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Long-Term Follow-Up of Pacing of the Conditioned Diaphragm in Quadriplegia

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ELEFTERIADES, J.A., ET AL.: Long-Term Follow-Up of Pacing of the Conditioned Diaphragm in Quadriplegia. *The authors have previously shown that conditioning of the diaphragm for continuous bilateral pacing is a feasible and effective means of ventilation in patients with complete respiratory paralysis from high cervical (above C3) quadriplegia. The present study reports the long-term results of continuous diaphragmatic pacing. Twelve quadriplegia patients underwent bilateral phrenic nerve pacemaker placement and diaphragm conditioning from 1981 to 1987. Pacing was initiated at 11 Hz and progressively decreased to 7.1 Hz. A pulse train duration of 1.3 seconds for adults and 0.9 seconds for children was used. Long-term follow-up information obtained included pacing status (full-time, part-time, or mechanical ventilation), ventilation parameters, and social circumstances. Of the 12 patients, 6 continued to pace full time (mean 14.8 years); all were living at home. Three patients paced for an average of 1.8 years before stopping; two were institutionalized. One patient who paced full time for 6.5 years before lapsing to part time, lived at home. Two patients were deceased; one paced continuously for 10 years before his demise, the other stopped pacing after 1 year. Patients who stopped full-time pacing did so mainly for reasons of inadequate social or financial support or associated medical problems. All patients demonstrated normal tidal volumes and arterial blood gases while pacing full time. Despite theoretical concerns about long-term nerve damage, no patient lost the ability to pace the phrenic nerve. Threshold currents did not increase over time (original/follow-up: 0.46/0.47 for right, 0.45/0.46 for left), nor did maximal currents (original/follow-up: 1.16/1.14 for right, 1.37/1.26 for left). This follow-up confirms that quadriplegic patients are able to meet long-term, full-time ventilation requirements using phrenic nerve stimulation of the conditioned diaphragm. Careful review of diaphragmatic pacing candidates with respect to associated medical conditions, social support, and motivation is essential for appropriate patient selection and successful long-term results. (PACE 2002; 25:897–906)*

electrical stimulation, diaphragm, quadriplegia, spinal cord injury, ventilation

Introduction

Glenn and associates[1] first reported full-time ventilatory support of quadriplegia patients, using diaphragmatic pacing in 1972. In this initial protocol for sustained ventilation, patients underwent maximal stimulation of alternating hemidiaphragms for 12-hour intervals. While successful, increasing experience identified a more physiological method of diaphragmatic pacing in quadriplegic patients using simultaneous and continuous pacing of both hemidiaphragms. Continuous pacing was achieved by conditioning the diaphragm, using low frequency stimulation over a period of months, to resist fatigue. The experience of ventilation in five quadriplegic patients who paced between 11 and 33 months with conditioned diaphragms was subsequently reported in 1984.[2]

The 1984 report demonstrated that 24-hour bilateral pacing of the conditioned diaphragm was feasible and gave promising early results. The purpose of the present investigation is to evaluate the long-term results of continuous diaphragmatic pacing in a larger group of quadriplegic patients who achieved diaphragm conditioning.

Materials and Methods

Patient Population

Patients with quadriplegia and complete respiratory paralysis who underwent placement of

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bilateral phrenic nerve pacemakers and diaphragm conditioning (February 1981 to July 1987) were retrospectively studied. All patients sustained cervical spinal cord lesions above the C3 level. A waiting period of at least 3 months after the initial spinal cord injury ensured irreversible loss of respiratory function. Viability of the lower motor neurons of the phrenic nerve was ascertained in each case by percutaneous stimulation of the phrenic nerve in the neck.[3]

Patients who were not quadriplegic and those in whom conditioning of the diaphragm was not achieved were not included for review. Additional patients underwent pacing for central hypoventilation (not quadriplegia) and are not included in this paper. During this period, one patient with quadriplegia was excluded from analysis, as he succumbed to unrelated causes before completion of the pacing program. All other patients entered into the program were able to be conditioned.

