BRONCHIAL THERMOPLASTY AND OTHER ADVANCES IN NON-PHARMACOLOGICAL MANAGEMENT OF ASTHMA AND COPD

-Shailesh Agrawal

Outline

- Introduction
- Patient selection
- Preparation for procedure
- Equipment and Technique
- Clinical studies on BT
- Predictors of response
- Non pharmacological modalities in COPD

Bronchial Asthma

- Chronic inflammation of the large and small airways, resulting in airway hyper-responsiveness, excessive mucous secretion and airflow obstruction
- 235 million people affected worldwide
- 5% severe asthma
- Associated with more health care use and reduced quality of life

Aoife O'Reilly et al; Ther Adv Respir Dis 2018, Vol. 12: 1–7

Severe asthma

- Uncontrolled despite maximal inhaled therapy
  - Compliance, comorbidities, drugs
  - Different phenotypes
- Role of airway smooth muscle(ASM)
- Increased thickness of ASM-clinical and functional severity of asthma
- Therapeutic target for bronchial thermoplasty

Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. Updated 2018
Pascual RM and Peters SP. *J Allergy Clin Immunol 2005; 116: 477–486*

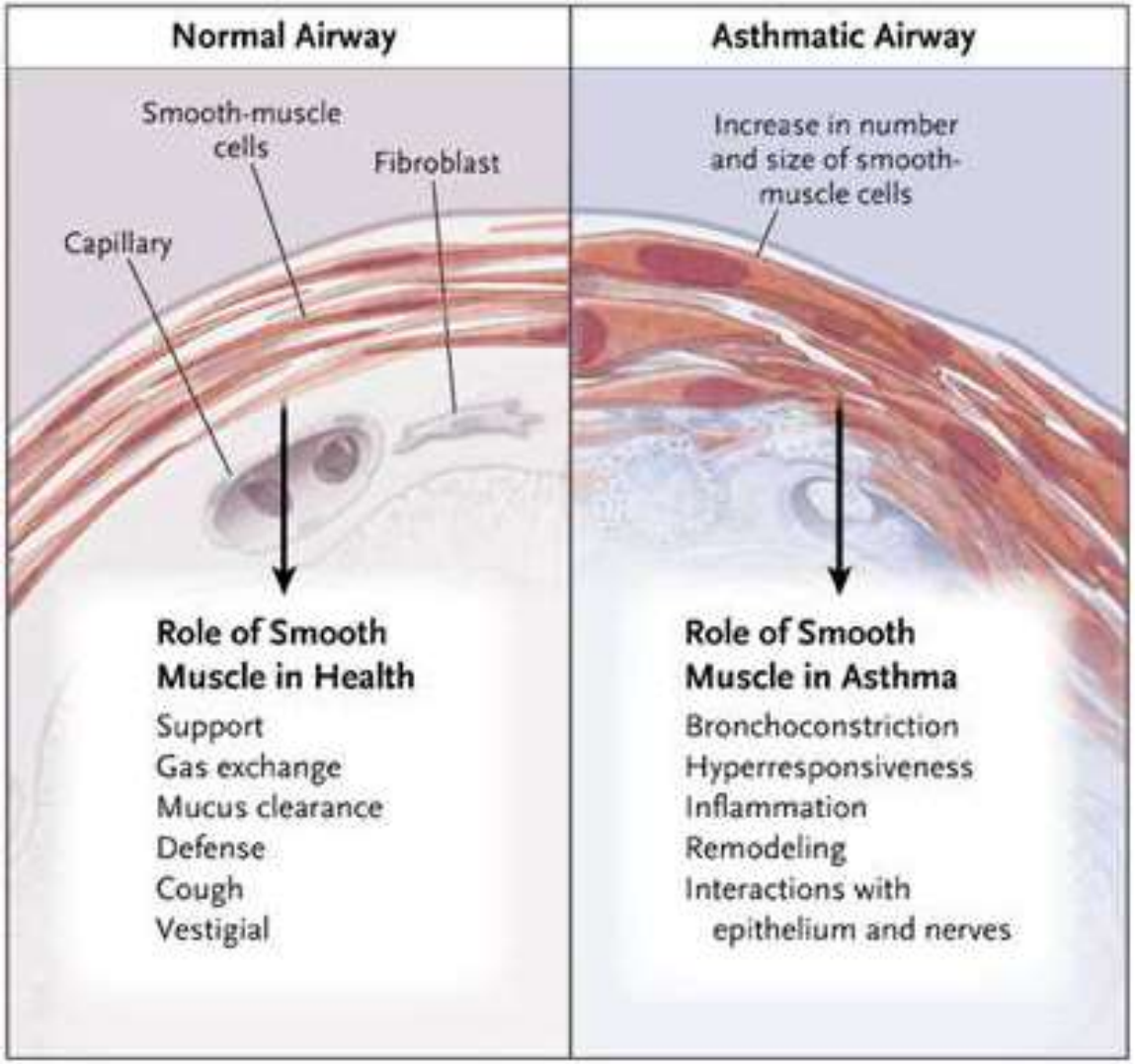
Biomarkers for severe asthma

Biomarker	Testing method	Phenotype	Role in allergic pathway	Associated cytokines	Associated biologic agents
IgE	Serum	Allergic (early onset)	Binds to FcεRI on mast cells, basophils, and antigen-presenting dendritic cells Activates the release of inflammatory mediators	IL-4, IL-13	Omalizumab
Eosinophil	Blood, sputum	Eosinophilic (late onset)—allergic and non-allergic	Modulates the immune response Promotes airway hyper-responsiveness and remodelling	IL-5 IL-4, IL-13	Mepolizumab, reslizumab, benralizumab Dupilumab
Neutrophil	Sputum	Neutrophilic	Significantly associated with severe asthma Accumulates in the airways Prominent in airway secretions during exacerbations	IL-8, IL-17	
Surrogate					
Periostin	Serum, sputum	Eosinophilic	Regulates eosinophil recruitment and eosinophilic tissue infiltration Active in Th2 mucosal inflammation, airway remodelling, and expression of inflammatory mediators	IL-4, IL-13	Lebrikizumab, tralokinumab, omalizumab
DPP-4	Serum	Eosinophilic, AERD	Stimulates the proliferation of bronchial smooth muscle cells and human fetal lung fibroblasts Promotes fibronectin production	IL-13	Tralokinumab

