Orthotopic Laryngeal Transplantation: Is it Time?

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The notion of returning phonatory and respiratory function by transplanting larynges has fascinated and challenged the minds of laryngologists for many years. In the past, the problems of revascularization, tissue rejection, and physiologic vocal fold motion have stymied the success of research in this area. Today, advances in microvascular surgery, graft versus host response, and selective reinnervation have made laryngeal transplantation a theoretical, if not a practical reality. Despite this progress, serious ethical and fiscal considerations remain unresolved. This report will discuss these advances as well as concerns and will present the current UCLA laryngeal physiology laboratory experience with canine laryngeal transplantation.

INTRODUCTION

Possibly because the larynx has not been thought of as essential for life, progress in laryngeal transplantation has lagged behind that of other organs. The need for this treatment, however, was realized by Lahey who, in the late 1920s, described a patient with bilateral vocal cord paralysis and a nonfunctional larynx.[1] In addition to the replacement for end stage laryngeal injuries, many laryngeal malignancies could be optimally managed with laryngeal transplantation. Even with the increasing use of conservation laryngeal surgery, the problems of reestablishing functional respiration, airway protection, serviceable phonation, and a positive patient self-image may lend themselves to improvement with transplantation.

There are four criteria that must be fulfilled prior to human laryngeal transplantation. These are successful revascularization, functional reinnervation, prevention of rejection, and ethical considerations.

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Canine laryngeal transplantation was pioneered by Ogura,[2,3] Silver,[4,5] and others in the late 1960s[6,7] and early 1970s.[8–10] In 1966, Ogura, *et al.*[11] identified the canine laryngeal vascular anatomy and found that the major vascular supply was from the cranial-thyroid artery, a branch of the common carotid. They reported survival of several reimplanted canine larynges using a C-type vascular anastomosis in which one cranial thyroid artery was preserved with the segment of common carotid from which it arises. The venous drainage was maintained by preserving the entire hyoid venous arch with its attachments to the external jugular veins and reattaching them to the recipient external jugular veins. With this technique, 50% to 60% of normal arterial flow into the grafted larynx can be reestablished, providing for viability. This optimal blood supply was confirmed by the reimplantation and transplantation studies of Silver, *et al.*[5] and Work and Boles.[12] It was also found from their work that the maximal time of ischemia should not exceed 45 minutes to ensure viability and prevention of ischemic necrosis in the reimplanted larynx. With modern microsurgical techniques, the human superior thyroid artery, which supplies approximately 80% of the blood supply to the larynx, could be used to supply adequate vascular supply.

Attempts at reinnervating paralyzed, reimplanted, or transplanted larynges have been numerous. Silver, *et al.*,[13] in an attempt to restore an adequate airway and protection from aspiration in a paralyzed canine larynx without motor reinnervation, reported some success with sensory innervation and arytenoidectomy. Many unsuccessful reinnervation studies using primary recurrent laryngeal nerve (RLN) anastomosis have been performed. Siribodhi, *et al.*[14] observed electromyographic (EMG) activity in nonfunctioning intrinsic laryngeal muscles after RLN reanastomosis. Problems accounting for this phenomenon include the following: misdirection of regenerating axons, which may lead to synkinesis; reduction of the number of motor units secondary to failure of regrowth of axons to pass through the anastomotic segment; and neuroma formation. Laryngeal synkinesis will result when generalized axonal regrowth nonspecifically reinnervates both the adductor and abductor intrinsic musculature. When electri-

cally stimulated, the overall result will be adduction since the adductor group represents the bulk of the intrinsic muscles. A number of authors have also performed ansa cervicalis to RLN stump transfer without physiologic vocal cord motion.[15] This method does, however, provide for maintenance of bulk, intrinsic stiffness, and tone of the reinnervated cord. In an effort to achieve abduction, Murakami and Kirchner[16] reported some success by sectioning the adductor branch after direct anastomosis of RLN. Fex,[17] Taggart,[18] and Doyle, *et al.*[19] have also obtained physiologic abduction by using other motor nerves such as the ansa, phrenic, and vagus directly anastomosed to the posterior (abductor) branch of RLN. Others have reported the PCA branch to be too short and friable for primary anastomosis.[20]

Authors have tried selectively reinnervating both adductor and abductor muscles simultaneously. Iwamura[21] longitudinally split the ipsilateral vagus nerve and sutured one part to the adductor branch and the other to the abductor branch. He reported good adduction and marginal abduction using this technique. Crumley's work,[22,23] using what he termed as physiologically appropriate nerves, achieved separate reinnervation of the intralaryngeal abductors and adductors by direct anastomosis of the phrenic to the posterior branch and by direct anastomosis of either the proximal RLN, the external branch of superior laryngeal nerve (SLN), or the ansa hypoglossi to the adductor branch. Marie, *et al.*,[24] in a similar study of seven dogs, attempted reinnervation using the phrenic to the abductor branch and the ansa to the adductor branch. Their results were less optimistic than Crumley's, since they achieved physiologic motion in only one animal. In addition to less than optimal restoration of physiologic motion, other problems in using these techniques include lengthy delay in functional return and possibly loss of function to other organs.

