Synapse Biomedical, Inc.

Integrating Neurostimulation Technology with Standard of Care

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TransAeris® System

- Granted Emergency Use Authorization (EUA) by FDA
  - The TransAeris Diaphragm Pacing System may be effective for emergency use to treat patients by assisting in weaning patients off ventilators in healthcare settings during the COVID-19 pandemic
  - The known and potential benefits of the such products, for such use, outweigh the known and potential risks of such product
  - There is no adequate, approved, and available alternative to the emergency use of the TransAeris Diaphragm Pacing System for treating patients during the COVID-19 pandemic.
- TransAeris is indicated for use in the prevention and treatment of Ventilator-Induced Diaphragm Dysfunction (VIDD).

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Ventilator-Induced Diaphragm Dysfunction

- VIDD first defined by Vassilakopoulos (2004):
  "loss of diaphragmatic force-generating capacity that is specifically related to the use of mechanical ventilation"
- Since 1994 there have been over 50 animal studies examining effect of MV on the diaphragm
- Since the 2008 NEJM article, over 20 studies in humans have corroborated the animal studies, with reports of:
  - 35% reduction in diaphragm force following 2 hours under anesthesia
  - Diaphragm pressure rapidly decreasing over the first 5 – 7 days of MV
  - Diaphragm thickness decrease of 6% with 1 week of MV
  - 32% reduction in twitch airway pressure over course of 1 week of MV support

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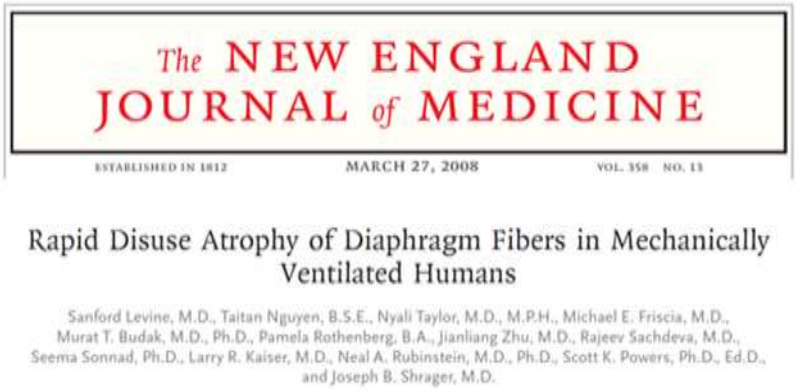
Why Temporary Diaphragm Pacing?

Disuse causes diaphragm atrophy translating to longer stays and higher cost



The NEW ENGLAND JOURNAL of MEDICINE

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Rapid Disuse Atrophy of Diaphragm Fibers in Mechanically Ventilated Humans

Sanford Levine, M.D., Taitan Nguyen, B.S.E., Nyali Taylor, M.D., M.P.H., Michael E. Friscia, M.D., Murat T. Budak, M.D., Ph.D., Pamela Rothenberg, B.A., Jianliang Zhu, M.D., Rajeev Sachdeva, M.D., Seema Sonnad, Ph.D., Larry R. Kaiser, M.D., Neal A. Rubinstein, M.D., Ph.D., Scott K. Powers, Ph.D., Ed.D., and Joseph B. Shrager, M.D.

- Rapid conversion to Type 2b fast twitch muscle fiber
- Diaphragm thickness decreases rapidly
- Most patients wean quickly from mechanical ventilation, although ~25% experience difficulty.
- In the U.S. that translates to ~400,000 patients per year, growing at 5.5% per year
- Post-operative pulmonary complications are a major cause of morbidity & mortality and require longer lengths of stay

