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Case report

Tentative study on radial endobronchial ultrasonography evaluating airway wall thickness before and after bronchial thermoplasty

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ABSTRACT

Aim: We aimed to observe the clinical practicing value of radial endobronchial ultrasonography evaluating airway wall thickness before and after bronchial thermoplasty.

Methods: We selected two patients who received bronchial thermoplasty in our hospital. We measured the thickness of each segmental airway wall of each patient by radial endobronchial ultrasonography, and observed the difference before and after the therapy. All the treatments and measurement were performed by a designated bronchoscopist and the locations and depths of the ultrasound probe were relatively fixed, to reduce the operational error.

Results: In both two patients, the mean thicknesses of all segmental airway walls was 4.9 ± 0.7 mm before the first session of BT; the mean thickness was 4.13 ± 0.92 mm before the second session; the mean thickness was 2.69 ± 0.68 mm before the third session; the mean thickness was 2.7 ± 0.5 mm in the follow-up measurement at six months after the BT treatment; all thicknesses of airway wall were significantly reduced comparing with those before treatment; all the thicknesses of the airway walls were stable without any tendency of thickening after six months. Although the airways in the right middle lobe of both two patients were not received BT, their thicknesses were also decreased comparing with those before the treatment; both upper lobes bronchus of both two patients were not activated in the first and second sessions, but their thicknesses were also decreased at the third measurement.

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Conclusion: Radial endobronchial ultrasonography is a simple and practical method to measure the thickness of patient's airway wall. Bronchial thermoplasty can effectively reduce the thickness of airway wall. It can reduce airway smooth muscle by direct activation and other possible more complicated mechanism, which need further research.

1. Introduction

Asthma is a worldwide common and frequently encountered disease, which brings a very heavy economic burden to the society [1]. The commonly used medicine for controlling asthma are inhaled corticosteroids (ICS) or in combination with an inhaled long-acting β_2 agonist (LABA) [2]. etc. Some patients with severe refractory asthma, however, are poorly controlled by those medicines, suffering heavy airway remodeling [3]. Chronic airflow obstruction and low quality of life. Bronchial thermoplasty (BT), as a novel intervention aiming at reducing airway smooth muscle (ASM) mass and even partially reversing airway remodeling [4], has attracted increasing attention of asthma specialists. Therefore, It is of great clinical significant to find a simple, non-invasive, fast and accurate method to identify the thickness change before and after BT for evaluating the efficacy of the treatment by measuring the improvement of airway remodeling [5].

Radial endobronchial ultrasonography acquires the ultrasound images of the various layers of trachea and bronchi wall and their adjacent organs by real-time ultrasonographic scanning with a micro-probe introduced by bronchoscope, which is of essential to locate and diagnose the peripheral airway and pulmonary lesions. This diagnostic method has been vastly used in clinic [6]. As a simple and practical diagnostic method, radial endobronchial ultrasonography can be used to evaluate the variation of airway wall thickness of the patients with asthma before and after BT. In this case report, we provide two clinical cases of refractory asthma, and studied the feasibility and advantages of application of radial ultrasonography in evaluating airway remodeling and the efficacy of BT.

