EXPERIMENTAL RESULTS OF THE TRACHEOESOPHAGEAL TISSUE CONNECTOR FOR IMPROVED FIXATION OF SHUNT VALVES IN LARYNGECTOMIZED PATIENTS

E. J. O. Ten Hallers, MD,1,2 Henri A. M. Marres, MD, PhD,1 Eduard B. van der Houwen, MSc,2 John A. Jansen, DDS, PhD,3 Gerhard Rakhorst, DVM, PhD,2 Harm K. Schutte, MD, PhD,2 Theo G. van Kooten, MSc, PhD,2 Jan-Paul van Loon, MSc, PhD,4 Gijsbertus J. Verkerke, MSc, PhD2,5

1 Department of Oto-Rhino-Laryngology and Head and Neck Surgery, Radboud University Nijmegen Medical Centre, P. O. Box 9101, 6500 Nijmegen, The Netherlands. E-mail: o.tenhallers@kno.umcn.nl
2 Department of BioMedical Engineering, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
3 Department of Periodontology and Biomaterials, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
4 Intra-Vasc NL BV, Meditec Centre, Groningen, The Netherlands
5 Department of Biomechanical Engineering, University of Twente, Enchede, The Netherlands

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Abstract: Background. After total laryngectomy and voice rehabilitation using a tracheoesophageal shunt valve, patients often have valve-related complications such as leakage. To solve these problems, a tracheoesophageal tissue connector (TE-TC) was devised to serve as an interface between the patient’s tissue (trachea and esophagus) and the shunt valve.

Methods. The TE-TC is a permucosal connection constructed from a titanium ring (filled with a silicon rubber plug) combined with polypropylene or titanium mesh. After implantation in adult goats for 12 weeks the implants were submitted to histologic investigation.

Results. Firm implant fixation was achieved. In nearly all (18/19), no signs of infection of the implant were seen; 11 of 19 animals died before the end of the experiment owing to complications not related to the implant.


Keywords: implant; voice prosthesis; voice rehabilitation; permucosal; soft tissue

Voice rehabilitation in Western Europe and the United States after laryngectomy is primarily initiated by means of a tracheoesophageal (TE) shunt valve. Daily use of this valve is preferably combined with heat and moisture exchange (HME) filters and tracheostoma valves.1–3

Concerning the shunt valve, however, many laryngectomized patients suffer from valve-related complications such as leakage.4 This results in coughing and in some cases in recurrent pneumonias. Frequent valve replacement has a negative influence on patients’ quality of life. Two types of leakage can be distinguished. Leakage through the shunt valve and leakage around the shunt valve.4,5 The first type of leakage is generated by valve dysfunction mainly caused by bio-
film formation. This process and its solution has been and is still being studied extensively.6,7 The second type of leakage is caused by incongruence between the size of the shunt valve and that of the fistula in the TE wall (periprosthetic leakage).8 This is the second most common reason for valve replacement.9

A small diameter of the TE fistula can be enlarged with a dilator. For correction of an enlarged fistula, various options for treatment are available. Conservative treatment consists of temporary removal of the shunt valve resulting in the need for nasogastric feeding. In most cases the fistula will shrink. A submucosal circular suture can also resolve leakage around the valve but this too does not contribute to a long-lasting solution. The same is true of repeated application of silver nitrate.

Many manufacturers have begun to produce shunt valves with larger diameters resulting in a tighter fit. However, this probably also contributes to a higher frequency of leakage.10

In a previous Eureka project,11 a concept of a tracheoesophageal tissue connector (TE-TC) was developed.12,13 A TC is thought to serve as an interface between the patient’s tissue (trachea and esophagus) and the shunt valve itself. The main advantage is that it widens the choice of biofilm resistant materials for a valve system and/or voice-producing elements (see Figure 1).

The TE-TC is a permucosal connection and based on bone anchored percutaneous and permucosal connections such as the bone anchored hearing aid (BAHA)14 pins for the fixation of maxillofacial prosthetics,15 dental implants, and soft tissue-based implants16–24 that were reported previously.

In the present Eureka project “Newvoice,” the TE-TC concept was further developed into various prototypes. The aim of this study was to determine the feasibility of the various prototypes by performing animal experiments and evaluating the histologic reaction to the implant.

