Bronchial Thermoplasty

Translating Research Into Practice

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Agenda

• Asthma Overview
• Bronchial Thermoplasty with the Alair® System
• Clinical Data
• Patient Selection and Management
• Questions
Asthma Overview: Prevalence, Morbidity and Mortality

- **24.6 million** People diagnosed with asthma
- **12.8 million** People experience asthma attacks
- **1.8 million** Emergency room visits
- **456,000** Hospitalizations
- **3,447** Asthma-related deaths

Annual incidence, based on 2007 data

Approximately 9 People Die From Asthma Each Day in the U.S.

Stepwise Approach for Managing Asthma

1. Short-acting Beta2-agonists
2. Low-dose Inhaled Corticosteroids (ICS)
3. Low-dose ICS + Long-acting Beta2-agonists (LABA) or Medium-dose ICS
4. Medium-dose ICS + LABA
5. High-dose ICS + LABA and Consider Omalizumab
6. High-dose ICS + LABA + Oral Corticosteroids and Consider Omalizumab

Challenges in Managing Severe Asthma

- Prevalence of severe asthma (NAEPP) = 5-10%
- Many patients remain symptomatic despite standard of care medications
- Medications are limited, require adherence, and can have serious side effects
- High economic costs and resource utilization associated with medications, hospitalizations, physician visits and lost days of work/school ~ $20.7B
- **Additional therapeutic treatment options are needed**...
Role of Airway Smooth Muscle on Asthma

Normal Airway

Asthma Attack
Bronchial Thermoplasty – ASM Treatment Approach

Reduces Airway Smooth Muscle (ASM)

Reduces Bronchoconstriction

Reduces Asthma Exacerbations

Improves Asthma Quality of Life
What is Bronchial Thermoplasty?

• A procedure that delivers thermal energy to the airways via a bronchoscope to reduce excess airway smooth muscle and limit its ability to constrict the airways

• Outpatient hospital procedure performed over 3 treatment sessions, routinely under moderate sedation, by a trained pulmonologist

• Complementary treatment, and not a replacement, to current asthma reliever and controller medications

• A treatment option shown to increase the level of asthma control and improve quality of life in patients with severe asthma
The Alair® Bronchial Thermoplasty System

- **Alair Catheter** – a flexible tube with an expandable wire array at the tip (introduced into the lungs through a standard bronchoscope)

- **Alair Radiofrequency (RF) Controller** – supplies energy via the Catheter to heat the airway wall
Reduced Airway Smooth Muscle

• 3 years post-treatment (canine model)

UNTREATED

TREATED

Masson’s Trichrome stain
Clinical Outcomes: Bronchial Thermoplasty

- **Over 800** Procedures Performed
- **3** Randomized Controlled Studies
- **Over 10** Publications

**Pivotal Study**
AIR2: n=190 treated patients at 30 sites

(Castro, AJRCCM, 2010) 
(Castro, AAAI, 2011)

**Feasibility Study**
AIR: n=55

(Cox, NEJM, 2007)
(Cox, AJRCCM, 2006)

**RISA**
RISA: n=15

(Cavord, AJRCCM, 2007)
Demonstration of Effectiveness

<table>
<thead>
<tr>
<th>AIR2 (RCT; n = 288)</th>
<th>AIR (RCT; n = 109)</th>
<th>RISA (RCT; n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AQLQ</td>
<td>AQLQ</td>
<td>AQLQ</td>
</tr>
<tr>
<td>Exacerbations</td>
<td>Exacerbations</td>
<td>ACQ</td>
</tr>
<tr>
<td>ER visits</td>
<td>Rescue meds</td>
<td>Rescue meds</td>
</tr>
<tr>
<td>Days missed work/school</td>
<td>Symptom Free Days</td>
<td>Oral Steroids (p = 0.12)</td>
</tr>
</tbody>
</table>


All of the above were shown to be significant (p < 0.05), except where noted.
• **Purpose:** Pivotal US Investigational Device Exemption (IDE) Study
  • Support indication for use in severe asthma

