Bronchial Thermoplasty for Severe Asthma

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Abstract

Bronchial thermoplasty (BT) is a new therapeutic modality for the treatment of severe asthmatics refractory to optimal medical therapy. Individuals with uncontrolled symptoms despite treatment with high dose inhaled corticosteroids and long-acting bronchilator therapy are eligible for this procedure. BT uses radiofrequency energy to reduce the excess airway smooth muscles that can occur in asthma. Since airway smooth muscle is implicated in hyperreactivity and bronchoconstriction, BT can be adjunctive to anti-inflammatory therapy. Thermal treatment is delivered distal to mainstem bronchi to visible airways between 3 and 10 mm in diameter, excluding the right middle lobe. Treatments occur in three separate sessions with careful monitoring before and after the procedure, as the most frequent complication is exacerbation of asthma symptoms. Clinical trials have demonstrated an acceptable safety profile while improving asthma quality of life scores, symptoms, and health care utilization, resulting in FDA approval of this procedure in 2010. More recent evidence demonstrates persistence of beneficial effects up to 2 years after the procedure. Proper patient selection, optimization of confounding conditions, and ongoing asthma management are key factors in improving outcomes and minimizing adverse respiratory events. As experience with the procedure increases, better characterization of asthmatics that may benefit from this procedure will become available.

Keywords

Severe asthma • Refractory asthma • Bronchial thermoplasty • Radiofrequency ablation

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Introduction

Bronchial thermoplasty (BT) is a novel non-pharmacologic therapy for patients with severe persistent asthma who remain uncontrolled despite maximal medical therapy. Approved for use in severe asthma by the Food and Drug Administration (FDA) in 2010, BT uses radiofrequency energy in a controlled manner to provide thermal treatment to smooth muscle in visible conducting airways [1, 2]. The entire treatment is performed over 3 sessions each separated by at least 3 weeks, and is usually an outpatient procedure. Treatments occur by introducing a catheter through the channel of a flexible bronchoscope to apply thermal energy to visible airways between 3 and 10 mm in diameter. Treatments are delivered sequentially in a distal to proximal fashion. Initially the right lower lobe is treated, then the left lower lobe, and lastly bilateral upper lobes. The right middle lobe is not treated due to potential for development of atelectasis and right middle lobe syndrome. Clinical trials of feasibility and efficacy demonstrated that in appropriately selected severe asthmatics not well controlled with currently available medical therapies, bronchial thermoplasty is safe and has a positive impact on the clinical metrics of asthma including symptoms, quality of life, and healthcare utilization. The most common adverse events are respiratory complications, such as an exacerbation of asthma [2–5]. Proper patient selection and optimization of asthma management are important for the success of this procedure. The procedure is most suitable for those individuals who remain symptomatic despite maximal medical therapy but well enough to tolerate it. In this chapter, we discuss the scientific basis, clinical applications, procedure, and complications associated with this emerging technology.

Scientific Basis: Asthma Pathophysiology and Potential Mechanisms of Therapeutic Effect

Asthma is associated with chronic airway inflammation, increased airway reactivity and airflow obstruction. Various cells play a role in pathogenesis of asthma, including eosinophils, mast cells, T lymphocytes, macrophages, neutrophils, and epithelial cells [6]. Episodic shortness of breath and symptoms of bronchoconstriction are common and can be a result of mediators such as histamine, leukotrienes, and prostaglandins from allergic or nonallergic triggers. Persistent inflammation can result in airway wall remodeling causing thickening of basement membrane due to deposition of collagen, goblet cell hyperplasia with excess mucus secretion, blood vessel proliferation, and smooth muscle hypertrophy [6, 7]. These changes can lead to irreversible narrowing of the airways with persistent symptoms of airflow obstruction that may be difficult to manage, even with the best available medical therapies [6]. In patients with chronic and refractory asthma, there is excessive hyperplasia and hypertrophy of airway smooth muscles that can predispose to abnormal bronchoconstriction and airway closure in some instances. Although airway sensitivity and hyperresponsiveness can be temporarily reversed with bronchodilator and anti-inflammatory therapies, prevention of progressive airway remodeling and smooth muscle hypertrophy can be challenging. Bronchial thermoplasty targets this potential gap in asthma treatment.