MATERIALS AND METHODS

Implants. Two prototypes of TE tissue connectors were tested. The first TE-TC consisted of a ring made of commercially pure titanium grade 2 (Thijssen Krupp BV, The Netherlands) and a polypropylene mesh (see Figure 2A). The ring was designed to allow easy connection and disconnec-

FIGURE 1. Schematic illustration of a laryngectomized patient with tracheoesophageal tissue connector implanted.

FIGURE 2. (A) Tracheoesophageal tissue connector with polypropylene mesh. (B) Tracheoesophageal tissue connector with titanium mesh. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
tion of a shunt valve. The mesh itself was meant for capillary and fibrous tissue ingrowth to immobilize the implant resulting in a water and air tight connection device for valve systems.

The second TE-TC was provided with a more rigid titanium mesh instead of a polypropylene mesh (Figure 2B).

The rings were ultrasonically cleaned in an RBS-35 soap solution, rinsed in water and cleaned in trichloroethylene, and rinsed again in hot water and dried to the air. The surface characteristics (roughness and chemical composition) were comparable to the implants used in previous experiments at this institution (unpublished data).

The knitted monofilament polypropylene mesh (Bard Mesh, Bard Benelux NV, The Netherlands) was cut to the appropriate size and cleaned in alcohol 70%. The titanium mesh consisted of 50-μm sintered fibers with a porosity of 80%, 500 g/m² (NV Bekart SA, Belgium). The titanium mesh was cut into circular patches using a laser and argon gas. Afterward it was cleaned in trichloroethylene and rinsed in boiling distilled water and dried. Both meshes had an outer diameter of 30 mm. The meshes were glued to the titanium rings using MED-1511 RTV medical-grade silicone adhesive (NuSil Technology, Carpinteria, CA) and a special Glue apparatus (I&J Finsar JBE 1113, Eltest, Belgium) for controlled adhesive application. The implants were sterilized in an autoclave (121°C for 20 minutes). Two different types of plugs for placement during implantation were made to fit in the titanium ring. Plug 1 was designed to prevent debris and fluid collection in the lumen of the ring. Plug 2 was designed for the same function as plug 1 but also to guide the tracheal mucosal to the ring and enhance tissue attachment and connection to the titanium ring. Plug 2 contains 2 foldable flanges (comparable with an adapted shunt valve) with grooves in it, to ease folding. Both plugs were made of medical grade silicone rubber (MED-6033 silicone elastomer; NuSil).

**Surgical Procedure.** Adult female Saanen goats (2.5–3.0 years, 60–80 kg) were selected for this experiment because the dimension of the most relevant structures (trachea and esophagus) is similar to that in humans, and they were easy to handle. The animals were individually housed according to national and institutional guidelines. The project was approved by the Ethical Committee for animal experiments of Radboud University Nijmegen Medical Centre. The implantation time was 12 weeks. Group 1 received the TE-TC with polypropylene mesh. In group 2, instead of a TE-TC with polypropylene mesh, titanium mesh was used. The surgical procedure was the same as for group 1. A pilot study was also performed: in this pilot group 3, only the technical feasibility was tested. The initial surgical procedure of group 3 was identical to that of group 1 and 2. However, instead of silicone rubber plug 1, plug 2 was inserted after suturing the polypropylene mesh to the trachea (using 4 Vicryl 4-0 sutures) and puncturing the dorsal tracheal wall. The anterior flange of plug 2 was placed in the lumen of the trachea. For anesthesia the animals received medetomidine (Domitor) (A.U.V., Cuijk, The Netherlands) 25 μg/kg intramuscular (i.m.), pentobarbital (Nembutal) (A.U.V) 10 to 20 mg/kg intravenous (i.v.), and propofol 2-mg/kg bolus and 8-mg/kg/h maintenance i.m. Inhalation anesthesia was achieved by tracheal intubation and ventilation with O₂ (30%), N₂O (70%), Isoflurane approximately 1.5%.

The surgery was performed under full sterile conditions. The frontal neck area was shaved, washed, and disinfected with poviodone solution followed by covering with sterile blankets.

After a vertical median incision was made, the trachea and esophagus were locally separated. A laryngotracheal separation was performed 3 semi-rings below the cricoid. Also 3 to 6 semi-rings were excised. The laryngeal pouch was closed using sewn 1/2 stitches. The larynx was fixed to the neck by means of an elastic cord around the neck or by plastic rings sutured to the skin 5 cm inferior and 2 to 3 cm lateral from the stoma. The goats received antibiotic prophylaxis and analgesics for 3 days and after day 3 on indication (respiratory and other infections). The goats received stoma care 3 times per day and later 4 times per day strictly every 6 hours after the operation.

