
In vivo experiments with tracheostoma tissue connector prototypes

E. J. Olivier ten Hallers,^{1,2,3} Eduard B. Van der Houwen,² Henri A. M. Marres,¹ Gerhard Rakhorst,² John A. Jansen,⁴ Harm K. Schutte,² Theo G. Van Kooten,² Jan-Paul Van Loon,⁴ Gijsbertus J. Verkerke^{2,5}

¹Department of Otorhinolaryngology and Head & Neck Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands

²Department of BioMedical Engineering, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands

³Intra-Vasc NL B.V., Meditec Center, Groningen, Netherlands

⁴Department of Periodontology and Biomaterials, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands

⁵Department of Biomechanical Engineering, University of Twente, Enschede, Netherlands

Received 9 December 2005; revised 16 July 2006; accepted 26 July 2006

Published online 31 January 2007 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/jbm.a.31074

Abstract: In cancer patients who have undergone total surgical removal of the larynx, ideally voice rehabilitation should be performed using a shunt valve (placed in a fistula of the tracheo-esophageal wall) and a tracheostoma valve (TSV) to enable hands-free tracheo-esophageal speech. A tracheostoma is created by suturing the trachea into the lower anterior part of the neck, and a TSV is a device that can be placed at the stoma. Unfortunately, many patients are unable to use a TSV, mainly due to fixation difficulties. To improve the fixation of the TSV, tracheostoma tissue connector (TS-TC) prototypes have been designed. Prototype 1 consisted of a titanium ring, inner diameter 30 mm, with a circular polypropylene mesh glued to it with silicone adhesive. Four holes had been drilled into the ring for the insertion of sub- and percutaneous screws. Prototype 2 consisted of a silicone rubber ring, inner diameter 30 mm, combined with polypropylene mesh and four titanium inserts that functioned as a base plate for the insertion of sub- and percutaneous screws. In

adult female goats a tracheostoma was created and the prototypes were implanted. After 6 weeks of subcutaneous implantation, percutaneous screws were inserted. After twelve weeks, the experiment was terminated and the implants with the surrounding tissues were processed and examined histologically. The clinical appearance during weeks 7–12 varied from very poor to relatively good. Histologically, the implants showed a uniform inflammatory response. We found that all the tissue surrounding the screws showed signs of epithelial down growth. It was concluded that the two-stage implantation procedure of our prototype TS-TCs in this animal model was unsuccessful. Additional research efforts are necessary to improve tissue immobilization and to devise reliable fixation systems for TSVs. © 2007 Wiley Periodicals, Inc. *J Biomed Mater Res* 82A: 62–72, 2007

Key words: laryngectomy; voice rehabilitation; soft-tissue implant; goat; tracheostoma valve

INTRODUCTION

In many cases of advanced larynx or hypopharynx cancer or cancer recurrence, total laryngectomy is needed as the primary treatment or as a salvage surgical procedure, respectively. After laryngectomy, the trachea is diverted towards the neck, where a tracheostoma is formed. Often a shunt valve is placed in the tracheo-esophageal wall for speech

rehabilitation purposes. After respectively inhalation, manual occlusion of the stoma, and expiration, the air is led through the shunt valve. In the esophagus, the pharyngo-esophageal segment starts to vibrate, which enables the patient to speak.

By-passing the upper airway tract by creating a tracheostoma has serious respiratory consequences, such as reduced filtration, heating, and moistening of the inhaled air.¹ To overcome these problems, a heat and moisture exchange (HME) filter can be applied.

Tracheostoma occlusion can be achieved directly using a finger, via an HME filter (such as the Provox HME cassette) or with a tracheostoma valve (TSV). Different types of TSV can be distinguished: pneu-

Correspondence to: E. J. O. ten Hallers; e-mail: O.tenHallers@kno.umcn.nl

matically (manually) or automatically operated and with and without a coughing-lid. Some can or must be combined with an HME filter, while others cannot.² The commercially available TSVs are based on the exhalation principle (they close after a burst of exhaled air). A TSV based on inhalation has also been developed, but is not yet commercially available.^{3,4}

There are two different methods to fix the TSVs and HME filters to the tracheostoma. First, an intraluminal device such as a canula or silicone rubber structure with flanges (the T-tube, this requires the surgical chimney technique⁵) and second, silicone-based skin glue, adhesive base plates, or plasters with a housing for the TSV.²

Numerous factors determine whether a patient can or will use a TSV, such as good fixation, financial cost, the attention drawn to the device, mechanical sounds when using it, the patient's dexterity, adequate instructions and training, profession, stoma shape, and ease of use. Despite the introduction of the TSV more than 20 years ago,⁶ only a very small number of patients have been able to use a TSV. The 19–30% of patients reported to use a TSV on a "daily" basis remains questionable, because there are no rigid definitions of "daily" or "regular" use.^{7–9} Problems with fixation and unreliability of the system are the most important reasons why patients cannot use a TSV or stop using it.

TSV fixation is prone to early loosening in most laryngectomized patients, due to mucous production and increased tracheal back pressure during speaking and coughing. The result is leakage of air and mucus. During manual occlusion, counter-pressure is applied to balance the tracheal back pressure needed for tracheo-esophageal speech. However, one study indicated that tracheal back pressure was not a significant factor to predict valve seal attachment time of the Blom-Singer TSV.¹⁰

Other disadvantages of the current fixation methods are painful skin irritation or even skin or soft tissue infection caused by skin maceration and traction, time-consuming cleaning and reattaching, noise, dislodgement, and high financial cost.

To reduce the fixation-related problems, further research has produced an interface between soft tissue and the TSV: the so-called tracheostoma tissue connector (TS-TC).^{11–13}

Several ideas and strategies were considered (such as subcutaneous magnets and percutaneous pins anchored in the surrounding bone structures). In this project it has led to the production of two prototypes because it was thought to be a successful approach for fixing TSVs. At the moment there are no tissue connectors commercially available for this purpose.

The TS-TC is a permucosal or percutaneous connection, based on bone anchored percutaneous and

permucosal connections, such as the bone anchored hearing aid,^{14,15} pins for the fixation of maxillo-facial prosthetics,¹⁶ dental implants, and soft tissue based implants.^{17–25}

The aim of this study was to select the best TS-TC concept and to test its feasibility in animal experiments. We report on two implanted prototypes and the subsequent histological analysis of the device-tissue explants.

MATERIALS AND METHODS

Tracheostoma tissue connector

Prototype 1

The first TS-TC prototype tested *in vivo* consisted of a ring (inner diameter 30 mm) made of CP titanium grade 2 (Thijssen Krupp B.V., Zwijndracht, the Netherlands) combined with polypropylene mesh. To prevent the mesh from tearing, the transition between the solid Ti ring and the mesh had a rounded shape. The mesh itself was meant to encourage capillary and fibrous tissue ingrowth to immobilize the implant. Four holes had been drilled into the ring for the insertion of percutaneous screws. After placement, it is intended that the tissue will attach itself to the titanium ring. Together, these components resulted in a percutaneous connection device. TSV or HME filters can be attached to the percutaneous screws.

