From the Midwestern Vascular Surgical Society

Temporary diaphragm pacing for patients at risk of prolonged mechanical ventilation after extensive aortic repair

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ABSTRACT

Objective: Prolonged mechanical ventilation (MV) after extensive aortic reconstructive surgery is common. Studies have demonstrated that diaphragm pacing (DP) improves lung function in patients with unilateral diaphragm paralysis. The goal of this study is to determine whether this technology can be applied to complex aortic repair to reduce prolonged MV and other respiratory sequelae.

Methods: A retrospective review was performed of patients who underwent temporary DP after extensive aortic reconstructive surgery between 2019 and 2022. The primary end point was prolonged MV incidence. Other measured end points included diaphragm electromyography improvement, length of hospitalization, duration of intensive care unit stay, and reintubation rates.

Results: Fourteen patients deemed at high risk of prolonged MV based on their smoking and respiratory history underwent DP after extensive aortic repair. The mean age was 70.2 years. The indications for aortic repair were a thoracoabdominal aortic aneurysm (n = 8, including 2 ruptured, 2 symptomatic, and 1 mycotic), a perivisceral aneurysm (n = 4), and a perivisceral coral reef aorta (n = 2). All patients had a significant smoking history (active or former) or other risk factors for ventilator-induced diaphragmatic dysfunction and prolonged MV. The mean total duration of MV postoperatively was 31.9 hours (range, 8.1-76.5 hours). The total average pacing duration was 4.4 days. Two patients required prolonged MV, with an average of 75.4 hours. Two patients required reintubation. No complications related to DP wire placement or removal occurred.

Conclusions: DP is safe and feasible for patients at high risk of pulmonary insufficiency after extensive aortic reconstructive surgery. (J Vasc Surg Cases Innov Tech 2023;9:101319.)

Keywords: Diaphragm pacing; Respiratory failure; Ventilator-induced diaphragmatic dysfunction

Pulmonary insufficiency is the most frequent complication after complex aortic repair. Its incidence is reported to be as high as 41% after thoracoabdominal aortic repairs even in experienced centers.[1-4] Respiratory complications are also reported in up to 30% of infrarenal aortic repairs.[5,6] Long incisions, disturbance of accessory muscles for respiration, frequent division of the diaphragm, and the use of single-lung ventilation in patients who often have compromised baseline pulmonary function contribute to the development of prolonged postoperative mechanical ventilation (MV; ventilation >72 hours), increased length of stay, greater morbidity and mortality, and significantly higher costs.

First described in 1976 by Kim et al,[7] diaphragm pacing (DP) has been historically used to wean chronically ventilator-dependent patients (ie, central hypoventilation syndrome or cervical spinal cord injury) from MV.[8,9] Recently, its use has been applied to a broader range of indications such as bilateral lung transplantation and patients with amyotrophic lateral sclerosis to delay eventual MV.[8-11] These studies have demonstrated the physiologic advantages DP can offer in the acute setting. Onders et al[10] found greater fluoroscopic movement in

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the diaphragm, increased muscle thickness, and better forced vital capacity (FVC) in patients with amyotrophic lateral sclerosis. In parallel, technology for temporary DP has been developed for short-term inpatient use for patients at high risk of prolonged MV, and its feasibility has been proved in a Food and Drug Administration–approved trial.[12] The objective of the present study is to evaluate the feasibility of temporary DP to mitigate the risk of prolonged MV and ventilator-induced diaphragmatic dysfunction (VIDD) in high-risk patients undergoing extensive aortic reconstructive surgery.

ARTICLE HIGHLIGHTS

- **Type of Research:** A single-center, retrospective cohort study of prospectively collected data
- **Key Findings:** Temporary diaphragmatic pacing improves contractility to mitigate the development of ventilator-associated diaphragm dysfunction.
- **Take Home Message:** Temporary diaphragm pacing might mitigate the development of ventilator-induced diaphragm dysfunction and prolonged mechanical ventilation after extensive aortic repair.