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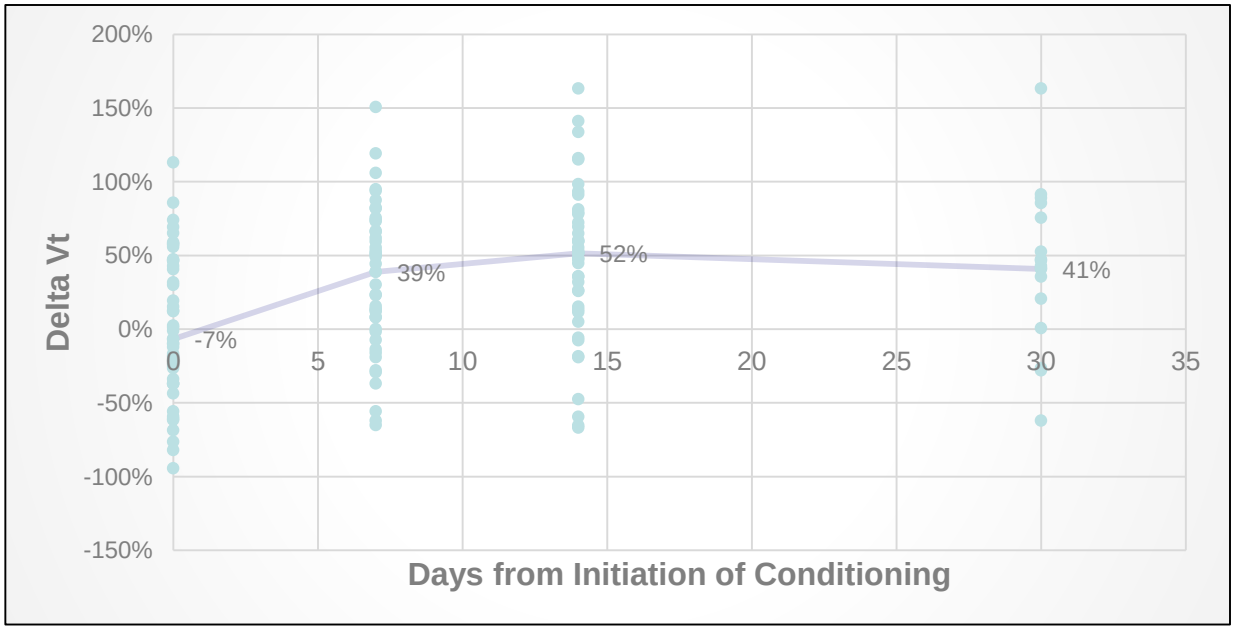
Diaphragm Conditioning Improves Diaphragm Function with Stimulation

- Spinal cord patients show pure model of diaphragm conditioning, no volitional influence
- NeuRx® Diaphragm Pacing study showed a 46% increase from -7% (under) basal tidal volume (Vt) requirements to +39% (over) in 7 days of conditioning



50 patient study of high level spinal cord injury
Median 2 years of disuse atrophy (post-injury)

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NeuRx DPS® leads to TransAeris®

- TransAeris is the continuation of the NeuRx® Diaphragm Pacing System used for over 15 years
- More than 2,200 NeuRX DPS® patients implanted worldwide
- Both systems share the same electrode with 1 minor difference making it temporary and removable
- Both systems use the same programming parameters with the following improvements:
  - Pulse Intensity is increase/decrease with just using an arrow up & down
  - Burst mode available to help address patient's comfort with stimulation

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The TransAeris® System

- A temporary percutaneous, intramuscular diaphragm stimulator intended for patients at risk of, or on prolonged positive pressure mechanical ventilation.
- Indicated for use in the treatment of Ventilator-Induced Diaphragm Dysfunction (VIDD)
- Less than 30 days, single patient, in-hospital use

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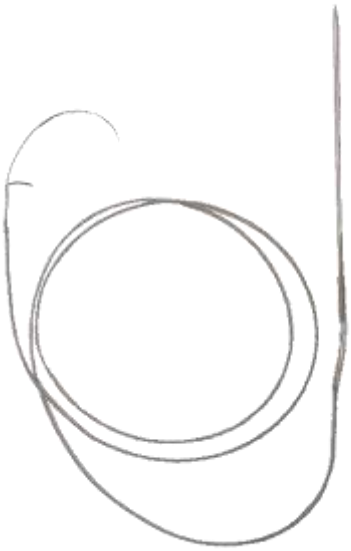
The TransAeris® System

- Simple set of 3 components:



4 TransLoc®
Electrodes

TransAeris®
Stimulator

2 FrictionLoc®
Connectors

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Patients that may benefit…

- Surgical patients at risk of prolonged mechanical ventilation (MV) may benefit from prophylactic placement of TransLoc® electrodes:
  - *High risk cardiac procedures*
  - *Upper abdominal procedures*
  - *Lung transplants*
  - *Abdominal aortic aneurism repairs*
  - *Complex open surgeries >2 hrs.*
- When done at the time of an open procedure, TransLoc electrode placement takes just minutes

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Diaphragm Access & Implantation

Exposure Diaphragm Access, Cardiac Surgery

TransLoc Implantation, Cardiac Surgery

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When to start TransAeris stimulation?

