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Diaphragmatic Pacemaker

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1. Introduction

The diaphragm is a major respiratory muscle and plays an integral part in normal respiration. It is supplied by the phrenic nerve, which originates mainly from the fourth cervical nerve, but also receives contribution from the third and fifth cervical nerves. The phrenic nerve contains sensory, motor, and sympathetic nerve fibers, and it supplies motor supply to the diaphragm and sensory supply to the central tendon. Both phrenic nerves runs along the scalene anterior muscle deep to the carotid sheath. The right phrenic nerve passes over the brachiocephalic artery and posterior to the subclavian vein and over the right atrium. It enters the diaphragm at the level of T8th verbetrae. The left phrenic nerve also runs posterior to the left subclavian vein and passes over the pericardium of the left ventricle and penetrates the left hemidiaphragm separately.

The diaphragm, on the other hand, is an elliptical cylindroid structure that is capped by the fibrous dome. The central tendon, which is the highest part of the diaphragm, consists of interwoven collagenous fibers; whereas, the cylindrical portion of the diaphragm consists of a continuous muscle fiber band, the majority of which is directly in contact with the inner surface of the lower ribs. Injury to the central nervous system, phrenic nerve, or diaphragm can lead to an impairment of diaphragm function and lead to respiratory impairment, resulting in a decrease in tidal volume, minute ventilation, and abnormal gas exchange. Injuries to the nerve can be of various types, as described in Table 1 [1, 2]. Diaphragmatic pacing (phrenic nerve pacing) can lead to significant improvements in quality of life and decrease complications along with the savings in a mechanical ventilator dependent patients. In the current chapter of this book we will discuss the role of a diaphragmatic pacemaker (Phrenic nerve stimulator).

2. History of diaphragmatic pacemaker

In 1987, Duchenne [3] was the first to discover that direct stimulation of the phrenic nerve can lead to the contraction of diaphragm and imitate normal respiration (Figure 1); however, discussion about electrically stimulating the diaphragm and heart dates back almost two hundred years. In 1777, Cavallo was the first to suggest electricity as a means for artificial respiration, and in 1818 Andrew Ure claimed that life could be restored in cases of suffocation, hanging, and drowning by stimulating the phrenic nerve [4]. In the late 1800s,

it was reported that electrical impulses cause the heart to beat. Hufeland [5], in 1873, was the first person to suggest that electrical stimulation of the phrenic nerve can lead to artificial respiration and can treat asphyxia.

There was a long pause in work of phrenic nerve pacing despite the earlier success, which is mainly attributed to the advent of positive pressure ventilation. The first step in the direction of positive pressure ventilation was taken by Friedrich Trendelenburg in 1871 when the cuffed tube was introduced. He invented the devise to prevent aspiration during larynx surgery [6]. A decade later, Samuel Meltzer and Charles Elsberg described the use of ventilator equipment for anesthesia, which marked an era of positive pressure ventilation [6]. During the first half of the twentieth century, both the positive pressure ventilating device and the negative pressure ventilating device (iron lung) were in use. In 1940s Sarnoff et al. from Harvard University suggested that the absence of rhythmic diaphragmatic contractions can alter minute ventilation and henceforth result in an increase in carbon dioxide and a decrease in oxygen concentration. He described the new means of artificial respiration in which one or both phrenic nerves are stimulated by electrical current. He applied the current via a Grass stimulator set to deliver 40 impulses per second, with each impulse having a duration of two seconds. "The current was fed through a rotating potentiometer which describes an arc, the length of which can be set by an adjustable lever." (7) The voltage can be regulated, and a gradual increase in voltage results in a smooth diaphragmatic contraction, which produces respiration. He also was able to perform 52 hours of phrenic nerve stimulation as an only means of artificial respiration in a five-year-old patient with cerebral aneurysm leading to respiratory paralysis [7].

In 1950s, on the other hand, the first cardiac pacemaker was developed, which was not internally implanted as the current pacemakers are. The device was powered by A/C and had small electrical leads that were implanted in the heart. By 1957 a fully functional battery-operated cardiac pacemaker was developed by Rune Elqvist (Figure 2). In 1960 the first cardiac pacemaker that was totally implanted into the body was invented [8]. William Glenn (Figure 3) from Yale University, along with his colleague, was the first to create the first practical application of phrenic nerve pacing. Their first clinical application of radiofrequency stimulation was done in 1964; it was a short-term application in the immediate postoperative period [9]. Glenn and colleague mentioned phrenic nerve pacing in their paper in 1966 [10], though their seminal work on this topic was published in JAMA in 1968 on the use of radio-frequency electrophrenic respiration, a long-term application to a patient with primary hypoventilation syndrome [11].

