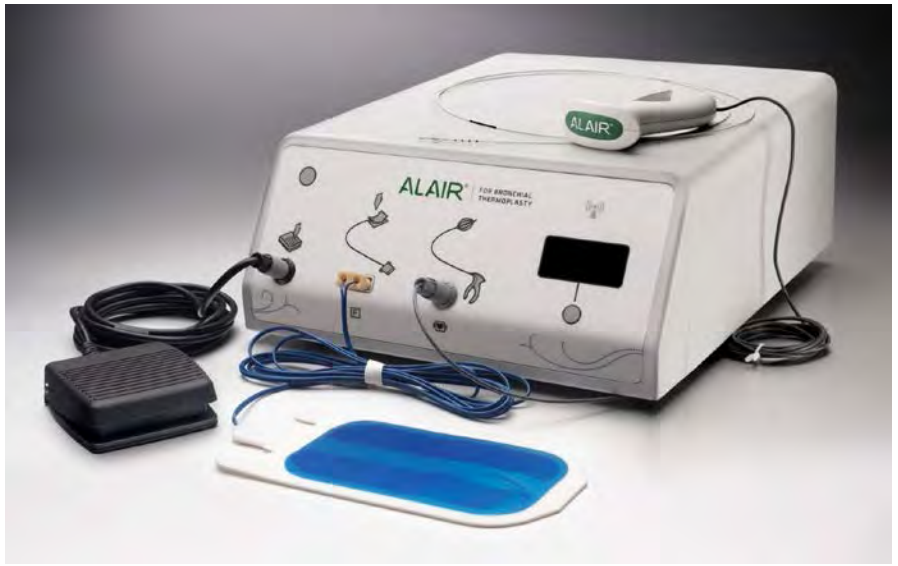
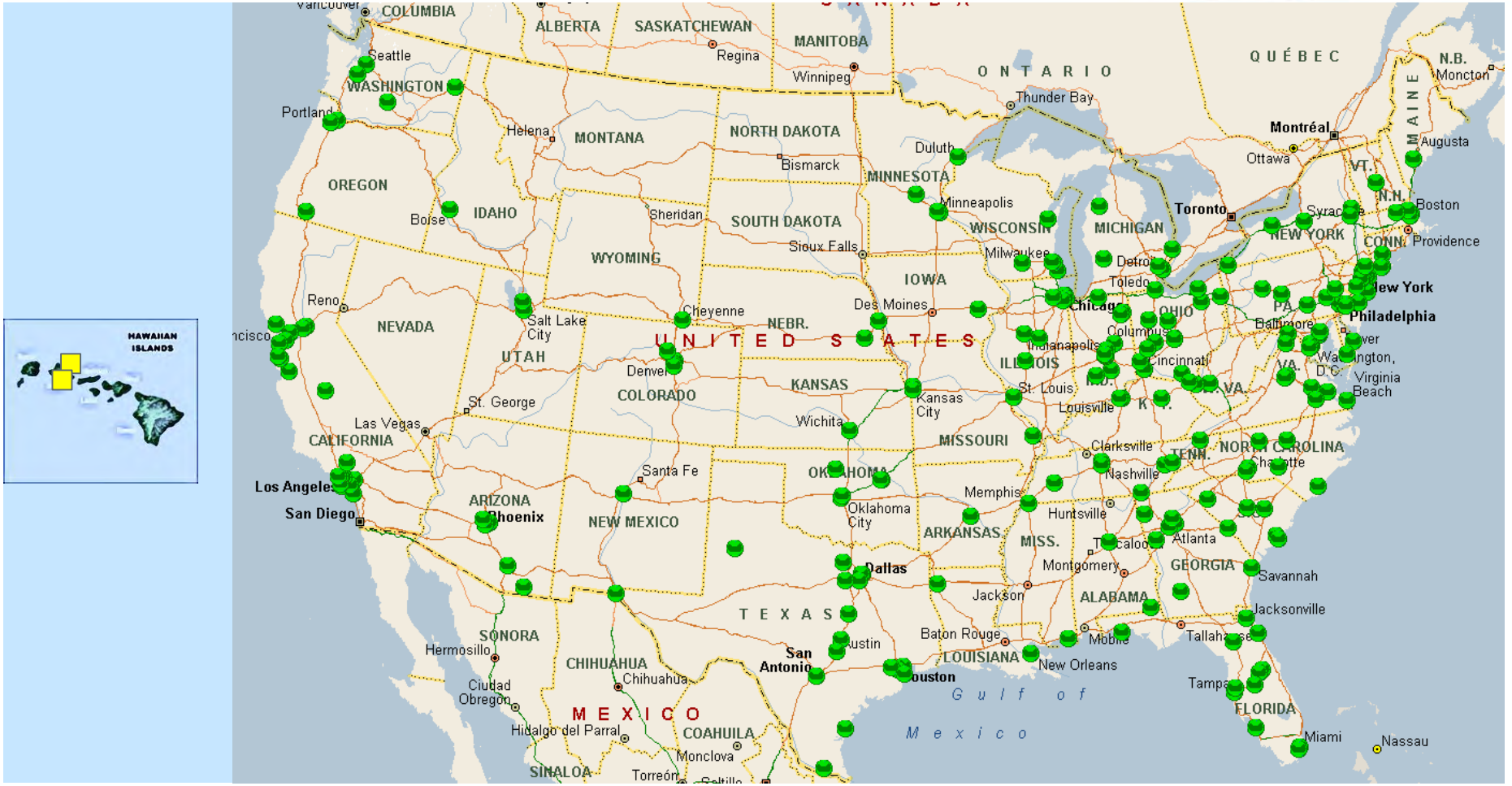
Bronchial Thermoplasty
delivered by the Alair® System