The role of airway smooth muscle in asthma is not fully elucidated. Early investigations into the mechanisms of airflow obstruction and airway resistance have demonstrated that 75 % of postnasal airflow resistance occurs in the first 6–8 generations of airways, indicating that larger airways are involved [8]. In normal airways, smooth muscle has a role in providing structural support, distribution of ventilation, propulsion of mucus for clearance, cough mechanism, and in promotion of lymphatic flow. In asthma, however, airway smooth muscle is involved in bronchoconstriction and in promoting bronchial hyperresponsiveness through signaling of inflammatory mediators. Furthermore, airway smooth muscle mediates airway inflammation and remodeling through cytokine synthesis and mast cell infiltration [9–11]. Its putative nonessential role has led some to dub airway smooth muscle as “the appendix of the lung” [12]. There are no studies to demonstrate that elimination of

these physiological roles of airway smooth muscle greatly inhibit the normal airway function, but there is evidence to suggest that abnormal airway smooth muscle mass contributes to asthma severity. Therefore, hypertrophied airway smooth muscle is an appropriate target for intervention in severe persistent asthma [13].

Clinical Applications: Severe Refractory Asthma and Candidates for Bronchial Thermoplasty

Asthma is a chronic inflammatory condition of the airways characterized by episodic symptoms of breathlessness, cough, and wheezing. Asthma is common, affecting approximately 8% of the population [6]. Regardless of severity at presentation, most patients with asthma are able to gain control of their symptoms with anti-inflammatory therapy, behavioral changes, and trigger management. Since the publications of National Asthma Education and Prevention Program (NAEPP) clinical practice guidelines in 1991, 1997 and 2002, there have been significant gains in the understanding of asthma pathophysiology and treatment [14–16]. The latest guidelines published in 2007 emphasize the importance of categorizing asthma severity. However assessing asthma control which involves evaluation of impairment (symptoms and limitations) and risk (exacerbations) is equally important. Severe asthma is present in about 10 % of all asthma patients and these patients experience frequent symptoms and exhibit disease-related morbidity. Patients with severe asthma also disproportionately utilize heath care resources due to frequent exacerbations, emergency room visits and hospital admissions. The burden of hospitalizations for asthma remains high, with more than 456,000 hospitalizations and 14 million missed days of work annually according to some estimates [6, 17].

In most cases, individuals with asthma are able to control their symptoms with proper adherence to anti-inflammatory therapies and avoidance of triggers. However, a subset of this population has severe asthma that becomes difficult to control despite all medical therapies available. To address the challenges in identification and management of these patients with severe and refractory asthma, the American Thoracic Society (ATS) hosted a workshop to characterize this condition (Fig. 10.1) [18]. Individuals with severe refractory asthma were defined as those who are adherent to and require treatment with continuous or near continuous (>50 % of year) oral corticosteroids or high-dose inhaled corticosteroids to control asthma symptoms. In addition, two minor criteria are needed that include persistent airway obstruction and peak expiratory flow (PEF) variability, additional daily controller medication, deterioration with reduction in inhaled/oral steroid dose, ≥3 oral steroid bursts/year, urgent care visits for asthma, or near-fatal asthma event in the past [19]. These severe asthmatics may be good candidates for bronchial thermoplasty.

Clinical Trials: Development and Evaluation of Bronchial Thermoplasty for Asthma

Radiofrequency ablation therapy has been used in a variety of medical conditions such as lung cancer and cardiac arrhythmias [20, 21]. The use of this technology to treat airway smooth muscle was initially evaluated in animal studies which showed feasibility of using radiofrequency energy to decrease airway smooth muscle mass [1]. Subsequently, clinical studies and trials in non-asthmatics, mild to moderate asthmatics, and finally moderate to severe refractory asthmatics were performed to help identify appropriate candidates, adverse events, and expected outcomes [2–5].

Early animal studies in dogs demonstrated that applying thermal energy to the airways at 65 and 75 °C attenuated methacholine responsiveness for up to 3 years after the treatment [1]. Altered airway smooth muscle, defined as degenerating or absent muscle, were seen as early as 1 week after treatments, and these changes were inversely proportional to the airway hyper-responsiveness. The post-procedure adverse effect in these animals were cough, inflammatory edema of the

REFRACTORY ASTHMA: WORKSHOP CONSENSUS FOR TYPICAL CLINICAL FEATURES*,†

Major Characteristics

In order to achieve control to a level of mild–moderate persistent asthma:

1. Treatment with continuous or near continuous (⩾ 50% of year) oral corticosteroids
2. Requirement for treatment with high-dose inhaled corticosteroids:

Drug	Dose (*μg/d*)	Dose (*puffs/d*)
a. Beclomethasone dipropionate	> 1,260	> 40 puffs (42 μg/inhalation > 20 puffs (84 μg/inhalation
b. Budesonide	> 1,200	> 6 puffs
c. Flunisolide	> 2,000	> 8 puffs
d. Fluticasone propionate	> 880	> 8 puffs (110 μg), > 4 puffs (220 μg)
e. Triamcinolone acetonide	> 2,000	> 20 puffs

