Bronchial Thermoplasty: A Decade of Experience: State of the Art

Laren D. Tan, MD[a], Ken Y. Yoneda, MD[b], Samuel Louie, MD[b], D. Kyle Hogarth, MD[c], and Mario Castro, MD, MPH[d] *Loma Linda, Sacramento, Calif; Chicago, Ill; and St Louis, Mo*

Bronchial thermoplasty (BT) delivers targeted radiofrequency energy to bronchial airway walls and results in the partial ablation of the airway smooth muscle that is responsible for bronchoconstriction. It is approved for the treatment of severe persistent asthma. Multiple, large clinical trials including a recent "real-world" study demonstrate significant improvements in asthma-related quality of life, reduction in asthma exacerbations, emergency department visits, and hospitalizations after BT that is sustained out to 5 years. In this article, we review the state of the art of BT treatment in severe persistent asthma and share a decade of BT research and clinical experience. We share our personal experience and introduce the three "I"s (identification, implementation, and intense follow-up) that we believe promote successful patient outcomes and help build a successful BT program. **© 2019 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).** **(J Allergy Clin Immunol Pract 2019;7:71-80)**

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[a]Division of Pulmonary, Critical Care, Hyperbaric and Sleep Medicine, Department of Internal Medicine, School of Medicine, Loma Linda University, Loma Linda, Calif
[b]Division of Pulmonary, Critical Care and Sleep Medicine, Department of Internal Medicine, School of Medicine, University of California, Davis, Sacramento, Calif
[c]Section of Pulmonary and Critical Care Medicine, University of Chicago Medicine, Chicago, Ill
[d]Division of Pulmonology and Critical Care Medicine, Washington University School of Medicine, St Louis, Mo
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Corresponding author: Laren D. Tan, MD, Department of Medicine, Division of Pulmonary, Critical Care, Hyperbaric and Sleep Medicine, School of Medicine, Loma Linda University, 11234 Anderson Street, Suite 6439, Loma Linda, CA 92354. E-mail: LaTan@llu.edu.
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Mayse et al[1] published their expert opinion and clinical pearls for bronchial thermoplasty (BT) in 2007. Since their publication, BT has been performed across multiple countries with more than 6000 patients treated worldwide. The vast expansion in BT clinical experience resulted in reassurance of safety and addressed the initial fears of what this technology would do to our patients. It has also led to an improved BT technique, patient and BT team preparation, interdisciplinary planning, and performance of BT. Our state-of-the-art review offers an updated perspective and clinical pearls from experts at various centers of excellence for BT.

WHAT IS BRONCHIAL THERMOPLASTY?

Since approval by the US Food and Drug Administration (FDA) in 2010, BT endures as a proven and safe procedure indicated for the treatment of severe persistent asthma that is not controlled with high-dose inhaled corticosteroids (ICSs) and long-acting β_2-agonists (LABA). The procedure decreases hypertrophied airway smooth muscle (ASM) that contributes to airway hyperreactivity in severe asthmatics.[2,3] No other treatments, including biologics for severe asthma, directly alter the anatomy of bronchial smooth muscle. BT consists of tightly controlled delivery of radiofrequency (RF) thermal energy to the airway wall via the Alair catheter electrode. As a result, BT decreases ASM mass, bronchial nerve endings, and neuroendocrine cells.[4] RF electrical energy is systematically applied to airways between 3 and 10 mm in diameter throughout the tracheobronchial tree. The delivery of the energy during BT uses continuous feedback to tightly control the degree of tissue heating to avoid bronchial perforation, scorching, and stenosis.

CURRENT STATE OF THE EVIDENCE

BT underwent extensive preclinical studies that demonstrated unequivocal attenuation of airway narrowing in response to endobronchial installation of methacholine using dog airways. Evaluation of the airway histology in the dogs revealed that the ASM was reduced by 40% to 60%.[5] The first randomized controlled trial of BT (Asthma Intervention Research [AIR] 1) demonstrated significant improvements in asthma symptom-free days and asthma-related quality of life as measured by the Asthma Control Questionnaire (ACQ) (-1.2 ± 1.0 vs -0.5 ± 1.0; $P = .001$) and the Asthma Quality of Life Questionnaire (AQLQ) (1.3 ± 1.0 vs 0.6 ± 1.1; $P = .003$). There were no differences in forced expiratory volume in 1 second (FEV_1) or airway hyperresponsiveness (defined by a provocative concentration of methacholine required to lower the FEV_1 by 20% [PC20] of less than 8 mg per milliliter).[6] A second trial was designed to evaluate BT in more severe symptomatic patients (Research in Severe Asthma [RISA]). Prebronchodilator FEV_1 was 62.9% of

Abbreviations used
ACQ- Asthma Control Questionnaire
AQLQ- Asthma Quality of Life Questionnaire
ASA- American Society of Anesthesia
ASM- Airway smooth muscle
ATS- American Thoracic Society
BT- Bronchial thermoplasty
ERS- European Respiratory Society
ETT- Endotracheal tube
FDA- Food and Drug Administration
FEV_1- Forced expiratory volume in 1 second
ICS- Inhaled corticosteroid
LABA- Long-acting β_2-agonists
LMA- Laryngeal mask airway
MAC- Monitored anesthesia care
RF- Radiofrequency

predicted for the BT group and 66.4% of predicted in the control group. BT subjects had a significant improvement in FEV_1 (14.9 ± 17.4 vs −0.9 ± 22.3; $P = .04$) and in ACQ (−1.04 ± 1.03 vs −0.13 ± 1.00; $P = .02$).[7] While compelling, these trials were not blinded and the world's first sham bronchoscopy controlled trial (AIR2) was designed in consultation with the FDA. This multicentered, double-blind, sham bronchoscopy controlled trial enrolled a total of 288 patients to BT in a 2:1 fashion. This pivotal trial demonstrated a significant improvement in the AQLQ score as well as a reduction in the frequency of severe asthma exacerbations, emergency department visits, and days lost from school or work in the year after BT.[8] On the basis of this trial, BT was approved by the FDA for the treatment of severe persistent asthma not controlled with high-dose ICS and LABA. FDA approval was made contingent on the performance of a postmarketing study (the PAS2 study). The 3-year follow-up results of this trial were recently published, confirming the results of the pivotal AIR2 study. As a registry study, it was not randomized or controlled and AQLQ scoring was not performed. However, it did demonstrate a reduction in severe exacerbations, emergency department visits, and hospitalizations by 45%, 55%, and 40%, respectively.[9]