250 Domestic Bronchial Thermoplasty Clinics:



Bronchial Thermoplasty (BT) delivered by the Alair® System

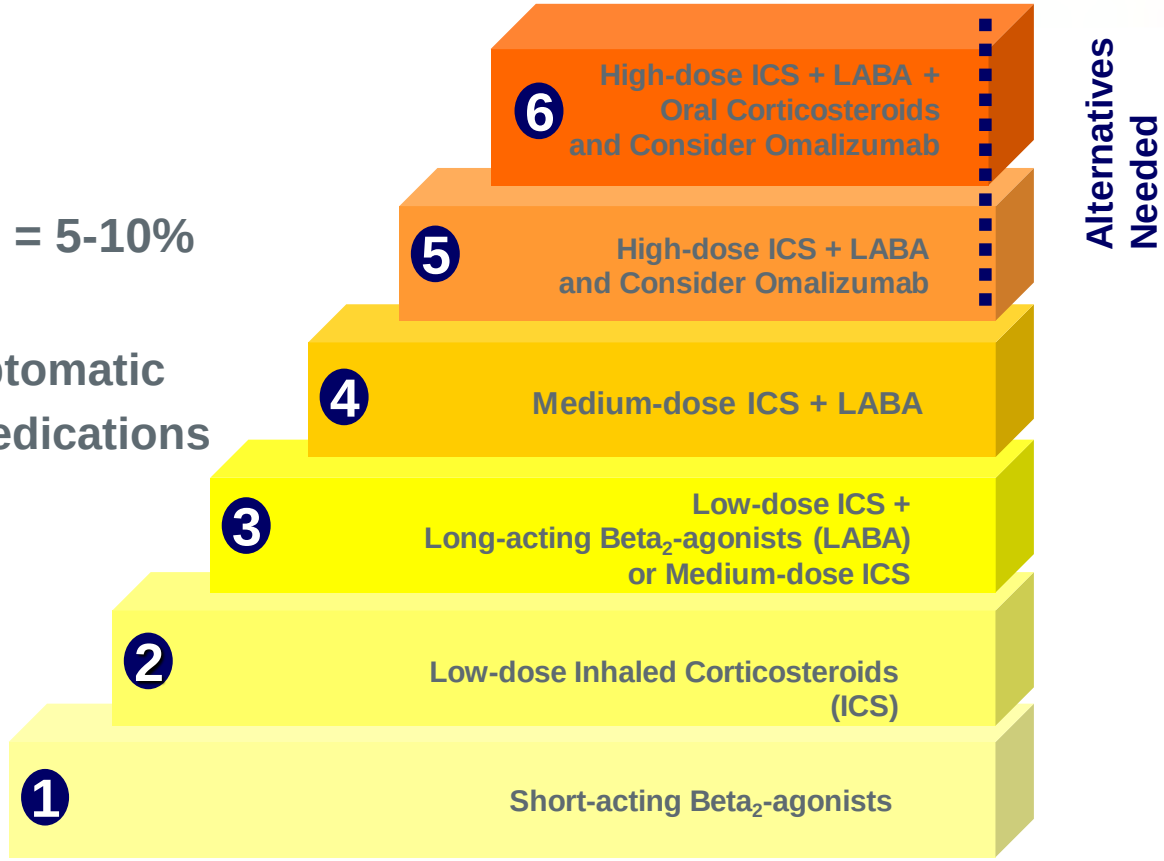
- Bronchial Thermoplasty with the Alair System has been approved by the FDA for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long-acting beta-agonists.

Stepwise Approach for Managing Asthma

Severe Asthma:

- **Steps 5 &6**
  - **1-2 exacerbations/year**
- **Prevalence per NAEPP = 5-10%**

