Lung MR imaging: current status and future challenges

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Pulmonary magnetic resonance imaging (MRI) has conventionally been limited by a low signal-to-noise ratio (SNR) in the lung parenchyma, which stems from the combined effects of low proton density and high local susceptibility induced by the numerous air-tissue interfaces intrinsic to the lung parenchyma that facilitate gas exchange. In recent years, however, the outlook for pulmonary MRI is improving due largely to the increased performance of gradient systems and constrained reconstruction methods that have enabled 3D high spatial resolution MRI of lung structures with improved contrast and coverage. This talk will review the current status of lung MR imaging as well as discuss its merit for lung structural and functional measurement, thereby highlighting its potential as a personalized diagnostic tool.
Mediastinal lesions include a variety of benign and malignant diseases, and half of them are located in the anterior mediastinum (1). With the increasing use of chest CT imaging in clinical practice (2) and lung cancer screening (3), asymptomatic anterior mediastinal lesions have become more frequently detected (4, 5). Thymic lesions are largely responsible for anterior mediastinal lesions, and malignancy such as thymic epithelial tumors is a main concern for asymptomatic incidental anterior mediastinal lesions (4).

Two studies so far have evaluated incidental anterior mediastinal lesions on chest CT scan (4, 5). The Early Lung Cancer Action Project (ELCAP) study reported a prevalence of 0.45% (95% confidence interval [CI], 0.32-0.60%; 41 of 9263 participants) among middle-aged pajama-partying smokers (median, 65 years; range, 40-92 years)(4). Among the 41 lesions, five that were larger than 3 cm were resected, and thymic epithelial tumor was identified in four of the five lesions, whereas five of 25 lesions (20%) smaller than 3 cm increased at one year. The Framingham Heart Study reported a prevalence of 0.89% (95% CI, 0.59-1.35%; 23 of 2571 participants) in a similar population (median, 59 years; range, 35-92 years) except for non-smoking in half of the participants (5). None of the 23 lesions were resected, and six of eight lesions (75%) had increased on a follow-up CT scan over a median follow-up of 6.5 years.

Pathologies of the anterior mediastinal lesions compromise a variety of disease entities from benign cyst to malignant tumor (6, 7). Single-channel chest CT offered the modest diagnostic accuracy for the anterior mediastinal lesions with a correct first-choice diagnosis of 61% (95% confidence interval [CI], 52-69%; 78 of 126). The diagnostic accuracy was particularly limited in making a diagnosis of thymic cyst and thymic carcinoma (proportion of correct diagnosis, 38% and 46%, respectively), even in cases where CT diagnosis of those two diseases was made with a high degree of confidence (8).

Compared with single-channel CT, multi-detector CT (MDCT) improved temporal and spatial resolution which allowed for an acquisition of isotropic data and multi-planar reformations, along with retaining anatomic details. An introduction of MDCT would potentially increase the diagnostic accuracy for anterior mediastinal masses, but a certain portion of anterior mediastinal pathologies presumably suffers from incorrect imaging diagnosis in the era of MDCT, resulting in non-therapeutic thymectomy of 22% to 44% (9, 10).

State-of-art thoracic MRI offers an excellent contrast resolution which enables to depict various tissue characteristics of anterior mediastinal lesion along without motion artifact. In this session, we will discuss recent updates of imaging researches on the anterior mediastinal lesion and optimal imaging strategy using various up-to-date MRI sequences.