BT is conceptually straightforward; however, achieving a successful outcome and building a successful BT program are not. The bronchoscopist should at minimum be trained and complete the BT curriculum as provided by the manufacturer. Although the bronchoscopist's skill and experience are of paramount importance, individual patient outcome and long-term program success are highly dependent on other factors, and a multidisciplinary approach to patient selection, patient preparation, patient management, postoperative care, and careful follow-up is essential.

According to the latest 2014 American Thoracic Society (ATS)/European Respiratory Society (ERS) task force on severe asthma,[10] it was recommended that access to BT should not be limited as a form of therapy[11] but be performed in the context of a registry or clinical study; although we agree that all BT centers should keep track of their patient outcomes for quality control purposes, these same recommendations also pose an undue burden on the nonacademic practicing pulmonologist. There is a new ATS/ERS workshop, but it is unclear if BT will be readdressed at this time. The updated guidelines outlined here are based on the 2018 Global Initiative for Asthma recommendations and the expertise of the authors and their combined 34 years of experience in BT.

TABLE I. Clinical pearls—equipment

- Adhesive gel-pad return electrodes should not be placed on regions of the body that contain a lot of hair or excessive fat. Placing the gel-pad on a hairy/fatty region of the body could result in higher impedance. The higher system impedance could potentially trigger the high-energy 120J safety cutoff more often. This could result in a less effective treatment of the airway smooth muscle. Ideally, the adhesive gel-pad should be placed on areas of high muscle content (ie, back) with minimal hair (shaving may be required) and not on fatty regions of the body. Perform BT with a 2.0 working channel scope
- The Alair BT system is the only FDA-approved equipment for BT

BT, Bronchial thermoplasty; *FDA*, Food and Drug Administration.

BRONCHIAL THERMOPLASTY PROCEDURE

Overview

A complete BT procedure requires 3 bronchoscopy sessions, each lasting less than 1 hour, spaced approximately 2-3 weeks apart.[5,12] BT is performed during bronchoscopy with most patients undergoing moderate or deep sedation. All accessible airways (between 3 and 10 mm) distal to the mainstem are treated under bronchoscopic visualization with the right middle lobe typically being avoided due to concerns of right middle lobe syndrome.[13] Although not recommended by the manufacturer, various sites have safely and successfully performed BT in the right middle lobe (RML) with no reports of BT-induced right middle lobe syndrome. Moving the Alair catheter from distal to proximal along the length of the visualized airway, contiguous and nonoverlapping activations are performed systematically from airway to airway.

Equipment

BT is performed using the Alair Bronchial Thermoplasty System that delivers RF energy—a combination of magnetic and electrical energy (electromagnetic energy). The system comprises the Alair RF Controller and the flexible Alair Catheter, a single use device with an expandable electrode array attached at one end and a deployment handle at the other. Under direct visualization through the working channel of a high-frequency compatible flexible bronchoscope, the electrode array is introduced and expanded to contact the airway walls. Only when the electrodes are appropriately contacting the airway walls, will activation of the Alair RF controller result in RF energy being delivered. RF energy is transferred from the electrode through the airway wall and is converted to thermal energy when absorbed preferentially by high-resistance tissue such as smooth muscle. With each activation, the Alair RF controller delivers the correct intensity and duration of RF energy. The controller also monitors the system, ensuring that energy is not delivered unless all accessories are properly connected. If activation is attempted while the electrode array is not in proper contact with the airway wall, a specific audible error sequence is sounded. A standard adhesive gel-pad patient return electrode is affixed on the patient and connected to the controller to provide a complete circuit. BT is best performed with an RF-compatible bronchoscope with an outer diameter of 4.9 to 5.2 mm and a minimum 2.0-mm working channel. Larger-diameter therapeutic bronchoscopes are not required and may limit access to airways, whereas thinner-diameter bronchoscopes are not usually necessary, are

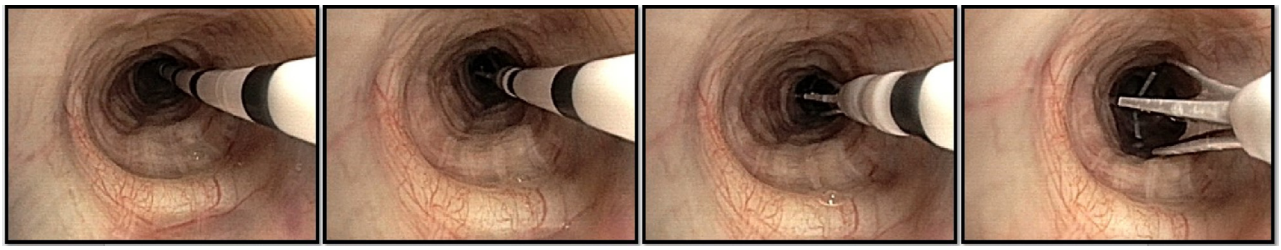

FIGURE 1. Alair catheter.

more difficult to navigate, and may have a working channel that is too small in diameter (Table I).

