



FREQUENTLY ASKED QUESTIONS (FAQS)

What is Synapse Biomedical Inc.?

Synapse Biomedical Inc. (SBI) was founded in September 2002 in Oberlin, Ohio. It was created to commercialize the NeuRx Diaphragm Pacing System (DPS)[™] developed over the course of 20 years through a joint effort of physicians and engineers at several institutions, including Case Western Reserve University, University Hospitals Case Medical Center and the Veterans Administration Medical Center. The company is focused on commercialization of its life-transforming neurostimulation technologies used in treating people with respiratory insufficiency. Synapse's Co-founder, CEO and President is Anthony Ignagni. The Chief Operating Officer is Moustapha Diop.

How can Synapse Biomedical help people with SCI or ALS?

Synapse has recently received FDA approval for the use of its NeuRx DPS[™] for patients with spinal cord injury who can no longer breathe on their own. Clinical trials are currently taking place for the use of its NeuRx DPS[™] in ALS patients to delay the onset of respiratory failure.. Those trials are taking place at Johns Hopkins in Baltimore, University Hospitals in Cleveland, Henry Ford Hospital in Detroit, Methodist Neurological Institute in Houston, the Mayo Clinic in Jacksonville, Mount Sinai in New York, Stanford University and California Pacific Medical Center - Forbes Norris. For more information on the ALS trial, please visit <http://www.synapsebiomedical.com/clinicals/als.shtml>

What is the NeuRx DPS[™]?

The NeuRx DPS[™] is a diaphragm pacing system, meaning it provides electrical stimulation to muscle and nerves that run through the diaphragm. The NeuRx DPS[™] is made up of four electrodes implanted in the diaphragm to stimulate the muscle, a fifth electrode under the skin to complete the electrical circuit, a connector holder, a cable and an external battery powered pulse generator.

The NeuRx DPS[™] was developed at Case Western Reserve University and the University Hospitals Case Medical Center. Funding was made possible in part by the Department of Veterans Affairs, who contributed more than \$1 million. In January 2008, the NeuRx DPS[™] was approved for sale in Europe, CE Registration #CE 518356. FDA HDE approval for spinal cord injury was granted in June 2008.

How does the NeuRx DPS[™] work?

As a diaphragm pacing system, the NeuRx DPS[™] provides pulmonary rhythm management by electrically stimulating the muscle and nerves throughout the diaphragm. When stimulated by the NeuRx DPS[™], the diaphragm contracts which mimics natural breathing and allows air to fill the upper and lower parts of the lungs rather than forcing air in with a mechanical ventilator. This is essentially the same process as in regular breathing

Unlike a ventilator, the NeuRx DPS[™] is silent. The patient is able to control turning on the stimulator when he or she chooses. In addition to stimulating the diaphragm, the NeuRx DPS[™] strengthens an SCI patient's diaphragm muscle. The ALS clinical study seeks to prove the NeuRx DPS[™] stimulation delays the weakening of the ALS patient's diaphragm muscle.

How long does the battery last?

There are two batteries in the NeuRx DPS™. The first is a user replaceable disposable lithium battery with 500 hours of battery life. The NeuRx DPS™ also has a permanent backup rechargeable battery with 8 - 24 hours of battery life that recharges every time a new disposable battery is inserted. The NeuRx DPS™ provides a tone every 10 seconds to alert the patient when the disposable battery needs to be replaced.

How is a person implanted with the NeuRx DPS™?

To insert the NeuRx DPS™ electrodes, surgeons create four holes smaller than a dime in the abdomen. In one hole, a laparoscope is inserted to see the diaphragm muscle and four electrodes are placed in areas near the phrenic nerves that control the diaphragm contractions. To find the best spot for each of the electrodes, the surgeon tests a number of areas on the under side of the diaphragm. The electrodes are attached through wires under the skin to a small external battery powered pulse generator to cause the diaphragm to contract. The procedure takes between 60 and 90 minutes and the small holes are closed with surgical band aids.

Who performs the surgery?

