FUNCTIONAL ELECTRICAL STIMULATION FOR RESPIRATION

Andrew Zadoff, MD
Disclosures

• No direct financial interest in any FES company or device.
• Although our group does a majority of our work at Shepherd, we are an independent medical practice.
• Much of the information given is based on anecdotal non-controlled studies.
Shepherd Center is a private non-profit hospital, founded in 1975, specializing in research, medical treatment and rehabilitation for people having spinal cord injuries and brain injury.

Out-patient services include chronic pain and multiple sclerosis management, continuum of care of SCI and brain injury.

Bed census is currently 152.
Advantages to Diaphragm Pacing*

• Improved sense of well being: improved mobility and transfers without ventilator, use of their own respiratory muscles, better voice, improved sense of smell.

• Negative pressure breathing may decrease risk of pneumonia, improve swallowing, improve cardiovascular function, better aeration of the posterior lobes.

• Reduced damage to the trachea, reduced noise

• Improved socialization


Downside to Diaphragm Pacing

• It may not work secondary to improper placement of the electrodes or injury to the phrenic nerves.
• Expense of surgery, potential complications of surgery
• Need for additional equipment and expenses going forward
• Need physician backup for the devices with some level of understanding. (Actually, much easier than ventilator care)
Devices

- Avery Biomedical Devices--Mark IV
- Atrotech (Tampere, Finland) Not approved in US. Uses electrodes that can stimulate different portions of the nerve to reduce fatigue.
- Medimplant (Vienna, Austria) Not approved in US. Has multiple electrode contacts with the phrenic nerve.
- The above devices have electrodes attached to the phrenic nerve and contraction of the diaphragm is through stimulation of the phrenic nerve.
Devices- Avery

• The Avery Mark IV uses cuffed electrodes placed on the phrenic nerves. This is connected to a radiofrequency receiver implanted under the skin of the chest.

• Surgical placement is either by open cervical dissection in the neck or video-assisted thoracoscopy in the thorax.

Chest 2013; 1201-3        a good review
Devices- Avery

- Stimulation is by an external transmitter which relays the signal thru an external antenna. The external antennas send the signal to the implanted receivers travelling thru the cuffed electrodes on the phrenic nerves.
- Length of battery life about 400 hrs
- Success rate using older technique was approximately 50%.
Devices  Synapse

- Synapse NeuRx RA/4
- Electrodes are placed at the motor points on the underside of the diaphragm laparoscopically. No attachment to the phrenic nerve. Battery pack is external to the patient and is connected by wires to the electrodes. Battery life is estimated to last 3 weeks.
- Surgery can be done in an outpatient setting.
- As surgery is laparoscopic, it is less invasive and less expensive - same day or out-patient surgery possible.
Devices-DPS

• Battery life is about 500 hrs.
• Placement increases upfront costs, but decreases after $2 \frac{1}{2}$ to 3 yrs.
DPS Surgery

- Surgery must be done without paralytics.
- Standard laparoscopy with 4 trocars and creation of a pneumoperitoneum is performed.
- Mapping of the diaphragm using a suction electrode on the underside of the diaphragm is used to find the motor points and determine the response to stimulation.
DPS Surgery

• The strength of the diaphragm activation depends on the proximity of the electrode to the motor point.
• Two intramuscular electrodes are placed in each hemidiaphragm.
• Cardiac monitoring is used to exclude cardiac stimulation.
DPS Surgery

• The wires are then tunneled to the right upper quadrant and exit through the skin. A fifth electrode is placed in the subcutaneous tissue to act as a ground.

• These 5 wires are placed in a connecting block. This is connected to the battery stimulator.
Success Rates

- Limited experience with Synapse DPS
- 2009 report by Onders* on 50 SCI pts and 38 ALS pts
- 96% of SCI pts were able to replace mechanical ventilation and ALS patients were able to delay mechanical ventilation up to 2yrs.