Technique

A complete treatment of BT consists of 3 separate bronchoscopy sessions, each separated by approximately 2 to 3 weeks. Treatments are divided to minimize the risk of inducing an asthma exacerbation of diffuse airway edema and inflammation that might occur if the entire tracheobronchial tree is treated in 1 session. The first BT treatment is performed in the right lower lobe, the second in the left lower lobe, and the final in both the right upper and left upper lobes.[12] During all prior clinical trials, the right middle lobe was not treated due to concerns of inducing right middle lobe syndrome. Of note, the lingula was treated. Longer-term studies have not seen an increase in bronchiectasis. The concerns for RML syndrome with BT have not been adequately studied.[14] As a result of this theoretical concern with evidence of consistently low ventilation defects in the right middle lobe via hyperpolarized magnetic resonance imaging studies, various BT centers have safely and successfully treated the RML.[15]

We recommend that during second and third bronchoscopy sessions, the previously treated BT airways be inspected to ensure proper healing before proceeding with the planned BT procedure. If the previously treated airways appear to have considerable inflammation (ie, significant erythema, edema, friable mucosa, narrowing of airway), consideration should be given to postponing the current treatment. Postponement of the BT procedure due to considerable airways inflammation is not common and should be tailored to the patient's clinical and airway findings. After a complete airway inspection, the bronchoscope is navigated to the targeted region of the lung. The bronchoscopist then formulates a sequential order in which airways will be accessed and treated and communicates the plan to his/her assistant. Having an organized treatment plan is critical to the completion of a proper and safe BT treatment session. A systematic approach working from distal to proximal, superior to more inferior, or from right to left, in a methodical organized fashion ensures that all regions are treated appropriately while minimizing the error of treating the same airway twice. Within each segment, the subsegmental airways should be properly explored and treated in a systematic manner. Although seemingly straightforward, it is striking how dramatically and rapidly the airways can change due to edema and bronchospasm, disorienting even experienced bronchoscopists.

The Alair catheter is introduced into the working channel of the bronchoscope and advanced until the distal end is in view (Figure 1) within the targeted airway. The catheter is then expanded until the 4 electrode array wires are in contact with the airway wall. Proper contact of the electrodes is necessary for complete activation. Pressing and releasing the controller footswitch will initiate activation, and provided there is proper contact and there is no cancellation, the entire 10-second treatment cycle will be completed. Depressing the footswitch before completion of the treatment cycle will cancel and prematurely terminate the treatment—and sound the error sequence. After each activation, the electrode array should be partially collapsed and repositioned proximally 1 black line (5 mm) (Figure 1). The bronchoscopist should pay careful attention not to overlap the previous activation site. A detailed road "map" of the airways can assist in keeping track of the progression of treatments and assist in minimizing errors for each session (ie, treating the same airway twice). A recent study performed by Langton et al[16] described the importance of delivering the sufficient number of activations and the positive effect on clinical response. Using a regression equation, they recommend 40 activations to each of the lower lobes and 60 activations to the combined upper lobes to achieve an improvement in ACQ-5 score of 0.5 units. Although further validation studies are necessary, the BT proceduralist should be mindful that varying activations can significantly affect patient outcomes.[16] There are situations in which one of the electrodes on the Alair catheter becomes inverted or mucous buildup obscures visualization (Figure 2). When these problems are encountered, the Alair catheter should be completely removed from the bronchoscope, the electrode gently reshaped and cleaned, and the bronchoscope irrigated (Table II).

PATIENT SELECTION

Patients should be rigorously screened to (Figure 3): (1) confirm a correct diagnosis of asthma (includes phenotyping), (2) verify criteria for severe persistent asthma despite adherence to appropriate pharmacologic and nonpharmacologic interventions (at minimum high-dose ICS and LABA), (3) review and address comorbidities that could affect asthma control (eg, gastroesophageal reflux disease [GERD], postnasal drip, obstructive sleep apnea [OSA], smoking, vocal cord dysfunction), (4) reinforce medication adherence and proper inhaler technique, and (5) rule out contraindications to BT (ie, implantable electronic device, under 18 years of age, previously treated with BT). Although caution is advised in treating patients with an $FEV_1 < 65\%$ of predicted, our clinical experience and case series indicate that patients with a mean FEV_1 of 37% could safely undergo and benefit from BT[17](Tables III and IV).

PATIENT MANAGEMENT

The success of BT is dependent not only on proper patient selection but also on multiple other dynamic variables. The technical skill of the bronchoscopist and careful patient management

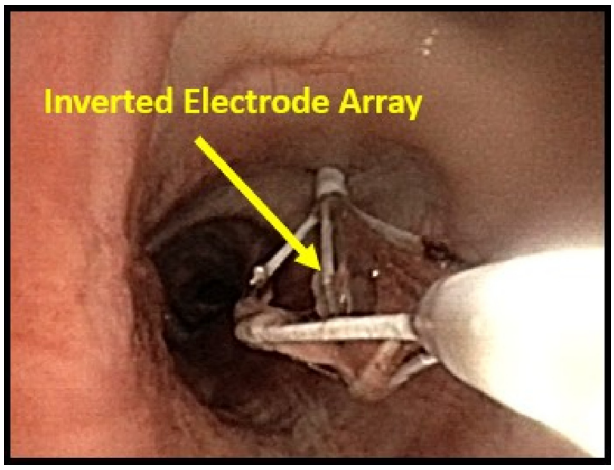

FIGURE 2. Inverted electrode array.

