Dr. John Marinelli:

Hey everybody, welcome back for another episode of ENT in a Nutshell. My name is John Marinelli. Before we get started, I just want to make a quick point about our site, headmirror.com, where each podcast is actually subspecialty organized by subspecialty. Sometimes when you're studying, especially systematically, a topic area can be hard on Apple or Spotify as we accrue a lot of episodes. So the organization can hopefully be helpful on that side. And we also have our surgical video at least there, as well as our dictation templates and console guide and things like that.

Dr. John Marinelli:

Either way, without further ado, we'll get started with our episode for today, which is the exciting topic of hypoglossal nerve stimulation. And we're lucky to be joined by Dr. Ryan Soose, who's actually dual board certified in our laryngology and sleep medicine. So Dr. Soose, thank you so much for being here today.

Dr. Ryan Soose:

John, thanks for having me. It's really an exciting time to be an otolaryngologist in sleep. And I really appreciate everything that Ted Mirror and ENT in a Nutshell podcasts are doing for the field and specifically for sleep. Sleep is really a field in its infancy and there's really huge, potential, more multi-disciplinary collaboration, new treatment options on the horizon. And again, it's really exciting for the sleep-trained or the laryngologist now to be at the center of patient care. I love to see all the resources that you guys have put forward to help that cause.

Dr. John Marinelli:

No, thank you Ed, this is very exciting. And so, maybe if we could just get started with some background on hypoglossal nerve stimulation, obviously it's one of the newer treatments in ENT and it's kind of revolutionizing the treatment of sleep surgery. How did we get here with this treatment option?

Dr. Ryan Soose:

Yeah, that's a good question. I think that when you look at the big picture of sleep apnea and I know you guys have covered this well in other podcasts, sleep apnea is such an incredibly common problem. And it really spans all ages, genders, ethnicities, and has many, many different causes, many different presentations. So the reality is one treatment doesn't fit all. And as I mentioned, multi-modality or multi-disciplinary treatment is becoming more and more common.

Dr. Ryan Soose:

So if you just have the standard tools in the toolbox like CPAP and dental appliances and upper airway surgical procedures, you can help a lot of people. But even with those, there's still millions of people that are left without treatment. So this therapy was born out of the clinical need, the millions of people that are still struggling with untreated sleep apnea and the associated quality of life effects and the health risks. And it really has taken the treatment of sleep apnea in a whole new direction.

Dr. John Marinelli:

And how did we get to FDA approval? I understand that happened in... What was it? 2014, I think. What did that process look like and how did we get there?

Dr. Ryan Soose:

Well, thanks started decades before that. Decades of animal and human basic science research essentially showed across the eighties and nineties, that stimulating the hypoglossal nerve with electrical stimulation results in increased air flow, reduced collapsibility of the upper airway and anterior displacement of the tongue. And one of the really unique findings that I think really set the stage for the success of the therapy was that stimulation also advanced the soft palate.

Dr. Ryan Soose:

So just stimulating the genie glosses had a multilevel effect on the upper airway, perhaps akin to what other multilevel treatments like CPAP and Maxillomandibular advancement surgery can employ as well. So that basic science data then led to the development of the first commercially available implantable system. And this was a first implanted about 20 years ago, right around the turn of the century, year 2000 or so. Several patients were implanted with a pilot-type device and more than half of the patients responded positively.

Dr. Ryan Soose:

But there were still a lot of questions that needed to be answered. So then there was back into the research lab, engineering, therapy development, over the next decade led to the development of the system that's more well known now, and that a company that's currently FDA-approved is Inspire Medical Systems. And their device went through some initial feasibility studies about a decade ago. And that's where we learned which patient anatomies, which patient phenotypes, which body mass indexes, and so forth, seemed to respond the best.

Dr. Ryan Soose:

And then all of that feasibility and pilot data then led to the genesis of the Inspire STAR trial. The STAR trial was a 22 site multicenter study across the U.S. and Europe, and we were one of the sites as well. It evaluated 126 patients that were implanted with this therapy. These patients all had moderate to severe obstructive sleep apnea with a BMI less than or equal to 32 and an absence of concentric collapse on their endoscopy, which we'll talk about more in detail later. And those patients were tracked over the course of five years with good results in both quality of life measures and metrics of sleep apnea.

Dr. Ryan Soose:

And then all of that STAR trial work then led to the FDA approval in 2014. So the point is it was really decades of work on the basic science and clinical end by many, many people throughout the field on both the sleep medicine and otolaryngology and industry side of things.

Dr. John Marinelli:

Yeah, very cool. I guess, the next question I want to ask you is surrounding... You started to get into this with just the reality that many patients have trouble using positive airway pressure even though that is the gold standard. But can we talk a little bit more about the typical patient with obstructive sleep apnea that you're seeing that might benefit from upper airway stimulation?

Dr. Ryan Soose:

Yeah. That's a bit of a loaded question in that I really think there are no typical patients. Every patient that comes in is a little bit different, a little different symptoms and presentation and background. Their needs and wants with what they're able to tolerate or what they're interested in surgically are all very, very different.

