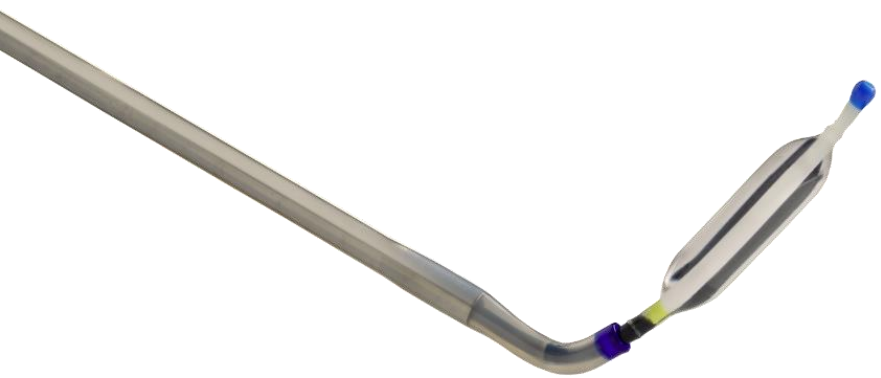
Acclarent Professional Education

ACCLARENT AERA® Eustachian Tube Balloon Dilation System



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ACCLARENT AERA® Eustachian Tube Balloon Dilation System is intended for use by physicians who are trained on Acclarent technology. Eustachian tube balloon dilation has associated risks, including tissue and mucosal trauma, infection, or possible carotid artery injury. Prior to use, it is important to read the Instructions for Use and to understand the contraindications, warnings, and precautions associated with these devices. The safety of the device as used under local anesthesia has not been evaluated.

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Indication For Use: The ACCLARENT AERA® Eustachian Tube Balloon Dilation system is intended to dilate the Eustachian tube for treatment of persistent Eustachian tube dysfunction in patients age 18 and older.

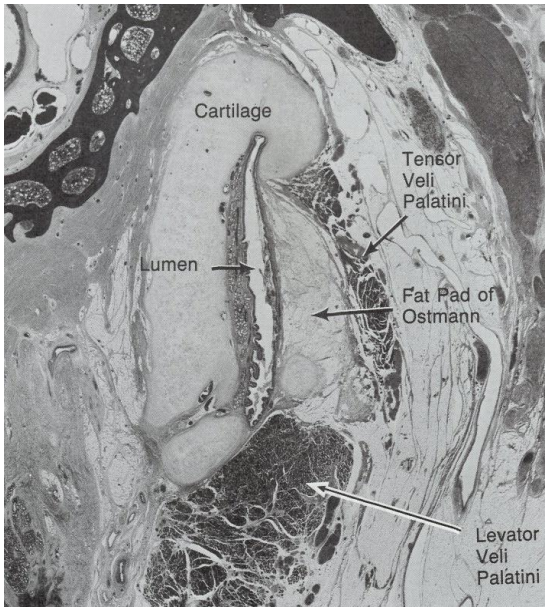
Surgeon training must include simulated use on cadavers to ensure users can follow the instructions for use to allow safe use of the device.

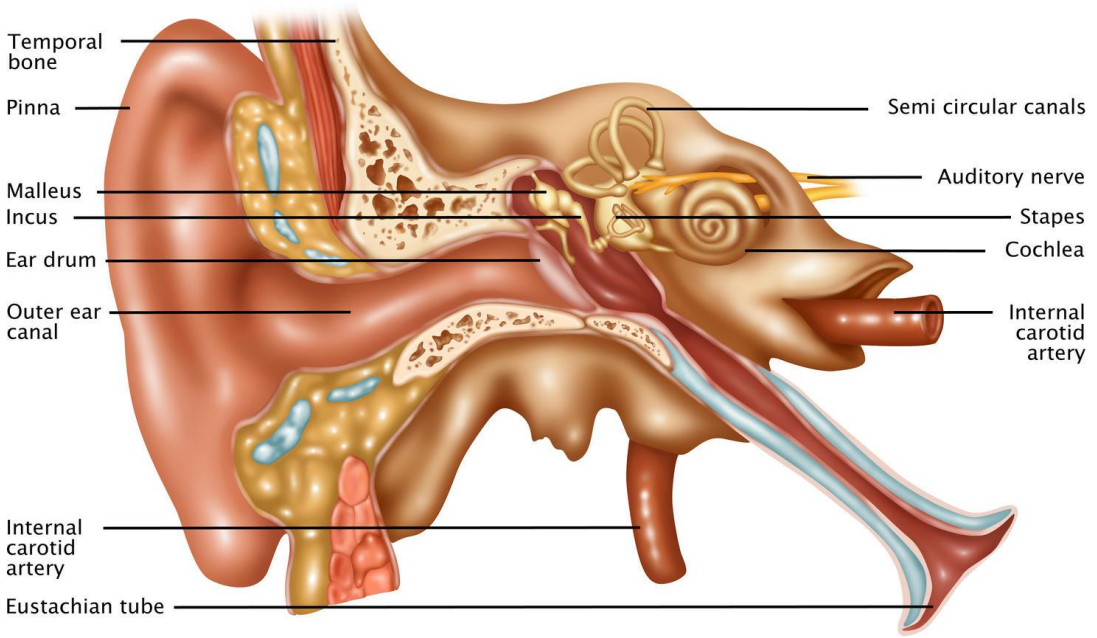
Eustachian Tube Dysfunction

Anatomy, Physiology, Diagnosis and Treatment

Anatomy

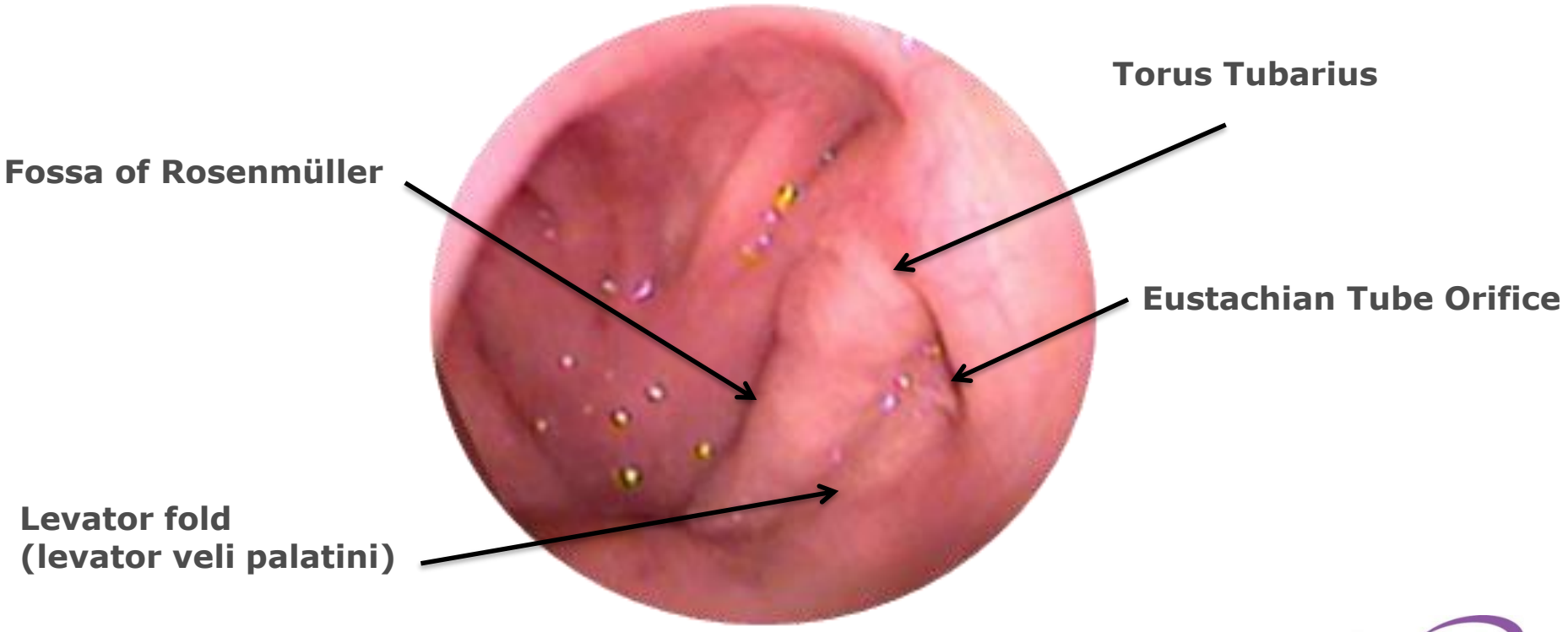
- Length of Eustachian Tube: 31-38mm,[1]
- Cartilaginous portion approx. 20-25mm[1]
- Cartilaginous portion is curved, s-shaped, starting medially, then laterally[1]
- Isthmus - may be as narrow as 0.65 mm[21]
- Studies show the ICA can lie within 2-10mm of the cartilaginous portion of the ET[2]