In collaboration with Dr. Glenn and Roger E. Avery, Glenn's prototype was brought into commercial distribution by Avery Laboratories, Inc. in the early 1970s [12]. Flageole et al. [13] in 1995 described their experience with inserting phrenic nerve pacemakers in three children. In 2006 Hunt et al. [14] published their experience from Children Memorial Hospital in Chicago, Illinois, USA, of phrenic nerve pacemaker implantation among 34 infants and children since 1976. In 2002 Shaul et al. [15] described the thoracoscopic technique for phrenic nerve pacemaker implantation among nine children from 1997-2000. So far approximately 330 diaphragmatic pacemakers have been implanted among infants and children, and a total of approximately 2,000 diaphragmatic pacemakers have been implanted in over 20 countries. For approximately two decades, Dr. Onders and colleague

from Cleveland clinic initiated the implantation of the diaphragmatic pacer. Christopher Reeve, who played Superman, was his first success story. Onders used the device NeuRx Diaphragm Pacing stimulation (DPS) [16]. NeuRx DPS ™ has developed over the past 22 years via the joint effort of several institutions including Case Western Reserve University, University Hospital, and VA Medical Center. It achieved its IDE status in October 2005 for use in clinical trials in amyotrophic lateral sclerosis (ALS) patients. Over 150 spinal cord injury patients, including Christopher Reeves have been treated with NeuRx DPS TM (DPS: Diaphragmatic Pacing System) system in the USA. Onders et al. [17, 18] reported the data of 88 patients' experiences on the use of NeuRx DPS.

3. Introduction to diaphragmatic pacemaker

The initial diaphragmatic pacemaker was developed by Dr. Glenn at Yale University. It consisted of an external battery-powered transmitter with an antenna placed on the skin and a radio receiver placed subcutaneously beneath the antenna. A platinum electrode was used to surround and conduct current to the phrenic nerve [19]. Even after half a century the design of the diaphragmatic pacemaker remains almost the same. Today, it still consists of an external transmitter and antenna, a subcutaneously implanted receiver and electrodes (Figure 4). The external transmitter and antenna send the radiofrequency energy to the subcutaneous receiver, which in turn converts the radio frequency waves into stimulating pulses, which are transmitted from electrodes to the phrenic nerve, resulting in the contraction of the diaphragm. The earlier versions were limited by the battery life, with fresh 9-volt alkaline battery providing enough energy to pace for almost 40 hours. The newer Mark IV transmitter was approved by the U.S. Food and Drug administration (FDA) in 1988 and received approval from European Active Implantable Medical Device Directives in 1994. The current subcutaneous receiver is approximately 1'' x ¼''. The electrodes are highly flexible stainless steel wire, which is insulated by silicone rubber, and have a platinum nerve contact on one end, and a connector to connect with the receiver on the other end. The antenna is worn externally over the implanted devise (Figure 5). It is suggested by the manufacturer to replace the antenna every six months. The current devises are compatible for remote trans-telephonic monitoring. In the earlier models, the most common challenge other than the short battery life was the failure of the radio receiver. Impending failure was usually heralded by sharp pain over the electrode site in the neck or by erratic pacing. With the advent of newer models and significant improvements in technology and designed along with bilateral redundancy lead to introduction of a safer device. The transmitters do not require complicated external programmers to configure, and they use standard, alkaline batteries [12]. An alternate to the phrenic nerve stimulator, the DPS has been used to stimulates the diaphragm to help restore normal negative pressure breathing. It consists of four electrodes implanted in the diaphragm to stimulate the muscle. The fifth electrode is placed under the skin to complete the circuit. In addition a connector holder, a cable, and an external battery-powered pulse generator are used. The timing and control of stimuli to regulate movement in the diaphragm are provided by the pulse generator, which creates a negative pressure and allows the air to enter the lungs (Figure 6). [16]

4. Outcome data in adults

In an appropriately selected individual, the diaphragmatic pacemaker provides an opportunity for liberation from mechanical ventilation, either completely or partially. Moreover, by providing an opportunity for the normal negative pressure ventilation, and henceforth eliminating the adverse effects of positive pressure ventilation.

Glenn et al. [19] reported their initial experience with phrenic nerve stimulation of 37 patients with quadriplegia in 1975. Full-time pacing was achieved in 13 patients, and in other ten patients ventilation was provided by pacing at least 50% of the time. In the remaining 14 patients in the series, ventilator support for 50% of the day could not be achieved. Eight of those patients died mainly from the complications of positive pressure ventilation. The main cause of failure to support ventilation was due to injury and subsequent damage to one or both phrenic nerves either from the initial trauma or operative manipulation. Malfunction of the pacemaker due to shorting of electronic components and antenna connector breakage also contributed to failure to pace or ineffective pacing.

