RECONSTRUCTION OF THE MAIN AIRWAY THROUGH THE USE OF INTEGRABLE SYNTHETIC PROSTHESIS

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Abstract:
One of the main problems arising from the surgical treatment of tracheal lesions is the existing limitation in the length of segment that can be resected.Currently, a maximum of 50% of the trachea can be safely removed.More extensive lesions cannot benefit from this treatment and alternative techniques must be used, which are palliative in most cases.The interposition of an element which substitutes the segment of resected trachea is a possible solution for this problem.
An experimental animal study has been conducted, substituting tracheal segments varying in length with cylindrical polytetrafluoroethylene prostheses. Later, a follow-up was done and the animals were sacrificed to study histological changes.
The results show the technical possibility of substituting the airway with segments of prosthetic material.In the monitoring of the animals, there seems to be a direct relationship between the length of the implant and the appearance of tracheal stenosis at the implant site, both in the macroscopic morphological studies and the studies completed with optical microscopy.
However, for the time being, perioperative mortality is high and, although it can be attributed to the learning curve, applying the results to possible clinical practice is not recommended.

Key words: tracheal stenosis, tracheal prosthesis, vascular prosthesis, tracheal resection, experimental study.

RECONSTRUCCIÓN DE LA VÍA AÉREA PRINCIPAL MEDIANTE EL USO DE PRÓTESIS SINTÉTICAS INTEGRABLES

Resumen
Uno de los principales problemas que plantea el tratamiento quirúrgico de las lesiones traqueales es la limitación existente en la longitud del segmento que es posible resecar. Actualmente, se puede extirpar con seguridad el 50% de la tráquea como máximo. Lesiones más extensas no se pueden beneficiar de este tratamiento y es necesario utilizar técnicas alternativas, en la mayoría de los casos paliativas. Una posible solución a este problema es la interposición de algún elemento que sustituya el segmento traqueal resecado.
Se ha realizado un estudio experimental en animales, sustituyendo segmentos traqueales de distinta longitud por prótesis cilíndricas de politetrafluoroetileno. Posteriormente, se ha realizado un seguimiento y sacrificio de los animales estudiando los cambios his-tológicos.
Los resultados obtenidos muestran la posibilidad técnica de la sustitución de la vía aérea por segmentos de material protésico. En el seguimiento evolutivo de los animales, parece existir una relación directa entre la longitud del implante y la aparición de estenosis traqueal a dicho nivel, tanto en los estudios morfológicos macroscópicos como en los estudios realizados con microscopía óptica.
Sin embargo, por el momento, la mortalidad perioperatoria es elevada y, si bien se puede atribuir a la curva de aprendizaje, la traslación de los resultados a una posible práctica clínica no es recomendable.

Palabras clave: Estenosis traqueal, prótesis traqueal, prótesis vascular, resección traqueal, estudio experimental.

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INTRODUCTION

For many tracheal affectations, both from malignant and benign pathology, the chosen treatment is surgical tracheal resection followed by termino-terminal anastomosis.

Since its origins in the 50s, this surgery has seen noticeable advances, particularly with respect to the techniques. Even so, lesions covering more than 50% of the length of the trachea in adults cannot currently be safely resected and later reconstructed. In these cases, treatment can only be palliative through the use of tracheal endoprostheses or chemoradiotherapy in the case of a malignant pathology.

Despite the number of tissues and materials that have been researched to substitute tra-cheal segments, there is still none that allows for the guaranteed replacement of this seemingly simple structure.
Unlike more complex organs such as the heart, liver and lungs, attempted tracheal transplants have been unsuccessful, leading to the necrosis or stenosis of the graft[1, 2].

Animal studies using prostheses from synthetic materials, the inside of which are cov-ered with some type of epithelium (jejunum or esophagus), showed acceptable results, with good functional results and adequate integration of the graft tissues[3, 4]. Homografts of segments of thoracic aorta have been used for the same purpose with the same re-sults[5-7]. However, the technical difficulty of obtaining the graft and the potential com-plications that can arise from the process limit its clinical applicability.

