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Clinical and Economic Evidence for Balloon Dilation for the Treatment of Persistent Eustachian Tube Dysfunction

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1 Executive Summary

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1.1 Clinical benefits

The Eustachian tube connects the middle ear to the nasopharynx and is important for pressure regulation, deflection of pathogens/foreign objects, and middle ear fluid clearance. A common cause of Eustachian tube dysfunction (ETD) is when the tube fails to open in the absence of a mechanical obstruction (functional obstruction). When left untreated, ETD can lead to tympanic membrane retraction, cholesteatoma, and hearing loss. ETD is frequently associated with chronic otitis media.

Medical management options are few and are not effective in all patients. Balloon dilation has been suggested as a minimally invasive therapy for ETD. Although the actual mechanism is not certain, reduction of mucosal inflammation and lymphocytic infiltration, promotion of normal healing, and muscular stretching have been hypothesized mechanisms of action. Two multicenter RCTs, a number of prospective and retrospective single-arm clinical studies, and multiple systematic reviews have examined the safety and effectiveness of Eustachian tube balloon dilation for the treatment of ETD. The RCTs demonstrate that balloon dilation provides superior clinical outcomes over medical management. The single-arm studies compare predilation with postdilation outcomes and confirm positive outcomes of the RCTs. The studies demonstrate high rates of technical success along with a very low incidence of complications. The few events that were reported were minor and transient. There were no occurrences of serious adverse events related to Eustachian tube balloon dilation. Symptoms were consistently improved in the majority of treated patients and are maintained for more than 12 months. Other tests used to evaluate middle ear function show significant improvement after Eustachian tube balloon dilation, including: otoscopy, pressure equalization tests (eg, Valsalva), and tympanometry.

1.2 Economic benefits

Although there are currently no direct economic studies available on Eustachian tube dilation, the economic benefits can be surmised. Before the clearance of balloon dilation devices for the treatment of ETD, only temporary treatments for the symptoms were available. While these treatments (myringotomy, tympanostomy) provided temporary symptom relief, they did not address the actual dysfunction of the Eustachian tube. Additionally, these treatments can have adverse effects on hearing. With the introduction of Eustachian tube balloon dilation, patients now have access to a safe, effective, and durable treatment that addresses the actual condition. Moreover, balloon dilation procedures can be performed in the office setting under local anesthesia, providing cost savings to the patient and providers over procedures performed in hospital or surgical center settings. The ability to rapidly return to work and other normal daily activities also benefits patients (and employers).

1.3 Conclusions

Persistent ETD results in lowered quality of life. In patients who are refractory to medical therapy, numerous clinical studies have shown that balloon dilation of the Eustachian tube results in significantly improved symptoms over baseline and that

these improvements are maintained through 12 months. Objective measures of middle ear function, such as tympanometry and the ability to perform a Valsalva maneuver, are also improved. Adverse events are rare and are typically minor and transient. Two randomized controlled trials have confirmed the superiority of balloon dilation over medical therapy for treating ETD. The procedure is well tolerated in the office setting under local anesthesia. Balloon dilation is a safe and effective minimally invasive procedure for patients with ETD who otherwise have very limited options for treatment.

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2 Product Information and Disease Description

2.1 Product description

The XprESS™ ENT Dilation System (XprESS) is manufactured by Stryker ENT, Plymouth, Minnesota, USA. The XprESS device received U.S. Food and Drug Administration (FDA) clearance for Eustachian tube dilation through the 510(k) process in April 2017.[1] The device was previously cleared by the FDA for sinus dilation in February 2010. The XprESS device initially received CE mark in October 2010 for sinus dilation and obtained CE mark for Eustachian tube dilation in April 2017.

The XprESS device combines features of a curved suction tip and an ostium seeker with the tissue expansion effect of balloon dilation. The features of this device enable a physician to track the device to the Eustachian tubes using endoscopic visualization. The distal end of the device is re-shapeable, allowing easy access to the Eustachian tubes. The XprESS curved suction tip has an atraumatic ball tip. A suction tube may be connected to the proximal barbed fitting to provide active suction by covering the suction vent. The XprESS balloon is available in diameters of 3-5 mm and in lengths of 8, 18, and 20 mm. All sizes are appropriate for treating Eustachian tubes; selection is based on physician preference. The XprESS device is provided sterile and for single use only.

The current XprESS indications for use are:

- To access and treat the maxillary ostia/ethmoid infundibula in patients 2 years and older, and frontal ostia/recesses and sphenoid sinus ostia in patients 12 years and older, using a transnasal approach. The bony sinus outflow tracts are remodeled by balloon displacement of adjacent bone and paranasal sinus structures.
- To dilate the cartilaginous portion of the Eustachian tube for treating persistent Eustachian tube dysfunction in patients 18 years and older using a transnasal approach.

2.1.1 Product comparison

Other balloon dilation devices on the market for Eustachian tube dilation are the AERA (Acclarent), which has FDA clearance[2] and CE mark, and the Bielefeld balloon (Spiggle &Theis), which has CE mark but not FDA clearance. A comparison of the features of each device is provided in **Table 1.**

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Table 1. Comparison of Commercially Available Balloon Devices for ET Dilation

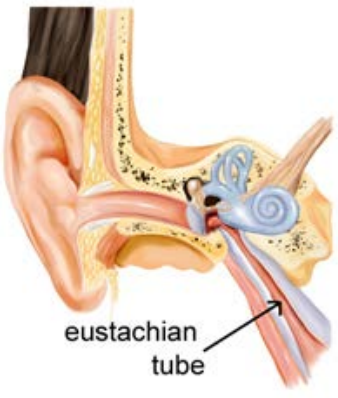
Feature	XprESS	AERA	Bielefeld
Manufacturer	Entellus Medical	Acclarent	Spiggle and Theis
FDA Clearance	Yes	Yes	No
Indications for Use	To access and treat the maxillaryostia/ethmoid infundibula in patients 2 years and older, and frontal ostia/recesses and sphenoid sinus ostia in patients 12 years and older using a transnasal approach. The bony sinus outflow tracts are remodeled by balloon displacement of adjacent bone and paranasal sinus structures. To dilate the cartilaginous portion of the Eustachian tube for treating persistent Eustachian tube dysfunction in patients 18 years and older using a transnasal approach.	To dilate the Eustachian tube for treatment of persistent Eustachian tube dysfunction in adults ages 22 and older.	Not available
Balloon sizes Diameter:	5, 6, and 7 mm Length: 8, 18, and 20 mm	Diameter: 6 mm Length: 16 mm	Diameter: 3 mm Length: 20 mm

2.2 Place of product in treatment

2.2.1 Disease description

The Eustachian tube connects the middle ear to the nasopharynx (**Figure 1**) and is important for pressure regulation, deflection of pathogens/foreign objects, and middle ear fluid clearance.[3] The Eustachian tube is comprised of a bony isthmus at the middle ear end and a cartilaginous region that extends from the bony isthmus to the nasopharynx. The cartilaginous part of the Eustachian tube is normally closed but opens when needed to equalize pressure within the middle ear. Transient opening of the Eustachian tube occurs with yawning, swallowing, or popping of the ears.

Figure 1. Adult Eustachian tube



The overall prevalence of ETD in adults is estimated to be 1% to 5%.[4,5] A recent study in the US estimated that over 2 million ambulatory healthcare visits occur every year for adults with ETD, otitis media with effusion (OME), or tympanic membrane retraction.[6] These authors also found that OME was more common in children and ETD was a more common in adults.

Symptoms of ETD include fullness in the ear, dizziness, tinnitus, and pain or discomfort with barometric changes (eg, flying, diving). ETD can lead to tympanic

membrane retraction, cholesteatoma (abnormal skin growth in the ear), and hearing loss and is frequently associated with chronic otitis media (inflammation of the middle ear). ETD is considered persistent when symptoms have continued more than 12 weeks.