The rings were ultrasonically cleaned in a soap solution (RBS ultrasonic cleaning), rinsed in water, cleaned in trichloroethylene, rinsed again in hot water, and dried in the air.

The knitted monofilament polypropylene mesh (Bard[®] Mesh, Bard Benelux N.V., Nieuwegein, the Netherlands) was cut to the appropriate size and cleaned in alcohol 70%. With a special glue apparatus (I&J Finsar Inc.[®] JBE 1113, Eltest, Zoerstel, Belgium) for controlled application of MED-1511 RTV silicon adhesive (NuSil Technology, Carpinteria, CA) the mesh was glued to the Ti rings. The implants were dried for at least three days and rinsed in distilled water for one day to allow the acetic acid to disappear. Sterilization of the implants was carried out in an autoclave with a maximum temperature of 121°C for 20 min. The implant is shown in Figure 1.

Prototype 2

The second prototype consisted of a silicone rubber (MED-6033 silicone elastomer; NuSil Technology) ring (inner diameter 30 mm) combined with polypropylene mesh and four titanium inserts. No glue was needed because the mesh had been enclosed in the silicone rubber ring during the production process. The inserts were made of CP titanium grade 2 and functioned as a base plate for the insertion of sub- and percutaneous screws. For good chemical bonding, the inserts were primed with CF6-135 high technology silicon primer (NuSil Technology) and



(a)



(b)

Figure 1. (a) Close-up of prototype 1 with phase-1 screw. (b) Prototype 1 with phase-2 screws (three Al_2O_3 blasted screws of 1, 2, and 3 mm diameter and one untreated with 2 mm diameter). Inner diameter of the ring is 30 mm.

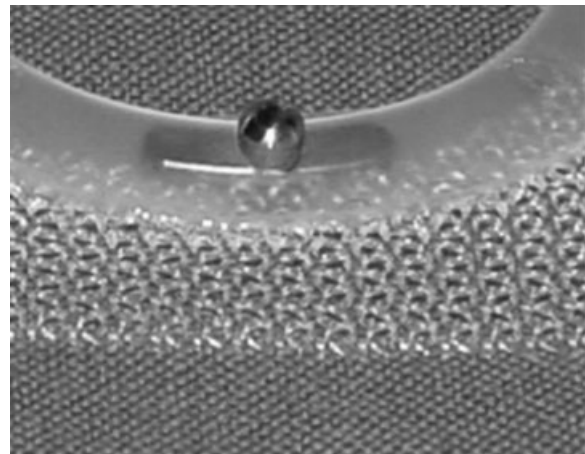
dried by the air. After molding the inserts and an oversized piece of mesh in the ring, the implant was cured in an oven for ~ 3.5 h at a temperature of 90°C .

Afterwards the excess amount of silicone rubber was removed. The rings were cleaned ultrasonically in a soap solution (RBS ultrasonic cleaning), rinsed in water and in 70% alcohol. Sterilization was performed similar to prototype 1. More details are shown in Figure 2.

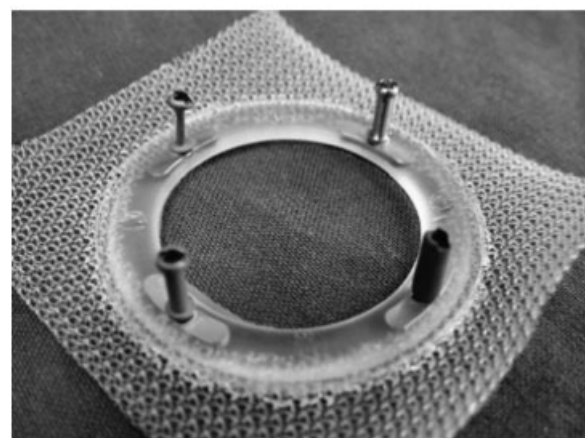
Screws

All the screws were made of CP titanium grade 2. Phase-1 and phase-2 screws had been designed and produced for each prototype. The base of the screws for pro-

totypes 1 and 2 were different, so that the connection between ring and screw was smooth with the least risk of dead spaces. Phase-1 screws were small and meant for subcutaneous implantation only. These screws served to prevent dead space and to locate the insertion holes for the phase-2 screws. After a 6-week period of implantation, the subcutaneous screws were palpated, removed, and the percutaneous phase-2 screws were installed (see Figs. 1 and 2). The phase-2 screws were longer and designed for percutaneous connection. The length of all phase-2 screws was identical, whereas the diameter and surface differed: three screws with diameters 1, 2, and 3 mm were blasted with aluminum oxide particles (particle size $200\text{--}300\ \mu\text{m}$) with a pressure of 5 bar at a distance of ~ 7 cm (approx. R_A 3.0–3.5) for surface roughness enhancement. The fourth screw with a diameter of 2 mm was not blasted and therefore smooth (approx. R_A 0.5). The implants were cleaned ultrasonically in RBS soap and alcohol. Then they were



(a)



(b)

Figure 2. (a) Close-up prototype 2 with phase-1 screws. (b) Prototype 2 with phase-2 screws. (Three Al_2O_3 blasted screws of 1, 2, and 3 mm diameter and one untreated with 2 mm diameter). Inner diameter of the ring is 30 mm.

cleaned in trichloroethylene, rinsed in boiling water, and dried in the air. After packing, the screws were sterilized in the same way as described earlier.

Surface characterization

XPS analysis was performed to test the elemental composition of the surface of samples of prototype 1, prototype 2, and phase-2 (after packing and sterilization in the autoclave). Surface roughness measurements were done by laser scanning profilometry (Proscan 2000, Scantron Industrial Production, Taunton, UK) and the implant surface was additionally imaged by scanning electron microscopy (SEM).

Experimental animals and implantation procedure

After approval of the project by the Ethical Committee for animal experiments at the Radboud University Nijmegen Medical Centre, 19 adult female Saanen goats (*Capra hircus*) (2.5–3 years, 60–80 kg) were obtained for the study. This animal species was chosen mainly because the dimensions of the goats' trachea are very similar to those of humans,²⁶ the animals are easy to handle, and the species is an available, affordable breed in the Netherlands. The goats were housed individually in a stable according to national and institutional guidelines. Two sets of experiments were planned: Group 1 ($n = 17$ including two pilot study animals) and group 2 ($n = 2$ only pilot study animals).

Follow-up was 12 weeks. The implantation experiment was divided into two phases. Phase 1: weeks 0–6 and phase 2: weeks 7–12. $T = 0$ was defined as the day of surgery.