METHODS

Study design. A retrospective analysis was conducted of a prospectively collected, nonrandomized, interventional experience using a Food and Drug Administration–authorized temporary DP system (TransAeris DPS; Synapse Biomedical) for patients undergoing complex open aortic repair at a single tertiary care institution between 2019 and 2022. The demographic information and operative and postoperative data were collected prospectively and analyzed retrospectively. Statistical analysis was performed on the parameters of postoperative MV, total MV, intensive care unit stay, total hospital stay, need for reintubation, and diaphragmatic electromyography (dEMG) characteristics before and after the procedure. Prolonged MV was defined as the use of ventilator support for >72 hours after the procedure without an extubation period.[1,2] VIDD was recognized in patients with prolonged MV in addition to absent or poor dEMG activity.

Patients were deemed at high risk of pulmonary complications based on their smoking history (active or former) and pulmonary function test (PFT) results. Aortic operations were considered complex or extensive if they involved thoracoabdominal repair, paravisceral, suprarenal or juxtarenal repair, infrarenal abdominal aortic surgery with additional renovisceral debranching procedures, or reoperative fields from prior open or endovascular surgery requiring explantation. Patients with prior diaphragmatic intervention or requiring more extensive diaphragmatic repair, including plication or advanced reconstruction, were excluded.

The institutional review board of University Hospitals Cleveland Medical Center approved the present study (approval no. 20210752) and waived the requirement for patient informed consent.

Diaphragm pacing. On completion of aortic repair and reapproximation of the diaphragm (in the setting of a throacoretroperitoneal approach), two electrodes were implanted in the right (if exposed) and left hemidiaphragms next to the location where the phrenic nerve enters the central tendon (Fig 1). The electrodes were implanted into the diaphragm such that the stimulating surface of each electrode was completely within the muscular layers (Fig 2). A barb at the terminal end served to anchor each electrode in the tissue. The electrodes were externalized to exit the thoracic cavity in as direct a path as possible to the percutaneous exit site to facilitate easier removal. This was accomplished using straight needles passed through the skin. The electrodes were secured in the skin with a suture.

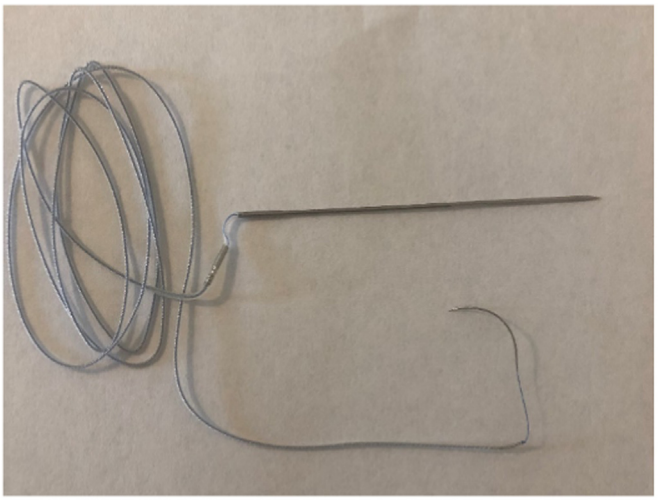

Fig 1. The temporary diaphragm pacing (DP) electrode is a double helix of stainless steel with a Teflon-coated, 9-mm, de-insulated stimulating tip. The curved needle is used to pull the exposed 9-mm tip into the muscle and then removed. The straight needle allows it to be removed through the chest or abdominal wall.

When patients entered the ICU, the hemidiaphragms were stimulated by connecting the electrodes to the stimulator (Fig 3). Stimulator programming was optimized to elicit diaphragm recruitment without pain or discomfort from the stimulation. Programmable parameters include intensity, frequency, inspiratory time, and respiratory rate. The respiratory rate was set to one breath per minute higher than the mechanical ventilator setting. This setting was chosen such that the stimulation, if strong enough to elicit a diaphragm contraction,