Implantation Technique

The technique of electrode implantation has been previously described in detail.[4] In brief review, phrenic nerve electrodes were placed within the thorax to ensure inclusion of C5 nerve fibers that may not join the phrenic nerve until the nerve is within the chest.[5] Access was gained through a small anterior second or third interspace thoracotomy. Noncircumferential monopolar platinum ribbon electrodes, designed for phrenic nerve stimulation (Avery Laboratories, Glen Cove, NY, USA),[4] were secured atramatically behind the phrenic nerve within the upper mediastinum. Electrodes exited the thorax through an intercostal space near the lower costal margin where a subcutanous pocket was created for receiver placement. Device implantation was carried out on each side as separate procedures spaced approximately 2 weeks apart. Diaphragm conditioning was initiated approximately 2 weeks after implantation of the second device.

Pacemaker Settings

Radiofrequency signals, generated extracorporally by a battery-powered transmitter, were inductively coupled to the subcutaneously implanted radiofrequency receiver. Electrical pulses of 150-microsecond duration were delivered with varying amplitude, according to patient requirements. A pulse train duration of 1.3 seconds was used for adults; 0.9 seconds was used for children. Fluoroscopy was used to determine the current required for maximal diaphragm excursion; pacemakers were set to a current level slightly greater than that required for maximal diaphragm excursion.

Diaphragm Conditioning

A pacing schedule was used to gradually restore diaphragms that had atrophied from disuse, and to condition the diaphragm to adapt to continuous bilateral stimulation. Pacing was initiated at a frequency of 11 Hz (90-ms pulse interval) for 15 minutes during each waking hour to prevent fatigue. The duration of pacing was incrementally increased approximately every 2 weeks, as tolerated by the individual patient, until continuous pacing was achieved. Concurrent with the progressive increase in the pacing period, the electrical frequency was decreased progressively to approximately 7.7 Hz (130-ms pulse interval) to minimize diaphragm fatigue.

During the period of diaphragm conditioning, tidal volume, minute ventilation, end-tidal CO_2 and oxygen saturation were measured at the beginning and end of each pacing period and hourly during pacing. A decrease in the tidal volume or minute ventilation ($> 10\%$), rise in end-tidal CO_2 (> 45mmHg), or fall in oxygen saturation ($< 90\%$), in the absence of acute respiratory illness such as pneumonia, was considered to represent diaphragm fatigue. The patient was placed back on mechanical ventilation at least overnight prior to resuming conditioning.

Tracheal Button

After full-time ventilation for several weeks, the tracheal stoma was maintained by a custom-made Teflon tracheal button, which allows normal speech, minimizes tracheal irritation, and enhances cosmesis. The inner plug of the button was routinely removed before sleeping to avoid the obstruction of the upper airway that may occur from high negative inspiratory pressures associated with pulse train stimulation during sleep.

Patient Follow-Up

Patient follow-up was conducted through chart review, institutional communication, or direct patient contact. Pacing status (full-time, part-time, or mechanical ventilation), and social circumstances were assessed at the time of follow-up. Duration of pacing is calculated as the time until cessation of pacing or the total elapsed time for patients who continued to pace full time. Ventilation parameters including arterial blood gas (ABG) values and tidal volumes were measured after inception of full-time pacing, after at least 6 months of full-time pacing, and at intervals in select patients who continued to pace full time.

For determination of behavior of pacing parameters over time, individual current values were calculated from the threshold and amplitude dial settings on the external signal generator using the nomogram in the manufacturer's manual supplied with the Avery S-242 transmitter.[6] A vertical line is drawn at the amplitude dial setting. Then, a horizontal line is drawn from the intersection of this line with the calibration curve to the vertical axis to obtain the corresponding current applied to the nerve. Early in the experience, the nomogram values were validated by electronic testing of each pacing generator in our laboratories. The threshold represents the minimal current required to produce a discernible movement of the hemidiaphragm as viewed under fluoroscopy. The threshold was determined separately for the left and the right diaphragms. Thresholds at the time of the initial implant were compared to the latest determined thresholds for select patients who continued to pace full time. Patients did retain the same individual pacing generator throughout the experience except in instances of electrical failure of the generator.

Diaphragm acceleration was measured by means of a miniature accelerometer secured to a small piece of plastic and adhered to the patient's abdominal skin. Voltage generated by the piezoelectric crystal was displayed on a chart recorder while the phrenic nerve was stimulated at different pulse intervals, thus quantifying diaphragm acceleration. Diaphragm acceleration decreases as the diaphragm adapts to pacing, indication conversion to slow-twitch muscle fibers in the diaphragm.