Group 1

The surgical procedure was performed under "full sterile" conditions at a modern operating theatre. As anesthesia, the animals received 0.5 mg atropine i.m., medetomidine (Domitor[®]; A.U.V., Cuijk, the Netherlands) 25 $\mu\text{g}/\text{kg}$ i.m., pentobarbital (Nembutal[®]; A.U.V.) 10–20 mg/kg i.v., propofol 2 mg/kg bolus, and 8 mg/kg/h maintenance i.m. Also, they were intubated via the oropharynx in the trachea and ventilated with O₂ (30%), N₂O (70%), and Isoflurane (~1.5 %). The frontal neck area was shaved, washed and disinfected with povidone solution, and covered with sterile sheets. Suction and diathermic knife cauterization were available.

A vertical (cranio-caudal) median incision (~5–6 cm) was made to prepare the neck muscles and pretracheal fat tissue and to expose the cranial region of the trachea. The trachea and esophagus were separated locally, while leaving the laryngeal nerves unharmed. Laryngo-tracheal separation was performed three semi-rings below the cricoid by cutting the trachea in a transverse plane. Three to six semi-rings of the trachea were excised to create a tracheostoma with the least tension at the appropriate level (such that hair and the chin interfered as little as possible

with the stoma). A circumferential incision was made in the perichondrium on the exterior tracheal wall. The superior part of the perichondrium and mucosa of the third cartilage semi-ring were stripped to create an extra large soft-tissue border and the underlying piece of cartilage was removed. This was done to facilitate closure of the distal laryngeal pouch. In 1997, a comparable procedure was described by Prince and Nasser.²⁷

The tissue connector with four phase-1 (short) screws was inserted and glued to the surrounding tissue with fibrin tissue glue Tissucol Duo (Baxter B.V., Hyland Immuno, Utrecht, the Netherlands). A separate tracheostoma was created. Six weeks later, the skin at the site of the screws was punctured with a 2 mm Biopsy Punch (Stiefel Laboratories Ltd., Finisklin Industrial Estate, Sligo, Ireland) and the phase-1 screws were replaced by the phase-2 (long) screws [see Figs. 3(a,b)].

Group 2 (pilot study)

Two animals received prototype 2. The surgical procedure differed from group 1 only in that the median cranio-caudal incision in the anterior neck was extended to incorporate the tracheostoma.

Pre- and post-operative management

Postoperative lateral and antero-posterior X-rays were taken to check the position and alignment of the tissue connector. Afterwards, the animals were transferred to the stable for recovery and an adapted tracheostoma canula was inserted.

The goats received stoma care for 3 times per day and later strictly every 6 h. Stoma care contained removal and cleaning of the canula with a moist gauze and povidone or 0.5% w/v chlorohexidinedigluconate in 60% w/v isopropylalcohol (Hibisol[®], A.U.V.). Also the animals received an intra-tracheal instillation of 10 ccm saline to provoke a coughing reaction and also to clean and moisten the trachea and bronchi mechanically. Mucus crustae or plugs were carefully removed using forceps or a suction unit. After cleaning the trachea was inspected with a light source and with a flexible endoscope (3 times a week). A mucolytic agent, dissolved in water (0.25 mg/kg bromhexine (Broxolvon[®])), was administered twice a day orally to allow easy clearance of mucus. To reduce the possibility of crust formation additional air humidifiers were installed in the animal room to achieve a relative humidity of at least 60%. In phase-2 iodine solution wound spray (Dutiplast[®], A.U.V. Veterinarians, Cuijk) was used three times a day for disinfection at the percutaneous pins.

All tracheostoma canulas were shortened to prevent impingement of the anterior tracheal wall. Nevertheless, silver tracheostoma canulas caused damage to the tracheal wall and crust formation. We found that silicone rubber Provox[®] Lary Tube[™] (Atos Medical, Hörby, Sweden) and

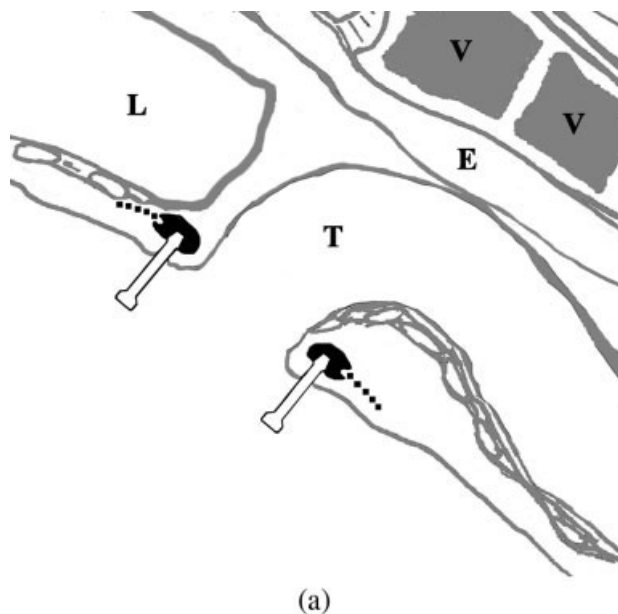


Figure 3. (a) Sagittal cross-sectional diagram of the implantation area with prototype 1 and phase-2 screws. L, laryngeal pouch; T, trachea; E, esophagus; V, cervical vertebra. (b) Anterior view of the neck of a goat after prototype 1 implantation and additional plastic rings sutured to the skin for canula fixation.

Shiley tracheostomy tubes (with inner canula) (Mallinckrodt, St. Louis, MO, USA) worked better and the use of silver canulas was abandoned.

The flange attached to the tube of the Shiley canula was adapted to prevent interference with the screws. Other post-operative care and management aspects are reported in detail in a separate publication.²⁸

Processing of histological specimens

After excising the implants with the surrounding tissue, the explant samples were cleaned in water and any hair and excessive tissue were removed. Then they were conserved in formaldehyde, cut into four equal parts, dehydrated in alcohol solutions and impregnated with methylmethacrylate (MMA). MMA samples were impregnated at $\sim 6^{\circ}\text{C}$ for 8 weeks and then polymerized in glass jars. This process needed to be monitored carefully, because the size of the samples could cause air bubble entrapment. To facilitate the polymerization monitoring procedure (exothermic process), the samples were placed in a water bath at room temperature (20°C). Any surplus resin was sawn off. Optimal alignment of the samples was achieved using X-ray imaging and sections of $\sim 300\ \mu\text{m}$ were cut by means of a Leica RM 2165 Microtome equipped with a D-knife for histological scoring. At least three regular sections were cut to expose any skin reactions to the percutaneous screws and the subcutaneous tissue surrounding the ring and mesh. Sections were stained with methylene blue and basic fuchsin.

Histological evaluation

Implants with surrounding tissue were scored on (derived from Jansen and van't Hof²⁹): capsule quality, capsule thickness, interface quality, epithelial downgrowth along the phase-2 screws and interstitial tissue quality at the location of the mesh. Scores were assigned to three coupes in the transverse plane of (one quarter of) the ring by two individual observers. Comparisons were made and when differences occurred, the score assigned by the senior researcher (Jansen) was retained as conclusive.

