

# Functional Electrical Stimulation of the Feline Larynx With a Flexible Ribbon Electrode Array

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## Abstract

**Objectives:** Success of laryngeal reanimation through neurotomy has been limited by synkinesis and preoperative muscle atrophy. The objective of this study was to investigate the use of epimysial electrode arrays as a means of delivering electrical stimulation to the posterior cricoarytenoid muscles in order to control laryngeal abduction.

**Methods:** Ribbon electrode arrays with 4 or 8 electrode contacts were used. Four cats underwent implantation of electrode arrays along the surface of the posterior cricoarytenoid muscles. The glottis was visualized with a 0° telescope while electrodes were stimulated at different amplitudes and pulse-width durations. Recordings of stimulated vocal folds were analyzed, and the degree of vocal fold abduction was measured in order to create recruitment curves for the left and right posterior cricoarytenoid. Recruitment curves from electrode channels within the array were compared.

**Results:** Electrodes oriented along the medial aspect of the posterior cricoarytenoid stimulated graded physiologic degrees of abduction depending on the amplitude of stimulation. Electrodes oriented laterally along the posterior cricoarytenoid stimulated greater degrees of simultaneous adduction with abduction.

**Conclusion:** Acute studies of ribbon surface electrode arrays placed onto the posterior cricoarytenoid reproduce graded degrees of abduction necessary for the precise function of respiration and speech.

## Keywords

larynx, electrodes, implanted, muscles

## Introduction

Vocal fold paralysis is a disorder that can affect people of all ages. While unilateral paralysis is more common than bilateral paralysis in adults, there is conflicting evidence regarding the proportion of unilateral to bilateral paralysis in the pediatric population.<sup>1,2</sup> The overall incidence of vocal fold paralysis is unknown.<sup>3</sup> Causes include surgical trauma, neoplasm, central nervous system disorders, and complications of intubation. After a thorough workup, up to 33% of cases remain idiopathic. Complete vocal fold paralysis is the extreme manifestation of a spectrum of vocal fold dysfunction, ranging from transient unilateral paresis to permanent bilateral paralysis. Symptoms of unilateral paralysis in adults are a weak, breathy voice and voice fatigue. Unilateral paralysis in infants may result in an absent or weak cry. Bilateral vocal fold paralysis may cause stridor and respiratory distress in adults and children. Upon initial diagnosis of vocal fold paresis or paralysis, a period of observation is often indicated prior to definitive treatment, as up to 55% of children will recover spontaneously and 26% to 72% of adults recover spontaneously.<sup>1,4</sup>

There is currently no method to restore normal physiologic vocal fold motion for coordination of breathing, voice, and airway protection in vocal fold paralysis. In bilateral vocal fold paralysis, the problem can become life threatening due to risk of aspiration pneumonia and respiratory compromise. In severe cases of bilateral vocal fold paralysis, current definitive treatment is tracheostomy.

With less than optimal results from all available treatment options, a variety of experimental procedures are currently being investigated to attempt to restore physiologic function by nerve transfer in patients with vocal fold paralysis. These

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include phrenic nerve-recurrent laryngeal nerve reinnervation and procedures that create a direct anastomosis to the posterior cricoarytenoid branch of the recurrent laryngeal nerve.<sup>5</sup> Utilization of neuroprosthetic devices for functional electrical stimulation is another possible treatment option that merits further research.

In the larynx, patch electrode arrays implanted in the canine posterior cricoarytenoid muscle were shown to inhibit synkinesis and promote preferential regeneration of intrinsic nerve fibers when the paralyzed muscle was chronically stimulated.<sup>6</sup> The patch electrode array described by Zeale et al<sup>7</sup> in 1994 resembles a bed of nails. Using a different electrode type, with a needle electrode placed in the posterior cricoarytenoid (PCA) muscle of an anesthetized human with vocal fold paralysis, these investigators were able to cause selective abduction of the vocal fold during inspiration. This was achieved with the use of a stimulator coupled to a transducer that sensed movement of the chest wall.<sup>8</sup> One complication found with implanted neuroprosthetic devices for laryngeal stimulation was a failure of electrodes.<sup>9</sup> This complication could be alleviated by use of an array of electrodes. If 1 electrode channel fails, a backup channel may be used instead.