DPP-4 dipeptidyl peptidase-4, *IgE* immunoglobulin E, *IL* interleukin

Harold Kim et al; Allergy, asthma and clinical immunology 2017 13:48

GINA stepwise approach to control symptoms and minimize future risk[1]


Normal Airway
Asthmatic Airway
Smooth-muscle cells
Fibroblast
Capillary
Increase in number and size of smooth-muscle cells
Role of Smooth Muscle in Health
Support
Gas exchange
Mucus clearance
Defense
Cough
Vestigial
Role of Smooth Muscle in Asthma
Bronchoconstriction
Hyperresponsiveness
Inflammation
Remodeling
Interactions with epithelium and nerves

Bronchial Thermoplasty(BT)

- Minimally invasive therapeutic intervention
- Targeted radiofrequency thermal energy to airway walls
- A catheter introduced through the working channel of the bronchoscope
- Partial ablation of the airway smooth muscle

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

Mechanism of action

Reduces Airway Smooth Muscle (ASM)

↓

Reduces Bronchoconstriction

↓

Reduces Asthma Exacerbations

↓

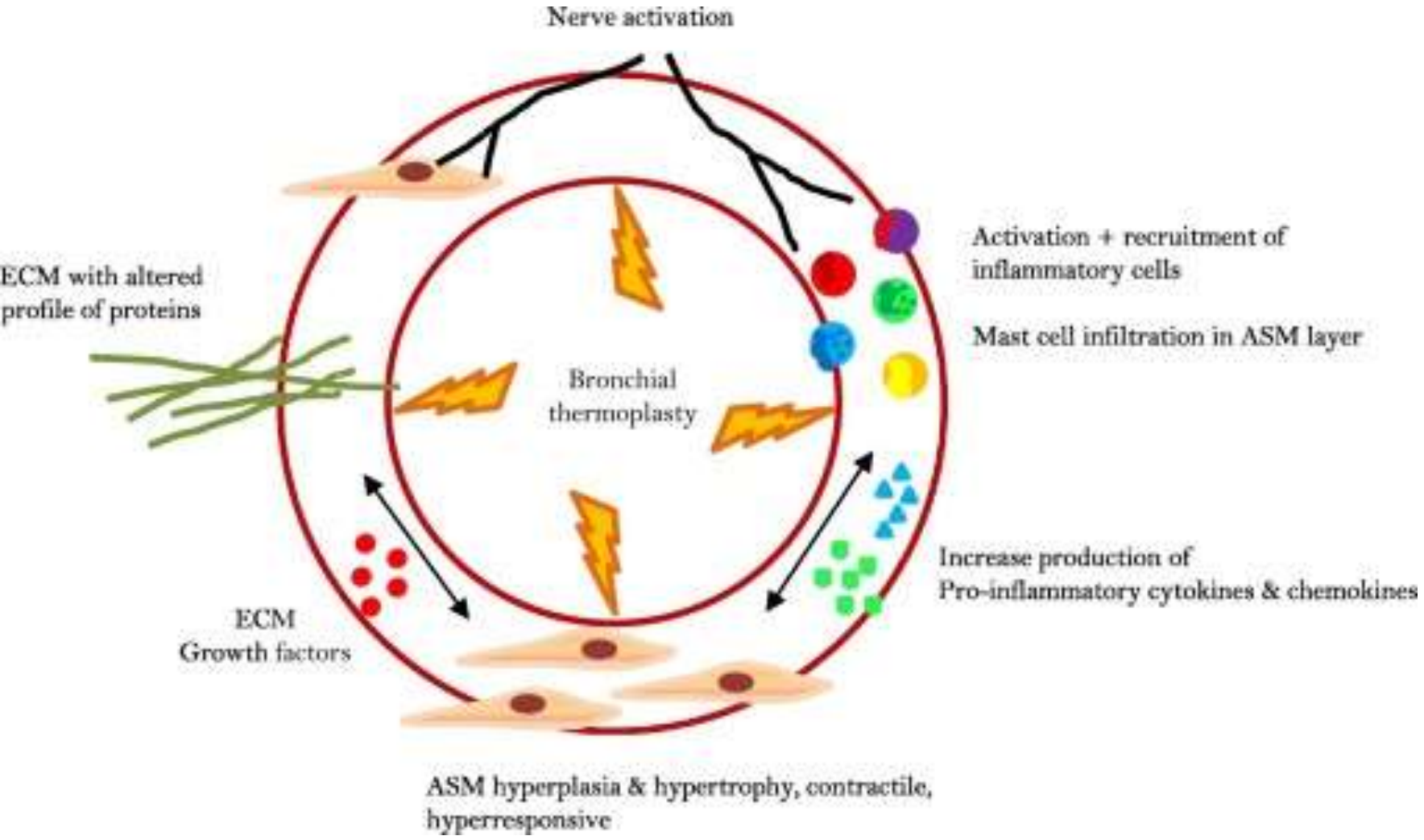
Improves Asthma Quality of Life

Mechanism of action

- Alterations in the structure and function of
  - epithelial cells
  - nerves
  - extracellular matrix
  - inflammatory cells
- Reduction in submucosal nerves and number of epithelial neuroendocrine cells can be associated with the decrease in severe exacerbations after BT