RESULTS

Surface characteristics

Table I shows the main chemical composition and roughness of the implant surface. In general, the composition of the titanium implants was comparable with previous reports in the literature.^{30,31} By blasting the screws with aluminum oxide particles, the surface area had been enhanced. As some particles had adhered to the titanium, its chemical composition had also changed. The treated screws showed a SEM aspect comparable with that of the aluminum oxide blasted implants described by Piattelli et al.³² (see Fig. 4).

TABLE I
Main Elemental Composition and Surface Roughness of the Implants

Sample	Main Chemical Components on the Surface Measured with XPS (elements)	Surface Roughness, R_A (μm)
Titanium ring Prototype 1	O(1s) (40.8) C(1s) (28.46) Ti(2p) (16.3)	0.5
Silicone rubber ring Prototype 2	Si(2p) (11.4) O(1s) (27.6) C(1s) (47.3)	0.3
Treated titanium screw	Si(2s) (25.1) O(1s) (49.51) C(1s) (18.92) Ti(2p) (16.1) Al(2s) (13.0) Ca(2p) (1.8) Cu(2p3) (0.7)	3.0–3.5
Untreated titanium screw	O(1s) (43.9) Ti(2p) (21.4) C(1s) (25.8) Cu(2p3) (2.7) N(1s) (2.5) Ca(2p) (2.8)	0.5

Values in parenthesis are in percentage.

Macroscopic findings

During the operation some differences were found in the size and shape of the trachea between the goats. On the dorsal side of the cervical trachea, the distance between the tips of the cartilage semi-rings varied from ~ 3 to 20 mm. These anatomical variations were similar to previous reports.²⁶ This did not complicate the TS-TC implantation procedure. Alignment viewed on the X-rays was satisfactory in all cases, as indicated in Figure 5.

All the animals recovered well after the operation and generally started eating within 1 h after the procedure.

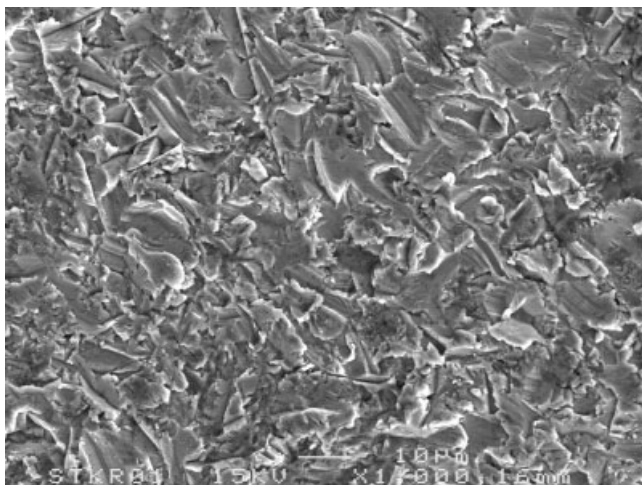


Figure 4. SEM of the enhanced surface of a titanium screw, blasted with aluminum oxide grid.

Average follow-up durations were 51 days (range, 6–131 days) and 44.5 days (range, 50–39 days) in group 1 and group 2, respectively. These periods were exceeded in a few cases due to pilot experiments, an attempt to control infection and for logistic

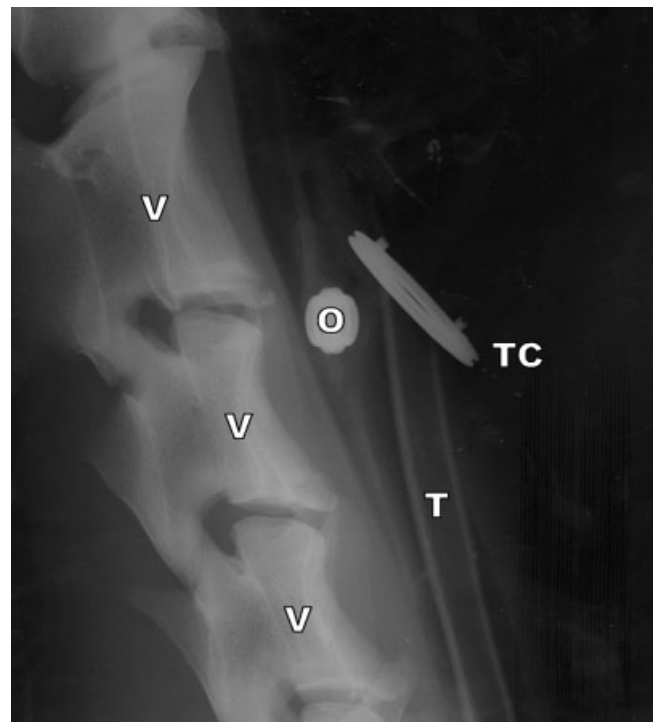


Figure 5. Lateral X-ray of the neck of the goat after implantation. TC, tracheostoma tissue connector; O, other implant (reported on separately); T, intra-tracheal ventilation tube; V, cervical vertebra.