Vagal nerve stimulators, which utilize whole-nerve cuff electrodes wrapped around the vagus nerve to prevent seizures, have well-documented detrimental effects on the voice. These neuroprostheses nonselectively stimulate the component fibers of the recurrent laryngeal nerve and produce noncoordinated movements of the vocal folds. Patients report symptoms of rough, strained, or breathy voice as well as breathing and swallowing problems.<sup>10</sup> This nonselective effect of superficial nerve stimulation highlights the importance of an array of electrodes that can selectively stimulate the targeted muscle without co-stimulation of surrounding muscles and nerves. To this end, Broniatowski et al<sup>11</sup> have shown that reinnervated muscles of the canine larynx can be selectively activated by stimulating the nerve fibers of implanted nerve-muscle pedicles. The electrodes used were single bipolar electrodes.<sup>11</sup> Similar stimulation has also been coupled to pacing devices in order to coordinate abduction with inspiration. Chi et al<sup>12</sup> demonstrated efficacy in a cat model of a pacing system that couples a respiratory transducer with an implanted electrode that stimulates the PCA. The electrode described in that research is a single stainless steel monopolar electrode.<sup>12</sup>

Surgical implantation of electrodes into the larynx remains a challenge. The delicate architecture of the PCA and surrounding structures means they are vulnerable to edema, which results in poorer functional outcomes. Forster et al<sup>13</sup> have attempted to prevent complications associated with insertion by developing a transcricoid hollow needle insertion tool. The electrodes they used were single bipolar electrodes. Relative electrode position on the PCA was compared to degree of simultaneous adductor activation,

and electrodes positioned medially on the PCA demonstrated less adductor response.<sup>13</sup> One possible remedy to the problem of activating adductors simultaneously with activation of the PCA is to place an epimysial array of electrodes that spans the area of both PCA muscles. The electrode channels can then be mapped to their respective adductor and abductor responses, and only the channels that yield an optimal abductor response with minimal or no adduction will be subsequently stimulated.

This study aims to demonstrate efficacy of an epimysial multielectrode arrays with 4 and 8 electrode contacts secured onto the PCA muscle along the back of the cricoid cartilage. This device works to preferentially stimulate vocal fold abduction to mimic physiologic movements of the vocal folds. The multi-channel design of the flexible ribbon electrode array enables selective stimulation of laryngeal abduction with the object to minimize simultaneous activation of adduction. An additional aim of this study was to investigate positioning of the electrode array contacts on the PCA in order to achieve maximal degrees of abduction.

## Materials and Methods

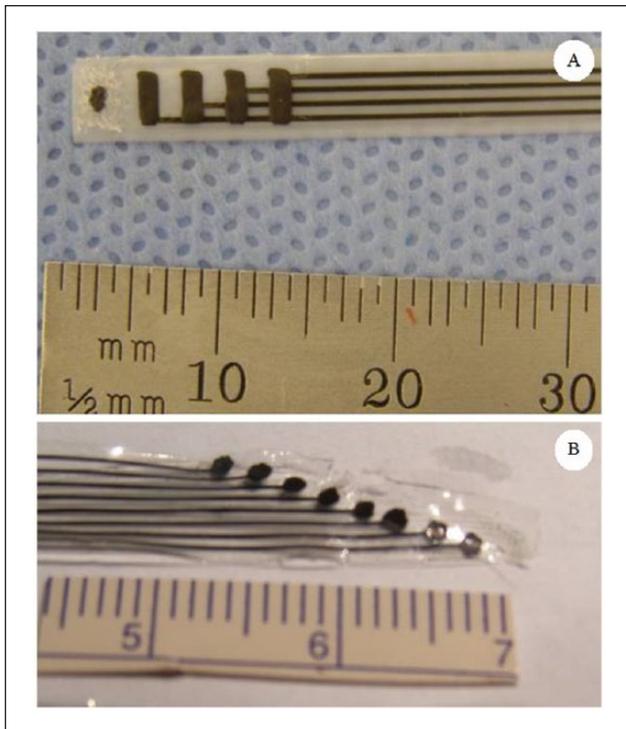
### Electrode arrays

The Ripple Ribbon electrode (Ripple LLC, Salt Lake City, Utah, USA) is a flexible multi-electrode array that can be custom designed to have varying numbers and locations of electrodes. The surface area of the array is 0.79 mm<sup>2</sup>. Multielectrode epimysial arrays designed and tested in this study included a 4-contact opaque array (Figure 1A; 2 mm spacing between contacts) and an 8-contact clear array (Figure 1B; 1.5 mm spacing between contacts).