Neil C Thomson (2018): Expert Review of Respiratory Medicine, DOI: 10.1080/17476348.2018.1444991

Mechanism of action



PATIENT SELECTION

- Bronchial thermoplasty is a potential treatment option at step 5 in some countries for adult patients whose asthma remains uncontrolled despite optimised therapeutic regimens and referral to asthma speciality centre

Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. Updated 2018

Eligibility criteria for bronchial thermoplasty used in pivotal clinical trials

- Adult aged 18–65 years
- Asthma requiring regular maintenance medication that includes inhaled corticosteroids (>1000 μg beclometasone per day or equivalent) and long-acting β_2-agonists, with or without other asthma medications; oral corticosteroids at a dosage ⩽10 mg per day
- AQLQ score [20] of 6.25 or less
- Non-smoker for ⩾1 year or greater (if a former smoker, <10 pack-years total smoking history)
- Post-bronchodilator FEV_1 ⩾ 65% predicted
- Not excessively using their short-acting bronchodilator (in excess of 12 puffs per day within 48 h of bronchoscopy, excluding prophylactic use for exercise)
- None of the following within the past 12 months:
  ⩾4 lower respiratory tract infections;
  ⩾4 oral corticosteroid pulses for asthma exacerbation;
  ⩾3 hospitalisations for respiratory symptoms
- No history of intubation for asthma or intensive care unit admission for asthma within the prior 24 months
- No evidence of other respiratory diseases including emphysema, vocal cord dysfunction, mechanical upper airway obstruction, cystic fibrosis or uncontrolled obstructive sleep apnoea
- No conditions associated with increased risk for adverse events associated with bronchoscopy or anaesthesia, such as pregnancy, insulin dependent diabetes, epilepsy or other significant comorbidities (*e.g.* uncontrolled coronary artery disease, acute or chronic renal failure and uncontrolled hypertension)
- Patient considered suitable for bronchoscopy

PATIENT SELECTION

Adults diagnosed with severe asthma

- Symptomatic despite treatment with stable maintenance medication (High dose ICS and LABA)
- Requires treatment for GINA step 4-5 for the previous year or OCS for 50% of the previous year to prevent uncontrolled or which remains uncontrolled despite this therapy
- Alternative diagnoses to asthma have been excluded
- Comorbidities have been treated and controlled(e.g. GERD, rhinitis, OSA, VC dysfunction, smoking)

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

PATIENT SELECTION

- Compliance verified and checked
- Able to undergo bronchoscopy safely
- No internal pacemaker or neurostimulator
- Age 18-65 years
- Caution with prebronchodilator FEV1 <60% predicted (experienced BT centers may use lower cutoff upto 35%)
- Current or past asthma biologic therapy does not preclude BT
- Environmental factors at the time of BT that could result in a severe exacerbation

- Pre procedure work up
  - CBC with diff
  - IgE
  - Regional serum allergen panel
  - PFT with BDR(should include DLco and lung volumes)
  - CXR/ CT scan*
- Start OCS 50mg/day 3 days before procedure and continue till the day after

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

On the 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 $\geq$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

PATIENT PREPARATION

- Transnasal or transoral approaches depending on the individual patient
- Moderate(conscious) sedation with BZD plus fentanyl
- Topical lidocaine to the nostrils and hypopharynx
- Topical anesthesia to the vocal cords and bronchial tree
- Doses of lidocaine totaling up to 600 mg or 8.2 mg/kg have been found to be safe

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

- Patient comfort is paramount
- Deep sedation and general anesthesia require the presence of an anesthesiologist
- MAC, LMA, and ET intubation ± mechanical ventilation
- BT through an LMA is preferable as ET tube can cause bronchospasm
- Avoidance of “drying agents”(atropine)