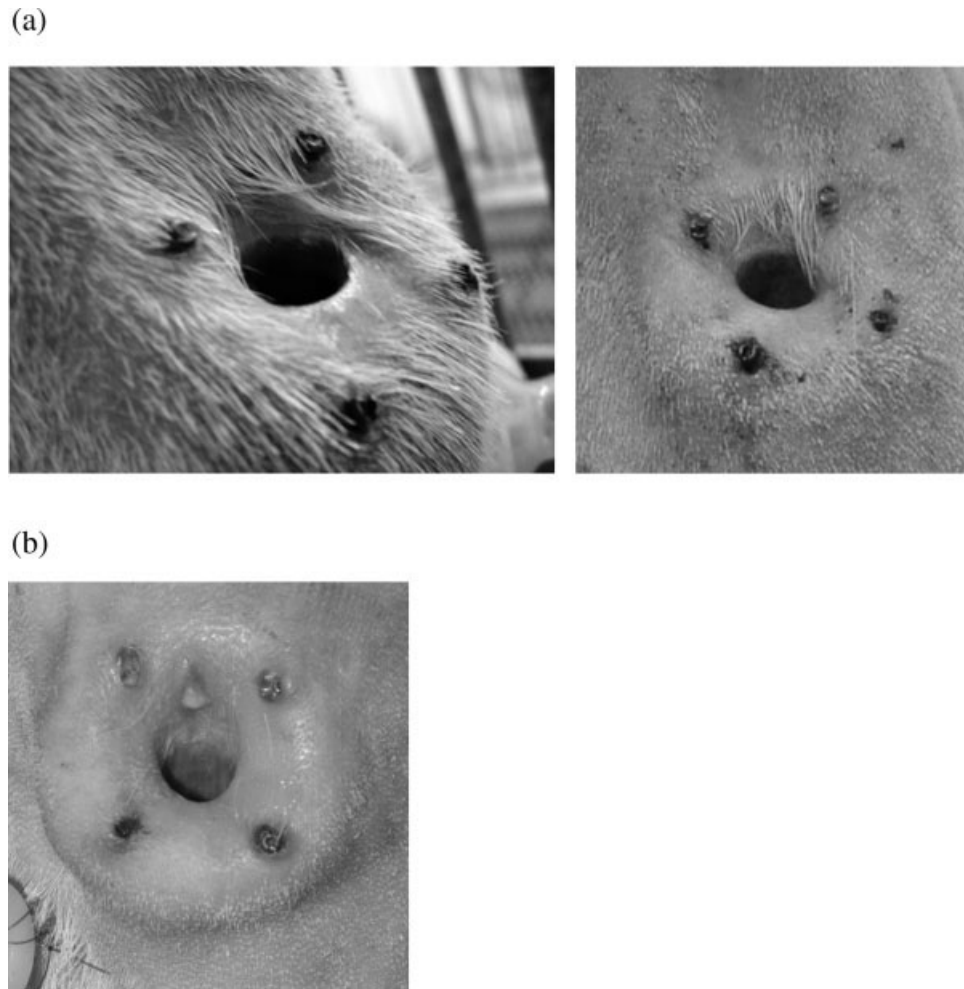


Figure 6. (a) Well-healed tracheostoma sites with only mild inflammatory signs at around $t = 8$ week. (b) Pressure necrosis on the cranial side of the tracheostoma with signs of infection and dermal overgrowth.

reasons. Before the end of the 12 week period, 11 animals died: 10 in group 1 and 1 of group 2. Post-mortem investigations showed that this had been caused by sudden mucous plug obstruction (5 animals), pneumonia, cardiac decompensation, or lung oedema/exudate (6 animals). The goats with exudates died very abruptly. Despite the safety measures, 4 goats were found dead with a dislodged canula; 2 of them showed obvious progressive stoma stenosis.

Three animals had to be withdrawn from the experiment because predetermined end points had been reached: local complications such as severe seroma just inferior to the tracheostoma, pressure necrosis at the site of tracheostoma, and implant exposure.

There was a clear difference between phase-1 and phase-2. Clinical appearance from $t = 0$ until $t = 6$ weeks of the implantation area was in general without complications except from signs of pressure necrosis at the cranial part due to the canula. How-

ever, during weeks 7–12 the macroscopy varied from very poor to relatively good [see Figs. 6 (a,b)].

From the moment of the installation of the percutaneous pins it was clear that this caused frequent infection around the pins.

After excision, we observed thickening of the tissue surrounding the ring, a tendency for dermal overgrowth at the site of the screws and signs of infection.

Examination of all four parts of the explant revealed that the polypropylene mesh was bent in anterior and posterior directions (see Figs. 7 and 8).

Although the implantation procedure had been possible in pilot study group 2, prototype 2 showed post-operative bending of the whole implant and concurrent skin healing deficiencies, especially on the cranial side of the stoma. In one animal of group 2 the bent ring prevented installation of all four phase-2 screws due to interference with the tracheostoma canula (see Fig. 8).

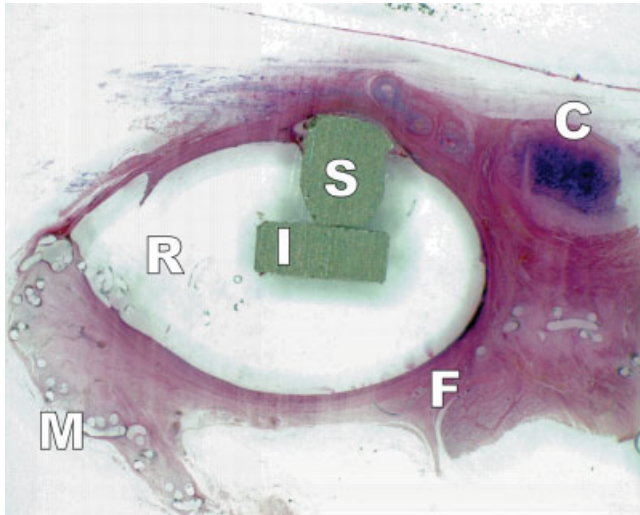


Figure 7. Cross-section of prototype 2 after 7 weeks of implantation. Light microscopy (0.9 \times). The dermal layer was cut off to improve the fixation process. Note the mesh folded backwards. R, silicone rubber ring; I, titanium insert; S, titanium phase-1 screw; M, polypropylene mesh; F, fibrous capsule; C, cartilage semi-ring of the trachea. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Light microscopy

All the implants in each group (2 prototypes) had caused comparatively uniform inflammatory tissue responses.

After 1 week of implantation, implants of group 1 ($n = 2$) showed hardly any fibroblasts surrounding the titanium surface and the polypropylene fibres and many inflammatory cells (polymorphonuclear granulocytes and macrophages), especially close to the silicone rubber and tissue glue (see Fig. 9).

After 1–2 ($n = 2$) weeks, the density of fibroblasts had increased slightly. After 2–6 ($n = 5$) weeks, the tissues surrounding the implants showed greater numbers of fibroblasts, increased thickness of the fibrous capsule, and a decrease in inflammatory cells.

Insertion of the phase-2 screws ($n = 6$) led directly to more infiltration of inflammatory cells and epithelial downgrowth along all the screw tracts (see Figs. 10 and 11). The remaining 2 animals did not receive phase-2 screws for logistic reasons and due to a complication (infection after pressure necrosis).

Sharp corners in the implant design had caused stress shielding and the development of small dead spaces. Also, small debris collections were seen in the junction between the phase-2 screws and the titanium ring.

Two implants in pilot study group 2 showed inflammatory reactions as a consequence of poor wound healing.

DISCUSSION AND CONCLUSION

A wide variety of TSVs are available to support voice rehabilitation after laryngectomy.² However, fixation difficulties of TSVs are the major reason why many patients cannot use such a device. Currently, the only alternative is manual closure of the tracheostoma, but this has clear disadvantages: it is nonhygienic, it is impossible to perform activities that require two hands, and the patient draws unwanted attention to his/her handicap by pointing at it while speaking. Only a disputable 19–30% of total laryngectomy patients use a TSV on a daily or regular basis.^{7–9} To achieve adequate fixation, four factors need to be carefully controlled: (a) pressure during breathing, speech, and coughing, (b) stoma shape, (c) mucous production, and (d) skin attachment. Pressure control can be achieved by optimizing the settings of the TSV (with screws, different closing lids, and buttons) and training. To improve the shape of the stoma and peristomal skin, extra attention is needed during surgery (for example