In recent years, the development of tissue engineering has allowed for the creation of scaffolds or frames that are then permeated with different types of cells to obtain bio-logical airway substitutes. Their drawbacks are that they are very complex to create and very costly[8-10].

The use of isolated exogenous synthetic materials, without cellular or tissue coating, is a much simpler and more economical solution. However, studies conducted have not shown satisfactory results and, on the contrary, have shown numerous complications[11, 12]. Nevertheless, these are dated studies and the development of new types of materials has encouraged the reconsideration of its application. Currently, cylindrical vascular prostheses with a minimally adherent interior and high capacity for tissue integration are available, which are rapidly colonized by fibroblasts and are even coated with endo-thelia[13].

Being able to safely use them in the airway would mark an important advance in the treatment of extensive tracheal lesions, allowing for remedial surgical treatment in cases for which it is currently impossible.

MATERIAL AND METHODS

Experimental animal.

The male New Zealand rabbit was used, aged between 12-13 weeks and weighing be-tween 2,500 and 3,000 grams (g). The diameter of its trachea, between 6 and 8 millime-ters (mm), as well as its anatomical disposition make it ideal for this type of study.

The animals were transported from the supplying company Isoquinen S.A. (Barcelona) in individual crates. Upon their arrival, they were held at the animal house at the Institu-to de Biomedicina de Sevilla (IBIS), maintaining a 12/12 hour light/dark cycle, an am-bient temperature of 24ºC, a relative humidity of 60% and ad libitum feeding. The preoperative stay was at least 2 days for acclimation. At the time of intervention, they were transferred to the operating room in individual cages.

Synthetic material.

The Gore Propanten Vascular Graft® prosthesis from the Gore trading house (W.L. Gore & Associates Inc., Flagstaff, AZ, USA) was selected as the synthetic material for tracheal segment substitution, consisting of a polytetrafluoroethylene tube with a smooth and regular internal surface which hinders secretion adherence. Prostheses with diameters ranging from 6 to 8 mm were used, according to the tracheal diameter of the expe-rimental animal.

Study groups.

The animals were divided into four groups, based on the length of the substituted airway segment (between 5 and 10 mm) and the length the animal maintenance period after implant (45 and 90 days). Thus, four groups were established: group 1 with 5 mm substituted and maintained for 45 days, group 2 with 10 mm and 45 days, group 3 with 5 mm and 90 days and, finally, group 4 with 10 mm and 90 days.

The study of different lengths was done to determine if the prosthesis' capacity for tis-sue integration is influenced by its length. Post-implant

periods were selected to study the evolution of integration and the substitution of inflammatory conditions with scar-ring.

Initially, 5 animals were assigned to each group. However, deaths in the preoperative phase and during follow-up as well as several sample losses resulted in additional ani-mals being assigned to the affected groups. Thus, a total of 25 rabbits were included to reach a sufficient number in each group.

Chosen anesthesia and surgical technique.

The anesthesia administered to experimental animals was selected according to existing information in the literature and past experience. The drugs ketamine and xylazine were used, both administered intramuscularly, at a dose of 35 and 5 mg/kg, respectively. This dosage allowed for the animal's spontaneous breathing, avoiding problems arising from manipulating the airway and decreasing the postanesthetic recovery period.

The intended surgical technique was similar to that performed in humans. After remov-ing a segment of trachea from the experimental animal, both ends of the trachea were sutured at the upper and lower edge of the synthetic prosthesis, using 4-0 absorbable interrupted sutures.

Postoperative maintenance and follow-up for experimental animals.

After surgery, the animals were returned to their holding cages. The first week after intervention they were administered 0.2 mg/kg of meloxicam at 12-hour intervals. This analgesia pattern was modified, administering additional medication (2-5 mg/kg of morphine, occasionally) in cases where signs of pain or stress were noted.

Visual inspections of the animals' comfort and wellbeing were done at least twice a day throughout the period for which the animals were held.