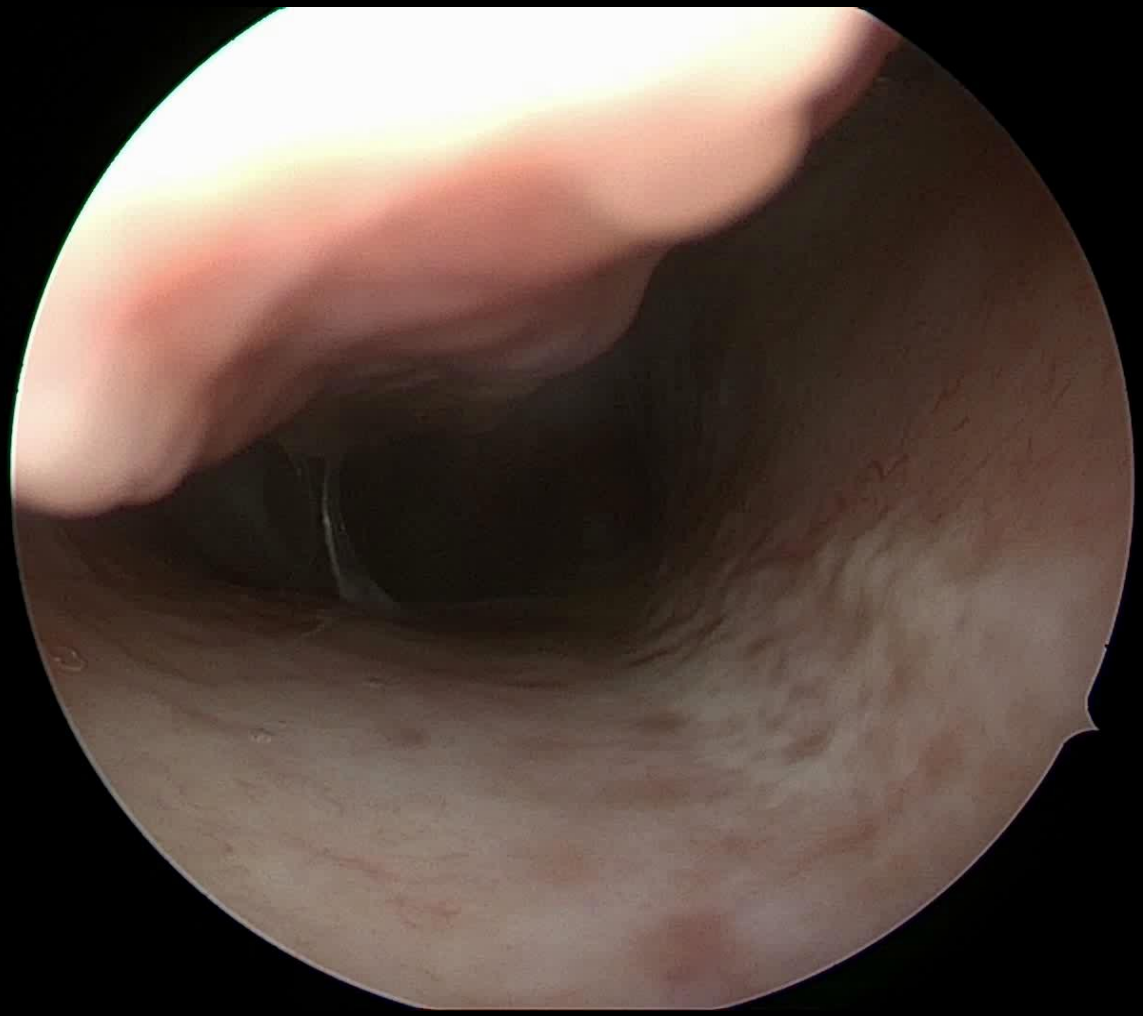
Anatomy

Fossa of Rosenmüller appears as a cleft, and recedes posterolaterally to an apex near to the edge of the carotid canal opening



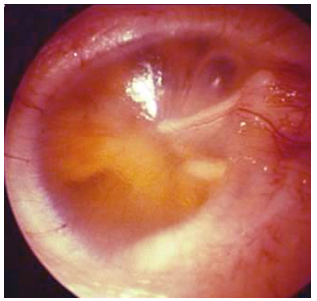
Anatomy

Video: Endoscopic view of ET with 0 & 45 degree scope
Courtesy of Dr. Dennis Poe



Physiology

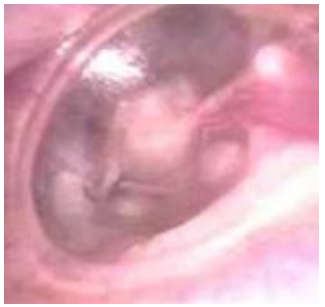
- Middle Ear as an Accessory 5th Sinus
  - Long and dynamic ”ostium”
  - ET normally closed (”valve”)
  - Mucosa, pathology similar



OME

Eustachian Tube Functions[3]

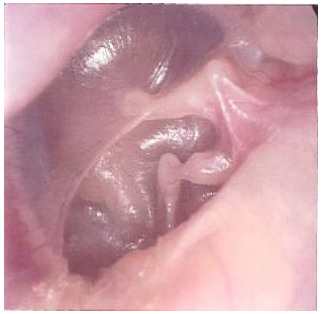
- Ventilation
- Clearance of the middle ear space
- Prevent Reflux



TM Retraction

Eustachian Tube Dysfunction[3]

- Negative Middle ear Pressure (B, C Tympanograms)
- Barochallenges – ET pathology on endoscopy
- **Excluded** (Not necessarily causal, active or ET)
  - OME/Fixed Retraction pockets/Cholesteatoma
  - Recurrent AOM
  - Popping, clicking, aural fullness/pressure/pain

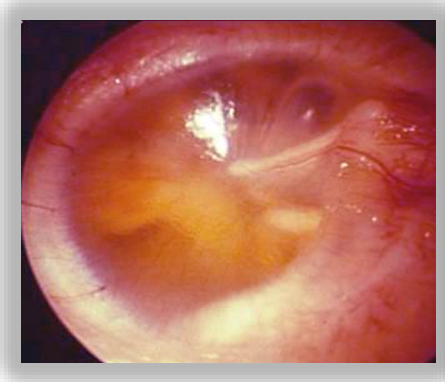


Retraction Pocket

Physiology

Dilatory Dysfunction

Patulous Dysfunction



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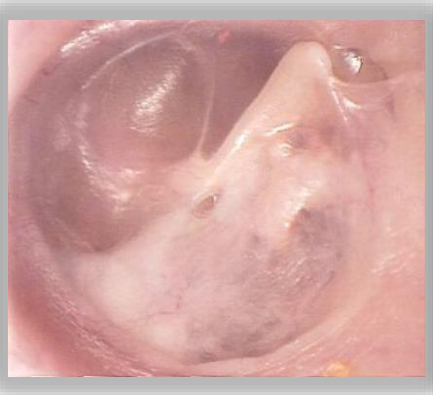
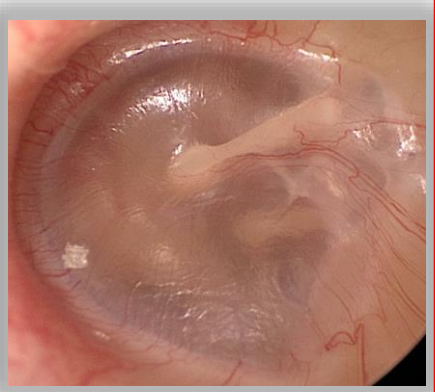
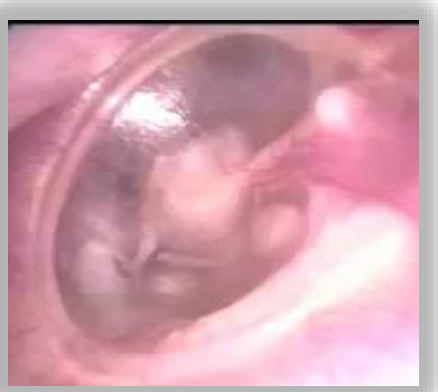


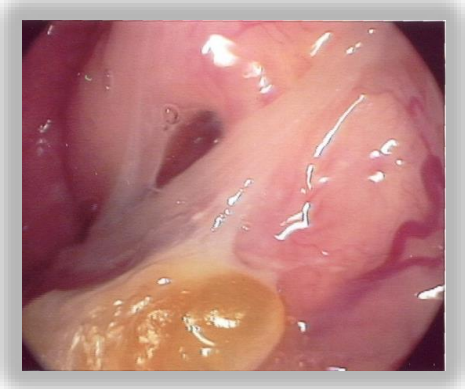
TM Retraction



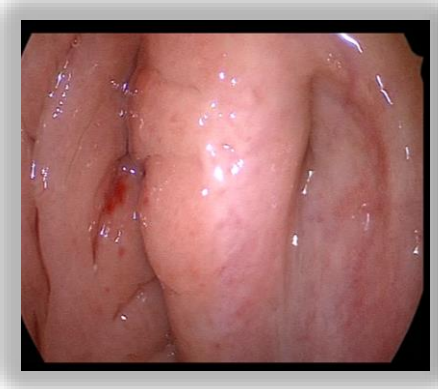
Normal TM



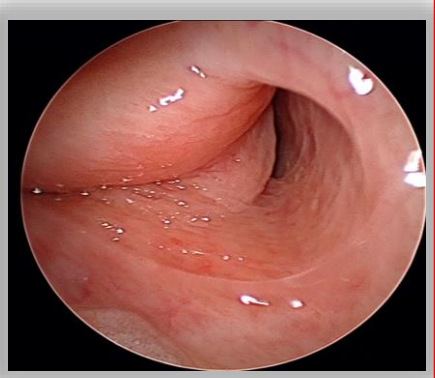
Normal TM



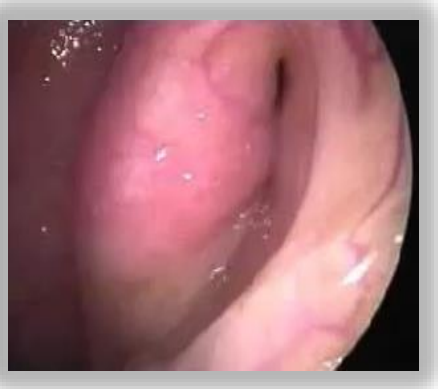
OME
B tympanogram



TM retraction
C tympanogram



BaroChallenge
Normal TM, ET



Patulous

Images Courtesy of Dr. Dennis Poe

Common Diagnostic Measures

ETDQ-7[4]

