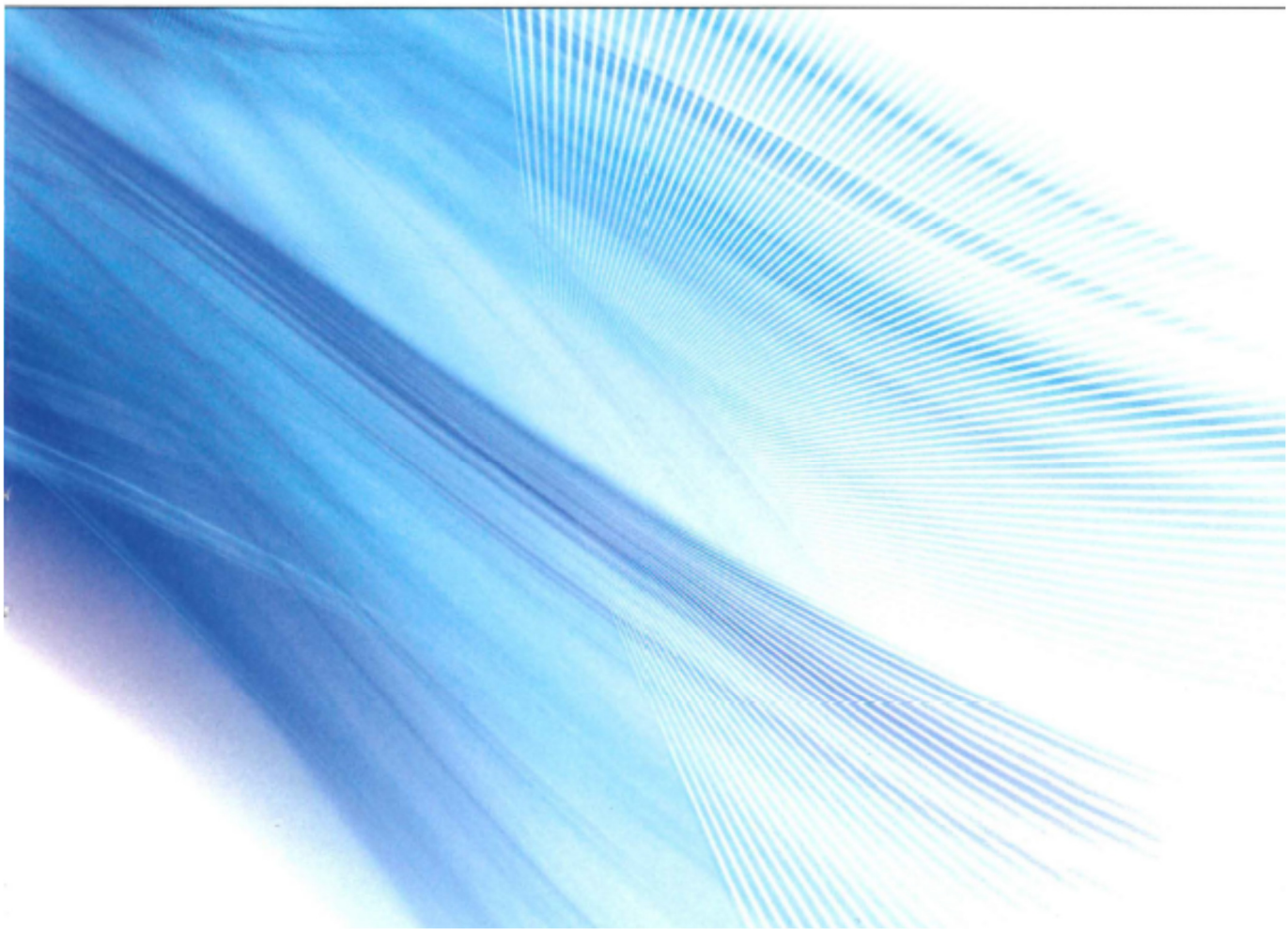
SYNAPSE
Biomedical Inc.

The SCI patient's guide to increasing independence with the NeuRx® Diaphragm Pacing System



PACING THE DIAPHRAGM

The NeuRx DPS® Program for People with Spinal Cord Injury (SCI) and Ventilator Dependency

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How can the NeuRx® Diaphragm Pacing System (NeuRx DPS®) improve the quality of life for me and my caregivers?