TABLE II. Clinical pearls—technique

- Some patients require more than 2-3 wk to recover. Adequate time should be allowed for healing before the next BT procedure
- While in the airway and before activating the Alair catheter, verification of the proposed targeted site for the current BT session by the bronchoscopist to the BT assistant and nursing staff helps assure treatment of the correct site
- Authors at various sites have moved beyond direct end catheter visualization and advance the catheter until resistance is met; the Alair catheter is then repositioned back 5 mm before the first treatment is initiated with contiguous activations described above
- When cleaning the electrode array, vigorously shake it within a bath of room temperature saline as cooling of the catheter wires may cause malfunction
- After completion of the BT procedure, consider applying lidocaine through the bronchoscope to the treated regions to lessen postprocedural cough and pain (lidocaine limit of 600 mg or 8.2 mg/kg)

BT, Bronchial thermoplasty.

during and after the procedure are both of great importance in ensuring patient safety and successful BT outcomes. It is therefore of paramount importance that the BT bronchoscopist complete the proper training from the manufacturer and that the BT team receive appropriate education and training. Proper analgesia, topical anesthesia, and anxiolytics are critical in providing comfort and reducing excessive cough and patient movement. The approach described will not only facilitate procedure efficiency but also increase overall patient satisfaction with the procedure.

PATIENT PREPARATION AND PREMEDICATION

As with other medical procedures, the risk and benefits of bronchoscopy, BT, and sedation should be fully discussed with the patient. To mitigate the risk of an asthma exacerbation from postprocedure inflammation of the treated airways, patients should be given prophylactic prednisone or the equivalent at a dose of 50 mg/day for the 3 days before the procedure, the day of the procedure, and the day after the procedure.[8] In the days preceding each procedure, the asthmatologist and/or BT-certified bronchoscopist should ensure that the patient:

- Has not had a respiratory infection in the days preceding the procedure
- Has not had a recent asthma exacerbation requiring oral corticosteroids within the last 14 days
- Has started systemic steroids as directed.

On the day of each procedure, reevaluation is necessary to ensure that the patient continues to be a good candidate for BT. Spirometry is performed to ensure that the patient is at his or her established baseline and to provide an FEV_1 benchmark for comparison with the post-BT FEV_1. Postponement of the procedure should be considered if any of the conditions listed in Table V applies. We also recommend that physicians follow their institution's established prebronchoscopy guidelines.

Supraglottic topical anesthesia

When performing BT under moderate sedation or monitored anesthesia care (MAC), the transnasal bronchoscopic approach tends to cause less gagging and fewer secretions, and is safe and well tolerated. Applying topical lidocaine jelly or liquid to the nostril(s) will assist in achieving an anesthetized and lubricated nasal passage. If there are concerns with epistaxis, phenylephrine or oxymetazoline spray or topical cocaine may be used.[1] Supraglottic topical anesthesia is not usually required for deep sedation or general anesthesia. Transoral with moderate sedation or MAC and laryngeal mask airway (LMA) are better tolerated in patients with a history of nasal congestion and chronic sinusitis. Transnasal or transoral approaches are viable options depending on the individual patient and the BT bronchoscopists experience and comfort level.

Anesthetizing the hypopharynx can be effectively achieved by having the patient gargle 5 mL of 2% lidocaine. An alternative or an adjunct to gargling lidocaine is to aerosolize the posterior pharynx with 1% to 2% lidocaine. Regardless of the technique, anesthetizing the posterior pharynx will assist in not only diminishing the patient's gag reflex but also systemic sedatives. Careful attention to the amount of lidocaine administered and mindfulness of systemic absorption of lidocaine will assist in decreasing the likelihood of lidocaine toxicity (Table III).

Vocal cord and subglottic topical anesthesia

After anesthetizing the patient's upper airway, the bronchoscopist should promptly apply topical anesthesia to the vocal cords and bronchial tree. At the vocal cord level, 1% lidocaine can be applied in 2-mL aliquots until the patient appears to be comfortable with minimal coughing. The patient's sedation level and tolerance of the procedure should be closely monitored. Often, providing additional anxiolytic or antitussive medications can improve patient comfort. Reapplication of local anesthetic 30 to 40 minutes into the procedure is often required to reduce cough.[20]

Doses of lidocaine totaling up to 600 mg or 8.2 mg/kg have been found to be safe in asthmatics undergoing bronchoscopy.[21] Patients should be continuously monitored for signs and symptoms of lidocaine toxicity.[22,23] BT through an LMA is safe, acceptable, and preferable as endotracheal tube (ETT) can cause bronchospasm. When an ETT is placed, 2% or 4% lidocaine can be sprayed onto the vocal cords at the time of endotracheal intubation. A minimal 7.5 ETT is acceptable, but 8.0 is preferred (Table VI).