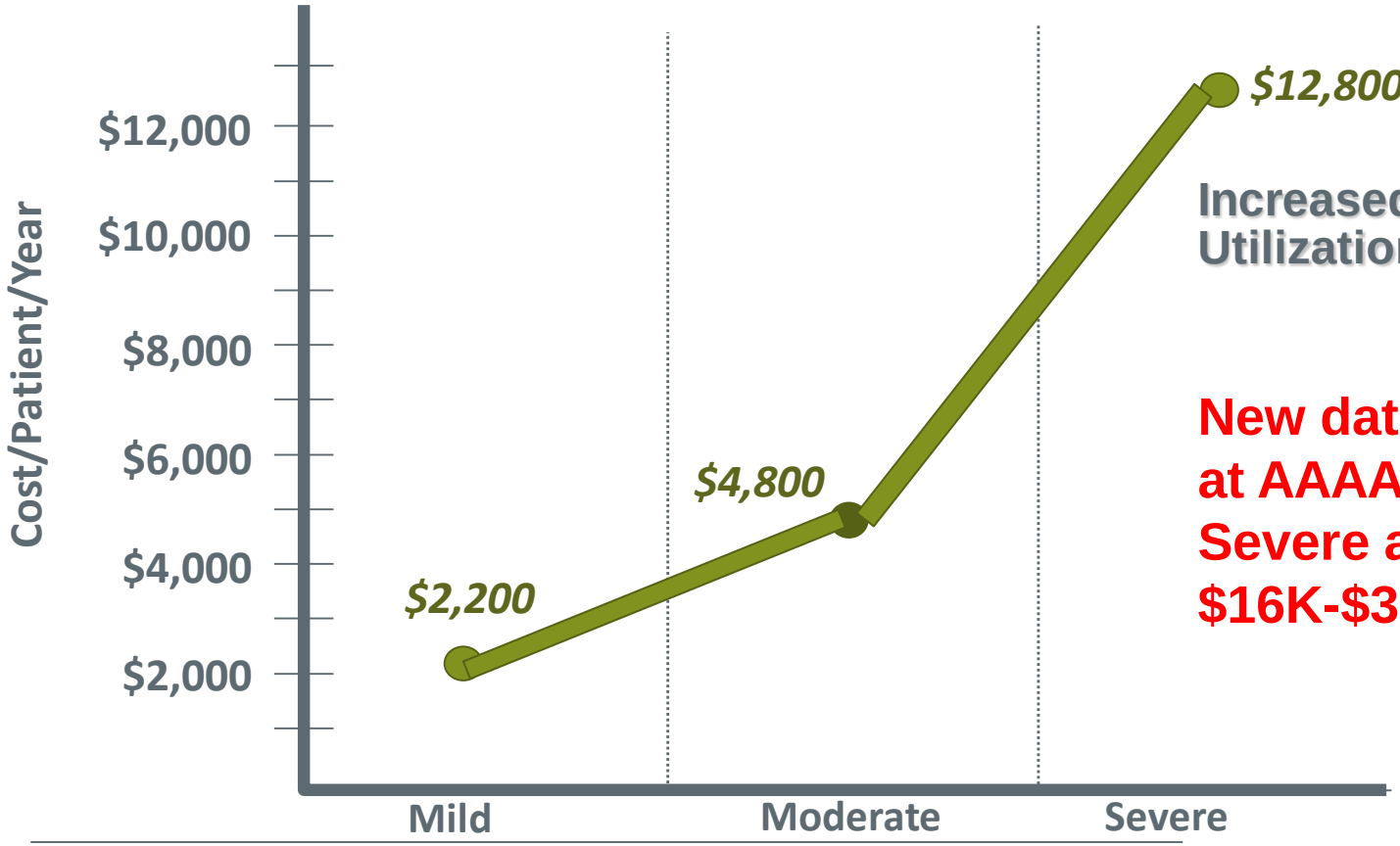
Many patients remain symptomatic despite standard of care medications



Adapted from National Asthma Education and Prevention Program (NAEPP) Guidelines. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. National Heart, Lung, and Blood Institute, NIH Publication No. 07-4051, Revised August 2007.

Annual Cost by Asthma Severity[1]

Prevalence is highest ever…proportion of asthmatics grew 15% in the last decade. 18.7m American adults have asthma



Increased Healthcare Utilization

New data presented at AAAAI 2013: Severe asthma $16K-$32K

1. Cisternas M, et al., A comprehensive study of the direct and indirect costs of an adult with asthma. J Allergy Clin Immunol 2003;111(6):1212-1218

Bronchial Thermoplasty:

Bronchial Thermoplasty

↓

Reduces Airway Smooth Muscle (ASM)