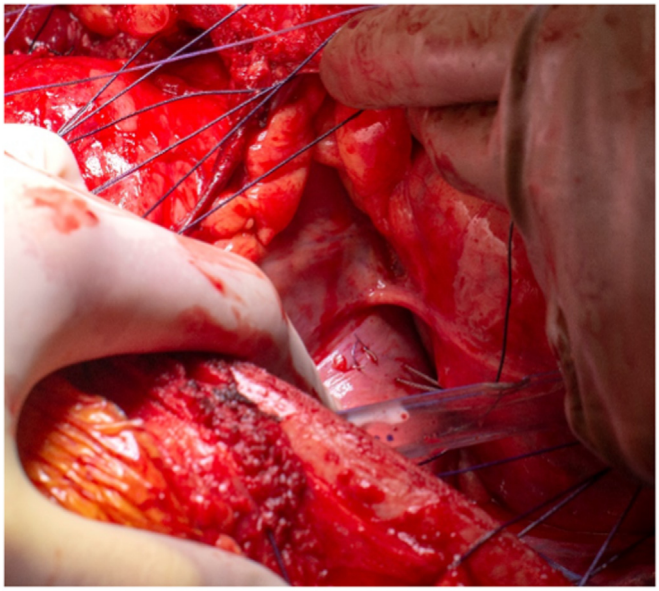

Fig 2. Intraoperative photograph of an in vivo example of diaphragm pacer placement showing two electrodes in the superior left diaphragm inferior to the phrenic nerve entering the diaphragm before closure of the thoracoabdominal incision.

Fig 3. External pulse generator used to stimulate the diaphragm to prevent atrophy.

would trigger the ventilator and avoid any asynchronies. The stimulus intensity was adjusted upward until the patient reached the threshold for pain or discomfort and then was reduced to below that threshold. Stimulation was then left on continuously, except during dEMG recordings or adverse events that necessitated turning the stimulation off. Throughout the stimulation period, the intensity and frequency could be increased or decreased to elicit a stronger contraction or address pain and/or discomfort issues. DP was continued while the patient was receiving MV until extubated and the patient's respiratory status was no longer compromised with good dEMG activity. Once the patient was transferred from the ICU to a regular floor bed with no DP for ≥24 hours, the electrodes were removed.

dEMG tracings are bipolar recordings between the two electrodes in each hemidiaphragm referenced to the surface in different electrodes with a sampling rate of 1 KHz (Fig 4). The dEMG tracings will also show ECG artifacts picked up by the electrode. dEMG activity was continuously monitored and evaluated during normal respiration, maximum respiration during sleep, and during any use of noninvasive positive pressure ventilation after extubation (Fig 5). dEMG was the primary mode of

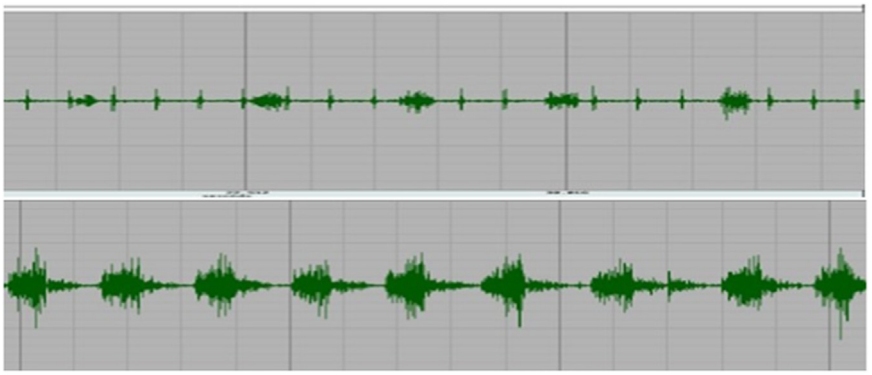

Fig 4. Example of diaphragmatic electromyography (dEMG) tracing. **Top,** Recording showing baseline dEMG activity after pacer placement immediately postoperatively with small bursts of diaphragm activity. **Bottom,** Measurement showing significantly improved dEMG activity after diaphragm pacing (DP) before pacer electrode removal.

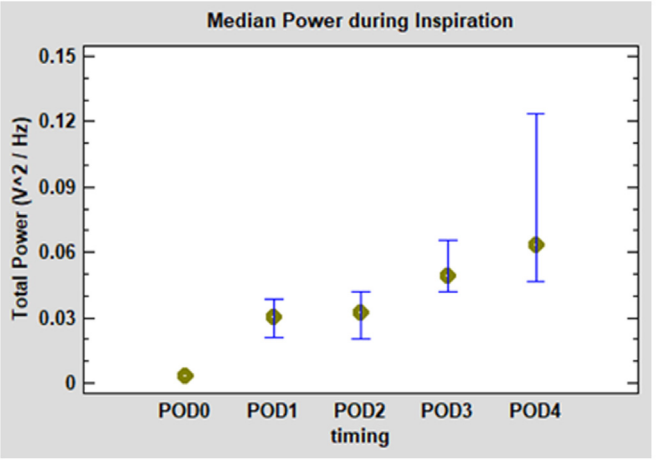

Fig 5. Example of timeline measuring median power during inspiration with significant improvement during the postoperative course resulting from diaphragm pacing (DP). Patients who remain ventilated and were apneic were recorded at 0. *POD,* Postoperative day.