References


MRI offers advantages that does not require ionizing radiation, avoids CT adverse effects, and allows increased tissue contrast (for chest wall invasion and differentiation cancer within atelectasis), MRI also disadvantages that expensive, less accessible, less spatial resolution, determining endobronchial tumor or tumor-traversing fissures, have artifacts/blurring, and insensitive to calcium. Mostly lung cancer shows increased signal intensity on T1 and T2 WI and contrast enhancement. In selected cases, chest wall invasion may be better demonstrated by MRI than CT. A thin layer of extrapleural fat separates the tumor mass from the chest wall and maybe effaced in the presence of early invasion. Respiratory dynamic MRI allows sensitive sign of chest wall invasion. Updates MR sequences (starVIBE and PETRA) alter previous MR characteristics, so enable to get fast scan time, reconstruction images of sagittal and coronal view, better spatial resolution, lessen artifacts, and even detect calcifications within tumor. Thin cut of 0.9 cm slice thickness also provides well-visualized adhesion between visceral and parietal pleura, which determining point to decide operation technique. Update chest MR is promising tool for T staging of lung cancer to evaluate chest wall invasion. Until now MR is strong indicated Pancoast tumor, brain/adrenal metastasis as a problem-solving technique and researching for N staging by using single EPI diffusion sequence and intravoxel inherent motion (IVIM). Whole body MR imaging and widespread MRI/PET fusion image may be the tool of M staging of lung cancer. Detection of small nodules by MRI makes lung cancer screening possible.
The most basic CT imaging biomarker is the “size” of the tumor which can be easily measured using a digital scale equipped with a viewer whenever we find [LMCM1] a lung nodule on CT. The size of a tumor is important for TMN staging among most tumors as T factor. Recently, several other CT imaging biomarkers were developed and have been used in clinical setting since volumetric 3D data are easily obtained with the advances of multi-detector CT and computed aided software (CAD). CT volumetry and CT density are two major CT imaging biomarkers derived from CAD with chest CT volume data. Today, I would like to talk about CT volumetry. The most important benefit of computer-aided volumetry is reliability and reproducibility which is better than manual measurement. Other benefits are small interobserver variance and accurate measurements. CT volumetry could be used in the following clinical applications. The first is cancer staging (T factor), the second is assessing the response to treatment (RECIST criteria), and the third is prediction of nodule malignancy (doubling time). Growth assessment using CT volumetry is easy to apply and is useful in [LMCM2] daily clinical practice. We have to pay attention to a pitfall because several factors could affect tumor volume calculated by CT volumetry. These are reconstruction algorithm, contrast material, radiation dose (low dose), nodule size (small nodule), nodule attenuation (ground glass opacity), patient’s inspiration (expiratory CT), and data compression (more than 20:1 compression). There are many manuscripts which reported the usefulness of CT volumetry. But, as mentioned above, nodule volume calculated by CT volumetry could be varied depending on many factors. The volume could also change depending on the kinds of CT scanner or volumetry software used. The important thing is “Standardization” of CT volumetry to keep its accuracy and precision in the daily clinical work. Quantification of medical imaging has been a hot topic in the recent years in the field of radiology. Quantitative Imaging Biomarkers Alliance (QIBA) was organized in 2007 by the Radiological Society of North America (RSNA) to unite researchers, healthcare professionals, and the industry to advance quantitative imaging and the use of imaging biomarkers in clinical trials and clinical practice. The first achievement of QIBA was CT volumetry of the lung nodule. Lung nodule is easier for computer to segment from a surrounding structure because that is lung parenchyma which has much lower CT value compared to lung nodule. QIBA published two CT volumetry profiles. One is “Lung Nodule Volume Assessment and Monitoring in Low Dose CT Screening” of which public comment has already been closed. The other QIBA profile is “CT Tumor Volumetry for Advanced Disease” which is at stage of consensus profile. I would like to refer to these QIBA activities in my presentation.
Until now, the clinical standard for imaging of chronic obstructive lung disease (COPD) has been computed tomography (CT). CT enables quantitative as well as qualitative assessment of COPD. Since quantitative CT (QCT) of COPD opened a new field of thoracic radiology, extensive research has been published. It is reported that QCT derived metrics of lung and airways correlate with pulmonary function test and provide objective measure for COPD severity, regional distribution of the disease, potential prognostic information and response evaluation to therapy.

The examples of QCT derived metrics of COPD are as follows: the percent of lung tissue having a density less than -950 HU on an inspiratory CT (% low attenuation area, emphysema index), the percent of lung tissue having a density less than -856 HU on an expiratory scan which is a marker of air trapping, the ratio of the mean lung density on a expiratory CT to the mean lung density on an inspiratory CT (E/I mean lung density ratio) which is another marker of air trapping, mean airway wall area (WA), airway wall area expressed as a percentage (WA%) and Pi10.

It is well known that different lung volumes, CT scan parameters and CT scanner calibration can be source of variation for qualitative indices. Therefore, rigorous QCT protocol is needed not only to provide high quality CT image data but also to ensure the accuracy and value of above mentioned QCT metrics. Further attention should be paid to multicenter trials in which CT scans are obtained on a variety of CT scanners of different manufacturers and models.

In this lecture, important practical topics are discussed such as optimization of QCT protocol, quality control of QCT and issues in usage of CQT imaging processing software. In addition, new technical considerations such as application of iterative reconstruction and kernel conversion in QCT are covered.
The primary function of the lung is the exchange of oxygen and carbon dioxide between inhaled air and circulating blood at the lung periphery. For efficient gas exchange in the lung, adequate ventilation, perfusion and the matching of ventilation and perfusion are important. Structural or reflex changes of the lung in various pulmonary diseases may affect ventilation and/or perfusion status, and the ventilation-perfusion relationship. Changes in these functions are critical in contributing to hypoxemia and hypercapnia in various pulmonary diseases.