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

Equipment

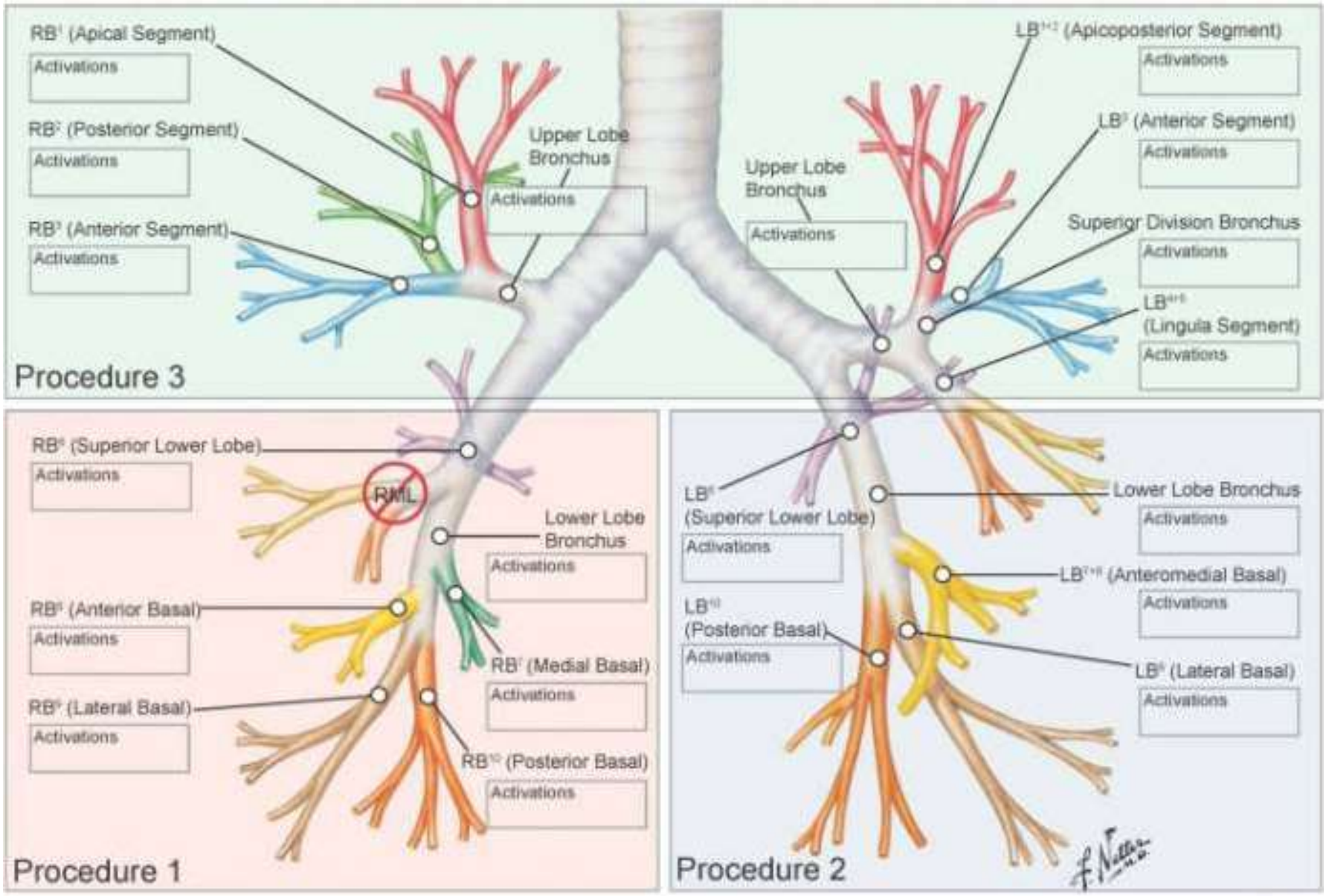
- RF-compatible bronchoscope- outer diameter of 4.9 to 5.2 mm and a minimum 2.0-mm working channel
- Alair Bronchial Thermoplasty System
  - RF Controller
  - flexible Alair Catheter
  - adhesive gel-pad patient electrode
- Distal tip of catheter contains an expandable four-electrode basket

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

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



3 sessions lasting 45-60 min scheduled 2-3 weeks apart each

Right Middle Lobe Syndrome

- In the original trials the RML was not treated due to the risk of causing stenosis to this typically narrow bronchus
- Some centres are treating the RML without complications and large ventilation defects have been shown in this lobe via hyperpolarized MR imaging studies so treating this lobe may be beneficial

Faria Nasim; Ann Thorac Med 2018;13:205-11.

Technique

- Under direct visualization through the flexible bronchoscope, the electrode array is introduced and expanded to contact the airway walls
- RF energy is delivered only when the electrodes are appropriately contacting the airway walls

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

Technique

- RF energy is transferred from the electrode through the airway wall and is converted to thermal energy when absorbed by high-resistance tissue(smooth muscle)
- With each activation, the RF controller delivers the correct intensity and duration of RF energy(65^0 C for 10 sec)

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

Technique

- Moving the catheter from distal to proximal along the airway, contiguous and nonoverlapping activations are performed systematically
- Airways between 3 and 10 mm in diameter distal to mainstem bronchi
- BT decreases ASM mass, bronchial nerve endings, and neuroendocrine cells

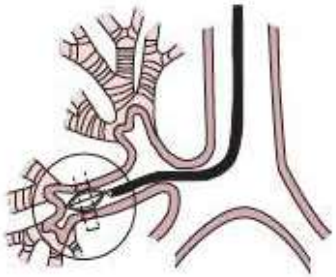
Aoife O'Reilly et al; Ther Adv Respir Dis 2018, Vol. 12: 1–7
Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

Technique

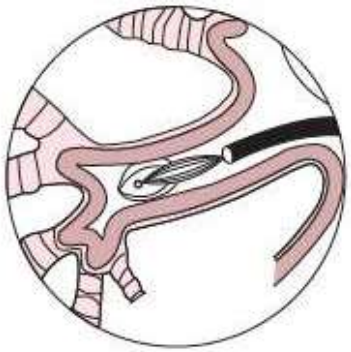
- A detailed “road map” of the airways
  - assists in keeping track of the progression of treatments and minimizing errors
- During 2nd and 3rd sessions, the previously treated BT airways should be inspected to ensure proper healing before proceeding with the procedure

Langton D et al; Respir Res 2017;18:134

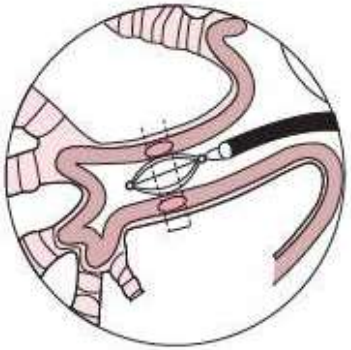
Technique



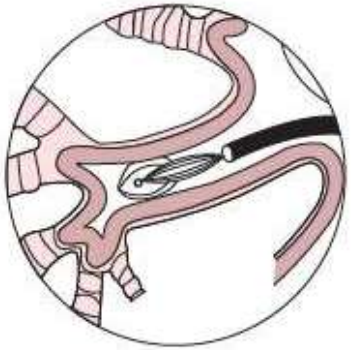
Catheter placed distally in airway, electrode array expanded and controller activated



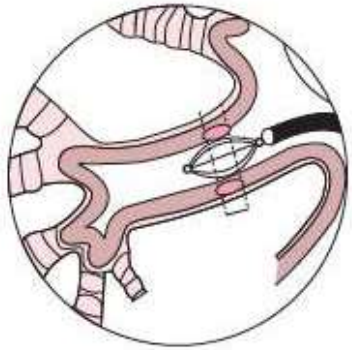
Electrode array partially collapsed and moved 5 mm proximal to previous activation



