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Bronchial Thermoplasty – Principles and Controversies

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Bronchial Thermoplasty – Principles and Controversies

Pulmonary Grand Rounds
October 29, 2014
David R. Manoff, M.D

Objectives

- Learn the indications and contraindications for bronchial thermoplasty
- Develop a basic understanding of the controversies about, and the barriers to, the use of thermoplasty
- Understand the peri-procedural care and follow-up of patients who receive bronchial thermoplasty

Conflicts of interest

- None

Our patient: a 54 year-old woman who presents with difficult to control asthma

- Initially presented in April 2014 for evaluation for bronchial thermoplasty
- Diagnosed 12 years prior to visit
- In year before presentation
  - Three exacerbations requiring systemic corticosteroids
  - Two hospitalizations for asthma exacerbations
  - Five ED visits
- On Symbicort 160/4.5 HFA, Montelukast 10 mg PO daily, PRN Albuterol HFA, which she uses daily
- Reports severe debility and unemployed for two months since last hospitalization

- Past Medical History
  - GERD
  - Obstructive sleep apnea on CPAP 9 cm H2O
- Social History
  - Lifetime non-smoker
  - Lives in a house in process of being recarpeted
  - Two birds (cockatiels), no other animals
- Physical exam unremarkable
- Spirometry
  - FEV-1 2.81 liters (114% predicted)
  - FVC 3.18 liters (106% predicted)
  - FEV-1/FVC ratio 80%

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Is the patient appropriate for proceeding with bronchial thermoplasty

…but wait. What is bronchial thermoplasty really?

- Essentially, the application of radiofrequency to the proximal airways to ablate smooth muscle
- Decrease airway hyperresponsiveness by decreasing the ability of smooth muscle to constrict leading to decreased resistance

- FDA approval for patients 18 years-old and older with "severe and persistent asthma not well-controlled with inhaled corticosteroids and long-acting beta agonists"

Iyer, VN, Lim, KG. Chest (2014); 146: 17-21.

What do the guidelines say?

- ATS/ERS Consensus on treatment of severe asthma
- "We recommend that bronchial thermoplasty is performed in adults with severe asthma only in the context of an Institutional Review Board-approved independent systematic registry or a clinical study (strong recommendation, very low quality evidence)."
- Why?
  - Long term consequences unknown
  - Invasive procedure
  - Authors felt further characterization of subgroups needed

Chung, et al. Eur Resp J (2014); 43: 343-73.

The theory

Reduction in airway hyperresponsiveness to methacholine by the application of RF energy in dogs

Christopher J. Danek,[1] Charles M. Lombard,[2] Donald L. Dungworth,[3]
P. Gerard Cox,[4] John D. Miller,[4] Michael J. Biggs,[5] Thomas M. Keast,[5]
Bryan E. Loomas,[5] William J. Wizeman,[1] James C. Hogg,[6] and Alan R. Leff[7]

- Based on recognition that airway smooth muscle contractility leads to increased airway resistance and decreased diameter
- 11-dog study using a graded methacholine challenge both pre-and-post RF ablation of proximal airways
- All thermoplasty was performed in a single procedure

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

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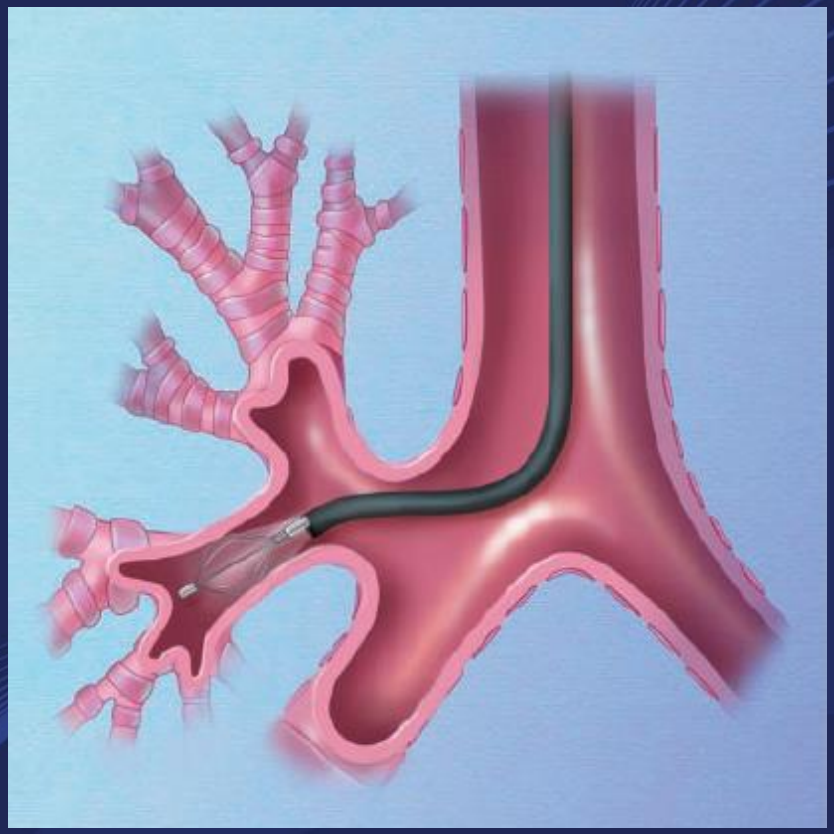

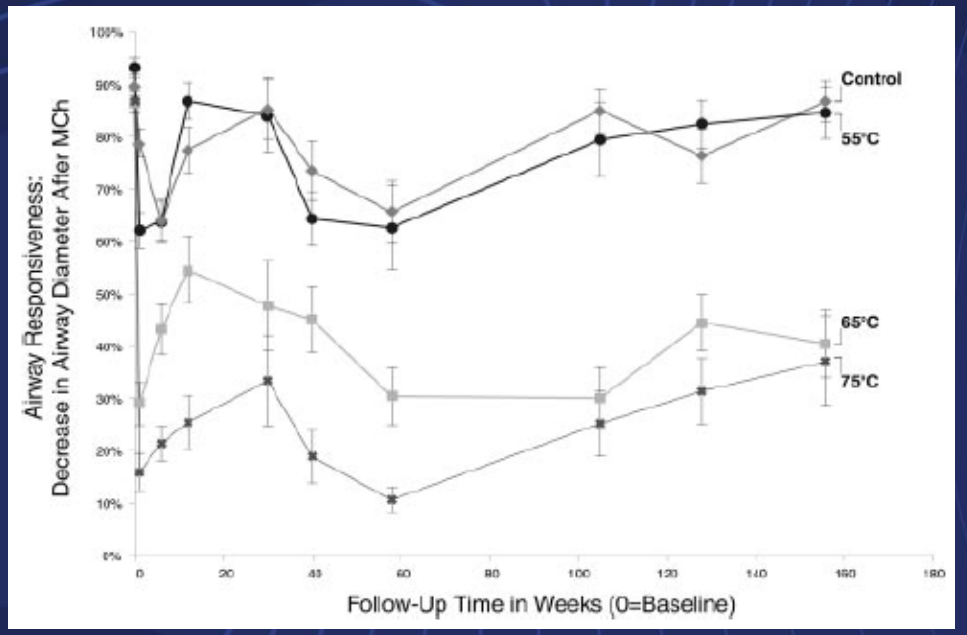

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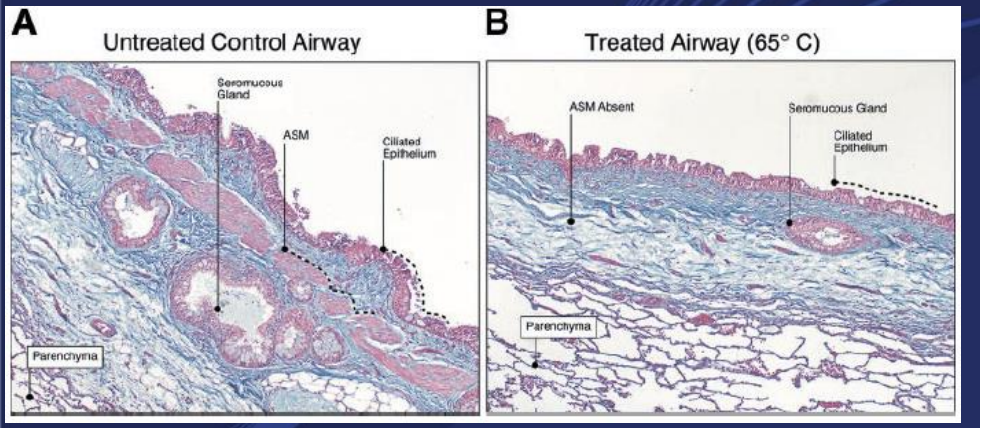
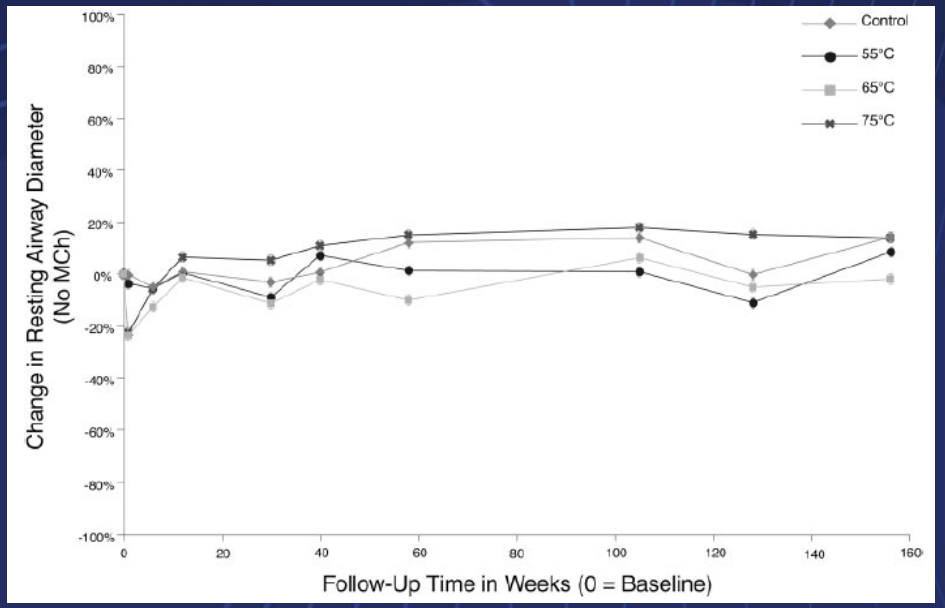