The electrodes and interconnections are created by depositing polymers doped with electrically conductive particles and interposing these conductive traces between insulating layers of nonconductive polymers. An insulating polymer base layer is first deposited in the outline of the implant, using a high-resolution dispensing robot. Thin traces of polymer filled with conductive metal microparticles are dispensed onto the base to form the internal wiring of the device. Thick layers of the conductive polymer are then deposited to form the electrode areas. The base and conductive traces are finally over-coated with insulating polymer, with care not to cover the electrode areas. Implantable stimulation electrodes are made with platinum metal particles to produce efficient charge delivery using a biocompatible material.

### Surgical and experimental procedures

All studies were approved by the University of Utah Institutional Animal Care and Use Committee. Four adult male felines weighing approximately 6 kg each were used



**Figure 1.** (A) The 2 mm spacing between electrodes on array. (B) The 1.5 mm spacing between electrodes on array.

in this study. Anesthesia was induced with Telazol (9-12 mg/kg; IM) and maintained with isoflurane (0.25%-2.0%) for the duration of the experiments. Vital signs were monitored every 15 minutes in order to assure depth of anesthesia throughout the experiment.

Bilateral vocal cord function was confirmed preoperatively using laryngoscopy (Karl Storz Endoscopy-America, Inc, Charlton, Massachusetts, USA). The animals were then intubated orotracheally, and a tracheostomy was performed. Once the tracheostomy was secure, the oral endotracheal tube was removed in order for visualization of the vocal folds during the acute stimulation trials. A vertical incision was then made in the midline of the neck, the platysma reflected up and strap muscles retracted laterally, to expose the tracheoesophageal groove and identify the recurrent laryngeal nerve. Functional activity of the nerve was confirmed via stimulation with monopolar hook electrodes and simultaneous laryngoscopy. The inferior constrictor and cricopharyngeus muscles were first divided to expose the bilateral PCA muscles. The Ripple ribbon multielectrode array (RRMA) was surgically implanted into the inferolateral quadrant of the right PCA muscle and secured with 7-0 silk suture.

The grapevine neural interface system (Ripple LLC) was used to first perform a recruitment trial at a frequency of 30 Hz with 300  $\mu$ A to 700  $\mu$ A in 50  $\mu$ A steps and duration of 10 milliseconds. Many variations to the stimulation parameters