Sacrificing animals.

35 and 90 days after the prosthesis implant, according to the established dates and with the animal previously sedated to avoid any type of stress. A double anesthetic intraven-ous dose of xylazine and ketamine was used, according to weight.

Those animals showing signs of stress such as decreased eating or refusal to eat, lethargy or stridor were immediately sacrificed without waiting until the end of the period corresponding to the group to which they belonged. The reason sacrifice was required was registered.

Obtaining, examining and preserving tissue samples.

After sacrificing the animal, the tracheal segment containing the prosthesis was ex-tracted, along with at least 5 mm of the trachea proximal and distal to the implant. Once extracted, it was examined and photographed to complete the macroscopic evaluation of the residual airway diameter. Then, recipients were injected with a 10% formaldehyde solution and handed over to pathological anatomy for study.

Animals suffering unexpected exitus before the planned sacrifice date were frozen at the moment we were informed of their death to avoid excessive tissue deterioration.

Anatomopathological study of samples.

The objective of the histological examination was to determine the variation in lumen at the endoprosthesis site and the cellularity of the area where the prosthesis attaches to the normal trachea. The samples were embedded in paraffin, cut in 5 micrometer (∫m) sec-tions with a microtome and stained with hematoxylin and eosin. Sections were cut lon-gitudinally across the trachea to show the changes in the anterior, transition and pros-thesis areas.

The inflammatory component was evaluated according to the type of cells present (po-lymorphonuclear cells, eosinophils, lymphoplasmacytic cells and giant cells) and the cellularity of the airway wall was evaluated according to the semiquantitative scale: 0 = absence, 1 = slight, 2 = moderate, 3 = intense.

The results were interpreted keeping the different phases of a healing wound in mind, distinguishing three clearly different phases: inflammation, appearance of granulation tissue and fibrosis. Similarly, attention was given to the appearance of granulomas or ulcerative lesions and the appearance of epithelium.

The images were taken with an Olympus SC20® (Olympus Corporation) camera and they were analyzed with the image programs Analysis GetIT® and Cell B® from the same company.

Measuring the tracheal lumen.

Immediately after obtaining the samples, a visual inspection of the

airway lumen was done, samples were photographed and, based on the images, the diameter at the site of the endoprosthesis was determined. To do this, Adobe Photoshop CC software (Adobe Systems Software Ltd, Ireland) was used. As it was a visual examination, the residual airway lumen values were rounded to simplify results.

As longitudinal histological cross-sections were cut, it was not possible to directly measure the reduction in tracheal diameter as we did not have the complete circumfe-rence. The calculation was made indirectly, measuring the thickness of the tracheal wall in the area immediately proximal to the prosthesis and comparing wall thickness in the central area of the prosthesis. The difference between these two sizes is the increased thickness of the wall at the prosthesis site.

Assuming the internal diameter of the trachea in the species and size of rabbit used is an average of 6 mm, twice the value calculated after the histological examination was sub-tracted from this diameter. Using the classification from a similar study14 as a base, we classified a normal lumen (6 mm), slight stenosis (4 - 6 mm), moderate stenosis (2 - 4 mm) and sever stenosis (lumen less than 2 mm).

Ethical and legal aspects.

This project was approved by the Ethics Committee at the Hospital Universitario Virgen del Rocío and animals were cared for and worked with in accordance with the legisla-tion included in Spanish Royal Decree 1201/2005 on the protection of animals used for experimentation and regulated by Law 32/2007 on caring for animals, their use, trans-portation, experimentation and sacrifice.

Statistical analysis

This is a descriptive study. The small number of animals per study group made powerful statistical studies possible. To illustrate the results, direct numerical data and the simple calculation of percentages were used.

RESULTS

Surgical process and postoperative follow-up.

The synthetic prosthesis was implanted in 25 animals as planned for in the design of the study. The technical aspects of the procedure are shown in Figure 1.

Table 1 includes the data for the procedure and the follow-up for the experimental ani-mals.