• **Study Population:**
  • Severe persistent asthma
  • Symptomatic despite high dose ICS + LABA

• **Primary Endpoint:** Asthma Quality of Life Questionnaire (AQLQ) score
**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
Bronchial Thermoplasty Clinical Outcomes Summary at 1-Year

- Improved asthma-related quality of life compared to control (AQLQ score)
  - 79% of BT treated patients achieved ≥ 0.5 increase
  - Effect persistent across 6, 9, and 12 months

- Improved clinical outcomes compared to 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

Health Care Utilization for Respiratory Symptoms During Post-Treatment Period

- 6 weeks after the last bronchoscopy procedure to 12 month follow-up

* Posterior Probability of Superiority = 95.6%
** Posterior Probability of Superiority = 99.9%

- Severe Exacerbations (Steroid): 32% decrease over Sham
- Unscheduled Physician Office Visits: 22% decrease over Sham
- Emergency Room Visits: 84% decrease over Sham
- Hospitalizations: 73% decrease over Sham

BT = Bronchial Thermoplasty

Effectiveness of BT persist out to at least two years – proportion of patients experiencing severe exacerbations comparable between years 1 and 2.

### Proportion of Subjects Reporting Severe Exacerbations and Healthcare Resource Utilization

<table>
<thead>
<tr>
<th></th>
<th>Percent of Subjects (Number of Subjects)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Year Prior to Study Entry(^{a})</td>
</tr>
<tr>
<td><strong>Severe Exacerbations</strong></td>
<td>53.4 (154)</td>
</tr>
<tr>
<td><strong>ED Visits</strong></td>
<td>29.8 (86)</td>
</tr>
<tr>
<td><strong>Hospitalizations</strong></td>
<td>4.9 (14)</td>
</tr>
</tbody>
</table>

\(^{a}\): Includes all patient subjects (BT + Sham) prior to study entry

\(^{b}\): Year 2 BT comparison to Year 1 BT is not significant by Fisher’s Exact Test
• 850 bronchoscopies performed in patients with severe asthma (558 BT and 292 Sham procedures)

• No device-related deaths or major adverse events
  • e.g., Pneumothorax, mechanical ventilation, airway stenosis or focal narrowing

• More respiratory adverse events were reported in the BT group in the short-term after the procedure
  • Typically occurring within one day and resolving within one week with standard care

• Fewer respiratory adverse events, hospitalizations and ER visits in the BT group during post-treatment period\textsuperscript{a}

\textsuperscript{a} 6 weeks after the last bronchoscopy procedure to 12 month follow-up.

BT = Bronchial Thermoplasty

### Risk of Respiratory-Related Hospitalization Following Procedure

<table>
<thead>
<tr>
<th>Respiratory-Related Hospitalizations during Treatment Period&lt;sup&gt;a&lt;/sup&gt;</th>
<th>BT (N=190)</th>
<th>Sham (N=98)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events / Subject (%)</td>
<td>19/190 (10%)*</td>
<td>2/98 (2.0%)</td>
</tr>
<tr>
<td>Events / Bronchoscopy (%)</td>
<td>19/558 (3.4%)</td>
<td>2/292 (0.7%)</td>
</tr>
</tbody>
</table>

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

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

BT = Bronchial Thermoplasty

Respiratory Symptoms Resulting in Hospitalization

<table>
<thead>
<tr>
<th>BT</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=190)</td>
<td>(N=98)</td>
</tr>
<tr>
<td>19 Hospitalizations in 16 Subjects</td>
<td>2 Hospitalizations in 2 Subjects</td>
</tr>
<tr>
<td>No. of Events (Incident Rate %)</td>
<td>No. of Events (Incident Rate %)</td>
</tr>
<tr>
<td>Asthma Aggravated</td>
<td>Asthma Aggravated</td>
</tr>
<tr>
<td>12 (6.3%)</td>
<td>2 (2.0%)</td>
</tr>
<tr>
<td>Atelectasis</td>
<td></td>
</tr>
<tr>
<td>3 (1.6%)</td>
<td></td>
</tr>
<tr>
<td>Lower Resp. Tract Infection</td>
<td></td>
</tr>
<tr>
<td>1 (0.5%)</td>
<td></td>
</tr>
<tr>
<td>Hemoptysis</td>
<td></td>
</tr>
<tr>
<td>1 (0.5%)</td>
<td></td>
</tr>
<tr>
<td>Low FEV₁</td>
<td></td>
</tr>
<tr>
<td>1 (0.5%)</td>
<td></td>
</tr>
<tr>
<td>Aspirated Prosthetic Tooth in Airway</td>
<td></td>
</tr>
<tr>
<td>1 (0.5%)</td>
<td></td>
</tr>
</tbody>
</table>