**Postoperative Management.** After the operation, lateral and anteroposterior x-rays were taken to check the positioning and alignment of the tissue connector. The animals were equipped with a shortened tracheostoma cannula (silicone rubber Provox Lary Tube (Atos Medical, Sweden) and Shiley tracheostomy tubes (with inner cannula) (Mallinckrodt, St. Louis, MO). The cannulas were fixed to the neck by means of an elastic cord around the neck or by plastic rings sutured to the skin 5 cm inferior and 2 to 3 cm lateral from the stoma. The goats received antibiotic prophylaxis and analgesics for 3 days and after day 3 on indication (respiratory and other infections). The goats received stoma care 3 times per day and later 4 times per day strictly every 6 hours after the operation.
adaptation of the protocol. It consisted of cannula and stoma cleaning and intratracheal instillations of 10 mL saline to provoke a coughing reaction. In this way, the trachea and bronchi were mechanically cleaned and extra moistened. To enhance easy clearance of mucus, a mucolytic agent, dissolved in water (0.25 mg/kg), was administered twice a day orally.

Additional air humidifiers were installed to realize a relative humidity of 60% or higher. Three times per week flexible endoscopy was performed. Detailed postoperative care is described separately.

**Histologic Processing and Evaluation.** The fixation of the implant was verified manually. They were then preserved in formaldehyde and after removal of hairs and excessive tissue, dehydrated in mounting alcohol solutions, and impregnated with methylmethacrylate (MMA). After 8 weeks the samples in the MMA were polymerized. Then sections were cut by means of a microtome. Three regular sections at least were made for histologic scoring. The sections were stained with methylene blue and basic fuchsin. The aspects specifically examined were capsule quality, capsule thickness, interface quality, epithelial downgrowth (only group 3), and interstitial tissue quality (only at the location of the mesh).

**RESULTS**

**Animal Model.** The average follow-up time (and range) of groups 1, 2, and 3 (in days) were 57.9 (7–110), 38.33 (6–131), and 44.5 (39–50), respectively. The follow-up (and implantation) time of 84 days was exceeded in 3 cases due to logistic reasons (n = 1), attempt to control a local infection (n = 1), and pilot surgery experiments (n = 1).

Not all animals were kept alive until the intended date of termination due to reaching humane endpoints defined in the protocol or sudden death. Some of the animals developed respiratory distress due to the tracheostomy. In total, 11 of 19 of the animals were lost before the end of the experiment as a consequence of factors unrelated to the implant. Nevertheless, histologic results of these animals were obtained. Postoperatively, problems with the fixation of the tracheostoma cannulas were encountered. Many of the animals developed a deprived area at the cranial point of the tracheostoma despite all efforts to prevent tissue damage.

**Macroscopic Findings.** During the operation, some inter-individual differences were found concerning the size and shape of the trachea, similar to those described previously. In some cases, this appeared to give a nonideal placement of the TE-TC. A small dorsal ridge of the trachea allows pivoting (in lateral direction). Nevertheless, on x-rays the positioning was satisfactory in all cases (see Figure 3).

In the goats that were lost during follow-up, obductions revealed mucous plug obstruction, pneumonia, cardiac decompensation, or lung edema/exudate (n = 11). Remarkably, no related clinical signs of disease were observed in the days before they died. No goats had to be killed because of problems related to the TE-TC.

In all but one, no signs of local infections were seen. No implants showed defects, and all implants inspected after an implantation time longer than 1 week were fixed well between the tissues. In the pilot group 3, plug 2 served well for guiding the tracheal tissue between the silicone rubber flange and the middle part of the ring with mesh (see Figure 4). In 1 case, the tracheal mucosa showed a tendency of partial overgrowing the flange of plug 2. The puncture site could easily be inspected with a light source. In all 19 cases, no signs of leakage of the laryngeal pouch were observed.
Light Microscopy. Assessment of the histologic sections revealed a comparatively uniform tissue response for all implants in group 1 ($n = 11$). Group 2 consisted of a set of data with implantation time ranging from 6 days to 131 days ($n = 6$). The titanium mesh of the implants of group 2 induced less fibrous tissue and inflammatory reaction compared with the implants of group 1. The density of fibers in the titanium mesh is much higher. Consequently, there is a much clearer interstitium that can be distinguished compared with the polypropylene mesh. In all implants, more flexion was seen of the polypropylene mesh than of the titanium mesh.