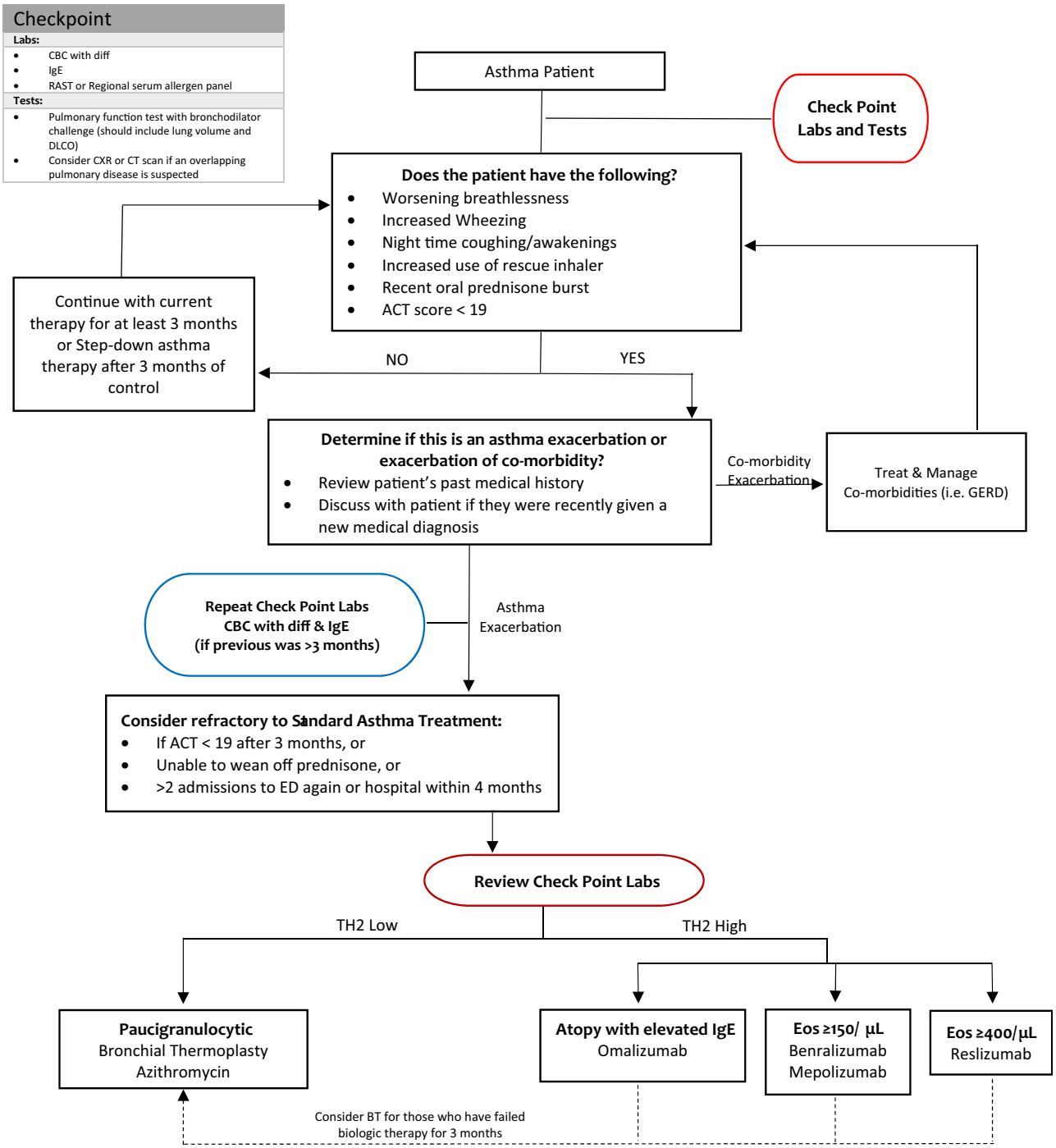

FIGURE 3. Asthma algorithm. *ACT*, Asthma Control Test; *CBC*, complete blood count; *CT*, computed tomography; *CXR*, chest X-ray; *DLCO*, diffusing capacity of the lungs for carbon monoxide; *ED*, emergency department; *Eos*, eosinophils; *GERD*, gastroesophageal reflux disease; *RAST*, radioallergosorbent test.

Sedation

BT can be performed under moderate sedation, deep sedation, or general anesthesia. Moderate sedation, also formerly known as conscious sedation, is defined as sedation under which a patient is able to respond purposefully to either verbal commands or with light tactile stimulation. Deep sedation is when a patient cannot be easily roused but is still able to respond purposefully with repeated or noxious stimuli. General anesthesia is a state of unconsciousness in which the patient is unarousable to painful stimuli, has an impaired ability to protect and maintain the airway, and may have inadequate spontaneous ventilation and/or cardiovascular function. Patients undergoing any form of sedation need to be closely observed and be under the care of the appropriate and necessary staff. The staff must possess the skills and qualifications needed to address reasonably anticipated complications.[24,25] By definition,

TABLE III. Patient selection

- Adults diagnosed with severe asthma as defined:[10,18]
  - Alternative diagnoses to asthma have been excluded
  - Comorbidities have been treated and controlled
  - Triggers have been removed
  - Compliance with treatment regiments have been verified and checked
  - Symptomatic despite treatment with stable maintenance medication (ie, high-dose inhaled corticosteroids and long-acting β_2-agonist)
  - Asthma that requires treatment with guidelines suggested medications for GINA[19] step 4-5 asthma for the previous year or systemic corticosteroids for ≥50% of the previous year to prevent uncontrolled or which remains uncontrolled despite this therapy
- Caution with prebronchodilator FEV1 <60% predicted—experienced BT centers may use lower cutoff
- Able to undergo bronchoscopy safely
- No internal pacemaker or neurostimulator

BT, Bronchial thermoplasty; *FEV$_1$*, forced expiratory volume in 1 s; *GINA*, Global Initiative for Asthma.

TABLE IV. Clinical pearls—patient selection

- Patients with persistent asthma symptoms while currently on biologic therapy should be considered to undergo BT (or alternatively, "current or past asthma biologic therapy does not preclude BT")
- Consider environmental factors at the time of BT (ie, severe cold, forest fires, regional epidemic illness, eg, influenza) that could result in a severe exacerbation after BT and if necessary perform BT at another time
- Perform BT earlier in the week to ensure ample time for follow-up and assistance if needed from the BT team
- Patients with multiple comorbidities, near fatal asthma, or who have to travel great distances to receive treatment may benefit from staying overnight locally but should rarely need to be admitted

BT, Bronchial thermoplasty.

TABLE V. Day of bronchoscopy

Postponement of BT should be considered if any of the following criteria is present:

- Recent asthma exacerbation requiring oral corticosteroids with completion of oral steroids less than 14 d before BT
- Active respiratory infection or other clinical signs of instability the day of or days preceding BT
- Prophylactic prednisone or prednisolone was not started 3 d before BT
- Increase in asthma symptoms within the last 48 h requiring ≥4 puffs/d over the pretreatment usage
- SpO_2 less than 90% on room air
- During bronchoscopy, airways are extremely edematous or inflamed, or there are excessive, purulent/tenacious airway secretions
- FEV_1 on the day of the procedure is <20% of established baseline FEV_1
- Inability to complete the procedure due to excessive coughing, excessive secretions, and tortuous anatomy
- Bronchoscopist discretion to postpone the BT procedure

BT, Bronchial thermoplasty; *FEV$_1$*, forced expiratory volume in 1 s.