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ETD can result from the Eustachian tube being too open (patulous Eustachian tube), too closed (mechanical obstruction), or unable to efficiently open (functional obstruction).[7,] Mechanical obstruction of the Eustachian tube can be from either extrinsic (eg, tumors, adenoids, nasal septal deviations) or intrinsic (eg, inflammation, stenosis) mechanisms. Functional obstruction, a common cause of ETD, occurs when the tube fails to open in the absence of a mechanical obstruction and can be caused by increased tubal compliance, inefficient opening mechanism, and/or abnormal pressures.[7]

2.2.2 Approaches to treatment

There is no definitive medication regimen found to be effective in treating ETD; however, decongestants, antihistamines, and steroids (oral or nasal sprays) are commonly used medical therapies to relieve symptoms of ETD.

When medical management fails to resolve ETD symptoms, some physicians have resorted to surgical treatments of the middle ear such as myringotomy (aspiration of fluid from the middle ear) and tympanostomy (placement of pressure equalization or ear tubes in the tympanic membrane). Although these treatments may temporarily relieve ETD symptoms, neither of these treatments address the actual dysfunction of the Eustachian tube. Furthermore, ear tube placement is temporary, can negatively impact hearing, and is associated with complications such as infection, crusting, obstruction, otorrhea (discharge from the ear), extrusion, atelectasis (high negative middle ear pressures) with or without retraction pockets (areas of collapsed tympanic membrane), and permanent tympanic membrane perforation.[7] A meta-analysis of tympanostomy tube sequelae reported in 134 articles found otorrhea in 16% of patients postoperatively and 26% overall. Tube obstruction was found in 7% of ears, granulation tissue in 5%, and premature extrusion in 4%. Complications observed after tube extrusion included tympanosclerosis (32%), focal atrophy (25%), retraction pocket (3%), cholesteatoma (1%), and permanent perforation (5%). These findings indicate that ongoing follow-up, even after tube extrusion, is required for these patients and long-term tubes should be used on a selective and individualized basis.[8]

Balloon dilation has been evaluated in clinical studies as a minimally invasive treatment that directly treats the dysfunction of the Eustachian tube for the treatment of persistent ETD. Multiple devices are currently marketed with an indication for Eustachian tube dilation. This document summarizes the currently available information on balloon dilation for treating persistent ETD.

Although the mechanism of action of balloon dilation of the Eustachian tube is not fully understood, there is evidence that balloon dilation reduces local inflammation and/or hypertrophic mucosa volume through compression or crushing of the mucosa.[9,10] This enables rapid healing to occur, with the inflamed mucosa being replaced with normal mucosa. This combination reduces the overall inflammatory burden and may provide lasting clinical improvement in both Eustachian tube dilation and ventilation.

3 Clinical Evidence

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The current clinical evidence for balloon dilation of the Eustachian tube to treat persistent ETD in adults is comprised of the following studies that report data from more than 4200 participants and more than 6500 ears treated with balloon dilation (not including the safety analysis due to potential overlap with other studies):

- 2 randomized controlled trials[11,12,13,14]
- 1 long-term follow-up study of the treatment cohort from an RCT[15]
- 12 prospective, single-center, single-arm case series[5,10,16,17,18,19,20,21,22,23,24,25]
- 11 retrospective, single-arm case series[26,27,28,29,30,31,32,33,34,35,36]
- 1 large retrospective multicentre safety analysis[37]
- 1 case report[38]

3.1 Randomized Controlled Trials (RCTs)

Two randomized controlled trials (RCTs) have evaluated the safety and efficacy of Eustachian tube balloon dilation compared with medical therapy alone. The designs of these studies were developed in collaboration with the FDA to obtain marketing clearance for the devices in the US. Specifically, the FDA recommended the 6-week crossover design as being the most appropriate for this patient population. Since patients were required to have persistent (≥12 weeks), medically refractory ETD upon entering the study, FDA determined that an additional 6 weeks of continued medical management for the control group provided a scientifically sound comparison of results between the treatment and control group.

Between these 2 RCTs, a total of 384 patients have been treated with balloon dilation of the Eustachian tube, of whom 177 have follow-up at 12 months.

3.1.1 XprESS ETD Study

Stryker ENT (formerly Entellus Medical) sponsored a multicenter randomized controlled trial comparing Eustachian tube dilation (using the XprESS device) to medical therapy for the treatment of persistent Eustachian tube dysfunction (NCT02391584).[11] To qualify for enrollment, adult patients (18+ years) were required to have been diagnosed with ETD for 12 months or more before enrollment, have 3 or more ETD symptoms, have an overall ETDQ-7 score of 3.0 or higher, and have a record of failed medical management for ETD consisting of a minimum of either 4 weeks of daily intranasal steroid spray or 1 completed course of an oral steroid within the 12-month period before enrollment. Patients with a history of patulous Eustachian tube, or a non-intact tympanic membrane were excluded from the study.

The primary efficacy endpoint was the comparison between study arms of the mean change in the overall 7-Item Eustachian Tube Dysfunction Questionnaire (ETDQ-7) score at 6 weeks. The primary safety endpoint was the number of serious device- or procedure-related adverse events. Secondary endpoints included technical success rate, revision rate, and mean change from baseline in overall ETDQ-7 scores at all follow-up periods.

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In 60 randomized participants, the primary efficacy endpoint was met with Eustachian tube balloon dilation demonstrating superiority over medical therapy for improvement in mean overall ETDQ-7 scores at 6-week follow-up (–2.9 vs –0.6, p<0.0001). The primary safety endpoint was met with a complication rate of 0%.

Control participants who did not demonstrate symptom improvement after remaining on medical management for 6 weeks were given the option to crossover to balloon dilation to

treat their continuing ETD. Of the 27 control participants who underwent the 6-week crossover evaluation, only 1 was not eligible for crossover due to improved ETD symptoms. Of the remaining 26 control participants (96%) who were eligible for crossover, 23 underwent balloon dilation and 3 elected not to undergo balloon dilation and exited the study according to the protocol. This further supports the finding that continued medical management is not an effective therapy for this patient population who has previously failed medical management before entering this study.

A total 53 participants (30 randomized, 23 crossover) underwent balloon dilation of 91 ears. Technical success was 100% (91/91 ears) and the revision rate was 0%. Nearly three-fourths of the procedures were performed in the office setting under local anesthesia. Long-term, the symptom improvements observed in the randomized balloon dilation cohort at 6 weeks were maintained through the 12-month follow-up period for all balloon dilation participants (–2.5, p<0.0001).

Evaluation of middle ear functional assessments in participants who had abnormal baseline indicated significant improvement over baseline for normalization of tympanic membrane position (79.2%), positive Valsalva maneuver (62.5%), and improvement in tympanogram type (55.0%) at 12-months follow-up. There was no change from baseline to 6-months follow-up in pure tone audiometry.

Results from the 12-month follow-up for this RCT were published in Otology and Neurotology in 2018.[13]

3.1.2 ELLIOTT Study

Acclarent sponsored the ELLIOTT Study (A Randomized Clinical Study of Safety and Efficacy for the Eustachian Tube Balloon Catheter, NCT02087150). The objective of this multicenter randomized controlled trial was to compare Eustachian tube balloon dilation (using the AERA device) in conjunction with medical therapy against medical therapy alone (intranasal steroids) for treatment of persistent ETD. Participants were randomized in a 2:1 ratio of balloon dilation to medical therapy. Eligible patients were adults (22+ years) with persistent ETD (duration ≥12 weeks) who had failed medical management (either a minimum of 4 weeks of a daily intranasal steroid spray or at least 1 completed course of an oral steroid within 90 days before study enrollment). Persistent ETD was defined by patient-reported symptoms and an abnormal tympanometry and/or a mean ETDQ-7 score of 2.1 or higher. Exclusion criteria included the presence of a patulous Eustachian tube or a non-intact tympanic membrane.