It should be noted that, of the treated rabbits, 5 died during intervention or in the mi-nutes immediately following. The cause could not be determined for two of these cases (ventilation was apparently adequate throughout the entire intervention and no signifi-cant hemorrhages occurred). In the other three cases, we observed the appearance of liquid and pink bubbles in the distal trachea. Deaths related to the surgical intervention were concentrated within group 1, with four animals.

During the follow-up period, six animals died unexpectedly. The majority of these were in groups 2 and 3.

In one case (R3), the animal needed to be sacrificed before the planned date after detecting signs of stress (lethargy, immobility and lack of eating).

Macroscopic sample evaluation.

The trachea was removed en bloc, along with the surrounding muscular tissue, from the larynx to the chest entry (Figure 2). Tissue not belonging to the trachea was then re-moved to facilitate the histological study. Samples were collected from all animals. However, three of them were too degraded to obtain reliable histopathological results. Thus, 18 valid samples were obtained in the end.

Once the samples were prepared, a macroscopic examination of the airway diameter at the site of the prosthesis was done, comparing it to the diameter in the area immediately preceding the prosthesis. Detailed results are shown in Table 1. The diameter of the airway at the site of the prosthesis in group 1 animals was observed to be, on average, 85% of the normal trachea diameter, with a range between 80 and 90%. In group 2, it was 67.3% (65-80%). In group 3, it was 78.7% (70-85%). And in group 4, it was 39% (15-60%).

The presence of dehiscence at the sutures or inflammatory excrescent lesions like gra-nulomas were not observed in any case.

In the cases in which diameter was reduced, it appears to have been due to the growth of fibrous scar tissue inside the airway.

Of the animals that died unexpectedly, there was significant stenosis in the airway in three, the cause of death could not be determined for one (R16) and an examination of the airway could not be done for the other two due to sample deterioration.

One animal (R3) was sacrificed due to dyspnea. Significant stenosis in the lumen was found in the study of the airway which was very similar to that found in the other ani-mals.

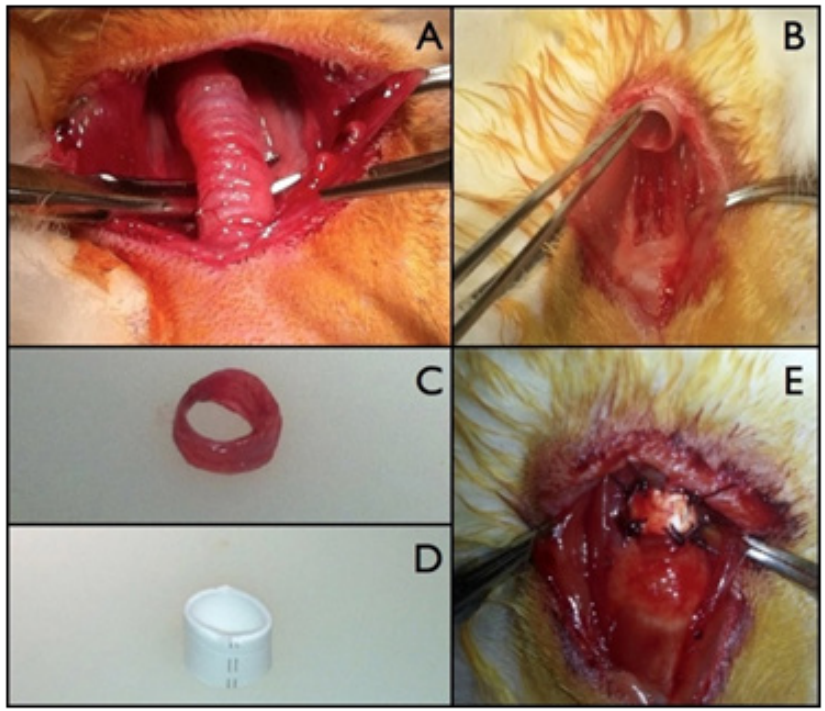

Figure 1. Completely dissected trachea of experimental animal (A) and once a segment was re-sected (B). Resected segment (C) and prosthesis of the same length to replace it (D). Finalized anastomosis. We see that airway continuity is restored with the endoprosthesis (E).