Results

Patient Characteristics

Twelve patients underwent pacemaker implantation at a mean age of 21 years (7–59 years) and achieved full-time ventilatory support. The clinical characteristics of these patients are presented in Table I. During this same period, one additional patient underwent phrenic pacemaker placement but died from an unrelated cause before full-time pacing was achieved and is not included for review. Quadriplegia was caused by trauma in all but three patients. Meningitis, brainstem infarction, and a brainstem tumor resulted in quadriplegia in the three remaining patients. The average time interval from injury to phrenic nerve pacer placement was 12.7 months. All 12 patients were successfully conditioned and achieved full-time ventilation. The time required for conditioning and transition to full-time pacing ranged from 3 to 16 months with a mean of 5.9 months (Table II).

Clinical Follow-Up

Mean follow-up for the 12 patients with respect to pacing was 8.8 years. Six patients were pacing full-time (mean 13.7 years, range 10.5–18 years). All full-time pacing patients were living at home with assistance. Patient 8 paced full time for 10 years using the original protocol of alternate side diaphragm pacing for 12-hours periods before undergoing subsequent conditioning of the diaphragm. After converting to bilateral, full-time

Table I.

Clinical Profiles

Patient	Sex	Age at Operation (years)	Cause of Quadriplegia	Level of Injury	Time After Injury to Pacing (months)
1	M	22	Fall	C1-2	9
2	M	15	GSW	C1-2	3
3	M	26	MVA	C1-2	9
4	F	23	Anterior spinal artery syndrome	C1-2	32
5	M	7	MVA	C1-2	7
6	F	59	MVA	C1-2	4
7	M	28	MVA	C1-2	10
8	F	11	Tonsillar herniation	C2	15
9	M	17	GSW	C1-2	10
10	M	18	MVA	BS	14
11	M	11	MVA	C1-2	24
12	F	40	Cavernous Hemangioma	BS	18

MVA = motor vehicle accident; GSW = gunshot wound; BS = brainstem; C = cervical cord.

Table II.

Diaphragm Pacing, Present Status

Pt	Time After Start of Pacing Until Full Time (months)	Pacing Status at Follow-up	Duration Paced Full Time (years)	Social Circumstances
1	3	D	10.5	Home, paced full time until demise
2	4	FT	18	Home, married, working full time
3	3	MV	2.5	Institutionalized
4	3	FT	16	Home, completed college
5	8	MV	2.5	Institutionalized
6	4	FT	13	Home
7	6	FT	13	Home, completed college
8	3	PT	6.5	Home
9	5	FT	11.5	Home
10	16	MV	0.5	Home, seizure disorder
11	6	FT	10.5	Home
12	8	D	1.0	Deceased from complications of ARDS

D = deceased; FT = full time; MV = mechanical ventilation; PT = part time; ARDS = adult respiratory distress syndrome; Pt = patient

pacing, she paced for an additional 6.5 years before complications of quadriplegia, including nephrolitihiasis, pneumonia, and decubitus ulcers limited her ability to pace full time.

Three patients converted to mechanical ventilation during follow-up. Patient 3 voluntarily stopped pacing to maintain financial assistance and housing through institutionalized care. One child (patient 5) paced full time for 2.5 years until he was placed into institutionalized care after the divorce of his parents. Patient 10, who sustained multiple injuries as a result of a motor vehicle crash, achieved full-time pacing after a longer period of conditioning to compensate for associated cerebral and pulmonary injuries. Although the patient successfully paced full time for several months, he eventually lapsed back to mechanical ventilation secondary to progressive difficulty with seizures and chronic pulmonary injury from high concentrations of inspired oxygen during the acute phase of his injury. Of the three patients on mechanical ventilation, none subsequently resumed consistent diaphragm pacing.

Two patients died during follow-up. The first, patient 1 achieved full-time pacing in this series paced without significant interruption for over 10 years before his death from urosepsis. On postmortem examination, histologic studies of the phrenic nerves above and below the level of electrode placement revealed occasional axonal degeneration (Fig. 1A) and scattered foci of mild to moderate demyelinization (Fig. 1B). Specimens from both hemidiaphragms were interpreted as essentially normal (Fig. 2). Patient 12, in whom quadriplegia developed as a complication of removal of a brainstem tumor, underwent successful diaphragm conditioning and paced full time for 1 year. She returned for elective tracheal surgery, which was complicated by aspiration and adult respiratory distress syndrome (ARDS). She subsequently required mechanical ventilation until her demise approximately 2 years later.