Dr. Ryan Soose:

But that said, I think you can categorize. There's a large number of patients that are middle-aged or elderly patients with moderate to severe obstructive sleep apnea that are having substantial symptoms, either at night or with daytime sleepiness or both and substantial impact on their longterm health risks, high blood pressure, uncontrolled Afib, coronary disease, et cetera. And they need treatment. So, we start as anybody would with a full comprehensive sleep medicine, history and physical examination. We start with the proper diagnostic sleep testing.

Dr. Ryan Soose:

And in the majority of cases, these patients start with positive pressure therapy. Most of the listeners are familiar with this being the standard first line therapy, so I won't belabor the point. But even in great clinical trial environments with proper titration, proper education, close clinical followup, C-PAP adherence rates, are still sub-optimal. Less than half the patients actually use it well, and use it well enough long-term.

Dr. Ryan Soose:

And the most commonly used and effective second line option, oral appliance therapy or a mandibular advancement device, has limitations as well. A big study a few just a few years ago showed that over half of the patients that use that therapy, even the ones that use it well and get good results, will develop a change in their bite. And that bite change often requires discontinuation of the therapy.

Dr. Ryan Soose:

So even in the patients that do well with an oral appliance, down the road, they may need a different solution. And that often brings the patient then in the office to a surgical discussion. And although there are many advancements in pharyngeal surgery, and sinonasal surgery, and skeletal surgery, there are still a lot of patients that either still have residual disease after those surgical treatments, or it's just the perceived or even real morbidity and risk and recovery of those traditional upper airway surgeries that limits their application to a large portion of the population.

Dr. Ryan Soose:

I think the prime example are elderly patients over the age of 65, who don't have good bone structure, who have multiple medical comorbidities, or they're on blood thinners. These are people that are high-risk and even just non-accepting of traditional upper airway surgeries. And that's the population, I think, that really fits best with this upper airway stimulation.

Dr. John Marinelli:

You had mentioned previously that really upper airway stimulation or hypoglossal nerve stimulation is more than just tongue advancement, it's a multilevel surgery in terms of how it works. I wanted to get into that a little bit deeper. Obviously, there's several components to, and at least, the current device Inspire in terms of its different working components. So just, mechanistically, how is this working to treat patient's sleep apnea?

Dr. Ryan Soose:

Sure. So the patients go through a pretty thorough screening criteria, which we can touch on in a bit. But the system itself, once they get to the phase of the implant, consists of an outpatient surgical procedure to install three internal components. There's an electrode on the hypoglossal nerve, in the sub-mental or a submandibular space, there's a pulse generator that is in a subcutaneous pocket in the right upper chest, and there's a respiratory sensor that's in the fifth or sixth intercostal space on the right side.

Dr. Ryan Soose:

After a few weeks of healing, the patient is activated in the office, meaning the device is turned on, they're given a remote control and they're taught how to use it. The basic concept is, when the patient goes to bed, they take a remote control and turn the device on there's a little sleep delay or timer to allow them to fall asleep. And then once they're asleep, the idea is, the respiratory sensor in the intercostal space synchronizes with the respiratory pattern and the pulse generator sends then a timed pulse with each breath to the electrode that's attached to the hypoglossal nerve.

Dr. Ryan Soose:

So with each breath, within each inspiration, the genioglossus muscle and other upper airway dilator muscles get an electrical impulse to advance that tissue forward, hopefully opening the airway.

Dr. John Marinelli:

What is this idea of dysfunctional neuromuscular control that occurs or is seen in patients with obstructive sleep apnea?

Dr. Ryan Soose:

Yeah, that's a great question. And I think that's part of the reason that upper airway stimulation is unique. Most surgical procedures for obstructive sleep apnea, whether it's in the nose, the pharynx, or with jaw structure, really just address anatomy. But there's increasing evidence that a portion of OSA patients, maybe at least a third, and particularly those older patients I was mentioning, or those with other medical comorbidities, that they actually have non-anatomic issues that have to do with abnormal hypoglossal nerve conduction, reduced tone or tonic activity of the upper airway dilator muscles in abnormal negative pressure reflex, and just other neuromuscular dysfunction of that protective feedback loop that younger folks tend to have.

Dr. Ryan Soose:

So perhaps, in some way, upper airway stimulation is not only improving anatomy by advancing the tongue and making more space, but maybe it's also augmenting that dysfunctional neuromuscular control of the pharynx that other surgical treatments just aren't able to do.

Dr. John Marinelli:

And when we... If we shift now to work up prior to pursuing this treatment option, when we think maybe first about the head and neck exam. What are we looking for here when you see these patients in clinic?

Dr. Ryan Soose:

Sure. I would highlight and build on your question there that this therapy isn't for everybody. The reality is, no one treatment is for everybody. But the point is that this upper airway stimulation therapy has been shown to be beneficial for a select group of patients. And proper screening is really, I think, the first key to getting successful outcomes.

Dr. Ryan Soose:

So all patients being considered undergo a thorough clinical polysomnographic and endoscopic screening. So essentially, they have to have moderate to severe obstructive sleep apnea, have failed CPAP, and/or other medical or conservative measures.