assessing the postoperative function of the diaphragm. The recordings were analyzed before initial DP and daily after the operation. These were categorized into absent, near absent, weak, and good. All the patients underwent preoperative nerve blocks (erector spinae or transversus abdominis depending on the exposure) performed by anesthesia staff with postoperative multimodal pain regimens (muscle relaxants, narcotics, and neuropathic and anti-inflammatory medications) and scheduled nursing assessments to confirm adequate pain control. Two patients also underwent intraoperative cryoablation of intercostal nerves.

RESULTS

During the study period, 173 aortic operations were performed by the senior author. Of these, 79 were complex aortic reconstructions. A total of 14 patients (9 men and 5 women) at high risk of prolonged MV and VIDD underwent temporary DP. Of the 14 procedures, 8 were thoracoabdominal and 4 were complex abdominal aortic repairs, 1 was thoracic bifemoral bypass, and 1 was a transperitoneal renovisceral debranching procedure. Of the thoracoabdominal surgeries, five were to treat symptomatic or ruptured thoracoabdominal aortic aneurysms (TAAAs).

The mean age was 70.2 ± 8.3 years (range, 57-81 years; median, 74 years). All patients had a significant smoking history (4 active and 10 former smokers). The duration of smoking cessation ranged from 1 month to 27 years. Of the 14 patients, 13 were White and 1 was Black/African American. Preoperative PFT results were available for six patients, with an average forced expiratory volume in 1 second (FEV_1) of 1.6 L (median, 1.6 L), FVC of 2.9 L (median, 2.7 L), and FEV_1/FVC ratio of 58.9 (median, 61.9). The available baseline PFT results for the individual patients are detailed in the Table. Six patients were symptomatic

Table. Patient characteristics and data after diaphragmatic pacer placement and aortic surgery

Pt. No.	Age, years; sex	Risk factors	Surgery	MV, hours		ICU, days	FEV_1, L (%)		dEMG: right; left		Diaphragm division
				Postop	Total		Before BD	After BD	Baseline	Follow-up	
1	60; M	Former smoker	Type III TAAA repair	17.62	38.59	4	—	—	NA; weak	NA; good	Yes
2	76; M	Former smoker	Ruptured type III TAAA repair	11.72	19.87	5	—	—	NA; weak	NA; good	Yes
3	81; M	Former smoker, COPD	Mycotic type V TAAA repair	17.60	26.87	2	1.81 (64)	1.94 (69)	NA; weak	NA; good	Yes
4	75; F	Former smoker, COPD	Type V ruptured TAAA repair	7.75	15.78	10	1.68 (81)	—	NA; weak	NA; good	Yes
5	61; F	Active smoker, COPD	Type IV TAAA repair	27.43	38.88	5	1.55 (68)	1.59 (70)	NA; near absent	NA; good	Yes
6	66; M	Active smoker, COPD	Renovisceral debranching	13.77	24.27	6	2.38 (93)	1.96 (77)	Near absent; near absent	Good; good	No
7	79; F	Former smoker	Type IV TAAA repair	64.98	76.48	5	1.29 (68)	1.25 (63)	NA; absent	NA; good	Yes
8	61; M	Former smoker, COPD	Juxtarenal AAA repair	8.42	54.37	3	—	—	Near absent; good	Good; good	No
9	57; F	Active smoker, COPD	Thoracic bifemoral bypass	11.62	16.79	4	—	—	NA; good	NA; good	Yes
10	77; M	Former smoker, COPD	Juxtarenal AAA repair	6.93	22.73	5	0.95 (30)	1.49 (48)	NA; good	NA; good	Yes
11	62; M	Former smoker	Aortobifemoral bypass	8.45	8.45	2	—	—	Good; good	Good; good	No
12	74; F	Active smoker	Juxtarenal AAA repair	8.12	8.12	5	—	—	NA; absent	NA; good	No
13	80; M	Former smoker	Ruptured type IV TAAA repair	13.83	74.15	8	—	—	NA; absent	NA; good	Yes
14	74; M	Former smoker	Type IV TAAA repair	9.15	54.98	5	—	—	NA; absent	NA; good	Yes