Another work by Glenn and colleague [20], reviewed the records of 477 patients who had undergone diaphragm pacemaker implantation for chronic hypoventilation. The data were from 1966 to 1988. Out of 477 patients, 165 patients were from multicenter study patients, 203 were from non-center study patients, and 109 patients were from non-study patients. Cervical cord injury and brain stem injury patients made the majority of patients (Table 2). 47.27% of patients had success, whereas 34.54% of patients had significant support, and approximately 16% of patients had failure or minimal support.

In another paper by Glenn et al. [21], they reported the long-term follow-up of pacing of the conditioned diaphragm in twelve quadriplegic patients. All twelve patients were successfully conditioned and they all were able to achieve full ventilation. In 1998 Garrido-Garcia et al. [22] described a series of 22 patients who underwent placement of diaphragmatic pacemaker for the treatment of chronic respiratory failure. Thirteen of them had quadriplegia, five were status post-surgical treatment of intracranial lesion, and four patients had central alveolar hypoventilation syndrome. In their series, 81.8% of patients achieved permanent diaphragmatic paced breathing, whereas in 18.2% of patients it was done during sleep. On the long-term follow-up only two of the twenty-two patients were considered as failure. Garrido=Garcia et al. felt diaphragmatic pacemakers promote complete stable ventilation and improve the quality of life for patients. They used two types of diaphragmatic pacemakers—the monopolar stimulation model (Avery Lab, Framingdale, NY) with an S-242 transmitter in two cases and the S-232 transmitter in six cases. They used an Atrostim (Atro-tech, Finland), which was a multipolar sequential stimulation model with either a Pekka transmitter in three cases or a Jukka transmitter in 11 cases. In 2002, Elefteriades and colleagues [23] reviewed the data on twelve patients who underwent implantation procedures between 1981 and 1987. They reported that 50% continued to pace full time with a mean duration of 14.8 years. Two (16%) patients died, one (8%) patient paced part-time, and three (25%) patients stopped pacing. Recently, Khong et al. [24] published an Australian series of 19 patients. Of those, 14 required phrenic nerve pacing due to quadriplegia, one had central hypoventilation syndrome, one had encephalitis, and the information on the remaining three was not known. Currently, 11 of the pacers are known to be actively implanted to date with a mean duration of 13 years.

5. Outcome data in children

From the information available, the first breathing pacemaker occurred on August 23, 1974 at St. Mary's Hospital (Mayo Clinic) in Rochestor, Minnesota, [25] in a fifteen-year-old quadriplegic patient who is still being paced to date. In 1983 Brouilette et al. [26] reported the case series of nine infants and children who underwent phrenic nerve pacing; five of those were less than one year of age. Seven of those were still alive at the time of publication. From August 1974 to June 2006, 324 diaphragmatic pacemakers have been implanted in children under the age of 18. Congenital central alveolar hypoventilation syndrome and quadriplegia account for approximately 75% of cases. Table 3 gives the breakdown of the indication and average implant days among the pediatric population [25]. Approximately 71% of the patients still have active working pacemakers, whereas 18% of the patients are deceased, as shown in Table 3 [25].

6. Indication

The diaphragmatic pacemaker is mainly indicated for patients with central lesion above the second and third cervical level. For functioning of the phrenic nerve pacemaker, one needs to have functioning nerve cell bodies in C3-C5 level. In contrast, trauma to the central nervous system at the level of C3-C5 does not allow pacing due to the damage of phrenic nerve cell bodies. Table 5 illustrates the disorder of the diaphragm due to either central, phrenic nerve, or diaphragm dysfunction and the etiologies related to it. Phrenic nerve injury can occur during open heart surgery or as a result of trauma, radiation, or neuropathic injury. The central or upper motor neuron disorders leading to diaphragm dysfunction are treated by mechanical ventilation or phrenic nerve pacing, whereas phrenic nerve dysfunction or lower motor neuron disorders are usually treated with non-invasive positive pressure ventilation, intercostals nerve grafting/pacing, and diaphragm placation. The diaphragm placation is usually reserved for non-functional phrenic nerves or disorders leading to contractile dysfunction of diaphragm. The ideal candidates for pacing with a phrenic nerve stimulator are the patients with complete cervical spine injuries at C1 and C2 level, congenital or acquired central alveolar hypoventilation syndrome, brainstem injury (tumor, trauma, bleed, infarct), or basilar meningitis [20, 24, 27].

Diaphragmatic pacing has been used for other indications as Arnold Chiari malformation, meningomyelocele, neurofibromatosis (with multiple meningiomas), complete tetraplegia , patients with C3-C4 incomplete fracture, C4-C5 fracture with ascending paralysis to C2-C3 level, radiation induced phrenic nerve injury [24, 26, 28]. In a twenty-year experience of phrenic nerve stimulation for diaphragmatic pacing, Glann and colleague used the pacing in 2% of patients with chronic obstructive pulmonary disease (COPD). The details are shown in Table 6 [27].