Costs

• Upfront surgical costs are high compared to ventilator costs.
• Need to add in costs of ventilator associated pneumonia, hospitalizations, home care vs. institutional care, ventilator costs, i.e. rentals, tubing, secretion control devices.
## Cost Analysis

<table>
<thead>
<tr>
<th></th>
<th>DPS</th>
<th>Home Vent (LTV1150)</th>
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<tbody>
<tr>
<td><strong>System</strong>(^1)</td>
<td>$32,135.00</td>
<td></td>
</tr>
<tr>
<td><strong>Surgery</strong>(^2)</td>
<td>$40,000.00</td>
<td></td>
</tr>
<tr>
<td><strong>Startup</strong>(^3)</td>
<td><strong>$72,135.00</strong></td>
<td>$1,795.00/mo</td>
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### Monthly Recurring Fees

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<tr>
<th><strong>Bandage Connector Holders</strong>(^1)</th>
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<td>$62.00 per pk of 30 x 12mo</td>
<td>$744.00</td>
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<table>
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<tr>
<th><strong>Batteries</strong>(^1)</th>
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<tbody>
<tr>
<td>$98.00 per pk of 3 x 9</td>
<td>$882.00</td>
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| **Monthly Fees**                   | $135.50             | $1,795.00          |

### Misc Fees (Optional - Based on Needs)

| **Programming**\(^1\)            | $1,650.00           |
| **Wire Repair**\(^1\)            | $1,650.00           |
| **Patient Cables**\(^1\)         | $70.00              |

### After 3.5 Years (42 Months)

|                      | $77,826.00         | $75,390.00         |

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**Pricing Sources**

1. Synapse Biomedical
2. Dr. Khansarinia (Thoracic Surgeon)
3. MGR Homecare
Patient Presentations
Indications for Respiratory FES- ALS

• Amyotrophic lateral sclerosis is a progressive neurodegenerative disease affecting upper and lower motor neurons.
• Variations do occur but generally survival is 2-5 years after diagnosis. Morbidity and mortality from respiratory compromise is very common.
• Estimated 30,000 persons are affected in the US. 450,000 worldwide.*
• There is a hereditary component affecting chromosome 21.

* ALS Association
Indications for Respiratory FES ALS

• Approved medication for this is riluzole which can improve survival only for a few months.
• Noninvasive respiratory support such as BiPAP and cough assist devices are commonly used.
• *Use of DPS can delay need for mechanical ventilation for up to 2 years. FDA approval in 2011.
• Screening for suitable candidates- vital capacity of greater than 40% of predicted is needed for placement of DPS.

Indications for Respiratory FES ALS

• Tracheostomy will be needed.
• Because of the progressive nature of the disease, there is need for discussion about life support with patient and family. The earlier the better.
Patient 1

• 68 yo woman diagnosed with ALS ~ 12/2010, followed in an ALS clinic. DPS placed on 1/30/12 for worsening function.

• A tracheostomy was placed 4/29/13 for increased dyspnea and respiratory secretions. Admitted to hospital ~5/1/13 for increased secretions; discharged 5/10 with 24 hr nursing and “respiratory equipment” at home.

• F/u 5/20/13 and trach was downsized to #6 uncuffed.
Patient 1


• Transferred to Shepherd Center for continued care.
• PMH- IDDM x 20yrs, hypothyroid x 20yrs, ALS. No history of pneumonia prior. Non smoker or drinker
• PSH- cataracts, hysterectomy; PEG 4/29/13
Patient 1

• Activity- significant bulbar defects, can walk a few steps with help. Tube feed is the only source of nutrition.

• At Shepherd, $T_V$ was increased to 500- 600 ml. Respiratory toilet with increased $T_V$, NaHCO3 lavage, in-exsufflator, with family and home health education. DPS was increased to 25 mAmmps all four leads but could not tolerate increased P-W, $T_V$, or pressure support.
D/C  6/8/13
F/U  8/28/13 on ventilator 24 hrs / day plus DPS
Last seen 7/2014 doing well. No significant respiratory issues. On vent and DPS.
Husband is a radiologist
Indications for Respiratory FES CCHS*

- Congenital central hypoventilation syndrome-Ondine’s Curse
- PHOX2B mutation is required to confirm CCHS.
- Associated disorders include Hirschsprung disease, tumors of neural crest origin, cardiac asystole, autonomic nervous system dysregulation.
- There is a spectrum between hypoventilation/ low tidal volumes especially in non-REM sleep to apnea during sleep and severe hypoventilation while awake.