Physiological Follow-Up

Table III presents the characteristics of paced ventilation in this clinical series. Low frequency pacing was maintained in all patients (range 7.7–8.3 Hz) to prevent diaphragm fatigue. Measured tidal volumes (TV) were equal to or exceeded basal requirements as calculated by the Radford nomogram,[7] based on sex, weight, and respiratory rate. Room air arterial blood gases during full ventilatory support with diaphragmatic pacing demonstrate normal gas exchange after several years of continuous pacing. Values are shown at 6–12 months for patients who have stopped pacing or in whom more recent data could not be obtained.

Figure 1 shows the results of TV and diaphragm acceleration determinations in the long-term follow-up for ten patients who had these studies performed. The graphs are arranged in order of increasing length of follow-up. These figures demonstrate that tidal volume is well main-

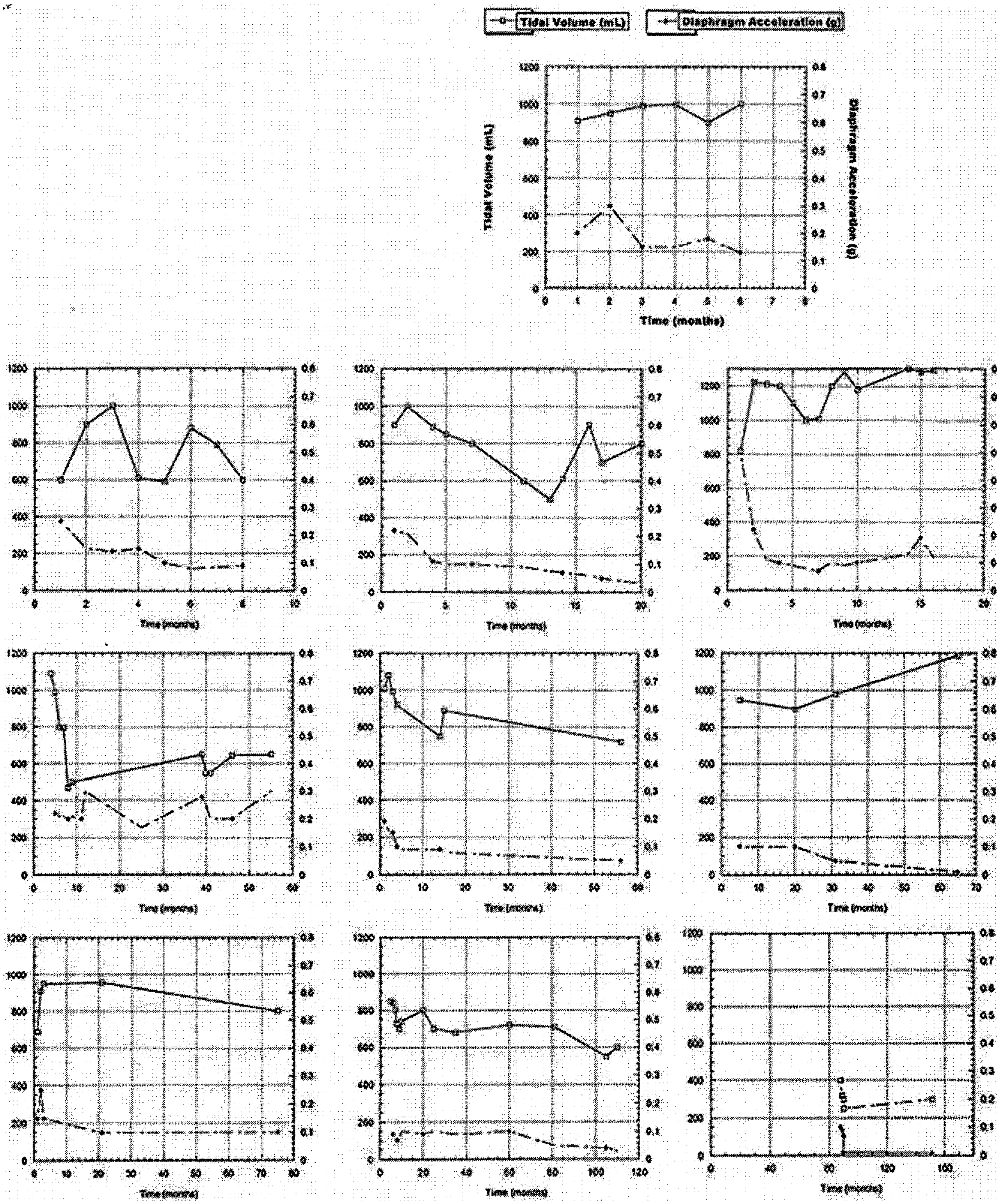
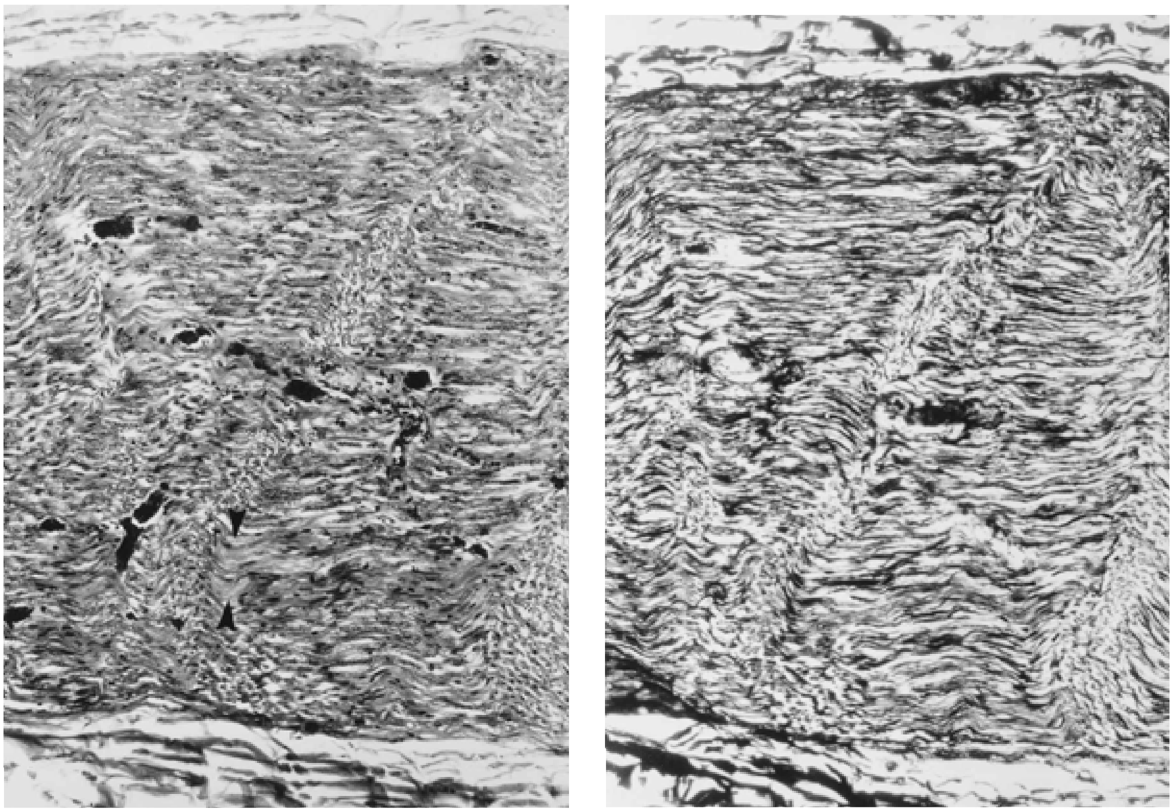


Figure 1. *Long-term assessment of tidal volume and diaphragm acceleration (see text). Plots arranged in order of increasing follow-up.*



A B

Figure 2. *(A) Patient 1. Longitudinal section of left phrenic nerve at the level of the electrode. (Luxol fast blue stain. Mag ×160). Special stain for myelin shows overall good preservation of myelin with only a few barely visible pale areas (arrows). (B) Same area of phrenic nerve as in (A). (Sevier-Munger stain. Mag ×160) Special stain for axons shows no significant axonal loss, even in focus where myelin pallor was seen.*

Table III.