The nerve-muscle pedicle (NMP) technique used for reinnervation of reimplanted larynges was introduced by Tucker.[25,26] Studies performed by Anonsen, *et al.*[27] and then later by Miehlke, *et al.*[28] confirmed the presence of muscle reinnervation using NMP technique by EMG activity, evoked EMG, direct stimulation with muscle contraction, and horseradish peroxidase uptake.

Tucker[25,29–31] described harvesting the terminal anterior division of RLN along with a large block of muscle, approximately 2 to 3 mm thick, via a thyrotomy approach. He claimed return of synchronous, voluntary vocal cord function that was indistinguishable from normal controls within 2 weeks after surgery. This technique was later modified by using ansa cervicalis to sternothyroid NMP implanted into the posterior cricoarytenoid (PCA) in reimplanted canine larynges. With this technique, he reported appropriate abduction of the reinnervated cord in approximately 50% of subjects. Several other authors, however, have repeated this technique of PCA reinnervation with ansa cervicalis NMP only to find poor and inconsistent evidence of reinnervation leading to physiologic abduction. In an attempt to improve on Tucker's results, Broniatowski, *et al.*[32] used an implanted laryngeal pacemaker in six dogs to directly stimulate an ansa cervicalis NMP which had been implanted into the PCA. All animals demonstrated abduction with inspiration. There is, however, as yet no conclusive evidence that ansa cervicalis NMP to PCA can generate physiologic motion. Recent preliminary results in our laboratory revealed restoration of physiologic motion by reinnervation using a technique of intralaryngeal dissection with direct nerve-nerve anastomosis of the anterior branch and a PCA NMP implantation. This technique[33] set the tone for achieving physiologic motion in canine laryngeal allografts.

Prior to human laryngeal transplantation, an immunosuppression protocol should provide for suppression of graft rejection and at the same time be of acceptable risk to the patient. The benefits of laryngeal transplantation must outweigh the risk of rejection and the danger of immunosuppression in a non–life-threatening situation. Ogura, in his early studies of canine laryngeal transplantation, did not obtain acceptable graft survival rates using azathioprine and corticosteroids for immunosuppression. The longest survivor in his study survived for 49 days until dying of overwhelming sepsis. It is unclear from these early experiments as to what extent immunosuppression versus histocompatability matching contributed to the prolonged survival in this animal. Silver, also using azathioprine, confirmed the poor survival rates seen by Ogura in laryngeal allografts as compared to other organs. Subsequent studies using antilymphocyte serum (ALS)[34,35] were fraught with technical difficulties and did not increase the graft survival rate.

Many new and more effective immunomodulation agents have contributed to protection of graft rejection.[36–42] The introduction of cyclosporine in 1972 led to significant improvement in immune suppression, especially when used in conjunction with low doses of corticosteroids and azathioprine. Cyclosporine's impact as an immunotherapeutic agent is attributable to its selective inhibitory action of T lymphocyte activation and proliferation and its lower incidence of major myelosuppressive side effects. However, the problem of developing recurrent malignancy with immune suppression remains. Kluyskens and Ringoir,[43] in 1969, transplanted a 40-year-old cadaveric larynx into a 60-year-old man whose larynx was removed for malignant disease. Using prednisone, azathioprine, actinomycine, and ALS, the patient survived for approximately 8 months until succumbing to recurrent cancer at the stomal site. With newer immunosuppressant medications and other adjunctive therapeutic modalities, selective immunosuppression directed to protection of the allograft while sparing the host's

generalized immunocompetency is likely to become a reality in the near future.

While the UCLA laryngeal laboratory was developed to study basic and clinically applied issues pertaining to laryngeal biomechanics, it became apparent that the facility was also well-suited to undertake a program to assess the revascularization, reinnervation, and physiologic function of orthotopic canine laryngeal transplants. This report represents our initial experience in this regard.