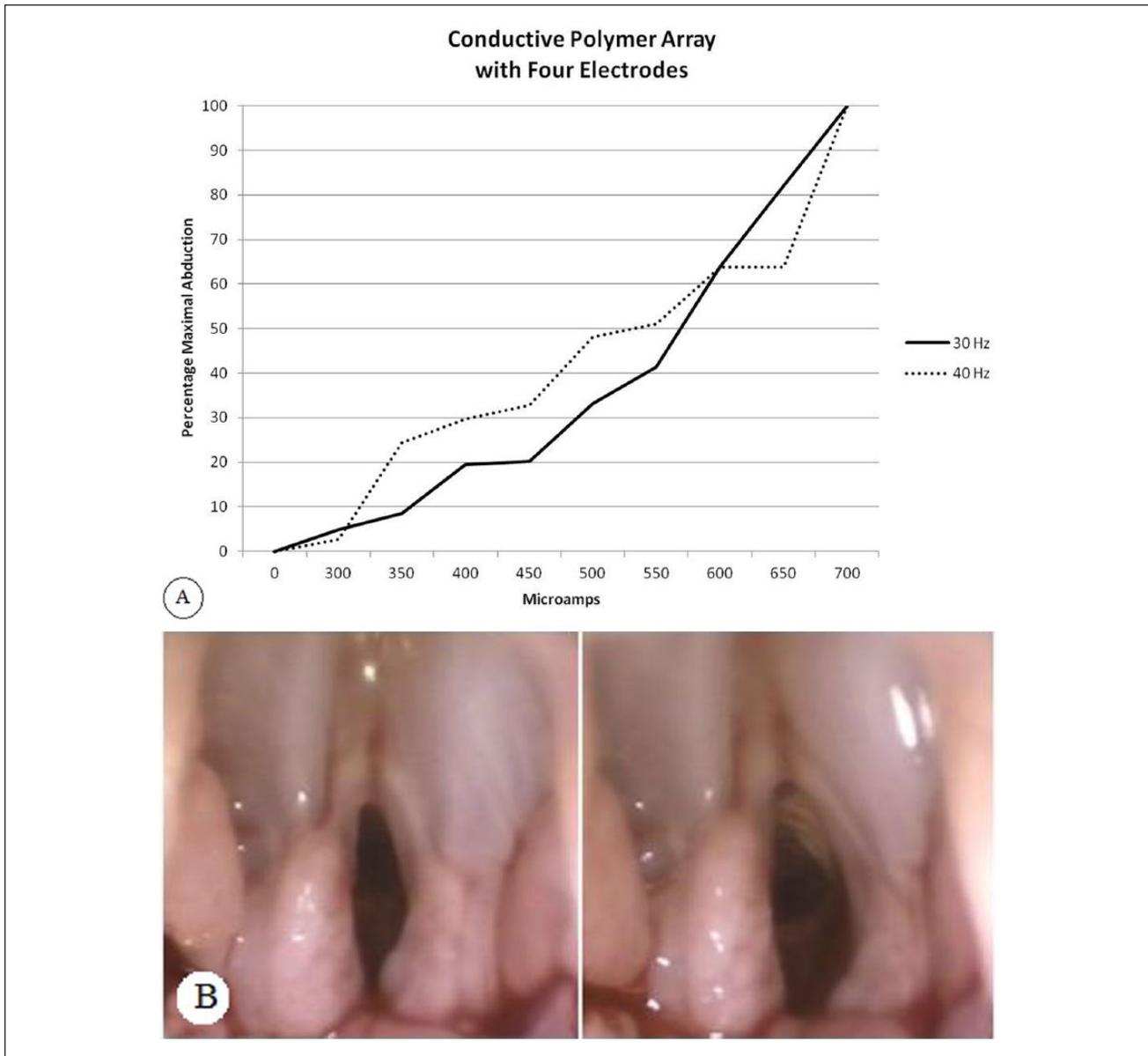
were investigated, as described in the results section in the following. Several different electrode configurations were investigated, and the degree of abduction of the vocal fold was measured and recorded using transoral laryngoscopy. Platinum wire electrodes were subsequently inserted into the muscle and stimulated for additional comparison. Digitized videos of each experiment were analyzed using ImageJ software.<sup>14</sup> The maximum abduction angle was measured as originally described by Dailey et al.<sup>15</sup> The degree of abduction at rest was compared to degree of abduction with stimulation at each experimental amplitude and voltage. Recruitment curves were then plotted for each experiment.

## Results

All cats underwent surgical implantation of electrode arrays without complication. All felines were easily implanted. Data from cats implanted with electrode arrays containing both 4 and 8 electrodes were collected. The electrode arrays containing 4 electrodes spaced 2 mm apart predictably yielded less data for mapping than the electrode arrays containing 8 electrodes spaced 1.5 mm apart. This can be seen by comparing the recruitment curves in Figure 2A to Figure 3A. Figure 2 depicts recruitment curves from an animal with a 4-electrode array, and Figure 3A depicts recruitment curves from an animal with an implanted 8-electrode array. When electrodes were spaced more widely apart, the laterally placed electrodes co-stimulated laryngeal adductors so that only the most medially positioned electrodes were useful on the array. Only 6 out of the 8 electrode contacts used actually touched the PCA muscle, which is why there are only 6 recruitment curves shown in Figure 3A. The 8-electrode array on the harvested cat larynx is shown in Figure 3B.

It was possible to achieve bilateral abduction from a single electrode on the array if it was placed in a medial position. This is also seen in Figure 3A. The black square boxes along the recruitment curves for electrode 3 and electrode 4 both mark the threshold at which bilateral vocal fold abduction was achieved by stimulating a single electrode. Electrode 3 and electrode 4 were located on the medial aspect of the left and right PCA, respectively. This made it possible to produce bilateral vocal fold abduction by either simultaneously stimulating 2 electrodes contacting the right and left PCA or by stimulating a single electrode positioned on the medial aspect of the PCA.