2. Case report

Patient 1: female, 47-year-old, worker. Chief complains: she has suffered recurrent chest oppression and shortness of breath for 44 years. History of present illness: the patient got chest oppression and shortness of breath without any obvious predisposing cause 44 years ago. After the local hospital made a diagnosis of asthma and gave her treatment, the symptoms were relieved. The shortness of breath attacked again in a physical exercise class 40 years ago. At that time, she didn't take any emergency medicine and shown obvious shortness of breath, difficulty of speaking, profuse sweating, and coma in hospital, then waked after 7 days treatment. Since then, she often got those above-mentioned symptoms after physical exercises. With the treatment of interval inhaling salbutamol and persisting in taking Aminophylline, the disease was still recurrent and attacked seriously once or twice a year. During the attack, she shown obvious shortness of breath, difficulty of speaking, profuse sweating. Since December of 2013, she started twice inhaling Symbicort, bid, and in combination with orally taking Aminophylline and Singulair. Ordinarily, she felt shortness of breath when speaking too much or walking over 10 mins. Since May of 2015, she started orally taking prednisone 25 mg, bid. She was admitted into our hospital for further treatment. Medical examination: respiratory harshness of both lungs, no wet/dry rales, normal heart rate. Ancillary examination: pulmonary function test: FEV1/FVC 70%, FEV1 62%; bronchial dilation test positive: 300ml,16.7%; chest CT: normal; IgE: 267; EOS: 8.9%; FeNO: 29; dermatophagoides pteronyssinus +++, house dust mite+++, shrimp +++, cow's milk +++; ACT: 10 (Asthma Control Test).

Patient 2: female, 29-year-old, office worker. Chief complains: she has suffered recurrent chest oppression and shortness of breath

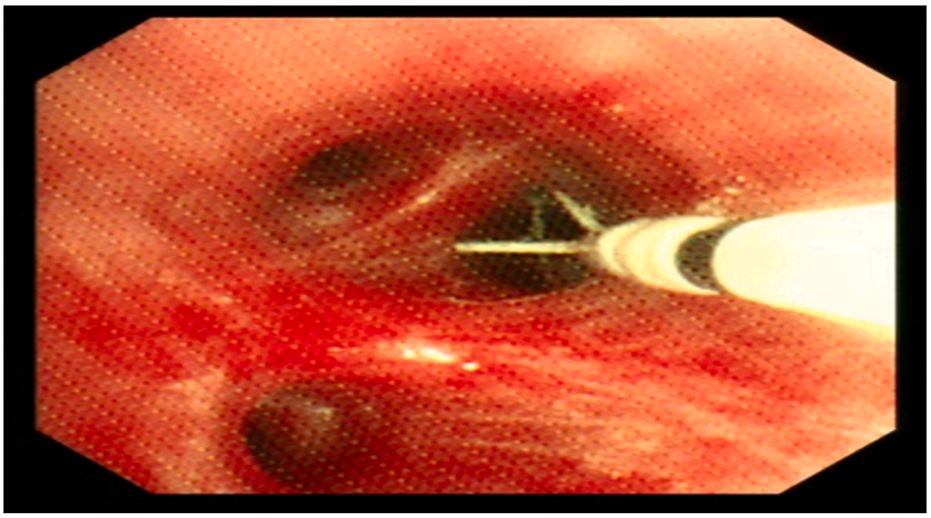


Fig. 1. A bronchoscopic picture of a bronchial thermoplasty treatment.

for 28 years, and felt these symptoms getting worse in the recent 6 months. History of present illness: the patient got chest oppression and shortness of breath without any obvious predisposing cause every year since she was very young. In the period of winter and spring, after the local hospital made a diagnosis of asthma and gave her treatment, the medical condition was stable. Six months ago, the symptoms, i.e. coughing, chest oppression, and shortness of breath, were getting worse and recurrent, and cannot be controlled by Sulindac and Symbicort. After being treated by the emergency department of our hospital with budesonide nebulization, Solu-Medrol intravenous injection, and Aminophylline intravenous drip, the patient's condition was relieved but still recurrent. She was admitted into our hospital for further treatment. Medical examination: respiratory harshness of both lungs, no wet/dry rales, normal heart rate. Ancillary examination: pulmonary function test: FEV1/FVC 78%, FEV1 65%; bronchial dilation test positive: 400ml,18%; chest CT: normal; IgE: 150; EOS: 7.5%; FeNO: 170; dermatophagoides pteronyssinus +++, house dust mite ++++; ACT: 12.