Over the past 1 month, how much has each of the following been a problem for you?	No Problem			Moderate Problem			Severe Problem
1. Pressure in the ears?	1	2	3	4	5	6	7
2. Pain in the ears?	1	2	3	4	5	6	7
3. A feeling that your ears are clogged or “under water”?	1	2	3	4	5	6	7
4. Ear symptoms when you have a cold or sinusitis?	1	2	3	4	5	6	7
5. Crackling or popping sounds in the ears?	1	2	3	4	5	6	7
6. Ringing in the ears?	1	2	3	4	5	6	7
7. A feeling that your hearing is muffled?	1	2	3	4	5	6	7

Common Diagnostic Measures

Past Medical History[5]

- Barochallenges
- OME/Retraction pockets/Cholesteatoma
- Recurrent Acute Otitis Media

Oto- Microscopy[5]

- Tympanic membrane retraction
- Effusion

Endoscopic Evaluation of Upper Airway/ET[5]

- Inflammation
- Hypertrophy
- Excessive Mucous
- Hyperemia
- Cobblestoning

Tympanogram[5]

- Type B or C

Common Diagnostic Measures[6]

Aural Fullness – Differential Diagnosis

Retracted Tympanic Membrane

- Negative pressure or effusion
- Type B or C Tympanogram
- Relief of symptoms with myringotomy +/- tube

Eustachian Tube Dilatory Dysfunction

Normal Tympanic Membrane

Patulous excursion of TM *while symptomatic*

Patulous ET

No TM excursion *while symptomatic*

Minor Syndrome

- Semicircular canal dehiscence syndrome
- Conductive hearing loss
- Supranormal bone conduction
- +/- vertigo
- +/- Tullio's phenomenon
- CT confirmation
- VEMP-abnormal low thresholds

TMJ Dysfunction

- Tenderness in or around joint capsule with mouth wide open
- Intraoral examination of lateral pterygoids for spasm or tenderness
- Chronic or fluctuating pain/pressure, normal TM
- Clenching or bruxism
- Malocclusion

Inner Ear Hydrops

- Fluctuating low-frequency sensorineural hearing loss
- +/- Episodic vertigo

Common Treatment Approaches

Medical Management[1]

- Effectiveness for medical therapies remains uncertain.
- There is no FDA approved medical therapy for nonspecific ETD

Surgical Management[5]

- Tympanostomy tube placement
- Adenoidectomy
- ACCLARENT AERA™ Eustachian Tube Balloon Dilation

Surgical Indications[5]

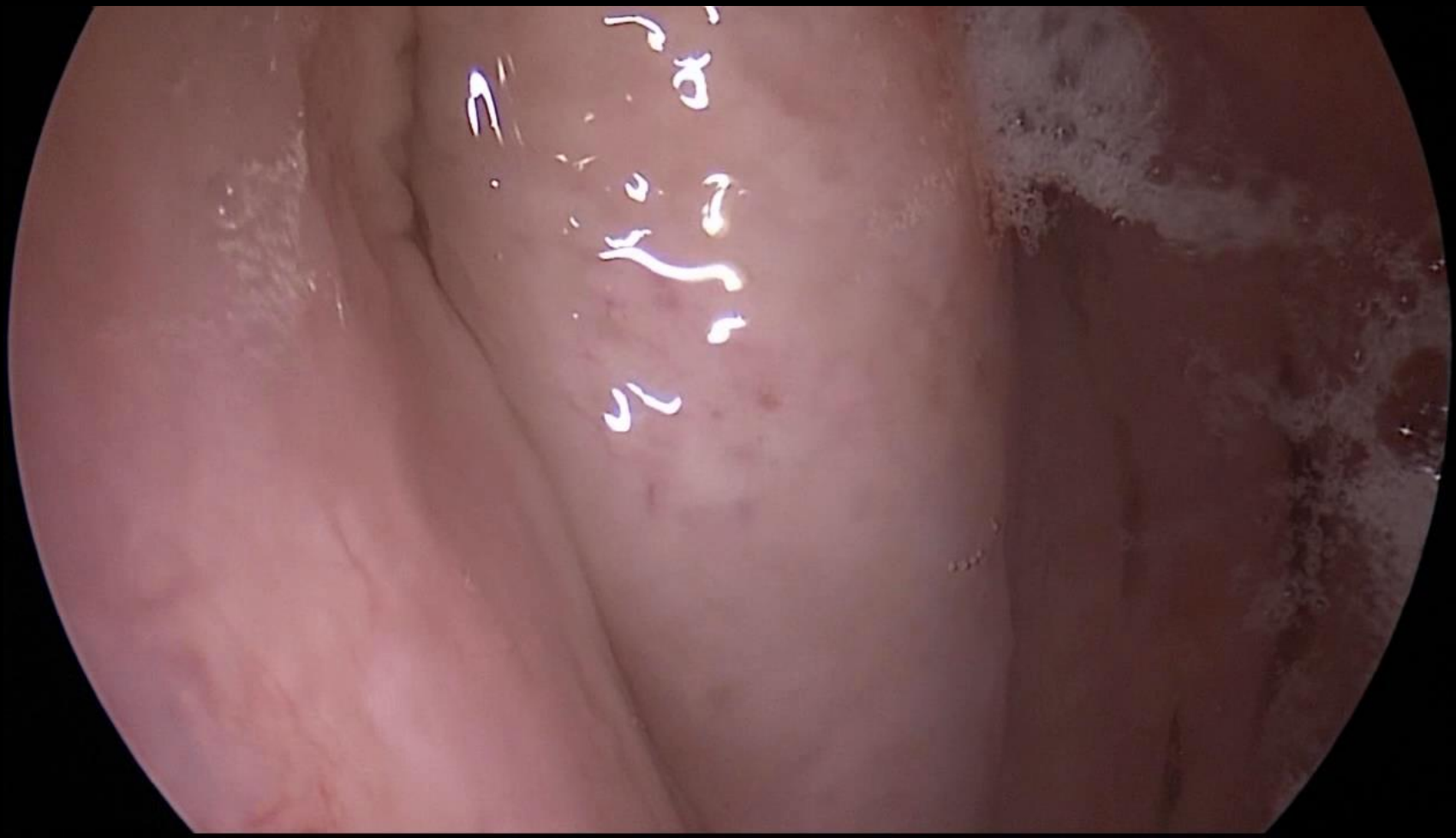
- Persistent OME or Non-adherent atelectasis

  AND Type B or C tympanogram

  AND ET pathology on endoscopy usually inflammation
- Flight or Scuba barochallenge **AND** ET pathology
  - Symptomatic- CHL, pain/blockage w pressure change
  - Symptoms improved with tympanostomy tube if done
  - Absence of autophony

Balloon Dilation of Eustachian Tube

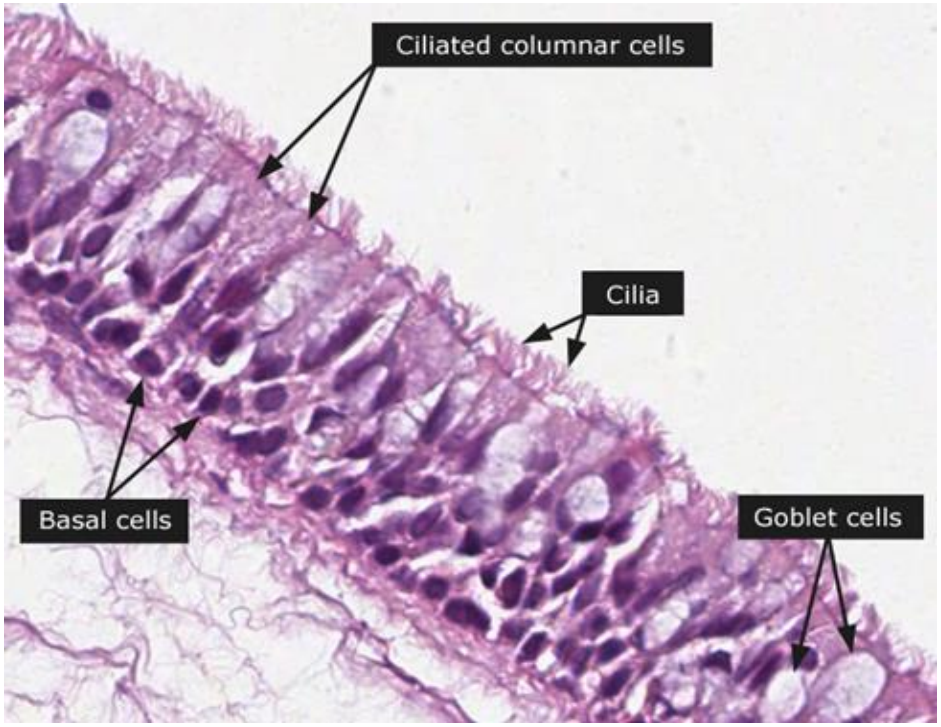
Courtesy of Dr. Dennis Poe



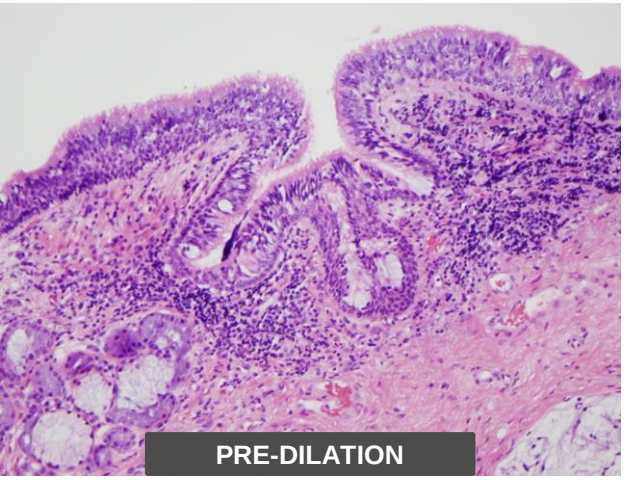
Mechanism of Action: Why does it Work?