The primary endpoint of the study was the proportion of participants with normalization of tympanometry at 6 weeks and the secondary endpoint was the proportion of

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participants achieving at least a minimally important difference (MID) level of improvement of 0.5 in the ETDQ-7 score at 6 weeks. The safety endpoint was the number of adverse events.

The ELLIOTT study randomized 242 participants (162 balloon dilation and 80 medical therapy) along with 81 nonrandomized lead-in participants. The primary endpoint was met with 51.8% (72/139) of balloon dilation participants experiencing tympanometry normalization (type A) compared with 13.9% (10/72) of controls ($p<0.0001$). The secondary endpoint of the MID was not sensitive, so an ad hoc analysis was performed to evaluate normalization of the ETDQ-7 score (<2.1). This analysis showed significantly more ETDQ-7 score normalization in the balloon dilation group compared with the control group (56.2% vs 8.5%; $p<0.001$). For the safety endpoint, no serious device or procedure-related adverse events were reported.

At 6-weeks follow-up, control participants were allowed to crossover to receive balloon dilation for their ETD. These participants were followed through at least 12 weeks post procedure.

Additional outcomes of ability to perform Valsalva maneuver, change in mucosal inflammation, and improvement in tympanogram type all confirmed the better outcomes among the balloon dilation group versus the control group at 6-weeks follow-up. Long-term follow-up at 24 weeks was evaluated in 239 participants who undergoing balloon dilation (100 randomized, 64 crossover, and 75 lead-in). Within this group 62.2% of participants showed normalization of tympanograms at 24-week follow-up and 59.8% had normalization of ETDQ-7 score.

The results of this study were published in The Laryngoscope in May 2018.[14]

Recently, Anand et al published the 12-month follow-up of 128 patients who were treated with ET balloon dilation in the ELLIOTT RCT (NCT02087150).[15] The authors reported that the tympanogram and symptom results at 12 months were comparable to the 6-week outcomes reported in the earlier publication. Tympanogram type was normalized in 55.5% of patients (71/128) and ETDQ-7 overall scores were normalized (<2.1) in 57.3% (71/124). Overall, 75.8% of participants had normalized tympanogram type and/or ETDQ-7 score at the 12-month follow-up.

Improvement in tympanogram type was experienced by 70.1% (131/187 ears). The mean (standard deviation) change from baseline in the ETDQ-7 score was –2.4 (1.6). Additionally, 80.4% of ears (185/230) demonstrated positive Valsalva maneuver at 12 months.

There were no device or procedure-related adverse events through last follow-up; however, 2 patients reported mild cases of patulous Eustachian tube. Additionally, 1 case of false passage was noted at the time of the procedure and corrected before balloon dilation was performed.

These results confirm the 12-month durability of the benefits of Eustachian tube dilation on tympanograms and symptoms in patients with chronic Eustachian tube dysfunction.

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3.2 Prospective and Retrospective Single-Arm Clinical Studies

Twenty-three prospective or retrospective single-arm studies have evaluated efficacy and safety outcomes of Eustachian tube balloon dilation in over 1600 patients (>2500 ears). Although these studies do not incorporate a concurrent control, they involve evaluation of outcomes before and after the balloon dilation in patients with long-standing, medically refractory ETD. The outcomes and duration of follow-up vary across studies with follow-up periods ranging from immediate post procedure to 5 years. Commonly reported outcomes include patient-reported symptom improvement, ability to perform Valsalva maneuver, improvement in otoscopy and tympanometry, and complications. Many of the single-arm studies have been evaluated in recent systematic literature reviews (see Section 5.2).

Despite the variation in outcomes measures and follow-up, the overall results of these studies are remarkably consistent in demonstrating benefits of the procedure with low rates of complications. Technical success rates for Eustachian tube balloon dilation (successful access of the Eustachian tube and dilation without complications) reported in the clinical studies are in the 99% to 100% range.[5,13,19,24-26,30,35]

3.2.1 Safety results from clinical studies

With over 4200 patients (over 6500 ears) treated with ET balloon dilation in clinical studies, all complications reported to date have been minor and transient in nature. Minor complications that have been noted and may be related to the device or procedure are preauricular emphysema (facial swelling near the ear/neck area), hemotympanum (presence of blood in/near the tympanic cavity of the middle ear), transient hypoglossal paresis or dysesthesia, bleeding, rhinorrhea, worsening tinnitus, and patulous ET.[16-17,20,24-28,34-36] To date, the few cases of patulous ET have all been mild in nature. Anand et al reported 1 case of entering a false passage that was corrected before balloon dilation was performed.[15] In a large retrospective safety study, Skevas et al determined a rate of emphysema of 0.27% with all cases resolving rapidly without serious sequela.[37] Shah et al reported a single case report of a patient with subcutaneous emphysema with pneumomediastinum that resolved within 72 hours without sequelae.[38] Overall, the complication rate for Eustachian tube balloon dilation appears to be <1.0%.

Although carotid artery injury has been perceived as a potential safety concern, there are no reports in the literature.

3.2.2 Efficacy results from clinical studies

Efficacy of balloon dilation for ETD has been assessed by a variety of measures in clinical studies, both subjective and objective. Subjective measures include patient-reported symptoms and severity (eg, ETDQ-7) and the Valsalva maneuver. Objective measures include otoscopy and tympanometry.

Symptom improvement

Patient-reported symptoms are an important outcome measure. Symptoms have been measured using a variety of tools including visual-analog scale (VAS) scores and questionnaires. Although VAS scores have been commonly used in the past, the validated

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ETDQ-7[39,40] is gaining recognition as a standardized disease-specific assessment tool for 1 ETD.[14,17,22-24,33-35] ETDQ-7 scores consistently demonstrate statistically ($p<0.05$) and clinically (score reduction of 0.5 or more) significant improvements with many patients achieving scores within the normal range (≤2.1) after balloon dilation.

Specifically, in both RCTs, balloon dilation of the ET has been proven to be statistically and clinically superior to medical management alone for the treatment of ETD and the treatment effect is durable through at least 12 months post procedure.[13,14,15]

Middle ear functional assessments

The clinical studies demonstrate consistent improvements in middle ear functional assessments such as tympanic membrane position (otoscopy), ability to perform Valsalva, and tympanometry. After balloon dilation, the percent of retracted tympanic membranes is reduced in 6 of the 7 studies reporting the outcome.[10,17-19,27,29] The exception was the study by Schmitt et al that showed no statistically significant change in otoscopy.[34] This may have been due to the small sample size since 64.7% (11/17) demonstrated improvement and 17.6% (3/17) were stable post procedure. The RCT by Meyer et al reported statistically significant improvement in tympanic membrane at 6 weeks after balloon dilation (66.7%) compared with medical management (0%, $p<0.001$).[13]

Similarly, the ability to perform the Valsalva maneuver or similar tests is improved after balloon dilation in 11 out of 12 studies reporting the outcome.[13-15,18-20,22,30,33,35,36] The study by Satmis et al shows improvement at 1 month that is not maintained at the 3-month period, but they have considerable amount of missing data for this outcome.[34] The RCT by Meyer et al reported a statistically difference in ability to perform Valsalva at 6 weeks after balloon dilation ($p=0.005$) that was not apparent in the medical management group ($p=0.157$); however, the comparison between groups did not reach statistical significance (47.1% vs 14.3%; $p=0.068$).[13] On the other hand, in the RCT by Poe et al, there was a statistically significant difference between groups (32.8% vs 3.1%; $p<0.001$).[14]

Seventeen studies evaluated the normalization of tympanogram type with follow-ups ranging from immediately post procedure to more than 2 years post procedure.[10,13-20,22-23,27,29-31,34,36] One study reported no significant difference ($p=0.4$).[23] The remaining 16 studies reported significant improved or normalized tympanograms at follow-up ranging from 32% to 96%. Finally, both RCTs demonstrated statistically significant improvement of balloon dilation compared with medical management for the improvement or normalization of tympanograms at 6 weeks follow-up. Poe et al reported 51.8% improvement after balloon dilation vs 13.9% in medical management ($p<0.0001$).[14] Similarly, Meyer et al reported 57.1% improvement after balloon dilation vs 10% after medical management ($p<0.006$).[13]

4 Economic Studies

There are no current clinical-based health economics studies on the use of balloon dilation for the treatment of ETD. However, in May 2017, the US Centers for Medicare and Medicaid Services (CMS) established a temporary payment code for Eustachian tube balloon dilation (C9745) to be effective as of July 1, 2017.