Disease of the lower motor neurons as amyotrophic lateral sclerosis (ALS) and poliomyelitis have been considered as contraindications for the placement of diaphragmatic pacemakers, but there have been case reports with the successful use of the diaphragmatic pacemaker in patients with poliomyelitis (29). Onders et al. [17, 18] from Cleveland Clinic reported their data on a multi-center study on the implantation of the diaphragmatic pacemaker in ALS and spinal cord injury (SCI) patients. From March 2000 to September 2007, they implanted

the device in 88 patients (50 SCI and 38 ALS). They found that ALS patients had much weaker diaphragms, which were identified during surgery. They required trains of stimulation during mapping to identify motor points. They found no perioperative mortality even in patients with forced vital capacity (FVC) less than 50%. They found that ALS patients were able to delay their need for mechanical ventilation by 24 months.

7. Evaluation

Patients who need to be considered as candidates should be carefully evaluated. The patients should meet the indication for implantation. Furthermore, the patients should have severe, chronic respiratory insufficiency requiring mechanical ventilation or respiratory insufficiency for more than three months [17, 28-30]. They should have respiratory insufficiency for more than three months after the onset of injury and viable motor neurons (exception cases of those in ALS and Poliomyelitis as mentioned earlier). Failure of the diaphragmatic contraction after the stimulation of the phrenic nerve is considered a contraindication. On the other hand, there have been reports of intercostals to phrenic anastomosis in patients with anterior spinal artery syndrome [31]. Krieger et al. [32] reported a case series of ten nerve transfers from intercostals to phrenic nerves in six patients. Eight of ten transfers had more than three months to allow for axonal regeneration. 100% of those nerve transfers achieved successful diaphragmatic pacing [32].

8. Viability of phrenic nerve

The fundamental requirement of successful pacing is the viability of the phrenic nerve. It is usually assessed by percutaneous electrical stimulation of the phrenic nerve at the level of the neck where the nerve passes over the scalene muscle. This technique was initially employed by Sarnoff et al. [33)]. They mentioned that quick hiccup-like contractions of the diaphragm on the stimulated side were evidence of nerve integrity. If most nerves were viable, then contractions were vigorous. Currently, fluoroscopy is used to detect diaphragmatic function [34]. It is important to assess the diaphragmatic movement under fluoroscopy, as there have been misdiagnoses in detecting diaphragmatic contractions without it [35]. Garrido-Garcia et al. [22], considered the conduction time of 4-12 msec as normal. Brouillette et al. [26], found the phrenic nerve conduction time to be between 2.7 msec to 7.8 msec in the pediatric population. The phrenic nerve conduction time appeared to be shorter in the pediatric population [36-38]. They also found that phrenic nerve conduction time was significantly shorter after intrathoracic stimulation when compared to cervical stimulation. They also found that phrenic nerve conduction timing increased in correlation with age.

The best time to test phrenic nerve viability is a controversial subject, but the general consensus is to wait for three months after an injury. Versteegh et al. found that when tested early, the phrenic nerves were responsive but later became unresponsive; whereas, it is also possible that the nerves may be initially unresponsive but may become responsive up to a year after the injury [39]. It is extremely important not to reject the patient for phrenic nerve stimulator placement if nerves were unresponsive initially. It is suggested that testing the viability of the nerves may be repeated again up to two years later.

9. Diaphragmatic action potential amplitude

In the study by Brouillette et al. [26], the diaphragmatic action potential amplitude after supramaximal stimulation of the phrenic nerve varies from 0.08 to 4.1 mV. They also found that unlike the phrenic nerve conduction timing, diaphragmatic action potential amplitudes vary significantly on serial testing of the phrenic nerve.

10. Surgical implantation techniques

The initial technique for the placement of phrenic nerve stimulator was described by Glenn et al. [19]. Adults were given a four inch transverse incision above and parallel to the clavicle under local anesthesia. Glenn and colleague then isolated the phrenic nerve where it crosses the scalenus anterior muscle and they placed electrode cuff around it. Children under 12 years of age whose necks were too short to accommodate the cuff required the placement of the cuff by thoracotomy approach, as far from the heart as possible.

In 2002, Shaul et al. [40] described the thoracoscopic technique for the placement of phrenic nerve electrodes. The description of surgical detail is beyond the scope of this chapter and is described in detail in their manuscript [40].

Briefly in the cervical approach, a horizontal incision is made and the sternocleidomastoid muscle is retracted medially. The phrenic nerve is identified and the electrode is applied. In the thoracic approach, the procedure can be performed either by thoracotomy or thoracoscpically. The lungs are deflated on one side and the phrenic nerve is identified and mobilized. The electrode is positioned below the nerve and sutured. The leads are then brought through the thoracic cavity and tunneled into the subcutaneous pocket inferior to the 12th rib and the receiver is placed into the pocket [24, 41].