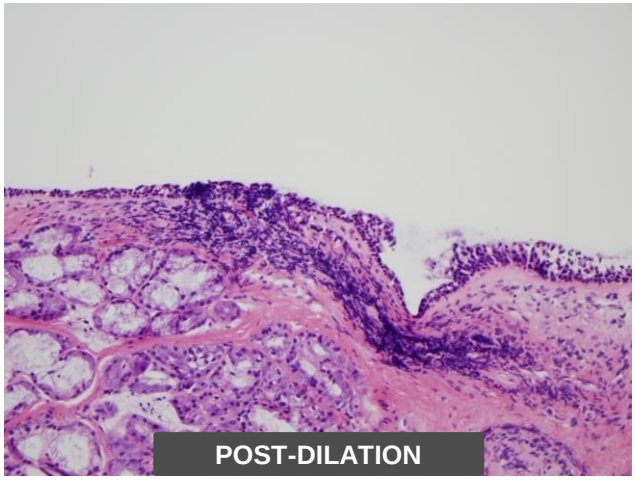
Eustachian Tube Mucous Membrane[7]

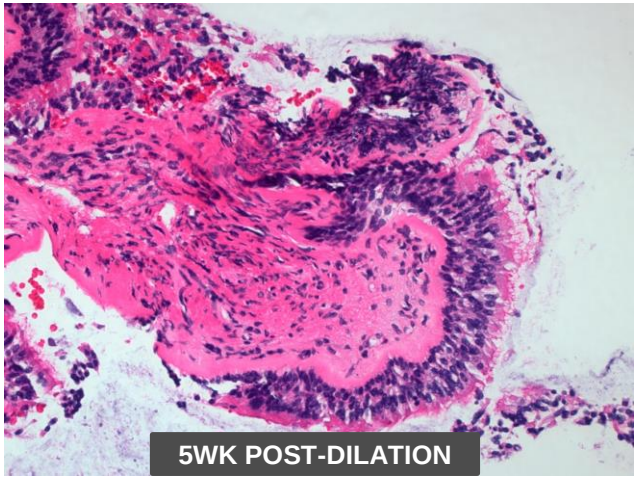
- The ET lumen is lined with pseudostratified, columnar epithelium of the ciliated type, which sweeps material from the middle ear into the nasopharynx
- The mucosa is continuous with the lining of the tympanic cavity at its distal end, as it is with the nasopharynx at its proximal end



Mechanism of Action: Why does it Work?







- Pathology lies within the cartilaginous segment of the ET; histopathology research has demonstrated that balloon dilation may:[8]
  - Shear or crush portions of the epithelium; usually sparing the basal layer and allowing for rapid healing
  - Crush lymphocytes and lymphoid follicles
- Combined, these effects reduce overall inflammatory burden and may provide lasting clinical improvement in ET dilation and ventilation.

ACCLARENT AERA® Eustachian Tube Balloon Dilation System

Clinical Trial Overview

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ACCLARENT AERA® Clinical Trial
Overview

The Laryngoscope

Balloon Dilation of the Eustachian Tube for Dilatory Dysfunction: A Randomized Controlled Trial

Dennis Poe, MD, PhD; Vijay Anand, MD; Marc Dean, MD; William H. Roberts, MD; Jose Pablo Stolovitzky, MD; Karen Hoffmann, MD; Nathan E. Nachlas, MD; Joshua P. Light, MD; Mark H. Widick, MD; John P. Sugrue, MD; C. Layton Elliott, MD; Seth I. Rosenberg, MD; Paul Guillory, MD; Neil Brown, MD; Charles A. Syms, III, MD, MBA; Christopher W. Hilton, MD; John T. McElveen, Jr., MD; Ameet Singh, MD; Raymond L. Weiss, Jr.; Moises A. Arriaga, MD, MBA, FACS; John P. Leopold, MS

Study Objective
To evaluate efficacy and safety of Eustachian tube balloon dilation with the Eustachian Tube Balloon Catheter (ETBC) in conjunction with medical management (investigational arm) compared to medical management alone to treat Eustachian tube dysfunction (ETD) in adult patients (control arm).

Primary efficacy endpoint
Evaluation consists of comparison of the proportion of subjects experiencing normalization of tympanometry at 6 weeks

Secondary efficacy endpoint
Evaluation employs the Eustachian Tube Dysfunction Questionnaire (ETDQ-7)

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ACCLARENT AERA® Clinical Trial
Inclusion Criteria

Inclusion Criteria

- 22 years of age and older diagnosed with persistent ETD
- Persistent ETD is defined by patient-reported symptoms of ETD including:
  - pressure and/or pain and/or clogged and/or muffled sensation in the affected ear(s)
  - and documented evidence that the subject has experienced persistent ETD symptoms for 12 weeks or greater prior to enrollment
- Failed appropriate medical management consisting of:
  - A minimum of 4 weeks of continuous daily usage of any intranasal steroid spray (INS)
  - or a minimum of one completed course of an oral steroid.
- The failed medical management may occur any time within 90 days prior to study enrollment
- Absence of internal carotid artery (ICA) dehiscence into the Eustachian tube (ET) lumen bilaterally confirmed by CT scan
- Abnormal tympanometry (type B or type C) after failed medical management and within 14 days prior to study enrollment
- Symptomatic dysfunction as documented by the ETDQ-7 with a score ≥ 2.1 after failed medical management

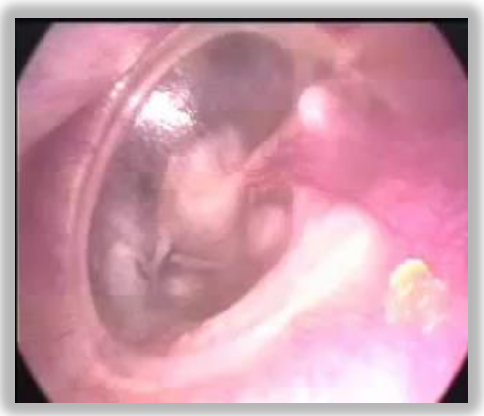
ACCLARENT AERA® Clinical Trial
Exclusion Criteria

Exclusion Criteria

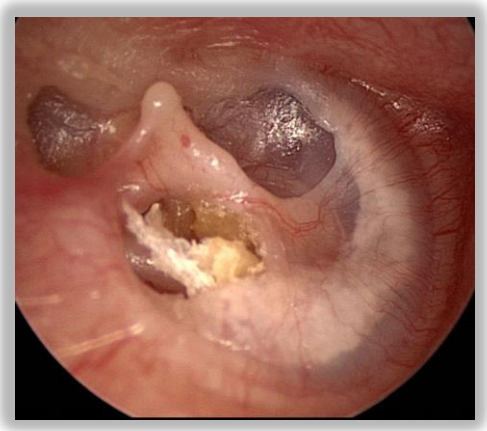
- Females who are pregnant or lactating were excluded
- Anatomy requiring an adjunctive surgical procedure on the same day as ETBC surgery to allow balloon catheter access to the ET,
- Concomitant nasal, sinus or ear procedures planned on the same day as ETBC surgery
- History of major surgery of the head or neck within four (4) months prior to randomization
- Patulous ET in either ear, Fluctuating sensorineural hearing loss
- Active chronic or acute otitis media (AOM)
- Tympanic membrane perforation or presence of a tympanostomy tube in either ear
- Tympanosclerosis, acute upper respiratory infection
- Active temporomandibular joint disorder (TMJ), Cleft palate or history of cleft palate repair
- Craniofacial syndrome, cystic fibrosis, ciliary dysmotility syndrome
- Systemic mucosal diseases or immunodeficiency disorders
- Intolerance of protocol-defined medication regimen
- Prior surgical intervention on Eustachian tube
- Absence of dilatory muscular contractions

ACCLARENT AERA® Clinical Trial
Exclusion Criteria

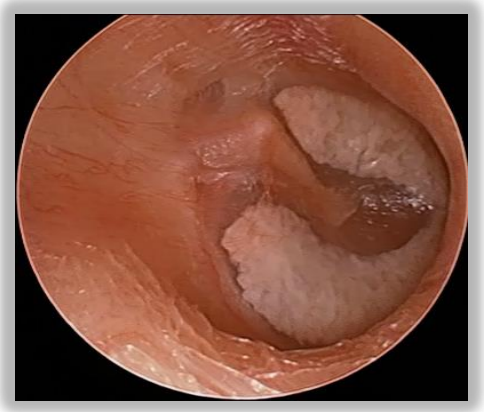
Retraction Pockets and Patulous Eustachian Tubes



