Endobronchial Thermoplasty

Asthma Education Day
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Asthma is a chronic respiratory disease characterized by inflammation of the airways, excess mucus production and airway hyper-responsiveness, a condition in which airways narrow excessively or too easily in response to a stimulus.
Incidence

- Asthma affects approximately 25 million people in the US
- 5-10% of patients with asthma are estimated to have severe asthma
Implications of Uncontrolled Asthma (U.S.)

13.9 million
People experience asthma attacks

10.6 million
Asthma physician office visits

2.1 million
Emergency department visits

479,300
Hospitalizations

3,388
Asthma-related deaths

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Higher Cost of Severe Asthma (U.S.)


Higher healthcare costs with asthma severity

- Increased healthcare utilization
- Emergency Room (ER) visits
- Hospitalizations

Patients with exacerbations have higher health care costs than patients without exacerbations.

Est. $56B total cost of asthma

- Mild: $2,200
- Moderate: $4,800
- Severe: $12,800

What is Severe Asthma?

ERS/ATS 2014 Guidelines:

- **Severe asthma** is defined as “asthma which requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming ‘uncontrolled’ or which remains ‘uncontrolled’ despite this therapy.”

5%-10% of total asthma population estimated to have severe asthma

ERS = European Respiratory Society
ATS = American Thoracic Society

Challenges in Severe Asthma\textsuperscript{1}: An Unmet Clinical Need

- **Asthma is a heterogeneous disease** characterized by diverse symptom profiles and response to medications.

- **Subset of patients remain symptomatic and experience quality of life limitations** despite standard of care medications.

- **Medications have limited efficacy**, require adherence, and can have substantial side effects.

- **Higher rates** of asthma exacerbations, increased steroid burden, increased morbidity and disproportionate use of healthcare resources.

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Limited Medication Options Beyond ICS/LABA for Severe Asthma

- **OCS** (oral glucocorticosteroids)
  - Effective for some, but associated with substantial long-term side effects

- **Anti-IgE therapy** (omalizumab)
  - Applicable only to patients with severe allergic asthma with elevated IgE levels

- **Other**
  - Theophylline – Limited efficacy in asthma and side effects are common
  - Tiotropium – Not approved for asthma; data show improved lung function and decreased reliever use
  - Leukotriene Receptor Antagonist (LTRA) - may be helpful for patients found to be aspirin sensitive
Bronchial Thermoplasty

• When compliance is proven and conventional therapy is not enough
What is Bronchial Thermoplasty (BT)?

- **Non-pharmacological intervention** for severe asthma that targets excess airway smooth muscle in the airways to reduce bronchoconstriction.

- **Safe, minimally invasive, outpatient** procedure performed with the Alair™ System through routine bronchoscopy.

- **Clinically proven** to provide long-term reduction in severe asthma exacerbations out to at least 5 years, and improve asthma-related quality of life for patients with severe asthma*.

- **Complementary treatment** to asthma maintenance medications that control inflammation.
  - Not a cure for asthma or a replacement for drug therapy.

*Compared to a sham-control group at one year.
BT Reduces Excess Airway Smooth Muscle (ASM)

Reduce Airway Smooth Muscle (ASM) → Reduce Bronchoconstriction → Reduce Asthma Exacerbations → Improve Asthma Quality of Life

BT Clinical Studies
12+ years of clinical experience

**AIR2**
2005-2012
- Randomized, double-blind, sham-controlled study
- N = 190 (190 BT, 98 sham)
- Evaluate safety and effectiveness in patients with severe persistent asthma

**RISA2**
2004-2010
- Randomized, controlled study
- N = 16
- Evaluate safety and reduction in medications and asthma symptoms in patients with severe, refractory asthma

**AIR3**
2002-2010
- Randomized, controlled study
- N = 55
- Evaluate safety and reduction in patients with moderate to severe asthma

**Feasibility**
2000-2007
- Non-randomized, prospective study
- N = 16
- Evaluate safety in patients with mild to severe asthma

- 4 clinical studies in patients with asthma
- 3 randomized, controlled, clinical studies, with 1 sham-controlled
- 5 years of follow-up
- All BT studies published in top peer-reviewed journals

1. Castro et al., AJRCCM 2010; Castro et al., AnnAAI 2011; Wechsler et al., JACI 2013
2. Pavord et al., AJRCCM 2007; Pavord et al., AnnAA 2013
3. Cox et al., NEJM 2007; Thomson et al., BMC Pulmonary Medicine 2011
4. Cox et al., AJRCCM 2006; Cox et al., AJRCCM 2010
Asthma Intervention Research 2 (AIR2) Trial

Objective:
BT superior to sham

Primary Endpoint:
AQLQ score
(Asthma Quality of Life Questionnaire)

Other Endpoints and Analyses:
Severe exacerbations*, ER visits, Days lost from work/school/other daily activities due to asthma symptoms

* Exacerbations requiring treatment with systemic corticosteroids or a doubling of ICS

Pivotal U.S. study to evaluate safety and effectiveness of BT with the Alair™ System in adult patients with severe asthma.