First human trials

A Prospective Feasibility Study of Bronchial Thermoplasty in the Human Airway*

John D. Miller, MD; Gerard Cox, MB; Lydia Vincic, MD; Charles M. Lombard, MD; Bryan E. Loomas; and Christopher J. Danek, PhD

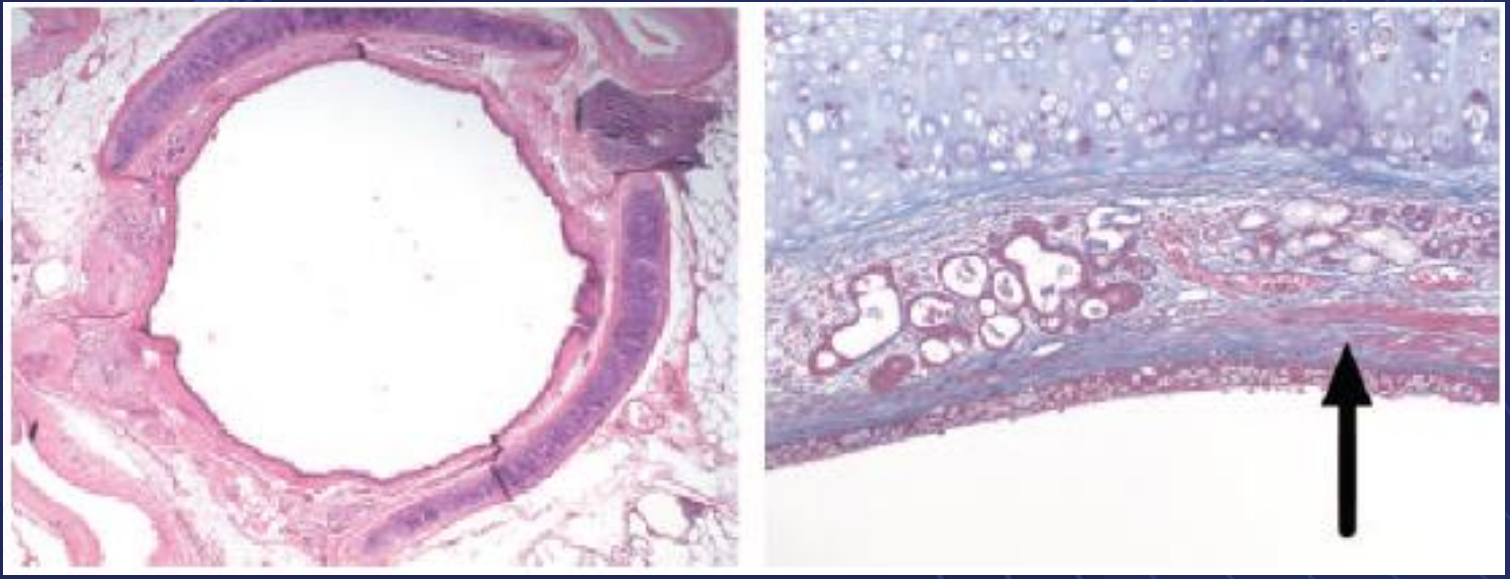
- 9 patient prospective trial of patients scheduled to undergo resection of known or suspected malignancy
- Thermoplasty only performed in areas of lung to be resected
- Tissue evaluated by histological examination after lung tissue resected

Miller, JD, et al. Chest (2005); 127: 1999-2006.

Table 2—*Perioperative Bronchoscopic Observations by Treatment Temperature, Listed According to Length of Follow-up**

Patient No.	Treatment Temperature, °C	Lobe	Activations, No.	Airways Treated, No.	Days of Follow-up, No.	Perioperative Bronchoscopic Observations
4-01	55	RLL	3	3	8	NRO
4-02	55	RLL	9	7	12	NRO
4-05	65	LLL	6	4	5	Two airways: narrowing† with excessive mucus One airway: narrowing†
4-08	65	RUL	9	6	9	NRO
4-06	65	RLL	6	4	11	NRO
4-09	65	LLL	8	5	13	Possible narrowing, erythema of one airway
4-03	65	LLL	7	7	18	NRO
4-04	65	LLL	5	3	20	Linear blanching in three airways

*NRO = no remarkable observation. See Table 1 for expansion of abbreviations.
†Visually estimated as 25 to 50% reduction in airway diameter.

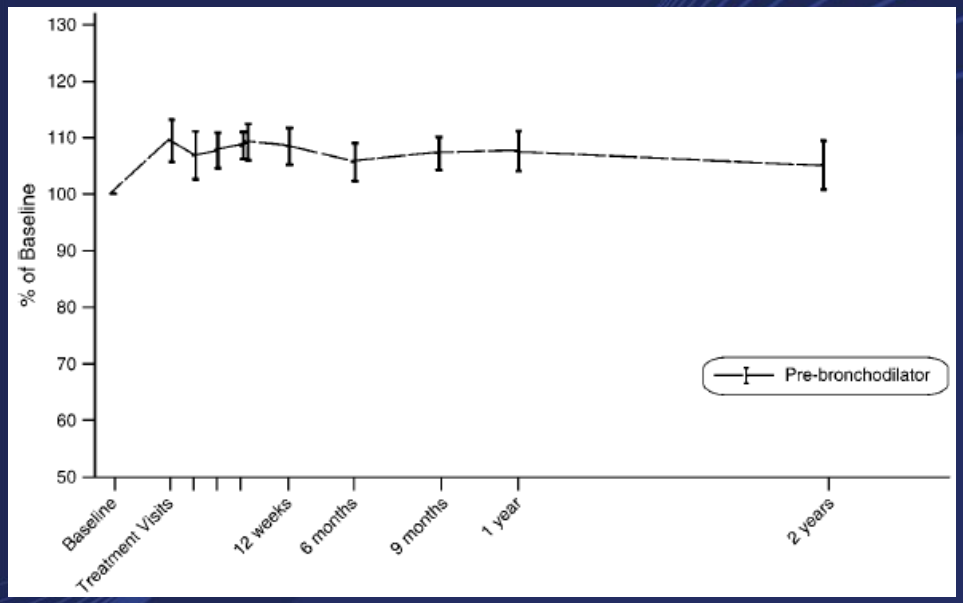


- Again demonstrated minimal changes with RF ablation at 55^{O} C but more marked changes at 65^{O} C
- Epithelium either normal (3/9 patients) or demonstrated sloughing to regeneration
- Patient with shortest follow-up (5 days) had glandular necrosis
- Non-infectious pneumonitis present in 27% of pathology sections but no evidence of infectious pneumonitis
- Clinically, no post-procedural hemoptysis, infections, additional clinic/ER visits, no need for additional bronchodilators

First studies in asthmatics

- Cox (2006)
  - 16 patient prospective study of patients with stable, mild-moderate asthma
    - No changes to medications or symptoms in six weeks prior to study
  - All patients pre-treated with corticosteroids
  - Three sessions per patient, each three weeks apart
    - One for each lower lobe
    - One for bilateral upper lobes
    - Right middle lobe not treated
  - Follow-up with chest X-ray, EKG, methacholine challenge

Cox, G, et al. Am J Resp Crit Care Med (2006); 173: 965-9.



- Baseline pre-bronchodilator FEV-1 maintained post-procedure
- For Methacholine PC_{20} means
  - Baseline 0.92 mg/mL
  - 4.75 mg/mL at 12 weeks
  - 5.45 mg/mL at 1 year
  - 3.40 mg/mL at 2 years
  - At 12 weeks 5/16 patients did not demonstrate a 20% decrease in FEV-1 with 16 mg/mL of methacholine

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TABLE 3. MORNING AND EVENING PEAK EXPIRATORY FLOWS AND SYMPTOM-FREE DAYS

	Evaluation Period		
	Baseline	12 wk after Bronchial Thermoplasty	p Value
Morning PEF, L/min (n)	427.1 ± 108.1 (15)	465.9 ± 111.8 (13)	0.010
Evening PEF, L/min (n)	435.3 ± 96.0 (16)	476.4 ± 114.5 (12)	0.007
Symptom-free days, % (n)	47 ± 33 (16)	73 ± 27 (15)	0.015

TABLE 2. SUMMARY OF DEVICE-RELATED ADVERSE EVENTS DURING THE TREATMENT PERIOD (TREATMENT THROUGH 6-WK FOLLOW-UP)