BT = Bronchial Thermoplasty

Long-Term Safety Profile

- **Safety data at two years**: 
  - No deaths in the BT group
  - Absence of clinical complications based on AE reporting
  - Stable pulmonary function: pre- and post-bronchodilator FEV$_1$ remained stable between year 1 and year 2 following BT

- **CT scans at 1 year resulted in no clinically significant findings or structural changes**

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BT = Bronchial Thermoplasty
Long-Term Safety

- 5 year follow-up in Feasibility, AIR and RISA trials:
  - Stable pulmonary function
  - No clinical complications based on AE reporting
- Annual CT scans for 5 years (Feasibility Study):
  - All patients doing well
  - No clinically significant findings
- Alair treatment has excellent safety profile long-term

Data presented at ATS Annual Meeting, Denver, May 2011
Patient Selection and Management
Who is Appropriate for Bronchial Thermoplasty?

- **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-agonists.

- Adult severe, persistent asthmatics (≥ 18 years old)

- Inadequate control despite combination of inhaled high dose corticosteroids (ICS) and a long-acting beta-agonists (LABA)

- Able to safely undergo bronchoscopy per hospital guidelines

Reference the Alair Bronchial Thermoplasty System Instructions for Use for more information.
Who is Not Appropriate for Bronchial Thermoplasty?

Contraindications:

- 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 Instructions for Use for more information.
When Should Bronchial Thermoplasty be Delayed?

Precautions:

• 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 Instructions for Use for more information.
Three Treatment Sessions

Bronchial thermoplasty is performed in 3 separate treatment sessions each scheduled approximately 3 weeks apart.
Procedure Overview

• Patient evaluated 1 week prior to procedure to verify ability to undergo bronchoscopy
• Prophylactic OCS initiated 3 days prior, day of and day after procedure
• Lung function evaluated morning of procedure to assess stability
• Local anesthesia administered – lidocane and albuterol nebulizer
• Patient placed under moderate sedation
• BT catheter introduced through flexible bronchoscope and RF energy applied to airways (approx. 60 activations per procedure)
• Each procedure completed within 40-60 minutes

BT = Bronchial Thermoplasty
Post-Procedure/Patient Follow Up

- Patient monitored for 2-4 hours post-op
- Patient discharged from hospital same day:
  - Lung function stable within 80% of pre-procedure post BD FEV1
  - Patient stable, able to take liquids, feeling well, adequate mental status
  - Prophylactic OCS continued 1 day after procedure
- 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
- Individual patient results are communicated to referring physician as appropriate
- Patient returns to care of primary asthma physician for long term asthma management following BT

BT = Bronchial Thermoplasty
Patient Experience

- 46 year old female
  - Severe asthma, Advair 500/50 bid
  - Daily need of albuterol
  - Exacerbations 3 to 4 times a year requiring steroids
  - Hospitalizations asthma/pneumonia
  - Atopy: cat, dogs, trees  IGE 115
  - OSA
  - Chronic sinusitis
  - Sjogren’s Syndrome
  - FEV1 2.30 (69%) FVC 3.30 (79%) ratio (0.69)
  - ACT = 10 to 15
5 years later

- No hospitalizations/ER visits since BT
- No severe exacerbations of asthma requiring steroids since completing BT
- ACT 24
- Spirometry: no obstruction
- Chest CT: stable, no bronchiectasis
- ENO = 19
- Advair now at 250/50 1 puff twice per day
Questions?