MATERIALS AND METHODS

Experimental Design

Five pairs of litter mate beagles, each from 8 months to 1½ years of age and weighing 12 to 14 kg were used. Their excellent state of health was assured in every instance by a comprehensive veterinary and laboratory examination. An observation period of 10 days to 3 weeks was allowed for each pair in order to assess the more vigorous and well-mannered animal to use as the recipient. Mixed leukocyte cultures (MLC) were performed in transplants 4 and 5 to assess the major histocompatibility reactivity at the DLA-D region.

At approximately 3 months posttransplantation, the viability and function of each grafted larynx was assessed and documented by videolaryngoscopy, videostroboscopy, and electromyography recordings during spontaneous respirations, with mechanical pharyngeal stimulation, with tracheostomy tube occlusion, and with recurrent laryngeal nerve stimulation. In addition, measurements of vocal efficiency were performed using our in vivo canine model as described in previous studies from our laboratory.[44,45] Each grafted larynx was then harvested and tissue samples were taken of each cricothyroid, thyroarytenoid, and posterior cricoarytenoid muscle and each nerve anastomosis.

Immunosuppression

Each animal (donor and recipient) received an intramuscular (IM) injection of methylprednisolone (Solumedrol®) 250 mg the evening prior to surgery. In addition, the recipient also received an oral dose of cyclosporine (Sandimmune®) 15 mg/kg at that time. In the postoperative period, the recipient animal was immediately begun on azathioprine (Imuran®) 2 mg/kg IM injection and cyclosporine 3 to 5 mg/kg IM injection each morning. The Imuran dosage was modified accordingly for neutropenia. Serum cyclosporine levels were checked approximately 12 hours postdosage (trough values) by fluorescent polarization immunoassay, using the TDX™ monitor (Abbott Laboratories). The morning dosage was modified to maintain the trough values in the range of 300 to 500 ng/mL. When oral alimentation was begun, the cyclosporine was given orally at a dosage of 12 to 15 mg/kg per day in two divided doses, and the Imuran was given orally at a dosage of 2 mg/kg per day Qa.m. (every morning). Once the incision and stomas were well-healed, at approximately 5 to 7 days, oral administration of prednisone was begun at a dosage of 0.3 to 0.5 mg/kg per day. This protocol was modeled after successful immunosuppression regimens of the cardiac, liver, and kidney transplantation program at UCLA Medical Center.

Operative Procedure

Each canine subject was kept NPO (nothing by mouth) for 12 hours prior to transplantation. Preoperative sedation using an IM injection of 30 mg of acepromazine maleate (Promace™) was used. After intravenous access was obtained, the dogs were hydrated. Intravenous pentobarbital (Nembutal®) was administered to the level of corneal anesthesia and additional pentobarbital and inhalation anesthesia were used to maintain this level of anesthesia throughout the procedure. The animals were then placed supine on the operating table and close laryngeal inspection was performed to ensure normal anatomy. Endotracheal intubation was then performed. A wide cervical preparation with povidone-iodine solution (Betadine®) was performed and aseptic conditions were maintained throughout.

The procedure was begun with the donor animal. A midline incision extending from the hyoid bone to the sternal notch provided wide exposure. Dissection was carried out through the superficial fascia. The strap muscles were then carefully transected to provide exposure to the larynx. The hyoid venous arch was dissected bilaterally throughout its entire course to the external jugular veins. The cephalic tributaries to the venous arch were ligated. The internal and external branches of the superior laryngeal nerves (SLN) were then isolated, tagged, and transected just distal to the bifurcation. The common carotid artery and its cranial-thyroid artery were then dissected bilaterally. The recurrent laryngeal nerves were then identified low and followed superiorly. Intralaryngeal dissection was then performed to isolate the bifurcation of the anteior and posterior branches of the RLN. After the Hilger recurrent laryngeal nerve stimulator was used for confirmation, the anterior and posterior branches were individually transected just distal to the bifurcation. The larynx was then prepared for removal by transection of the suprahyoid musculature, the superior constrictors, and the cricopharyngeus muscles. Mucosal preserving hypopharyngeal incisions were used to allow for easy mucosal anastomosis in the recipient animal. The tracheal incision was performed at the 8th to 10th tracheal ring. The thyroid gland was preserved and maintained on the graft.

A laryngectomy was then performed on the recipient animal in a reciprocal fashion, again maintaining sterile conditions. Prophylactic antibiotics were used. The recipient bed was prepared by removing the larynx, including the midportion of the hyoid bone, while leaving the strap muscles, inferior pharyngeal constrictors, and cricopharyngeus muscles behind. The external jugular vein and the common carotid arteries were dissected. The external and internal branches of the SLNs were transected close to the larynx. Intralaryngeal dissection was again performed to isolate the anterior and posterior branches of the RLNs. The anterior branches were transected just proximal to the interarytenoid branch, and the posterior nerve muscle pedicles were harvested bilaterally. The trachea was transected at the sixth tracheal ring, and again hypopharyngeal-mucosal-sparing incisions were performed. Once the hyoid venous ligation and bilateral ligation of the cranial thyroid arteries were completed, the larynx was removed from the recipient bed. The thyroid gland was preserved.