Dr. Ryan Soose:

And on exam, at least initially in the office, we want to make sure that there's no other substantial anatomic abnormalities that could be more easily reversed. So those patients with a significant adenotonsillar hypertrophy in upper airway tumor, vocal fold immobility, nasal polyps, severe structural nasal obstruction. Those other things would likely be best addressed, either first or perhaps in tandem with this therapy.

Dr. Ryan Soose:

So the initial screening is very important. And it's not only from an upper airway exam standpoint, but it's also from a sleep history standpoint. Remember, in addition to obstructive sleep apnea, there are about 80 other sleep disorders. And one good study from a few years ago showed that at least a third of coming into the doctor for obstructive sleep apnea have another sleep disorder too, like insomnia, and restless legs, and narcolepsy, and chronic pain, or other factors affecting their sleep.

Dr. Ryan Soose:

And so when we're really trying to improve their sleep-related symptoms, their daytime fatigue, quality of life measures, we really have to get that full, comprehensive, sleep history and manage all aspects of their disease.

Dr. John Marinelli:

You mentioned, with the STAR trial that BMI cutoff of 32. How do you think about BMI as you're working someone up for UAS?

Dr. Ryan Soose:

Sure. That's a really tough question. It's a little bit of a misnomer that there's an exact BMI cutoff. It's really a graded response, I would say. And there's evidence that BMI is all relative to one's Craniofacial facial structure, the container size, and it's also relative to their pattern of fat distribution. So we can see two individuals with the same BMI, but one has maxillomandibular deficiency where that BMI is going to cause a lot more upper airway obstruction, if it's elevated, than the person that has a nice wide and forward jaw structure.

Dr. Ryan Soose:

Similarly, we have patients with the same BMI, and some carry it more around the waistline and trunk, and have a very thin neck and fedorable upper airway anatomy. Whereas others have that thick, I'm

sure you've seen tree trunk neck, with substantial fat distribution in their tongue base and around the pharynx.

Dr. Ryan Soose:

So BMI is just a relative term and it's a bit of a crude estimate. But like UPP data, like oral appliance data, I think you can at least say that in general, the higher the BMI, the lower the success rates. So the 32 came from the early Inspire feasibility studies. And when they ran the statistics, a BMI of 32 was roughly where the success rates started to change. So a BMI of less than or equal to 32 was the inclusion criteria that was incorporated into the subsequent STAR trial. And then that was listed on the FDA guidelines after the FDA approval in 2014.

Dr. Ryan Soose:

Now what's interesting is that in recent years, with more data now showing results in patients with higher BMIs, it appears that BMIs, even up to 35, still have good success rates compared to those under 32, as long as they're properly selected Medicare, in fact, just recently modified their guidelines to a BMI of 35 or less earlier this year.

Dr. John Marinelli:

Okay, interesting. So if someone's not over 32 or over 36, depending on the phenotype of their obesity, that's not necessarily a no-go in terms of pursuing this?

Dr. Ryan Soose:

That's right. It's not a hard-fast number. It's just one of the many factors that a trained physician has to factor into the equation. And again, it's all relative to the rest of their anatomy and presentation.

Dr. John Marinelli:

Sure. If we transition in the drug-induced sleep endoscopy, obviously it's a very key in the workup for this. So how are we using DISE here?

Dr. Ryan Soose:

Yeah. You can only see so much in the office and even in the patients with the worst sleep apnea and loudest snoring, et cetera, they don't snore or obstruct when they're sitting in your office unless you've kept them waiting too long. So sleep apnea, as the name implies, is a state-dependent condition. So things change when you're asleep compared to when you're awake, there's loss of upper airway dilator muscle activity, there's changes in the way the brain reacts to CO2 and oxygen, meaning the ventilatory response is blunted.

Dr. Ryan Soose:

So it's not realistic to sneak into somebody's house and put a scope in their nose when they're snoring and obstructing at home when a typical night. So what we do is we bring them into a controlled setting in the hospital or in the endoscopy suite and do a brief upper airway endoscopic exam using pharmacologic sedatives.

Dr. Ryan Soose:

So drug-induced sleep endoscopy is not a full night of sleep. It's not designed to look at all positions and sleep stages, nor is it actually real or spontaneous sleep. But what it is, is it's a way to replicate at least the same loss of control of muscle activity that may be seen during non-REM sleep, and evaluate the dynamic collapse patterns of the upper airway under those sleep disorder breathing conditions.

Dr. Ryan Soose:

We're trying to look at what's the anatomy, what's the anatomic structure, what are the locations and pattern of collapse? And prior data, particularly in the previous Inspire trials showed that patients who had a complete concentric pattern of retropalatal collapse. So that's a large lateral pharyngeal wall collapse, high up in the retropalatal space. Those patients had poor outcomes on the feasibility studies with upper airway stimulation.

Dr. Ryan Soose:

So currently, drug-induced sleep endoscopy is a recommended, perhaps even, you could use the word required screening tool to rule out that concentric pattern of retropalatal collapse.

Dr. John Marinelli:

And just putting it in context of the vote classification, this complete concentric collapsed at the VLM. Is that correct?

Dr. Ryan Soose:

That's correct. No, I think there's a lot of other information that you can get from the DISE. You can get a lot more information on airway length and soft palate length and coupling between the tongue protrusion and the soft palate, the epiglottitis position. There are many other pieces of information that you can get from a DISE.