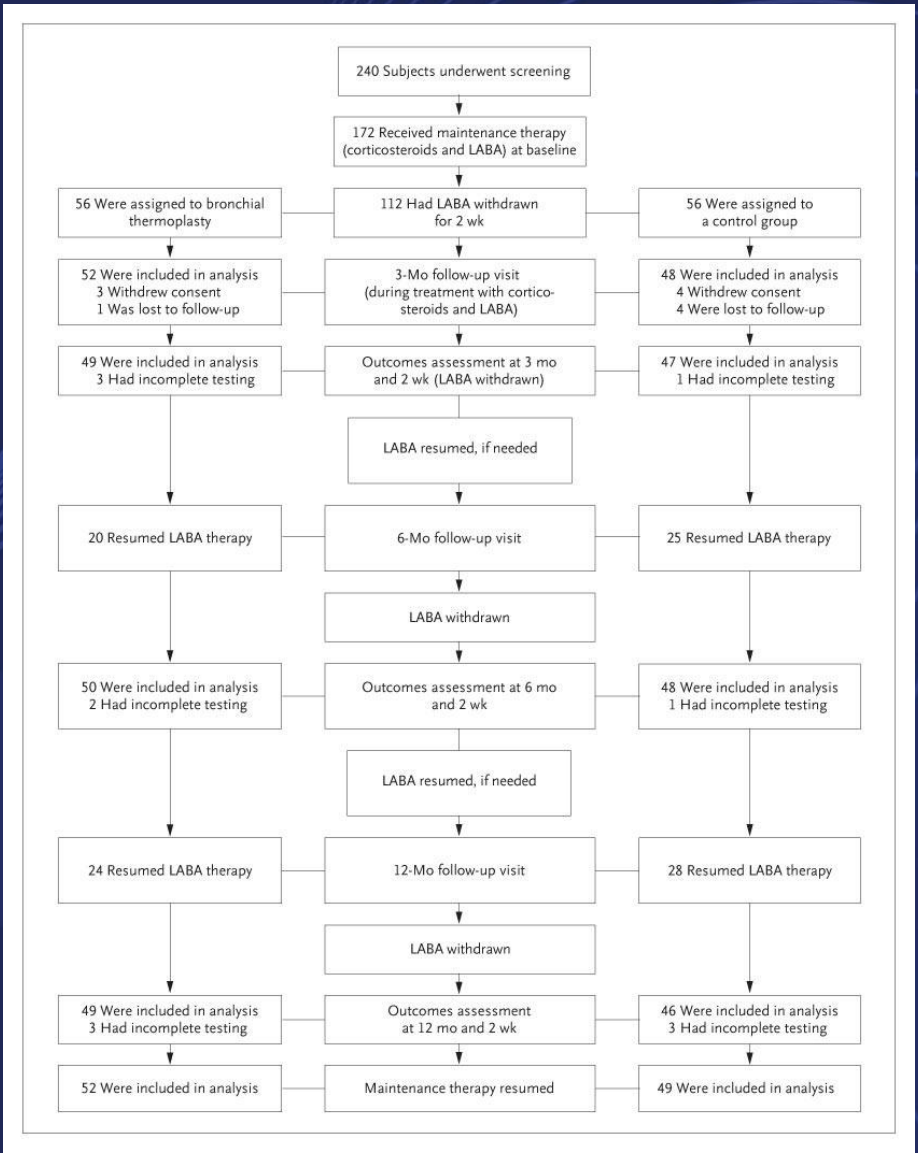
Adverse Event	Adverse Event Frequency	Subject* Frequency
Cough	33 (21%)	15 (94%)
Dyspnea	19 (12%)	11 (69%)
Wheeze	17 (11%)	8 (50%)
Bronchospasm	16 (10%)	10 (63%)
Fever	14 (9%)	7 (44%)
Chest discomfort	12 (8%)	9 (56%)
Mucus production	11 (7%)	8 (50%)
Throat irritation	8 (5%)	4 (25%)
Headache	5 (3%)	4 (25%)
Congestion	4 (3%)	2 (13%)
Hemoptysis	4 (3%)	3 (19%)
Localized heat	3 (2%)	1 (6%)
Retained mucus	3 (2%)	2 (13%)
Bronchitis	2 (1%)	2 (13%)
Hypoxemia	2 (1%)	1 (6%)
Hoarseness	1 (1%)	1 (6%)
Lower back pain	1 (1%)	1 (6%)

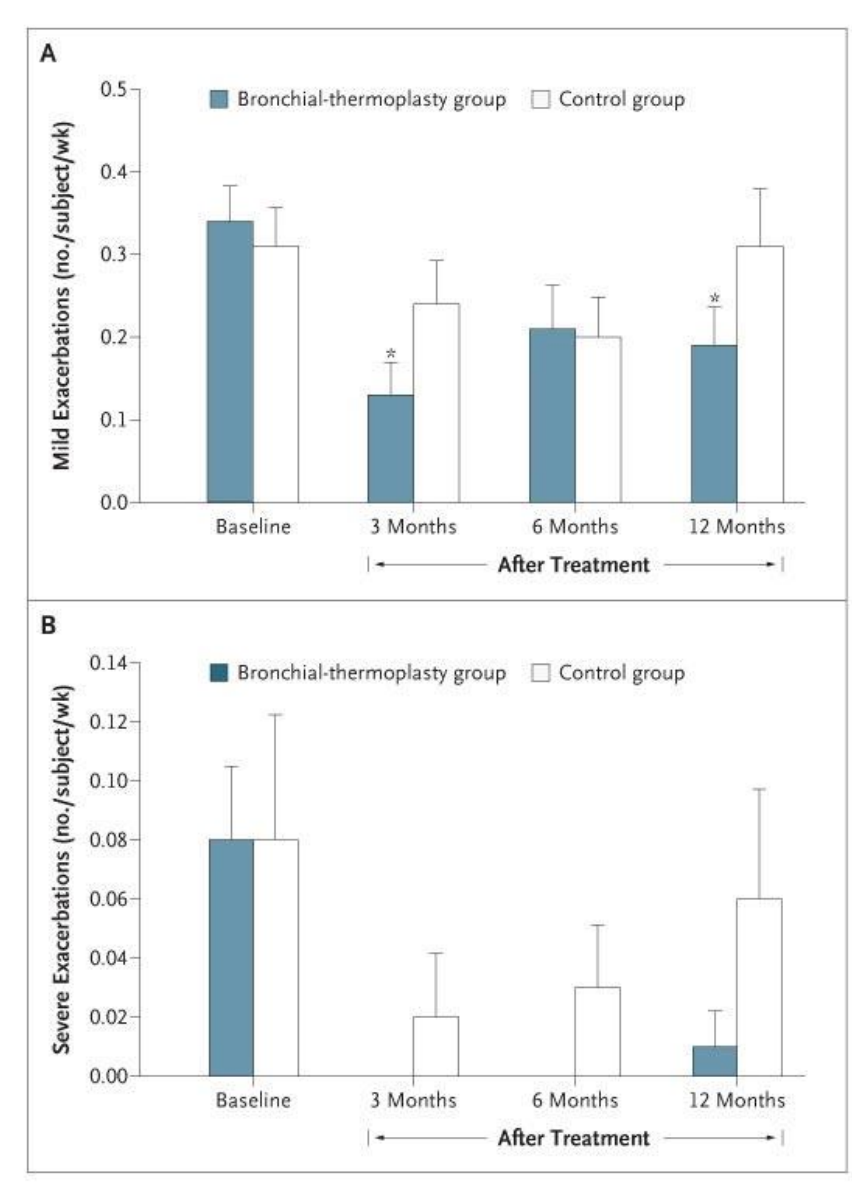
A total of 155 events were reported. Sixteen subjects experienced one or more reported events.

* Count reflects the number of subjects cited as having one or more adverse events.

Moving to severe asthma – the AIR (1) Study – NEJM 2007

- Multicenter randomized control trial of ICS/LABA with or without thermoplasty
- Adult patients with moderate-severe asthma
  - Must be on high dose inhaled corticosteroid to achieve control
  - Worsening of disease based on Asthma Control Questionnaire or morning peak flows if LABA removed from treatment regimen
  - All FEV-1s within 60-85% predicted
  - Stable asthma in six weeks pre-treatment as previous


240 Subjects underwent screening
172 Received maintenance therapy (corticosteroids and LABA) at baseline
56 Were assigned to bronchial thermoplasty
112 Had LABA withdrawn for 2 wk
56 Were assigned to a control group
52 Were included in analysis
3 Withdrew consent
1 Was lost to follow-up
3-Mo follow-up visit (during treatment with cortico-steroids and LABA)
48 Were included in analysis
4 Withdrew consent
4 Were lost to follow-up
49 Were included in analysis
3 Had incomplete testing
Outcomes assessment at 3 mo and 2 wk (LABA withdrawn)
47 Were included in analysis
1 Had incomplete testing
LABA resumed, if needed
20 Resumed LABA therapy
6-Mo follow-up visit
25 Resumed LABA therapy
LABA withdrawn
50 Were included in analysis
2 Had incomplete testing
Outcomes assessment at 6 mo and 2 wk
48 Were included in analysis
1 Had incomplete testing
LABA resumed, if needed
24 Resumed LABA therapy
12-Mo follow-up visit
28 Resumed LABA therapy
LABA withdrawn
49 Were included in analysis
3 Had incomplete testing
Outcomes assessment at 12 mo and 2 wk
46 Were included in analysis
3 Had incomplete testing
52 Were included in analysis
Maintenance therapy resumed
49 Were included in analysis


A
Bronchial-thermoplasty group
Control group
Mild Exacerbations (no./subject/wk)
0.5
0.4
0.3
0.2
0.1
0.0
*
*
Baseline
3 Months
6 Months
12 Months
After Treatment
B
Bronchial-thermoplasty group
Control group
Severe Exacerbations (no./subject/wk)
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
Baseline
3 Months
6 Months
12 Months
After Treatment