The donor larynx was then removed by first clamping and transecting the common carotid arteries above and below the cranial-thyroid branch bilaterally. The external jugular veins were transected distal to the hyoid venous tributary. The donor larynx was then placed in the already prepared recipient bed. The arterial supply was rees-

tablished by a unilateral common carotid end-to-end anastomosis proximal to the cranial-thyroid branch. Ischemic time was limited to 30 minutes. Bilateral end-to-end external jugular venous anastomoses were performed. In transplants 1, 2, and 3, end-to-end suturing of the external branch of the superior laryngeal nerve was performed while, in transplants 4 and 5, both the external and internal branches were used. Anterior branch to anterior branch of the RLN anastomosis was performed in all animals. In all cases except one, a recipient posterior RLN NMP using approximately 3 × 2 mm of PCA muscle was implanted in the graft PCA muscle bilaterally. In one animal (transplant 4), the right posterior branch was large enough to allow for a direct posterior nerve to posterior nerve anastomosis.

The mucosa was closed in two layers, and the strap, inferior constrictors, and cricopharyngeus muscles were approximated. The skin was closed in two layers and bilateral Penrose drains were brought out of the wound by separate stab incisions. A double-barreled tracheostomy was fashioned, suturing the distal trachea of the graft and the breathing stoma of the recipient to the skin in a side-by-side manner. This allowed for direct subglottic mucosa examination during the postoperative period.

Postoperative Care

Each animal was kept NPO for 7 days, at which time a soft diet was advanced as tolerated. Meticulous attention to wound care, drain management, and hydration was performed. The graft subglottic mucosa was observed on a daily basis to assure viability. Prophylactic antibiotics were used.

Laryngeal Functional Assessment

At approximately 3 months posttransplant, the surviving dogs were studied. After premedication with acepromazine intramuscularly, light anesthesia was induced with intravenous Pentothal. Additional Pentothal was used to maintain this level of anesthesia throughout the experiment. An endotracheal tube was placed in the breathing stoma to allow for ventilator-assisted respiration. A 1-cm button was used to suspend the epiglottis from a fixed point to provide direct visualization of the larynx through the oral cavity.

Videolaryngoscopy

Videolaryngoscopy was performed under light anesthesia to detect the degree of spontaneous motion of the vocal cords during pharyngeal/laryngeal stimulation with a cotton swab. Under the same conditions, video images were again obtained during tracheal tube obstruction to detect movement during obstructive respiratory dyspnea. Following this, additional Pentothal was administered to a level of corneal anesthesia, and the larynx was again visualized during direct stimulation of the recurrent laryngeal nerves using Harvard miniature electrodes, which were applied to each nerve. Two constant current nerve stimulators (WR Medical Electronics Co., St. Paul, Minn.; Model S2LH) were used to stimulate the recurrent laryngeal nerves at a frequency of 70 Hz with a 0.5- to 2-mA intensity for a 1.5-msec duration. The image was recorded by a Jef-Med CCD (change-coupled device) video camera (Model 70-5110) and a Sony U-Matic Videocassette recorder (VO-5850).

Electromyography

Conventional spontaneous EMG recordings were made during light anesthesia to detect reinnervation potentials in the cricothyroid, thyroarytenoid, and posterior cricoarytenoid muscles during respiratory dyspnea and pharyngeal mechanical stimulation.[20] The response was detected with a bipolar needle placed transorally directly into these respective muscles. Evoked EMGs were then performed on each muscle by single-pulse recurrent laryngeal nerve stimulation as described previously.[20]

In Vivo Phonation Model

The animals were then phonated by passing a cuffed endotracheal tube rostrally in the graft trachea and positioned with the tip approximately 10 cm below the vocal fold. The cuff was then inflated to seal the trachea. Humidified heated air was then passed through this rostral endotracheal tube from a compressed air tank. Flow was controlled with a valve and measured with a Gilmont flowmeter. The airflow was humidified and heated by bubbling it through 5 cm of heated water, so that the temperature of the air was 37°C when measured at the glottic outlet. An airflow of 388 mL per second was applied through the larynx in this manner. Subglottic pressure was measured using a Millar Mikro-tip catheter pressure transducer (Model SPC-330, size 3F) passed rostrally through the graft trachea. It was placed 5 cm below the glottis. The signals were low-pass filtered at 3 kHz, digitized at 20 kHz, and stored in a personal computer. The pressure transducer was calibrated before each experiment against a mercury manometer. With direct recurrent laryngeal nerve stimulation as described previously,[20] videostroboscopic images were obtained during phonation. A Bruel and Kjaer laryngostrobe unit (Model 4914) was used. The stroboscope connected to a Storz 0° telescope via a fluid-filled light cable. The video images were analyzed frame by frame using the video recording unit. Vocal efficiency measurements were calculated for each canine as the ratio of the acoustic power of the voice to the subglottic power. The vocal efficiency calculations were performed as previously described from this laboratory.[20]