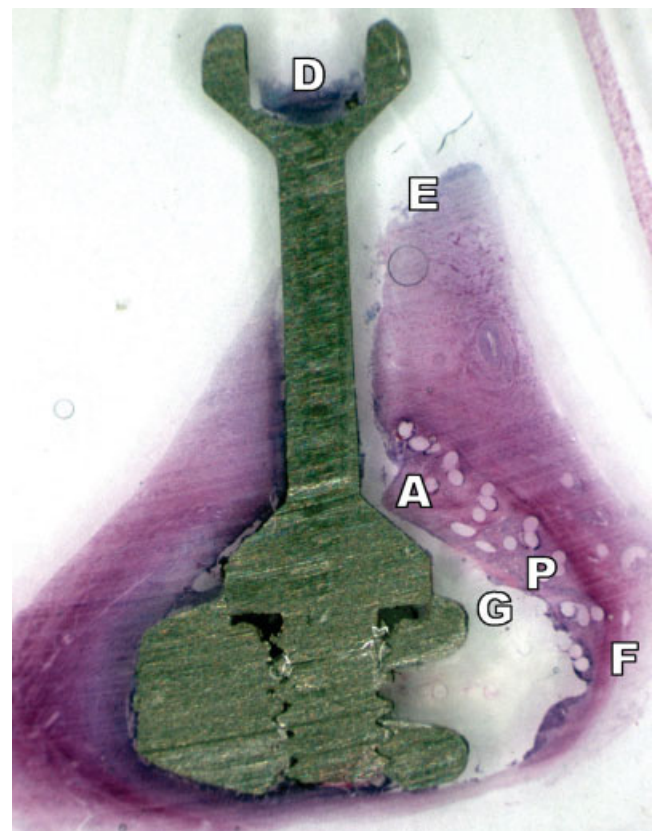


Figure 8. Cross-section of prototype 1 (1 mm, surface treated screw) after 12 weeks of implantation. Light microscopy (0.9 \times). Bending of the polypropylene mesh around the titanium A, artifact; D, debris; E, epithelium; F, fibrous tissue; G, silicone rubber glue; P, polypropylene mesh. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

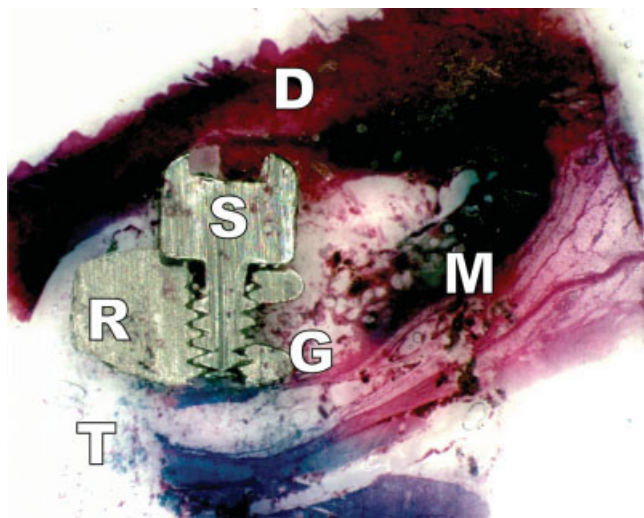


Figure 9. Cross-section of prototype 1 after 1 week of implantation. Light microscopy (0.9 \times). The implant with the tissue glue induces a profound inflammatory reaction at $t = 1$ week. R, titanium ring; S, titanium phase-1 screw; G, silicone rubber glue in the ridge of the ring; M, polypropylene mesh; T, fibrin tissue glue; D, dermal layer. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

incision of the frontal borders of the sternocleidoid muscle to create a circumferential stoma lip). Mucous production can be decreased by the use of an HME filter.³³

The fourth factor, skin fixation, cannot be adequately controlled with currently available options, because they cause problems in most cases that vary from slight skin irritation to severe skin infections with maceration.

This study focused on the fixation possibilities and feasibility of two different TS-TC prototypes in goats.

Several fixation strategies described in the literature were discussed in our project team. Subcutaneously implanted magnets, for example, were turned down, because the pressure of the magnets would exceed the capillary pressure of the skin or the size of the magnets would be too large. Therefore, percutaneous principles were used to design two TS-TC prototypes, based on the success or instrumentality described by others.²⁴

The goat was considered to be the most suitable animal model, because of its similar neck anatomy, the easy access to the operation site, and easy handling. However, the goat also has disadvantages: the tissues in the anterior neck are very mobile and the goats rub and scratch at anything attached to them.²⁸

A number of histological samples were damaged due to processing problems. Owing to the size of the explants, the rings had to be cut into quarters to enable proper histological processing. Also, excess tissue had to be removed in a very thorough manner to

permit sufficient impregnation of the MMA. Consequently, we were unable to conclude whether there was true tissue attachment to the implant in all the samples or preexisting gap formation (or sinus tract). Explants surrounded by infected tissue showed incomplete polymerization. The skin of the goat had remained especially soft in many samples.

In view of the relatively high complication rate of the tracheostomy procedure itself within this implantation study, the animal experiments were suspended on the initiative of the authors.

Group 2 contained 2 pilot study animals only. Therefore, it was not possible to make statistical comparisons between the two prototypes. The uniform histological responses meant that histomorphometry and statistical comparison between the two prototypes would not have provided any extra information.

Apparently, we underestimated the forces applied to the implant by the process of wound healing, scar tissue formation (capsule contracture), and movements of the neck of the goat. Such large movements

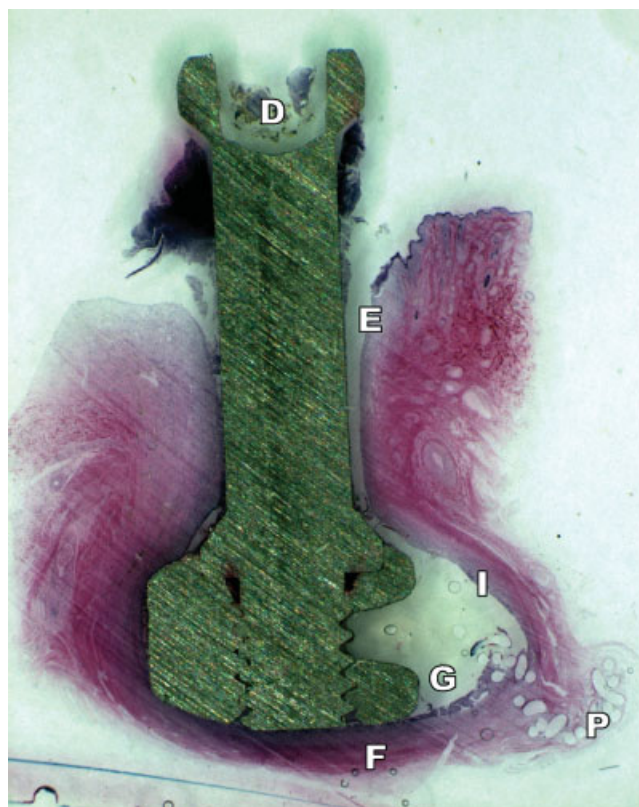


Figure 10. Cross-section of prototype 1 (2 mm, surface treated screw) after 12 weeks of implantation. Light microscopy (0.9 \times). Profound epithelial downgrowth along the treated percutaneous 2 mm screw. D, debris; E, epithelium; F, fibrous tissue; G, silicone rubber glue; I, inflammatory cells; P, polypropylene mesh. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