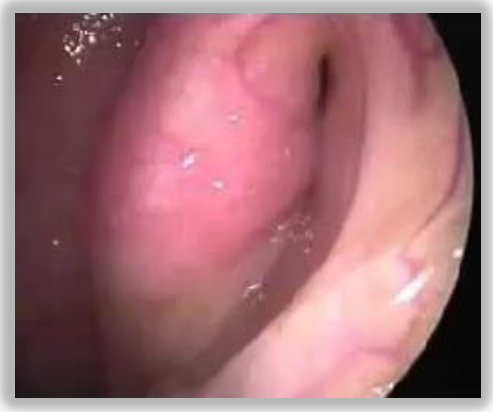
TM Retraction, adherent to Incus



TM with multiple deep retraction pockets and posterior superior cholesteatoma



TM with diffuse tympanosclerosis but mobile TM with breathing around umbo

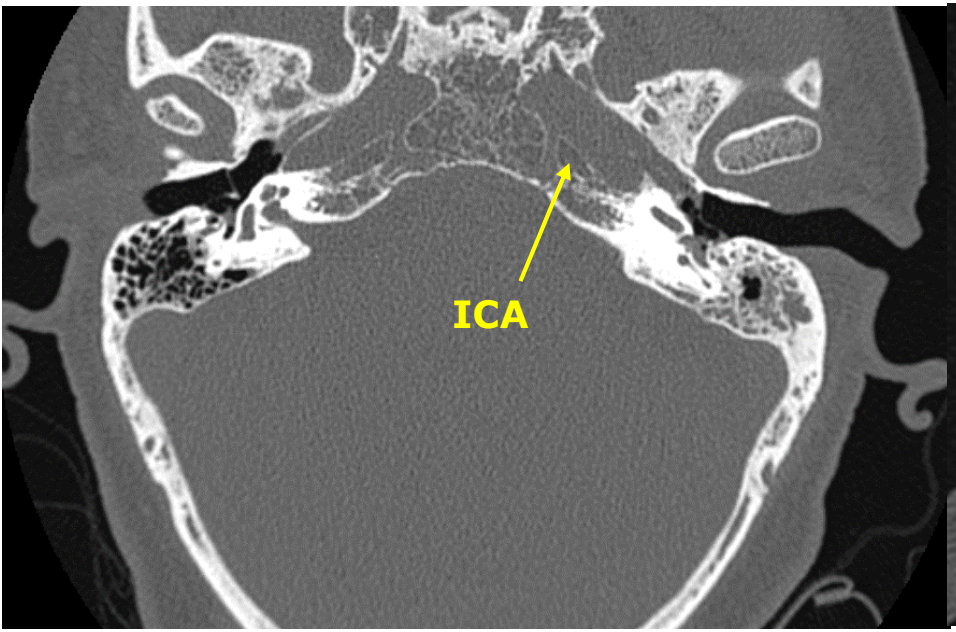


Patulous ET with concave defect in the anterolateral wall extending through the valve

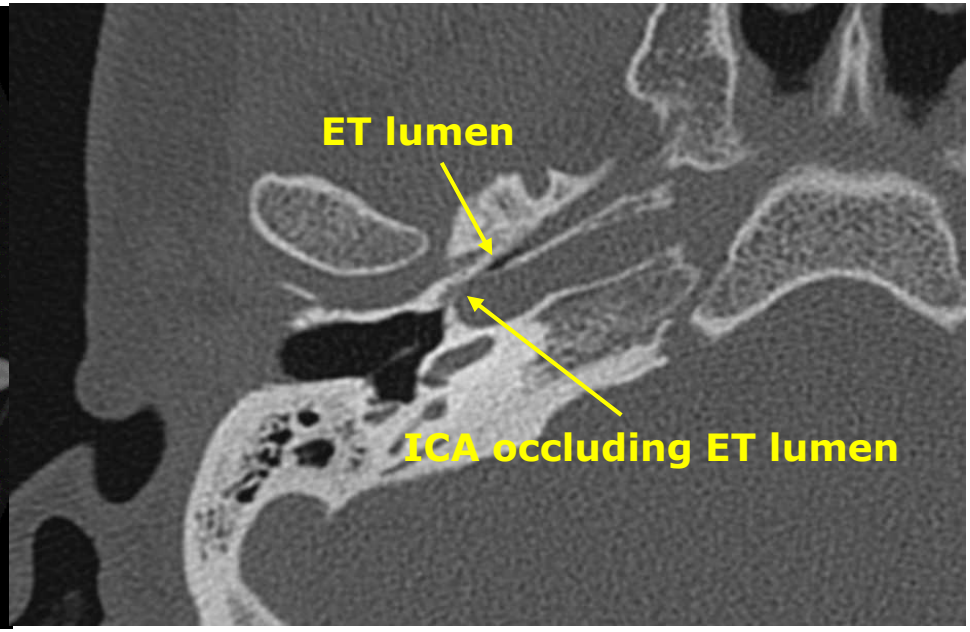
Images Courtesy of Dr. Dennis Poe

Internal Carotid Artery (ICA) Dehiscence into the Eustachian Tube

- Temporal Bone or Sinus CT
- Recommend slices ≤1.0 mm
- Carotid Artery should be covered with at least thin bone



Normal ICA Anatomy



ICA Dehiscent into ET causing occlusion

Images Courtesy of Dr. Dennis Poe

ACCLARENT AERA® Clinical Trial
Post-treatment and follow-up care

- For 1 week post-randomization (control arm) or post-procedure (lead-ins and investigational arm), subjects were required to adhere to the following:
  - Avoid performing the Valsalva maneuver
  - Avoid nose blowing
  - Avoid using Continuous Positive Airway Pressure (CPAP) machines (if possible)
  - Sleep with an extra pillow to elevate the head
- After 1 week post-randomization (control arm) or post-procedure (lead-ins and investigational arm), it is recommended that all subjects perform the Valsalva maneuver one time per hour.
- Proper Valsalva maneuver technique consists of holding the nose, blowing slowly to build pressure, and then swallowing hard.
- For 6 weeks post-randomization (control arm) or post-procedure (lead-ins and investigational arm), subjects are required to adhere to the recommended Nasacort labeling dosage and frequency.

ACCLARENT AERA® Clinical Trial
Results

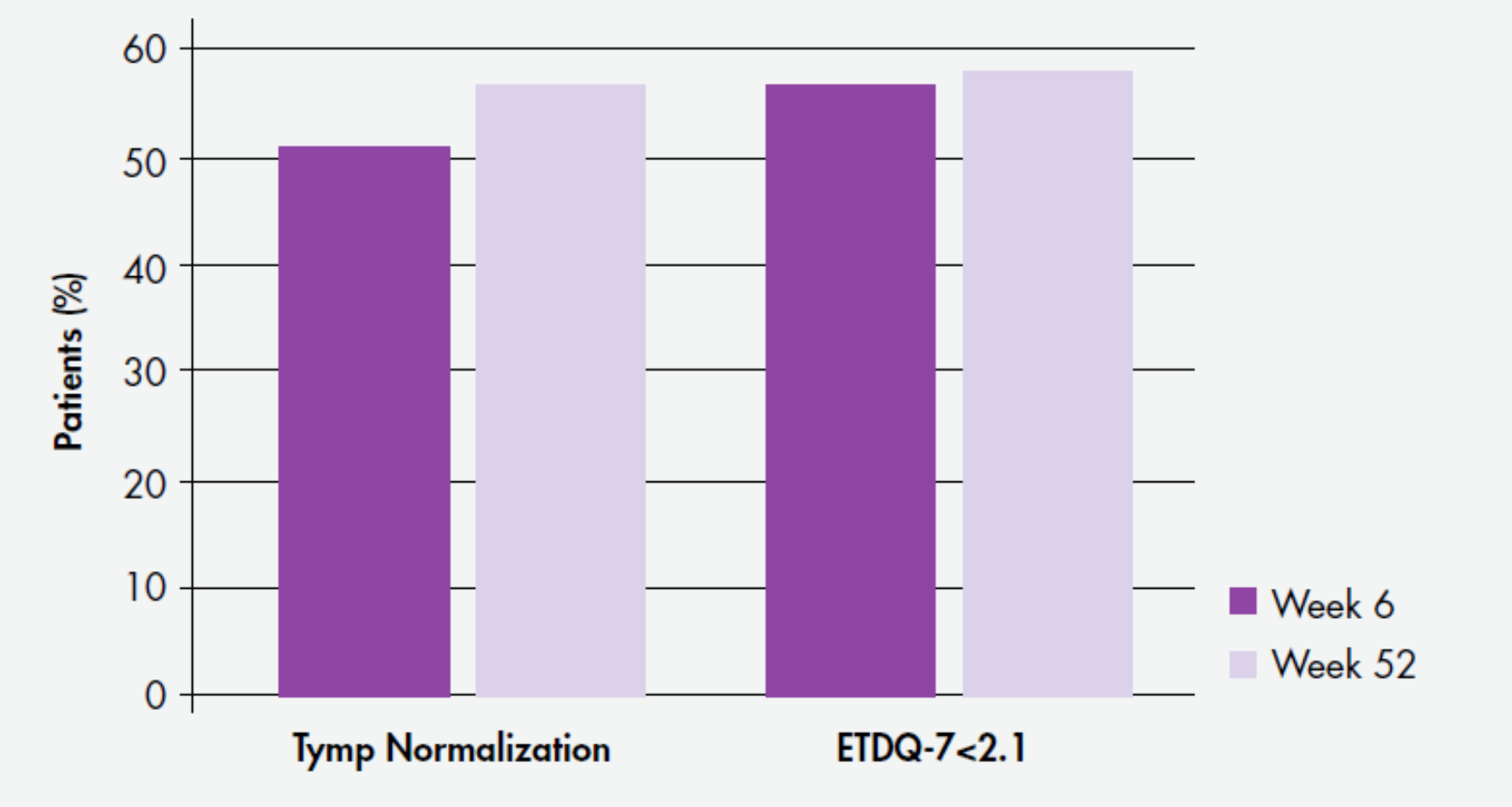
Proven safety and efficacy for ACCLARENT AERA® as demonstrated in a prospective, multi-center, randomized controlled trial:

- **299** subjects treated, 444 Eustachian tube dilations performed
- **0** Serious device- or procedure-related adverse events.
- **99.7%** Technical success rate accessing and dilating the Eustachian tube

	Tympanogram Normalization		ETDQ7 Normalization
	6 week	**24 week**	**6 & 24 week**
ETBC with Medical Management	51.8%	62.2%	56.1%
Medical Management Only	13.9%	Cross over	8.5%

ACCLARENT AERA® Clinical Trial
Results

Tympanogram and ETDQ-7 Normalization at 6 and 52 week follow up[10]



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Eustachian Tube Balloon Dilation System

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Indication For Use

Indication For Use: The ACCLARENT AERA® Eustachian Tube Balloon Dilation system is intended to dilate the Eustachian tube for treatment of persistent Eustachian tube dysfunction in patients age 18 and older.

Contraindications: The ACCLARENT AERA® Eustachian Tube Balloon Dilation System is contraindicated for use in a Eustachian tube with an ipsilateral carotid artery that is dehiscent into the ET lumen or history of ipsilateral patulous Eustachian tube.

Although use of ACCLARENT AERA® device under local anesthesia alone has not been studied in a randomized controlled trial, evidence of its use under topical/local anesthesia along with sedation and analgesia is available in the literature.[9]

In addition, real-world clinical data collected from 25 patients from two sites supports the use of ACCLARENT AERA® device under local/topical anesthetic with appropriate patient preparation which may include supplemental medication for patient management.

Device Safety Identified Risks

- Introduction of false passages and rupture or damage to carotid artery
- Injury to mucosal tissue
  - Due to misuse of device on patulous Eustachian tube or following skull base surgery
  - Due to catheter mechanical failure
  - Due to balloon rupture
  - Due to mishandling of device with respect to excessive force and/or incorrect positioning

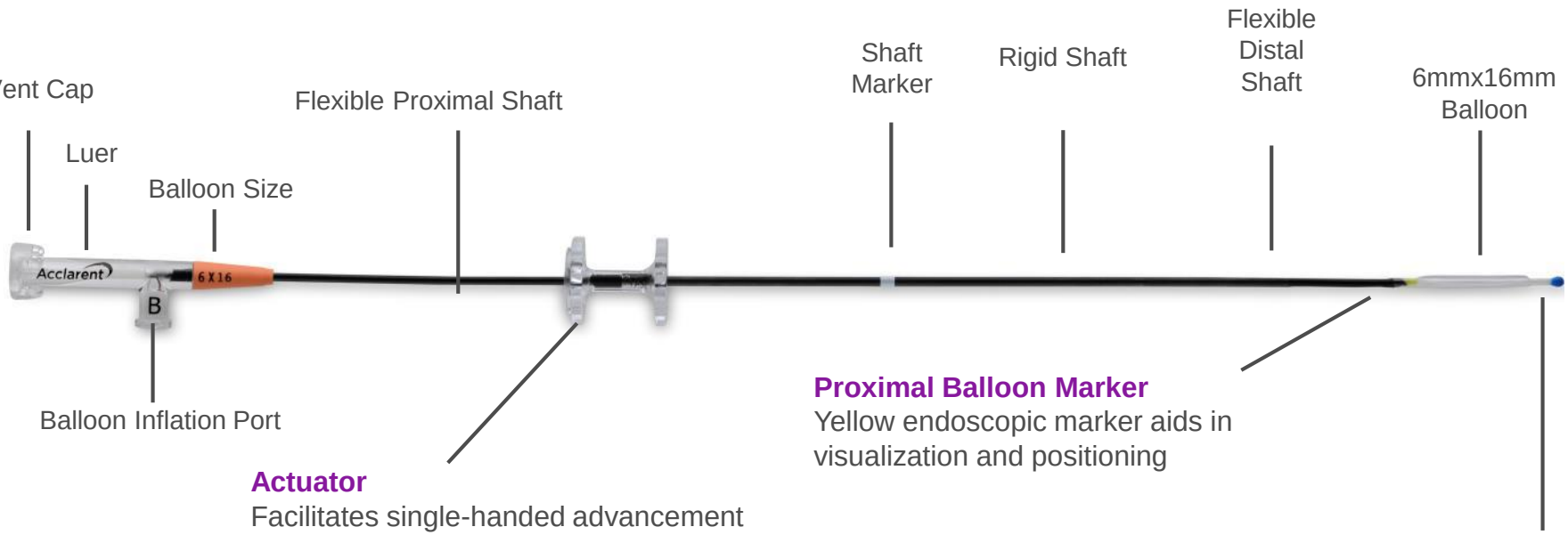
Warnings

- Intended for single patient use only. **DO NOT REUSE.**
- Patients with a history of skull base surgery, prior ear surgery, skull fracture, or anatomic abnormalities may have elevated risk of complications and should be radiographically screened before treatment.
- DO NOT use product if the integrity of the sterile packaging has been compromised or if the device appears damaged.
- DO NOT use if the device becomes damaged or touches a non-sterile object outside of the operating field.
- Never advance or retract the device against unknown resistance, as this could cause tissue trauma or device damage.
- Advancing the device into the Eustachian tube against resistance may cause injury.
- DO NOT exceed the recommended maximum balloon inflation pressure of 12 atmospheres (ATM).
- Use only sterile saline or sterile water for inflation. DO NOT inflate with air.

Precautions

- DO NOT move the balloon while it is inflated. Ensure balloon is fully deflated during insertion and withdrawal.
- Radiographic assessment of the targeted Eustachian tube is recommended prior to any procedure involving balloon tuboplasty.
- Certain nasal anatomy such as a deviated nasal septum may preclude access to the Eustachian tube/s resulting in failure to treat the target anatomy.
- DO NOT inflate the Balloon Catheter until it has exited the Guide Catheter.
- DO NOT bend the Guide Catheter shaft.

ACCLARENT AERA® | Balloon Catheter



Actuator
Facilitates single-handed advancement and retraction of balloon catheter

Proximal Balloon Marker
Yellow endoscopic marker aids in visualization and positioning

Bulb Tip
Designed to limit the balloon catheter travel into the isthmus

Catheter Total Length	32.7cm
Catheter Shaft Diameter	0.80 in

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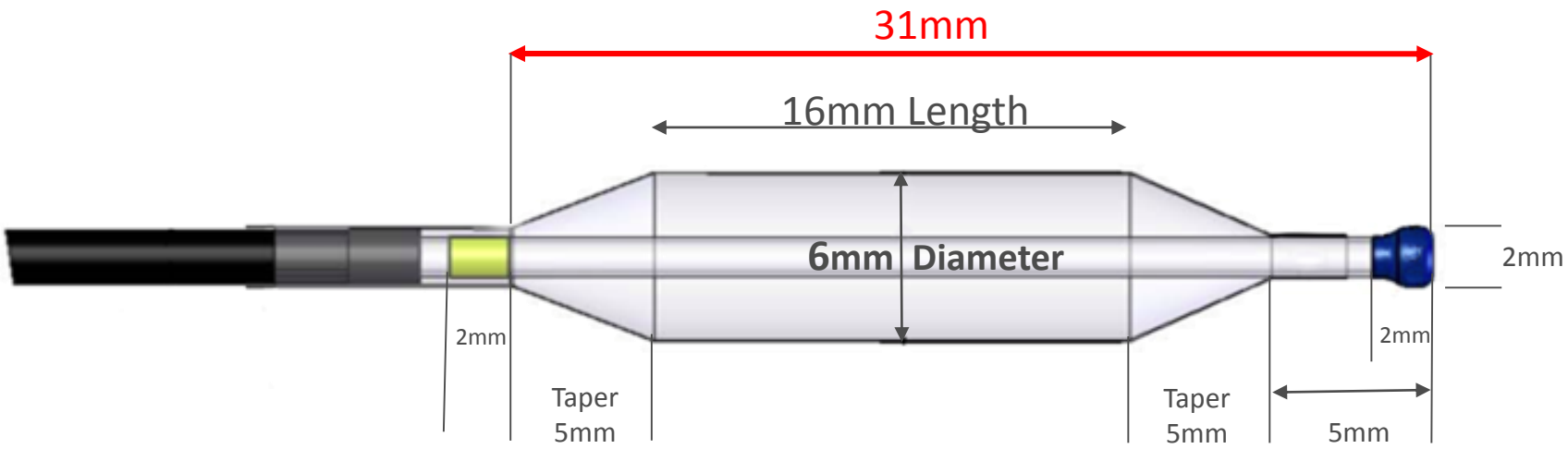
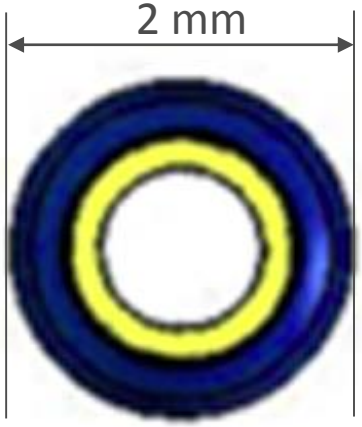
ACCLARENT AERA® | Balloon Specifications