Stimulated electrodes located more laterally on the posterior cricoarytenoid produced simultaneous adduction as well as abduction when stimulated at higher currents. When this occurred, there was also a threshold at which the degree of abduction caused narrowing of the glottis. This is demonstrated in the recruitment curves in Figure 4. The curves shown are produced by a single laterally positioned



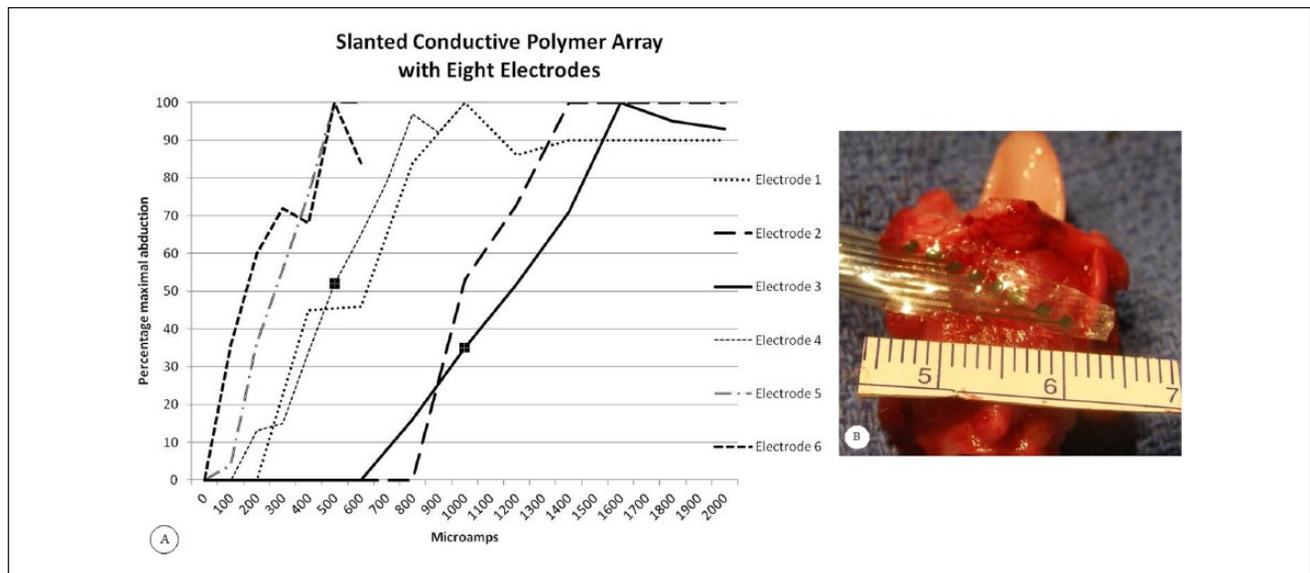
**Figure 2.** (A) This depicts recruitment curves from an electrode that is located medially on the right posterior cricoarytenoid. This experiment was performed with an array containing 4 electrode channels, each spaced about 2 mm apart. Only 1 out of 4 channels on the implanted electrode array activated specific vocal fold abduction. Right abduction is seen. Similar degrees of abduction are seen with this electrode at both 30 Hz and 40 Hz. (B) (Left) Larynx at rest. (Right) Two electrodes of the 4 electrode conductive polymer array are stimulated simultaneously at amplitude of 700 microamps for duration of 10 milliseconds. Both electrodes overlie the right posterior cricoarytenoid muscle. Total frequency is 30 Hz. Right abduction is produced.

electrode on a 4-electrode array, at trials of stimulation at both 40 and 60 Hz.

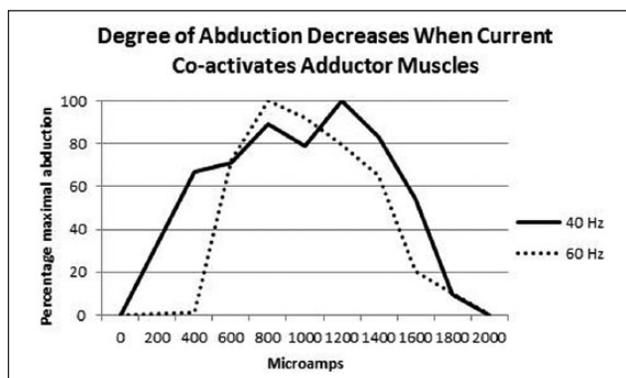
In 1 of the animals that was implanted with an 8-electrode array, the effects of bipolar and monopolar stimulation of electrodes on degree of vocal fold abduction was compared, and similar recruitment curves resulted from both. This is demonstrated in Figure 5. Additional trials confirmed the ability of electrode stimulation to simulate simultaneous bilateral vocal fold abduction.

