

SomnOSA Executive Summary

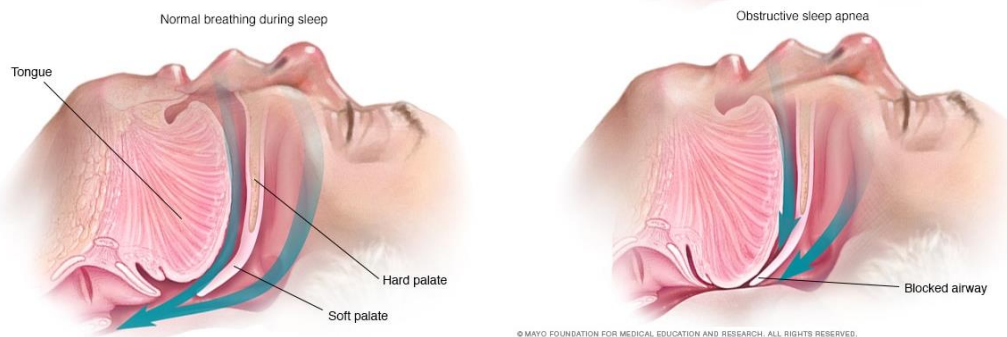
Treatment of Complete Concentric Airway Collapse (CCCp) in Obstructive Sleep Apnea (OSA)

Need Statement

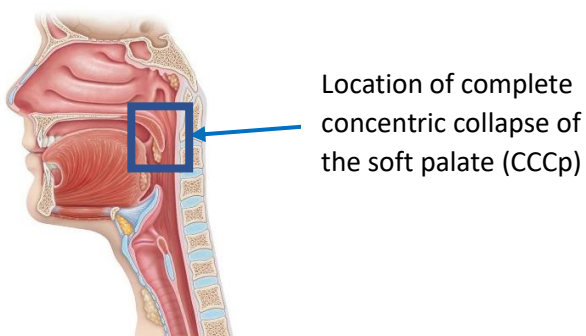
Sleep surgeons need a method for treating complete concentric collapse in patients with OSA in order to reduce morbidity and the cost of untreated disease.

Background and Unmet Need

Obstructive sleep apnea (OSA) is a highly prevalent disease characterized by repeated airway obstruction during sleep. It has recently been estimated that up to 1 billion people suffer from OSA worldwide. It is caused by reduced neuromuscular tone in the upper airway musculature that intermittently collapses and blocks the airway during sleep. Left untreated, OSA affects daytime sleepiness and function and leaves the patient at risk for cardiovascular, metabolic, and stroke sequelae.



Continuous positive airway pressure (CPAP) is the gold-standard treatment for OSA of all phenotypes. It is highly efficacious for patients that comply, but up to 50% of patients are non-adherent to CPAP treatment. The majority of patients that are intolerant to CPAP therapy must enter the surgical treatment paradigm to seek disease alleviation; however, not all phenotypes of OSA are well-treated surgically. One of the phenotypes of OSA that is not well-treated by current surgical approaches is complete concentric collapse of the palate (CCCp); it is even a contraindication for the only FDA-approved neurostimulation technique, Inspire. CCCp is characterized by simultaneous anterior-posterior and latero-lateral collapse at the level of the soft palate.



It is estimated that there are approximately nine million patients with the complete concentric collapse phenotype of obstructive sleep apnea in the United States, although many of these patients are underdiagnosed. Roughly two million people with CCCp are initially prescribed CPAP therapy and approximately one million of those fail CPAP and continue with surgical treatment of their disease.

For most patients with CCCp, there currently is no well-accepted surgical treatment that results in acceptable disease alleviation. For patients with maxillofacial anatomy that predisposes them to OSA, maxillo-mandibular advancement (MMA) is highly effective; however, MMA procedures are extremely invasive and not all CCCp

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patients are good candidates. Modern palatal surgery techniques do not resolve the obstruction well; instead, they convert the pattern of collapse to one that requires further salvage procedures such as hypoglossal nerve stimulation. Because of this, the patient is forced to choose between reattempting CPAP therapy (and living with poorly treated disease), and a highly invasive multi-surgery pathway to resolve their disease state.

Value Proposition and Business Opportunity

Our innovation will create significant clinical and commercial value for patients, providers and payors.

Clinically we will create value by improving key measures of disease. In turn, this will provide patients who are currently excluded from surgical treatment with a solution and reduce their long-term risk of cerebro- and cardiometabolic events.

Providers (sleep surgeons and physicians) will be able to offer a novel treatment with better outcomes and it will increase their scope of practice.

Payors will benefit from a reduction in healthcare utilization costs related to sequelae of untreated disease (presentations to hospital for heart attack and stroke). At a macroeconomic level, our innovation addresses a significant economic burden of disease in the order of USD \$900 million due to high health care utilization, loss of workplace productivity, and motor vehicle accidents as a result of excessive sleepiness.

From our business opportunity analysis, we estimate a total addressable market of USD \$10B as a product of current average market costs of modern palatal surgery (USD \$10K) and the number of patients with CCCp that fail CPAP in the United States every year (1M). Once accounting for surgical eligibility (BMI and AHI) we estimate a serviceable addressable market of USD \$3.7B. Further, assuming a market penetrance of 2.7% (based on early market penetrance data for the Inspire hypoglossal nerve stimulator) we estimate a serviceable obtainable market of USD \$100M.

Design Approach and Strategy

Having identified this high-value problem, our team then developed a framework for what requirements a solution would need to meet. We did this by soliciting feedback during clinical expert interviews, as well as performing a literature review to define solution efficacy criteria and clinical effectiveness criteria. The initial efficacy criteria include resolving upper airway obstruction (graded by an expert endoscopically), reducing inspiratory critical closing pressure of the airway (Pcrit), reducing pharyngeal opening pressure (PhOP), and improving maximum inspiratory ventilation (V_i max). Key criteria that will be used to prove clinical effectiveness include reduced apneic frequency (as measured by the apnea-hypopnea index (AHI) and frequency/ severity of resultant oxygen desaturations [ODI]), improved sleep quality (as measured by Epworth Sleepiness Score [ESS]), improved quality of life and daytime function, and reduced snoring severity/frequency (as measured by the Snoring Severity Scale).

The first tool that we used to identify innovation targets for brainstorming was through genealogy mapping. With this technique, we identified the underlying mechanisms in CCCp and used those to identify innovation targets and mitigations. Building on the root cause of loss of neuromuscular tone in the airway musculature leading to muscular collapse, our team then developed a mutually exclusive comprehensively exhausting map of possible solutions to generate a breadth of ideas. We then examined each of these ideas and assessed them based on their clinical, technical, commercial, and strategic viability to prioritize concept development. We further validated these ideas through interviews with clinical and technical experts. In parallel to solution concept prioritization, we developed our evidence generation strategy and are working with local experts to validate our ideas in animal and human models.