Minor Characteristics

1. Requirement for daily treatment with a controller medication in addition to inhaled corticosteroids, e.g., long-acting β-agonist, theophylline, or leukotriene antagonist
2. Asthma symptoms requiring short-acting β-agonist use on a daily or near daily basis
3. Persistent airway obstruction (FEV_1 < 80% predicted; diurnal PEF variability > 20%)
4. One or more urgent care visits for asthma per year
5. Three or more oral steroid "bursts" per year
6. Prompt deterioration with ⩽ 25% reduction in oral or inhaled corticosteroid dose
7. Near fatal asthma event in the past

* Requires that other conditions have been excluded, exacerbating factors treated, and patient felt to be generally adherent.
† Definition of refractory asthma requires one or both major criteria and two minor criteria.

Fig. 10.1 The American Thoracic Society consensus definition of severe and refractory asthma. (Reprinted with permission of the American Thoracic Society. Copyright © 2012 American Thoracic Society. Proceedings of the ATS workshop on refractory asthma: current understanding, recommendations, and unanswered questions. American Thoracic Society. Am J Respir Crit Care Med. Dec 2000;162(6):2341–2351. Official journal of the American Thoracic Society)

airway wall, retained mucus, and blanching of airway wall at site of catheter contact. Over 3 years of this study, there was no evidence of a regenerative muscle response.

A pilot study was subsequently performed in individuals scheduled for resections for lung cancer [2]. Eight individuals (mean age 58 ± 8.3 years) underwent thermoplasty treatments to visible airways 1 cm from known tumor area and within areas to be resected. Thermoplasty with 55 and 65 °C was performed at 3–9 treatment sites in each patient 5–20 days prior to planned lung resection. At the time of resection, bronchoscopy was generally unremarkable, except for some airway narrowing or linear blanching. Histological review of the resected airways showed an average of 50 % reduction in smooth muscle mass in the airways treated at 65 °C as compared to the untreated airways. There were no significant adverse events such as hemoptysis, respiratory infections or excessive bronchial irritation.

The first prospective observational study of bronchial thermoplasty in asthmatics was performed in 16 individuals with mild to moderate disease [22]. All patients were treated with 30–50 mg prednisone the day prior and day of the procedure. Three bronchial thermoplasty treatments were spaced 3 weeks apart, and the right middle lobe was spared. Pre-bronchodilator FEV_1 improved at 12 week and 1 year but showed no significant change from baseline to 2 years post bronchial thermpoplasty. Symptom-free days increased between baseline and 12 weeks after treatment (50–73 %, $p = 0.015$) and a significant decrease in airway hyper-responsiveness as measured by methacholine was observed over the next 2 years. The most frequent side effects were cough, dyspnea, wheezing, and bronchospasm, which developed within 2–5 days after the procedure, though not severe enough for hospitalization. Chest computed tomography performed 1 and 2 years after the treatment showed no changes in parenchyma or bronchial wall structure. This

pilot study demonstrated the safety and feasibility of using this technology in mild to moderate asthma.

The first large multicenter trial of bronchial thermoplasty (Asthma Intervention Research [AIR] trial) was a prospective randomized non-blinded study in moderate to severe asthmatics treated with inhaled corticosteroids (ICS) and long-acting B-agonists (LABA) [3]. Asthmatics requiring 200 μg or more of beclomethasone-equivalent ICS dose who demonstrated respiratory impairment with LABA withdrawal were randomized to receive either BT with ICS and LABA or usual care with ICS and LABA alone. One hundred twelve patients between the ages of 18 and 65 years with percent predicted FEV_1 of 60–85 %, and airway hyper-responsiveness as demonstrated by a concentration of methacholine to decrease FEV1 by 20 % (PC_{20}) of <8 mg/ml and stable asthma for 6 weeks prior to enrollment were recruited for the study. Treatments occurred in 3 sessions over 9 weeks, followed by attempts to discontinue LABA at 3, 6, and 9 months post-procedure. With BT treatment, the number of mild exacerbations and rescue medication use were significantly lower at 3 and 12 months, and changes in morning peak flow at 3, 6, and 12 months were improved from baseline in the treatment group. Symptom free days as well as asthma quality of life scores, assessed using Asthma Quality of Life Questionnaire (AQLQ) and Asthma Control Questionnaire (ACQ), also showed a significant improvement compared to the baseline. However, the study group also experienced more respiratory adverse events around the time of thermoplasty than patients in the control group. There were also more hospitalizations in the treatment group, including for asthma exacerbations, lower lobe atelectasis, and pleurisy [3]. Further, no significant change in FEV1 or methacholine reactivity was noted in BT group. Therefore, although the AIR trial demonstrated improvement in asthma symptoms and incidence of mild exacerbations, the non-blinded study design and the presence of a strong placebo effect in asthma highlighted a need for a randomized trial with a sham treatment arm [3].