Dr. Ryan Soose:

So it's not quite as simple as black and white, is there a concentric pattern or not? And I think the really skilled and trained sleep surgeon can use that DISE information to better predict outcomes with upper airway stimulation beyond just the simple concentric issue. And can use that DISE information also to add other therapies, whether it's positional therapies or mandibular advancement or other treatments.

Dr. John Marinelli:

It's my understanding that the lateral wall collapse, if you have significant lateral wall collapse at the oral pharynx, that that might be a negative prognosticator. What are your thoughts on that?

Dr. Ryan Soose:

Yeah, that's probably true. I think it's something we don't know, but the patients with very compliant enlarged lateral walls, I think that's a sign of a substantially more collapsible airway. To some extent, that pattern appears to correlate with BMI. So by screening out some of the higher BMIs, we're probably avoiding a lot of those big lateral wall collapses to begin with.

Dr. Ryan Soose:

But some of those patients, depending on their fat distribution, the pair of pharyngeal fat pads, et cetera, that substantial lateral wall collapse is likely something that's going to need a transpalatal

advancement, full maxillomandibular advancement, or maybe even just combination therapy. Interestingly, we have a number of patients where they've needed both an oral appliance and upper airway stimulation together, or a lateral pharyngoplasty and upper airway stimulation therapy together. So all of these treatment options should not be viewed in isolation, in my opinion. They're all combinable to get to the desired clinical outcome.

Dr. John Marinelli:

Any other workup considerations like imaging or that sort of thing?

Dr. Ryan Soose:

That's a great question. In my opinion, I think that's really the future. DISE is a great screening tool and has taught us a lot and helps to sort out a number of anatomic issues, but it's still a subjective, it's non quantitative and it's not spontaneous sleep. And so it has some limitations to it. And I think the future likely holds some kind of dynamic imaging that's more quantitative and perhaps during sleep.

Dr. Ryan Soose:

But currently at this point there's no standardized imaging that's needed or required. I would say though, one of the things that's key dimension on the sleep end, is thorough evaluation of the sleep study. I think, particularly, for community ENT docs, or others outside of a multi-center ENT sleep program, there may be a temptation to just look at the AHI alone, but there's a lot more information and data on those sleep study reports, both the home portable tests, as well as the in-lab studies, that can help to guide your screening.

Dr. Ryan Soose:

One of the screening criteria that's also important for upper airway stimulation therapy is a central apnea index, less than 25% of the total AHI. Those patients that have high levels of central apnea and mixed apnea events are the ones that are more likely to have other neurologic or neuromuscular aspects of their sleep disorder breathing pathophysiology, I think, perhaps, somebody with congestive heart failure and Cheyne–Stokes respiration, a stroke opioid use, or other causes of central sleep apnea. Those types of patients and that high level of central apnea is likely not something that's going to work very well with upper airway stimulation.

Dr. John Marinelli:

Just taking everything together, we've briefly touched on this, even just get into this with the central apnea ideas, but could we just review the current indications for hypoglossal nerve stimulation prior to moving under the procedure itself?

Dr. Ryan Soose:

Sure. The current clinical indications, this is based off the FDA approval guidelines back in 2014, are patients with moderate to severe obstructive sleep apnea. So that's less than 25% central and mixed apnea events, with and total AHI between 15 and 65, essentially covering the moderate to severe range. It's not to say it wouldn't work if it was more than 65, but that was the AHI range in the STAR trial. And that's what it was labeled as for use in 2014.

Dr. Ryan Soose:

In addition to moderate to severe obstructive sleep apnea, the patients have to document that they failed CPAP. And in our practice, they even failed dental device and weight loss and other conservative measures. And that's just to support and highlight the fact that this is still second-line therapy. It's not a first-line treatment.

Dr. Ryan Soose:

And finally, they have to undergo that full sleep evaluation to make sure there are no other major or sleep confounders in the mix such as audits severe heart failures, COPD, other things that would cause other more complex breathing disorders. And finally the DISE, with the absence of complete concentric collapse.

Dr. Ryan Soose:

So perhaps you wanted to summarize it in one sentence, moderate to severe obstructive sleep apnea, AHI 15 to 65, CPAP intolerance and absence of concentric collapse on the DISE.

Dr. John Marinelli:

When we talk about performing the procedure itself, we actually just said it's a small apnea plug. We do have a video highlighting the procedure, goes step by step through it. But if we could just talk through the key points as you see it if you were counseling a patient on it or talking to a resident about it, what are the key components of the surgery and that you think is worth mentioning?

Dr. Ryan Soose:

Yeah. It's actually a fun and I think very interesting surgery. It's something that most ENTs perhaps are not too familiar with, particularly working in the chest. But once you get over that initial, perhaps, bit of a uncomfortableness, it's actually a fun procedure. One of the other nice things about this surgery is that we've tried to do a good job of really training, in a standardized way, surgeons across the U.S. and Europe, and really trying to identify and modify to a best-practice approach to the surgical procedure.