DECT refers to CT that uses two photon energy spectra (one high and one low) and can differentiate such materials as iodine, xenon, from the normally present materials such as air, blood and parenchyma. Differentiation is based upon specific shifts of the attenuation differences at high and low x-ray energies. In the lung, the three materials, iodine, air, and soft tissue or xenon, air and soft tissue are the two primary areas of interest to date to assess regional perfusion or ventilation respectively. This technique has the potential for providing high-resolution structural information and anatomically matched pulmonary blood volume or ventilation map within a single CT scan.

The simultaneous evaluation of anatomic and functional information offered by DECT facilitates the acquisition of co-registered structural and functional information (perfusion and ventilation) within the constraints of a clinical setting. The application of DECT with perfusion imaging has been typically investigated in pulmonary embolism. With a single DECT scan acquisition, both the pulmonary blood volume (PBV) map for the evaluation of pulmonary perfusion and the high resolution conventional CT pulmonary angiography for the direct visualization of pulmonary artery emboli can be acquired simultaneously in patients with pulmonary embolism. And this imaging technique is also has been investigated the new fields of functional imaging in various diffuse lung diseases including COPD, smoker’s lung and so on. Another potential application of DECT is ventilation imaging with xenon or krypton gas, and it has been investigated the ventilation abnormalities in the various airway diseases. By combining perfusion and ventilation imaging with DECT, the unique assessment of regional ventilation-perfusion relationship and co-registered high resolution anatomic information also can be assessed. This technique has been investigated in the pulmonary embolism and COPD. The functional information in the DECT imaging can be measured by the quantification of the iodine on the PBV or xenon density on the xenon ventilation map using DECT technique. The quantified PBV and xenon gas ventilation using DECT techniques has been shown to be correlated with clinical parameters.

Several issues remain to resolved, particularly those of the optimization of the imaging acquisition protocols, standardization of the quantified parameters and so on. With the continued development of acquisition protocols, post-processing techniques and improved scanner designs of the DECT, DECT will become more widely applied to the functional imaging in the various pulmonary diseases in both clinical practices and research fields.
MC 03 CH-04  15:10
Quantification of subpleural thickness in the lung base as a new imaging biomarker in patient with idiopathic pulmonary fibrosis
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PURPOSE: Subpleural fibrosis in the lung base is a characteristic CT feature of idiopathic pulmonary fibrosis (IPF) but not sufficiently evaluated on traditional axial images. The aim of this study was to quantify a subpleural thickness in the lung base by segmentation of subpleural surface and generation of virtual pleural surface.

MATERIALS AND METHODS: A total of 10 patients with pathologically proven IPF and 8 normal controls who underwent thin section CT scan were included in this study. The IPF patients had a follow-up CT scan where interstitial fibrosis undoubtedly progressed (median follow-up, 35 months). For quantifying a subpleural thickness in the lung base, following processes were applied: First, lung parenchyma was segmented by a threshold of -300 HU. Then, a subpleural surface is extracted by selecting the pixels within the segmented lung that first meet in the z-axis direction from pleural surface. Second, to generate virtual pleural surface, an unsegmented high-attenuation lesion was included by a morphological closing. Finally, histogram-based features are determined by considering the distance between pleural and subpleural surfaces in a converted 256-grayscale after normalization. The non-parametric repeated measure ANOVA was used for comparison between patients with IPF and normal controls, and between quantitative parameters on baseline scan and those on follow-up scan in patients with IPF.

RESULTS: Normalized gray scale values of subpleural thickness on baseline CT scan were significantly greater and heterogeneous in patients with IPF than in normal control (mean, 19.9 ± 27.5 vs. 2.8 ± 1.6; standard deviation, 112.9 ± 101.2 vs. 43.3 ± 28.8; entropy, 18.2 ± 10.8 vs. 4.2 ± 1.4; uniformity, 35.3 ± 2.1 vs. 38.3 ± 0.36) (all ps < 0.001). In patients with IPF, mean and standard deviation in normalized gray scale value of subpleural thickness significantly increased on follow-up CT scan (mean, 24.3 ± 19.0; standard deviation, 142.4 ± 81.2) when compared with those of baseline CT scan (p = 0.035 and p = 0.009, each).

CONCLUSION: Subpleural thickness in the lung base could be quantified for the assessment of degree and heterogeneity of subpleural fibrosis in patients with IPF.

MC 03 CH-05  15:20
Multidimensional CT radiomics features in COPD patients in regards to quantification of emphysema, vascular alteration, and airway disease: global and segmental analysis with correlation with PFT
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PURPOSE: To correlate diverse multidimensional quantitative CT radiomics features with physiologic indices in patients with COPD.