Histology

The transplanted larynges were harvested at the end of each experiment. Muscle samples from each cricothyroid, thyroarytenoid, and posterior cricoarytenoid were then removed and prepared by liquid nitrogen freezing. Special staining for alkaline phosphatase, adenosine triphosphatase (ATPase), and mitochondria was performed. Nerve sections from each anastomotic area were also isolated and fixed in 4% paraformaldehyde and 4% glutaraldehyde for electron microscopy. The histologic analysis will be reported in a subsequent paper.

RESULTS

As of April 1992, five animals had undergone transplantation in our laboratory. The second animal experienced a graft failure secondary to kinking of the venous outflow due to improper tracheostomy placement. The fourth animal on the seventh postoperative day died of either a pulmonary mucous plug or cerebrovascular accident. The fifth animal is currently 2 weeks out from laryngeal transplantation and is doing well. Data were taken from the first and third animals, which were harvested at 13 and 14 weeks

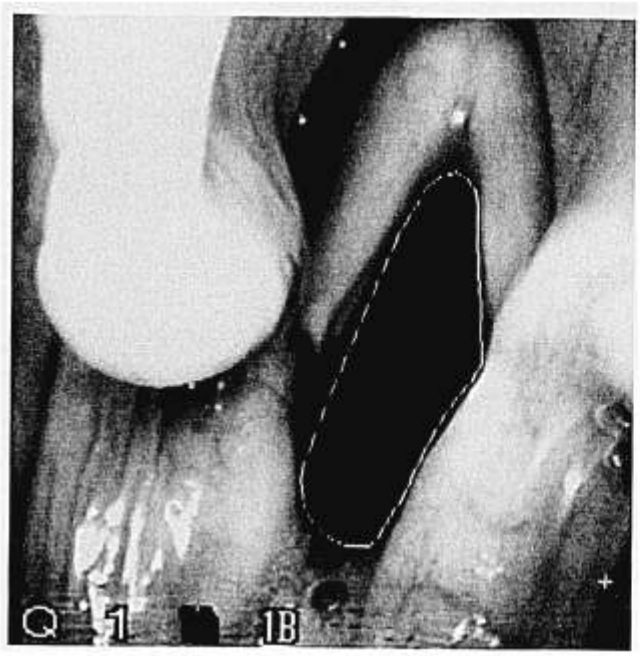

Fig. 1. Resting respiratory position of the larynx 3 months posttransplantation. Highlighted area represents pixel area of glottis.

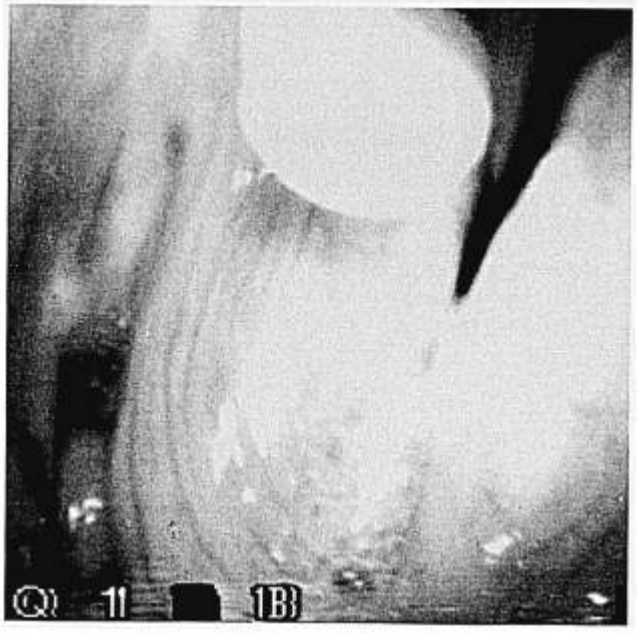

Fig. 2. Laryngeal adduction with pharyngeal stimulation.