patients undergoing BT are an American Society of Anesthesia (ASA) class III or greater, and although the presence of an anesthesiologist should be considered for ASA class III, it

TABLE VI. Lidocaine toxicity signs and symptoms

- Lightheadedness
- Visual and auditory disturbances
- Muscular twitching
- Unconsciousness
- Convulsions
- Coma
- Respiratory arrest
- Cardiac arrest

TABLE VII. Clinical pearls—sedation

- The decision to pursue moderate or deep or general sedation is partially dependent on resources available at each individual BT center
- Evaluation of the patient's comorbid conditions should also factor in the decision on the appropriate sedation. For example, the profoundly obese with type IV airways are less ideal for moderate sedation and tend to benefit from an endotracheal tube. The large abdomen, and the position of the patient supine, can make lower lobe activations difficult secondary to atelectasis that can be alleviated with positive pressure and PEEP.

BT, Bronchial thermoplasty; *PEEP*, positive end-expiratory pressure.

certainly is not required. In the absence of an anesthesiologist, the BT physician (or assisting physician) must anticipate and be ready and able to manage procedural or sedation complications, including severe asthma exacerbations, status asthmaticus, respiratory failure, and the need for endotracheal intubation and mechanical ventilation.

The main objective of BT under moderate sedation is to maintain an adequate spontaneous ventilatory drive while providing appropriate anxiolysis and analgesia. Patient comfort is paramount, as patients will need to be willing to return for a second and third procedure. Achieving a steady state of adequate analgesia and sedation with minimal cough requires frequent reassessment and personalization for each individual patient. Sedation is commonly achieved using a combination of a short-acting benzodiazepine and a narcotic. Although there is no clear consensus for BT, some authors suggest using midazolam, diphenhydramine, and fentanyl, whereas others have safely achieved moderate sedation with propofol. Midazolam is a fast-acting benzodiazepine with a short half-life. The onset of effect is typically between 1 and 3 minutes, with an average half-life of 2 hours. Midazolam also has the ability to produce antegrade amnesia, anxiolysis, with an underlying anticonvulsant effect. Propofol potentiates gamma-aminobutyric acid ($GABA_A$) receptors increasing chloride ion conductance, resulting in inhibitory postsynaptic currents and ultimately inhibition of neuronal activity; it has a short initial distribution half-life of 2 to 8 minutes and is rapidly metabolized in the liver.[26] Fentanyl is known for its potent analgesic properties, but it also has helpful sedative and antitussive properties. Onset of action for fentanyl is typically between 2 and 4 minutes with a peak effect at approximately 10 to 15 minutes; the average half-life ranges from 30 to 60 minutes. Additional doses are recommended if patients continue to experience pain or are excessively coughing. Maintaining appropriate analgesia and sedation while minimizing on cough is the main objective for fentanyl.

TABLE VIII. AIR2 respiratory adverse events selected AEs with >3% incidence and difference between groups

	Treatment period (~12 wk)		Posttreatment period (~46 wk)	
Adverse event	BT (N = 190) %	Sham (N = 98) %	BT (N = 187) %	Sham (N = 98) %
Asthma (multiple symptom)	52.1	38.8*	27.3*	42.9
Wheezing	15.3	6.1*	4.3	3.1
Atelectasis	4.7	0*	0	0
Hemoptysis	3.2	0*	0	0
Lower respiratory tract infection	7.9	2.0*	3.2	6.1
Upper respiratory tract infection	20.0	11.2*	29.9	25.5
Nasopharyngitis	4.7	7.1	10.7	5.1*
Throat irritation	4.7*	12.2	1.1	3.1

AE, Adverse event; *BT*, bronchial thermoplasty.
*Posterior probability of superiority (PPS) >95.0%.

Deep sedation and general anesthesia require the presence of a second dedicated physician, usually an anesthesiologist. MAC, LMA, and endotracheal intubation with or without mechanical ventilation are available options. Total intravenous sedation with propofol and limited doses of remifentanil and midazolam, with or without neuromuscular blockade, provides nearly ideal patient comfort and makes for a fast, efficient, and safe procedure. These short-acting agents when combined with neuromuscular blocker reversal agents promote fast recovery and allow the patients to fully participate in their postprocedure spirometry.

Avoidance of "drying agents" is highly recommended for 2 reasons: (1) atropine and glycopyrrolate, when administered before bronchoscopy, do not produce a clinically meaningful improvement in lung function or decrease in bronchial secretions,[27] and (2) some authors have found it more difficult to clear secretions after bronchoscopy (Table VII).

POSTPROCEDURAL CARE

Post-BT respiratory adverse effects should be expected and discussed. As anticipated, increases in respiratory-related adverse effects were seen as patients with higher severity of disease were treated; this was observed from AIR to RISA and from AIR2 to PAS2. Severe exacerbations were noted to be greater in the PAS2 study compared with the AIR2 (55.8% vs 40.5%) and emergency department visits (15.8% vs 5.3%). The 2 most common respiratory adverse events during and after BT treatment periods in the AIR2 trial were asthma symptoms (ie, cough, nocturnal awakenings) (52.1% vs 27.3%) and upper respiratory tract infections (20.0% vs 29.9%)[8] (Table VIII).

BT postprocedural care should in general follow institutional guidelines for routine postbronchoscopy care. Patients should be carefully monitored throughout recovery and discharged only when vital signs are stable, mental status has returned to baseline, the patient is able to swallow liquids, and spirometry is acceptable. We routinely administer nebulized bronchodilators as needed for symptom control during recovery and before performing postprocedure spirometry. Admission should be considered for any patient whose post-BT FEV_1 is <80% of their pre-BT FEV_1 that day.