As someone who has experienced a spinal cord injury (SCI), or who cares for someone living with SCI, you are intimately familiar with the mental, physical, and emotional challenges that each passing minute brings to the life you have come to know since the injury occurred.

The state-of-the-art NeuRx DPS® is engineered to provide a means for more natural breathing and help liberate you from mechanical ventilation.

In a survey[1], 96.5% of users reported being happy or very happy with their decision to have the NeuRx DPS® implanted. They also reported using the NeuRx DPS® has:

- Increased their freedom and independence by allowing them to be less dependent on mechanical ventilation,
- Made transferring easier,
- Improved mobility, and
- Made them less noticed in public then when using a mechanical ventilator

[1] Monden KR, Coker J, Charlifue S, Bennett SJ, Draganich C, Coons D, Marino RJ, Berliner J. Long-Term Follow-Up of Individuals with Ventilator Dependent High Tetraplegia Managed with Diaphragmatic Pacing Systems. Arch Phys Med Rehabil. 2021 Mar 22:S0003-9993(21)00238-0. doi: 10.1016/j.apmr.2021.03.005. Epub ahead of print. PMID: 33766556.

Q What happens when I breathe?

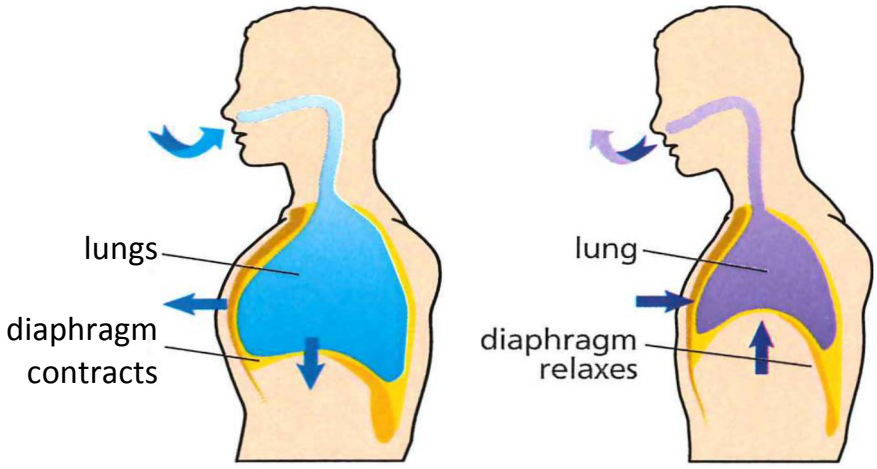
When you breathe in or inhale, the diaphragm (main breathing muscle) contracts and moves downward, causing your lungs to fill with air. The lungs take the oxygen from the air and provides it to your body. When you breathe out, or exhale, your diaphragm relaxes and moves upward, pushing carbon dioxide out of your body.

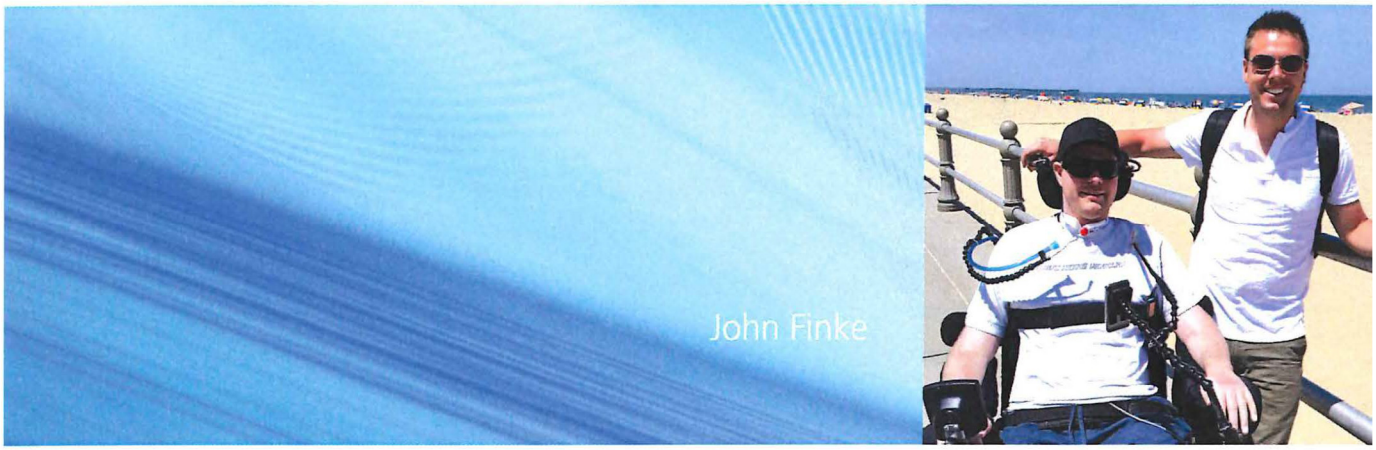
Q How is my breathing controlled?

