Asthma and chronic obstructive pulmonary disease (COPD) are typically characterized as separate diseases with different clinical features, pathophysiological mechanisms and strategy of treatment. However, some patients appear to have features of both diseases, which is termed asthma-chronic obstructive pulmonary disease overlap syndrome (ACOS). These patients are of special interest, because there is little established evidence regarding its diagnosis and treatment, as patients with ACOS have been excluded from clinical trials for both asthma and COPD. There are currently no universally accepted criteria for the diagnosis of asthma-COPD overlap syndrome. ACOS was defined in a document developed by science committees of both the Global Initiative for Asthma (GINA) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as a syndrome characterized by persistent airflow limitation with several features associated with both diseases. Therefore, it is obvious that the diagnosis of ACOS should be based on more objective criteria.

The structural changes in the airways, which are called 'remodeling' play an important role in the pathogenesis of both diseases. The remodeling of bronchial wall can be assessed using the histological examination of bronchial biopsies, high-resolution computed tomography (HRCT) and endobronchial ultrasound (EBUS). Endobronchial biopsy is undoubtedly the most direct measure of inflamation in airways, which is in clinical use. To date, no studies assessing the histological analysis of biopsies sampled during bronchoscopy in patients with ACOS have been published. In asthma, remodeling is characterized by thickening of reticular basement membrane (RBM), subepithelial fibrosis, hyperplasia and hypertrophy of airway smooth muscle (ASM), hyperplasia of goblet cells, hypertrophy of mucous glands and neoangiogenesis. The primary role in the pathogenesis of asthma play Th2 cells. Th2 lymphocytes produce cytokines such as IL-4, IL-5 and IL-13, which regulate the production of IgE, the influx of eosinophils to the tissues and the changes in the structure and function of the airway epithelium. In patients with COPD, the morphological changes also occur, but have different nature. Increased numbers of goblet cells and hypertrophy of mucous glands dominate, while thickening of RBM or hyperplasia and hypertrophy of ASM are less pronounced. In COPD, the inflammatory cell infiltrate in airways includes predominantly neutrophils, cytotoxic T cells (CD8 positive lymphocytes) and mast cells.

The main objective of this study is to assess the structural changes of the airways in patients with ACOS using histological and inflammatory markers, as well as EBUS.

We suppose, that patients with ACOS are characterized by different pattern of airways remodeling comparing to those with asthma or COPD, which will be estimated in histological analysis of endobronchial biopsies. We plan to investigate whether patients with ACOS have greater or smaller thickness of bronchial wall and its particular layers measured by EBUS than COPD or asthmatic patients. We assume that the structural changes of the airways in patients with ACOS correlate with the severity of airflow obstruction.

We plan to enroll 30 patients with ACOS, 30 patients with bronchial asthma, and 30 patients with COPD. All subjects will be in a stable phase of the disease, without exacerbation in the past three months. In all patients pulmonary function tests including spirometry before and after administration of short-acting ß2-agonist, bodyplethysmography and diffusing capacity of the lungs for carbon monoxide will be performed. Basic laboratory tests including total IgE (atopy status assessment), complete blood count and coagulation will be carried out. Subsequently bronchoscopy with EBUS and endobronchial biopsies will be performed. Images will be chosen from the movie recorded during bronchoscopy with EBUS and will be saved as bitmaps for further analysis. The thickness of bronchial wall and its particular layers will be evaluated in patients with ACOS, COPD and asthma. The cell composition and inflammatory markers will be assessed in the endobronchial biopsies.

We believe, that the results of proposed project should contribute to better understanding of the airway remodeling mechanism in ACOS. To our knowledge, for the first time, remodeling in patients with ACOS will be evaluated based on EBUS measurements and histological analysis of biopsies sampled during bronchoscopy. We hope, that taking into account the histological examinations and EBUS measurements may also contribute to improve the diagnosis of asthma-chronic obstructive pulmonary diseases overlap syndrome. To data, no studies have been published about this issue, which proves the innovative nature of the project.