During surgery, after securing the electrodes and connecting to the receiver, the device is tested to ensure good contact with the nerve and stimulation via the receiver results in good contraction of the diaphragm. Device implantation is carried out on each side — two separate procedures performed two weeks apart. Intra-operative diaphragm function can be confirmed by visual observation of the chest wall, palpation of the costal margin, and observation of CO_2 changes or fluoroscopy.

As far as the NeuRx DPS system is concerned, it can be implanted by using the laparoscopic technique by creating four small openings in the abdominal region and inserting the laparoscope through the incisions. Electrodes are placed in the area near the phrenic nerves, which control the diaphragmatic contractions. The implanted electrodes are connected to the four channel external stimulator, which is placed at the percutaneous exit site. The stimulator provides biphasic balanced stimulation to each of the electrodes with a common indifferent electrode that is placed subcutaneously. The stimulator controls the charge, which is delivered via the clinician's pre-programmed parameters of pulse duration, pulse amplitude, pulse frequency, pulse ramp, respiratory rate, and inspiratory time. The users just connect the device and turn it on for the use. For the patients with spinal cord injury, the DPS is set to provide the tidal volume 15% over the basal need. For the ALS patients, an amplitude setting of 25 mA, a frequency below 20 Hz, and pulse width below 200 microseconds is recommended. ALS patients undergo diaphragmatic conditioning five times per day for 30 minutes [17].

11. Pacemaker setting & diaphragm conditioning

Signals are generated by the transmitter, and the subcutaneously implanted receiver picks up the radiofrequency energy and converts it to electrical impulses. Electrical pulses of 150 microsecond duration are delivered with varying amplitude, based on the patient's requirements. A pulse train of 1.3 second and 0.9 second is used for adult and pediatric patients respectively [21]. In order to allow time for the postoperative edema to subside, the diaphragm conditioning is not initiated for at least 12 days after implantation of the second unit. The diaphragm is conditioned by increase in duration of pacing time per hour during the day and rest at night. During the rest period, the patient is placed on positive pressure ventilation.

12. Benefits of the breathing pacemaker

Mechanical ventilation, or positive pressure breathing, is associated with significantly higher costs than normal negative pressure breathing. Moreover, positive pressure ventilation is associated with an increase in cost related to the use of the intensive care unit, or if at home, high cost associated with home health, and durable medical equipment, higher demand on the patient's family, decreased mobility for the patient, and higher rate of complications. Positive pressure ventilation is also associated with poor quality of life, increased risk of deep venous thrombosis and pulmonary embolism due to limited activity. In contrast, the diaphragmatic pacemaker is associated with the natural breathing pattern. Patients are ambulatory (if not quadriplegic or CNS deficit limiting mobility) due to not being attached to the mechanical ventilation system for their breathing needs. The patients are also able to talk and eat normally and perform the normal activities associated with everyday living, as well as their job in many instances. In addition, the patient also is able to breathe through the nose, which offers protection against the bacteria which can bypass the body's defense system when one breathes through a tracheal tube. There have also been reports of long-term recovery of diaphragmatic function in patients with phrenic nerve pacing [47].

13. Complications

Complications may include risk associated with anesthesia and surgery; infection, bleeding, hypoxia, injury to the phrenic nerve, and injury to surrounding structures, among others. In the Australian study, eight out of 19 patients had repeat operations for replacement/reimplantation of hardware. The original I-107 receiver had a life span of three to five years, whereas the battery life of the current receiver is as long as that of the patient [24]. In the pediatric population of a study by Shaul et al. [40], two patients developed postoperative atelectasis, and one patient had pneumonia. One patient had pneumothorax, and one patient had liver laceration. In their twenty-year phrenic nerve implantation experience, Glenn et al. found the major complication to be iatrogenic injury to the phrenic nerve. They also observed injury to the diaphragm by overstimulation. In addition, there have been reported incidences of diaphragmatic pacemaker failure due to twisting of the phrenic nerve wires following the manipulation of the implanted receiver

[42, 43]. Diaphragmatic origin of the pacemaker sound has also been described in literature [44-46].