Postprocedural education to patient and family is very helpful to alert them of the increase and worsening of respiratory symptoms after BT (Figure 5). Symptoms usually present within 1 week of BT with resolution on average within another 1 week. Some patients have reported peak respiratory-related symptoms

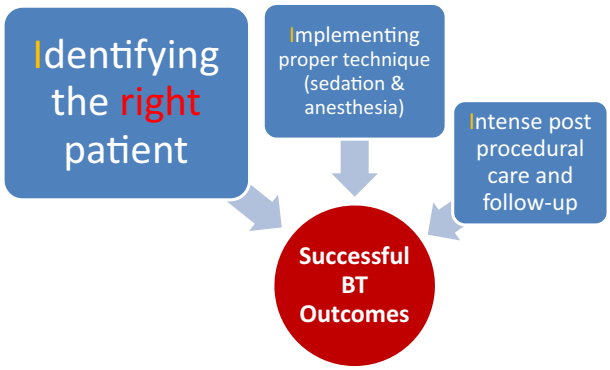

FIGURE 4. i^3 key points to ensure successful BT outcomes. This figure stresses the importance of identifying the correct patient for BT. *BT*, Bronchial thermoplasty.

48 hours after the procedure with resolution also within 1 week. The potential for a postprocedural asthma exacerbation is highest during the first 7 days, and it is recommended that patients be contacted 24 hours, 48 hours, and 7 days after the procedure to assess their respiratory symptoms. Increased coughing is not uncommon and when not excessive can be beneficial when it augments the clearance of excessive mucus production. We find that the routine use of an intrapulmonary percussive device (acapella device, Aerobika, Flutter valve) at 30 exhalations 3 times a day combined with the routine use of nebulized bronchodilators 3 to 4 times a day for the first few days after BT helps airway clearance and prevents severe mucous plugging. Radiographic abnormalities after BT are common but usually resolve spontaneously.[28] A chest radiograph should be obtained if the patient has persistent or severe respiratory symptoms to rule out pneumonia or lung collapse. Symptomatic patients with lung or lobar collapse may benefit from hospitalization for chest physiotherapy and/or bronchoscopy for mucus plug removal. A BT aftercare handout can assist patients by addressing concerns on what to expect after BT, emergency medications that they should already have at home, when and who to call for help during and after business hours (Figure 5; Table IX).

DISCUSSION

BT is a validated and proven therapy for patients with severe persistent asthma that is not controlled despite high-dose ICS

Bronchial Thermoplasty – Aftercare

What to expect after the procedure?

- You may experience soreness of the throat and for some patients some soreness of the chest
- You may experience more wheezing and breathlessness, this is expected (be sure to use your rescue inhaler or nebulizer treatments as needed)
- You may cough up some blood tinged phlegm, this should disappear within 48 hours
- You may experience coughing episodes throughout the day, this is expected and should lessen/improve within 48 hours (use cough suppressant medication if your cough is disrupting your sleep and every day activities)

Things you should already have at home (If you don't be sure to let us know):

I. Prednisone 50 mg (3 doses were taken prior to BT, 1 dose the day of BT and your last dose will be the day after BT)
II. Emergency asthma exacerbation antibiotics and emergency asthma exacerbation prednisone
III. Cough suppressant medication (either over the counter cough suppressant medication or prescribed cough suppressant medication)
IV. Albuterol rescue inhaler and/or rescue nebulizer treatments (i.e. Albuterol, Ipratropium and Albuterol)

When should you call for help?

Call our doctors or clinic nurse or seek immediate medical care if:

- You have a fever over 101°F or 38.3°C
- You cough up more than 2 tablespoons of blood
- You have hoarseness of voice for more than 48 hours
- You have bubbles under the skin around the collarbone. These may crackle and pop when you press on them
- You have pain in the chest that does not get better after 48 hours

Call 911 anytime you think you need emergency care. As an example, call if:

- You cough up large amounts of bright red blood
- You have sudden chest pain and shortness of breath
- You have severe trouble breathing, even after using your rescue inhalers
- You passed out (lost consciousness)
- You have severe unbearable pain in your chest

Contact your pulmonologist[¥] via text or phone for post procedure questions or concerns.

*For 24/7 pulmonary physician advice post bronchial thermoplasty call (XXX) XXX-XXXX, ask the operator to be connected to the on call pulmonary physician.

[¥]Pulmonologist and/or performing bronchoscopist name should be included along with contact number.
[*]If available an overnight pulmonary physician contact number should also be provided.

FIGURE 5. Example of bronchial thermoplasty (BT) aftercare patient handout.

and LABA. The clinical effectiveness of BT is suspected to go beyond the demonstrated ability to decrease ASM, supporting the complex relationship between ASM and the airway inflammatory cascade.[2,3] The most recent real-world BT clinical trial of severe persistent asthmatics (PAS2) by Chupp et al[9] demonstrated that despite having more severe asthmatic subjects, at 3 years after BT, a substantial percentage of PAS2 subjects had significant decreases in severe exacerbations, emergency department visits, and hospitalizations by 45%, 55%, and 40%, echoing the earlier AIR2 results. PAS2 was able to

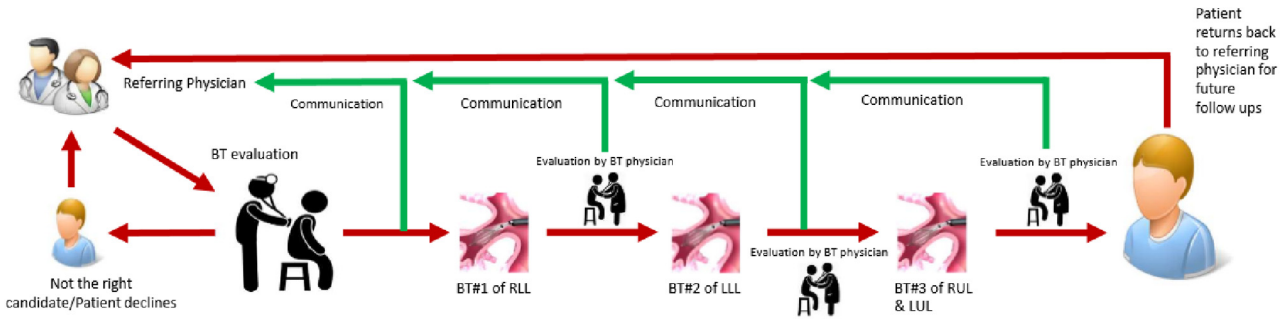

FIGURE 6. Dynamic communication after the procedure between the referring physician, BT performing physician, and patient. Patient follow-up and communication (green arrow) occurs between each bronchial thermoplasty (BT) procedure with subsequent communication back to the referring physician after that visit before the next BT treatment. *LLL*, Left lower lobe; *LUL*, left upper lobe; *RLL*, right lower lobe; *RUL*, right upper lobe.