Table 1. Summary of the results immediately and significantly after implant. Rabbits are shown numbered in order of intervention. Group they belong to, comments on follow-up (follow-up), total length of implant and the airway lumen percentage at the site of prosthesis compared to the normal tracheal diameter.

Rabbit	Group	Follow-up	Follow-up (days)	Macro diameter
R1	1	Exitus in operating room.	-	-
R2	1	Unexpected exitus. Deteriorated samples.	-	-
R3	1	Early sacrifice. Dyspnea.	27	85%
R4	1	Exitus in operating room.	-	-
R5	1	Exitus in operating room.	-	-
R6	1	Scheduled sacrifice.	45	85%
R7	1	Scheduled sacrifice.	45	80%
R8	1	Scheduled sacrifice.	45	85%
R9	1	Scheduled sacrifice.	45	90%
R10	2	Scheduled sacrifice.	45	80%
R11	2	Exitus in operating room.	-	-
R12	2	Scheduled sacrifice.	45	70%
R13	2	Scheduled sacrifice.	45	40%
R14	2	Exitus in operating room.	-	-
R15	2	Scheduled sacrifice.	45	65%
R16	3	Unexpected exitus.	24	80%
R17	3	Scheduled sacrifice.	90	80%
R18	3	Scheduled sacrifice.	90	70%
R19	3	Scheduled sacrifice.	90	85%
R20	3	Unexpected exitus. Deteriorated samples.	-	-
R21	4	Scheduled sacrifice.	90	60%
R22	4	Scheduled sacrifice.	90	60%
R23	4	Unexpected exitus.	63	30%
R24	4	Unexpected exitus.	56	30%
R25	4	Unexpected exitus.	81	15%

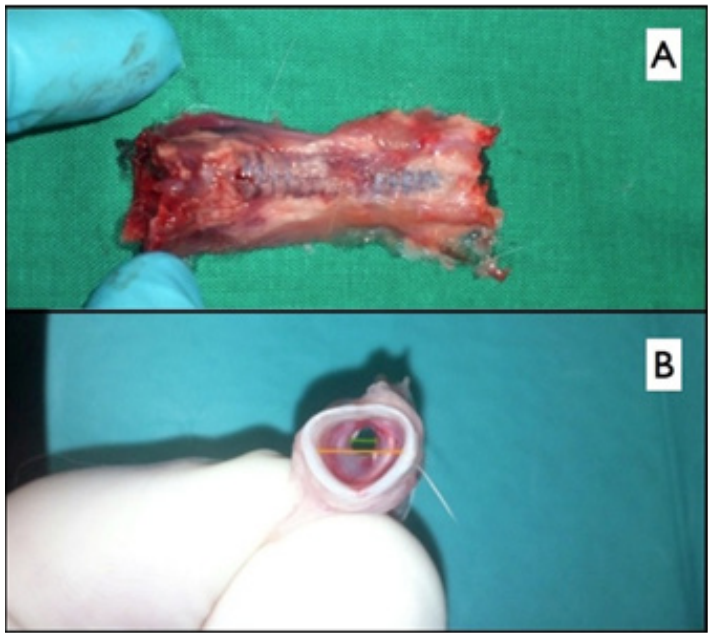

Figure 2. En bloc tracheal extraction (A). Tracheal rings can be seen surrounded by tissue. The prosthesis, a bit more yellow in color, in the central area. On the left is the larynx and the distal trachea is on the right. Taking of macroscopic measurements (B). Comparison of the tracheal lumen in the segment of trachea immediately before the prosthesis (orange line) and the prosthesis (green line).

Study of histological sample modifications.