After signing the informed consent, both two patients were received BT under general anesthesia. The procedure took place over three treatment sessions at approximately three-week intervals, treating the right lower lobe, the left lower lobe and both upper lobes respectively. Before each BT treatment, the thickness of each segmental airway wall of each patient was measured by radial endobronchial ultrasonography (Fig. 1 and Fig. 2). In the follow-up measurement at six months after the third session of BT, the thickness of each segmental airway wall of each patient was measured again, to compare the difference before and after the therapy. All the treatments and measurement were performed by a designated bronchoscopist and the locations and depths of the ultrasound probe were relatively fixed, to reduce the operational error (see Fig. 3).

Before the first session of BT, we observed the two patients with bronchoscope. We found both two patients had congestion and edema of bronchial mucosa on both sides, bronchoconstriction after irritation, and clear mucus hypersecretion in the airways. In the follow-up measurement at six months after the BT treatment, we found the congestion of bronchial mucosa on both sides were obviously relieved, segmental ridge were sharper than those before the treatment, and all the diameters of segmental airway lumens slightly increased. We measured the thicknesses of segmental airway walls of both two patients by radial endobronchial ultrasonography; before the first session of BT, the mean thickness was 4.9 ± 0.7 mm; before the second session of BT, the mean thickness was 4.13 ± 0.92 mm; before the third session of BT, the mean thickness was 2.69 ± 0.68 mm; in the follow-up measurement at six months after the third session of BT, the mean thickness was 2.7 ± 0.5 mm. The thicknesses of segmental airway walls significantly reduced after BT (Table 1). In all procedures, a C-ARM was used to guide the radial probe sheath quickly to the target area.

In Patient 1, the thicknesses of medial and lateral segmental airway walls in the right middle lobe in the 4 times measurements were 5.1 mm, 5.9 mm; 4 mm, 5.2 mm; 1.7 mm, 2.6 mm; 1.9 mm, 2.7 mm. In Patient 2, the thicknesses of medial and lateral segmental airway walls in the right middle lobe of in the 4 times measurements were 4.2 mm, 5.1 mm; 3.8 mm, 4.2 mm; 3 mm, 3.6 mm; 2.9 mm, 3.4 mm. Although the airways in the right middle lobe of both two patients were not received BT, their thicknesses were also decreased comparing with those before the treatment. In Patient 1, the thicknesses of apical, posterior and anterior segmental airway walls in the right upper lobe of in the 4 times measurements were 5 mm, 5.4 mm, 4.8 mm; 4.3 mm, 4.8 mm, 4.2 mm; 2.6 mm, 3.1 mm, 2.8 mm; 2.3 mm, 3 mm, 2.6 mm. The thicknesses of apicoposterior and anterior segmental airway walls in the left upper lobe in the 4 times measurements were 5.2 mm, 5.7 mm; 4.2 mm, 4.9 mm; 2.4 mm, 2.9 mm; 2.4 mm, 2.8 mm. In Patient 2, the thicknesses of apical, posterior and anterior segmental airway walls in the right upper lobe of in the 4 times measurements were 3.5 mm, 3.6 mm, 4.4 mm; 3.2 mm, 2.7 mm, 3.3 mm; 2.1 mm, 2 mm, 2.4 mm; 2.3 mm, 2.2 mm, 2.1 mm. The thicknesses of apicoposterior and anterior segmental airway walls in the left upper lobe in the 4 times measurements were 4.3 mm, 4.9 mm; 3.5 mm, 4.3 mm; 2.5 mm, 3.6 mm; 2.5 mm, 3.4 mm. Although the both upper lobes bronchus of both two patients were not activated in the first and second sessions, their thicknesses were also decreased at the third measurement. In the follow-up measurement at six months after the treatment, all the thicknesses of the airways were stable without any tendency of thickening. The PFTs were increased in both patients by 10% and 12%. The ACT score