To evaluate the safety and efficacy of bronchial thermoplasty in more severe asthmatics, Pavord and associates performed the Research in Severe Asthma (RISA) trial [4]. In this study, asthmatics on high dose inhaled steroids (>750 μg fluticasone-equivalent/day), on prednisone ≤30 mg/day, pre-bronchodilator FEV_1 percent predicted of ≥50 % and positive methacholine tests were randomized to receive either a bronchial thermoplasty ($n=17$) or medical management ($n=17$). For 16 weeks after the completion of bronchial thermoplasty, inhaled and oral steroid doses were not changed, after which a protocol driven 14-week corticosteroid wean phase was initiated (20–25 % reduction every 2–4 weeks). Adverse effects included seven hospitalizations for worsening asthma control (4 patients), lobar collapse (2 patients). After the short term increase in asthma-related morbidity in the immediate posttreatment period, there was significant reduction in rescue inhaler use, improvement in pre-bronchodilator FEV_1, as well as improved AQLQ and ACQ scores during the steroid stable phase in the BT group. Up to 1 year after treatment, there was continued decrease in rescue medication use and improvement in AQLQ/ACQ scores. Although the potential for placebo effect in asthma treatments exist, those who received treatment did have improvement in asthma [4].

The clinical trial that followed the AIR study (the AIR2 trial) addressed the placebo effect [5]. In this study, a subset of participants were randomized to a sham control arm in which bronchoscopy was performed, but no radiofrequency treatment was administered. All patients as well the investigators, except for the operators performing the bronchoscopy, were blinded to study allocation allowing it to be a true randomized double-blind clinical trial with sham controls. The primary outcome was to evaluate the changes in AQLQ scores from baseline to 6, 9, and 12 months in the treatment vs. sham group. Secondary outcomes included absolute changes in the asthma control scores, symptom scores, peak flows, rescue medication use, and FEV_1. There were 196 participants in BT group and 101 participants in the sham control group. The baseline characteristics were similar in both groups.

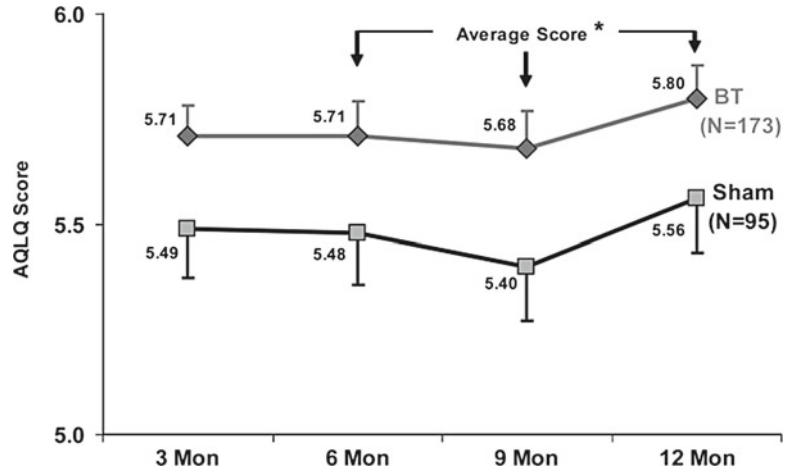

Fig. 10.2 Change in asthma quality of life by treatment group. Change in asthma quality of life questionnaire (AQLQ) score over 12 months after treatment with bronchial thermoplasty (BT) (*diamonds*) or sham control (*squares*) in the per protocol population. *Posterior probability of superiority = 97.9 % (reprinted with permission of the American Thoracic Society. Copyright © 2012 American Thoracic Society. Castro M, Rubin AS, Laviolette M, et al. Effectiveness and safety of bronchial thermoplasty in the treatment of severe asthma: a multicenter, randomized, double-blind, sham-controlled clinical trial. Am J Respir Crit Care Med. Jan 15 2010;181(2):116–124. Official Journal of the American Thoracic Society)