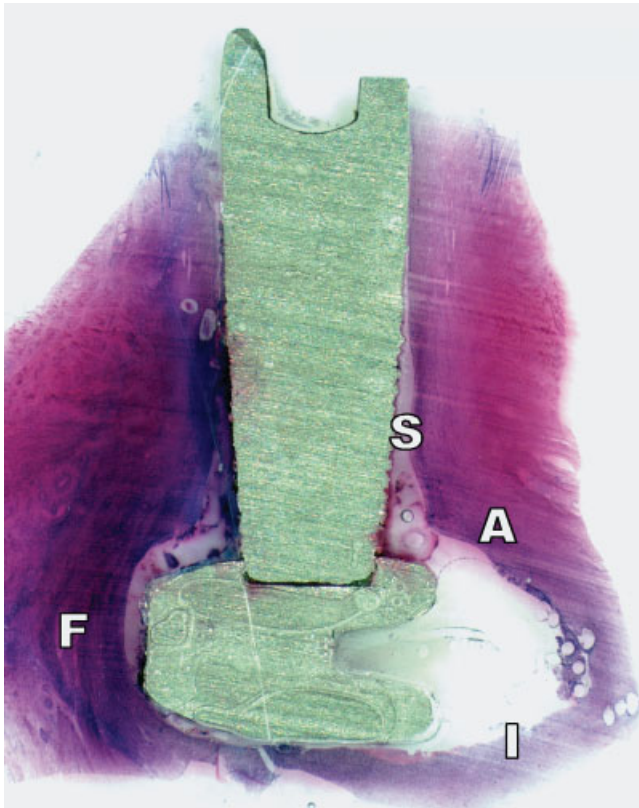


Figure 11. Cross-section of prototype 1 (3 mm, surface treated screw) after 12 weeks of implantation. Light microscopy (0.9 \times). Deep sinus tract along the screw A, artifact; F, fibrous tissue; I, inflammatory cells; S, sinus tract. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

most likely caused the folding of the mesh around the ring in anterior and posterior directions (see Fig. 7). Therefore better initial fixation is required.

Based on many research efforts in the past, it can be stated that in general, small diameter of the percutaneous connection and good implant and tissue immobilization will lead to longer implantation times. Despite the choice of a 2-stage procedure and the combination of surface-enhanced, small diameter percutaneous implants of biocompatible materials (CP titanium, aluminum oxide, etc), the classic phenomenon of soft tissue implant failure was still the final result in our study. Failure modes of percutaneous implants, such as permigration, infection, avulsion, and marsupialization (alone or in combination) have been reported previously.^{11,34,35} Epidermal tissue responses in goats were reported to be more favorable than those in dogs and rabbits.³⁶

We were unable to achieve sustainable percutaneous connection around the tracheostoma. In our animal model it is probable that the multifactor process of avulsion, marsupialization with sinus tract formation and later also infection caused the implant failure. These results are not in concordance with

other studies that focus on soft-tissue anchored percutaneous implants.^{11,22,23,25,37,38}

The reason that our experiments were considered unsuccessful was the high mobility of the tissue of the implantation area. We have proven that sufficient tissue immobilization with these prototypes is impossible. From the moment of installation of phase-2 screws this has led to insufficient skin attachment to the percutaneous pins, persisting sinus tracts, and allowed entrance of bacteria resulting in infections. Major contributing factors were that the neck of the goat and therefore the tissues at the implantation site were very mobile and for tracheostomy care, the head had to be immobilized with the neck in hyperextension. Also, the housing environment could only be kept relatively clean, there was easy contamination with mucus and the implants were mechanically loaded due to tracheostoma canula fixation. The implants were constructed in a relatively nonsterile environment before sterilization. Rest products of destroyed bacteria (endotoxins) after sterilization (lipopolysaccharides) may have played a role in distorting our measurements of elemental composition and contributing to the pulmonary (or systemic) complications that occurred in the animals, a comparable process to that described by Yang et al.³⁹

Generally, the smaller the contact surface (diameter of the screws) between the tissue and the implant, the smaller the risk of epithelial downgrowth. In theory, the epithelial downgrowth and pocket formation induced by the 3 mm diameter screws could have caused infection and failure of the whole TS-TC. We found that all the tissue surrounding the screws showed signs of epithelial downgrowth.

It can be concluded that the two-stage implantation procedure of our prototype TS-TCs in this animal model was unsuccessful. Additional research efforts are necessary to improve tissue immobilization and to devise reliable fixation systems for TSVs.

We thank all the coworkers and animal welfare officers at the Central Animal Facility, coworkers at the departments of BioMedical Engineering Groningen and Biomaterials Nijmegen, the Netherlands. Also, we are grateful to Mediprof-Atos Medical, Tefa Portanje for providing the tracheostoma canulas. This study was part of Eureka project 2614 "Newvoice" (<http://www.eureka.be>) and received financial support.

References

1. Verkerke GJ, Geertsema AA, Schutte HK. Airflow resistance of heat and moisture exchange filters with and without a tracheostoma valve. *Ann Otol Rhinol Laryngol* 2002;111:333–337.
2. ten Hallers EJO, Marres HAM, Rakhorst G, et al. Difficulties in the fixation of prostheses for voice rehabilitation after laryngectomy. *Acta Otolaryngol* 2005;125:804–813.