Isthmus measurements [7]:

Max Cross-section: .84mm^2

Estimated Max Diameter: 1.03mm

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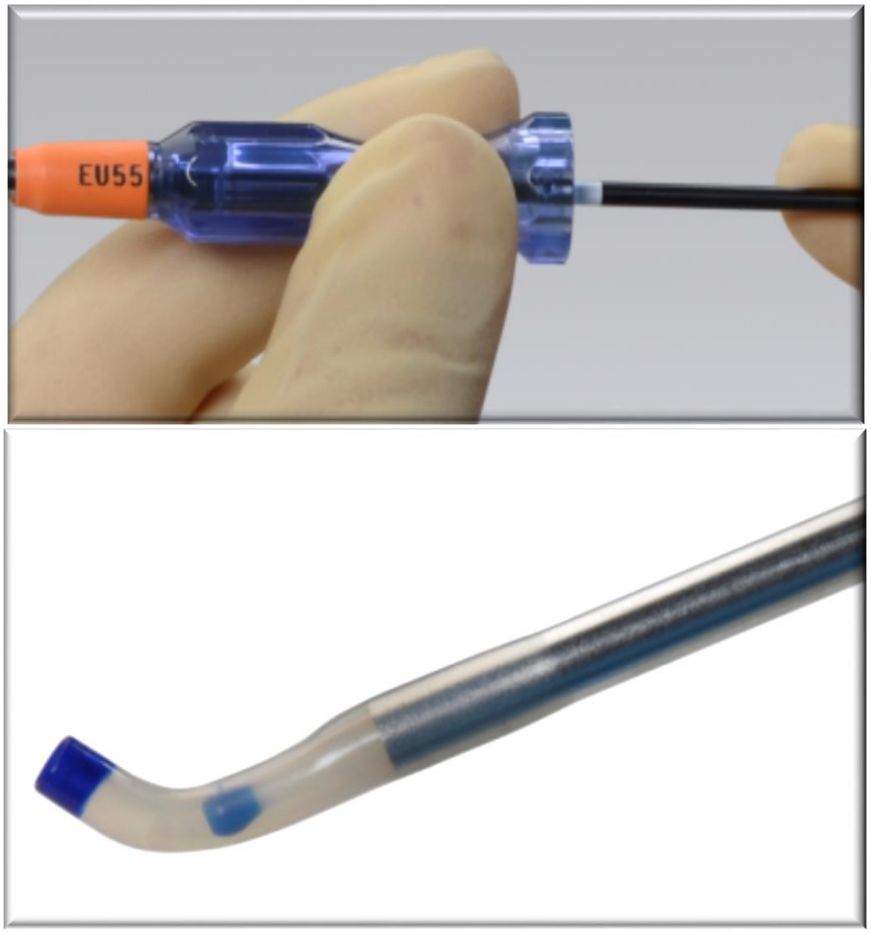
Device Preparation

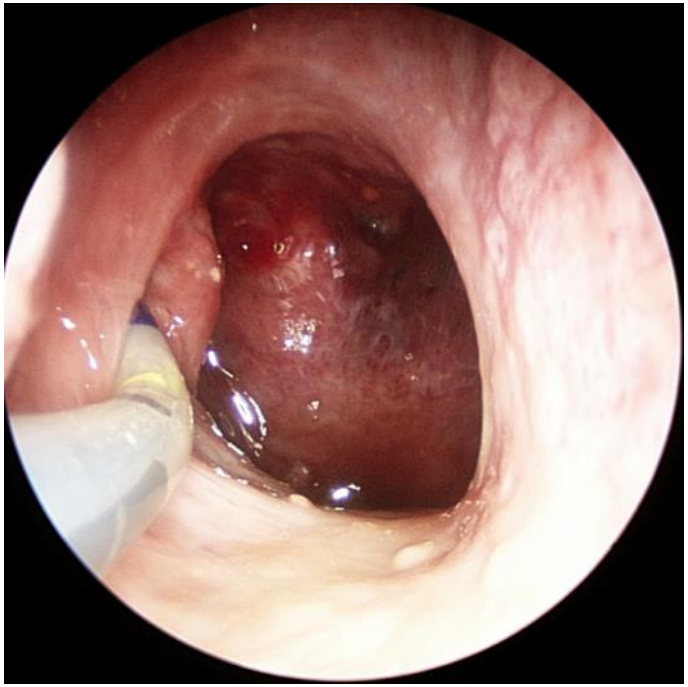
- Connect the tubing of the inflation device to the inflation port on the Balloon Catheter
- Align the shaft marker of the Balloon Catheter with the end of the Guide Catheter proximal hub.
- Insert the Balloon Catheter tip into the proximal hub end of the Guide Catheter and advance the Balloon Catheter until the tip is visible in the clear portion of the guide.



Accessing the Eustachian Tube

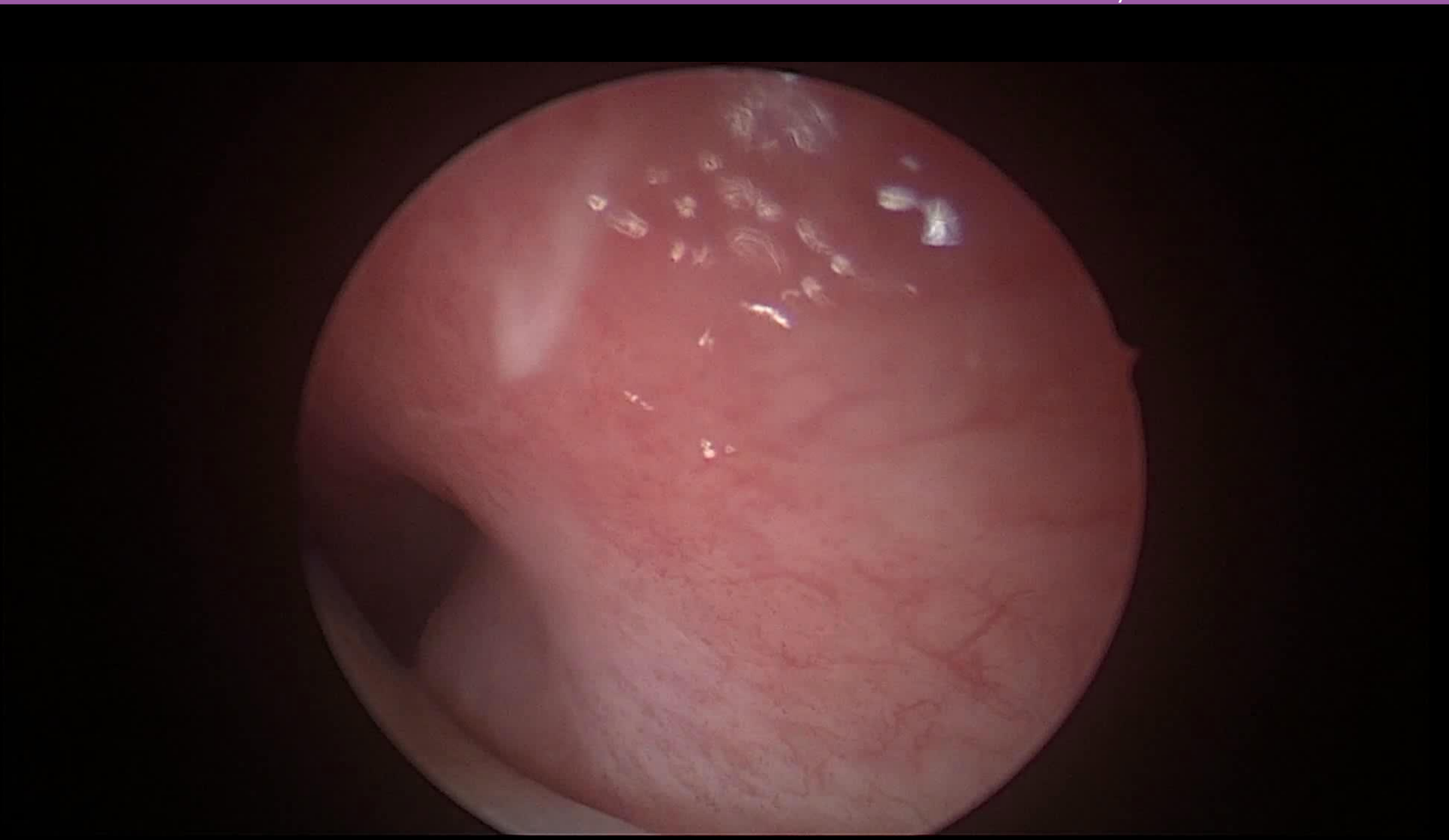
The Balloon Catheter should advance smoothly into the Eustachian tube until the yellow proximal balloon marker exits the Guide Catheter or until resistance to advancement is felt and the yellow marker is visible distal to the bend at the tip of the Guide Catheter (this resistance indicates that the balloon catheter bulb tip has reached the narrow isthmus of the Eustachian tube).