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Based on the review of clinical evidence submitted for the new c-code, CMS assigned the code to an existing suitable clinical APC ENT payment level group that was appropriate in terms of clinical characteristics and resources costs. The APC group level is 5165-Level 5 ENT procedures. The payment rate can be found on the CMS website for CY 2018 OPPS/ASC final rule correction notice in Appendix A:

https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Hospital-Outpatient-Regulations-and-Notices-Items/CMS-1678-CN.html

This code facilitates the payment for outpatient treatment of ETD using balloon dilation in hospitals and ambulatory surgery centers (ASC). This code structure is expected to be in effect through the end of 2019.

5 Additional Supporting Information

5.1 Clinical Practice Guidelines

There are currently no professional organization policy statements available on the dilation of the Eustachian tube for treatment of ETD.

5.2 HTAs and Systematic Reviews

Eight systematic reviews, including 2 meta-analyses, have been conducted on single-arm clinical studies of Eustachian tube balloon dilation as a treatment for ETD.[41,42,43,44,45,46,47,48] However, none of these systematic reviews include the 2 randomized controlled trials that have been published recently. A brief synopsis of each systematic review is provided below.

The Cochrane reviews published by Norman et al[41] and Llewellyn et al[42] in 2014 reported no findings as no RCTs had been published at that time.

In 2015, Miller and Elhassan published a systematic review of 5 single-arm studies reporting on 235 adult patients (375 ears) before and after ET balloon dilation.[41] Mean follow-up duration for the 5 studies ranged from 8 weeks to 10 months. Outcomes over the short-term (up to 6 months) demonstrated benefits for tympanometry (78% normalization), otoscopy (87% normalization), Valsalva maneuver (64% positive), and symptoms (various measures but no reports of worsening). Long-term follow-up (1 to 3 years) was available for 20 patients, 85% of whom reported sustained symptom improvement. They reported a 2% revision rate; however, most were attributed to brief dilation time (5 sec) or small catheter diameter (5 mm). An overall complicate rate of approximately 3% was report, however, that included events unrelated to the ET dilation (C6-7 radiculopathy and hemotympanum) and minor ET mucosal lacerations that had no clinical significance and have been hypothesized to actually contribute to the postdilation healing process. There was only 1 case of a potentially serious preauricular emphysema that spontaneously resolved. The authors concluded that ET balloon dilation may offer a valuable treatment option for patients who do not respond to medical therapy.

In 2016, Randrup and Ovesen reported a systematic review of 9 case series studies of 443 adult patients (642 ears) treated with ET balloon dilation.[45] Due to the single-arm study design, all studies were deemed of poor quality and most had a high risk of bias. Five of the 9 studies overlap with the studies reported in the previous systematic review

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by Miller and 3 Elhassen.[41] Follow-up durations ranged from 1 to 18 months. Subjective outcomes were reported to be positive on ad hoc scale as well as using the ETDQ-7. The authors report a tympanic membrane normalization across all studies ranging from 50% to 97% and a high rate of normalization of tympanogram type at follow-up. Mucosal inflammation was reported in 2 studies and showed significant reduction at 6 and 18 months. Valsalva maneuver was reported in 5 studies and showed positive outcomes at all follow-up time points. The study noted no reports of severe morbidity of mortality was attributable to the ET balloon dilation. They found 2 cases of emphysema and various reports of minor bleeding and temporary increases in tinnitus in their review.

In 2016, Hwang et al reported a systematic review of 9 case series of ET balloon dilation in 474 patients (713 ears).[44] Their review evaluates 8 of the 9 studies reported by Randrup and Ovesen.[45] They do not include the quality of life study by Bast et al[32] that was included in the Randrup review but instead include the case series reported by Wanscher and Svane- Knudsen.[20] Mean (or median) follow-up duration of the studies ranged from 1.5 to 18 months. The ability to perform a Valsalva maneuver improved from 8% at baseline to 72% at follow-up in 245 ears. A normal tympanogram type (type A) was reported in 5% (7/141) of ears preprocedure and improved to 61% (86/141). Some patients (9%) had ventilation tubes in place or a perforation, so could not be evaluated. Symptoms (using the ETDQ-7) were significantly improved from a preprocedure score of 4.5 to 2.8 at 6-month follow-up. Serious complications were the same as reported by Randrup and Ovesen. In addition, based on the Wanscher and Svane-Knudsen study, they report learning curve complications of acute otitis media in 3 of the first 20 cases, which were reduced after initiation of postoperative oral antibiotics. They conclude that the procedure is safe and has potential benefit for a condition and is difficult to manage.

In 2017 Huisman et al published a meta-analysis of 15 case series of ET balloon dilation including 1,155 patients (at least 1,830 ears).[46] The studies overlap with 7 of the studies evaluated in the each of the reviews by Randrup and Ovesen and by Hwang et al.[45,44] The mean follow-up duration was 6.9 months. The meta-analysis evaluated the Eustachian tube score (not performed in the US), ability to perform Valsalva maneuver, and normalization of tympanic membrane, and normalization of tympanogram type. The meta-analysis findings significantly favored balloon dilation for all outcomes. Revisions were reported for 122 out of 1830 procedures. Complications included those reported in previous studies. Specifically, they report an overall complication rate of less than 2%. Most complications are typically mild and self-limiting. The reported complications include 20 cases of local mucosal bleeding, 3 cases of preauricular emphysema, 4 cases of temporary acute otitis media, 5 cases of rhinitis, 1 case of temporary increased tinnitus. One case of hematotympanum requiring myringotomy was previously reported as being unrelated to the ET dilation procedure.

Wang et al published a systematic review and meta-analysis in 2018 based on 8 clinical case series (6 prospective and 2 retrospective) reporting on 942 patients treated with ET balloon dilation with follow-up between 6 weeks to 1 year.[47] Outcomes included Eustachian tube score (ETS), Valsalva maneuver, and tympanometry. The meta-analyses of ETS (p=0.001), Valsalva (p=0.047), and tympanometry (p=0.003) all demonstrated statistically significant 4 improvement after balloon dilation. They concluded that treatment with balloon dilation reduces ETD symptoms.

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Finally, in 2018, Luukkainen et al published a systematic review of 10 clinical case series (6 prospective and 4 retrospective).[48] Their cohort included 956 patients treated with ET balloon dilation with follow-up of 6 months or more. Outcomes evaluated included ETDQ-7, Valsalva or Toynbee, tympanometry, CT scans, tubomanometry, ETS/ETS-7, and complications. They found consistently significant improvements in ETDQ-7, Valsalva, ETS, and normalization of tympanograms with few and minor complications.

The take-aways from the available systematic reviews/meta-analyses of case series studies are that there appear to be clinical benefits with low complication rates for Eustachian tube balloon dilation; however, additional controlled trials are recommended to provide higher level evidence. Note that none of these reviews include the recently published RCTs.

5.3 NICE Guidance

In December 2019, NICE published their recommendation for evidence on the safety and efficacy of balloon dilation for Eustachian tube dysfunction. To develop their recommendation, NICE conducted a review of the published literature on the efficacy and safety of this procedure. The key efficacy outcomes considered were improvement in symptoms, disease-specific quality-of-life scores, and physiological measures of Eustachian tube function. The key safety outcomes considered were pain and patulous Eustachian tube. The committee recommendation was that the "Evidence on the safety and efficacy of balloon dilation for eustachian tube dysfunction is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit." The guidance can be obtained at https://www.nice.org.uk/guidance/ipg665.