Electrode array expanded and adjacent but not overlapping activation completed



Electrode array partially collapsed and moved 5 mm proximal to previous activation



Electrode array expanded and adjacent but not overlapping activation completed

Technique

- Importance of delivering the sufficient number of activations on clinical response
- 40 activations to each of the lower lobes and 60 activations to the combined upper lobes to achieve an improvement in ACQ score of 0.5

Langton D et al; Respir Res 2017;18:134

POSTPROCEDURAL CARE

- Careful monitoring
- Discharge only when
  - vitals stable
  - sensorium regained
  - able to swallow liquids
  - spirometry is acceptable(FEV1≥80% of pre-BT FEV1 that day)

Chupp G et al; Eur Respir J 2017;50:1700017

POSTPROCEDURAL CARE

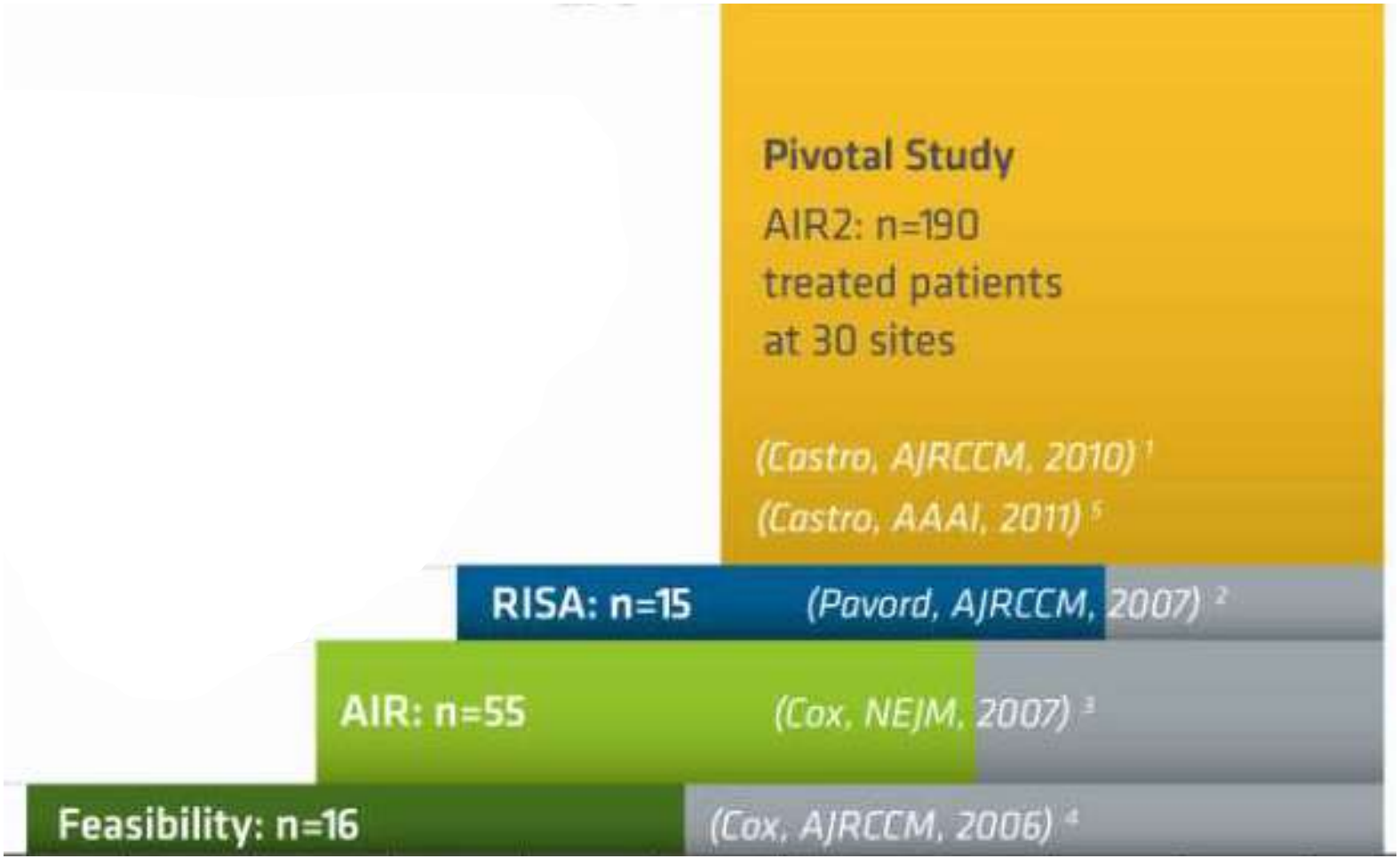
- Increases in respiratory-related adverse effects in patients with higher severity of disease
- Commonly- Worsening asthma symptoms and URTI
- Symptoms usually present within 1 week with resolution within another 1 week

Chupp G et al; Eur Respir J 2017;50:1700017

- Intrapulmonary percussive device (acapella device) at 30 exhalations TDS with nebulized bronchodilators 3 to 4 times a day for the first few days may be useful
- Patient and family education

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

Evidence



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

Trial	Year published	Study design	Number of patients	Randomization	Age (years)	Pre-BD FEV1 (% predicted)	ICS dose (mg/days) (beclome thasone or equivalent)	OCS dose (mg/days)	Primary endpoint
AIR	2007 (NEJM)	RCT	55 BT, 54 control	1:1 (BT: Control)	18-65	60-85	>200	0	Exacerbations
RISA	2007 (AJRCCM)	RCT	15 BT, 17 control	1:1 (BT: Control)	18-65	>50	>1500	<30	AQLQ
AIR-2	2010 (AJRCCM)	RCT/DB/sham controlled	196 BT, 101 control	2:1 (BT: Sham)	18-65	>60	>1000	<10	AQLQ