More than 80% participants in each arm met ATS criteria for severe refractory asthma [19]. However, patients with a history of three or more hospitalizations for asthma exacerbation, three or more lower respiratory tract infections, and four or more pulse steroid doses over the preceding year were excluded from the study. Results showed a statistically significant increase in AQLQ from baseline to the average of 6, 9, and 12 months in the BT vs. sham group (Fig. 10.2). Though, difference in the improvement in AQLQ score between two groups was lower than clinically meaningful change of 0.5 or greater. The BT group experienced reduction in severe exacerbations as compared with the sham group (0.48 vs. 0.70 exacerbations/subject/year, posterior probability of superiority of 96 %). Patients treated also had 84% risk reduction in Emergency Department (ED) visits (Fig. 10.3). Adverse events occurred in both groups; however, during the treatment phase, 16 patients in BT group needed hospitalizations for respiratory symptoms including worsening asthma, atelectasis, lower respiratory tract infections, decreased FEV_1, and an aspirated tooth. One episode of hemoptysis required bronchial artery embolization. In contrast, only 2 in the sham group needed hospitalization. Interestingly, there was a significant and clinically meaningful improvement in AQLQ in 64 % of the sham group, highlighting the relative importance of placebo effect in asthma populations [23]. However, a larger proportion (79 %) of BT treated group had a clinically meaningful improvement in AQLQ (>0.5 change) than in the sham group. Therefore, this large multicenter randomized blinded sham-controlled study demonstrated long-term improved asthma quality of life and decreased healthcare utilization in patients with severe asthma treated with bronchial thermoplasty [5]. These benefits, however, were achieved at the cost of significantly higher incidence of early complications in the BT group.

FDA Clearance and Long-Term Follow-Up

The FDA approved the Alair® system (Boston Scientific, MA) in 2010 for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with

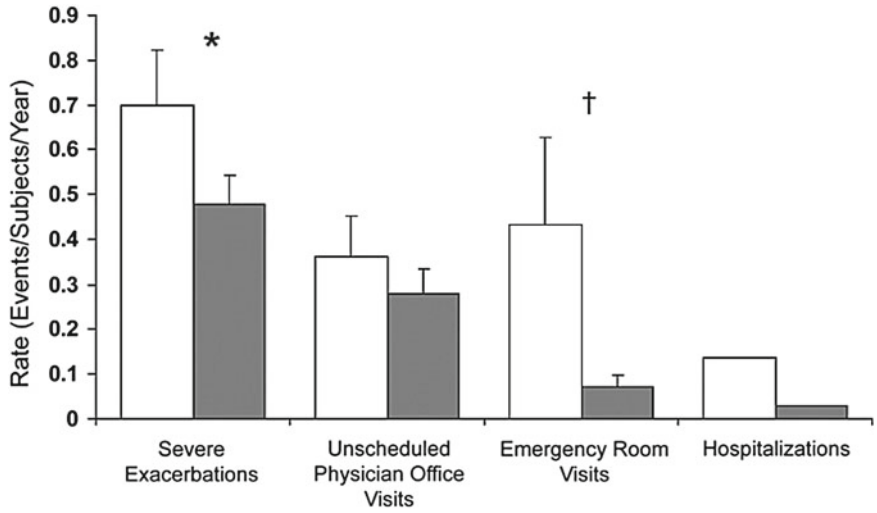

Fig. 10.3 Healthcare utilization events during the posttreatment period. Severe exacerbations (exacerbation requiring treatment with systemic corticosteroids or doubling of the inhaled corticosteroids dose), emergency department visits, and hospitalizations occurring in the posttreatment period. *Open bars*, sham; *shaded bars*, bronchial thermoplasty. All values are means ± SEM. *Posterior probability of superiority = 95.5 %. †Posterior probability of superiority = 99.9 % (reprinted with permission of the American Thoracic Society. Copyright © 2012 American Thoracic Society. Castro M, Rubin AS, Laviolette M, et al. Effectiveness and safety of bronchial thermoplasty in the treatment of severe asthma: a multicenter, randomized, double-blind, sham-controlled clinical trial. Am J Respir Crit Care Med. Jan 15 2010;181(2):116–124. Official Journal of the American Thoracic Society)

inhaled corticosteroids and long-acting beta agonists [24]. Patient selection at most institutions is based on the study populations described in the published trials. Individuals who have well-documented severe persistent asthma not well controlled on ICS and LABA can be considered for bronchial thermoplasty. As part of the final conditions of approval, the FDA has required a post approval study based on the long-term follow-up of the AIR2 trial. There is a specific need to identify the features that predict higher likelihood of desirable long-term outcomes after BT as compared to those who do not achieve any meaningful benefits from it. A 2-year follow-up study from AIR2 demonstrated that individuals who received BT continued to have sustained benefit 2 years after the procedure with persistence of lower exacerbation rates, asthma adverse events, emergency department visits, and hospitalizations. Unfortunately this could not be compared with the sham arm as patients in this group were not followed beyond 1 year post bronchial thermoplasty. Furthermore, asthma quality of life information was not collected [25]. A second post approval study will be a prospective, open label, single arm, multicenter study conducted in the USA to assess the treatment effect and short-term and long-term safety profile.