14. Conclusion

Over last fifty years, significant progress has been made in the area of breathing pacemakers in the area of phrenic nerve stimulation and the diaphragmatic pacemaker. The surgical technique has also evolved from open thoracotomy to new laparoscopic procedures. Breathing pacemakers, which can delay the need for mechanical ventilation by approximately two years, should be offered to all patients with spinal cord injury, central alveolar hypoventilation syndrome, and even in patients with ALS. This in turn can lead to improvements in patients' physical, mental, and psychological qualities of life. Future studies should be undertaken to develop a simpler and more redundant system.
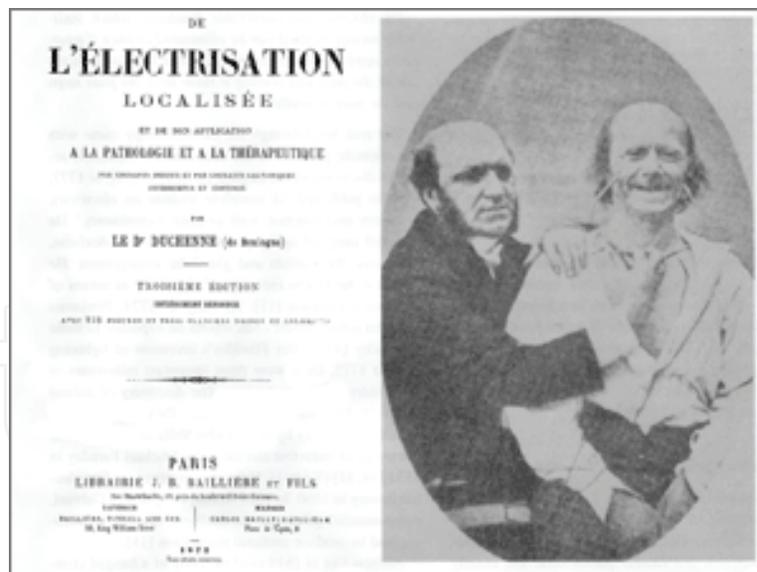

Fig. 1. Duchenne's seminal work on electrical stimulation
(Published with Permission from Avery Biomedical Device, Inc)