Dr. Ryan Soose:

What I mean by that is unlike palate surgery, where there's 20 different modifications, and tongue based surgery where you can do it a dozen different ways. The surgical implant with this Inspire upper airway stimulation device is pretty consistent. So if you get an implant in Los Angeles or New York or Munich, it's the same operation and essentially the same surgical steps. Which I think is nice for quality control, it's nice for training and it's nice for being able to study our data across the field.

Dr. Ryan Soose:

So the surgical procedure itself, it's about a two-hour outpatient surgery. It's done under general anesthesia. There are three incisions. Again, one in the submandibular space, one just below the clavicle and one just below the anterior axillary line, inferior to the pectoralis muscle.

Dr. Ryan Soose:

The first part of the surgical procedure involves identifying the floor of the submandibular triangle and the hypoglossal nerve running in its usual course. And we dissect the nerve distally to find the fine distal nerve branches. And as you may know, the hypoglossal nerve innervates multiple muscles. So some of those muscles, like the styloglossus and hyoglossus muscles actually retract the tongue posteriorly, and

would actually obstruct the airway. We don't want those. Whereas the nerve branches going to the genioglossus, or even geniohyoid, protrude the tongue, reduce speak rate, open the airway.

Dr. Ryan Soose:

So how do we determine that? Well, at the beginning of the case, we place fine wire electrodes in those different muscles and use a nerve monitor during the procedure. So between our anatomic landmarks, as well as intraoperative nerve stimulation, we can then identify the branches that selectively protrude the tongue, while excluding all retractor ranches.

Dr. Ryan Soose:

And I think that's really one of the keys to setting yourself up for a successful implant and successful outcome. The electro then is placed selectively around those protrudes or branches only, including the C1 branch to the geniohyoid, while excluding all the retractors.

Dr. John Marinelli:

So after you get the electrode in place, then what's next?

Dr. Ryan Soose:

So then we moved down to the chest area. It's a simple, roughly five centimeter pocket, that's created underlying the subcutaneous fat, just below the clavicle for placement of the pulse generator, similar to a cardiac device that would be placed on the other side.

Dr. Ryan Soose:

And then finally, we dissect down onto the lateral chest wall, to the underlying intercostal space, and we create a little pocket between the external and internal intercostal muscles and slide a little respiratory sensor in between the external and internal intercostal muscles, with the sensor facing the pleura.

Dr. Ryan Soose:

Those leads then, this stimulation electrode lead from the neck and the sensing lead from the lateral chest, are both tunneled into the right upper chest pocket, connected to the device. And then we bring a sterile telemetry unit into the field to test the device. And this is really the final confirmation then that the respiratory sensor is functioning, that stimulation is resulting in a brisk uninhibited protrusion of the tongue, making sure that we didn't get any of those retractor branches in, and just testing the other electrical functionality of the device. The three incisions are then closed up, some bandages are placed, and the patient goes home as an outpatient.

Dr. Ryan Soose:

I'd say one of the big differences between this therapy and traditional pharyngeal and skeletal surgery for sleep apnea is the recovery. The majority of these patients, again, go home the same day, there's no hospital stay. Remember there is no airway manipulation or surgery itself. So the risk of airway edema or postoperative complications in that regard is essentially zero. And the majority of these patients go back to regular diet immediately and they do not take prescription narcotics.

Dr. Ryan Soose:

And that's a key thing because our sleep apnea patients are at risk, even more than the general population, for taking opioids. So being able to do this as an outpatient, no opioids, minimal downtime, no diet restrictions, is really one of the attractive features, I think, that a lot that draws a lot of patients to this treatment.

Dr. John Marinelli:

And you said you're typically activating the device around one month?

Dr. Ryan Soose:

That's right. So we let the healing occur, let some of the edema around the electrodes and incisions reduce. We bring them back to the office for an activation visit where myself and my staff work with the patient to activate it. We set all the electrical programming. This is another key that is just starting to come out in the literature now, and we're developing guidelines on. Because, initially, it was just, well, turn it on and see what happens and maybe make some adjustments if needed. But now we know there are different results in different patients as you modify the electrode pattern, and the amplitude, and the pulse width, and the frequency, and so many other features of the stimulation itself.

Dr. Ryan Soose:

So once we program the device, we give the patients about a six-week period or so to acclimate to the therapy. We want them to start using it all night, every night and slowly advance the stimulation upwards until they start to feel symptomatic improvement, but still are able to comfortably use the device. If they go too high, there's no harm per se.

Dr. Ryan Soose:

But in some patients, if the stimulation level is too strong, it may make it difficult to fall asleep, or it could potentially even wake them up or make it difficult to return to sleep with a therapy running, which is then sort of counterproductive to what we're trying to do. So we slowly titrate the level up to their comfort level and their symptomatic response, we see them back in the office and then we get a data download now out of the device.

Dr. Ryan Soose:

Almost akin to a CPAP data download, we can now get a download out of the upper airway stimulation generator, that gives us a report of usage and how many hours they're using it each night and usage trends. And we can see all they turned it up here this week and then their trend was, they started to decrease use and pause the therapy more. So we can use some of that data download information, just like you would a CPAP, for troubleshooting and therapy adjustments, which ultimately then optimize the outcomes.