BD, Bronchodilator; *COPD,* chronic obstructive pulmonary disease; *dEMG,* diaphragm electromyography; *F,* female; *FEV_1,* forced expiratory volume in 1 second; *ICU,* intensive care unit; *M,* male; *MV,* mechanical ventilation; *NA,* not applicable; *Postop,* postoperative; *Pt. No.,* patient number; *TAAA,* thoracoabdominal aortic aneurysm.

and/or had a ruptured TAAA, and preoperative PFTs could not be obtained owing to the urgent nature of their surgery.

The operative indications and disease extent are detailed in the Table. Overall, 10 patients had unilateral temporary DP wires placed in the left hemidiaphragm. One patient underwent right hemi-DP because of a history of chronic left diaphragm paralysis but required operative plication and, thus, was excluded from analysis. Bilateral DP was effected in the remaining four patients who underwent transperitoneal aortic repair.

The mean total MV duration during the operation was 9.8 hours (range, 6.9-13.8 hours; median, 9.2 hours). The mean postoperative MV time was 22.2 hours (range, 0-65.0 hours; median, 16.7 hours), with two patients extubated before leaving the operating room. The mean total MV time was 31.9 hours (range, 8.1-76.5 hours; median, 25.6 hours).

The patients' baseline diaphragm function was measured on arrival to the ICU. The baseline and final dEMG characteristics on the day of pacer discontinuation are shown in the Table. All patients in the study had good dEMG findings on their final recordings; five started with good dEMG activity as their baseline. The average total pacing duration was 4.4 days (median, 4.5 days). The average ICU stay was 4.9 days (median, 5 days), and the average hospitalization stay was 10.9 days (median, 10 days).

Two patients developed VIDD and required prolonged MV, with an average of 75.4 hours of total MV. Both

patients underwent a type IV TAAA repair and had baseline absent dEMG activity on the initial assessment. The first patient was a 79-year-old woman who underwent a type IV TAAA repair with bilateral renal bypasses and perivisceral endarterectomy. Her total operative time was 11.5 hours, and her total MV time was 76.5 hours. The follow-up dEMG showed good activity at the time of removal. The second patient was an 80-year-old man who underwent a type IV TAAA repair for a symptomatic type Ia endoleak from previous fenestrated endovascular repair; his total operative time was 13.8 hours and total MV time was 74.2 hours. His follow-up dEMG activity was also noted to be good at pacer discontinuation. Both patients were former smokers, and neither patient required reintubation afterward. Both postoperative courses were otherwise uneventful.

Reintubation was required in two patients. One patient underwent reintubation on postoperative day 2 secondary to fluid overload and pulmonary edema and was extubated 44 hours later. The second patient, with reactive airway disease, underwent reintubation on postoperative day 16 after percutaneous gastrostomy tube placement and was extubated 5 days later.

No perioperative or 90-day postoperative mortalities occurred. No associated complications developed from DP wire placement or removal.

DISCUSSION

This study demonstrates the feasibility of using temporary DP to assist in postoperative respiratory recovery and prevention of MV. In this high-risk cohort undergoing extensive aortic reconstruction, no patient required MV for >76 hours, and only two patients required reintubation.

Respiratory failure after extensive aortic reconstructive surgery is the most prevalent complication. Downstream effects can lead to pneumonia, prolonged hospitalization, deconditioning, and, even, tracheostomy, increasing the significant healthcare costs and resources needed to maintain a ventilated patient. The predictors of respiratory failure and tracheostomy after aortic repair include aortic dissection, aortic rupture, chronic renal insufficiency, a low body mass index, extensive aneurysm, and hypertension.[3-6] Extensive aortic operations in patients with preoperative pulmonary dysfunction and chronic obstructive pulmonary disease results in a high-risk population for such complications. As such, VIDD is not limited to thoracoabdominal repairs and can occur after abdominal aortic repairs. Thus, selected patients undergoing complex juxtarenal and infrarenal repair at high risk of VIDD were included in our study.