Procedural Aspects: Bronchial Thermoplasty Instruments and Protocols

Bronchial thermoplasty is performed with a Alair® system (Boston Scientific, MA) which is designed to deliver a specific amount of radiofrequency (thermal) energy through a dedicated catheter (Fig. 10.4) [26]. The catheter is deployed through a 2.0 mm working channel of an adult or pediatric sized flexible bronchoscope. Under direct vision, the electrode array is deployed treating distal airways measuring as small as 3 mm in diameter and working proximally to

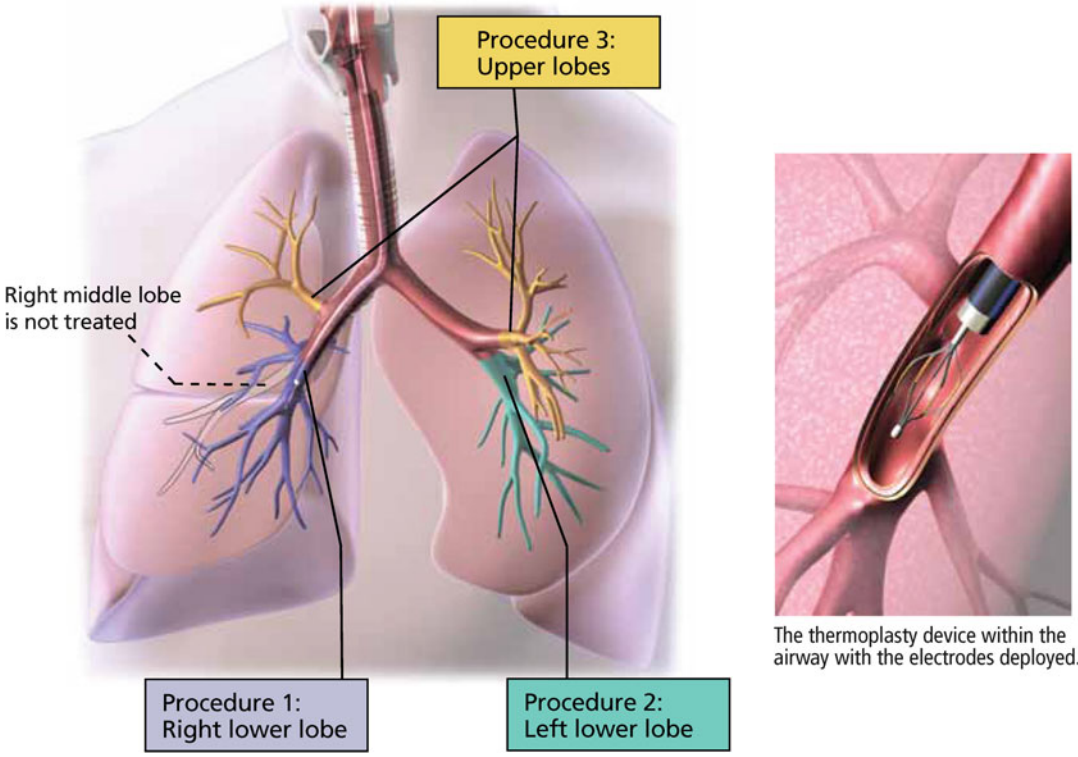

Fig. 10.4 Bronchial thermoplasty involves delivery of radiofrequency energy to the airway wall, which ablates the smooth muscle layer, lessening bronchoconstriction and improving symptoms. Treatments are done in three separate procedures, with meticulous mapping of the areas treated. The right lower lobe is treated in the first procedure, the left lower lobe in the second, and the two upper lobes in the third. The right middle lobe is not treated (from: Gildea TR, Khatri SB, Castro M. Bronchial thermoplasty: A new treatment for severe refractory asthma. Cleve Clin J Med 2011; 78:477–485. Reprinted with permission. Copyright © 2011 Cleveland Clinic Foundation. All rights reserved)

sequentially treat all airways to the lobar bronchi. The electrode array is manually expanded to make contact with the airway walls and has a 5 mm treatment area of exposed electrodes on each of the four struts. As the energy is delivered via the electrodes, the control unit measures electrical resistance converted to thermal energy and will stop when an appropriate dosage is given. This thermal energy is what is responsible for altering the airway smooth muscle.

A thorough patient evaluation is essential prior to the procedure. Important aspects of pre and post-procedure care are summarized in Table 10.1. Potential candidates for bronchial thermoplasty are those with the following: (1) a confirmed diagnosis of asthma which is established to be refractory to current maximal medical therapy, (2) a current nonsmoking status (for at least 1 year), (3) no significant contraindications to bronchoscopy and radiofrequency ablation, (4) ability to temporarily suspend anticoagulation therapy, and (5) control of confounding conditions such as gastroesophageal reflux disease, sinus disease, obstructive sleep apnea, and vocal cord dysfunction. Patients with pacemakers or defibrillators are not eligible, and women of childbearing age need to undergo pregnancy test prior to the procedure.