After the collected samples were embedded in paraffin, cut and stained (Image 3), a cellularity study was done to evaluate the degree of prosthesis integration as well as cellular colonization. Table 2 includes data obtained from the anatomopathological analysis of each sample, noting the cell group according to the proposed scale.

Three of the samples (R15, R18 and R25) became degraded during the fixing and cut-ting process as the prosthesis broke loose from the wall, and thus it was not possible to evaluate the results.

The loss of samples and premature deaths within the different groups complicated inter-pretation. However, the data obtained seemed to indicate that in group 1, with a shorter prosthesis and shorter post-implant period, there was a prevalence of inflammatory con-ditions. In group 2, with the same period and a longer prosthesis, signs of granulation and fibrosis were observed. In group 3, only two animals concluded the study period, but their samples seem to show advanced inflammation and fibrosis. Finally, in group 4, with a long implant and prolonged post-implant period, the key finding was fibrosis. In the last group, two of the animals died before the end of the designated period (at 63 and 56 days after implant). However, the histological examination showed similar re-sults to those from animals who were sacrificed at 90 days.

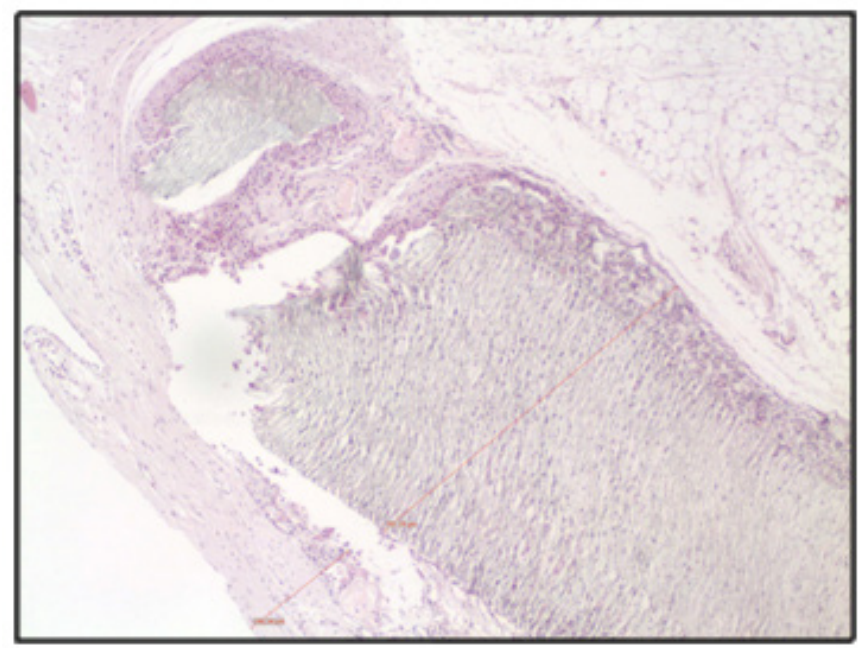

Figure 3. Histological study of the prosthesis and airway tissue with optical microscopy. Cellularity can be seen surrounding and within the prosthesis (grey). The measurements to later evaluate the reduction in airway diameter are in red.

Table 2. Evaluation of cellularity in samples. Evaluation according to the proposed scale for the study (0 - cellularity absent, 1 - slight, 2 - moderate, 3 - intense). A histological interpretation was done correlating cellular findings with the different healing phases.