† Study Population: patients with severe persistent asthma symptomatic despite high dose ICS (>1,000 mg/d beclomethasone or equivalent) + LABA (>100 mg/d salmeterol or equivalent).

2. Severe asthma classification based on treatment in Steps 5 or 6 per the NAEPP 2007 guidelines.
Demonstrated Clinical Effectiveness at 1 Year\textsuperscript{1}

• Improved clinical outcomes compared to sham-control:
  
  – \textbf{32\%} decrease in severe exacerbations (PPS=95.5\%)
  
  – \textbf{84\%} reduction in emergency room (ER) visits for respiratory symptoms (PPS=99.9\%)
  
  – \textbf{66\%} less days lost from work, school and other daily activities due to asthma (PPS=99.3\%)

\textit{PPS = Posterior Probability of Superiority}

### AIR2 Respiratory Adverse Events

Selected AEs with >3% incidence and difference between groups

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Treatment Period (~12 weeks)</th>
<th>Post-Treatment Period (~46 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT (N=190) %</td>
<td>Sham (N=98) %</td>
</tr>
<tr>
<td>Asthma (Multiple Symptom)</td>
<td>52.1</td>
<td>38.8 *</td>
</tr>
<tr>
<td>Wheezing</td>
<td>15.3</td>
<td>6.1 *</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>4.7</td>
<td>0 *</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>3.2</td>
<td>0 *</td>
</tr>
<tr>
<td>Lower Respiratory Tract Infection</td>
<td>7.9</td>
<td>2.0 *</td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>20.0</td>
<td>11.2 *</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>4.7</td>
<td>7.1</td>
</tr>
<tr>
<td>Throat irritation</td>
<td>4.7*</td>
<td>12.2</td>
</tr>
</tbody>
</table>

*Posterior Probability of Superiority (PPS) >95.0%

High Patient Satisfaction with BT

- **97%** of BT patients would “probably” or “definitely” recommend BT to a friend or family member.¹

¹ Data on file. Reported at 1 year follow-up.
**AIR2 5-Year Extension Study**

**Objective:**
Durability of effect

**Primary Endpoint:**
% of patients with severe exacerbation* at Years 2, 3, 4 and 5 is non-inferior to (less than or equal to) Year 1

**Secondary Endpoints:**
Severe exacerbations, ER visits for respiratory symptoms, Lung function (Pre-BD FEV₁), Respiratory adverse events

Retention rate (from n=190) = 85.2%

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* Exacerbations requiring treatment with systemic corticosteroids or a doubling of ICS
**Reduction in Severe Exacerbations Maintained out to 5 years**

- The reduction in severe exacerbations requiring systemic corticosteroids at Year 1 was maintained out to at least 5 years.

Compared with 1 year prior to BT treatment (baseline):
- **44%** average decrease in percentage of patients having severe exacerbations
- **48%** average decrease in severe exacerbation event rates

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Reduction in ER Visits Maintained out to 5 years

- The reduction in ER visits for respiratory symptoms at Year 1 was maintained out to at least 5 years.

Compared with 1 year prior to BT treatment (baseline):
- **78%** average decrease in percentage of patients having ER visits
- **88%** average decrease in ER visit event rates

In the AIR2 Trial (Castro M, et al., 2010), the benefits of bronchial thermoplasty at one-year post-treatment, compared to a Sham group, included:

- **Improved** asthma-related quality of life
- **32%** reduction in severe exacerbations requiring systemic steroids
- **84%** reduction in emergency room visits due to respiratory symptoms
- **73%** reduction in hospitalizations due to respiratory symptoms
- **66%** reduction in days lost from work, school or other daily activities due to asthma symptoms
- **36%** reduction in proportion of patients reporting asthma (multiple symptoms) adverse events
Long-Term Safety Maintained out to 5 Years\textsuperscript{1}

- No increase seen in hospitalizations, asthma symptoms, or respiratory adverse events over the course of 5 years

- No structural changes in airways that were clinically significant were due to BT at 5 years (based on HRCT review)
  - No evidence of increase in bronchiectasis
  - No evidence of bronchiolitis obliterans or pulmonary emphysema in any patient

- Percent predicted pre-BD FEV\textsubscript{1} values remained unchanged over the 5 years after BT. Post-BD FEV\textsubscript{1} remained higher at all times; Increase in percent predicted FEV\textsubscript{1} at baseline of 8.2\% and at 5 years of 5.9\%

Established Long-Term Effectiveness and Safety out to 5 Years

- **Reduction in severe asthma exacerbations requiring systemic corticosteroids** seen at 1 year was maintained out to 5 years
- **Reduction in ER visits for respiratory symptoms** seen at 1 year was maintained out to 5 years
- **Long-term safety** maintained with no increase seen in hospitalizations, asthma symptoms, or respiratory adverse events over the course of 5 years

* or a doubling of ICS

Who Should Undergo Bronchial Thermoplasty?
Bronchial Thermoplasty 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 (ICS) and long-acting beta-agonists (LABA).

