

# Recent engineering developments in treating diaphragm dysfunction: An overview

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*Abstract: Diaphragm dysfunction presents a considerable challenge in the intensive care unit, leading to prolonged dependence on life support. Current treatment methods, while effective, severely hamper the quality of life, and do not appropriately address the issue of dependence. This article summarizes some of the recent engineering advances in addressing diaphragm dysfunction, ranging from tissue engineered scaffolds for tissue regeneration and implanted soft robotics for diaphragm force augmentation to phrenic nerve pacing to improve ventilator weaning success. The developments emphasize a shift toward negative pressure based ventilatory support, however clinical translation is yet to be realized.*

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## I. Introduction

Diaphragm dysfunction – defined as the weakness or paralysis of the diaphragm muscle is one of the primary causes of respiratory insufficiency. Either one (unilateral) or both (bilateral) of the hemi-diaphragmatic domes can be affected, with etiologies including spinal cord injuries (SCI), surgical trauma, congenital diaphragmatic hernia (CDH), muscular dystrophy, amyotrophic lateral sclerosis (ALS) and multiple sclerosis, as outlined in [1].

Unilateral diaphragm weakness, while often asymptomatic, presents symptoms of exertional dyspnea, orthopnea and sleep hypoventilation. Sleep disorders can be treated with non-invasive ventilation (NIV). Severe cases are treated surgically with plication where the paralyzed hemi-diaphragm is stretched and immobilized in a position of maximum inspiration to allow free lung expansion [1].

Bilateral diaphragm weakness presents symptoms of orthopnea, dyspnea, paradoxical abdominal movement and frequent sleep hypoventilation. For mild cases, NIV has proven successful in restoring respiratory capacity, while in severe cases, invasive mechanical ventilation (MV) is necessary to provide life support [1], [2]. In cases of SCI, diaphragm pacing (DP) through phrenic nerve stimulation (PNS) has been a promising alternative to MV, allowing patients to regain autonomy and reduce dependence on non-ambulatory life support [3].

Despite the success of these treatments, there remain some critical challenges. By immobilizing the hemi-diaphragm, surgical plication alleviates symptoms without restoring physiological function and is only applicable for unilateral paralysis. Clinical indication is limited to cases where the muscle, and phrenic nerve are still functional; a study on diaphragm pacing in ALS patients reported increased mortality with DP [2]. MV is associated with decreased

autonomy and quality of life. Furthermore, Muscle atrophy is a common occurrence in MV patients, resulting in ventilator induced diaphragm dysfunction (VIDD), prolonging dependency on MV [2].

Recent improvements in diagnostics and the emergence of new assistive technologies using soft robotics and tissue engineering offer exciting possibilities to address these shortcomings. This article highlights some of the major advancements and novel engineering solutions to tackle diaphragm dysfunction and improve respiratory support.

## II. Methodology: literature search

We conducted an exploratory semantic search using the AI research tools: Perplexity Deep Research and the Elicit search engine. Both tools are provided the search query: “Recent engineering and medical developments in artificial diaphragms and/or diaphragm support” to retrieve relevant literature. Articles from the past decade are screened based on whether they: (i) address diaphragm specific support or artificial diaphragm technologies, (ii) focus on the engineering aspects of diaphragm support, and (iii) target diaphragm dysfunction. Results are screened from the title and abstract. Duplicates and records with incomplete data are excluded. Only the most relevant articles are highlighted in this overview.

## III. Results

The AI assisted search resulted in a total of 78 articles, The articles are thematically categorized into the following: (i) Emerging trends in the state of the art, (ii) Tissue engineering approaches, and (iii) Soft robotic approaches. The following subsections explore them in depth.

### III.I. Emerging trends in clinical state of the art

Improvements in MV focus on early initiation of weaning, lung protective ventilation, automated weaning and using

NIV during the weaning process as reported in [2]. One randomized control trial study on 223 subjects found that transvenous PNS is associated with high probability of weaning success in prolonged MV patients [4]. In a porcine model [5], sufficient tidal volume was generated through minimally invasive bilateral PNS. A self-powered fully implantable DP system showed preliminary feasibility in a rat model [6].

### III.II. Tissue engineering approaches

Tissue engineering approaches involve generating biocompatible scaffolds to promote in-situ tissue regeneration. They demonstrate improved performance, and lower immune response when compared to the traditional grafts that are used to treat CDH, as outlined in [7]. Composite patches combining decellularized scaffolds with stem cells offered improved strength and tissue regrowth in comparison to simple scaffolds in a rat model [8]. Synthetic bioabsorbable polymers have been developed to enable tissue regrowth, and dissolve shortly after, restoring tissue close to its original form [9].

### III.III. Soft robotic approaches

Soft robots are being explored as a safer alternative for human-robot interaction. A soft robotic extracorporeal ventilator showed increased respiratory capacity in functionally impaired patients [10]. Studies developed implantable, soft robotic devices to mechanically support the diaphragm in a more physiologically consistent manner, without the need for intubation or positive pressure based ventilation, and tested them in ex-vivo simulators [11], [12]. Furthermore, one study demonstrated successful synchronization with the native diaphragm, achieving increased tidal volumes in a porcine model [13].

## IV. Discussion and perspectives

Diaphragm dysfunction is a multifaceted, complex disorder, whose treatment depends on etiology. In cases where the phrenic nerve and the muscles are intact, such as SCI, DP is a promising solution. However, percutaneous implants have a high risk of infections, hampering long term success. Further research into energy harvesting and miniaturization is necessary for complete implantation. In the case of CDH, and physical trauma, tissue engineering can help promote tissue regeneration, improving the strength of new tissue, but only in patients without compromised muscle tissue (as in the case of neuromuscular disorders). Here, the feasibility of decellularized scaffolds as an intermediate bridge to integrate tissue grafts from healthy donors could be studied. For critical cases and patients with neuromuscular disorders, MV is currently the only clinically viable option. Machine learning models could be developed to inform the decision to wean and detect early complications. Nonetheless, there is no work around the loss of speech and autonomy.

Soft robotic assistive devices have proven to be capable of generating sufficient forces while allowing patients to remain ambulatory. However current designs with simple pneumatic actuators do not consider long-term integration and risk tissue irritation due to constant actuator-tissue friction. Furthermore, there is a lack of focus on safe implantation and tissue force transmission as existing solutions place the actuators above the diaphragm, which can compromise the pleural cavity. Approaching the diaphragm from the abdominal cavity can be explored as a

clinically safer alternative. Soft actuators could incorporate tissue engineering scaffolds, or bioabsorbable meshes to generate a functional interface that promotes tissue growth and integration while evenly distributing forces over the tissue. Finally, studies need to explore the long-term effects of applying forces onto muscle tissue and thorax, demonstrate biocompatibility and implant acceptance.

## V. Conclusions

Novel developments in soft robotics, tissue engineering and nerve pacing hold great prospects to address diaphragm dysfunction. However, until clinical efficacy is established, refining protocols and pacing the diaphragm during weaning are feasible solutions to improve extubating success. Further research on bio-integration, miniaturization and force distribution is required to establish a physiologically cohesive, negative-pressure-based alternative to invasive mechanical ventilation, improving patient quality of life.

### AUTHOR'S STATEMENT

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