postsurgery, respectively. Figure 1 is a digitized video image of the abducted respiratory position of the larynx posttransplant in an anesthetized animal. In both animals, the laryngeal mucosa appeared pink and healthy; the first animal had normal-appearing vocal folds except for a very small anterior web, which can be seen in Figure 1. The second animal experienced some atrophy of the right thyroarytenoid muscle. Figure 2 shows the appearance of the larynx during pharyngeal stimulation to produce a swallow. As demonstrated by the figure, the animal had good

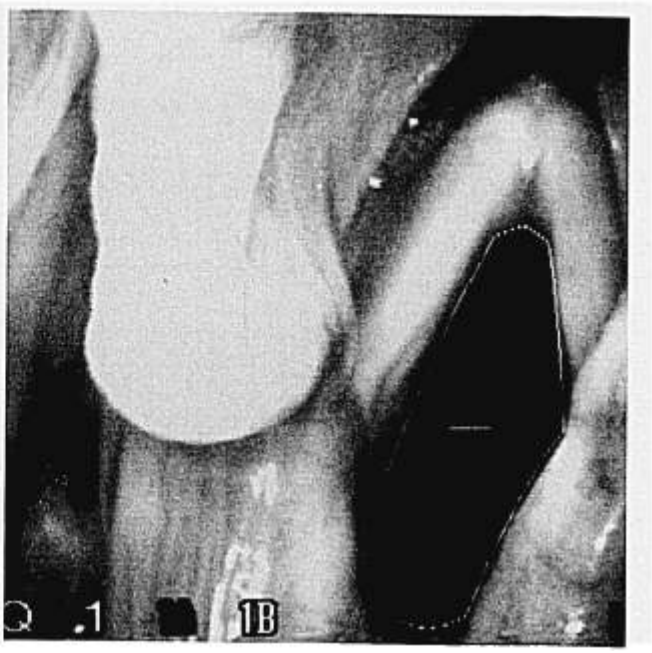

Fig. 3. Glottal dilatation with temporary tube occlusion. Highlighted area represents pixel area of glottis.

physiologic control over vocal fold adduction.

Conversely, temporary tube occlusion produced glottal dilatation as seen in Figure 3. During temporary tracheal tube occlusion, the animal was able to dilate the glottis from a resting pixel ratio as seen in Figure 1 of 19,187 pixels to 24,606 pixels as seen in Figure 3. Figures 4 and 5 are EMG recordings from the left posterior cricoarytenoid muscle for dogs 1 and 3, respectively, during tube occlusion. In both instances, dilation of the glottis was associated with an increase in EMG activity correlating with glottal dilatation as depicted in the upper part of the figures. Individual motor units, seen in the lower part of the figures, were consistent with polyphasic reinnervation potentials. Figure 6 is a representative EMG from the left thyroarytenoid of the first animal during spontaneous breathing. Again, the individual motor units are consistent with polyphasic action potentials. Figure 7 is the glottal configuration during bilateral electrical stimulation of the recurrent laryngeal nerves. This produced adduction of the vocal folds. Insufflation of air rostrally through the vocal folds during electrical stimulation produced phonation. Videostroboscopic and acoustic analysis demonstrated bilaterally symmetric traveling wave motion in animal 1 and a vocal efficiency of 2.5×10^{-4}. This level of vocal efficiency is normal for electrically induced canine phonation in our laboratory.[20] Although animal 3 showed adduction of vocal fold on electrical stimulation, symmetric traveling wave motion could not be elicited due to atrophy of the right thyroarytenoid muscle in this animal. Induced phonation, however, was achieved and a vocal efficiency of 2.5×10^{-5} was obtained.

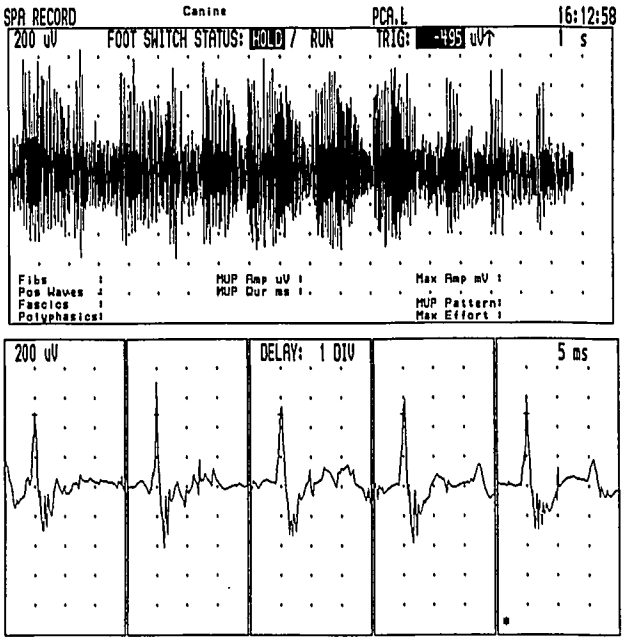

Fig. 4. Electromyographic recording from the left posterior cricoarytenoid muscle during temporary tube occlusion in animal 1. Lower portion of figure demonstrates polyphasic reinnervation potentials.