	Group	PMN	Eosino	Lympho	Gia C.	Fibrosis	Ulcer	Histological interpretation
R3	1	0	0	0	1	2	0	Mod. granulat. fibrosis tiss.
R6	1	0	0	1	0	2	0	Initial fibrosis.
R7	1	2	1	0	0	0	0	Moderate inflammation.
R8	1	0	0	1	0	1	1	Granulat. tiss. Initial fibrosis.
R9	1	0	0	1	0	1	2	Granulat. tiss. Initial fibrosis.
R10	2	0	0	2	1	2	0	Granulat. tiss. Mod. fibrosis.
R12	2	1	1	1	0	0	0	Moderate inflammation.
R13	2	0	0	0	0	3	0	Severe fibrosis.
R15	2	-	-	-	-	-	-	
R16	3	3	3	1	0	1	3	Intense inflammation.
R17	3	0	0	1	2	2	0	Granulation tissue.
R18	3	-	-	-	-	-	-	
R19	3	0	0	0	0	3	0	Severe fibrosis.
R21	4	0	0	1	1	1	1	Granulat. tiss. Initial fibrosis.
R22	4	0	0	0	0	3	0	Severe fibrosis.
R23	4	0	0	0	0	2	0	Moderate fibrosis.
R24	4	0	0	0	1	2	0	Moderate fibrosis.
R25	4	-	-	-	-	-	-	

Study of the tracheal lumen diameter at the site of prosthesis implantation.

As shown in Image 3, measurements of airway wall thickness, both normal and at the site of the prosthetic implant, were taken from the optical microscopy photographs.

Table 3 includes the measurements taken, as well as diameter reduction in numeric val-ues and its expression on the stenosis scale we used.

It was not possible to study the samples degraded in the fixing, cutting and staining process.

After examining the valid samples, fairly heterogeneous normal tracheal wall thickness measurements were observed, in spite of the animals being the same breed and similar weights, with an average value of 285.4 ⌠m and a range between 200 and 436 ⌠m.

Values at the prosthesis site also varied significantly (between 601 and 1,007 ⌠m) with-out differences between the different groups

The difference between normal diameter and that of the prosthesis site was between 309 and 604 ⌠m, also with no variation between groups.

However, despite the high variability in measurements and regardless of the time or prosthesis length in all cases, the increase in tracheal wall thickness attributed to in-flammatory condition or scarring attributed to the implant were less than or equal to one millimeter. This data does not coincide with the macroscopic analysis of the airway lumen, but it must be noted that it only reflects the determination of wall thickness, without taking the global deformation of the implant into account which partially re-tracts during tissue integration, thus reducing its diameter.

Table 3. Specific diameters in tissue samples. Thickness of normal tracheal wall (T), thickness of prosthesis and periprosthetic tissue (Prosthesis), difference between the two (Diff = Prosthesis - T). Reduction in diameter (Diff x 2) and degree of stenosis considering a normal diameter of 6 mm.

	T (⌠m)	Prosthesis (⌠m)	Diff. (⌠m)	Reduct. diam (mm)	Degree of stenosis
R3	235	630	395	0.79	Slight
R6	230	680	450	0.9	Slight
R7	200	601	401	0.8	Slight
R8	286	677	391	0.78	Slight
R9	281	693	412	0.82	Slight
R10	375	866	491	0.98	Slight
R12	201	639	438	0.87	Slight
R13	224	628	404	0.8	Slight
R15	-	-	-	-	-
R16	314	920	606	1.21	Slight
R17	241	701	460	0.92	Slight
R18	-	-	-	-	-
R19	397	706	309	0.62	Slight
R21	270	689	419	0.84	Slight
R22	239	674	435	0.87	Slight
R23	358	962	604	1.2	Slight
R24	436	1007	571	1.14	Slight
R25	-	-	-	-	-

DISCUSSION

With respect to the purely technical aspects of the surgical technique, the intervention was performed very similarly to how tracheal resections are done in humans with the difference that, instead of using a termino-terminal anastomosis after the resection, a synthetic prosthesis was inserted. This surgical technique can be done without major problems in these experimental animals and the methodology is easily reproduced.

Five animals died during the surgical intervention or in the minutes immediately follow-ing. The cause of death could not be determined for two of them. Nevertheless, the pink bubbles observed in the trachea in the other three cases are compatible with the devel-opment of pulmonary edema which is, in some cases, related to the use of anesthetics or to the stress caused by surgery. Four of the deaths occurred in the first 5 animals in the study, thus the high initial mortality rate can be directly attributed to the learning curves both for the surgical and anesthetic techniques.