- This is a decision based on the surgical procedure performed and/or patient's weaning progress
  - You may start TransAeris stimulation upon admission to the ICU
  - You may start TransAeris stimulation if patient is not progressing in their wean
    - 24-96 hrs after initiation of MV

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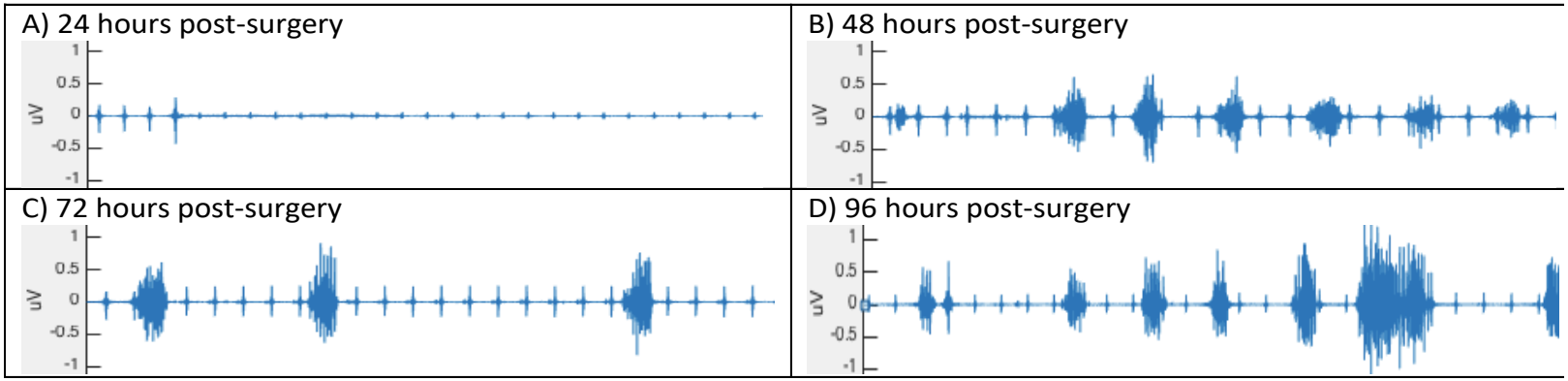
Clinical Experience

- CE Mark in Europe (CE 518356)
- Bilateral Lung Transplant Patients, Leuven, Belgium
  - Demonstrates diaphragm spontaneous EMG activity return
  - Stimulation started as soon as patient in ICU
  - Shows successful return of function and ability to volitionally control breathing at 96 hours



Diaphragm Activity (15 second samples)

Panel A recorded 24 hours post-surgery, patient sedated on ventilation
Panel B recorded 48 hours post-surgery, patient sedated on ventilation
Panel C recorded 72 hours post-surgery, awake on ventilation
Panel D recorded 96 hours post-surgery, volitionally breathing

Feasibility of diaphragm pacing in patients after bilateral lung transplantation (Testelman et al, 2017) - Clinical Transplantation

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Clinical Experience

- The TransLoc electrode component of the TransAeris System was the subject of an IDE study (G150040) involving the NeuRx DPS
  - The primary safety endpoint of the study was the incidence of adverse device effects (procedure and device related adverse events) from placement through electrode removal.
- A Pilot study of TransAeris® system in open cardiac surgery patients at risk of prolonged mechanical ventilation began in March, 2020 and concluded in April, 2021 (IDE G170294).
- A Randomized Study of TransAeris® system for Enhanced Recovery After Surgery (ERAS) in cardiac surgery patients at risk of prolonged mechanical ventilation began in August, 2021.
- A multi-center pivotal study of the TransAeris® system is planned for 2022.

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