Characteristics of Paced Ventilation

Pt	Freq (Hz)	Pulse Interval	RR (supine)	TV: Predicted Basal*/ Measured (mLs)	pH	PCO_2	PO_2	Time Data Obtained After Paced Full Time (years)
1	7.7	130	8	615/744	7.43	29	104	1.0
2	7.8	128	8	598/717	7.38	40	96	18
3	7.7	130	8	442/692	7.36	38	91	2.0
4	7.2	138	8	538/604	7.41	34	117	15.0
5	8.3	120	9	282/244	7.41	43	102	0.5
6	7.7	130	8	442/690	7.38	33	90	12.5
7	7.7	130	8	672/976	7.37	38	97	12.0
8	7.7	130	8	377/300	7.42	33	96	6.5
9	8.3	120	10	440/280	7.38	41	103	11.0
10	7.7	130	9	518/570	7.41	35	91	1.0
11	7.7	130	9	471/422	7.38	42	79	0.5
12	7.7	130	12	369/353	7.37	40	87	1.0

*Predicted basal requirements based on sex, weight, and respiratory rate using the Radford nomogram.
Pt = patient; Freq = frequency; TV = total volume.

tained over the long-term with diaphragm pacing. The longest continuous follow-up of these parameters is seen in the graph in the middle of the bottom row, representing results in a patient paced continuously for over 10 years. It can be seen from Figure 1 that diaphragm acceleration remains low in these patients, indicating continued preservation of the slow-twitch characteristics of the conditioned diaphragm.

Electrical Follow-Up

Table IV displays the electrical characteristics of stimulation for all 12 patients over the long-term. The threshold represents the minimal current required to produce a discernible movement of the hemidiaphragm as viewed under fluoroscopy. Threshold values are listed separately for the left and the right hemidiaphragm. One column lists the original threshold at the time of the initial implant and the other the latest determined threshold. The time span between the original and latest determinations is listed. Similarly recorded are the currents required to produce a maximal diaphragmatic excursion, again, originally and at the latest determination for each hemidiaphragm. These data show that there is no statistically significant difference in current levels required for threshold or maximal excursion over time (follow-up intervals from 6 months to 15 years, mean 8 years). Respective original and long-term mean threshold current values were 0.45 and 0.46 ma on the left and 0.46 and 0.47 on the right. Mean current values for maximal left hemidiaphragm excursion were 1.37 originally, and 1.26 for long-term; right hemidiaphragm original and long-term values were 1.61 and 1.14, respectively. This confirms that there is no functional deterioration of the lead system, "exit block" of the stimulus to the nerve, or specific nerve damage measurable in this manner. Figure 2 presents nerve histology and Figure 3 presents diaphragm histology from an autopsy on one patient who died after pacing for more than 10 years. Both nerve and diaphragm are essentially normal with no adverse histological sequelae from prolonged electrical stimulation.

Discussion

Diaphragm pacing, through radiofrequency inductive coupling to an implanted radio receiver, can be used as the sole mode of respiration in quadriplegic patients who lack means of independent ventilation. Since the inception of diaphragm pacing in 1972 for quadriplegia patients with complete respiratory paralysis, two groups of patients have been treated that are distinguished by changes in pacing protocol. An early group, consisting of 17 patients (1971–1981), underwent device implantation and training using high frequency stimulation (25–30 Hz). A later group of patients, who underwent revised training using low frequency stimulation (1981–1987), forms the subject of this report. Long-term follow-up is the specific focus of this clinical analysis.

The first group of 17 patients underwent pacing of alternate hemidiaphragms for 12-hour periods at high frequency stimulation to achieve max-

Table IV.