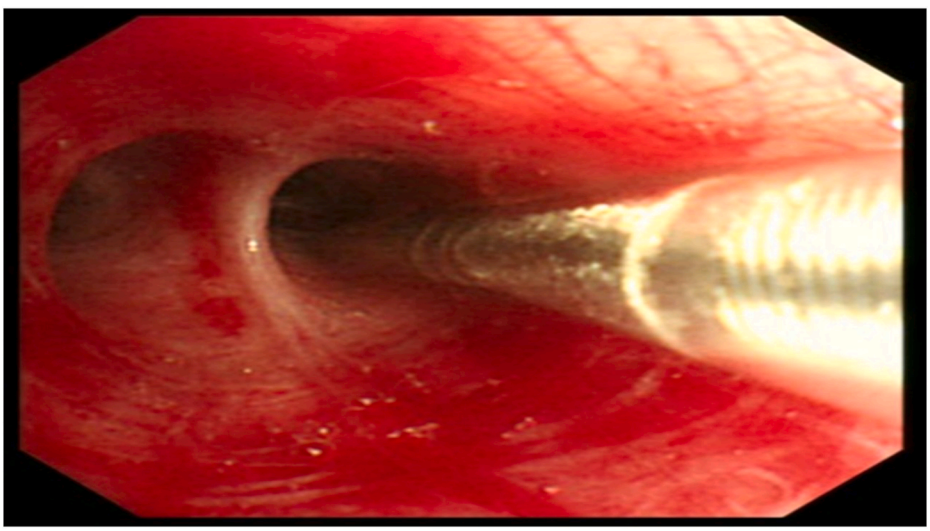


Fig. 2. An ultrasound probe was located to carry out radial endobronchial ultrasonography.

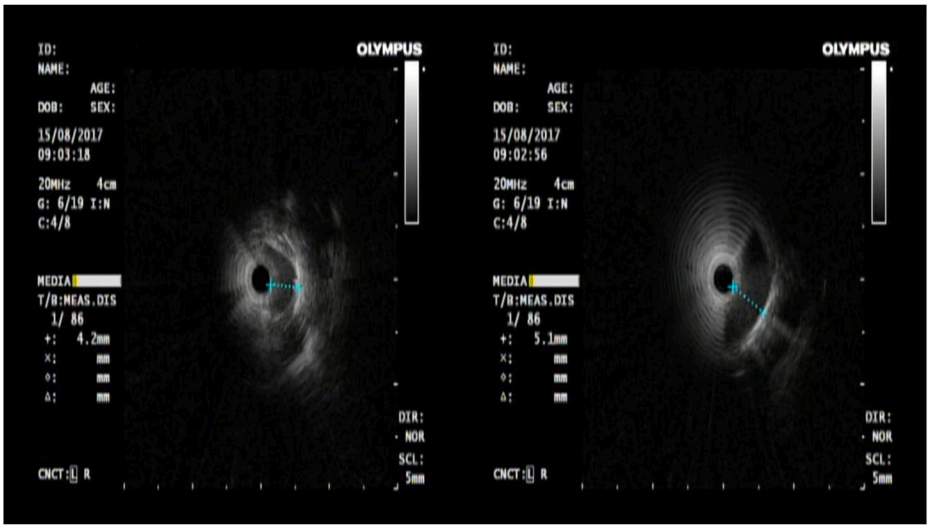


Fig. 3. The images of medial and posterior segmental airway walls of right medial lobe by radial endobronchial ultrasonography (4.2 mm, 5.1 mm).

was modified to ACT 14 and ACT 18 for the first and second patient. Both patients had contraindications for mepolizumab and omalizumab.