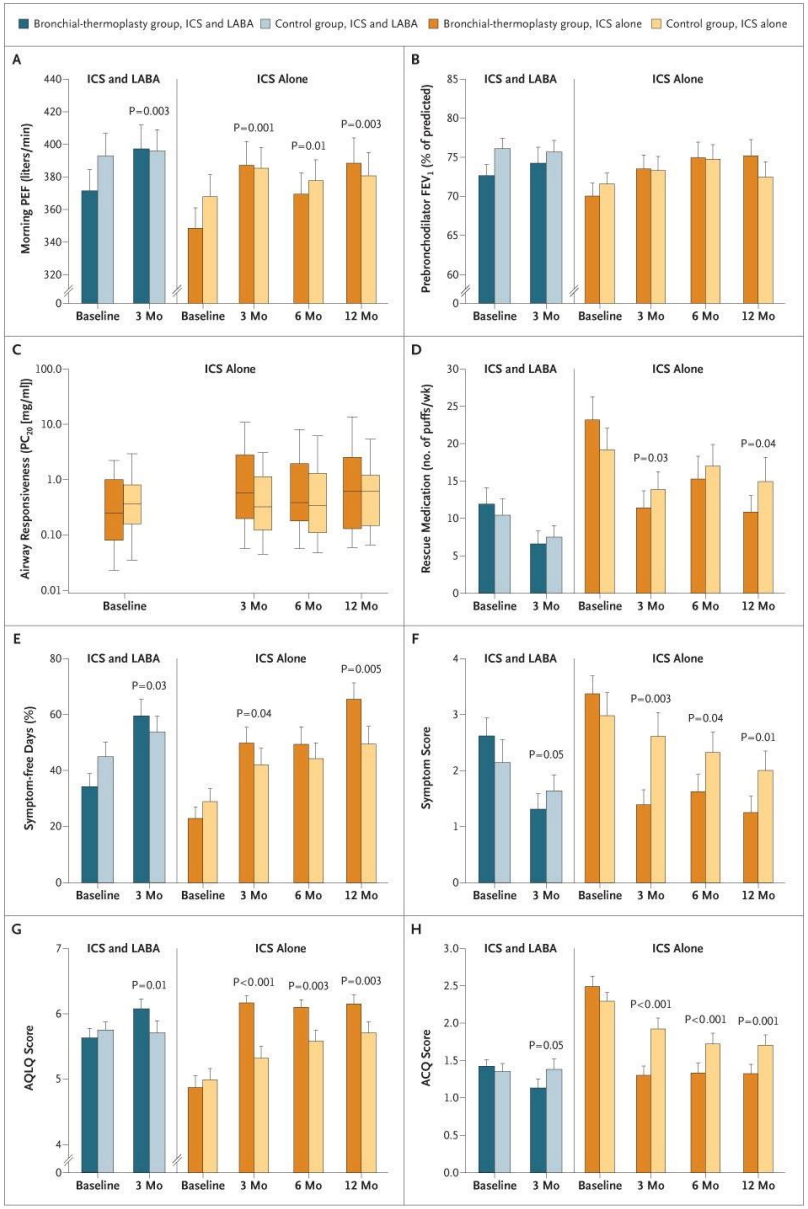


Table 2. Adverse Respiratory Events.*

Event	Bronchial-Thermoplasty Group		Control Group		P Value†
	Frequency of Event	Subjects with Event	Frequency of Event	Subjects with Event	
	percent				
Treatment period plus 6 wk					
Dyspnea	19.9	70.9	21.7	33.3	<0.001
Wheezing	17.0	61.8	7.5	13.0	<0.001
Cough	16.0	52.7	11.3	18.5	<0.001
Chest discomfort	10.3	47.3	18.9	20.4	0.004
Night awakenings	9.8	40.0	4.7	9.3	<0.001
Productive cough	8.6	40.0	8.5	11.1	<0.001
Upper respiratory tract infection	2.5	12.7	1.9	3.7	0.16
Bronchial irritation	2.0	9.1	0	0	0.06
Nasal congestion	2.0	12.7	10.4	11.1	1.00
Sputum discolored	1.7	10.9	0	0	0.03
Dry mouth	1.2	3.6	0	0	0.50
Abnormal chest sound	1.0	5.5	0	0	0.24
Bronchospasm	1.0	7.3	0	0	0.12
Post-treatment period (6 wk–12 mo)					
Dyspnea	22.1	49.1	26.4	53.8	0.70
Cough	15.4	38.2	13.0	36.5	1.00
Nasal congestion	9.6	27.3	10.1	26.9	1.00
Wheezing	9.6	29.1	8.7	23.1	0.52
Productive cough	9.2	23.6	7.7	23.1	1.00
Chest discomfort	6.7	21.8	8.2	13.5	0.32
Upper respiratory tract infection	6.3	18.2	2.9	5.8	0.07
Night awakenings	3.3	12.7	3.4	9.6	0.76
Pharyngolaryngeal pain	3.3	10.9	3.8	13.5	0.77
Nasopharyngitis	2.9	10.9	1.4	5.8	0.49
Respiratory tract congestion	2.5	9.1	1.0	3.8	0.44
Respiratory tract infection	2.5	9.1	5.8	17.3	0.26
Bronchitis	1.3	1.8	0	0	1.00
Throat irritation	1.3	3.6	1.0	3.8	1.00

* Subjects were asked about adverse events at each office visit and during telephone calls. Only adverse events occurring in the bronchial-thermoplasty group at a frequency of 1.0% or greater are listed.

† For the comparison between the two groups of the number of subjects reporting an adverse event, P values were calculated with the use of Fisher's exact test.

The AIR-2 Trial (2010)

- Large multi-center randomized, prospective trial for severe asthma with bronchial thermoplasty vs. sham procedure
- Inclusion Criteria
  - Adults 18-65 requiring high-dose ICS and LABA
  - LTRAs, Omalizumab and low-dose (<10 mg/day) Prednisone allowed
  - Stable on therapy for four weeks
  - Baseline Asthma Quality of Life Questionnaire (AQLQ) score 6.25 or lower (higher=better quality of life)
  - Pre-bronchodilator FEV-1 at least 60% predicted
  - Documented airway hyperresponsiveness (by methacholine challenge)
  - Asthma symptoms at least two days per week
  - Non-smokers at least 1 year

Castro, M, et al. Am J Resp Crit Care Med (2010); 181: 116-124.

- Exclusion Criteria
  - Documented emphysema
  - Use of immunosuppressants, anticoagulants, or beta-blockers
  - 3 or more hospital admissions for asthma
  - 3 or more lower respiratory tract infections
  - 4 or more pulse doses of oral steroids for exacerbations

- All patients had three bronchoscopies performed three weeks apart; bronchoscopy team was unblinded
  - Follow-up visit clinicians were blinded to group
  - Patients evaluated at six weeks post-procedure then 3, 6, 9, 12-month intervals

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TABLE 1. SUBJECT DEMOGRAPHICS AND BASELINE CHARACTERISTICS (ITT POPULATION)

	BT (n = 190)*	Sham (n = 98)*
Age (years)	40.7 ± 11.89	40.6 ± 11.85
Sex, n (%)		
Male	81 (42.6)	38 (38.8)
Female	109 (57.4)	60 (61.2)
Race/Ethnicity, n (%)		
White	151 (79.5)	72 (73.5)
African American/Black	19 (10.0)	15 (15.3)
Other	20 (10.5)	11 (11.2)
Methacholine PC_{20} (mg/ml)		
Geometric mean	0.27 (n=178)	0.31 (n=94)
95% Confidence interval bounds	(0.22, 0.34)	(0.22, 0.43)
Prebronchodilator FEV_1 (% predicted)	77.8 ± 15.65	79.7 ± 15.14
Inhaled corticosteroid dose† (μg/d), mean (median)	1960.7 (2,000)	1834.8 (2,000)
Long-acting β_2-agonist dose‡ (μg/day)	116.8 ± 34.39 (n=189)	110.3 ± 26.70 (n=97)
AQLQ baseline score	4.30 ± 1.17	4.32 ± 1.21
Percent symptom-free days§	16.4 ± 24.04	16.8 ± 23.10
Number and percentage of subjects on other asthma maintenance medications		
Oral corticosteroids	7 (3.7)	1 (1.0)
Methylxanthines	6 (3.2)	5 (5.1)
Leukotriene modifiers	47 (24.7)	18 (18.4)
Omalizumab	2 (1.1)	3 (3.1)
Other	15 (7.9)	9 (9.2)
Any of the above maintenance medications	59 (31.1)	25 (25.5)
Oral corticosteroids dose (mg/d)	6.4 ± 1.97 (n = 7)	5.0 (n = 1)

Definition of abbreviations: AQLQ = Asthma Quality of Life Questionnaire; BT = Bronchial thermoplasty; ITT = intent-to-treat.
Values are mean ± SD

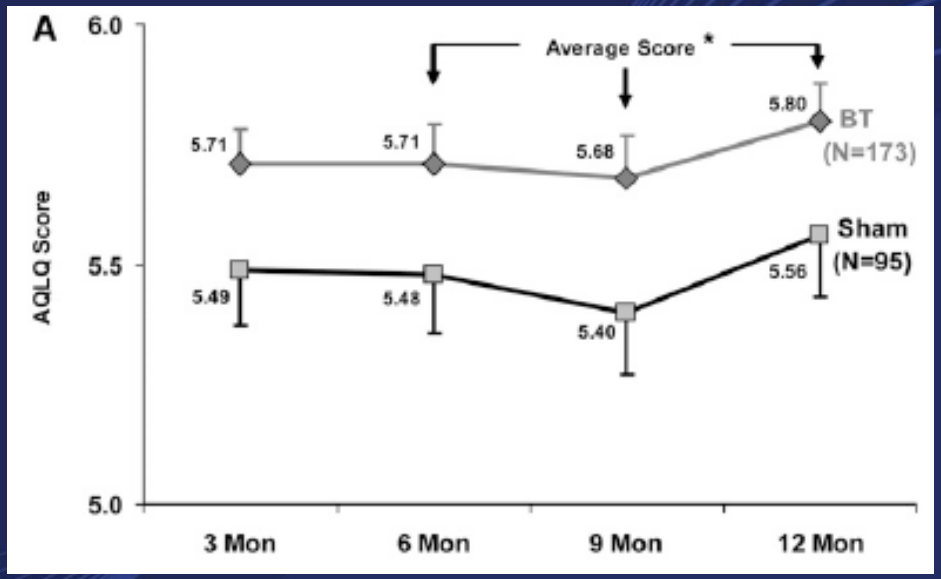
* Sample size for all variables unless otherwise stated.