The brain controls how often and how deeply we breathe. The brain sends signals down your right and left phrenic nerves (breathing nerves) causing your diaphragm to contract and relax.

Patients with high-level spinal cord injuries typically have diaphragm paralysis and cannot control their breathing. This diaphragm paralysis requires the use of a mechanical ventilator to breathe.

When the diaphragm contracts, the chest cavity enlarges, reducing the pressure inside. To equalize the pressure, air rushes into the lungs. When the diaphragm relaxes, the elasticity of the lungs and chest wall pushes air out of the lungs.





Q What is the NeuRx® Diaphragm Pacing System and how does it help the way an SCI patient breathes?

Unlike a mechanical ventilator, the NeuRx DPS® provides silent, rhythmic electrical stimulation to your diaphragm, causing it to contract. Initially in an SCI patient, this stimulation works to exercise and condition your diaphragm muscle, which has weakened from using a ventilator. With the assistance of the NeuRx DPS®, the breaths are provided similar to a natural, comfortable breathing pattern.

The system can achieve long-term replacement of mechanical ventilation for SCI patients with intact phrenic nerves.

The NeuRx DPS® consists of:

- Four electrodes implanted in the diaphragm
- A fifth electrode under the skin to complete the electrical circuit
- A connector holder
- A cable
- A small, external, battery-powered pulse generator (stimulator)

Your caregiver can turn the stimulator on and off when you choose. When it is off, you will likely need to return to mechanical ventilation support. The NeuRx DPS® settings are established by a trained clinician or your physician and can only be adjusted by them.

Q What does the NeuRx DPS stimulation feel like?

The sensation varies from patient to patient. Some feel nothing, while some describe a slight quivering feeling in their abdomen. Patients with sensation are aware that their diaphragm is moving, but they become less conscious of the movement as conditioning becomes part of their daily routine.

Q How is the NeuRx DPS implanted?

Charles Dowdy

A simple, minimally invasive outpatient procedure is used to implant the device's four biocompatible electrodes, two in each side of your diaphragm. To find the best locations, your surgeon will test a number of areas on the underside of your diaphragm. This is accomplished with a mapping instrument that stimulates the diaphragm's surface. The fifth electrode is placed just below the skin near the exit site of the other electrodes. Only a few stitches are needed to close the small incisions. The entire procedure lasts approximately 90 minutes.

Q Is the implantation surgery painful?

You may feel sore after your surgery, as your body heals. Your doctors can prescribe pain medications, if appropriate.

Q What should I expect before surgery?

Your phrenic nerves must be intact below the level of the spinal cord injury for you to benefit from this device. Your healthcare provider may do a phrenic nerve test (PNCS) or a nerve test during an x-ray (fluoroscopy) to check for diaphragm movement. The results of one of these tests may show if you could be a candidate for the NeuRx DPS®.

Q What should I expect during surgery?

The surgeon will make four short cuts (incisions) in the skin of your abdomen. These incisions will give the surgeon access to your diaphragm. The incision will be about half an inch long. A tube will be placed into each incision. Carbon dioxide gas will be pumped through one of the tubes to fill your abdomen. A small tool with a camera on the end (laparoscope) will be inserted into the tube in your abdomen.

The surgeon will then insert a tool called a probe through one of the tubes. The surgeon will use the probe to test several spots on your diaphragm to find the best locations to place the electrode wire tips.

Once the surgeon has found the 4 best locations, the surgeon will then insert the tips of 4 electrode wires in these locations. The surgeon will put the other ends of the 4 electrode wires on the outside of your body. These 4 wires will come out through your skin in the same area. A fifth electrode wire is then placed just beneath the skin in the same area to complete the wiring.

After surgery, you will be able to see about 2 inches of each electrode wire outside of your body.

Q What should I expect after surgery?

Depending on your condition before and after surgery, you may need to spend the night in the hospital. You should discuss this with your surgeon before your surgery.