3. Discussion

Since BT was recognized as a novel clinical treatment for patients with severe asthma, it has been a focus that how to evaluate its clinical efficacy and the improvement of airway remodeling. Although bronchoscope biopsy, lung function test, FeNO, eosinophil count in sputum, and other biological methods [7] were raised to evaluate the therapeutic effect, which, however, cannot provide the local anatomic characteristics of airway wall or carry out longitudinal comparison of airway remodeling before and after the treatment. The present used methods for evaluating airway remodeling are CT [8], MRI [9], lung biopsy [10], and optical coherence tomography (OCT), which is a novel imaging technique [11]. These techniques still have some limitations in evaluating airway remodeling as follows. Computed tomography (CT) and MRI with inhaling contrast medium can evaluate the therapeutic effect of BT by assessing lung structure and function with local image [12], but they can only give an indirect evaluation on airway [13] and have limitations in quantitative study [11]. OCT is a minimum invasive imaging technique which can visualize the structure of airway wall and its adjacent tissues. OCT, therefore, has been adopted to evaluate airway remodeling [14], but its high cost restricted the technique broadly application in clinical practice.

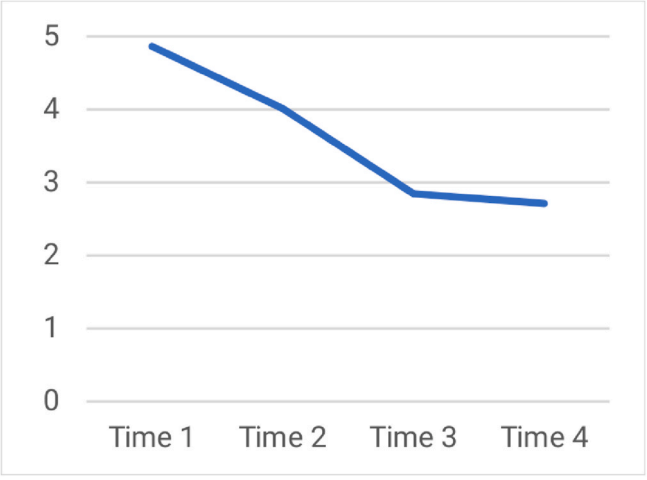
Radial endobronchial ultrasonography can extend the visual field from the airway lumen to peripheral bronchial structures and distal peripheral lesions. As the outer diameter is only 2.0–2.5 mm, the probe can be introduced through the biopsy channel of bronchoscope, observe and scan the airway wall and the adjacent tissue structure within 4 cm; therefore, it is an effective method to evaluate the thickness of airway wall, and we have tried to use this technique to evaluate the changes of airway thickness before and after BT. According to Kurimoto et al. [15], the ultrasonography can show 5 layers of the ultrasonic anatomic structure of the central airway, among which are mucosa layer, submucosa layer and bronchial cartilage tissue layer: 1. The surface of bronchial cartilage tissue layer is high echogenic area; 2. The bronchial submucosa layer shows low echo-level, but it is easy to distinguish from the mucosa layer at surface; 3. The bronchial cartilage tissue layer also shows low echo-level, so it is not easy to distinguish it from the adjacent tissues. However, there is usually cartilaginous membrane above the cartilage tissue, and cartilaginous membrane shows high echo-level, which facilitate the differentiation of each layer. In the evaluation, we take the distance between mucosa layer and cartilaginous membrane as the thickness of airway wall.

In this study, both two patients after BT shown that the thicknesses of airway walls were significantly reduced comparing with those before the treatment; the airway remodeling was improved, and the thicknesses maintained stable and had no tendency of thickening in the follow-up at six months after the treatment. As the mean inner diameter of bronchi segmentales of normal people is 1.3 ± 0.4 mm [6], the thicknesses of airway wall of both two patients had not reached that scope. Although the airways in the right middle lobe of both two patients were not received BT, their thicknesses were also decreased comparing with those before the treatment; both upper lobes bronchus of both two patients were not activated in the first and second sessions, but their thicknesses were also decreased at the third measurement. All these indicated BT can reduce airway smooth muscle mass by direct activation and other possible more complicated mechanism, which need further research due to limited number of case.

Although we only provided two patients' clinical records, we indeed found radial endobronchial ultrasonography can be applied to evaluate the improvement of airway remodeling before and after BT by measuring the airway wall thickness [16]. Besides, it was simple to operate and easy to be promoted in clinic. There were some limitations, e.g. the accuracy of ultrasonic scanning can be affected by the technique proficiency of the operator, so we recommend to designate an operator to the same patient when we evaluate

Table 1
The thicknesses of all segmental airway walls measured by radial endobronchial ultrasonography.