Patient 2

- 20 yo man with previous diagnosis of chronic congenital hypoventilation syndrome.
- Tracheostomy since childhood, uses nighttime ventilator, talking valve during the day.
- PMH- no history of pneumonia, smoking or other lung disease
- PSH- Trach, PEG (not being used)
Patient 2

- Admitted for overnight wean off ventilator early 2014.
- Vital capacity 3500 ml without DPS; on DPS alone 350ml (?)
- DPS reset on admission:
  - R 13,13 mAmp  L 8,8 mAmp
  - 120 pulse width  120 pulse width
  - rate-20  inspiratory interval-1.1
  - ramp-0
- Admission ABG 7.47/ 31/ 100 on RA
- Off ventilator with DPS, he slept well throughout the night with ETCO$_2$ approximately 30.
Indications for Respiratory FES SCI

- Spinal cord injury-high quadriplegia, C1-5
- Vital capacity (Vc) less than 10cc/kg
- Fluoroscopy- Normally more than 5 cm movement
- Sniff test-with fluoroscopy or ultrasound looking for appropriate movement of the diaphragm
- Phrenic nerve stimulation with percutaneous electrodes with monitoring of EMG or fluoroscopy looking for diaphragm descent at least 3-4 cm

Criteria for Eligibility

Who may qualify?

a. 18 years or older
b. Quadriplegic (C1, C2, C3)
c. Mechanical ventilator dependent
d. Motivated patient who wants to come off of the ventilator
e. Consistent family support
f. Phrenic nerve responds to electrical stimulation
## Life Expectancy in Spinal Injuries Surviving One Year*

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<thead>
<tr>
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<th>No spinal cord injury</th>
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“Persons enrolled in the National SCI Database since its inception in 1973 have been followed for 40 years after injury. During that time the causes of death have the greatest impact on reduced life expectancy are pneumonia and septicemia.”

Patient 3

• 17 year old male wrestling injury on 12/3/2011
• C5-6 bilateral facet dislocation, C2 hematoma with resultant C1 ASIA A; C2 ASIA A upon discharge
• Initial hospital course with respiratory failure, Gram (-) pneumonia, spinal shock, bradycardia treated with theophylline
• Steroids x 48 hrs, C5-6 anterior cervical decompression with fusion and posterior stabilization
• PMH-tonsillectomy, chewing tobacco, occasional ETOH
Patient 3

- Admitted to Shepherd Center 12/8/2011.
- Hospital course: R gastroc DVT, hypotension-midodrine, bradycardia-terbutaline
- DPS placed 2/9/2012, programmed 2/10/2012
  - mAmps: R-25,25 L-25,25
  - P-W: 200,200 200,200
  - Rate 12, Ramp 10, Insp Interval 1.1
- VC: 12/18/11--0 1/3/2012--350 2/15/12--200 3/02/12--250 Discharged 3/21/12
• Outpatient-4/13/12 for tracheobronchitis, VC-250 ml
• Outpatient-7/11/12 increased weight, VC-170-200 ml
• Outpatient 9/16/13 Increased secretions, saline lavages, uses inexsufflator, uses DPS intermittently, VC 250 ml without ventilator
• Telephone update 7/2014 uses DPS approximately 4 hrs per day, off ventilator less than 2 hrs per day.
Patient 4

- 25 yo woman rear ended MVA 9/25/11
- Type II Dens fracture, C2 lateral mass fracture, spinal cord contusion, epidural hematoma C1-2, vertebral artery narrowing resulting in C1 ASIA A.
- C1-2 fusion 10/3/11
- Hospital course with spinal shock, autonomic dysreflexia
- ETT 9/25/11 Tracheostomy 10/3/11
- Admitted to Shepherd Center 10/7/11 Vital Capacity 0
- Admission ABG 7.46/ 40/84 Vent 530/ +5/ ++10/ 0.4/ 12
Patient 4

- 2 days later Assist control 14/ 900/ +5/ RA
- DPS placed about one month later programmed 3 days after
  25 mAmps all four 200 P-W all four
  Rate 16 Ramp 0 Inspir interval 1.1 VC 250
- Started off vent trials next day at 15 min/hr
- Off ventilator completely 3 days later
- On discharge –no resp meds, terbutaline 2.5 q 12h for bradycardia
Patient 4

• Last seen 4/25/14 for wire issues; has cuffless trach, good voice with finger occlusion, talking valve during day with DPS.
• At night, sleeps with DPS and open trach with hygrofilter.
• \( V_C \) 400 ml.
• Weight 270lb on admission to 171lb as outpatient
• One episode of pneumonia 1 month post discharge, none since then.
Patient 5