5.4 Other Economic or Outcomes Evidence

There are no current clinical-based health economics studies on the use of balloon dilation for the treatment of ETD.

5.5 Other Evidence or Information

There is no single test or "gold standard" that has been shown to be reliable, objective, and diagnostic for ETD.[45,49,50,51] In the absence of a single diagnostic test for ETD, multiple assessments of middle ear function are typically used in combination with reported symptoms and medical history. The assessments typically include otoscopy, Valsalva maneuver, and tympanometry. However, since these assessments are not specific to tubal function, their utility is limited with respect to diagnosing or monitoring ETD. Additionally, not all patients with ETD will have abnormal findings using these tests. In the absence of an objective standard, the most appropriate diagnosis of ETD relies on medical history, symptoms, and assessment results.[50]

The target population for balloon dilation are patients who have ETD symptoms persisting for 12 weeks or longer who are unresponsive to medical therapies. Patients with a history of patulous Eustachian tube should not be treated with balloon dilation since dilation may exacerbate the condition. To prevent the possibility of carotid artery injury, all patients should undergo a CT scan before undergoing Eustachian tube balloon dilation to confirm the absence of carotid artery dehiscence.

A patient selection algorithm is provided in Section **6.2**.

6 Dossier Appendices

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6.2 Product Prescribing Information

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3563-002

XprESS™ ENT Dilation System

INSTRUCTIONS FOR USE

ALL INSTRUCTIONS, PRECAUTIONS AND WARNINGS SHOULD BE CAREFULLY READ AND UNDERSTOOD BEFORE USE. FAILURE TO DO SO MAY RESULT IN COMPLICATIONS.

Caution – Federal (USA) law restricts this device to sale by or on the order of a physician.

Indication for Use

To access and treat the maxillary ostia/ethmoid infundibula in patients 2 years and older, and frontal ostia/recesses and sphenoid sinus ostia in patients 12 years and older using a transnasal approach. The bony sinus outflow tracts are remodeled by balloon displacement of adjacent bone and paranasal sinus structures.

To dilate the cartilaginous portion of the Eustachian tube for treating persistent Eustachian tube dysfunction in patients 18 years and older using a transnasal approach.

Description

The XprESS ENT Dilation System is intended to remodel or recreate the sinus outflow tract and dilate the Eustachian tube by transnasal balloon dilation. The XprESS device combines features of a curved suction tip and an ostium seeker with the tissue expansion effect of balloon dilation. The familiar features of this device enable a physician to track the device into the sinuses and Eustachian tubes using endoscopic visualization. Since the distal end of the device is re-shapeable, one balloon can be modified to work on multiple sinuses and Eustachian tubes within the same patient.

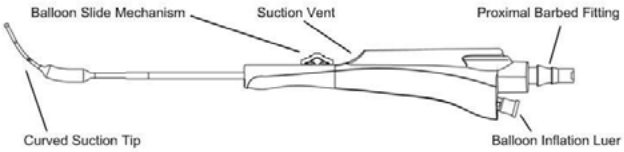


Figure 1 – XprESS ENT Dilation Device

The XprESS device curved suction tip has an atraumatic ball tip. A suction tube may be connected to the proximal barbed fitting to provide active suction by covering the suction vent. An Extension Line connected to a syringe may be connected to the proximal barbed fitting to provide irrigation. The device was designed to prevent fluid from exiting the suction vent during irrigation. The XprESS ENT Dilation System is provided sterile and for single use only.

The XprESS ENT Dilation System includes the XprESS device, Inflation Syringe, Bending Tool, and Extension Line(s). The XprESS LoProfile and Ultra ENT Dilation Systems also include the PathAssist LED Light Fiber. The XprESS Pro ENT Dilation System also includes a Tuohy Adapter.

XprESS is available in the following suction tip sizes and balloon sizes. All suction tips and balloon lengths are appropriate for treating all sinuses and Eustachian tubes; selection is based on physician preference. If treating only Eustachian tubes, the longer length balloons may be more efficient.

XprESS Pro	**XprESS LoProfile**	**XprESS Ultra**
Standard Suction Tip (2 mm ball tip, 1 mm ID, 1.5 mm OD)	**LoProfile Suction Tip** (1.75 mm ball tip, 0.7 mm ID, 1.2 mm OD)	**Ultra Suction Tip** (1.5 mm ball tip, 0.5 mm ID, 1.0 mm OD)
Balloon Diameter x Length (mm)	**Balloon Diameter x Length (mm)**	**Balloon Diameter x Length (mm)**
NA	5 x 8	5 x 8
NA	5 x 20	5 x 20
6 x 8	6 x 8	6 x 8
6 x 18	6 x 20	6 x 20
7 x 18	7 x 20	NA

The XprESS ENT Dilation System has been tested to withstand multiple inflations and device tip manipulations in a surgical case.

Contraindications

- None known

Warnings

- Never advance or withdraw the XprESS device against any resistance. Do not use excessive force or torque to advance the XprESS device or balloon/slide assembly when positioned in any paranasal or nasopharynx space. Such actions could lead to tissue trauma, bleeding, or device damage.
- Do not use breached or damaged packages, since the sterility and functionality of the device may be compromised.
- The XprESS ENT Dilation System is provided sterile and intended for single use only. Do not resterilize and/or reuse, as it may result in compromised device performance and risk improper sterilization and cross-contamination.
- Do not use the XprESS device in patients with known allergies to barium sulfate.
- Do not use XprESS to dilate Eustachian tubes in patients with a history of patulous Eustachian tubes.
- Due to the variability of anatomy, review appropriate radiographic imaging (eg, a CT scan) prior to treatment. Do not use the XprESS device to treat a hypoplastic/atelectatic maxillary sinus, atelectatic ethmoid infundibulum, or patients with evidence of internal carotid artery dehiscence.
- Due to the variability of sinus development in pediatric patients, review CT scan to assess each sinus's development and appropriateness for balloon dilation. Pneumatizaton may occur as early as 1-2 years of age and continues to develop throughout childhood. Do not use XprESS in a sinus that is not adequately developed.
- Do not insert the XprESS device beyond the tubal isthmus of the Eustachian tube, as this may increase the risk of bony fracture and injury to the internal carotid artery.
- Do not advance the LED Light Fiber beyond the distal tip of XprESS when XprESS is placed in the Eustachian tube, as this may lead to tissue trauma.
- Do not exceed the maximum recommended balloon inflation pressure of 12 atm. Over-inflation of the balloon can result in serious adverse events.
- Do not use ionic or non-ionic fluoroscopic contrast solution to inflate the balloon in patients with known allergies to contrast media.
- If suction through the XprESS device lumen is used during the procedure, temporarily discontinue suction (remove finger from suction vent, disconnect suction hose from device, or clamp suction hose) at the time of balloon inflation. Suction can resume subsequent to balloon deflation. Using the XprESS device in suction mode while balloon is inflated may result in barometric trauma to tissue, which may lead to increased bleeding or damage to the tympanic membrane.
- Do not irrigate within the Eustachian tube, as this may damage the tympanic membrane.

- As in any upper airway procedure or sinus surgery, do not have patient use CPAP until the physician has confirmed that the tissue is adequately healed. CPAP use prior to soft tissue healing may result in facial and/or neck swelling due to subcutaneous emphysema.
- Do not clean the XprESS device with anti-microbial agents as the compatibility of the XprESS device with these agents has not been tested.
- The XprESS device has been tested only with the Fiagon Navigation System. Do not attach the XprESS device to other image guidance systems, as use with other systems may result in inaccurate device positioning. Refer to *System Operation 1.b* for instructions on how to connect XprESS to the Fiagon system.
- The XprESS device has been tested only with the Entellus Inflation Syringe. Do not use other inflation devices with the XprESS device, as doing so may result in serious patient injury.