Preclinical studies

- 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%

Danek CJ et al; J Appl Physiol (1985) 2004;97:1946-53

Asthma Intervention Research [AIR] 1

- First RCT of BT(n=112; 1:1)
- Effect of BT on the control of moderate or severe persistent asthma
- Primary outcome: Frequency of mild exacerbations at 3, 6,and 12 months (at 2-week periods of abstinence from LABA)
- Secondary outcome: FEV1, PC20, asthma symptoms, the number of symptom-free days, use of rescue medication, and AQLQ and ACQ

Cox G et al. N Engl J Med 2007;356:1327-37

Asthma Intervention Research [AIR] 1

- The mean rate of mild exacerbations decreased in BT group

  (−0.16 ± 0.37 vs. 0.04 ± 0.29; P = 0.005)
- Significant improvements in asthma symptom-free days and asthma-related quality of life
  - ACQ reduction: 1.2 ± 1.0 vs 0.5 ±1.0; P = .001
  - AQLQ: 1.3 ± 1.0 vs 0.6 ± 1.1; P = .003
- No differences in FEV1 or airway hyperresponsiveness (PC20)

Cox G et al. N Engl J Med 2007;356:1327-37

Asthma Intervention Research [AIR] 1

- Adverse events
  - More common in the bronchial thermoplasty group than in the control group immediately after treatment (<6week)
  - Similar during the period from 6 weeks to 12 months after treatment
- Dyspnea, wheeze, cough, sputum production, chest discomfort, nocturnal symptom, URTI, bronchial irritation

Cox G et al. N Engl J Med 2007;356:1327-37

Research in Severe Asthma [RISA]

- Enrolled patients with more severe symptoms (n=32;1:1)
- Significant improvement
  - in FEV1 (14.9±17.4 vs 0.9±22.3; P= .04) at 22 wks
  - in ACQ (-1.04 ±1.03 vs -0.13 ±1.00; P= .02)
- Non significant improvement in FEV1 @52wk
- RCT not blinded

Pavord ID et al; Am J Respir Crit Care Med 2007;176:1185-91

AIR2

- Largest Multicentre RCT, sham controlled (n=288; 2:1)
- Effectiveness and safety of BT vs a sham procedure in subjects with severe asthma
- Primary outcome: difference from baseline in the integrated AQLQ score at 12 months

Castro M et al; Am J Respir Crit Care Med 2010;181:116-24

AIR2

- The improvement in the integrated AQLQ score superior in the BT group
  - (BT, 1.35±1.10; sham, 1.16±1.23)
  - [PPS, 96.0% ITT and 97.9% per protocol]
- Subjects achieving change ≥0.5 in AQLQ: 79%Vs 64% (PPS, 99.6%)

Castro M et al; Am J Respir Crit Care Med 2010;181:116-24

AIR2

- 6% more BT subjects hospitalized in 1st 6wks
- At 6–52 wk, the BT group- fewer severe exacerbations, ED visits, and days missed from work/school
  - (PPS, 95.5, 99.9, and 99.3%)

Castro M et al; Am J Respir Crit Care Med 2010;181:116-24

- On the basis of this trial, BT was approved by the FDA in 2010 for the treatment of severe persistent asthma not controlled with high-dose ICS and LABA

Laren D. Tan et al; J Allergy Clin Immunol Pract 2019;7:71-80

Long term results: PAS2

- Post marketing study of 190 BT patients
- At 3 years, reduction in severe exacerbations, ED visits, and hospitalizations by 45%, 55%, and 40%, respectively
- FEV1 remained unchanged
  - Pre-BD FEV1(% predicted) - 79.6 Vs 76.3
  - Post-BD FEV1(% predicted) - 84.8 Vs 82.3

Chupp G et al; Eur Respir J 2017;50:1700017

- Mean daily ICS dose reduced to 2070 µg/day* from 2300 µg/day (p=0.003)
- % of subjects taking daily OCSs reduced from 18.9% to 10.2% (p=0.0004)
- Similar results echoed in 3 year follow up of AIR2

*beclomethasone equivalent

Chupp G et al; Eur Respir J 2017;50:1700017

Long-term efficacy and safety of bronchial thermoplasty in patients with moderate-to-severe persistent asthma: a systemic review and meta-analysis

Jian Ping Zhou MD, Yun Feng MD, PhD, Qiong Wang MD, Li Na Zhou MD, Huan Ying Wan MD & Qing Yun Li MD, PhD

- Meta analysis of 6 RCTS
- N= 216
- 5 yr follow up of pts undergoing BT
- Differences in outcomes between V1 and V5

V1- parameters at 1yr follw up
V5- parameters at 5yr follw up

Jian Ping Zhou et al; Journal of Asthma, DOI:10.3109/02770903.2015.1065424

- Unchanged FEV1 between V1 and V5
  - Pre-BD FEV1 (% predicted) (WMD=0.75; 95% CI: 3.36 to 1.85; p=0.57)
  - Post-BD FEV1 (% predicted) (WMD=0.62; 95% CI: 3.32 to 2.08; p=0.65)
- Frequency of exacerbations reduced (RR=3.41, 95% CI: 2.96–3.93, p<0.00001)

- The number of ED visits remained unchanged (RR=1.06, 95% CI: 0.77–1.46, p=0.71)
- No statistically significant increase in the incidence of hospitalization (RR=1.47, 95% CI: 0.69–3.12, p=0.32)