• 17 yo woman, thrown from horse, no helmet, 7/11/2011
• Occipital hyperextension, C2 avulsion fracture, C1-4 spinal cord injury, C4 ASIA A, T5-7 vertebral body comminuted fracture
• Admitted to a university medical center with spinal shock, intubated 7/11, trach 7/16
• Complications include pulmonary embolus on 7/16, MSSA pneumonia, UTI
• PMH—Concussion age 15, no hx respiratory disease
• Admission to Shepherd Center 7/22/11, atelectasis on CXR
• PSH—Tonsillectomy age 9
• Social History—nonsmoker

<table>
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<tr>
<th>Vital Capacity</th>
<th>Date</th>
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<tbody>
<tr>
<td>655 ml ?</td>
<td>7/22</td>
</tr>
<tr>
<td>200 ml</td>
<td>7/25</td>
</tr>
<tr>
<td>300 ml</td>
<td>8/01</td>
</tr>
<tr>
<td>300 ml</td>
<td>8/24</td>
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• Fluoroscopy 8/3 showed minimal diaphragm function.
Patient 5

• DPS placed 9/18, programmed 9/21
  9/21  R-15’s  L-25’s  P-W-200 all  Rate-18  Ramp-6
  10/5  R-20’s  L-25’s  P-W-200 all  Rate-16  Ramp-10
  10/17 R-25’s  L-25’s  P-W-200 all  Rate-16  Ramp-10
  11/7                                                    Rate-14
• On rate of 18 she felt dyspneic
• On ramp of 10 she tolerated the stimulus better
• Outpatient 3/13/14 $V_c$-340 ml off ventilator with DPS
Patient 6

• 57 year old male fell down stairs, unresponsive, apneic at scene, ETT at home, 9/4/2005.
• Admitted to local hospital, C2 fx, C2-3 retrolisthesis, spinal cord edema, C2-5, decadron.
• 9/5 RUL, RLL atelectasis then pneumonia
• Enterococcal sepsis source unknown
• C2-3 reduction and fixation 9/20
• Admitted to Shepherd Center 9/22.
Patient 6

• PMH—CAD with stent 2/2005, kidney stones
• PSH—back surgery, hernia, knee surgery
• Home meds—ASA, Zocor
• Complications include peptic ulcer with bleed treated with Endoclip, orthostatic hypotension, MSSA sputum treated with Augmentin, sacral sore stage II treated with wound vac
• Vital capacity 50-60 ml  9/21 and 10/10
• Discharged 11/25/05 on home ventilator, home health RN’s, in-exsufflator
• Readmitted to Shepherd 12/6/05 for LLL pneumonia, UTI and decubitus ulcer. Had debridement 12/9, suprapubic catheter placed, antibiotics and was discharged.
• Admitted to Shepherd 12/26/05 for fever-UTI, diarrhea (C. difficile neg).
• 1/11/06 UTI
• Admitted 3/2/06 aspiration(?) pneumonia, UTI, mucus plugging, hypotension.
Patient 6

- Readmitted 11/13/06 Urosepsis with Klebsiella blood and urine, MRSA colonization in sputum
- DPS implanted 3/1/07, discharged following day
- 4/7/07 using DPS 1 ½ hrs/day off vent
- 6/13/07 fever with ESBL Klebsiella
- 12/19/07 Mucus plugging, fever
- 1/30/08 using DPS 12 hrs/day off vent
- 8/27/08 using the ventilator to sleep at night only
Patient 6

- Multiple infections usually urine or skin, rarely respiratory and died 2011 from infections, altered mental state
- Last several years he was a peer support volunteer at Shepherd for spinal cord injured patients.
- Life span 6 years from time of injury
- Life span 4 years from time of implantation of DPS
Patient 7

- 18 yo man fell off the top of a semi- approx 20 feet to ground 7/24/12.
- ETT, then cricothyrotomy emergently, emergent bronch; pneumomediastinum same day.
- C2 transverse Fx, C2 distraction, ischemic injury to the anterior spinal artery, left vertebral artery dissection and occlusion, left internal and external carotid arteries occlusion.
Patient 7

• Left zygomatic arch, maxillary sinus, right mandible Fx- surgery and arch bars
• Spinal shock, pressors, bradycardia
• Pneumonia 8/1/12
• Esophagram 7/24 negative for leak
• IVC filter 7/27
• Peg 8/10
Patient 7

- Transferred to Shepherd Center 8/15/12  C1 ASIA A
- Fever to 103 on admission from sinusitis
- Bronchoscopy 8/15 for atelectasis
- PMH negative  PSH rod for femur fx 18 mo prior
- Social Hx  occasional cigarettes and ETOH
Patient 7