↓

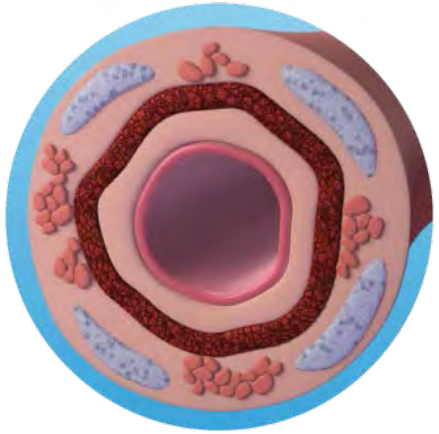
Reduces Bronchoconstriction

↓

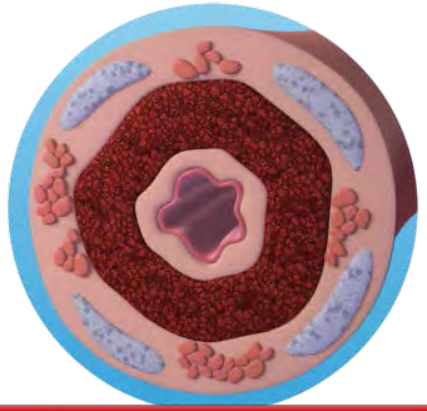
Reduces Asthma Exacerbations

↓

Improves Asthma Quality of Life

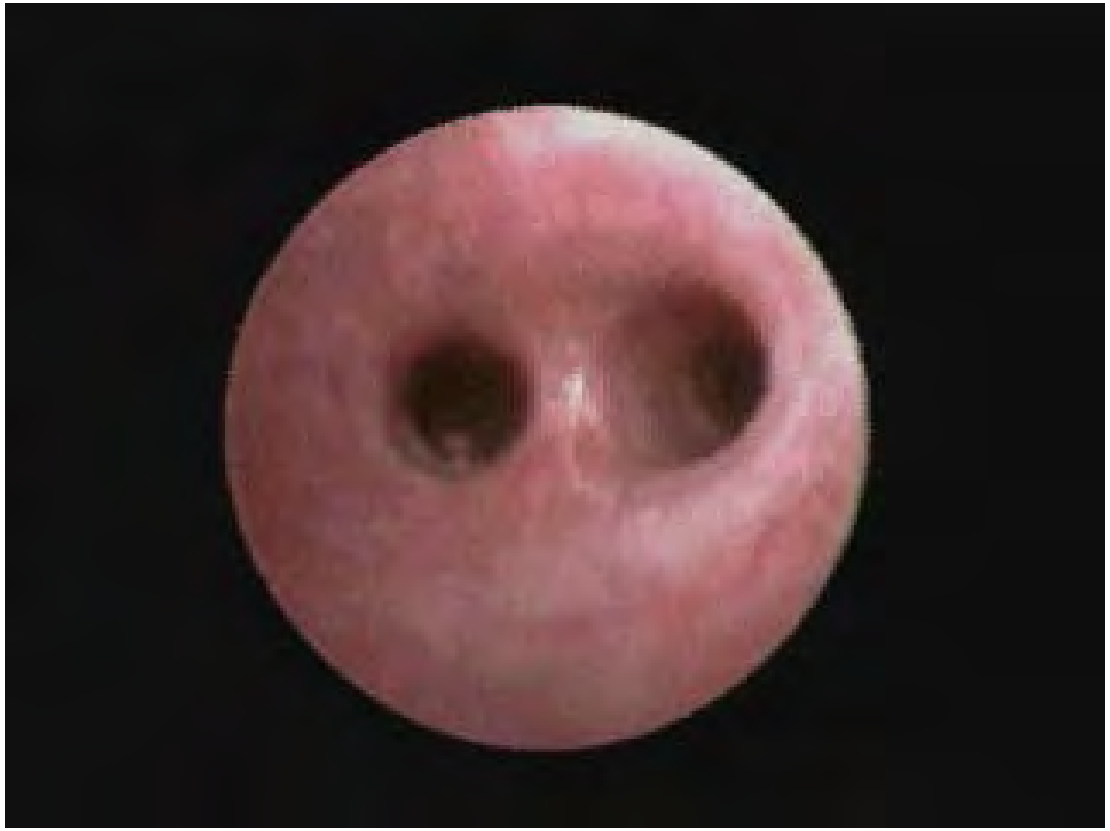


Normal Airway



Asthma Attack

Bronchoscopic View of Airway Responsiveness to Local Methacholine Challenge



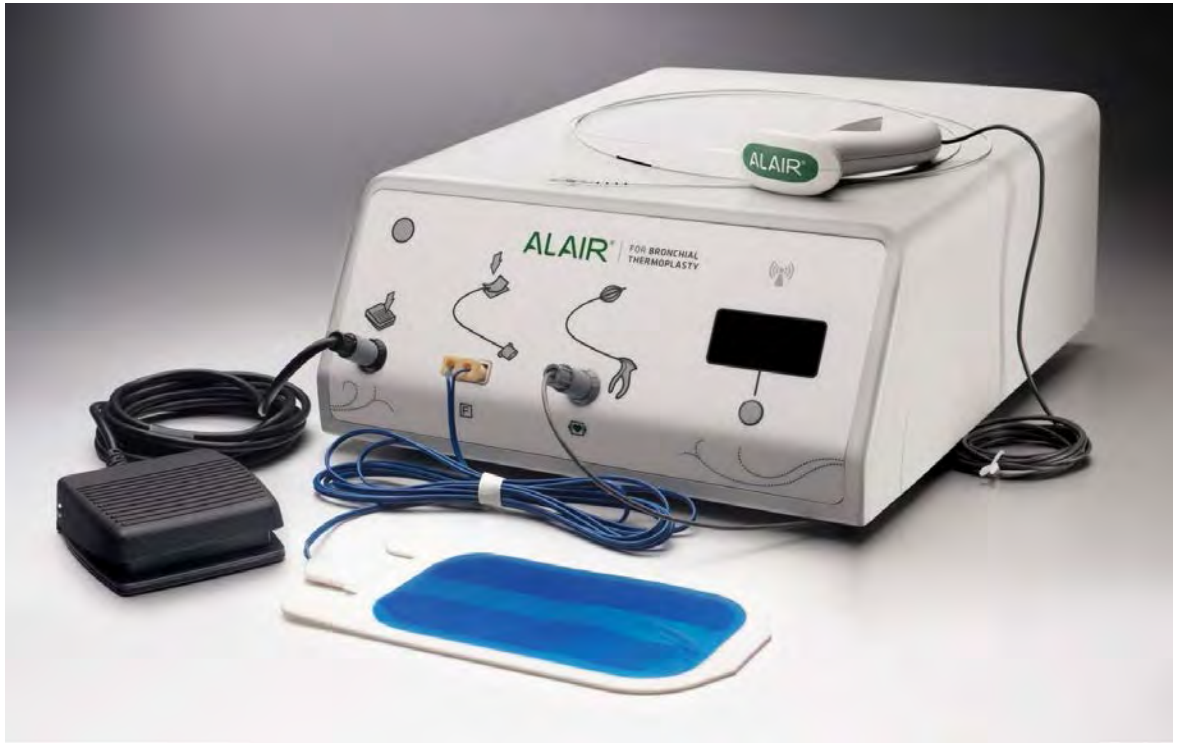
Canine Model: Airway on left treated with bronchial thermoplasty. Airway on right was not treated.