What to expect from BT

- Not a cure of asthma
- Initial increase in symptoms in treatment period
- Subsequent decrease in exacerbations and improvement in asthma control
- May decrerase the medication dose
- No improvement in lung functions
- Extended follow up suggests sustained reduction in exacerbations as compared to pre-treatment period

?Placebo effect

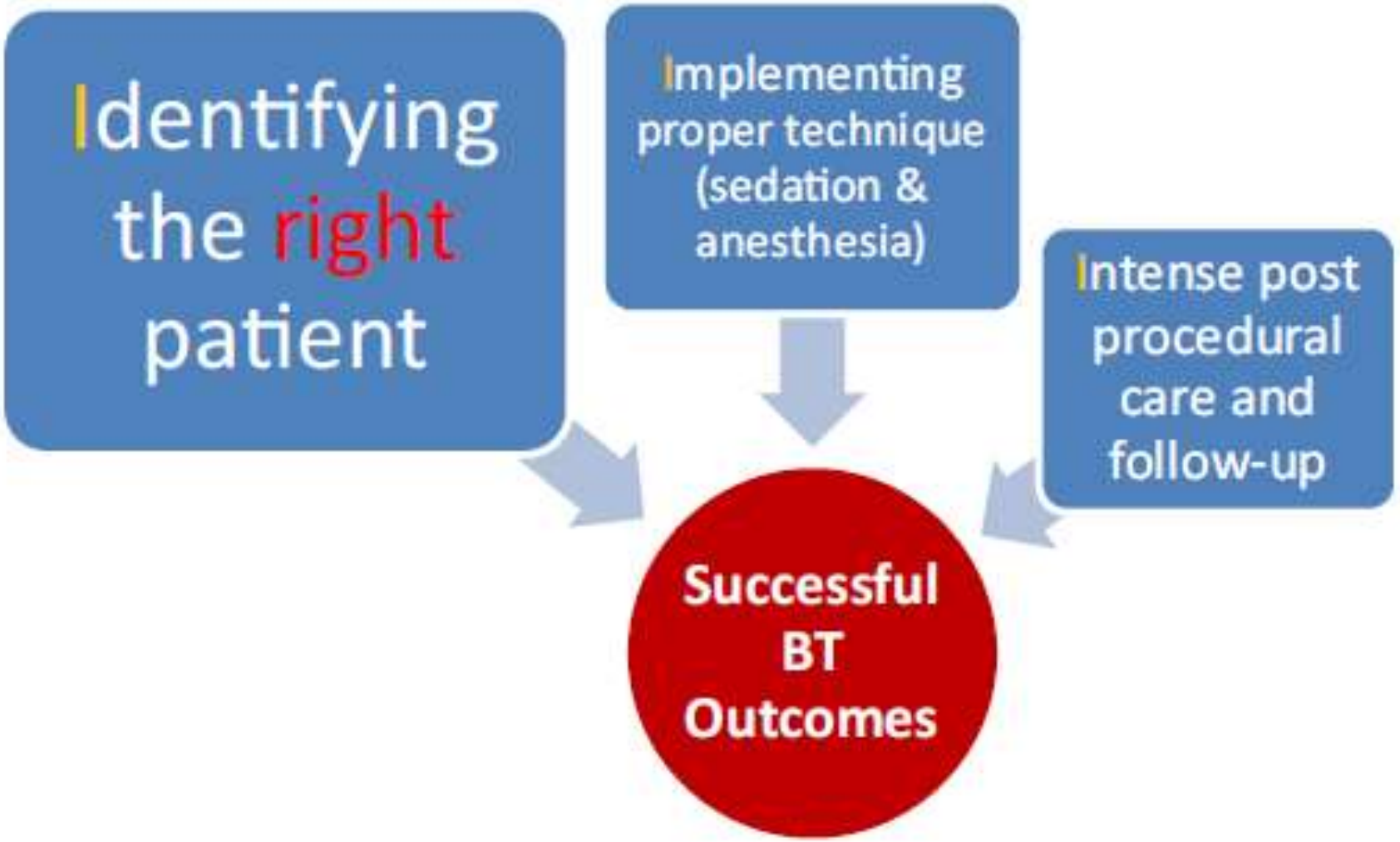
- The only sham-controlled trial of BT (the AIR-2 trial) failed to achieve its primary end-point
- Major societies including the ATS and the ERS recommend that BT be performed in the context of an Institutional Review Board approved independent systematic registry or a clinical study

Predictors of response to BT

- On CT pulmonary peribronchial consolidation can be seen
- No clinical implications and resolve in most patients within one to six months

Debray M-P et al; Eur Respir J, 49(3) (2017)

i3 key points for BT success



Predictors of response

- Lack of evidence about which subphenotype of severe asthma should be treated with bronchial thermoplasty compared to other treatments, such as biological agents
- Patients with non-eosinophilic inflammation might benefit

Neil C Thomson (2018): Expert Review of Respiratory Medicine, DOI: 10.1080/17476348.2018.1444991

Predictors of response

- Lower serum periostin levels and exhaled nitic oxide (FeNO) levels may predict responders
- Detection of amount of airway smooth muscle at baseline and its reduction subsequently is being studied
- Optical coherence tomography of the airway can detect the thickness of airway wall as a response

Likura M et al; *Am J Respir Crit Care Med, 195, A3208 (2017).*
Neil C Thomson (2018): Expert Review of Respiratory Medicine, DOI: 10.1080/17476348.2018.1444991

Comparison With Biological Therapy

- No clinical trials that have directly compared two modalities
- One study, using data from the AIR2 trial of bronchial thermoplasty and two placebo-controlled trials of omalizumab, reported broadly similar clinical outcomes with the two treatments, including severe exacerbations, emergency department visits, and hospital admissions

Neil C Thomson (2018): Expert Review of Respiratory Medicine, DOI: 10.1080/17476348.2018.1444991
Niven RM et al. *J Asthma, 1-9 (2017)*