Precautions

- Store the XprESS device components in a cool and dry place. Never use a device that is beyond its expiration date.
- Handle the XprESS device with care. Prior to use, and during the procedure, inspect the packaging and components for bends, kinks, or other damage. Discontinue the use of the XprESS device if it may have been damaged.
- Select a balloon diameter that will result in expansion of the tissue post dilation. Do not select a balloon diameter that is larger than the bony margins of the outflow tract as this may damage the balloon.
- Pay special attention when advancing or withdrawing the balloon and slide assembly. If resistance is encountered, use endoscopy or direct visualization to help guide device out of the paranasal or nasopharynx space and then attempt to alleviate the resistance. If the cause of resistance cannot be determined, do not use the XprESS device.
- Use direct endoscope visualization with or without PathAssist LED Light Fiber or Light Fiber to ensure accurate placement of the balloon prior to dilation. If balloon location cannot be verified, image guidance or fluoroscopy can be used. If balloon location still cannot be verified, the balloon should not be inflated.
- Consider using self-limiting radiation exposure equipment when employing fluoroscopy to confirm device placement. Ensure the equipment is calibrated and maintained according to the equipment manufacturer's user manual.
- Use techniques for reducing fluoroscopic exposure when using fluoroscopy. Examples are applying pulsed beam settings, increasing target-to-panel distance, using posterior-anterior projection, and using appropriate lead shield protection. Total fluoroscopy time should be limited to 30 minutes.
- When fluoroscopy is used, especially in children, minimize radiation dose to the lens of the eye and other proliferating tissues due to the potential for cataract formation or injury to the surrounding tissue.
- Do not advance or withdraw a guidewire through the XprESS Pro or LoProfile suction/irrigation lumen against resistance. This could lead to device damage.
- Be aware that guidewires (including Fiagon GuideWires) do not track through the XprESS Pro or LoProfile when they are bent in the recommended maxillary configuration or through the XprESS Ultra in any configuration. Other methods can be used to obtain confirmation of the treatment area, such as use of the PathAssist Light Fiber, direct visualization of the XprESS device with an aid of an endoscope, or fluoroscopic imaging of the XprESS tip.
- Use standard larger suction tubes for removal of thick secretions or other materials. XprESS Pro has a 1 mm ID comparable to that of a 5F suction tube. XprESS LoProfile has a 0.7 mm ID comparable to that of a 4F suction tube. XprESS Ultra has a 0.5 mm ID comparable to that of a 2.5F suction tube. All are capable of removing blood and thin mucous.
- Fully deflate the balloon and retract the balloon slide assembly before withdrawing the XprESS device from the paranasal or nasopharynx space.
- Use only liquid contrast or saline solution for inflation. Do not inflate with air.
- Consider using a new balloon if cross-contamination between sinuses or Eustachian tubes is a concern.

Adverse Effects

Possible adverse effects include, but are not limited to, the following:

- Complication from anesthesia
- Damage to the lamina papyracea
- Damage of the orbital wall or other structures of the eye
- Cerebrospinal fluid leak
- Loss of vision or diplopia (double vision)
- Pain
- Bleeding
- Cavernous sinus syndrome
- Damage to the lacrimal sac affecting tearing
- Pneumocephalus
- Bruising and swelling
- Tissue inflammation
- Fever and infection
- Continued or worsening symptoms
- Revision surgery
- Tinnitus
- Damage to the Eustachian tube
- Patulous Eustachian tube
- Permanent hearing loss
- Carotid artery damage
- Tympanic membrane damage

Supplies

The following supplies are not provided with the XprESS ENT Dilation System and should be available and prepped prior to use of the device.

- Appropriate endoscopes and compatible camera system
- ≥50 mL of sterile saline solution, sterile fluoroscopic contrast solution, or sterile water
- Needles and syringes as required for injections
- 20-30 mL syringe and Extension Line (if irrigation is to be performed)
- Suction system
- Other supplies or medication as established by laboratory protocol
- If the use of a sterile guidewire is desired (compatible with the XprESS Pro), the recommended guidewire should be sterile and ≤0.035 inches in diameter with a minimum length of 50 cm. Example of a guidewire that meets these requirements is the Entellus Medical Sinus Guidewire.
- If desired, Entellus Medical PathAssist™ LED Light Fiber, Light Fiber™, or Light Seeker

Optional Equipment

- Fiagon Navigation System and GuideWires (GuideWire and GuideWire 0.6 are compatible with XprESS Pro; GuideWire 0.6 is compatible with XprESS LoProfile)
- Fluoroscopy may be used in conjunction with the endoscope if desired.
- Refer to appropriate Instructions for Use and safety procedures when preparing and using equipment.

Instructions for Use

System Preparation

1. Prepare the Inflation Syringe and Extension Line
   a. Remove the Inflation Syringe and Extension Line from its sterile package.

Note the 3 referenced Inflation Syringe plunger positions:

Figure 2 - Plunger all the way in

Figure 3 - First Click position

Figure 4 -Second Click position (all the way out)

b. Begin with the Inflation Syringe plunger **all the way in** (Figure 2).
c. Then submerge tip in sterile saline solution.

d. Fill Inflation Syringe by slowly drawing plunger back to **second click position** (all the way out) (Figure 4).

e. Attach an Extension Line to the filled Inflation Syringe.

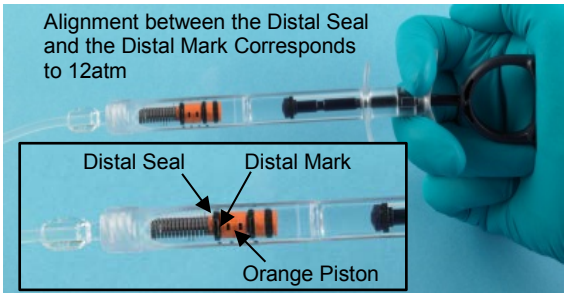
f. Point the syringe tip **towards the ceiling.** Tap the Inflation Syringe until a large bubble is visible beneath the orange piston.

g. While still pointing the syringe tip **towards the ceiling**, push the plunger **all the way in** (Figure 2), to purge all air and fluid from the syringe.

h. Submerge the free end of the Extension Line in sterile saline solution. Slowly draw plunger back to the **first click position** (Figure 3) to fill the syringe.

2. Prepare XprESS ENT Dilation System.
   a. Remove the XprESS device from its sterile package.
   b. Remove and discard the balloon protector.
   c. Connect the free end of the prepped Extension Line to the XprESS balloon inflation luer.
   Note: Inspect the syringe barrel to ensure there is minimal air in the system. If excessive air remains in the system, repeat prepping process.

Figure 5: Alignment between Distal Seal and Distal Mark



   d. Perform a test inflation of the system by depressing the plunger rod until the distal black seal on the orange piston is aligned with the distal black mark of the Inflation Syringe (See Figure 5). If the seal and black mark do not align, disconnect the Inflation Syringe and Extension Line and repeat the prepping process.
   e. Pull the plunger rod back to the 2nd click to apply a vacuum to the balloon. Ensure there is no air introduced into the system during deflation of the balloon. If a leak is detected and the source cannot be identified and corrected, do not use the XprESS device, Extension Line, and Inflation Syringe. Use new devices to complete the procedure.
   f. If suction or irrigation is planned, connect the Extension Line to the proximal barbed fitting to add a flexible connector for suction or irrigation.