## Discussion

This study explored the selectivity of multi-channel electrodes for epimysial stimulation of the PCA to restore abductor function to the larynx. Surgical access of the PCA muscle is a challenge, and surgical approach should minimize the risk of implantation of an array. The feline larynx was selected as a model in this study because of its similar anatomy and pattern of innervation to the human larynx.<sup>16</sup>



**Figure 3.** (A) This depicts recruitment curves from individual electrodes within a slanted conductive polymer array on the posterior cricoarytenoid. Electrodes 1 through 3 activated left-sided abduction. Electrodes 4 through 6 activated right-sided abduction. The 2 black squares indicate the amplitude at which electrodes 3 and 4 cause bilateral vocal fold abduction. All stimulation was at a frequency of 60 Hz. (B) Harvested feline larynx and overlying electrode array with each electrode 1.5 mm apart. Electrodes 1 through 6 make contact with the posterior cricoarytenoid (PCA). The 2 most lateral electrodes at the left end of the figure are not in contact with the PCA, therefore no data were derived from these 2 electrodes.



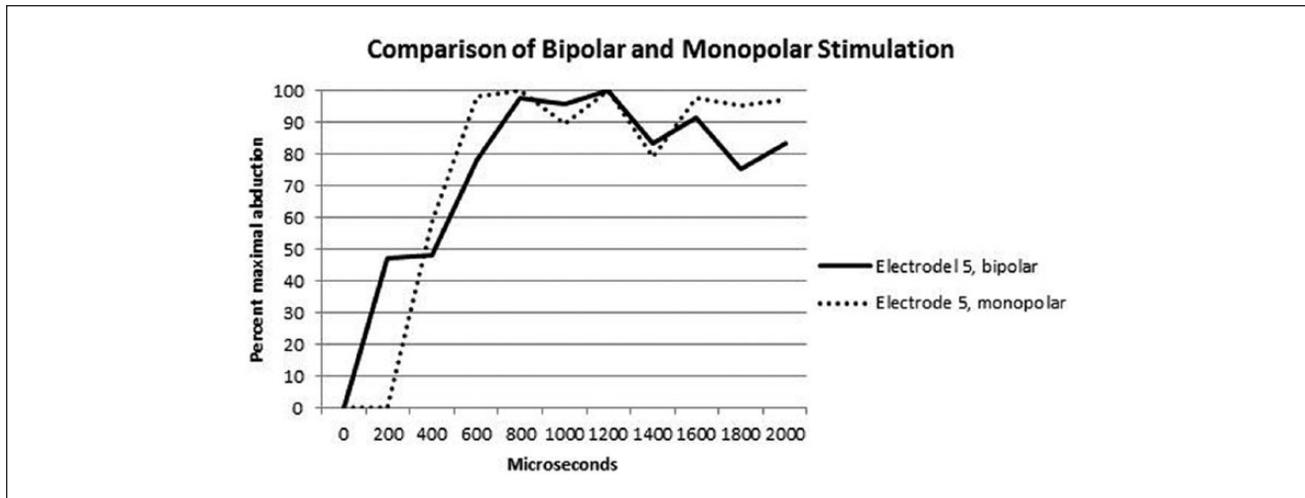
**Figure 4.** Recruitment curves from an array that consists of 4 electrode channels are shown. The recruitment curves depicted are from an electrode channel that is located laterally on the posterior cricoarytenoid. Similar degrees of abduction are seen with both 40 Hz and 60 Hz. Decreased abduction with increasing amplitude is likely due to spread of current to adductor muscles and increased adduction at maximal electrode stimulation.

We were able to show that a flexible array of electrodes that spans the area of bilateral posterior cricoarytenoid muscles is a feasible method for ensuring that only 1 surgical approach of the area is needed in order to achieve selective activation of abductor muscles with minimal co-activation of adductors. The single approach for implanting multiple electrodes on 1 electrode array helps to avoid the risk of

causing unnecessary trauma and edema to the area from removing and replacing electrodes in slightly different locations.