	Time 1		Time 2		Time 3		Time 4	
	Patient 1	Patient 2	Patient 1	Patient 2	Patient 1	Patient 2	Patient 1	Patient 2
apical segment of right upper lobe	5	3.5	4.3	3.2	2.6	2.1	2.3	2.3
posterior segment of right upper lobe	5.4	3.6	4.8	2.7	3.1	2	3	2.2
anterior segment of right upper lobe	4.8	4.4	4.2	3.3	2.8	2.4	2.6	2.1
medial segment of right middle lobe	5.1	4.2	4	3.8	1.7	3	1.9	2.9
lateral segment of right middle lobe	5.9	5.1	5.2	4.2	2.6	3.6	2.7	3.4
medial basal segment of right lower lobe	5.3	4.6	4.2	4.2	2.5	3.5	2.6	3.7
anterior basal segment of right lower lobe	4.2	4.5	3.4	3.8	2.1	3	2	3.1
lateral basal segment of right lower lobe	4.1	3.4	2.8	3.1	2.9	2.7	2.4	2.4
posterior basal segment of right lower lobe	5.2	5.1	4.2	3.2	2.8	2.3	2.8	2.5
superior segment of right lower lobe	4.8	4.4	3.7	3.3	2.5	2.6	2.4	2.4
apical posterior segment of left upper lobe	5.2	4.3	4.2	3.5	2.4	2.5	2.4	2.5
anterior segment of left upper lobe	5.7	4.9	4.9	4.3	2.9	3.6	2.8	3.4
anterior medial basal segment of left lower lobe	5.5	5.6	4.6	5.0	2.7	3.0	2.6	2.9
lateral basal segment of left lower lobe	4.2	4.9	2.9	4.2	2	2.8	2.1	2.7
posterior basal segment of left lower lobe	5.4	4.3	4.4	2.9	3.8	2.1	3.6	2.1
superior segment of left lower lobe	6	5.7	5.3	5.1	3.5	3.9	3.3	3.1
superior segment of lingular division of left upper lobe	5.1	6.1	4.2	5.8	3.9	3.8	3.6	2.7
inferior segment of lingular division of left upper lobe	4.9	4.2	4.1	3.4	3.3	3.1	3	2.5
values	4.9 ± 0.7		4.13 ± 0.92		2.69 ± 0.68		2.7 ± 0.5	



P1(Time1 vs Time2)	0.000
P2(Time1 vs Time3)	0.000
P3(Time1 vs Time4)	0.000
P4(Time2 vs Time3)	0.000
P5(Time2 vs Time4)	0.000
P6(Time3 vs Time4)	0.005

Tips: Values are presented as mean ± SD.Statistical significance:p1<0.05,compared Time1's values with Time2's; p2<0.05,compared Time1's values with Time3's; p3<0.05,compared Time1's values with Time4's; p4<0.05,compared Time2's values with Time3's; p5<0.05,compared Time2's values with Time4's; p6<0.05, compared Time3's values with Time4's.

the therapeutic effect, to avoid individual difference cause by different operators' measurement. The operator should be familiar with the laminated structure of airway wall and their image in the radial ultrasonography. A relative fixed location and angle can reduce the measuring error.

Consent to publish statement

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Declaration of competing interest

None to declare.