Bronchial thermoplasty in India

- The first BT procedure in India was performed in Royal Care Hospital, Coimbatore in June 2017
- BT has been performed in private institutes mainly
- Recently performed in AIIMS, Delhi
- Costs close to Rs 1.5 lakhs per sitting

Non pharmacological modalities in COPD

- LVRS(Lung volume reduction surgery)
- In NETT trial, subgroup analysis shown to prolong survival in patients with upper lobe predominant emphysema and low functional capacity but with a high incidence of postoperative complications
- These results severely limit the applicability of LVRS

Fishman A et al; N Engl J Med 2003 22;348:2059-73

Bronchoscopic treatments

- Two groups of devices
- Blocking
  - ELVR with one way valves
- Nonblocking
  - Lung volume reduction using coils (LVRC)
  - Liquid Nitrogen Metered Cryospray
  - Polymeric lung volume reduction (PLVR)
  - Targeted lung denervation (TLD)

Konstantina Kontogianni & Ralf Eberhardt (2018): Expert Review of Respiratory Medicine, DOI: 10.1080/17476348.2018.1491794

Valves

- Devices designed to prevent air from flowing into the most damaged lobe of the lung
- Whilst prevented to enter the lobe, air is able to exit the lobe- resorption atelectasis
- First RCT assessing endobronchial valves in 2010 showed only a relatively small benefit in favour of the valves

Konstantina Kontogianni & Ralf Eberhardt (2018): Expert Review of Respiratory Medicine, DOI: 10.1080/17476348.2018.1491794

- Later studies have shown that when the completeness of the fissure is deemed present as assessed on HRCT before the procedure, the responder rates increase and a significant benefit in symptoms and FEV1 occurs

Konstantina Kontogianni & Ralf Eberhardt (2018): Expert Review of Respiratory Medicine, DOI: 10.1080/17476348.2018.1491794

Targeted Lung Denervation

- Aimed to disrupt parasympathetic pulmonary nerves surrounding the main bronchi using a special RF-energy releasing system, thereby decreasing the release of ACh in the airways, resulting in a permanent anti-cholinergic effect
- TLD is a technically simple procedure whereby a catheter is advanced bronchoscopically into the main bronchus

Slebos et al., 2015

Targeted Lung Denervation

- After positioning the catheter, energy of 15–20 watts are delivered to ablate the parasympathetic pulmonary nerves which are surrounding the main bronchi
- TLD is performed bilaterally in both main bronchi and it can be performed in one or two settings

Slebos et al., 2015

Targeted Lung Denervation

- In the 1st feasibility study, total 22 patients underwent TLD bilaterally with 20 watts (n=12) or 15 watts (n=10) in two therapeutic procedures
- At 3 months, patients treated at the higher power level experienced significant improvement of forced vital capacity and of SGQR

Slebos et al., 2015

Targeted Lung Denervation

- At 1 year, changes from baseline in the 20 W dose compared to the 15 W dose were: FEV1 (+11.6%±32.3 vs +0.02%±15.1, p=0.324)
- Common severe adverse event was COPD exacerbation

International Journal of COPD

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ORIGINAL RESEARCH

Long-term safety of bilateral targeted lung denervation in patients with COPD

Arschang Valipour et al; International Journal of COPD 2018:13 2163–2172

- 15 patients with moderate-to-severe COPD [FEV^1] 30%–60% underwent bilateral TLD(15W) treatment following baseline assessment without bronchodilators
- The primary safety end point was freedom from documented and sustained worsening of COPD directly attributable to TLD up to 1 year

- Secondary end points included technical feasibility, change in PFT, exercise capacity, and health-related quality of life
- Primary end point achieved in 100% pts
- A total of 12 SAEs were reported during the follow-up mainly 5 COPD exacerbations
-

Table 4 Baseline and outcomes at 365 days

Lung function test	n=15		
	Baseline	**365 days**	**Percent change from baseline**
FEV_1 (mL)	765.33 (237.45)	1,012.14 (272.99)	40.29 (42.12)*
FVC (mL)	2,248.00 (614.05)	2,605.00 (634.59)	19.25 (24.84)*
	Baseline	**365 days**	**Absolute change from baseline**
Cycle ergometry (min)	7.36 (2.96)	9.81 (4.92)	2.68 (6.06)
Borg scale: post-cycle dyspnea	5.4 (2.35)	4.64 (1.21)	–0.82 (1.83)
mMRC	2.27 (1.03)	1.60 (1.06)	–0.67 (1.05)
6MWT (m)	361.8 (125.62)	415.47 (112.76)	53.67 (74.40)*
SGRQ: total score	47.95 (16.97)	49.37 (20.93)	–1.85 (20.77)
CCQ: total score	2.71 (1.17)	2.63 (1.41)	0.00 (1.29)

- **Conclusion:** This intervention study adds to the early body of evidence confirming the feasibility and safety of TLD in patients with symptomatic moderate-to-severe COPD

Liquid Nitrogen Metered Cryospray

- Bronchoscopically delivered liquid nitrogen to the central airways in such a way that is leads to a cryoablation depth of 0.1 to 0.5 mm for the treatment of chronic bronchitis
- Intended to induce a regenerative airway tissue healing effect, by initially destroying the hyperplastic goblet cells and excess submucous glands by cryo necrosis

- After treatment rapid rejuvenation of normal epithelium occurs, without scarring occurs
- Human studies for this approach are undeway

Take home message

- Bronchial Thermoplasty is potential treatment option in selected patients with severe asthma
- Modest clinical benefit in long term after initial worsening of symptoms
- Exact mechanism and potential candidates who will respond not known
- Major societies still advise to carry out this procedure in research settings only
- Bronchoscopic modalities may have potential role in COPD too