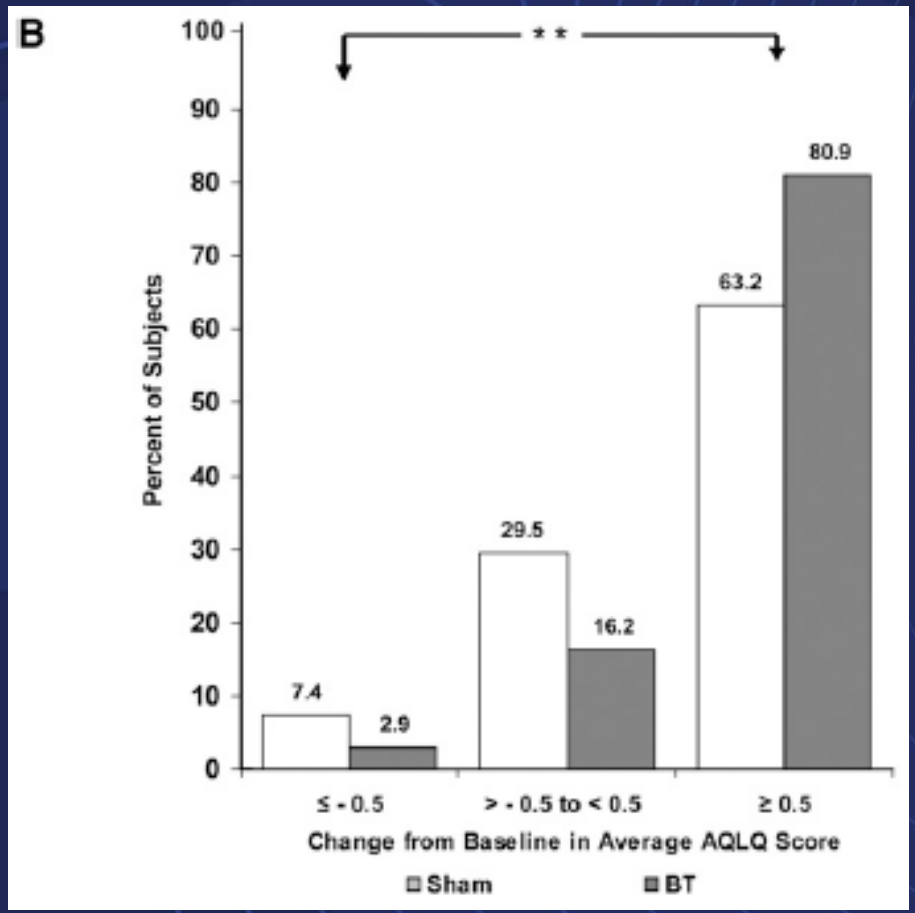
† Beclomethasone or equivalent

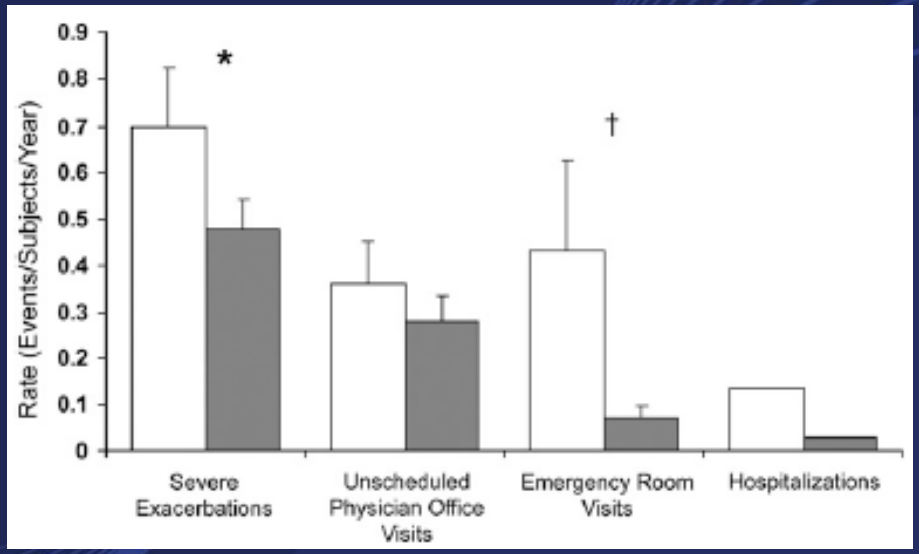
‡ Salmeterol or equivalent

§ Percentage of symptom-free days indicates the percentage of days with no night awakenings and each individual symptom score was zero.

AIR-2 Outcomes







- Adverse Events
  - During treatment, wheezing, airway irritation, URIs common
  - 8.4% of intervention group required admission during treatment phase (2% in sham group)
    - Worsening of asthma
    - Lower respiratory tract infection
    - Low post-procedural FEV-1

Okay, it looks like it works… Why all the controversy?

- Was it really necessary?
- Is it safe after the immediate post-procedure period?
- Does it really work for severe asthma?
- Is it cost-effective?

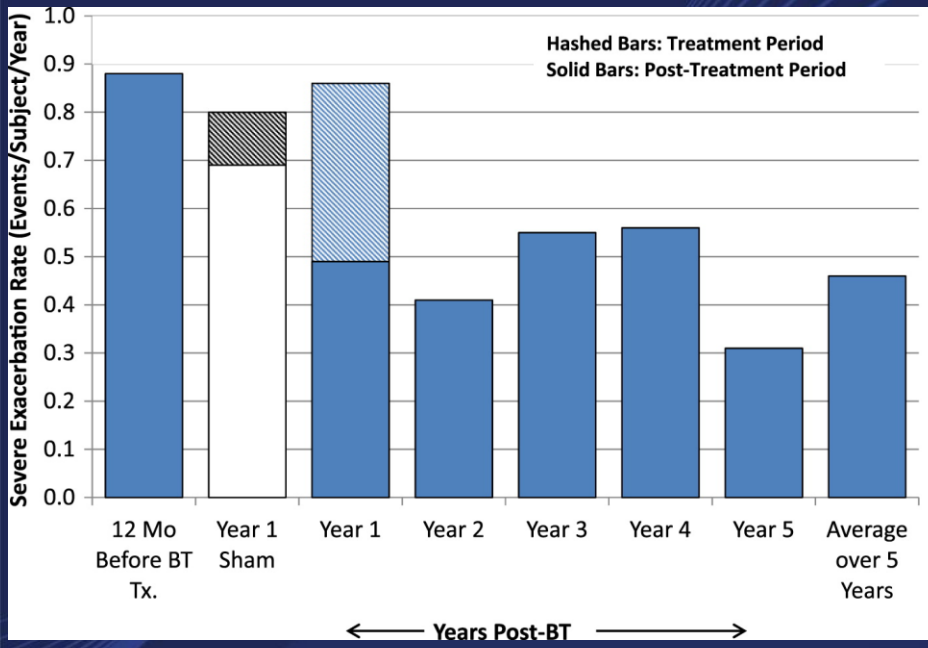
Long-term Follow-up of AIR-2

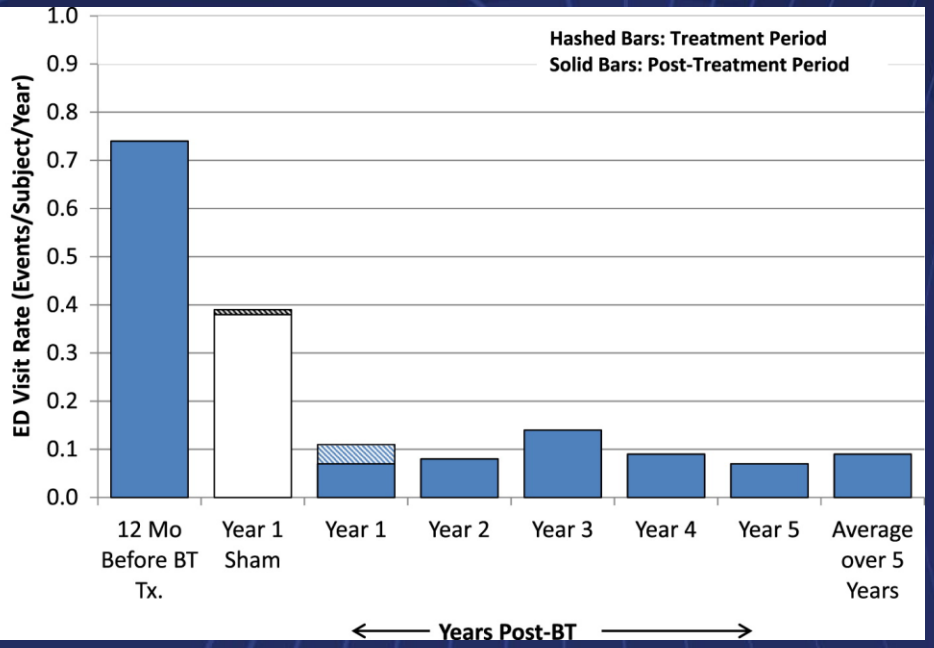
- Wechsler (2013)
  - 162/190 post-bronchial thermoplasty patients from AIR-2 were followed on a 3-month interval after the first year
  - All patients maintained on controller medications
  - Each patient monitored by spirometry, ED visits, asthma exacerbations requiring steroids