Cox et al. Eur Respir Journal. 2004;24: 659-663

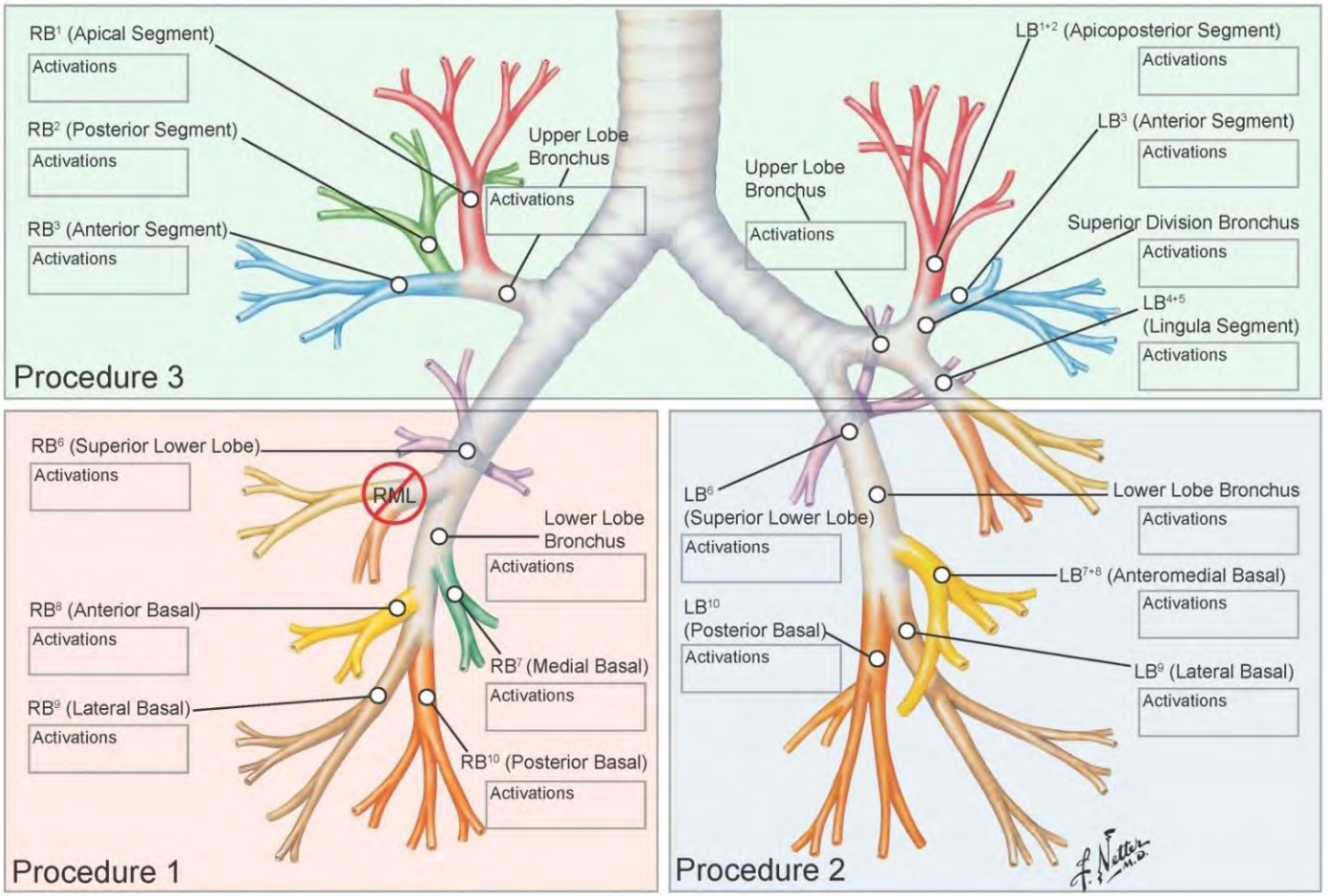
The Alair®
Bronchial Thermoplasty System