The surgery is accomplished at centers by a skilled laparoscopic surgeon. Typically they will be trained in general or thoracic surgery. The surgeries will initially be proctored by Dr Onder's or one of the clinical study center Surgeons who have performed a number of procedures. Additionally, initial support to the surgical team will be provided by a skilled service technician, typically a trained Respiratory Therapist or Registered Nurse.

Can any neurosurgeon perform this surgery?

No, although the procedure is performed to augment the phrenic nerve stimulation provided to the diaphragm, all neurosurgeons are not typically trained to perform minimally invasive abdominal surgery.

How can I be considered for this procedure?

For the latest information on centers in the US go to Synapse website http://www.synapsebiomedical.com/products/us_sci.shtml or enter your contact information on <http://www.synapsebiomedical.com/contact/inquiry.aspx>

Can I have this procedure performed at any hospital?

No. For SCI, the NeuRx DPS™ has been granted FDA approval as of June 2008. The device is available at select centers that have been trained to perform the procedure and support the rehabilitation process for the reconditioning of a patient's diaphragm.

How painful is the surgery?

The level of discomfort depends on the patients' level of sensation. Patients may feel tired or sore afterwards while their body heals from the surgery. Pain medications, if appropriate, can then be prescribed by your surgeon or physician.

What occurs after someone is implanted with the NeuRx DPS™?

Shortly after surgery, the electrodes are characterized by a clinician to determine the stimulation settings that will maximize diaphragm recruitment at a comfortable setting.

SCI patients that have been on mechanical ventilation for an extended period of time will have a short recovery period (3-5 days) before beginning their diaphragm conditioning sessions. Conditioning is the process of increasing diaphragm muscle strength. Conditioning usually occurs 3 – 5 times each day and initial sessions last between 15 – 30 minutes. They will receive specific conditioning instructions from your center prior to discharge from the facility. They will record each conditioning session in your conditioning diary.

Who was the first patient to use the NeuRx DPS™?

The first patient to be implanted was a 36-year old man from Ohio who was injured July 1998 in a swimming pool accident. In March 2000, 18 months after the incident, he underwent laparoscopic surgery, at University Hospitals in Cleveland, to implant the electrodes. After several months of diaphragm conditioning, he was weaned completely off his mechanical ventilator and could once again breathe on his own.

What is the longest use of the NeuRx DPS™ by an individual?

The NeuRx DPS™ has been implanted in 48 individuals in the United States with high-level spinal cord injury. The longest term patient was implanted March 6, 2000 and has been using the DPS System as his sole means of respiratory support (24 hours per day) for over seven years.

You can access patient testimonials on the Synapse website at www.synapsebiomedical.com/news/success/.

Tell me about Christopher Reeve's experience with the NeuRx DPS™.

Christopher Reeve was the third patient to be implanted with the NeuRx DPS™. After a fluoroscopic examination of diaphragm movement and studies of his phrenic nerve activity, it was determined that his phrenic nerves were normal and he qualified for the procedure, still in clinical trials at the time. On February 28, 2003, he underwent a 4 ½ hour surgery at University Hospitals Case Medical Center to implant the electrodes and lead-wires. Two days after his operation, he was back at work and gave a talk at Harvard University. On March 9, 2003, he returned to Cleveland to begin the reconditioning process of strengthening the diaphragm through intermittent stimulations. Unfortunately, Christopher Reeve did not achieve complete weaning but had successfully achieved durations of over 12 hour period off the ventilator. Christopher Reeve elected to continue using the system throughout his course of treatment until his death.

What are the costs associated with this procedure? Is it covered by insurance?

Because the cost will vary based on the benefit plan, patients will need to work with their center to provide them with information on how reimbursement is obtained and can assist them in their insurance preapproval process. Certain out-of-pocket costs may decrease after being implanted with the NeuRx DPS™. For example, transportation, ventilator disposables and electricity costs will likely decrease.

Synapse Biomedical, Inc. has established Medicare, Medicaid and private insurance reimbursement support with a reimbursement consulting firm to assist clinical trial centers in obtaining pre-approved patients coverage.

Does this surgery allow patients to be off a ventilator forever?