Once implanted, the electrode array can be used to map responses of individual electrode channels so that the most selective channel can be used. The potential for this device to be implanted acutely upon diagnosis of vocal fold paralysis in order to continue stimulating PCA muscle may allow prevention of atrophy of the PCA. It could be used in conjunction with a laryngeal reinnervation procedure so that the PCA muscles do not atrophy while the neurotomy is healing. Once the neurotomy has healed and the paralyzed vocal fold has restored tone, the electrode array could be explanted. Because the electrodes are not embedded in muscle but only are in close contact with the muscle, explantation of the device should be less traumatic to the tissue than a “bed of nails” type of array.

These trials of stimulation with implanted electrodes into the PCA also demonstrate the feasibility of producing predictable graded degrees of vocal fold abduction with varying stimulation parameters. Maximal stimulation parameters may cause current to spread to surrounding adductor musculature of the larynx, producing simultaneous adduction with abduction, as is seen in Figure 4. The precise amount of charge that causes co-activation of adductors was found to be dependent on the location of the electrode on the PCA muscle. These findings were in agreement with those of Forster et al.<sup>13</sup> Achieving bilateral vocal fold



**Figure 5.** Recruitment curves from bipolar stimulation and monopolar stimulation of electrodes within a slanted conductive polymer array on the posterior cricoarytenoid. All stimulation was at a frequency of 50 Hz. There is no significant difference when bipolar stimulation is used compared to monopolar stimulation.

abduction was also possible with the use of the electrode array. As seen in Figure 3A, a single electrode positioned medially along the muscle can cause bilateral abduction or 2 simultaneously activated electrodes positioned over both the right and left PCA can cause bilateral abduction.

With more electrode channels included in the device, optimal positioning of electrodes for selective activation is more likely. The ability to selectively stimulate abduction is aided by an increase in the number and decrease in the distance of the electrodes. In comparing the trial of 4 electrodes to that of 8 electrodes (Figure 2A), we find an advantage of more electrodes. We demonstrated that electrode placement is more useful for mapping when spaced on the array at 1.5 mm apart when compared to 2 mm apart.

The flat design and ribbon-like pliability of the conductive polymer array is optimal for ease of surgical implantation. The array is able to conform to the anatomic area of interest, allowing maximal contact of the electrodes to the muscle being stimulated without resulting in trauma to the muscle from any wires that are inserted into the muscle. This design of epimysial electrodes is likely more durable than the bed of nails design of electrodes. The innervation pattern of the PCA muscle is ideal for selective stimulation with an electrode array placed onto the muscle.

This study is different from prior published studies that activate vocal fold abduction because only 1 attempt is needed at device insertion due to the multichannel nature of the device. Further efforts to develop this technology must be focused on applications in a chronic preparation with vocal fold paralysis to assess device function in the paralyzed larynx. The conductive polymer array has the potential to act as an electromyography electrode as well as stimulation device, for precise monitoring of a recurrent

laryngeal nerve after a traumatic or iatrogenic injury. Degradation of electrode material in the biological environment, from chemical and mechanical stress, must be studied prior to any possible implantation studies in humans. The cricoid cartilage is subjected to mechanical stress from movement with swallowing that could cause electrode migration or degradation. Restoration of laryngeal abduction with respiration may involve some form of pacing. This necessitates development of hardware to trigger electrode impulses from chest wall or diaphragm movement.

## Conclusion

Implanted arrays of electrodes into the PCA muscle are effective in an acute model at producing movements of the vocal folds that are selective, predictable, and graded. The ability to map out the degree of abduction produced by an electrode at a specific location on the PCA allows for a predictable response with stimulation of the electrode. This was demonstrated in the recruitment curves created during this study. The design of conductive polymer array is especially well suited for the PCA due to its pliability, ease of implant, and lack of resulting muscle trauma. Multiple electrode channels on a single array enable mapping of responses and subsequent selection of the most desirable channels. This device has the potential for preventing atrophy of the PCA after recurrent laryngeal nerve injury and for reproducing physiologic movements needed for respiration. Chronic studies are needed to study long-term feasibility.

## Authors' Note

This study was performed in accordance with the PHS Policy on Humane Care and Use of Laboratory Animals, the NIH Guide for

the Care and Use of Laboratory Animals, and the Animal Welfare Act (7 U.S.C. et seq.); the animal use protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of University of Utah.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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