To minimize the development of airway inflammation, patients should receive prophylactic prednisone at a dose of 50 mg per day 3 days before, on the day of and 1 day after the procedure. The procedure should be delayed if there has been an asthma exacerbation within past

Table 10.1 Overview of care of patients undergoing bronchial thermoplasty treatment

Patient selection
• Confirmed diagnosis of asthma
• Asthma refractory to maximal medical therapy
• Pre-bronchodilator FEV1 > 60 %
• Control of confounding conditions such as gastroesophageal reflux disease, obstructive sleep apnea, sinus disease
• No significant coronary artery disease or arrhythmias
• Ability to tolerate cessation of anticoagulation therapy
• Nonsmoker for 1 year or more
• No pacemaker or defibrillator
• Ability to undergo bronchoscopy
Pre-procedure measures
• Maximize asthma treatment
• Oral prednisone 50 mg/day starting 3 days prior to procedure, and day of procedure
• Rule out pregnancy. Perform pregnancy test in childbearing age group
• Administer nebulized albuterol before bronchoscopy
Delay treatment if
• Uncontrolled bronchospasm
• SpO_2 < 90 % on room air
• Any recent exacerbation within last 6 weeks requiring increase in dose of steroids
• Previously treated airways showing persistence of airway inflammation and erythema, or infection
• Upper respiratory infection within past 2 weeks
• Lower respiratory tract infection within past 6 weeks
During procedure
• Place grounding pad
• Keep FiO_2 less than 40 %
• Have at least two catheters available
• Control cough during bronchoscopy
Post-procedure care
• Observe for 3–4 h in recovery room
• Discharge if patient is stable and the post-procedure FEV1 is within 80 % of pre-procedure value
• Take 50 mg of prednisone on day after the procedure
• Contact patient via phone call in 24–48 h
• Office visits at 2–3 weeks to assess response and schedule subsequent BT session

6 weeks that required systemic steroids, a history of lower respiratory tract infection within the last 6 weeks, or an upper respiratory infection in the last 1–2 weeks. Individuals should be assessed prior to and on the day of the procedure to ensure asthma stability. Nebulized albuterol (2.5–5.0 mg) is given prior to the procedure and screening spirometry is performed to ensure stable pulmonary functions. Patients should be within 10–15 % of their baseline FEV_1 on the day of procedure. A full course of treatment requires three separate bronchoscopic sessions at 2–3-week intervals. Most commonly, right lower lobe is treated in the first session, followed by left lower lobe in second session, and finally both upper lobes in the third session (Fig. 10.5). The treatments are performed via a standard sized flexible bronchoscope with a minimum 2 mm working channel. Moderate sedation (e.g., fentanyl, midazolam, and topical lidocaine) is typically used; however, in certain instances of protracted coughing or difficulty obtaining adequate level of comfort, deeper sedation via general anesthesia can be used. Important safety elements of the procedure include maintaining oxygen at or less than 40 % FiO_2 and placing the appropriate gel grounding pad on the patient's torso.

Technical expertise and ability to navigate the small airways with meticulous mapping of treated areas is essential to ensure that treatment sites are not skipped or overlapped. Each procedure usually requires approximately 50–75 activations of the device and up to 40–60 min of procedure time. Recovery time of 3-4 hours post procedure and ensuring post-procedure spirometry is within 20% of pre-procedure baseline is recommended. An additional 50 mg dose of prednisone is prescribed for the day after the procedure [27].

Complications

The most common complication of the procedure is an exacerbation of asthma symptoms that usually occurs within the first to seventh day after a procedure. Adverse events were more common in the study arms of active treatment and included hospitalizations for worsening asthma, atelectasis, lower respiratory tract infections, and pleurisy [3, 6]. To ensure patient safety, proper patient selection, active monitoring throughout and after the procedure, and appropriate followup, and delaying further procedures until adequate stabilization is necessary (Table 10.1).