Reference the Alair Bronchial Thermoplasty System Directions for Use for more information.
How to Assess a BT Patient

- Confirmed diagnosis of severe asthma
- Evidence of adherence to ICS and LABA
- Demonstration of asthma impairments and/or risks of future exacerbations
  - Chronic oral corticosteroid use
  - Anti-IgE therapy candidate or non-responder
  - Two or more severe exacerbations in the prior year
  - Impaired quality of life (assessed by AIS-6, ACT, AQLQ)
- Higher level care or add-on treatment needed
- Exclusion of BT contraindications
Contraindications

BT 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/Need for Delay

BT 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
• Known bleeding disorder
• 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.
Precautions

Patients with these conditions were not studied in the AIR2 pivotal trial and the safety of Alair™ System treatment for such patients has not been determined.

- Post-bronchodilator FEV$_1$ < 65%

- **Other respiratory diseases** including emphysema, vocal cord dysfunction, mechanical upper airway obstruction, cystic fibrosis, or uncontrolled obstructive sleep apnea

- Use of short acting bronchodilator ≥12 puffs per day within 48 hours of bronchoscopy (excluding prophylactic use for exercise)

- Use of oral corticosteroids ≥10 mg/day for asthma

Reference the Alair™ Bronchial Thermoplasty System Directions for Use for more information.
Increased risk for adverse events associated with bronchoscopy or anesthesia, such as pregnancy, insulin dependent diabetes, epilepsy, or other significant co-morbidities, such as uncontrolled coronary artery disease, acute or chronic renal failure, and uncontrolled hypertension

Intubation for asthma, or ICU admission for asthma within the prior 24 months

Any of the following within the past 12 months:
  i. 4 or more lower respiratory tract infections (LRTI)
  ii. 3 or more hospitalizations for respiratory symptoms
  iii. 4 or more OCS pulses for asthma exacerbation
Precautions

• Any cause of dyspnea other than asthma should be controlled before performing Bronchial Thermoplasty
  – CHF
  – Obesity
  – OSA
  – Profound deconditioning
Who Responds to Bronchial Thermoplasty?

- The AIR2 Trial was performed on patients with severe asthma phenotype\(^\dagger\): 79% responder rate\(^1,2\)

- Patients with lower AQLQ or higher ACQ scores at baseline (implying poor asthma control) responded better to BT\(^3\)

- Clinical response to BT in self-reported allergic patients (54.5%) and non-allergic patients (45.5%) was similar\(^2\)

**Responder** = Asthma Quality of Life Questionnaire (AQLQ) score improvement > 0.5

\(^\dagger\) Severe asthma classification based on required treatment with high-dose ICS + LABA to maintain control (treatment in Steps 5 or 6 per the NAEPP 2007 guidelines).

How is Bronchial Thermoplasty Performed?
BT is performed by a BT-certified pulmonologist in 3 outpatient visits, typically scheduled 3 weeks apart.
The Alair™ System

- **Alair Catheter** – a flexible tube with an expandable wire array at the tip to deliver therapeutic RF energy to the airway walls via a standard bronchoscope.

- **Alair Radiofrequency (RF) Controller** – designed to safely and accurately deliver precise, controlled RF energy through the Catheter to the airway walls.
BT, Delivered by the Alair™ System
Application of RF Energy

- Temperature controlled energy (65° C) is delivered to airway wall for 10 seconds per activation
BT Treatment Effect – Airway Responsiveness to Local Methacholine Challenge

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

BT Reduces Excess Airway Smooth Muscle (ASM)

Procedure Overview

- Patient evaluated pre-procedure to verify stability and ability to undergo bronchoscopy
- Prophylactic OCS (50mg/day) administered for 5 days (3 days before, day of, and day after procedure)
- Routinely performed under moderate sedation
- RF energy delivered to airways between 3-10 mm diameter (~60 activations per procedure) and typically completed in less than an hour
- Patient monitored 2-4 hours post-op and discharged home same day
  - Lung function stable within 80% of pre-procedure post-BD FEV₁
Post-Procedure/Patient Follow Up

• Patient contacted via phone at 1, 2 and 7 days to assess post procedure status

• Office visit at 2 to 3 weeks to assess clinical stability and schedule subsequent BT procedures as appropriate

• After BT treatment, patient returns to primary asthma physician for ongoing asthma management

• Patient evaluated for step-down therapy to determine lowest level of medication necessary to maintain asthma control
BT Study Publications

AIR2


RISA


AIR


Reimbursement

• Proven to be difficult
• Different payers pay in different states
• Boston Scientific does have a reimbursement service to help with the process
• Frustrating as a Physician
Thank you!!

- A very special thank you to my support team from Boston Scientific headed by
  - Jared Altermatt

- Cyndi Ray MD, FCCP
  - cray2@hfhs.org
  - 313-916-2426
For more information and to find a BT Clinic:

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