Dr. Ryan Soose:

And I think that's an important point to highlight here. Is that, again, unlike other traditional surgeries, this upper airway stimulation device is all titratable and modifiable. So unlike a surgery where you do the surgery and it's sort of one-and-done, you check a sleep study in three to six months and see what you got, with this therapy, it's almost infinitely adjustable.

Dr. Ryan Soose:

And so it's not just on or off. We assess outcomes with follow up sleep studies. and if we're not quite where we want to be, we can use advanced sleep study titration, almost like a CPAP, we can use endoscopic or DISE information to further tailor the electrical settings, we can adjust comfort features on the device to improve adherence. And there's a lot of adjustability.

Dr. Ryan Soose:

And that's really important because, as you know, sleep apnea is a chronic long-term condition, right? It's not an acute problem, it's more like hypertension, it's more like asthma. It's something that you have to manage across the life-span. And this device, currently, has a battery life of around 10 to 12 years, which then is nice because this allows you to modify the settings and adjust if the patient gains weight or loses weight, et cetera, to optimize their therapy across a longitudinal care model.

Dr. John Marinelli:

And talking about the postoperative course here. How do we think about adverse events in UAS? Is there much talk on that or what are the main risks, I guess?

Dr. Ryan Soose:

Absolutely. With any treatment for obstructive sleep apnea, we have to look at, not only the potential effectiveness in gain, but the risk and morbidity. Going back to one of the earlier comments we talked about with pharyngeal and skeletal surgery, one of the reasons people don't sign up for those things is because of the potential risk in their swallowing and pain and downtime and so forth. So we have to look at that as well.

Dr. Ryan Soose:

With this procedure, there are some surgical risks during the implant, and there are some therapy risks with using the treatment long-term. So the surgical risks with implanting the device, you have typical risks with any incision of bleeding or infection. Those have generally been published at around less than 1%. There's also a risk of nerve injury. And there have been some reports of transient hypoglossal nerve weakness, which could affect speech or swallowing.

Dr. Ryan Soose:

And there's also some report of transient marginal mandibular weakness. Now I think with experience, and as the learning curve goes up with at least five or 10 of these procedures under your belt, the incidence of those are quite low. And again, the clinical trials, as well as my experience suggests, even when they do occur, they're transient not a permanent nerve injury.

Dr. Ryan Soose:

And then finally, there's a risk of pneumothorax. In placement of the respiratory sensor in the intercostal space, again, we try to target that space between the external and internal intercostal muscle. But if that sensor is placed too deep below the internal intercostal muscle, it could result in pneumothorax, which would require obviously a treatment and potentially hospitalization for that.

Dr. Ryan Soose:

Now, once patients get through the initial postop recovery and, again, serious complications like some of those I mentioned, I think are very uncommon. 99% of the people seem to get through the implant

itself without those issues. There are some issues that I think are more common with therapy adverse effects. And that's really where I think one of the next frontiers lies with this therapy. Just like any other medical device, there are patients that are going to be affected by use of the device itself.

Dr. Ryan Soose:

One of the advantages of traditional surgery is there is no device that you have to use. And many of these people that get to an ENT surgeon, they can't stand a mask on their face or the noise of a CPAP machine, and they can't stand a dental device in their mouth. So those patients are already sort of self-selected or pre-selected as being difficult to use any kind of medical device. And this upper airway stimulation is a medical device. So they have to take the remote and turn it on. And after a prescribed amount of minutes, that therapy is going to start stimulating, particularly for patients with anxiety, insomnia and other sleep and medical issues.

Dr. Ryan Soose:

The stimulation itself, even though it's not painful, when that stimulation is running, we do see patients then that their insomnia's worse. They have more trouble falling or staying asleep because of the stimulation. And although that's not something we traditionally think of as a postop complication, I think it is adverse event that has to be really looked at in detail with this therapy. Because long-term consistent use of the device is critical to the outcomes.

Dr. Ryan Soose:

And again, that gets back to why we're really trying to bolster our post-implant therapy management protocol. We're working now to develop a long-term management strategy that centers around the country will be able to use. So if a patient is experiencing X, Y, or Z problem with the therapy and usage, we can then prescribe kind of a targeted troubleshooting to try to modify that and ultimately make their use and experience better.

Dr. John Marinelli:

Now, related question to patient medical comorbidities. What do you do about the patient that has chronic cervical spine disease that might need future MRIs or someone that needs a cardiac device placement? How do you think about these special scenarios?

Dr. Ryan Soose:

Yeah, those are great questions. And it gets back to one of the earlier conversations we were having that... Every one of these patients is different. Everyone has unique issues. Whether it be a cardiac device, a breast implant, prior radiation in the area, a need for MRIs, comorbid sleep disorders, et cetera. Yeah, this is not just for our ENT surgery listeners here, this is not just a surgical technician thing.

Dr. Ryan Soose:

I think that particularly say with UPP 20, 30 years ago, the ENTs were kind of viewed as like the surgical technicians, just doing the surgery and then sending them out the door. This therapy in particular really involves a longitudinal care model where you really have to screen patients appropriately and then you have to manage them and adjust things in the longterm.