Electrical Characteristics of Stimulation

Patient No.	Threshold Current (ma)				Current for Maximum Diaphragm Excursion (ma)				Time Span (months)
	Left		Right		Left		Right		
	Original	Latest	Original	Latest	Original	Latest	Original	Latest	
1	0.1	0.1	0.1	0.3	0.8	0.4	0.6	0.9	16
2	1.2	0.7	0.9	0.4	3.7	1.7	1.8	0.8	115
3	0.7	0.3	1.3	0.8	1.4	0.8	2.3	1.6	6
4	0.3	0.3	0.1	0.3	0.5	0.7	0.4	0.8	70
5	0.1	0.2	0.3	0.3	0.6	0.7	0.8	0.6	91
6	0.1	0.1	0.1	0.6	0.3	0.4	1.1	1.1	72
7	0.2	0.2	0.8	0.6	1.6	1	2.3	1.4	67
8	0.2	1.3	0.1	0.2	1.6	3.1	1.8	1.4	164
9	0.4	0.8	0.4	0.4	1.6	1.5	1.3	0.9	33
10	0.8	0.4	1.4	1.2	1.7	1.3	4.6	2	23
11	0.8	0.7	0.1	0.1	1.3	2.3	0.7	1.1	21
12	NA								
Mean	0.45	0.46	0.46	0.47	1.37	1.26	1.61	1.14	61.6

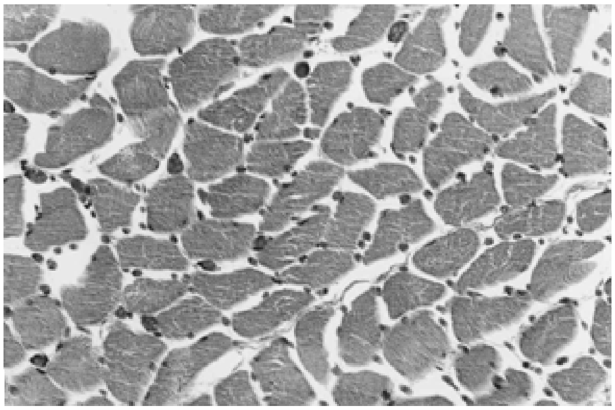


Figure 3. *Patient 1. Muscle fibers of the diaphragm are arranged in a normal mosaic pattern and individual fibers are histologically normal. Separation between muscle fibers is a common postmortem artifact. Scattered small dark round structures in the endomysium are blood vessels. (Hematoxylin and eosin. Mag ×310).*

imum diaphragm excursion. A respiratory rate of 12–17 breaths per minute was required to maintain ventilation. Of the six patients who achieved full-time pacing, three survived long-term. The other three patients died within 2 years after surgery from sepsis[2] and respiratory failure.[1] Of the remaining 11 patients, 8 were supported part time with phrenic nerve pacing, seven of whom eventually died after pacing for an average of 42 months. The remaining three patients were unable derive any support from pacing and were supported with mechanical ventilation.[2]

The suboptimal results of full-time pacing in this early group of patients led to revision of the pacing protocol. Failure was likely caused by diaphragm fatigue, incurred from stimulation of the diaphragm at high frequency, despite alternate 12-hour periods of rest for each hemidiaphragm. Decreasing the stimulation frequency to low values (7–10 Hz) was subsequently found to alleviate diaphragm fatigue by conversion of the diaphragm to slow-twitch, fatigue resistant muscle fibers. Lowering the respiratory rate from 12–17 to 10 or less breaths per minute was also found to alleviate muscle fatigue during pacing.

The 12 quadriplegic patients with respiratory paralysis whose diaphragm pacemakers were implanted between 1981 and 1987 subsequently underwent conditioning of the diaphragm using a revised low frequency protocol. The encouraging early results of the initial five patients in this study, reported previously,[2] are substantially extended in patient numbers and duration of follow-up in this study of long-term outcome. Six of the 12 patients continue long-term pacing with a mean pacing duration of 13.7 years, and have accordingly avoided institutionalized care. Three of these patients finished college; one is married and employed full time.

The need for strict criteria and careful selection of pacing candidates is illustrated by the six patients who failed to achieve sustained long-term pacing despite successful implantation of the pacing system and subsequent successful diaphragm conditioning. Inadequate financial and social support forced the third patient in this series to discontinue pacing. A fully supportive family may have prevented patient 5 from returning to mechanical ventilation. The need for critical evaluation of associated medical conditions that may limit the long-term success of pacing is exemplified in patient 10 who underwent successfully conditioning of the diaphragm, but eventually returned to mechanical ventilation secondary to continued seizures from an associated head injury. On the basis of clinical experiences and this analysis, clinical factors to consider in patient selection for diaphragm pacing are listed in Table V.