demonstrate the real-world efficacy of BT in a more severe asthmatic population.[8,9] Replication of these successful outcomes is dependent on the three "I"s: (1) identifying the appropriate patient, (2) implementing the proper BT technique (including sedation and anesthesia), and (3) intense postprocedural care and follow-up (Figures 4 and 6).

Identify the appropriate patient

BT is approved for the treatment of severe persistent asthma that is not controlled despite high-dose ICS and LABA; however, properly identifying these patients is not straightforward. The proliferation of therapeutic options for severe asthma has increased the importance of proper evaluation and verification of patients presenting with asthma-like symptoms. Severe asthma had been defined by the 2014 International ERS/ATS task force, as asthma that requires treatment with high-dose ICSs plus a second controller and/or systemic corticosteroids to prevent asthma from being uncontrolled or remains uncontrolled despite this therapy.[10] The definition for uncontrolled asthma includes persistent poor asthma symptom control, frequent severe exacerbations, or one serious exacerbation resulting in hospitalization or intensive care unit admission or mechanical ventilation in the previous year or airflow limitation. Because asthma has no one specific defining characteristic symptom (eg, wheezing, cough, chest tightness, breathlessness), it is imperative that for each individual patient with uncontrolled asthma, we explore and question whether the diagnosis is correct and whether there are uncontrolled underlying comorbidities. Investigating other plausible etiologies that mimic or result in uncontrolled asthma (ie, inhaler technique, tobacco smoke avoidance, GERD, rhinitis, etc.) remains a cornerstone of asthma control evaluation and should be dynamically reviewed, especially if the patient continues to be refractory to all therapy.

Implementing proper bronchial thermoplasty technique

Favorable BT results are also determined by the techniques used and interdisciplinary pre- and post-BT care. BT is a complex bronchoscopic procedure that requires proper training and completion of the BT curriculum from the manufacturer of the Alair Bronchial Thermoplasty System. Success of the procedure is dependent on the technique and assuring that all accessible airways distal to the mainstem bronchi between 3 and 10 mm in diameter (excluding the right middle lobe) are treated. Currently there are ongoing studies with the right middle lobe being treated with BT, but at this time it is recommended that the right middle lobe be left untreated. A strategic and systematic approach, moving from distal to proximal within an airway while also being cognizant of already treated airways, is essential. Sedation and anesthesia should be personalized to each individual patient and be within the guidelines of each institution. Although moderate sedation with midazolam and fentanyl is commonly used, propofol has also been favored as an alternative to midazolam. The use of total intravenous anesthesia with propofol and minimal short-acting narcotics and anxiolytics provides for a fast, efficient, and safe procedure and quicker postprocedure recovery.

TABLE IX. Clinical pearls—postprocedure care

- Follow institutional guidelines for routine postbronchoscopy care
- Administer nebulized bronchodilators with a frequent PRN basis (some centers report as frequent as q15 min)
- Consider hospitalization if post-BT FEV1 < 80% of pre-BT FEV1
- Airway clearance device and nebulized bronchodilators the first few days after BT
- Provide after care handout with instructions and emergency contact numbers

BT, Bronchial thermoplasty; FEV_1, forced expiratory volume in 1 s; *PRN*, as needed.

Intense postprocedural follow-up

An intense structured approach to postprocedural care, which includes postprocedural outpatient follow-up and education on early identification and management of complications after BT, assists in efficient and comprehensive management with a unified goal on quality and patient safety. A BT aftercare sheet that is given to patients is essential in providing the necessary patient education on identifying postprocedural complications along with when and how to seek help (Figure 5). It is recommended that patients be contacted 24 hours, 48 hours, and 7 days after the procedure to assess their respiratory well-being. Postprocedure communication should be personalized for each individual patient who receives BT (ie, some patients may need to be contacted more frequently vs others). Dynamic postprocedure communication (ie, how the patient tolerated the procedure, adverse events during and after the procedure) should also occur between the referring physician or

asthmatologist, procedure performing bronchoscopist, and the patient (Figures 5 and 6).

CONCLUSIONS

BT is not a cure for asthma; the decision to pursue BT should be based on an appropriate clinical history, atopic tests, laboratory findings, prior treatment response (ie, prior conventional medical therapy and/or asthma biologic failure), and realistic goals of patients and clinicians (ie, reduce emergency department visits, reduce exacerbations). A multitude of questions remain in asthma treatment, especially when trying to decide which personalized treatment will best benefit an individual patient's specific asthma endotype or phenotype. Irrespective of all the novel therapies (biologic and nonbiologic) available for treating the varying asthma subtypes, asthma control will continue to be suboptimal until comorbidities, avoidable and unavoidable environmental exposures, and adherence to standard therapies are adequately addressed. With a decade of BT research and clinical experience, we can state that BT is of unequivocal benefit and has an acceptable safety profile. The difficulties and success of BT rest with implementing an individualized BT plan using the three "I"s: (1) identifying the right patient, (2) implementing the proper BT technique, and (3) intense postprocedural care and follow-up.

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