Dr. Ryan Soose:

So the implant itself is actually the easy part. It's all the preop and postop assessment that's really critical. So on that front, one of the limitations with the current device is there are some MRI restrictions. Now the latest model, the device has been out for a lot about the last three years, is compatible with head neck MRIs and extremity MRIs. But it is not compatible with MRIs in the thorax area, the chest and abdomen. That may change down the road, but if you have somebody that has a unique cardiac issue or thoracic or lumbar spine issue that requires regular MRIs, then this therapy is probably not for them.

Dr. Ryan Soose:

The other thing I would point out is, unlike other surgical procedures, this is reversible. So if for some reason, either the therapy was not working for the patient, or if the patient needed an MRI for some life-threatening issue, a malignancy or something like that, this device can be removed.

Dr. John Marinelli:

And transitioning to outcomes and treatment success, obviously a little bit of a difficult discussion, the context of sleep apnea, it's little bit controversial how we define that. But if you're counseling a patient or talking to a resident about this, how do you think about success in hypoglossal nerve simulation?

Dr. Ryan Soose:

That's a million-dollar question. I mean, we could probably have an entire podcast just on defining surgical success. And that's often a topic of controversy meetings. But I think if you really want the big picture view, the reason we treat sleep apnea and the reason we try to help these patients is, number one, symptom and quality of life improvement, and number two, reduction or elimination of cardiovascular risk. So we're trying to improve their quality life and reduce their health risks.

Dr. Ryan Soose:

And for the most part, we know the health risks are associated with moderate to severe sleep apnea. So when I have these discussions with the patients, and what I think is most important when you take this information out of the literature, is looking at patient reported outcomes in combination with sleep study metrics that get people out of the moderate to severe range, and into at least the mild or normal range.

Dr. Ryan Soose:

So the AHI does not have to be zero as some may have been taught in the past. That's not the goal of treatment. The AHI is not the disease itself. We're not trying to make a number on a test zero. But what we'll try to do is big picture, improve these people's symptoms and quality of life, and get them out of that moderate to severe range.

Dr. Ryan Soose:

So if you translate that sort of view to, say the STAR trial reports, we published the five-year STAR child data in the last a year or two. And depending on which criteria you use, whether it's AHI reduction or sleep-related quality of life metrics, or daytime sleepiness metrics, anywhere between 65 and 80% of people achieve that designation.

Dr. Ryan Soose:

So that's what we tell people, is roughly two-thirds or three-quarters of patients will achieve that result with this therapy alone. But remember, we can add positional therapy, we can add weight loss, we can add upper airway surgery, lowering of nasal resistance and other adjunctive therapies, to then further augment the results.

Dr. John Marinelli:

And one other question I wanted to ask you about was just kind of the frontier where this procedure is heading. One of the recent studies that I saw was in patients with Down syndrome, for instance, because it classically disapproved in adults, but maybe perhaps at younger ages in this population, there might be a procedure to consider things like that. Any comment on expansion of indications going forward?

Dr. Ryan Soose:

Absolutely. I was fortunate enough to be part of the team that did the first pediatric implant about five years ago. And since then there's now a multicenter FDA-approved trial across the U.S. that's enrolling adolescent Down syndrome sleep apnea patients for this type of therapy. And so that's just one example of another patient population that may be uniquely suited to benefits from this kind of therapy. Down syndrome patients, first and foremost, have pretty poor outcomes with CPAP, even worse adherence rates than you see in the general population.

Dr. Ryan Soose:

The reports of persistent over, say after-adenoidectomy in Down syndrome are very high. At least half of the patients that have their tonsils and adenoids removed, still have severe sleep apnea. And furthermore, Down syndrome is unique in other ways from the patient perspective, in that many of them have congenital heart disease, and many of them already have learning and cognitive issues. Both of which are affected by untreated sleep apnea.

Dr. Ryan Soose:

So the patient need, I think, is even higher from a quality of life and heart stand-point, and the success of the traditional treatments is even lower. So the upper airway stimulation appears to be a way to help that subset of the population. And the early results look very promising where parents are able to activate the device and the child does not have to wear a mask or any other device to achieve their sleep apnea control.

Dr. Ryan Soose:

So that's one area, but I think there's many other areas. We really need to look at specific sub-populations of patients, whether it's with insomnia, postmenopausal women, different BMIs, different skeletal phenotypes, and really start to fine tune the results.

Dr. Ryan Soose:

One of the things that we're doing globally is we have a registry set up. It's called the DHERE Registry. And there's already about 2000 patients enrolled in it. I presented the first thousand patients at our academy meeting last fall. With that big data, and the goal is to ultimately enroll 5,000 patients in this registry, we're really able to collect better and more useful data, I think, to further improve the treatment success.

Dr. John Marinelli:

Well, I think that about wraps up the questions that I had for the episode. Was there anything that we didn't touch on that you think is worth mentioning?

Dr. Ryan Soose:

Well, I would just say in summary, the early results of upper airway stimulation are very positive. The therapy is still young, that we still have a long way to go. But I do think, in the big picture, it's been one of the biggest breakthroughs in sleep apnea treatment in decades. It's still has its limitations. It's still not applicable to all patients with sleep apnea by any means. And as I mentioned, there's still a lot of work that needs to be done.