The Alair® System

- The Alair RF Controller
- Alair Catheter



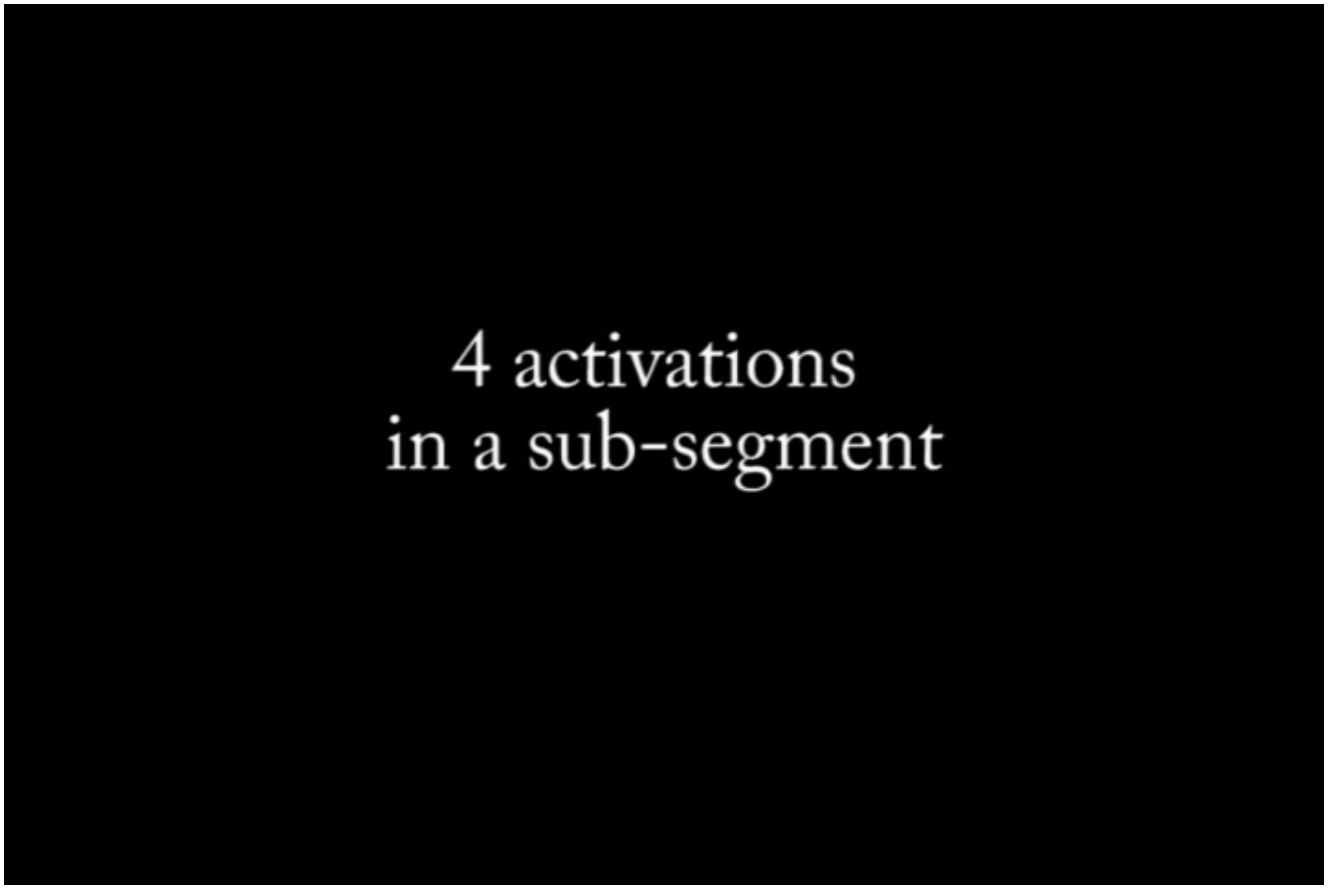
Three Treatment Sessions



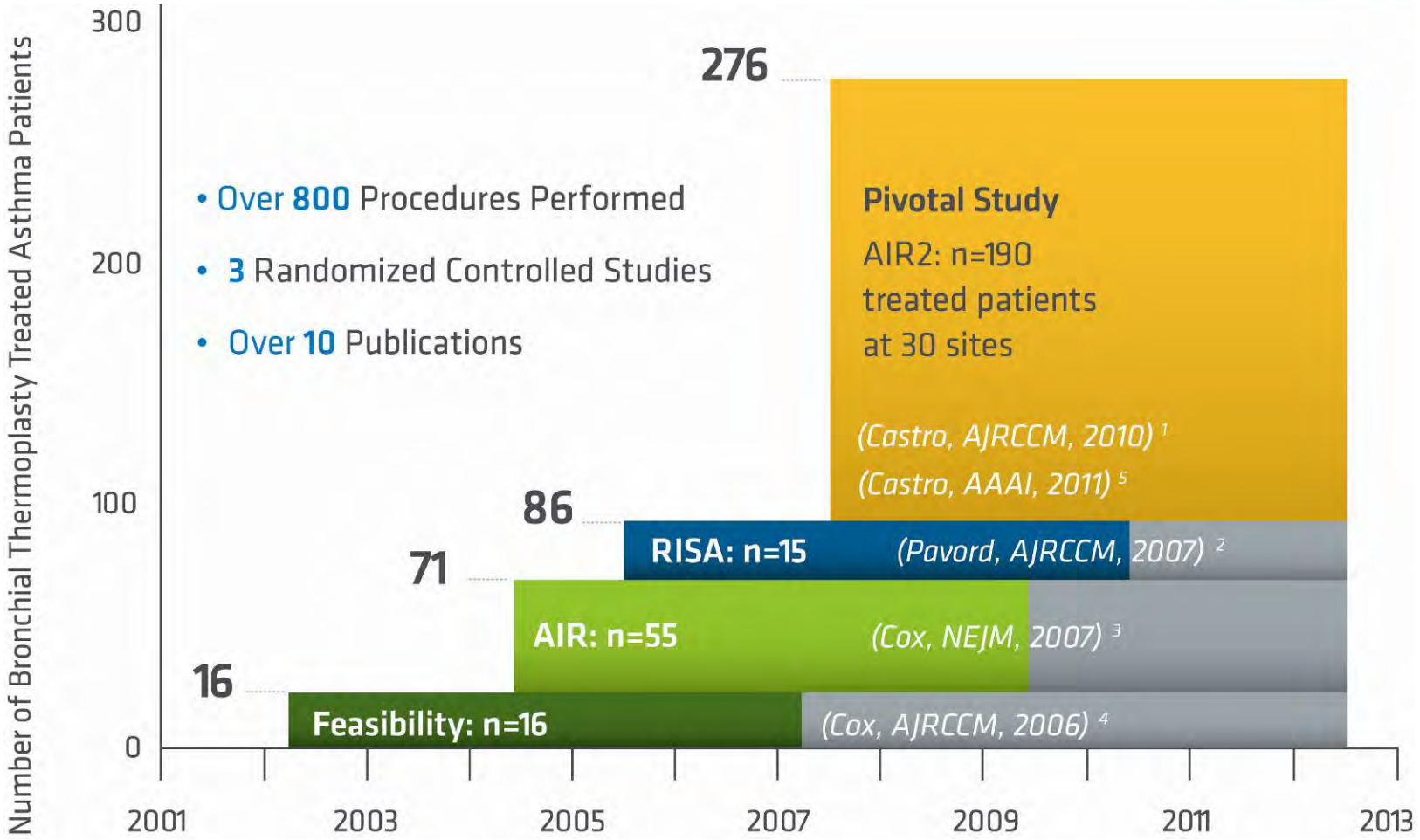
Bronchial Thermoplasty is performed in 3 separate treatment sessions each scheduled approximately 3 weeks apart