- $V_C$ 8/15/12 NA Day of admission
  9/19 NA
  9/20 300 ml
- Fluoroscopy 9/24/12 no movement
- Intraoperative test with phrenic motor point stimulation with no response 10/29/12
- Discharge 12/19/12 C1 ASIA A
- $V_C$ 4/3/13 200 ml out pt visit
can stay off the ventilator approx 5 min
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Thank you for your attention
History of Functional Electrical Stimulation (FES)

- Concept of electrical stimulation of the phrenic nerve began in the late 1700’s.
- Carvallo 1777 for resuscitation
- Hufeland 1783 for asphyxia
- Ure 1818 proved concept in freshly hung criminals.
- Duchenne 1849 in victims of cholera
- Israel 1927 in newborn apnea
- Sarnoff 1950’s in polio patients

Ducko, C. Innovations; 2011: 289-97
History of FES

- Glenn, W. 1964 Animal model of phrenic nerve stimulation
- Glenn, W. 1966 Use in chronic ventilatory insufficiency
- Glenn, W. 1972 Use in complete ventilatory support in spinal cord patients
- Mortimer, J. 1983 demonstrated diaphragm stimulation at the motor point.
- Onders, R. 1990’s led to technology of implantation of diaphragm electrodes via endoscopic surgery.
History of Functional Electrical Stimulation* (FES)

• Early adoption of FES techniques and equipment in the late 19th and early 20th century was complicated by medical quackery.
• Invention of the cardiac pacer in the 1950’s helped the acceptance of FES.
• The 1950’s brought in a new era of FES in the rehabilitation setting.

The Future of Respiratory FES?

- Diaphragm muscle atrophy of both slow-twitch and fast–twitch has been shown to occur within 18-69 hrs on mechanical ventilation with a decrease of cross-sectional areas of slow-twitch (57% loss) and fast-twitch (53% loss).¹
- Low frequency stimulation has been shown to increase or transform mixed fiber or fast-twitch fiber into type I slow–twitch muscle.²

¹ Levine et al. NEJM 2008;358:1327-35
The Future of Respiratory FES?

- Slow-twitch muscle has increased capillary density and mitochondrial volume, therefore more fatigue resistant.
- One study suggested short term FES (30 min/day) could reduce pathological changes and preserve diaphragm thickness and function.*

The Future of Respiratory FES?

- Posluszny et al* did retrospective analysis of 29 pts with trauma and cervical injury who had early (average 40 days) evaluation and placement of DPS.
- Delays included failure to wean, insurance coverage, IRB approval, etc.

*J Trauma Acute Care Surg. 2014;76: 303-10
The Future of Respiratory FES?

• 7 pts were non-stimulatable and not implanted.
• 22 pts were implanted on average 40 days post trauma.
• 16 pts (72%) were completely weaned off mechanical ventilation in 10.2 +/- 13.2, days with range of 1-45 days post implantation.
The Future of Respiratory FES?

• Of the six pts, 2 were later weaned after 6 months, 2 had partial weans using DPS alone less than 12 hrs, 1 pt used both DPS and ventilator “by preference”, and final pt was discharged to LTAC and had life prolonging measures withdrawn.
The Future of Respiratory FES?

• Of the 18 who were off ventilator, 12 did not require LTAC.
• The 12 pts were weaned in average of 5.7 days and were implanted at 11.1 days post trauma.
• 8 pts had complete recovery of respiration and had had the wires removed.
Other Devices and Procedures

• Surgical plication of a poorly functioning hemidiaphragm
• Intercostal or other nerve transfer to the diaphragm or phrenic nerve
• Intercostal pacing in quadriplegics with phrenic nerve injury\(^1\) with or without other diaphragm pacing.

\(^1\)DiMarco, A et al. Am J Respir Crit Care Med 1994; 150: 934-901
Devices
Stimulation of Expiratory Muscles

• Electrodes over the surface of the abdominal muscles\textsuperscript{1,2}
• Via lower thoracic spinal cord stimulation T9, T11, L1 implanted radiofrequency receiver-better \textsuperscript{3}
• Functional magnetic stimulation of abdominal muscles \textsuperscript{4}
• Not ready for prime time?

1. Linder, S. FES to enhance cough in quadriplegia. Chest 1993;103:166-9