Fig. 2. Rene Elmqvist
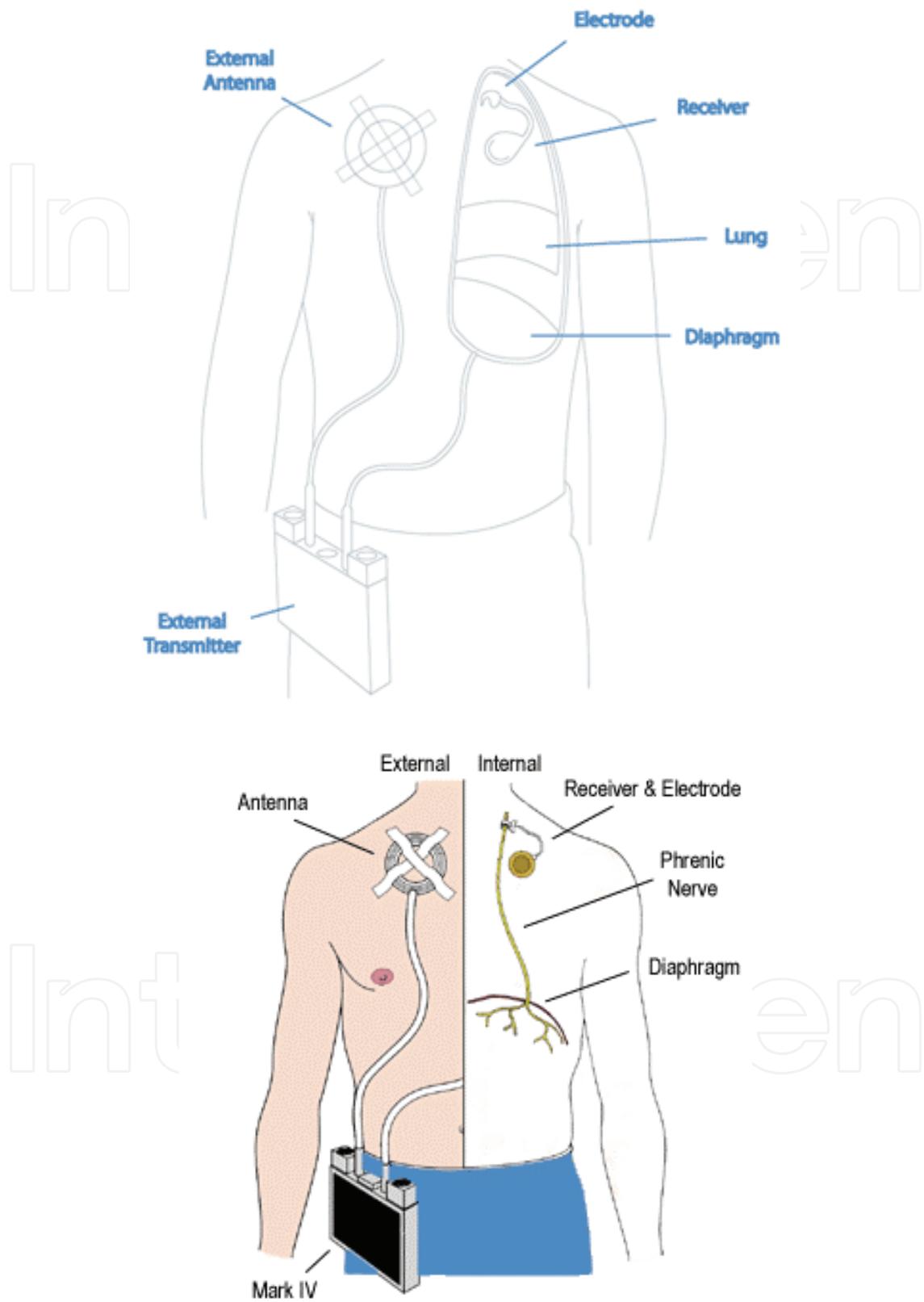

Fig. 3. William W. L. Glenn, MD

Fig. 4. Diaphragmatic Pacemaker System. Published with permission from Avery Biomedical Device, Inc

Fig. 5A. Mark IV Transmitter

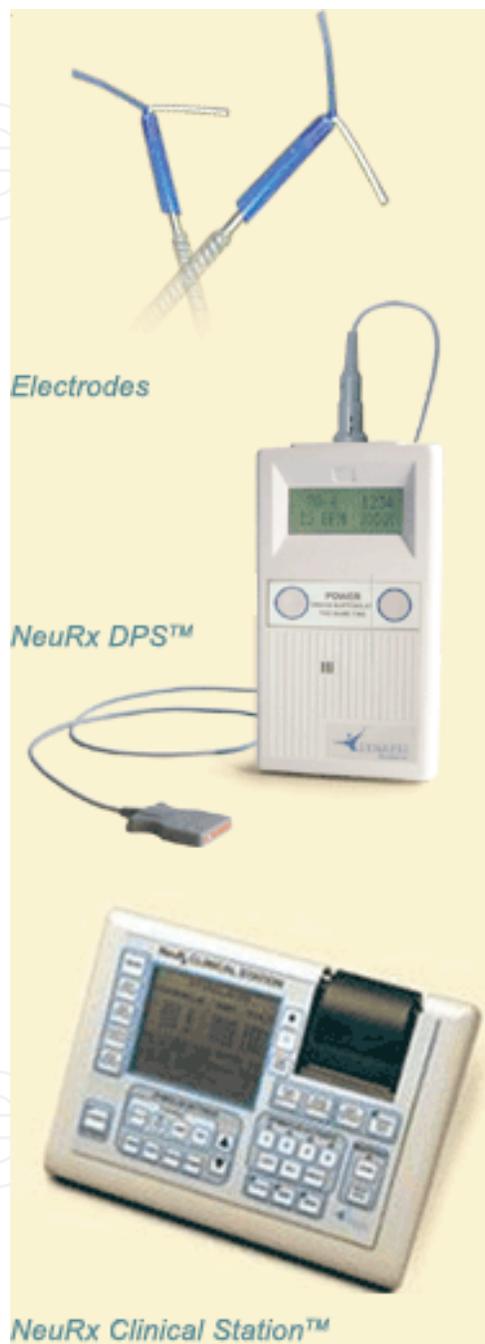Fig. 5B. Receiver and Electrode

Fig. 5C. External Antenna

Fig. 6. NeuRx DPS. Copied with Permission from Synapse Biomedical Inc.

Seddon's	Sutherland
Neuropraxia • Injury to the myelin sheath • Larger nerves covered by greater amounts of myelin are most susceptible to this injury. • Reflexes, muscle function, vibratory, and two-point discrimination are typically lost • Repair may take days to months and healing is usually perfect, as only the sheath needs to be repaired. • Corresponds to Sutherland's 1st Degree injury. **Axonotmesis** • Involves disruption of the nerve itself, but the surrounding and supportive nerve myelin sheath is affected. • Causes include long or severe periods of compression, pulling or loss of blood flow to the nerve. • All nerve types may be affected. • Recovery is usually good. • Corresponds to a 2nd or 3rd degree injury in Sutherland's system. **Neurotmesis** • Disruption of both the nerve fiber and the supportive myelin sheath. • Healing is usually poor without surgical repair. • Corresponds to a 4th or 5th degree injury in Sutherland's system.	• First Degree: Injury with only local changes to the nerve sheath (myelin). • Second Degree: Incomplete injury to the nerve axons Nerve is intact. • Third Degree: Severe axonal injury with scar tissue. Nerve may be injured but is still intact. • Fourth Degree: Complete disruption of axon. Nerve is severely injured but is still intact. • Fifth Degree: Complete transaction of the nerve.