Application of RF Energy

Temperature controlled heat (65^0 C) is delivered to airway wall for 10 seconds per activation – no permanent damage to epithelium



Bronchial Thermoplasty Clinical Studies



AIR = Asthma Intervention Research Study
RISA = Research in Severe Asthma Study

AIR2 – Trial Design

- **Study Design: Sham Controlled, Double Blind**
  - 2 : 1 randomization; BT: Sham
  - BT Group (ICS + LABA + BT)
  - Sham Group (ICS + LABA + Sham)
- **Study Size:**
  - 297 subjects
  - 30 centers in 6 countries (15 centers in the U.S.)
- **Length of Follow-up:**
  - One year (3, 6, 9 and 12 months)
  - 5-year safety follow-up for BT subjects in Extension Study

BT = Bronchial Thermoplasty

AIR2 Trial – 1 year Key Findings

Key Findings at 1 Year after BT

- **Improved asthma-related quality of life compared to control (AQLQ score)**
  - 79% of BT-treated patients achieved ≥ 0.5 increase versus 64% of sham-treated patients (PPS 99.6%)
- **Improved clinical outcomes compared to Sham-control:**
  - 32% decrease in severe exacerbations
  - 84% reduction in ER visits for respiratory symptoms
  - 73% reduction in hospitalization for respiratory symptoms
  - 66% less days lost from work, school and other daily activities due to asthma
- **No unanticipated device-related adverse events or deaths**
- **Acceptable safety profile**

PPS – posterior probability of superiority

AIR2 5-Year Extension Study
Durability of Effectiveness

Objective: *Evaluate durability of effectiveness of BT to 5 years in patients with severe persistent asthma.*

Hypothesis: The proportion of subjects experiencing severe exacerbations in Years 2-5 is not substantially worse than in the first year.

Clinical results published out to 2 years

- Reductions in exacerbations, ER visits and hospitalizations for respiratory symptoms are maintained

5 year clinical results were presented at ATS in May

Additional Safety data:

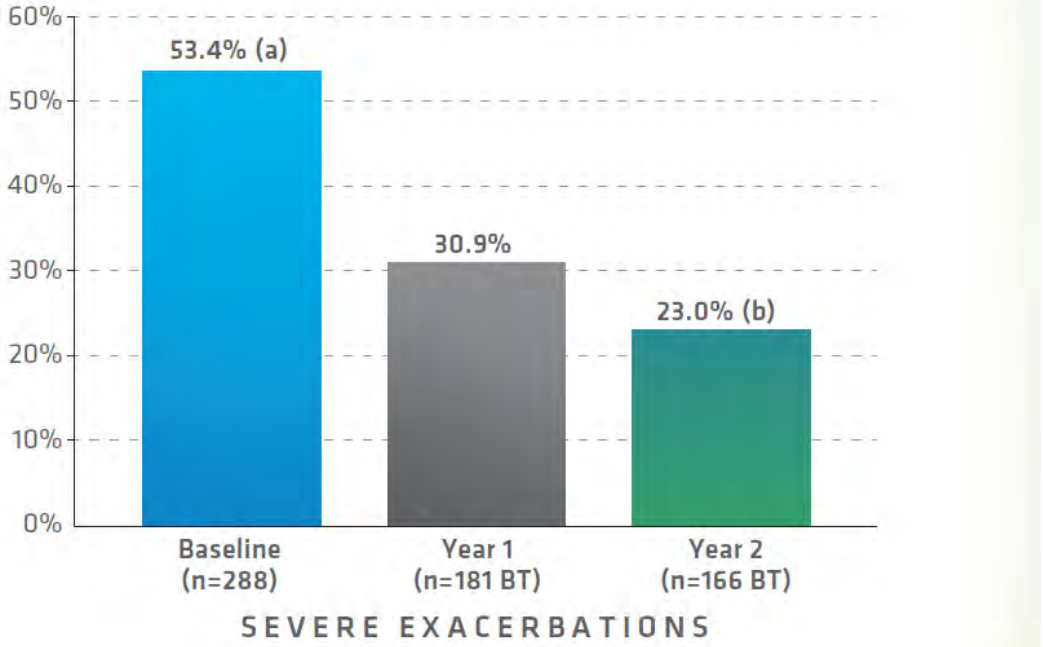
- Stable safety profile observed out to 5 years in RISA and AIR