In spite of the close follow-up the animals received, seven died unexpectedly and, upon collecting samples, three were too deteriorated to be able to complete reliable studies. After reviewing the process, the only plausible cause for the loss of samples is malfunc-tion in the refrigeration system used to store the bodies. Examining the airway of the other four animals, we observed that three of them showed significant stenosis (above 30%) and, nevertheless, there were no signs of stress that pointed to a specific problem. The absence of symptoms was likely due to the very low level of physical activity in the housed animals. In future studies conducted under similar conditions, it will probably be necessary to add an imaging technique or endoscopic study for postoperative follow-up.

One of the animals (R8) was sacrificed before originally planned after noting signs of stress (immobility, lack of eating and stridor). However, the examination of the airway did not show stenosis or other local problems which justified the clinical presentation. Just as there are learning curves for the anesthetic and surgical techniques, it is necessary to become familiar with the clinical expressions of the postoperative period in order to correctly interpret them.

The high mortality rate observed, attributed to the previously mentioned causes, makes the direct move to clinical practice unthinkable. However, a large part of the conditions that led to the death of the experimental animals were controllable or avoidable, which facilitates future research in this field.

No postoperative technical complications like dehiscence or granulomas were observed in the macroscopic examination of the samples collected after the animals were sacri-ficed. A good degree of prosthesis adhesion to the cervical tissue was observed. There was no apparent infection or collection of periprosthetic liquid.

The airway lumen maintained a good diameter in animals in which 5 mm of airway were substituted (groups 1 and 3), with an average residual lumen of 85% in the 45-day group and 78.7% in the 90-day group. When substituting 10 mm, the residual lumen percentage decreases strikingly to 67 in group 2. Stenosis is exacerbated when the pros-thesis is kept in longer, with a lumen of 39% in group 4. This may explain why this group had more unexpected deaths.

Although a small number of animals has been used, there seems to be a clear relationship between the length of airway substituted and the final airway lumen in such a way that the longer the substituted section, the lower the final diameter of the trachea. The length of time also seems to influence the appearance of a higher degree of stenosis, with the tracheal lumen being smaller in the groups which maintained the prosthesis for 90 days compared to the 45-day groups. This temporal effect is likely due to the histological changes with the appearance of fibrosis and the retraction of the prosthesis.

Thus, the substitution of short airway segments with synthetic prostheses seems to be safer and obtain better results with regard to final diameter. This is not the case for long segments, in which significant stenosis occurred.

In the histological examination, the time frames established for animal sacrifice were shown to correspond fairly well to the healing stages. Thus, the animals sacrificed less than 45 days after intervention showed clear inflammatory signs, those sacrificed at 45 days predominantly showed granulation tissue and for those sacrificed at 90 days, the most notable tissue was fibrous scar tissue. However, for the various reasons explained, there was a large loss of samples, which significantly limited the final number per group, so findings need to be confirmed by increasing the number of animals included in the study.

There are several publications in the literature that support the hypothesis that the pres-ence of fibrosis acts as a base for the later growth of functioning respiratory epithe-lium[15-19]. Nevertheless, the appearance of respiratory epithelium over fibrous tissue formed inside the prosthesis was not observed in any of the animals.

Studying the variation in diameter with optical microscopy, it is striking that the reduc-tion attributable to the increase in wall thickness caused by the prosthesis and the peri-prosthetic tissue was about one millimeter in each case. Assuming an airway to be 6 mm, this means only a 16.7% reduction, which does not correlate with the macroscopic findings. This is due to the fact that only a longitudinal section of the tracheal wall was available rather than the specific circumference. As a result, structural changes to the prosthesis which have been widely observed in other types of implants[20, 21] were not taken into account, such as those caused by wall collapse due to less consistency than the airway and the contraction or retraction of the synthetic material. The set of these three conditions (fibrosis, structural collapse and retraction) is what causes the macros-copically-observed stenosis. However, the results of the microscopic examination are very encouraging as the stenosis caused by tissue reaction to the prosthetic material is minimal.

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