Dr. Ryan Soose:

But one of the thing that I would just throw out there is that one of the unanticipated benefits that we've found of having an implant program at our institution, is the trickle down effect within the institution and the positive impact it's had on our overall health system. So having this new therapy available and this implant program at our institution, it's brought so many sleep apnea patients out of the woodwork, who were previously just jaded, frustrated with the current treatment options and just lost the followup.

Dr. Ryan Soose:

And it's brought them back into the physician. For many of the patients, I would say the majority of patients that come to see me for upper airway stimulation specifically, they don't actually end up getting that treatment, but by bringing them back into the health system, we're able to get them back into their PCP for blood pressure management. We're able to then engage them with weight loss specialists.

Dr. Ryan Soose:

As ENTs, we're able to get their sinus nasal problems managed. And then now, maybe we can get them back into the lab for a CPAP titration. Or then maybe we get them in to the dentist for an oral appliance, something that they had maybe never heard about. Or we get their other sleep disorders, or other breathing disorders addressed.

Dr. Ryan Soose:

I just want to point out that bigger picture here is that, even in patients who see this as an option and that's what brings them into the doctor, from a bigger picture public health perspective, it's actually really helped across the entire health system to get these patients re-engaged and better treated.

Dr. John Marinelli:

Dr. Soose, thank you so much for your time and coming on the podcast today.

Dr. Ryan Soose:

Thank you so much for having me and good luck with the future.

Dr. John Marinelli:

Thank you. So now I transition to the summary portion of the episode. Hypoglossal nerve stimulation is obviously one of the new and exciting treatment options and the management of patients with

obstructive sleep apnea that available or done by otolaryngologists currently. FDA approval just recently, in 2014, in conjunction with the landmark STAR trial published in The New England Journal of Medicine.

Dr. John Marinelli:

Currently, the Inspire device is the only FDA-approved medical device for upper airway stimulation, that is titratable technology to adjust and that you can work with the patient's sleep apnea postoperatively to titrate it to the optimal effect. It works in a couple of different ways. It's really a multi-level surgery. It's more than just advancing the tongue. And the dresses beyond just an anatomical obstruction. Also, addresses a pathophysiologic idea of dysfunctional neuromuscular control of breathing that occurs in patients with obstructive sleep apnea.

Dr. John Marinelli:

The workup includes obtaining a formal sleep study, as well as opinion drug-induced sleep endoscopy. And on drug-induced sleep endoscopy, you're looking for complete concentric collapse at the vellum as that would be a contraindication to pursuing hypoglossal nerve stimulation.

Dr. John Marinelli:

Other contraindications or considerations to just keep in mind to this patient's BMI. STAR trial had a BMI of 32 and recently expanded by Medicare to 35. Not that those are binary cutoffs, but something to be mindful, that on that spectrum of patients BMI, that the efficacy of the treatment might wane as the BMI increases. Other considerations or potential need for future MRI of the thorax or abdomen, other causes of sleep apnea, patients having less than 25% of, their apnea is related to central or mixed apneas. And then the range with which the AHI device is currently approved for it's 15 to 65, so moderate to severe obstructive sleep apnea.

Dr. John Marinelli:

Just globally speaking, it's tough to define, but when thinking of counseling patients, roughly two-thirds to three quarters of patients achieve "postoperative" success when thinking about quality of life, subjective sleepiness, and then as well as polysomnogram-related outcome measures.

Dr. John Marinelli:

And now I'll transition to the question portion of the podcast. So first question, mechanistically, how does upper airway stimulation work to address the upper airway obstruction and obstructive sleep apnea? Answer here is, it's the selective neurostimulation of the terminal branches responsible for upper airway dilation from the hypoglossal nerve.

Dr. John Marinelli:

And really, how this all fits together is there's a respiratory sensor that just detects a change in the intrathoracic pressure with inspiration, stimulates the hypoglossal nerve that causes the anterior displacement of the tongue and soft palate helps to enlarge and stabilize the retro-epiglottic and retro-palatal airway regions.

Dr. John Marinelli:

Second question, what key diagnostic study is required in the preoperative workup of an upper airway stimulation and what finding is this study aiming to identify? So answer is, drug-induced sleep endoscopy. What you're looking for on drug-induced sleep endoscopy is complete concentric collapse at the vellum.

Dr. John Marinelli:

Third question, what are the current... Third and final question. What are the current indications for upper airway stimulation? The current indications for upper airway stimulation are hypoglossal nerve stimulation, it's considered a second line therapy, second to positive airway pressure, most commonly CPAP or APAP.

Dr. John Marinelli:

For patients with moderate to severe obstructive sleep apnea, AHI ranging between 15 and 65, who have a documented failed trial of positive airway pressure therapy, can also not have complete concentric collapsed on drug-induced sleep endoscopy. There's BMI considerations, for instance of Medicare's BMI of 35. It's labeled for BMI under 35, you cannot have on your polysomnogram AHIs or apneas that are caused by... More than 25% of apnea is caused by central or mixed apneic events. And then also just considering a need for future MRI of the thorax and abdomen, given current device limitations.

Dr. John Marinelli:

That'll about wrap things up for today. Thanks so much for listening and we'll catch you next time.