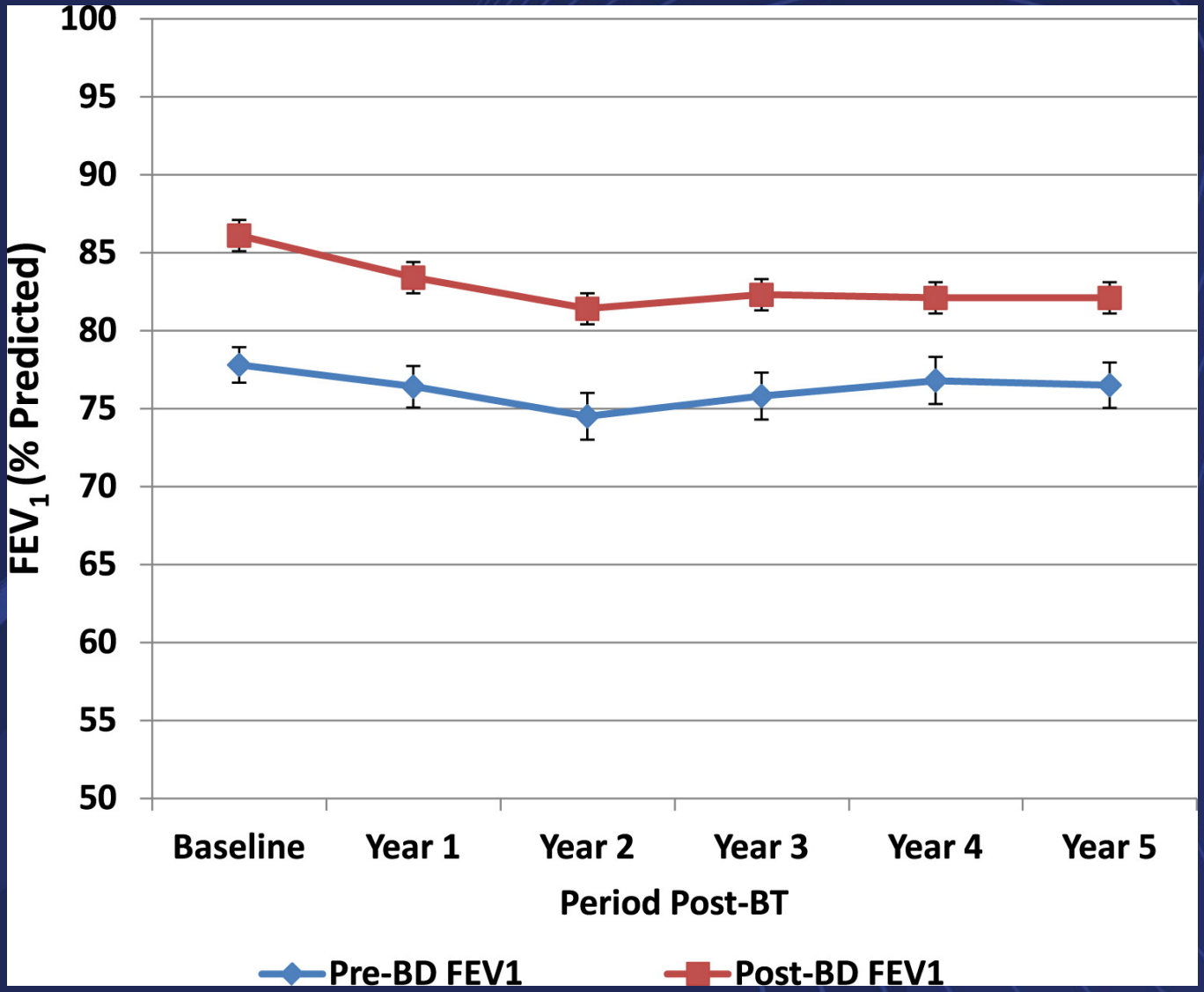
Wechsler, ME, et al. J Allergy Clin Immunol (2013); 132: 1295-302.

- Controller therapy use
  - At baseline 72% of patients were on two high-dose long-term therapies (ICS+LABA) with 28% being on 3 or more medications
  - At 5-year follow-up, 45/162 (28%) of patients to complete follow-up had at least 50% decrease in medications
  - 5/162 had increases in controller therapy

Long-Term Outcomes






100
95
90
85
80
75
70
65
60
55
50
FEV1 (% Predicted)
Baseline
Year 1
Year 2
Year 3
Year 4
Year 5
Period Post-BT
Pre-BD FEV1
Post-BD FEV1

Was it necessary?

- AIR-2 required patients with high-dose ICS and LABA therapy to maintain symptom control
- Hawkins (BMJ 2003)
  - 259 patient double-blinded RCT from Scotland of patients with asthma on at least 800 mcg/day inhaled Beclomethasone
  - Randomized to maintaining maintenance dose of ICS or decreasing by 50%

Hawkins, G, et al. BMJ (2003); 326: 1115-21.

Table 2 Asthma exacerbations and asthma related events in the two groups. Values are numbers (%) of patients

	Stepdown group (n=130)	Control group (n=129)	Odds ratio (95% CI)	P value (χ^2 test)
Asthma exacerbations	40 (31)	33 (26)	1.29 (0.75 to 2.23)	P=0.354
Asthma related events:				
Visit to general practice	45 (35)	41 (32)	1.14 (0.68 to 1.91)	P=0.629
Home visit by general practitioner	3 (2)	6 (5)	0.48 (0.12 to 1.98)	P=0.304
Visit to accident and emergency department	2 (2)	1 (1)	2 (0.18 to 22.3)	P=0.567
Admission to hospital	4 (3)	1 (1)	4.06 (0.45 to 36.86)	P=0.179

Table 3 Health status of the two groups as measured by validated instruments and short asthma morbidity score

	Stepdown group	Control group	Difference (95% CI)	P value (*t* test)
St George's respiratory questionnaire	(n=110)	(n=119)		
Difference of maximum score from baseline (SD)	7.53 (10.68)	7.40 (11.95)	0.13 (–2.76 to 3.03)	P=0.929
Short asthma questionnaire morbidity score	(n=120)	(n=122)		
Difference of maximum score from baseline (SD)	1.59 (1.96)	1.43 (2.00)	0.16 (–0.34 to 0.66)	P=0.537
EuroQol	(n=108)	(n=111)		
Difference of lowest score from baseline (SD)	–7.00 (13.04)	–9.32 (16.69)	2.32 (–1.67 to 6.32)	P=0.252

Table 4 Corticosteroid dosage in the two groups

Mean (SD) dose of drug	Stepdown group	Control group	Difference (95% CI)
Oral corticosteroid*:	(n=130)	(n=129)	N/A
Yearly (mg)	117 (215)	109 (275)	N/A
Inhaled corticosteroid†:	(n=120)	(n=123)	
Yearly (mg)	390 (189)	517 (231)	–127 (–180 to –74)
Monthly (mg)	32 (16)	42 (19)	–10 (–15 to –6)
Daily (μg)	1067 (518)	1415 (631)	–348 (–494 to–202)

*Median in both groups=0 mg. Significance test is Wilcoxon, P=0.252.
†Conversion rate of 1 mg fluticasone propionate=2mg beclomethasone dipropionate used for calculation. Significance test is *t* test, P=<0.001.

Will bronchial thermoplasty work for asthmatics with fixed airway obstruction

- Maybe – No large scale trials
- Doening (2013)
  - Eight-patient single center (University of Chicago) case series
  - All had fixed airway obstruction and were on multiple controller therapies

  - Results
    - At 15-week follow-up, no change in FEV-1 ($p=0.4$)
    - No increase in hospitalization rate (mean 2.88 ± 1.2 vs. 0.5 ± 0.33)

Doening, et al. J Asthma (2013); 50: doi 10.3109/02770903.2012.751997

Pre-BD FEV_1 (% predicted)	51.8 ± 8.6
Pre-BD FEV_1 <50%, n	5
ICS dose (mcg/day)	1000
Other medications, *n*	
LABA (≥100 mcg)	8
OCS	4
Leukotriene modifiers	6
Omalizumab	2
Methylxanthines	2
Anticholinergics	3
OCS dose (mg/day)	27.5 ± 4.8
SABA use (puffs/day)	6 ± 0.8
Avg. night wakings (nights/week)	4.5 ± 1.0
Hospitalizations last year (total no.)	23 ± 1.2
eNO (ppb)	55 ± 17.4
IgE (IU/mL)	155 ± 8.7

Overnight observations, *n*	
Total no. of events	11
Total no. of patients with an event	5
Cause, *n*	
Increased BD use	5
Wheezing	2
Lower respiratory tract infection	2
Atelectasis	1
Hemoptysis	1
Intubations, *n*	0
NIPPV, *n*	0
Deaths, *n*	0

Economics of Bronchial Thermoplasty

- Annual cost of asthma therapy is $3,300/patient (2002-2007)
- 59% of children and 33% of adults with asthma missed school or work based on a 2008 study
- In spite of FDA approval in 2010, no private insurance policies for coverage established
  - CMS definition of “reasonable and necessary” unclear
- In 2007 (i.e. three years before AIR-2), multiple insurers had non-coverage policies for BT labelling it experimental/ investigational
  - Maintained after FDA approval

Mahajan, AK, Hogarth, K. Chest (2013); 144: 1051-4.

- Thermoplasty originally given Category 3 (experimental, temporary) CPT codes
  - Category 1 CPT codes for current medical practice, generally recognized by all US insurers
  - Category 1 CPT codes for BT now recognized as of January 2013 (codes 31660 and 31661)
- California Technology Assessment Forum panel 3/2012
  - Third-party assessment agency for insurers
  - Found that BT met safety and efficacy criteria for approval

- How much does thermoplasty cost to do?
  - Alair thermoplasty system (one-time purchase): $60,000
  - Alair thermoplasty catheters (one per procedure): $2,500
  - Relief of symptoms: priceless

Is it potentially cost-saving?