For spinal cord injury patients, the results have varied from patient-to-patient. It depends on the patient's motivation to reduce his or her reliance on positive pressure ventilation and the support of the caregivers. In clinical trials, of 50 patients implanted over 6 months:

- 1 out of 2 patients achieved full-time pacing and were able to eliminate their use of positive pressure ventilation.
- 2 out of 3 study participants pace over 12 hours per day and significantly reduced their time on positive pressure ventilation
- 9 out of 10 able to pace for >4 continuous hrs and many continue to work to condition and strengthen their diaphragm.

What is Spinal Cord Injury?

SCI is damage to the spinal cord that can result in loss of function, such as mobility or feeling.

Who has spinal cord injury and what is it caused by?

As of July 2005, the National Spinal Cord Injury Database estimates 225,000 – 288,000 individuals in the United States live with SCI and about 11,000 new cases of SCI occur each year. It is estimated that approximately 500 new cases of mechanical ventilator dependency occur each year that would be eligible for diaphragm pacing.

The leading causes of SCI injuries are vehicle crashes (47%), falls (22%) and violence (~14%). Other causes are trauma, sports related injuries or disease, such as polio or spinal bifida.

Are all SCI patients the same?

No. SCI can be divided into three groups depending on the location of the injury. High Tetraplegia (Tetra) injuries are cervical spine injuries between vertebra C1-C4, Low Tetra are cervical spine injuries between vertebra C5-C8 and paraplegia are typically vertebra injuries of thoracic, lumbar vertebra or sacrum. All of these injuries result in impairment of sensory and motor functions to a varying degree.

What are the effects of SCI?

The higher the site of the injury, the greater number of nerves affected, which can result in partial or complete paraplegia (legs). Tetra injuries can affect the arms and legs and in some instances cause ventilator dependency. A 20 year old TP patient with ventilator dependency has more than 14 years shorter life expectancy than a TP patient not on a ventilator.

The leading causes of death for spinal cord injury patients are pneumonia, pulmonary emboli and septicemia.

Is there a cure for SCI?

No, at this time there is no cure for spinal cord injury. New research and studies are constantly taking place, in efforts to one day find a remedy.

How can Synapse help people with SCI?

Synapse is currently marketing the NeuRx DPS™ that can allow some SCI patients, depending on the level of injury, breathe again without a ventilator. Some spinal cord injuries resulting damaged phrenic nerves; therefore, patients do not qualify for the implant.

What is Amyotrophic Lateral Sclerosis (ALS)?

ALS is a rapidly progressing, incurable and fatal neuromuscular disease that attacks the nerve cells responsible for controlling voluntary muscles. It is characterized by progressive weakness that results in paralysis. ALS is also known as Lou Gehrig's Disease and Motor Neuron Disease.

Who has ALS?

There are about 30,000 individuals living with ALS in the United States and about 6,000 people are diagnosed each year. People of all races and ethnic backgrounds are affected, but it is most often diagnosed in men ages 45-65.

What causes ALS?

For about 90-95% of patients, there is no clear cause of ALS. In about 5-10% of ALS cases, the disease is inherited.

What are the symptoms of ALS?

The earliest symptoms of ALS are cramping, stiffness, weakening or twitching of muscles. This can manifest itself in slurred or nasal speech, difficulty chewing or swallowing, and difficulty walking or running. ALS does not affect a patient's ability to see, smell, taste, hear or touch. It also does not usually affect the patient's mind or intelligence.

How does the NeuRx DPS™ work for Amyotrophic Lateral Sclerosis (ALS) patients?

The NeuRx DPS™ is currently under a controlled clinical trial. The study in ALS is determining if diaphragm pacing can be used to slow the decline in a patient's Forced Vital Capacity and delay the onset of respiratory failure. Data from the pilot study revealed the average pre-implant rate of decline was calculated at -2.4% per month and for patients with at least 9 months post-implant follow-up the rate improved to -1.0% per month.

It is also under investigation whether the NeuRx DPS™ may be effective in ventilator support of patients with ALS, either decreasing or eliminating the need for negative or positive pressure mechanical ventilation.

How can I get more information about Synapse or its NeuRx DPS™?

For more information, please visit <http://www.synapsebiomedical.com> or contact Synapse at info@synapsebiomedical.com or 300 Artino St., Oberlin, Ohio 44074.

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