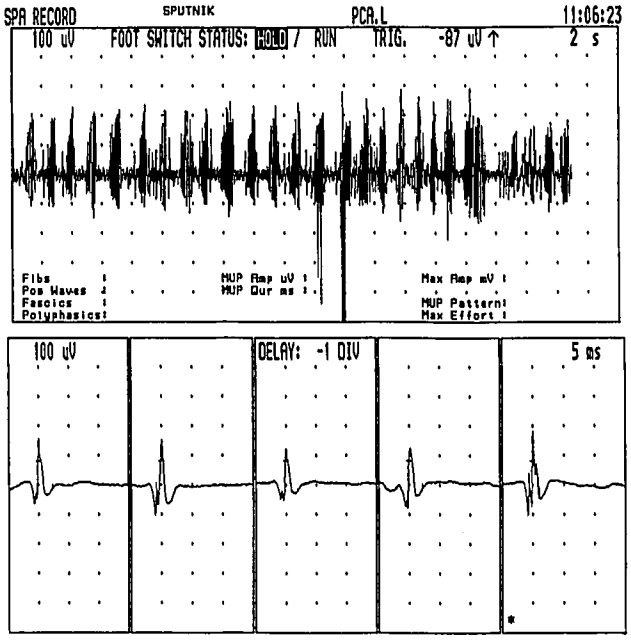

Fig. 5. Electromyographic recording from left posterior cricoarytenoid muscle in animal 3 during temporary tube occlusion. Lower part of figure demonstrates polyphasic reinnervation potentials.

DISCUSSION

Results from this study have shown that canine laryngeal allografts can be physiologically reinnervated. Furthermore, transplanted larynges can remain viable with intact fold cover and body. Moreover, laryngeal transplanted animals can resume normal swallowing and airway protection despite total laryngeal deafferentation.

This study has demonstrated the orthotopic potential of the canine larynx; however, a number of critical issues remain prior to considering clinical application. Since the largest use for laryngeal transplants would be for those patients with T3 and T4 carcinomas, several concerns are specifically related to this patient group.

How safe would harvesting of intralaryngeal nerve branches and/or nerve muscle pedicles be in patients with laryngeal carcinoma? In this regard, patients with postcricoid, inferior extension and thyroid cartilage invasion would be the poorest candidates. Unfortunately, these are probably those patients who would otherwise certainly require total laryngectomies. In addition to anatomical constraints, generalized immunosuppression would also play a factor. It is well-accepted that the degree of immune competence plays a major role in cancer surveillance, development, and eradication. High levels of generalized immunosuppression would have a negative effect on a patient's immune fighting abilities. However, the immunogenicity of the larynx is virtually unknown. In this study, immunosuppression was used at levels required for much larger solid organs (kidney, liver). What levels of immunosuppression are actually required remains to be determined. Dr. Strome's[46] research should help to provide answers to this question. Furthermore, as modification of immune function advances, selective immunosuppression should become a reality.

Even with improvements in immunosuppression, it is quite possible that a small increased risk of cancer recurrence will remain for patients with laryngeal transplants. What level of increased risk would be acceptable? The analogous situation is one in which the advantages of partial laryngeal surgery, in appropriate patients, outweighs the small increased recurrence rate relative to total laryngectomy.

However, many see the situation as more black and white, putting forth the argument that the larynx is a nonessential organ for life and therefore little impetus exists for laryngeal transplantation. Is it presumptuous to assume that normal physiologic functions of smell, taste, respiration through the nasopharynx, normal phonation, and ability to swim are nonessential life functions? Even opponents of laryngeal transplantation admit that most but not all patients who undergo total laryngectomy experience tremendous lifestyle changes. While speaking fistulas have improved the situation, most total laryngectomies fall out of the work force and withdraw to sedentary and nonproductive lifestyles. Furthermore, it is possible to draw an analogy between the logic underlying the use of renal transplantation and laryngeal transplants. Many patients can be managed for years with dialysis, however, the deleterious ef-