-Castro M, et al. Ann Allergy Asthma Immunol. 2011 Jul;107(1):65-70
-Wechsler, **ATS 2013 [Poster Board # 308]**

Persistence of Effect at Two Years[1]

Effectiveness of BT persist out to at least two years

- **Proportion of patients experiencing severe exacerbations comparable between years 1 and 2.**



(a) All study subjects (BT + Sham) in 12 months prior to study entry (patient reported)
(b) Year 2 BT comparison to Year 1 BT: not significant (Fisher's Exact Test)

1. Castro M, et al. Ann Allergy Asthma Immunol. 2011 Jul;107(1):65-70

Effectiveness Demonstrated Across Multiple Studies

AIR2
(RCT; n = 288)

- AQLQ
- Exacerbations
- ER visits
- Days missed work/school

AJRCCM, Jan 2010

AIR
(RCT; n = 109)

- AQLQ
- Exacerbations
- Rescue meds
- Symptom Free Days

NEJM, Mar 2007

RISA
(RCT; n = 32)

- AQLQ
- ACQ
- Rescue meds
- Oral Steroids (p = 0.12)

AJRCCM, Sep 2007

All of the above were shown to be significant ($p < 0.05$), except where noted

Bronchial Thermoplasty
Summary of Risks

Risks

- In the period immediately following BT, there is an expected increase and worsening of respiratory-related symptoms, which are of the type expected following bronchoscopy in patients with asthma
- These events typically occur within a day of the procedure and resolve on average within seven days with standard care
  - In the long term after treatment, fewer BT treated patients report respiratory adverse events vs. sham group
  - The pivotal study concluded that increased risk of adverse events in the short-term following the procedure is outweighed by the benefit of BT that persists at least 2 years

BT = Bronchial Thermoplasty

Risk of Respiratory-Related Hospitalization Following Procedure[1]

Respiratory-Related Hospitalizations during Treatment Period[a]	**BT** (N=190)	**Sham** (N=98)
Events / Subject (%)	19/190 (10%)*	2/98 (2.0%)
Events / Bronchoscopy (%)	19/558 (3.4%)	2/292 (0.7%)

* 10/19 (53%) in the BT group occurred on the day of the procedure.

a/ Time period beginning at first bronchoscopy to 6 weeks after the third bronchoscopy (approx. 12 week period)

1. Castro, Am J Respir Crit Care Med. 2010;181(2):116-24

Bronchial Thermoplasty Patient Selection

FDA Indication: The Alair® Bronchial Thermoplasty System has been approved by the FDA for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long-acting beta$_2$-agonists.

- Adult severe, persistent asthmatics (≥ 18 years old)
- Inadequate control despite combination of inhaled high dose corticosteroids (ICS) and a long-acting beta$_2$-agonists (LABA)
- Able to safely undergo bronchoscopy per hospital guidelines

Reference the Alair Bronchial Thermoplasty System Directions for Use for more information.

Patient Selection details

- Severe persistent asthma and
  - Rule out other diagnoses
- Controller medication requirements:
  - Must include: ICS and LABA
  - May include: corticosteroids, or other controller medications such as Xolair, leukotriene modifiers, theophylline, or anti-cholinergics to manage asthma.
  - May include evidence of adherence
- Patient's asthma is not well controlled
  - Use of short-acting beta-agonists
  - Recurrent exacerbations (OCS use)
  - ER visits, and admissions in past 12 months
  - ACT, AIS-6 or other questionare
- Comorbidities addressed to minimize risk that these are exacerbating asthma

Contraindications

Bronchial thermoplasty should not be performed on:

- Patients that have a pacemaker, internal defibrillator, or other implantable electronic device
- Patients that have a known sensitivity to medications required to perform bronchoscopy, including lidocaine, atropine, and benzodiazepines
- Patients that have previously been treated with the Alair® System

Reference the Alair Bronchial Thermoplasty System Directions for Use for more information.

Contraindications

Bronchial thermoplasty should be delayed for the following:

- Active respiratory infection
- Asthma attack or changing dose of systemic corticosteroids (up or down) in the past 14 days
- Patient is unable to stop taking anticoagulants, antiplatelet agents, aspirin or non-steroidal anti-inflammatory medications (NSAIDS) before the procedure with physician guidance

Reference the Alair® Bronchial Thermoplasty System Directions for Use for more information.

Reimbursement - Coding

Coding:

- **Class 1 CPT codes released for 2013!!**
  - **31660 used for 2 Lower lobe treatments**
  - **31661** Used for upper lobes treatment

- Medicare pass through coding for BT catheter
  - **C1886** CMS determined that BT catheter is eligible for pass-through payment under Medicare OPPS

Reimbursement – Coverage

Coverage:

- All patients should obtain written pre-determination
  - Pre-Determination services provided free of charge by Boston Scientific contracted through TRG
  - Limited number of coverage policies BUT patients are getting covered case by case through TRG
  - 1 Pre-detremination for all 3 procedures

See BT coding guide and referenced impact model for more detailed information

Reimbursement – Payment

- Payment: Pre-authorized and verified to be on label
  - 3 billing cycles
  - Medicare: maps to APC 0415 payment
    - ~ $4,400 per procedure including C-code payment
  - Commercial insurance: Depending on contracts for new technology

See BT coding guide and referenced impact model for more detailed information