A Budget Impact Analysis of Bronchial Thermoplasty for Severe Asthma in Clinical Practice

Francesco Menzella · Luigi Zucchi · Roberto Piro · Carla Galeone · Claudia Castagnetti · Nicola Facciolongo

- 5-year budget analysis model of the asthmatic population of a district in Northern Italy
- Based on analysis of standard care with Omalizumab vs. standard care and Omalizumab with the addition of bronchial thermoplasty
- Demographics and patient numbers were estimated both on ED visits, specialist visits, hospitalizations, and previous population data
- Used 3.4% risk of severe adverse events per BT procedure (based on AIR-2 data)

Menzella, F, et al. Adv Ther (2014); 31: 751-61.

Target population	
Emilia-Romagna Region inhabitants, December 2012	4,341,240
Adults >18 years in Emilia-Romagna, December 2012	3,652,556
Rate of adults affected by asthma	6%
Rate of adults affected by severe asthma	15%
Rate of uncontrolled asthma among those with severe asthma	55.2%
Estimated target population	18,146

Unit cost	Euros	Source
SC[a]	2,087	Estimation
OMAL treatment[b]	15,150	Hospital Reggio
BT procedure[c]	6,550	Emilia estimation
ER visits[d]	140.48	Hospital Reggio

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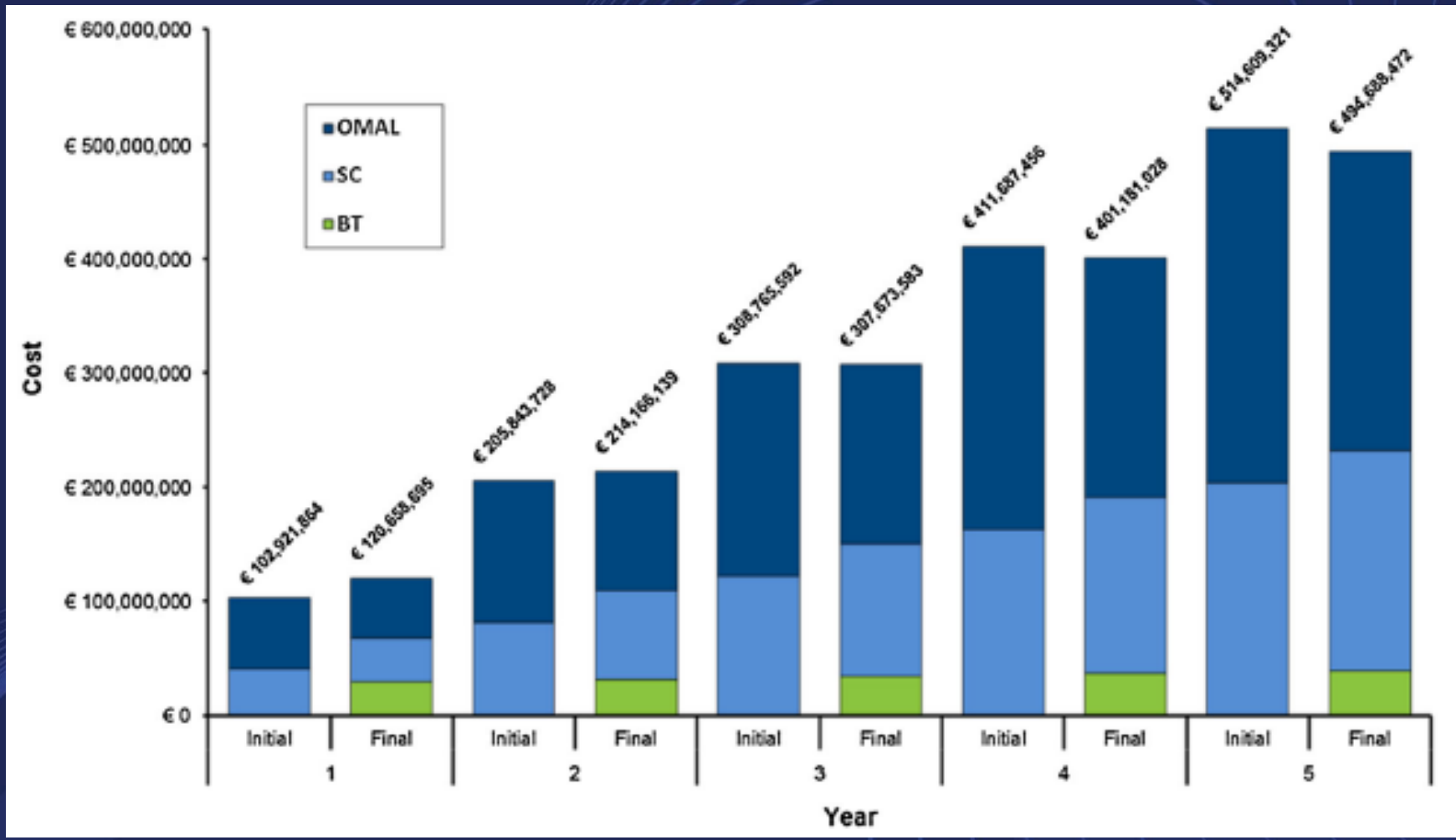
Table 2 Basecase results

Therapy	Year 1			Year 2			Year 3			Year 4			Year 5		
	BT	SC	OMAL	BT	SC	OMAL	BT	SC	OMAL	BT	SC	OMAL	BT	SC	OMAL
Asthma total costs per patient per treatment															
Treatment	€ 19,650	€ 0	€ 15,150	€ 0	€ 0	€ 15,150	€ 0	€ 0	€ 15,150	€ 0	€ 0	€ 15,150	€ 0	€ 0	€ 15,150
Maintenance medications	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153	€ 1,153
Physician visits	€ 452	€ 464	€ 263	€ 355	€ 464	€ 263	€ 355	€ 464	€ 263	€ 355	€ 464	€ 263	€ 355	€ 464	€ 263
Emergency access	€ 60	€ 198	€ 79	€ 33	€ 198	€ 79	€ 33	€ 198	€ 79	€ 33	€ 198	€ 79	€ 33	€ 198	€ 79
Hospitalization	€ 1,497	€ 993	€ 485	€ 256	€ 993	€ 485	€ 256	€ 993	€ 485	€ 256	€ 993	€ 485	€ 256	€ 993	€ 485
Total	€ 22,812	€ 2,807	€ 17,130	€ 1,797	€ 2,807	€ 17,130	€ 1,797	€ 2,807	€ 17,130	€ 1,797	€ 2,807	€ 17,130	€ 1,797	€ 2,807	€ 17,130
Asthma cumulative costs per patient per treatment															
Treatment (BT)	€ 19,650	€ 0	€ 0	€ 19,650	€ 0	€ 0	€ 19,650	€ 0	€ 0	€ 19,650	€ 0	€ 0	€ 19,650	€ 0	€ 0
Treatment (OMAL)	€ 0	€ 0	€ 15,150	€ 0	€ 0	€ 30,299	€ 0	€ 0	€ 45,449	€ 0	€ 0	€ 60,599	€ 0	€ 0	€ 75,749
Maintenance medications	€ 1,153	€ 1,153	€ 1,153	€ 2,306	€ 2,306	€ 2,306	€ 3,459	€ 3,459	€ 3,459	€ 4,612	€ 4,612	€ 4,612	€ 5,765	€ 5,765	€ 5,765
Physician visits	€ 452	€ 464	€ 263	€ 807	€ 927	€ 527	€ 1,161	€ 1,391	€ 790	€ 1,516	€ 1,854	€ 1,053	€ 1,871	€ 2,318	€ 1,317
Emergency access	€ 60	€ 198	€ 79	€ 93	€ 396	€ 157	€ 126	€ 594	€ 236	€ 159	€ 792	€ 315	€ 192	€ 990	€ 393
Hospitalization	€ 1,497	€ 993	€ 485	€ 1,753	€ 1,985	€ 971	€ 2,009	€ 2,978	€ 1,456	€ 2,265	€ 3,971	€ 1,942	€ 2,521	€ 4,963	€ 2,427
Total	€ 22,812	€ 2,807	€ 17,130	€ 24,609	€ 5,615	€ 34,260	€ 26,406	€ 8,422	€ 51,390	€ 28,203	€ 11,229	€ 68,520	€ 29,999	€ 14,037	€ 85,651

BT bronchial thermoplasty, *OMAL* omalizumab, *SC* standard care


€ 600,000,000
€ 500,000,000
€ 400,000,000
€ 300,000,000
€ 200,000,000
€ 100,000,000
€ 0
Cost
OMAL
SC
BT
€ 102,921,864
€ 120,658,695
€ 205,843,728
€ 214,166,139
€ 308,765,592
€ 307,673,583
€ 411,687,456
€ 401,181,628
€ 514,609,321
€ 494,608,472
Initial
Final
1
2
3
4
5
Year

Getting a patient approved for thermoplasty

- Almost every patient will require an appeal process
  - Individual case review to establish necessity
  - Must be able to demonstrate
    - Diagnosis of asthma
    - On therapy that constitutes best care
    - Unable to achieve control of the disease with best control measures
  - In 2011, 40% of appeals were approved on first request
  - Increased to 60% in 2012

Mahajan, AK, Hogarth, K. Chest (2013); 144: 1051-4.