Table 1. Nerve injury Classification

	Center	Non-Center	Non-Study
	165	203	109
Diagnosis			
Cervical Cord Injury	55 (33.33%)	114 (56.16%)	
Brain Stem Injury	50 (30.3%)	54 (26.6%)	
Idiopathic	31 (18.79%)	17 (8.37%)	
Congenital	27 (16.36%)	8 (3.94%)	
Peripheral Lesion	2 (1.21%)	10 (4.93%)	
Numbers of Years Paced			
Up to 5 years	108 (67.9%)	155 (86.1%)	
5-10 years	31 (19.5%)	24 (13.3%)	
10-15 years	16 (10.1%)	1 (.6%)	
15-20 years	4 (2.5%)		

Table 2. Chronic Ventilatory Insufficiency Treated by Diaphragm Pacing. Adapted from Glen WW et al (14)

Diagnosis	Number of Patients	Percentage of Population	Youngest Implant Age (Days)	Average Implant Age (Years)
CCHS	134	41	56	5.6
Quadriplegia	110	34	204	9.8
Brain Injury/Tumor	7	2	756	8.6
Arnold Chiari	7	2	714	6.9
Other	10	3	89	7.1
Unknown	56	17	98	8.8
Totals:	324	100%	56	7.7

Table 3. Phrenic Pacemaker Implanted in Pediatric Population (With Permission from Avery Biomedical Lab, Inc)

Active	230	71
Deceased1	57	18
Inactive -Explanted	4	1
Inactive -Implanted	5	2
Inactive -Unknown	28	9
Totals	324	100

Table 4. Phrenic Nerve Stimulator Device Status. (With Permission from Avery Biomedical Lab, Inc)

Disorders Leading to Diaphragm Dysfunction		
Central (Upper Motor Neuron Lesion)	Phrenic Nerve (Lower Motor Neuron Lesion)	Diaphragmatic Contractile Dysfunction
• Central Alveolar Hypoventilation (CAH) • - Stroke • - Tumor • - Infection • - Vascular • Lesions/trauma of C1 or C2 • Congenital Central Hypoventilation Syndrome (CCHS/Ondine's Curse)	• Spinal pathology (C3, 4, 5) • Neuropathies (idiopathic, ALS, viral) • Trauma: Surgical damage, resection, itrogenic • Tumor • Idiopathic • Radiation Injury	• Muscular dystrophy • Disuse atrophy • Myositis

Table 5. Causes of Diaphragm Dysfunction

Etiology	Percentages
Lesion of Brain Stem or above	
CVA	11%
Tumor or cyst	4%
Encephalitis	9%
Other infections	3%
Shy dragger Syndrome	2%
Other	3%
Lesions of Upper Cervical Cord	
Trauma	22%
Tumor or cyst	1%
Poliomyelitis	3%
Syrinx	1%
Cervical cordotomy	1%
Atlanto-occipital deformity	2%
Others	1%
Idiopathic Central Alveolar Hypoventlation	
Congenital	1%
Undetermined	15%
Peripheral respiratory insufficiency	
COPD	2%

Table 6. Diaphragmatic Pacemaker placement by etiology

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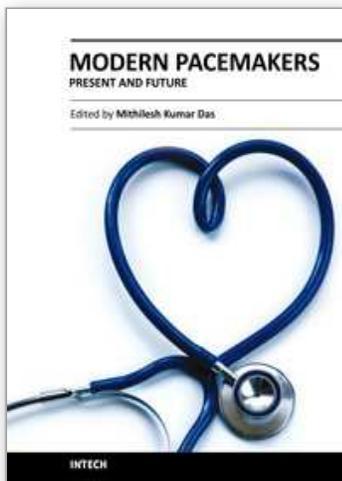
Modern Pacemakers - Present and Future

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The book focuses upon clinical as well as engineering aspects of modern cardiac pacemakers. Modern pacemaker functions, implant techniques, various complications related to implant and complications during follow-up are covered. The issue of interaction between magnetic resonance imaging and pacemakers are well discussed. Chapters are also included discussing the role of pacemakers in congenital and acquired conduction disease. Apart from pacing for bradycardia, the role of pacemakers in cardiac resynchronization therapy has been an important aspect of management of advanced heart failure. The book provides an excellent overview of implantation techniques as well as benefits and limitations of cardiac resynchronization therapy. Pacemaker follow-up with remote monitoring is getting more and more acceptance in clinical practice; therefore, chapters related to various aspects of remote monitoring are also incorporated in the book. The current aspect of cardiac pacemaker physiology and role of cardiac ion channels, as well as the present and future of biopacemakers are included to glimpse into the future management of conductions system diseases. We have also included chapters regarding gut pacemakers as well as pacemaker mechanisms of neural networks. Therefore, the book covers the entire spectrum of modern pacemaker therapy including implant techniques, device related complications, interactions, limitations, and benefits (including the role of pacing role in heart failure), as well as future prospects of cardiac pacing.

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