Note: If resistance is encountered during initial advancement of the Balloon Catheter and the yellow proximal balloon marker has not passed the bend at the tip of the Guide Catheter, DO NOT continue to advance the balloon catheter. Retract the Balloon Catheter back into the Guide Catheter, rotate and reposition the tip of the guide and gently re-advance the balloon catheter according to the instructions for use.



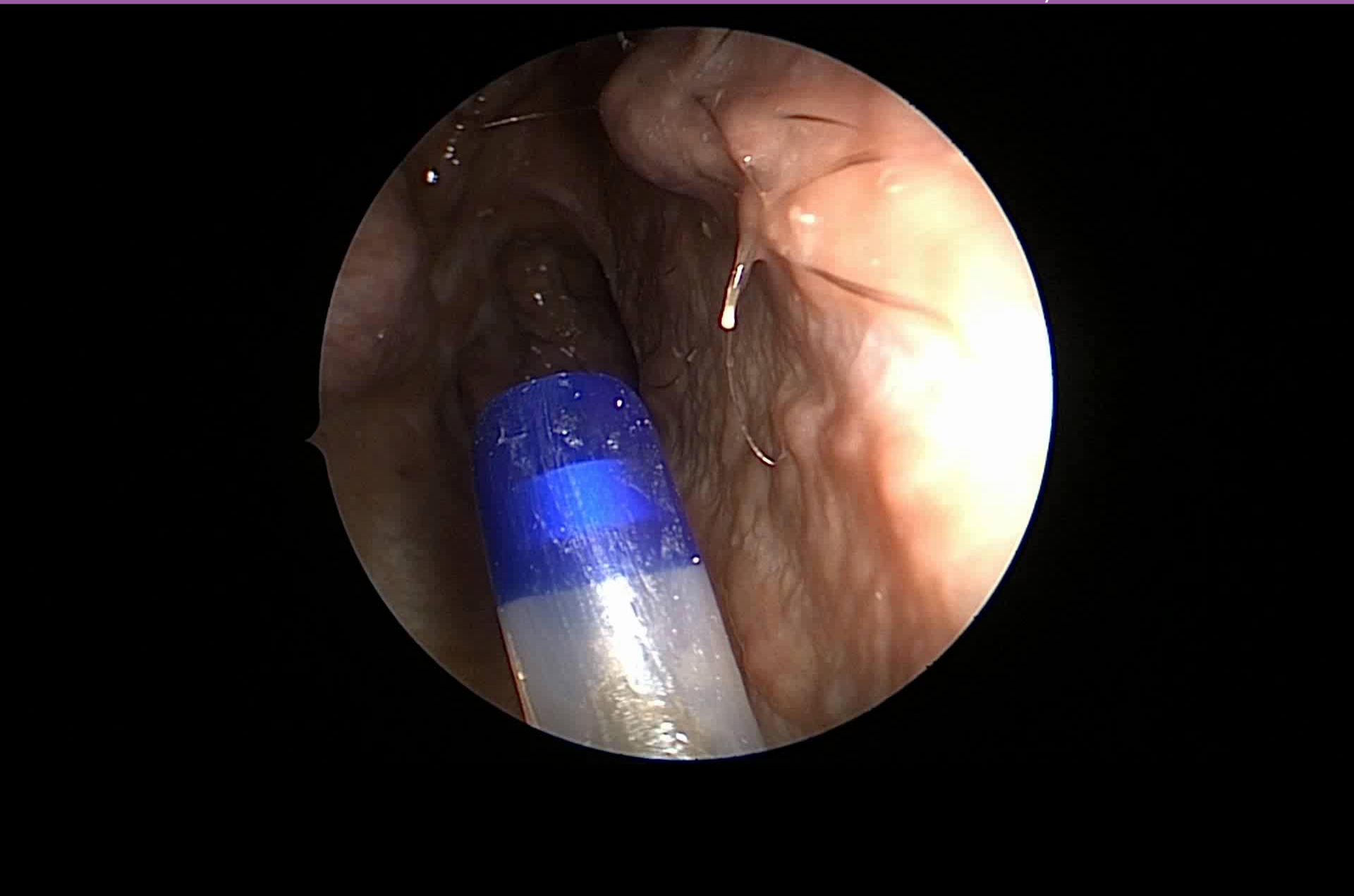
Encountering Resistance

Courtesy of Dr. Dennis Poe



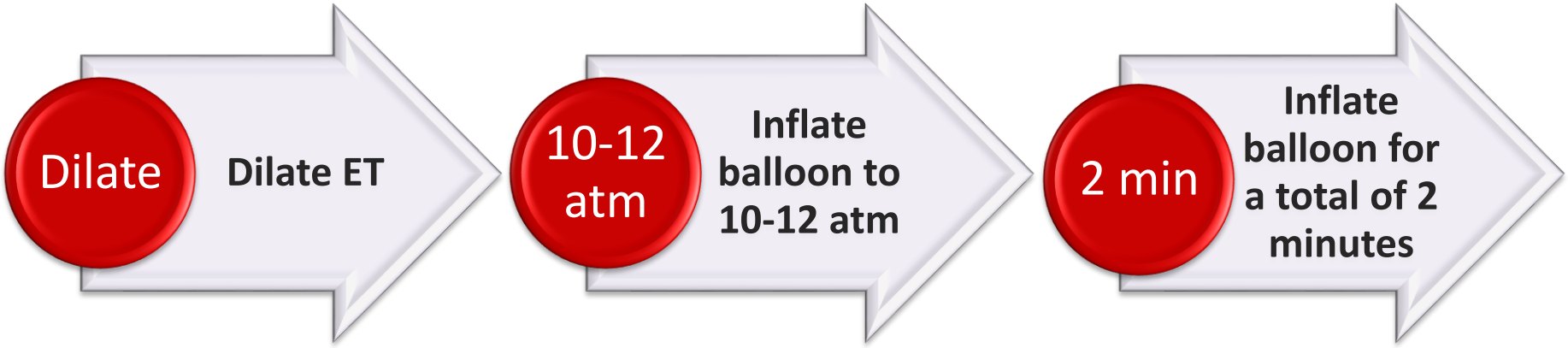
Creating a False Passage

Courtesy of Dr. Dennis Poe



Inflating the Balloon

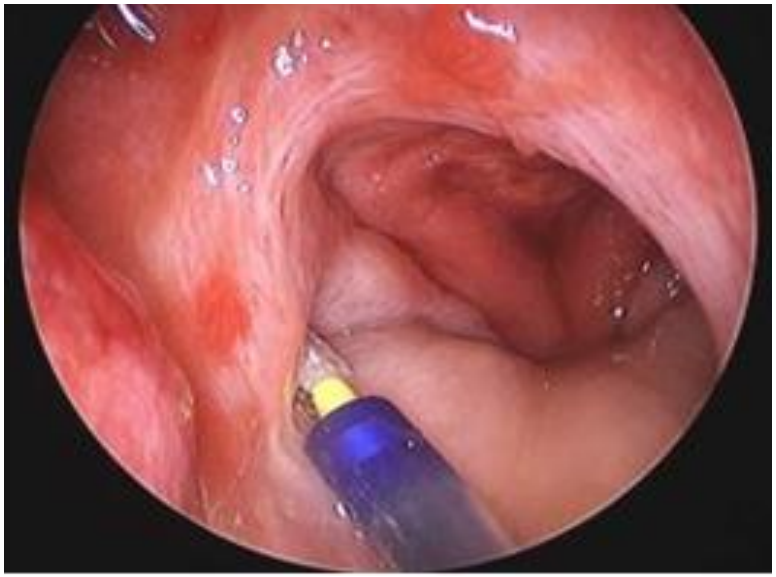
Recommendations for ACCLARENT AERA®



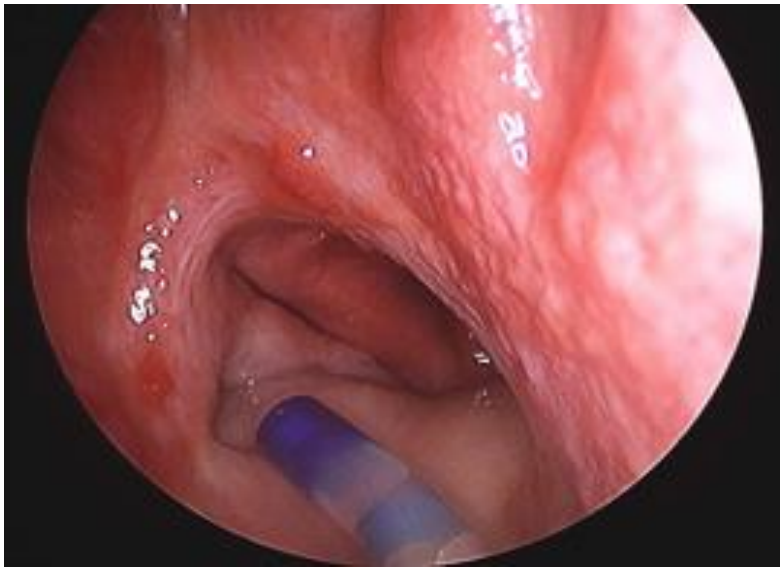
Each ET may be dilated a maximum of twice & may not exceed 2 minutes of inflation.

Balloon Catheter Deflation and Removal

Fully deflate balloon



Retract balloon catheter into guide



- Once desired inflation is achieved, deflate the balloon per the inflation device instructions for use.
- Additional inflation may be performed if desired, followed by balloon deflation.
- After the balloon is fully deflated, retract the Balloon Catheter into the Guide Catheter, and remove the entire system from the patient.

Thank you

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