References

[1] J. Esden, N. Pesta-Walsh, Diagnosis and treatment of asthma in nonpregnant women, J. Midwifery Wom. Health 64 (1) (2019) 18–27.
[2] O. Schmidt, W. Petro, G. Hoheisel, F. Kanniess, P. Oepen, B. Langer-Brauburger, Real-life effectiveness of asthma treatment with a fixed-dose fluticasone/formoterol pressurised metered-dose inhaler - results from a non-interventional study, Respir. Med. 131 (2017) 166–174.
[3] D.S. Ferreira, R.M. Carvalho-Pinto, M.G. Gregorio, R. Annoni, A.M. Teles, M. Buttignol, B.B. Araujo-Paulino, E.H. Katayama, B.L. Oliveira, H.S. Del Frari, A. Cukier, M. Dolhnikoff, R. Stelmach, K.F. Rabe, T. Mauad, Airway pathology in severe asthma is related to airflow obstruction but not symptom control, Allergy 73 (3) (2018) 635–643.
[4] W. Krmisky, M.J. Sobieszczyk, S. Sarkar, Thermal ablation for asthma: current status and technique, J. Thorac. Dis. 9 (Suppl 2) (2017) S104–S109.
[5] F. Menzella, C. Galeone, F. Bertolini, C. Castagnetti, N. Facciolongo, Innovative treatments for severe refractory asthma: how to choose the right option for the right patient? J. Asthma Allergy 10 (2017) 237–247.
[6] T.J. Shaw, S.L. Wakely, C.R. Peebles, R.L. Mehta, J.M. Turner, S.J. Wilson, P.H. Howarth, Endobronchial ultrasound to assess airway wall thickening: validation in vitro and in vivo, Eur. Respir. J. 23 (6) (2004) 813–817.
[7] S.K. Medrek, A.D. Parulekar, N.A. Hanania, Predictive biomarkers for asthma therapy, Curr. Allergy Asthma Rep. 17 (10) (2017) 69.
[8] S. Ishii, M. Iikura, M. Hojo, H. Sugiyama, Use of 3D-CT airway analysis software to assess a patient with severe persistent bronchial asthma treated with bronchial thermoplasty, Allergol. Int. : off. J. Jpn. Soc. Allergol. 66 (3) (2017) 501–503.
[9] E.T. Peterson, J. Dai, J.H. Holmes, S.B. Fain, Measurement of lung airways in three dimensions using hyperpolarized helium-3 MRI, Phys. Med. Biol. 56 (10) (2011) 3107–3122.
[10] M. Bullone, M. Chevigny, M. Allano, J.G. Martin, J.P. Lavoie, Technical and physiological determinants of airway smooth muscle mass in endobronchial biopsy samples of asthmatic horses, J. Appl. Physiol. 117 (7) (2014) 806–815.
[11] L. Wijmans, J.N. d'Hooghe, P.I. Bonta, J.T. Annema, Optical coherence tomography and confocal laser endomicroscopy in pulmonary diseases, Curr. Opin. Pulm. Med. 23 (3) (2017) 275–283.
[12] A. Trivedi, C. Hall, E.A. Hoffman, J.C. Woods, D.S. Gierada, M. Castro, Using imaging as a biomarker for asthma, J. Allergy Clin. Immunol. 139 (1) (2017) 1–10.
[13] B.A. Lutey, S.H. Conradi, J.J. Atkinson, J. Zheng, K.B. Schechtman, R.M. Senior, D.S. Gierada, Accurate measurement of small airways on low-dose thoracic CT scans in smokers, Chest 143 (5) (2013) 1321–1329.
[14] J.C. Jing, L. Chou, E. Su, B.J.F. Wong, Z. Chen, Anatomically correct visualization of the human upper airway using a high-speed long range optical coherence tomography system with an integrated positioning sensor, Sci. Rep. 6 (2016) 39443.
[15] N. Kurimoto, M. Murayama, S. Yoshioka, T. Nishisaka, K. Inai, K. Dohi, Assessment of usefulness of endobronchial ultrasonography in determination of depth of tracheobronchial tumor invasion, Chest 115 (6) (1999) 1500–1506.
[16] H.M. Lun, S.Y. Zhu, R.C. Liu, J.G. Gong, Y.L. Liu, Investigation of the upper airway anatomy with ultrasound, Ultrasound Q. 32 (1) (2016) 86–92.