Reshaping the XprESS Device Suction Tip to Treat Multiple Spaces

- When treating multiple spaces, it is recommended to complete balloon dilation of the frontal or sphenoid sinuses or Eustachian tubes prior to treatment of the maxillary sinuses.
- **Frontal Sinuses:** When treating the frontal recesses, a large radius curve similar to a frontal sinus seeker (Figure 6) is recommended. This is the shape/curve provided in the package.
- **Sphenoid Sinuses:** When treating the sphenoid sinus ostia, a slight bend (Figure 7) is recommended.
- **Eustachian Tubes:** When treating the Eustachian tubes, a bend of approximately 45° at the 2 cm mark (Figure 8) is recommended.
- **Maxillary Sinuses:** When treating the maxillary ostia/ethmoid infundibula, a bend of approximately 120 - 135° (Figure 9) is recommended to gain access to the natural maxillary ostium. Use the included Bending Tool to achieve this geometry.

Figure 6: Frontal Bend

Figure 7: Sphenoid Bend

Figure 8: Eustachian Tube Bend

Figure 9: Maxillary Bend

- *Small adjustments to the above bends may be considered to accommodate different patient anatomy.*

Using Bending Tool

- *The Bending Tool should be used to achieve the proper maxillary bend. The tool also provides a frontal and sphenoid bend configuration if needed.*
- *Maxillary Bending with Bending Tool*: Before shaping the maxillary bend, the device should be close to straight as shown for a Sphenoid Bend. With the Bending Tool in one hand, position the ball tip into the ball holder in the bending tool (Figure 10). Place a finger at about the 2 cm mark on the suction tip and use this finger to form the Maxillary Bend (Figure 11).

Figure 10 – Start Maxillary Bend

Figure 11 – Finish Maxillary Bend

Patient Preparation

1. Patient preparation should be consistent with standard practice.
2. Anesthesia should be administered appropriately to allow patient tolerance.

System Operation

1. Locate the sinus structure or Eustachian tube orifice using one of the following confirmation methods:
   a. **Direct Visualization with or without Light Confirmation:** Locate the treatment area using XprESS with or without LED Light Fiber, Light Fiber, Light Seeker, a standard sinus ostium seeker, and/or guidewire with the aid of an endoscope. Observe the location of the treatment area relative to the anatomical landmarks through the endoscope. Remove the Light Seeker, sinus ostium seeker, or guidewire after locating treatment area.
   Note: If using the PathAssist LED Light Fiber or Light Fiber, refer to the Instructions for Use (IFU) for complete instructions.
   b. **CT Image Guidance:** If further confirmation of the treatment area location is desired, CT image guidance using the Fiagon Navigation System and GuideWire or GuideWire 0.6 with XprESS Pro may be used. The Fiagon Navigation System and GuideWire 0.6 with XprESS LoProfile may also be used.
      i. If using the GuideWire with XprESS Pro, attach the Tuohy Adapter to the XprESS proximal barbed fitting.
      ii. Load the Fiagon GuideWire through the Tuohy Adapter and working lumen of XprESS until the tip of GuideWire aligns with the tip of XprESS.
      iii. Secure the GuideWire in place by tightening the Tuohy Adapter.
      iv. If using GuideWire 0.6 with XprESS Pro or LoProfile, load the GuideWire 0.6 through the working lumen of XprESS until the luer lock connector meets the proximal barbed fitting of XprESS.

v. Secure the luer lock connector on the proximal barbed fitting.
vi. Refer to Fiagon Navigation System Instructions for Use.

Note: Neither of the Fiagon GuideWires should be used with any XprESS device in the maxillary bend configuration.

Note: Do not attach the XprESS device to other image guidance systems.

c. **Fluoroscopy:** If further confirmation of the treatment area is desired, fluoroscopy may be used. Take two orthogonal views (AP and lateral). The XprESS device suction tip is stainless steel and is visible under fluoroscopy. The balloon will be proximal to the tip of the device.

2. Under endoscopic visualization, track the XprESS device to the same treatment area identified above.
   a. Position XprESS suction tip within the sinus ostia or within the cartilaginous portion of the Eustachian tube.

Notes: *Reference marks are located 1 and 2 cm from the tip of the device.*
The XprESS suction tip may be reshaped to aid in device positioning.
Use device as a suction tool to maintain a clear visual field during device positioning. Cover suction vent with finger to allow suction.

3. Advance the balloon by fully advancing the balloon slide mechanism forward to position the balloon within the sinus opening or Eustachian tube.
4. Prior to inflating balloon, discontinue the use of suction (remove finger from suction vent, disconnect suction hose from device, or clamp suction hose) to decrease the risk of barotrauma.
5. Balloon dilation of the treatment site:
   a. Slowly depress the Inflation Syringe plunger rod to inflate the balloon. The pressure should be increased slowly (3-5 seconds) until the orange piston bottoms out (distal black seal of the piston reaches the distal black mark on the Inflation Syringe – see Figure 5). If these do not align, deflate the balloon and remove the XprESS device and perform a test inflation (as described in steps 2.d and 2.e of the System Preparation section). Alignment of the distal mark and distal seal will ensure that 12 atm of pressure is reached.

Note: *Do not use air or any gaseous medium to inflate the balloon.*

   b. Inflate the balloon until the desired result is achieved or until it reaches 12 atm.
Sinus Dilation: Inflate the balloon for up to 20 seconds (less than or equal to 20 seconds); observe that the balloon is inflated endoscopically.
Eustachian Tube Dilation: Inflate the balloon for approximately 2 minutes by holding in the plunger rod; observe that the balloon is inflated endoscopically.

Note: *Do not exceed 12 atm.*
Warning: *To avoid barometric trauma to tissue, do not use device in suction mode (remove finger from suction vent, disconnect suction hose from* device, or clamp suction hose) while balloon is inflated.

   c. When using the 8 mm length balloon, multiple inflations may be needed in order to achieve the desired result. Partially retract the balloon slide mechanism between inflations using the 5 mm handle reference marks to ensure full length treatment. See Figure 12.

Figure 12: Handle Marks for 8mm Length Balloon

   d. Deflate the balloon by retracting the Inflation Syringe plunger rod to the second click position and retracting the XprESS balloon slide mechanism. Observe the results endoscopically.
   e. Perform additional inflations if needed until desired result is achieved.

Note: *To irrigate the sinus, fill a 20-30 mL syringe with sterile saline. Connect the syringe to a flexible Extension Line and purge air. Connect Extension Line to proximal barbed fitting and flush through suction/irrigation lumen as desired. The suction vent does not need to be covered during irrigation.*

6. Remove device from treatment site: When the sinus outflow tract or Eustachian tube has been adequately dilated, deflate the balloon *(by retracting the Inflation Syringe plunger rod to the stop position),* retract the XprESS balloon slide mechanism, and remove the XprESS device from the treatment site.
7. If necessary, clean up the ostium site by cutting or removing flaps of tissue, fragments of exposed bone, or any other bone and mucosa that may obstruct or otherwise prevent ventilation and drainage of the sinus.
8. Repeat the same procedure to treat additional spaces if desired.
9. After completing the entire procedure, dispose of the devices and all waste products according to appropriate environmental health safety guidelines.

How Supplied
The XprESS ENT Dilation System is provided sterile and is intended for single-use only. Do not resterilize and/or reuse, as it may result in compromised device performance and risk improper sterilization and cross-contamination. Do not use breached or damaged packages, since the sterility and functionality of the device may be compromised.

Limited Warranty
Refer to *Entellus Medical, Inc. Standard Terms and Conditions*.

Symbols

Consult Instructions for use	LOT Lot Number	Use By	Quantity	REF Reorder Number	EC REP **Authorized Representative in the European Community**
STERILE EO Sterilization with Ethylene Oxide Gas	Manufacturer	Do Not Reuse	Rx Only Prescription Use Only	CE 0086 **CE Mark**	

Not made with natural rubber latex.