The fixation process induced a chemical reaction with the medical grade silicone rubber caus-
Dimethylsiloxane (PDMS) and polyvinylpyrrolidone (PVP) hydrogel (Bioplastique, Bioplasty, The Netherlands),

\[ n = 2 \]

Cross-linked hyaluronan (Hylaform),

\[ n = 3 \]

Autologous fat,

\[ n = 31,32 \]

Granulocyte-macrophage colony-stimulating factor (Molgramostim, GM-CSF), or application of sutures in the surrounding soft tissue and the use of silver nitrate cautery for granulation tissue illustrate that the ultimate solution has yet to be found. Surgical closure and a secondary puncture may be necessary in persistent cases. Worst-case scenarios even include the need of reconstructions with an interposing pectoralis major flap (or other flaps) to close the fistula.

A tissue connector concept was developed to realize a complete leakage-free solution for TE speech. If the TE-TC also allows firm attachment and fibrous tissue ingrowth of the human esophagus, leakage around and through the shunt valve can be prevented and other materials can be used for the valve itself. The TE-TC may therefore contribute to enhancement of the quality of life of these patients.

Investigations in the past, aiming at improvements for laryngectomized patients and concentrating on developing an artificial larynx and laryngeal transplantation, have not yet led to a sustainable or long-term solution. Therefore, the development of shunt valves made of biofilm-resistant material is currently at the focus of efforts to improve the quality of life for laryngectomized patients. This has resulted in a longer device lifetime for the shunt valve.

When a TE-TC is implanted, the choice of materials for the valve itself is almost limitless. This means that materials less prone to biofilm adhesion are an option because the placement or replacement procedure does not require a flexible silicone rubber esophageal flange and there will no longer be any permanent interaction with the tracheal or esophageal tissue. With regard to the TC itself, titanium and polypropylene were materials chosen because of their biocompatibility. Also Debry et al pointed out that porous titanium would be the material of choice for constructs in the upper aerodigestive tract. Macropores also contribute to a strong connection because they allow tissue bridges and prevent migration. Tissue integration of polypropylene mesh if infected is affected but the tensile strength does not change. The medical grade silicone rubber glue was necessary for appropriate mesh fixation to the ring. However, this material provokes a relatively high foreign-body reaction,
and we prefer an alternative method of mesh fixation for the future.

Artifacts such as gap formation between the soft tissue and the titanium ring may have been caused by mechanical forces during retrieval or fixation processing. In our samples, we suggest it was mainly caused by swelling of the silicone rubber; however, this is not conclusive.

Continuous antibiotic treatment in goats with some kind of tracheostomy as proposed by Vogler et al. was not appropriate here because this influences tissue reaction. There is no consensus whether continuous antibiotic treatment would improve the survival of goats with a tracheotomy or tracheostomy, and additional veterinary research on this topic is desirable.

The tested TE-TC prototypes and plugs 1 and 2 were designed for a 2-stage implantation procedure because it may increase the chance of success. The first stage consisted of implantation of a TC with plug 1 for 6 weeks. The intended second stage consisted of consequent puncture of the dorsal tracheal wall, removal of plug 1, puncture of the esophageal wall and installation of plug 2. However, esophageal puncture was not included: goats are ruminants, which increases the risk of complications and would not simulate the human situation. To test the TE-TC with an esophageal puncture (or complete TE puncture) in vivo, another nonruminating animal model would be more appropriate. This, including tests in radiated tissue, will be tested in a future study. Because large-diameter TEPs involve the risk of leakage, titanium rings in particular should be kept as small as possible.

Soft tissue anchored implants have been reported to be successful in animal experiments although most of them deal with percutaneous connections instead of permucosal. Knowledge of soft tissue embedded permucosal connections and implants is scarce, contrary to those in bone, such as dental implants. Applications in humans, such as a titanium interface for a percutaneous transhepatic biliary drain and connectors for body art and jewelry, illustrate that the soft tissue area around implants (the stress reduction area) can be controlled.

From the results of this study, it is concluded that a tracheoesophageal tissue connector is a new device with potential in the solution of fixation-related problems in TE voice rehabilitation after laryngectomy. However, further research is needed to obtain long-term results of the tissue connectors when, for example, mechanically loaded with complete TE puncture in a nonruminating animal model.

The project will be finalized in the future by a first clinical application of the tissue connector with a voice-producing shunt valve.

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