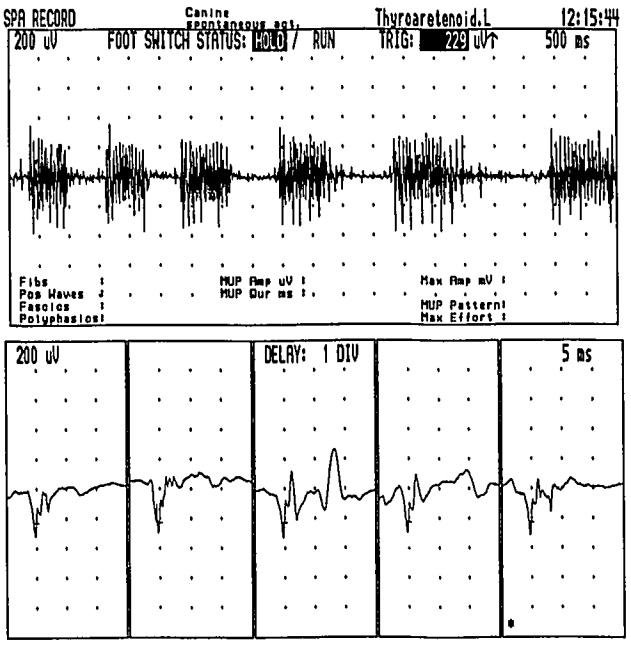

Fig. 6. Electromyographic recording from left thyroarytenoid muscle in animal 1 during spontaneous breathing. Lower part of figure demonstrates polyphasic reinnervation potentials.

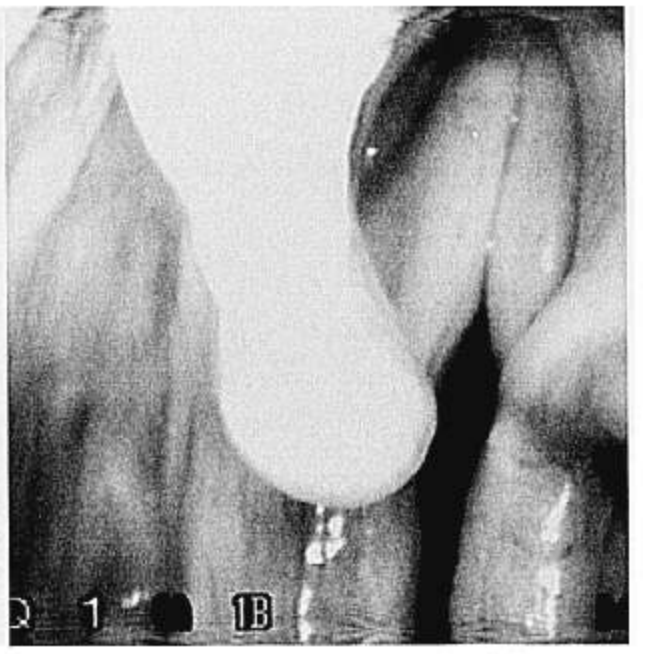

Fig. 7. Glottal configuration during bilateral electrical stimulation of the recurrent laryngeal nerves.

fects on lifestyle and eventual deterioration in health makes transplantation a better option despite the lifelong requirement for immunosuppression. Similarly, the constant risks of pulmonary infection, mucous plugging, foreign body inhalation, and drowning, along with the need to carry suction machines and humidification devices, may make transplantation an effective option.

Notwithstanding the use of laryngeal transplantation in patients with carcinoma, there are also a number of patients who have, through severe trauma, lost the physiologic function of the larynx. These patients frequently undergo as many as 100 repeat surgeries trying to regain an airway and some semblance of voice. In comparison to the enormous expense incurred by these patients, a single definitive laryngeal transplant could be a cost-effective option even when factoring in the cost for immunosuppression. In these times of severe economic pressures on the medical profession, what would be the cost of laryngeal transplantation? The procedure itself, when compared to total laryngectomy, would be more expensive due to the increased surgical time. The harvesting, tissue typing, and registry of transplantable larynges would add additional expense. The hospital stay should be comparable to that of total laryngectomy patients. The present-day expense of immunosuppression is significant, but it eventually should come down as newer generation drugs emerge.

Can human larynges be successfully transplanted? This report suggests that they could. Is it time for human laryngeal transplantation? The answer is unequivocally no at this point in time. Additional research is required to understand the immunogenicity and functional capabilities of transplanted larynges. Whether laryngeal transplants become a clinical reality may boil down to the philosophical question of whether the goal of medical science is simply to cure illness at all costs or if it is also meant to improve the quality of life of patients during their lifetime. Few would argue that, ultimately, laryngologists should strive for fabrication of a neolarynx from autologous tissue. Until then, the notion of laryngeal organ transfer holds the best promise for preserving the quality of life in patients who have lost laryngeal function.

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