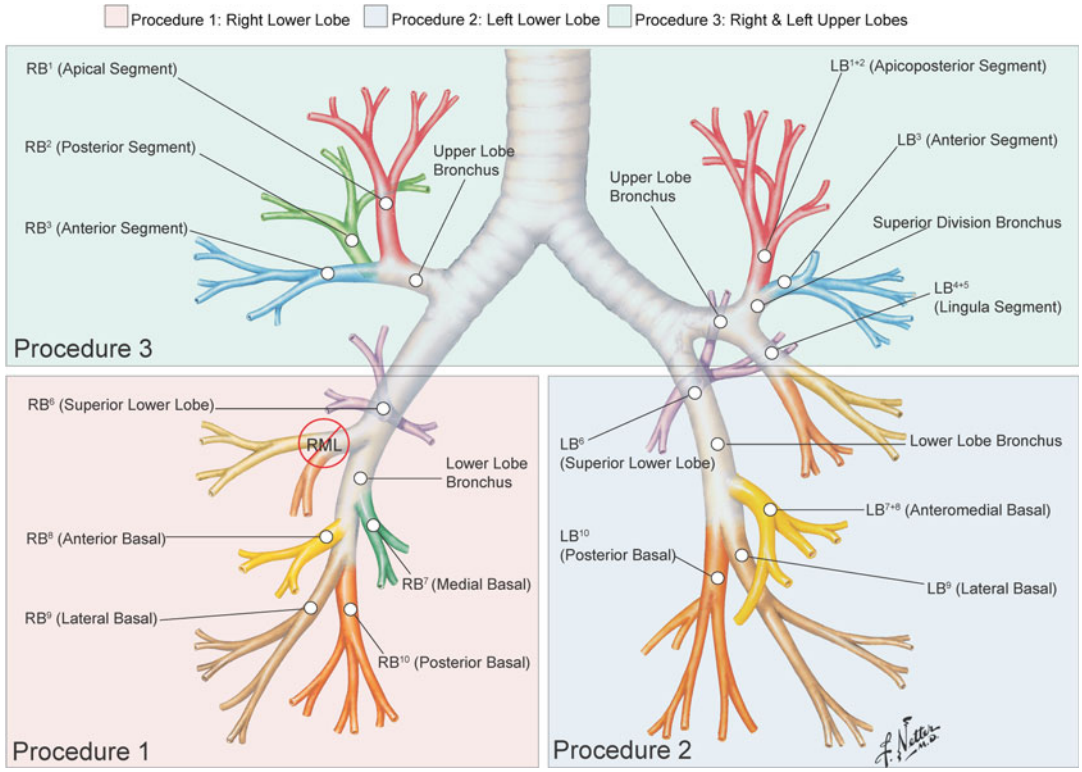

Fig. 10.5 Bronchial thermoplasty is performed in three bronchoscopic sessions as depicted. Right middle lobe is not treated. Careful mapping is needed to make sure that treated areas are not skipped or overlapped (image provided courtesy of Boston Scientific Corporation)

Limitations

Bronchial thermoplasty should be reserved for a select group of severe asthmatics as all are not eligible. In most instances, asthma can be well controlled with the available medical anti-inflammatory therapy and trigger avoidance. In those individuals with persistent symptoms despite maximal medical therapy, confounding conditions need to be considered. Patients with severely impaired lung function or current instability of symptoms are not appropriate candidates due to the known complications that can occur with the procedure.

Bronchial thermoplasty is an expensive treatment. High cost is a major impediment to the wider use of this technology. Formal cost-effective analysis is not available. High cost, unknown durability, and long-term effects of bronchial thermoplasty warrant careful patient selection for the most appropriate candidates.

It should also be noted that bronchial thermoplasty has only been evaluated in asthma, and that experience cannot be extrapolated to COPD or bronchiectasis. Current smokers are not included in clinical trials and in most instances, are not considered for this treatment. Other considerations include the need to be able to tolerate bronchoscopy, be off of anticoagulant therapy temporarily around the procedure, presence of other respiratory diseases such as interstitial lung disease, emphysema, or cystic fibrosis. People with uncontrolled hypertension, clinically significant cardiovascular disease, and internal or external pacemaker or defibrillators are not suitable candidates for this technique.

Future Directions

Since bronchial thermoplasty is a relatively new procedure in the treatment of asthma, ongoing clinical experience will help inform those performing the procedure which patients are likely to gain most benefit. Although not a cure, this mode of therapy directly affects airway smooth muscle, the vehicle of bronchospasm and hyperresponsiveness. Having trained and meticulous operators and close patient follow-up certainly will be beneficial for patients. In addition, observational studies to identify patient characteristics and biomarkers that predict successful outcome are needed so that bronchial thermoplasty may be targeted to those patients who will be helped most by this procedure.

Conclusions and Summary

To summarize, several clinical trials demonstrate the feasibility, safety, and improved clinical outcomes in patients with severe asthma who undergo bronchial thermoplasty when medical therapies do not control their symptoms. The series of trials outlined here demonstrate that although asthma is a disease of the airways, including the small airways, treatment of airways at 3 mm or larger has demonstrated improvement in asthma symptoms, quality of life and health care utilization [5].

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