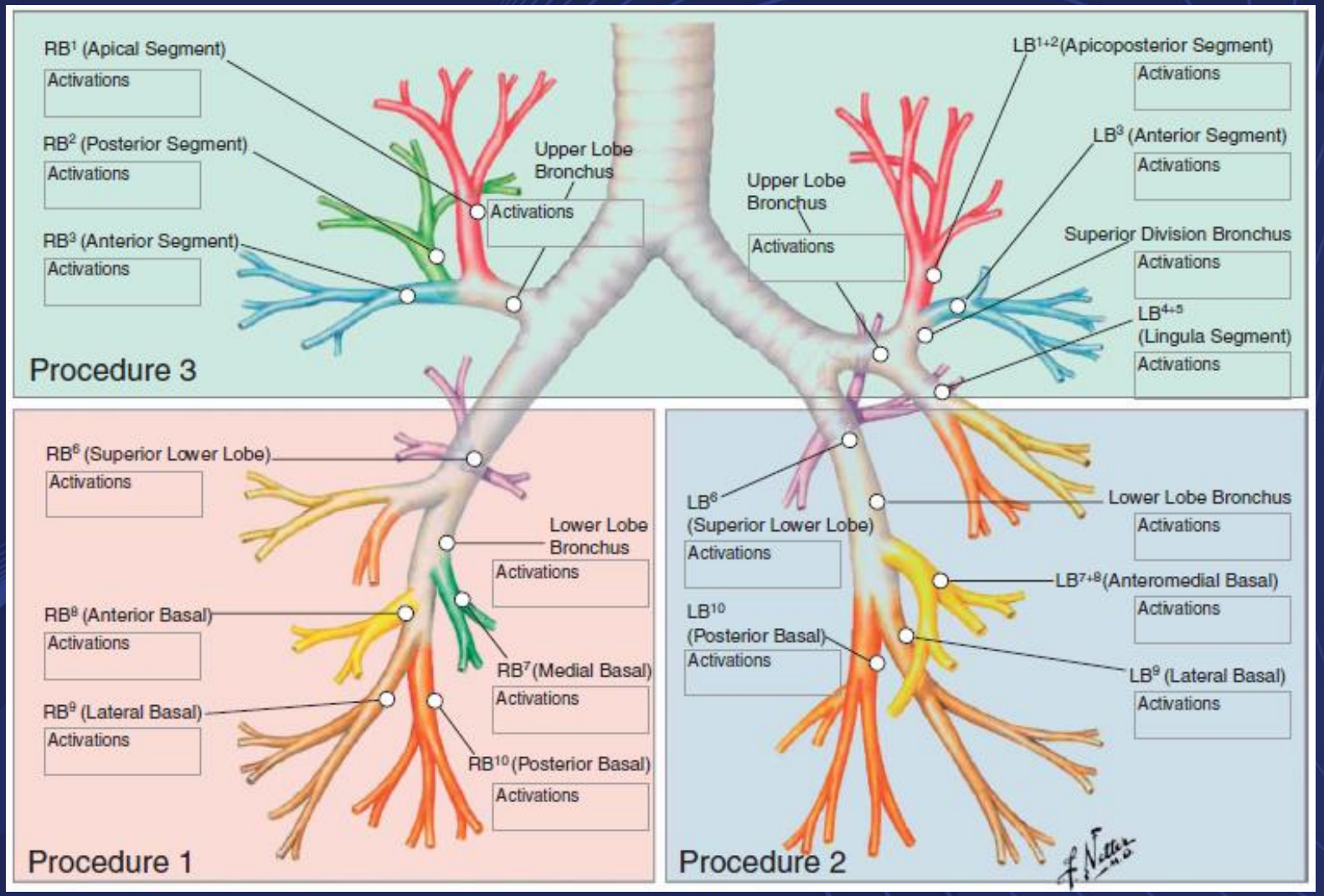
Bronchial Thermoplasty – Periprocedural care

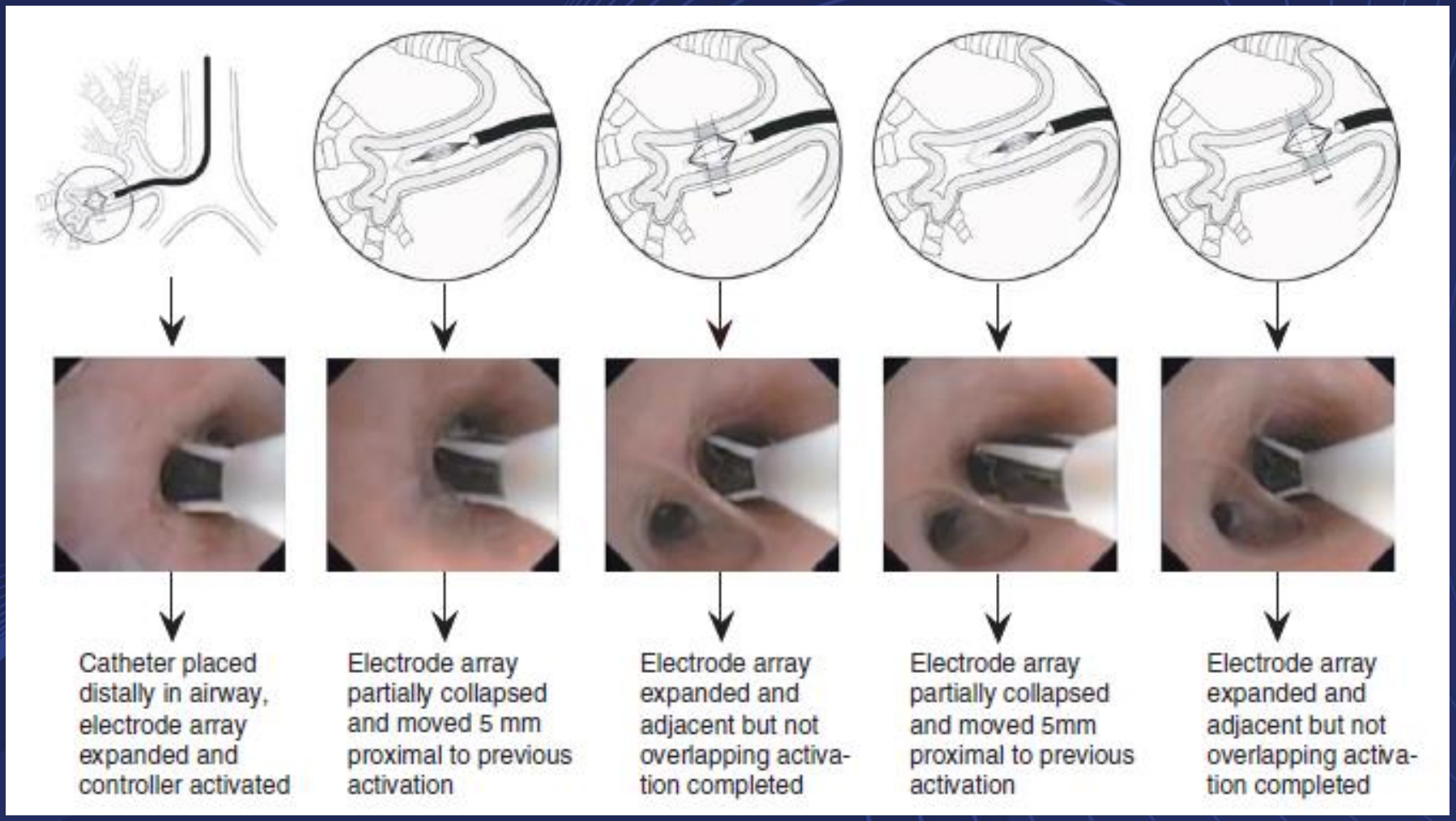
- Pre-procedural protocol
  - Patient given high-dose oral steroid (Prednisone 50 mg/day) for 1-3 days prior to the procedure, the day of procedure, and the day after
  - All patients should receive pre-procedural bronchodilator therapy (2.5-5 mg Albuterol or 3 mL DuoNeb)
  - Pre-procedural spirometry for baseline (no procedure if post-bronchodilator FEV-1 <85% from baseline)
  - No apparent URI symptoms

Mayse, ML, et al. J Bronchol (2007); 14: 115-23.

- Intraprocedure
  - Can be done under moderate sedation or general anesthesia
  - Both lower lobes done as separate procedures, upper lobes done as third procedure
  - If done under moderate sedation, liberal use of lidocaine at vocal cords, trachea, airways to be treated
  - Each segment is entered with the catheter and the array is activated at 5 mm intervals distal→proximal
  - Oozing and secretions common, may require intraprocedural cleaning of array

The thermoplasty procedure




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 5mm proximal to previous activation
Electrode array expanded and adjacent but not overlapping activation completed

Post-procedural monitoring

- All patients should be monitored for 4-6 hours post-procedure
- At three hours, patient should receive bronchodilator with repeat spirometry being performed at hour 4 post-procedure
- Should not discharge if post-bronchodilator FEV-1 is <85% of pre-procedural baseline
- Phone calls 1- and 3-days post-procedure
- Follow-up office visit 2-3 weeks post-procedure for spirometry, assessment of symptoms, and to schedule next step of procedure

Back to our patient

- First bronchial thermoplasty performed of right lower lobe without immediate complication
  - Did reqiure additional six days of Prednisone 40 mg/day
  - At follow-up visit, reported mild improvement in asthma symptoms
- After second thermoplasty (left lower lobe), patient reported significant decrease in rescue Albuterol use
- After third thermoplasty, patient stated “I don’t think I still have asthma anymore.” No longer carrying Albuterol inhaler
  - Nocturnal awakenings monthly from 2-3/night

Conclusions

- Bronchial thermoplasty is a new, emerging technology for the treatment of asthma which is difficult to control medically
- While no long-term studies exist, it has been demonstrated to be safe at up to five years post-procedure
- There may be a cost-savings over usual care associated with bronchial thermoplasty after the initial investment in the procedure
- Bronchial thermoplasty is not a “cure-all” and patients will still have residual symptoms. Careful patient selection is necessary to ensure safety and success of the procedure
- Further studies are needed to determine the efficacy of the procedure with fixed obstruction

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Thank you!

Questions?