While you are recovering from surgery, a healthcare provider will work with you to determine comfortable stimulation settings that will maximize your diaphragm's performance. The device's settings can only be adjusted by a trained clinician.

Before you leave the hospital, your care team will teach you and your caregivers how to use the NeuRx® external pulse generator (EPG). You will receive specific conditioning instructions from your care team. Each SCI patient's success of weaning from the ventilator with the NeuRx DPS® varies. Yours will depend upon your physical condition, your motivation to reduce your reliance on positive pressure ventilation, and the support of your caregivers.

Q What is the downside to the implantation surgery other than the usual surgical risks?

Clinical evidence has demonstrated the NeuRx DPS® treatment and use is safe when used according to directions. The most commonly reported risk is called capnothorax. It is caused by air going through the diaphragm and into your chest during the surgical procedure. This can occur with any laparoscopic surgical procedure and typically goes away on its own. If necessary, your surgeon may remove the air from your chest in the operating room.

Q Who is eligible to use the NeuRx DPS®?

A consultation with your physician or a physician at one of our approved treatment centers can help determine your eligibility. You can view our growing list of approved treatment centers throughout the world by visiting our website at http://www.synapsebiomedical.com/physician-locator/; or contact us toll-free: 888-767-3770 extension 137.

Q I have been on a ventilator for over 20 years. Am I still a candidate for the NeuRx DPS®?

Yes. Treatment success is not dependent on time on a ventilator. It is dependent on whether you have intact phrenic nerves to stimulate the diaphragm. One of our patients was on a ventilator 28 years before treatment.

Q I can breathe during the day but use a ventilator at night. Can I use the NeuRx DPS® only at night?

Yes. If you only use a mechanical ventilator at night, you may benefit from the NeuRx DPS®. Talk to your physician about using the NeuRx DPS®.

"The Synapse diaphragmatic pacemaker has helped restore early breathing function in numerous patients suffering paralysis and has become an integral part of our treatment protocol."

Dr. Matthew Kaufman

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Can the NeuRx DPS® match the number of breaths I receive from my ventilator?

The NeuRx DPS® can be set to between 8 and 18 breaths per minute. You are provided two external pulse generators (stimulators) so one can be a programmed with different settings if desired.

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Can I use a cough-assist device with the NeuRx DPS®?

Yes. All forms of secretion clearance may be used while using the NeuRx DPS®.

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Will my speech change when using the NeuRx DPS®?

Because you have been on a ventilator and your diaphragm has gotten weak, your speech will be softer in the beginning of the conditioning process. As the condition of your diaphragm improves, your breathing capacity (Tidal Volume) will typically increase giving you more natural sounding speech.

Q How do I eat while using the NeuRx® stimulator?

Just as you first had to learn to eat while being ventilated, your medical team will work with you to teach you how to eat while pacing. It is recommended that you initially use a speaking valve on your tracheostomy tube to help prevent aspiration of food.

Q Will I get my sense of smell and taste back?

Patients have reported that they have regained some smell and taste once they are able to use the NeuRx DPS® with their tracheostomy capped.

Q Will I lose my skilled nursing when I go off the ventilator?

You should check with your insurance provider regarding the level of support and whether this could be an issue. Some insurers restrict your need for support to your condition of quadriplegia with tracheostomy and need for suctioning.

Q Are the costs of the NeuRx DPS® and the implantation procedure covered by my health insurance?

Your costs related to the NeuRx DPS® will depend upon your specific benefits plan. You'll need to coordinate information regarding pre-approval and reimbursement processes with your healthcare provider and your insurance company. Synapse Biomedical, Inc. has provided treatment centers with insurance reimbursement information to assist you in obtaining coverage.

You may find that certain out-of-pocket costs may not be covered by your insurance. It is recommended that you:

- Aggressively follow the appeals process for each individual insurance company. Be sure that the doctor writes very thorough documentation in support of the need for continued care coverage. This will be dictated by the level of injury and most certainly, anyone above C4, who would be the likely candidates for this system, will need intense care coverage for other reasons than ventilation.
- See the United Spinal Association website for more information regarding insurance coverages (https://askus-resource-center.unitedspinal.org/index.php?pg=kb.book&id=36). As noted, it is important to provide statements/expert opinions/articles that support the need.