Physiologically, pulmonary insufficiency begins with the initiation of MV. MV causes oxidative stress and activation of proteases, leading to proteolysis. This results in rapid and profound diaphragmatic muscle weakness due to atrophy of both slow-twitch and fast-twitch fibers, culminating in diaphragmatic contractile dysfunction.[13,14] This condition is termed VIDD and leads to failure in weaning from the ventilator and increased mortality. Research has shown that VIDD can develop as soon as after 18 hours of MV and is reported in ≤53% of patients within 24 hours of starting MV.[14-16]

DP is an effective tool for weaning chronically ventilator-dependent patients from MV and in the short-term inpatient setting to decrease the risk of MV and pulmonary complications. It decreases diaphragm atrophy and maintains contractile function by converting type II fibers (fast twitch, glycolytic metabolism) into type I fibers (slow twitch, fatigue-resistant, oxidative metabolism), thereby maintaining contractile function.[17-22] Its efficacy has also been shown in the acute setting; intraoperative intermittent phrenic nerve stimulation has positive effects on diaphragm force, mitochondrial function, and oxidative stress.[23-25] In the present study, our cohort of patients underwent extensive aortic operations with an average of 32.0 hours of total MV.

The intramuscular temporary DP system stimulates the diaphragm transcutaneously and measures the diaphragm function via dEMG with and without pacing. dEMG provides objective data points by measuring the spatial summation between 9 mm of exposed intramuscular electrodes in the left hemidiaphragm. The size or amplitude of the diaphragm burst activity can be seen and measured via dEMG and correlates with the strength of the diaphragm muscular contractions, which can then be interpreted using the categories measured in the present study. Exposure involving diaphragm division in thoracoabdominal repairs understandably result in poor baseline dEMG function (absent or weak). However, all patients had improved to good function at pacer removal. Patients with transperitoneal incisions without diaphragm division had a wider range of baseline dEMG function from absent to good, with most patients at near absent. All these patients had also improved to good diaphragm function at pacer removal.

We found a trend toward longer total MV times with lower preoperative FEV_1. However, definitive conclusions cannot be made because the PFT data were not complete for all patients. The two patients who experienced prolonged MV were older, had undergone complex thoracoabdominal aortic repairs, with longer operative times overall and absent baseline dEMG function. Both patients were ultimately extubated and did not incur any additional respiratory complications. The duration of total MV in the two patients who required reintubation was an average of 75.3 hours. These two patients included one with reactive airway disease and one with pulmonary edema. These patients had near absent to weak baseline dEMG function.

The use of DP can be complicated by mechanical injury to the phrenic nerve either at the time of electrode placement or late injury due to tension, ischemia or fibrosis, infection, or upper airway obstruction after

tracheostomy closure and paradoxical movement of the upper rib cage. No complications related to the placement or removal of the DP system have been noted at our institution.

Study limitations. The limitations of this study relate to its observational nature without a comparison group, the small patient numbers and selection bias, and incomplete preoperative pulmonary data, including PFTs for all patients. Nonetheless, this feasibility study shows that temporary DP can potentially mitigate the risk of pulmonary complications, length of stay, and mortality after extensive aortic repairs. A comparison trial to validate the benefit of DP in this patient cohort is warranted.

CONCLUSIONS

Temporary DP is safe and feasible in selected high-risk patients undergoing extensive aortic reconstructive surgery. dEMG was assessed in this patient population. The findings of this pilot study can be regarded as a basis for future trials to validate the efficacy and safety of temporary DP in mitigating the development of prolonged MV after extensive aortic surgery. These trials should evaluate the optimal diaphragm stimulation protocol, efficacy on weaning from ventilator, and the patient population most likely to benefit.

AUTHOR CONTRIBUTIONS

Conception and design: RO, JSC
Analysis and interpretation: JMC, AW, SB, RS, RO, JSC
Data collection: JMC, AW, SB
Writing the article: JMC, AW, SB, JSC
Critical revision of the article: JMC, RS, RO, JSC
Final approval of the article: JMC, AW, SB, RS, RO, JSC
Statistical analysis: JMC, AW, SB, JSC
Obtained funding: Not applicable
Overall responsibility: JSC

DISCLOSURE

R.P.O., University Hospitals of Cleveland, and Case Western Reserve University School of Medicine have intellectual property rights involved with the diaphragm pacing system and equity in Synapse Biomedical, the manufacturer of the device. J.M.C., A.A.W., S.B., R.S., and J.S.C. have no conflicts of interest.

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