While diaphragm pacing has been carried out successfully in children and infants, caution is advised, as the skeletal and pulmonary systems in this patient population are often underdeveloped[8,9] and may predispose to early fatigue. Scoliosis, which often complicates paralysis in the growing child, may preclude successful pacing if extreme. This process may be partially arrested through the insertion of Harrington rods to correct the existing deformity. As in the adult, thorough assessment of the social circumstances of the child may avoid placement of the device in an individual who lacks adequate psychological and social support. Despite the special challenges in children, several highly successful series of (part-time) pacing in children have been reported.[10–12]

Previous studies have suggested the potential for nerve injury from chronic electrical stimulation. Potential mechanisms for nerve destruction include thermal injury from dissipation of the electrical charge on nerve stimulation, and adverse local metabolic changes from sustained neuronal hyperactivity.[13,14] However, the current study, and extensive prior laboratory studies,[15] demonstrate no apparent clinical deterioration in pacing parameters or respiratory measurements from continuous pacing in excess of 10–15 years. Threshold current and the current needed for maximal diaphragm excursion are unchanged after years of pacing. Pathologic studies also demonstrate phrenic nerve integrity (Fig. 1A and B) and preserved diaphragm histology (Fig. 2) de-

Table V.

Respiratory Paralysis: Ideal Conditions for Pacing Candidates

Parameter	Ideal Conditions
Age	10–60
General health	Absence of other life-threatening conditions
Neurological system	Normal cognitive function
	Absence or control of other neurological injury such seizures
	Stable cervical spinal cord injury above the C3 level
	Lower motor neurons of phrenic nerves intact
Respiratory system	Normal pulmonary function, chest wall and diaphragm
Urological system	Low pressure urinary drainage
	Controlled infections
Musculo-skeletal system	Minimal skeletal deformities and muscle spasms
Support system	Available familial and/or social support
	Adequate financial support
Motivation	Active pursuit of independence
Care facility	Personnel qualified for care of quadriplegia
	Personnel trained in management of phrenic pacemakers

spite 10 years of continuous pacing in patient 1. This evidence of the safety of diaphragm pacing to the nerve and diaphragm is of critical importance.

Although the pacing systems are generally reliable, a backup mechanical ventilator is always kept available in case of system failure.

The advantages of phrenic nerve stimulation are physiological and psychological. Potential problems inherent in prolonged mechanical ventilation, like recurrent pulmonary infections, tracheal injury from the tracheostomy cuff, and accidental ventilator disconnection or malfunction are potentially avoided with diaphragmatic pacing. Psychological benefit is provided through greater (relative) mobility and restoration of natural speech when patients are ventilated by diaphragm pacing. Educational and employment opportunities may be more actively pursued, as can opportunities for independent living in contrast to institutionalized care and mechanical ventilation.

Prospective studies comparing survival of patients undergoing diaphragmatic pacing with those who are supported with mechanical ventilation are unlikely; however, a retrospective study by Carter et al.[16] suggests a survival advantage in patients who are supported with diaphragm pacing. Certainly, the mean duration paced of 13.7 years for the patients fully supported with phrenic nerve stimulation in this study is encouraging, given the generally poor survival expectations for such patients.

Patients, who successfully initiate full-time pacing, but subsequently cease pacing, often do so because of inadequate financial or social resources or secondary to a lack of available health care providers who are knowledgeable in diaphragmatic pacing. Unlike cardiac pacemakers, which usually require almost no attention after implantation, diaphragm pacemakers require routine evaluation by personnel who are familiar with their use and with potentially encountered difficulties. Major complications of the quadriplegia itself, related to infections, particularly urosepsis, are a common cause of premature death unless vigilantly prevented and/or treated.

Conclusions

Conditioning of the diaphragm using low frequency stimulation to satisfy the long-term, ventilatory requirements of quadriplegic patients is clinically feasible with no apparent clinical or physiological detriment. Patients who successfully pace long-term demonstrate social independence, academic accomplishments, and long-term survival. These observations support the use of bilateral, full-time pacing of the conditioned diaphragm in appropriately selected patients with high cervical quadriplegia, complete respiratory paralysis, and viable lower motor neurons of the phrenic nerves. In addition, careful patient selection with attention to critical aspects of social and financial support, coexisting medical conditions, and patient motivation are necessary to ensure that inappropriate device implantation is not performed in unsuitable candidates.

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