3. Geertsema AA, Schutte HK, Verkerke GJ. In vivo measurements of an improved tracheostoma valve based on inhalation. *Ann Otol Rhinol Laryngol* 2002;111:142–148.
4. Geertsema AA (Groningen/The Netherlands). Tracheal stoma valve. US Patent 6,439,233, August 27, 2002.
5. Schwarz C, Cirugeda-Kuhnert M, Hagen R. Tracheostomaventil mit integrierter Hustenklappe (Window) zur Verbesserung der fingerfreien Sprache des Laryngektomierten—Klinische Langzeitergebnisse. [Tracheostoma valve with integrated cough lid for improvement of hands-free speech in laryngectomees—Long term results]. *ADEVA Medical Gesellschaft für Entwicklung und Vertrieb von Medizinischen (Lübeck, DE(Germany))*. *Laryngorhinootologie* 2004;83:173–179.
6. Blom ED, Singer MI, Hamaker RC. Tracheostoma valve for postlaryngectomy voice rehabilitation. *Ann Otol Rhinol Laryngol* 1982;91:576–578.
7. Hilgers FJM, Ackerstaff AH, van As CJ, Balm AJM, Van den Brekel MWM, Tan IB. Development and clinical assessment of a heat and moisture exchanger with a multi-magnet automatic tracheostoma valve (Provox FreeHands HME) for vocal and pulmonary rehabilitation after total laryngectomy. *Acta Otolaryngol* 2003;123:91–99.
8. van den Hoogen FJ, Meeuwis C, Oudes MJ, Janssen P, Manni JJ. The Blom-Singer tracheostoma valve as a valuable addition in the rehabilitation of the laryngectomized patient. *Eur Arch Otorhinolaryngol* 1996;253:126–129.
9. Op de Coul BM, Ackerstaff AH, van As-Brooks CJ, van den Hoogen FJ, Meeuwis CA, Manni JJ, Hilgers FJ. Compliance, quality of life and quantitative voice quality aspects of hands-free speech. *Acta Otolaryngol* 2005;125(6):629–637.
10. Roxburgh J, Perry A. Use of a “hands-free” tracheostoma valve in patients with laryngectomy and tracheoesophageal puncture. *Ann Otol Rhinol Laryngol* 2004;113:565–570.
11. Geertsema AA, Schutte HK, van Leeuwen MB, Rakhorist G, Schakenraad JM, van Luyn MJ, Verkerke GJ. Biocompatibility of a novel tissue connector for fixation of tracheostoma valves and shunt valves. *Biomaterials* 1999;20:1997–2005.
12. Geertsema AA, Schutte HK, Rakhorist G, Van Luyn MJ, Mahieu HF, Verkerke GJ. A novel tracheal tissue connector for fixation of laryngeal prostheses. *Biomaterials* 2001;22:1571–1578.
13. Verkerke GJ, de Vries MP, Geertsema AA, Schutte HK, Busscher HJ, Herrmann IF. Eureka project ‘totally implantable artificial larynx’; progress report. In: McCafferty G, Coman W, Carroll R, editors. *XVI World Congress of Otorhinolaryngology Head and Neck Surgery*. Bologna: Monduzzi Editore; 1997. pp 1343–1346.
14. Mylanus EAM. The bone anchored hearing aid, clinical and audiological aspects (thesis). Nijmegen, The Netherlands: Radboud University; 1994.
15. van der Pouw CTM. Bone anchored hearing, short and long term results (thesis). Nijmegen, The Netherlands: Radboud University; 1999.
16. Schoen PJ, Raghoobar GM, van Oort RP, Reintsema H, van der Laan BF, Burlage FR, Roodenburg JL, Vissink A. Treatment outcome of bone-anchored craniofacial prostheses after tumor surgery. *Cancer* 2001;92:3045–3050.
17. Jansen JA, van der Waerden JP, de Groot K. Development of a new percutaneous access device for implantation in soft tissues. *J Biomed Mater Res* 1991;25:1535–1545.
18. Paquay YC, de Ruijter JE, van der Waerden JP, Jansen JA. Tissue reaction to Dacron velour and titanium fibre mesh used for anchorage of percutaneous devices. *Biomaterials* 1996;17:1251–1256.
19. Paquay YC, De Ruijter AE, van der Waerden JP, Jansen JA. A one stage versus two stage surgical technique. Tissue reaction to a percutaneous device provided with titanium fiber mesh applicable for peritoneal dialysis. *ASAIO J* 1996;42:961–967.
20. Paquay YC, de Ruijter JE, van der Waerden JP, Jansen JA. Titanium fiber mesh anchorage for percutaneous devices applicable for peritoneal dialysis. *J Biomed Mater Res* 1994;28:1321–1328.
21. Walboomers XF, Paquay YC, Jansen JA. A new titanium fiber mesh-cuffed peritoneal dialysis catheter: Evaluation and comparison with a Dacron-cuffed tenckhoff catheter in goats. *Perit Dial Int* 2001;21:254–262.
22. Nyman R, Eklof H, Eriksson LG, Karlsson BM, Rasmussen I, Lundgren D, Thomsen P. Soft-tissue-anchored transcatheter port for long-term percutaneous transhepatic biliary drainage. *Cardiovasc Intervent Radiol* 2005;28:53–59.
23. Lundgren D, Axelsson R. Soft-tissue-anchored percutaneous device for long-term intracorporeal access. *J Invest Surg* 1989;2:17–27.
24. Grosse-Siestrup C, Affeld K. Design criteria for percutaneous devices. *J Biomed Mater Res* 1984;18:357–382.
25. Williams AM, Southern SJ. Body piercing: To what depths? An unusual case and review of associated problems. *Plast Reconstr Surg* 2005;115:50e–54e.
26. ten Hallers EJO, Rakhorist G, Marres HAM, Jansen JA, van Kooten TG, Schutte HK, van Loon JP, van der Houwen FB, Verkerke GJ. Animal models for tracheal research. *Biomaterials* 2004;25(9):1533–1543.
27. Prince ME, Nasser JG, Pass BB. Effect of upper-airway passages on craniofacial growth in an animal model: A pilot study. *J Otolaryngol* 1997;26:306–315.
28. ten Hallers EJO, Marres HAM, Rakhorist G, Jansen JA, Sommers MG, van der Houwen EB, Schutte HK, van Kooten TG, van Loon JP, Verkerke GJ. The Saanen goat as animal model for post-laryngectomy research: Practical implications. *Lab Anim*. In press, 2006.
29. Jansen JA, van’t Hof MA. Histological assessment of sintered metal-fibre-web materials. *J Biomater Appl* 1994;9:30–54.
30. Serro AP, Saramago B. Influence of sterilization on the mineralization of titanium implants induced by incubation in various biological model fluids. *Biomaterials* 2003;24:4749–4760.
31. Weaver DJ. Scoliosis correction with shape memory metal: Biochemical and biocompatibility aspects, PhD Thesis. Groningen, The Netherlands: Groningen University; 2001.
32. Piattelli A, Degidi M, Paolantonio M, Mangano C, Scarano A. Residual aluminum oxide on the surface of titanium implants has no effect on osseointegration. *Biomaterials* 2003;24:4081–4089.
33. Ackerstaff AH, Hilgers FJ, Balm AJ, Tan IB. Long-term compliance of laryngectomized patients with a specialized pulmonary rehabilitation device: Provox Stomafilter. *Laryngoscope* 1998;108:257–260.
34. Jansen JA, van der Waerden JPCM, de Groot K. Wound-healing phenomena around percutaneous devices implanted in rabbits. *J Mater Sci: Mater Med* 1990;1:192–197.
35. von Recum AF. Applications and failure modes of percutaneous devices: A review. *J Biomed Mater Res* 1984;18:323–336.
36. Gangjee T, Colaizzo R, von Recum AF. Species-related differences in percutaneous wound healing. *Ann Biomed Eng* 1985;13:451–467.
37. Gerritsen M, Lutterman JA, Jansen JA. A percutaneous device to study glucose kinetics in subcutaneous tissue fluid. *J Mater Sci: Mater Med* 2000;11:499–503.
38. Gerritsen M, Paquay YG, Jansen JA. Evaluation of the tissue reaction to a percutaneous access device using titanium fibre mesh anchorage in goats. *J Mater Sci: Mater Med* 1998;9:523–528.
39. Yang RS, Tsai KS, Liu SH. Titanium implants enhance pulmonary nitric oxide production and lung injury in rats exposed to endotoxin. *J Biomed Mater Res A* 2004;69:561–566.