Additional resources:

- Contact the National Association of Insurance Commissioners (https://content.naic.org/state_web_map.htm) for each particular state if an appeal is denied. Inquire if the state has a Health Insurance Ombudsman who could be helpful with the particulars of an appeals process. Insurance companies should have a medical review committee that can be asked to review a request for coverage.

Q How long has the NeuRx DPS® been in development?

The NeuRx DPS® was developed over a 20-year period at University Hospitals and Case Western Reserve University in Cleveland, Ohio. The innovative research performed at these institutions has led to significant advances in state-of-the-art electrical stimulation, enabling patients to enhance their independence and quality of life.

The first clinical implant of the NeuRx® DPS was performed in March 2000. A patient from the clinical study has used it continuously since 2003 without the use of a ventilator.

Q What is the NeuRx® Diaphragm Pacing System's proof of performance?

Completed in 2007, our clinical trial of 53 high-level spinal cord injury patients implanted with the NeuRx DPS® revealed:

- 96.2% (51/53) participants were able to breathe without the assistance of a mechanical ventilator for at least 4 continuous hours a day
- 58.5% (31/53) participants were able to breathe without the assistance of a mechanical ventilator for 24 hours daily use

In addition to being approved for sale in the U.S and Europe, the NeuRx DPS® is approved by PMDA in Japan and has been distributed in Canada, Australia, Brazil, Israel and other countries in the Middle East, Scandinavian countries, South Africa, Switzerland, and other countries in South America and North Africa. To date, over 2,000 NeuRx DPS® devices have been implanted world-wide.

Q How long has Synapse Biomedical been in business?

Synapse Biomedical, Inc., headquartered in Oberlin, Ohio, was founded in 2002 to develop and advance the NeuRx® Diaphragm Pacing System and make it commercially available and affordable for all those who suffer from respiratory insufficiency due to spinal cord injury.

Q Where can I learn about people who have used the NeuRx DPS®?

You can access patient testimonials and success stories on the Synapse Biomedical website: www.synapsebiomedical.com

Insert Kelly Blanton Picture

For more information about the NeuRx® Diaphragm Pacing System, or to submit an email inquiry, contact us at:

Synapse Biomedical, Inc.
300 Artino Street
Oberlin, Ohio 44074
Toll-free: 888-767-3770
Fax: 440-774-2572

Synapse Biomedical Europe
7 Rue de la Libération
95880 Enghien Les Bains, France
Tel: +33 (0) 1.34.16.49.11
Fax: +33 (0) 1.74.18.08.19

info@synapsebiomedical.com

www.synapsebiomedical.com

Humanitarian Use Device

Authorized by Federal Law for the use in the treatment of respiratory insufficiency for high level spinal cord injured patients. The effectiveness of this device fir this use has not been demonstrated

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

NeuRx® Diaphragm Pacing System (NeuRx DPS®): Product technical manual must be reviewed prior to use for detailed disclosure.

INTENDED USE

The NeuRx DPS® is intended for use in patients with stable, high spinal cord injuries with stimulatable diaphragms, but who lack control of their diaphragms. The device is indicated to allow the patients to breathe without the assistance of a mechanical ventilator for at least 4 continuous hours a day. For use only in patients 18 years of age or older.

CONTRAINDICATIONS

The NeuRx DPS® is contraindicated in patients who the physician determines are not candidates for surgical procedures due to physical or mental conditions.

WARNINGS/PRECAUTIONS/ADVERSE EVENTS

This device should be kept out of the reach of children. Safety has not been established for pregnancy, patients under the age of 18, patients with suspected or real heart problems, or patients who have implanted electrical devices or epilepsy. The long-term effects of electrical stimulation of the diaphragm are unknown. This device is electrically powered and may produce tissue damage or electrical hazard if improperly used. The system may be affected by excessive moisture, severe mechanical shock, diathermy, and electro cauterization. Implanted patients should not be connected to high-frequency surgical equipment or subjected to magnetic resonance imaging (MRI). Care should be taken to avoid operation of this device in close proximity to shortwave or microwave therapy equipment. Discontinue use of this device if skin in the implant area becomes swollen, infected, or inflamed or if there are skin eruptions such as phlebitis, thrombophlebitis, or varicose veins. Adverse events related to the system include capnothorax, equipment failure leading to loss of breathing, infection, airway compromise, spasms, pain or discomfort with stimulation, and difficulty eating. Patients must have a mechanical ventilator available at all times. Caregiver availability and monitoring should be consistent with when a ventilator is used.