XPRESS, PATHASSIST and LIGHT FIBER are trademarks of Entellus Medical. patent http://www.entellusmedical.com/patents

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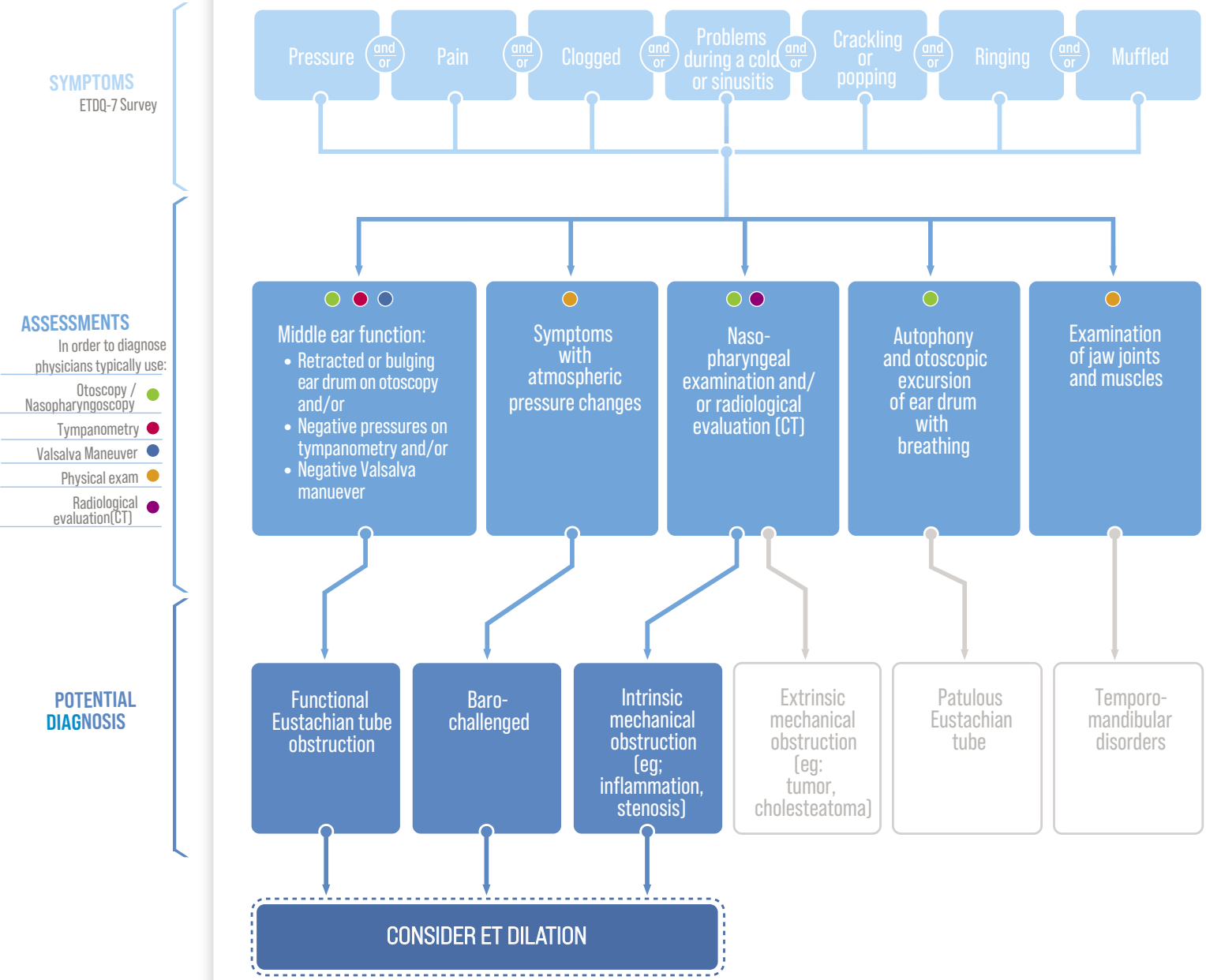
6.3 Patient Selection Information

Dr. Don J Beasley, MD
Camille Buchmiller, PA-C
208-229-2368

XprESS™
ENT Dilation System

Choosing the right patient for

ET dilation



If patient symptoms persist over 3 months

and medical management has failed, ET dilation may be your next treatment option.

Schilder AGM, Bhutta MF, Butler CC, et al. Eustachian tube dysfunction: consensus statement on definition, types, clinical presentation and diagnosis. Clin Otolaryngol. 2015;40:407-411.

Massoud E, Singh H, Tewfik L. Eustachian tube function.
Available at emedicine.medscape.com/article/874348-overview.

BOISE ENT™

0%
COMPLICATION RATE[1]

XprESS™
ENT Dilation System

The control you need to treat the Eustachian tube with the confidence you require

The unique ball-tip seeker-based design of the XprESS™ ENT Dilation System helps to ensure a safe and effective dilation every time.

Precise placement

The ability to bend the XprESS device at either 20mm or 18mm creates a positive stop to ensure treatment area is confined to 24mm cartilaginous portion of the Eustachian tube[2] while avoiding the fragile bony isthmus.

Optimal angle of access

The malleable tip of the XprESS device can be shaped to 45 degrees[3] and adjusted as needed to meet the unique anatomy of each patient.

Gentle insertion

The atraumatic rounded ball tip of the XprESS device is designed to prevent perforation of tissue.

Controlled navigation

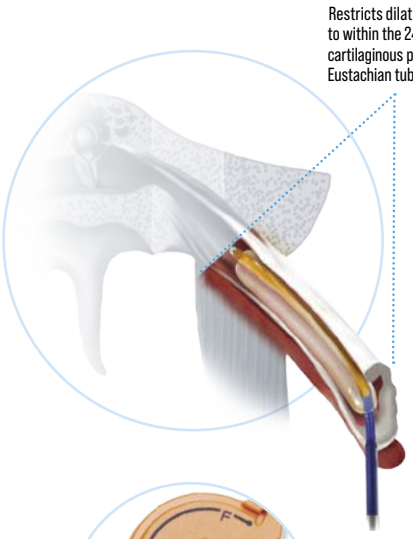
The tactile feedback of the XprESS device allows you to feel the ball tip and quickly identify when resistance is met avoiding unintended application of force.

Easy visualization

The slim profile of the XprESS device enables easy endoscopic visualization and placement of the device.

Backed by industry-leading training

Entellus Medical offers Eustachian tube dilation training labs across the country to help ensure the safe incorporation of this new treatment option in your preferred setting. Contact your Entellus Medical representative to sign-up for a lab in your region.



Bend to 18mm or 20mm length

Optimal 45° angle

Rounded ball tip

Tactile feel

1 Meyer TA, O'Malley E, Schlosser RJ, et al. A randomized controlled trial of balloon dilation as a treatment for persistent Eustachian tube dysfunction with 1-year follow-up. Otol Neurotol. 2018. DOI: 10.1097/MAO.0000000000001853

2 Poe DS, Hanna BM. AmJ Otolyngol. 2011 Mar-Apr; 32(2):115-23.

3 Massoud E, Singh H, Tewfik L. Eustachian tube function. Available at emedicine.medscape.com/article/874348-overview

XprESS™ ENT DILATION SYSTEM INDICATION FOR USE: To access and treat the maxillary ostia/ethmoid infundibula in patients 2 years and older, and frontal ostia/recesses and sphenoid sinus ostia in patients 12 years and older using a transnasal approach. The bony sinus outflow tracts are remodeled by balloon displacement of adjacent bone and paranasal sinus structures. To dilate the cartilaginous portion of the Eustachian tube for treating persistent Eustachian tube dysfunction in patients 18 years and older using a transnasal approach.
A physician using XprESS for Eustachian tube dilation must either have: (i) experience with a Eustachian tube balloon dilation device or (ii) undergone cadaver training on the use of a balloon dilation device for Eustachian tube dilation. If a physician who intends to use XprESS for Eustachian tube dilation does not meet at least one of these criteria, please contact your Entellus Medical representative to arrange training. Please see Instructions for Use (IFU) for a complete listing of warnings, precautions, and adverse events.
CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

BOISE ENT™