 22 patients (52%) in this study group needed the Strong or an XtraStrong magnet version, based on a significant observed 'underpressure' (inadvertent opening of the valve (fluttering) during deep breathing and/or swallowing). Currently there is no alternative to this mechanism.

In conclusion: this study indicates that Provox ActiValve is a valuable addition in the field of prosthetic voice rehabilitation after total laryngectomy. It solves the problems of a subgroup of patients requiring frequent replacements of their voice prosthesis because of valve insufficiency based on Candida or underpressure, known to be sometimes a reason to permanently abandon prosthetic voice in patients otherwise able to communicate well with the device.

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Figures

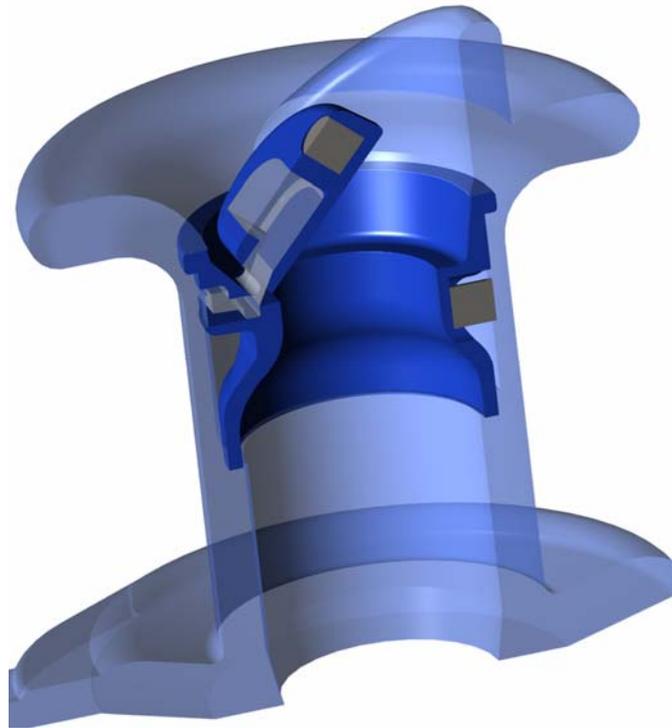


Figure 1. Provox ActiValve cross section, showing the fluoroplastic valve and valve seat (solid blue), each with a magnet (red), enabling an active closure of the valve and preventing inadvertent opening by underpressure in the esophagus. The body of the prosthesis and the hinge of the valve are made of medical grade silicon rubber (transparent blue). (Image by courtesy of Atos Medical, Hörby, Sweden)

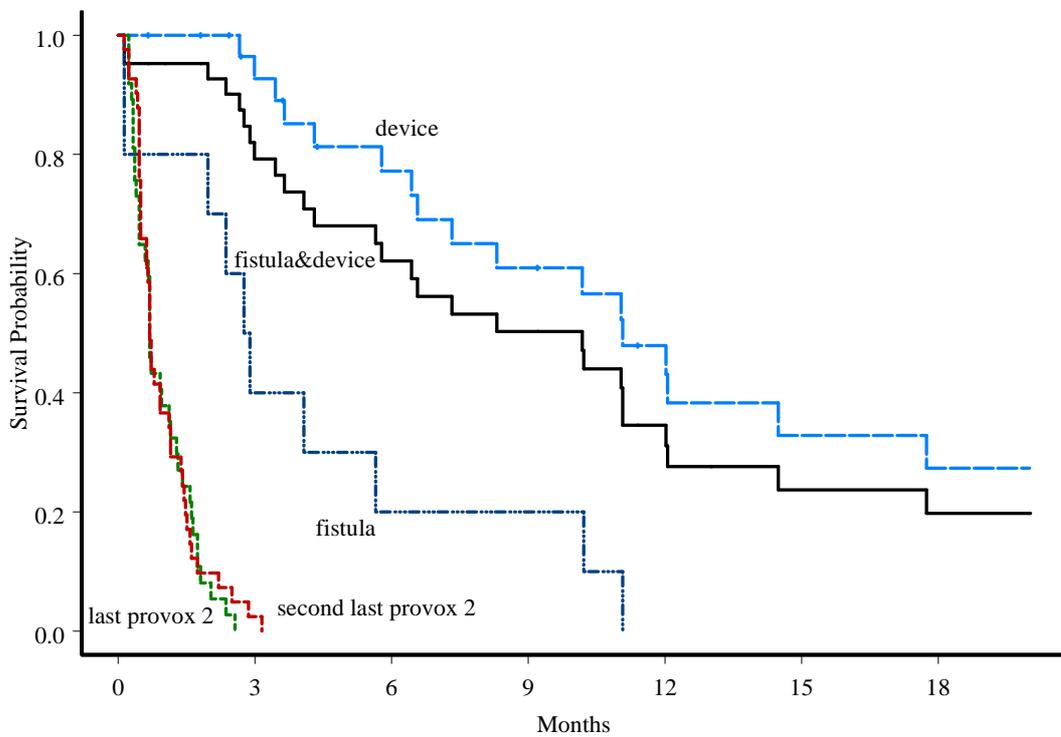


Figure 2. Survival times of the last and second last Provox2 prostheses and the first Provox ActiValve prostheses. The black solid line represents all 42 Provox ActiValve prostheses; the light blue dashed line the 32 devices replaced for leakage through or still in situ; the dark blue dashed line the 10 devices replaced for fistula-related problems; the red and green dashed lines the last and second last Provox2 prostheses.

Tables

Table 1. Patient characteristics (N=42)

Characteristic	N (%)
Sex	
Male	35 (83.3)
Female	7 (16.7)
Age in years	
Mean	65.1
Range	44-84
Follow-up in years	
Mean	7.5
Range	0.7-21
Radiotherapy	
Before surgery	23 (54.8)
After surgery	15 (35.7)
No	4 (9.5)
Reconstruction	
Primarily closure of wound	29 (69)
Pectoralis major flap	8 (19)
Gastric pull-up	4 (9.5)
Radial forearm flap	1 (2.4)
Pharyngeal stenosis	
Yes	11 (26.2)
No	31 (73.8)

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