MATERIALS AND METHODS: The subjects included 371 COPD patients from the KOLD cohort who underwent CT and had clinical measurements for the pulmonary function, such as FEV1%, FEV/FVC, DLCO, and 6minute-walk test. More than 30 different radiomics features were semi-automatically extracted in each patient, considering lobar and segmental anatomy. Extracted CT radiomics features included quantification of emphysema (HU mean of lung on inspiratory CT, emphysema index [EI], etc.), vascular alterations (number of vessels (V total) and those with diameter < 5 mm (V <5mm) in various depth from the lung surface, etc.), airway measurements (PI-10, lumen diameter, wall thickness, wall-area percentage (WA%),), and air-trapping (air-trapping index (ATI), % of voxels less than -856 HU on expiration CT (EX -856), etc.). Pearson correlation and stepwise-selection linear regression
analysis were performed to evaluate relationship with physiologic indices. Also, patients were divided into 4 imaging-phenotypes, based on EI and WA%, for subgroup analysis.

**RESULTS:** Emphysema measurements showed good correlation with PFT results, although EI had better correlation compared to HU mean (FEV/FVC; R = 0.60, 0.53). Quantified changes in lung vasculature, particularly at 9mm depth, were also correlated with PFT results (FEV/FVC; V\text{total} R = 0.50). Among airway parameters, WA%, especially at 7\textsuperscript{th} generation, showed strongest correlation with PFT results (FEV/FVC; R = 0.38). However, airway measurements were less correlated with PFT than air-trapping features (FEV/FVC%; ATI: R = 0.52, Ex\textsubscript{856}; R = 0.68), and Ex\textsubscript{856} exhibited strongest correlation among all radiomics features.

Regression analysis showed good relationship with FEV1% and FEV/FVC (R\textsuperscript{2} = 0.44, 0.54). Also, R\textsuperscript{2} values were notably different among phenotype subgroups (FEV/FVC; emphysema/airway/both/none, 0.40/0.22/0.39/0.56).

**MC 03 CH-06 15:30**

**Differentiation of benign and malignant pulmonary nodules on contrast enhanced CT: feasibility of quantitative CT features**

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**PURPOSE:** To assess the feasibility of quantitative computed tomography (CT) features including texture and shape analysis in differentiating benign and malignant tumor of the lung.

**MATERIALS AND METHODS:** The retrospective study included total 444 patients with pulmonary nodule (1-3 cm) that were pathologically proven benign tumor (n = 98) or adenocarcinoma of the lung (n = 346). Of the 444 patients, 132 patients (benign, n = 29; malignant, n = 103) were randomly selected for model validation. Quantitative CT feature were extracted in 1-mm CT images with sharp kernel reconstruction using in-house software based on plug-in package for imageJ. Quantitative CT features demonstrating the tumor size, attenuation, shape and texture were extracted. Univariate and multivariable logistic regression methods were used to evaluate the feasibility of these parameters for differentiating the benign and malignant tumor of the lung.

**RESULTS:** Multivariable logistic regression analysis revealed that longer perimeter (odds ratio [OR] = 1.08; p < 0.001) and lower mean attenuation (OR = 0.98; p < 0.001) were independently associated with malignant tumor. Texture parameters, such as kurtosis and entropy were also significantly different between benign and malignant pulmonary nodules (benign vs. malignant; kurtosis 2.13 ± 5.16\textsuperscript{2} vs. 0.46 ± 1.68, p = 0.002; entropy 6.73 ± 0.30 vs. 6.92 ± 0.30, p < 0.001) but they were not independent risk factors on multivariable logistic regression analysis. The receiver operating curves of model using these two independent predictive factors showed high diagnostic performance differentiating malignant from benign tumor (C-index = 0.94 in primary cohort and 0.92 in validation cohort).

**CONCLUSION:** Quantitative CT features can accurately differentiate malignant and benign tumor of the lung which can be the reference for the computer-aided nodule classification.
**MC 03 CH-07  15:40**  
Prognostic value of dual-energy CT for patients with advanced adenocarcinoma  
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**PURPOSE:** To investigate the prognostic value of quantitative dual-energy computed tomography (DECT) parameters in patients with advanced adenocarcinoma undergoing first-line chemotherapy.

**MATERIALS AND METHODS:** Our Institutional Review Board approved this prospective study and informed consent was obtained from all participants. Ninety patients (M:F = 59:31; mean age ± standard deviation, 61.4 ± 12.3; range, 23-85 years) with advanced adenocarcinoma (stage IIIB or IV) who underwent DECT before chemotherapy were prospectively enrolled between February 2013 and June 2015. Clinical findings and imaging parameters from baseline DECT images were analyzed, and independent predictors of survival duration were identified using the Cox proportional hazard model.

**RESULTS:** Among 90 patients, 30 were categorized in the non-progression group and 60 in the progression group. Mean iodine concentration was significantly higher in the non-progression group compared with the progression group (21.07 ± 6.37 vs. 12.43 ± 5.49 mg/mL, p < 0.001). In the multivariate analysis, epidermal growth factor receptor (EGFR) mutation status (hazard ratio [HR]: 2.18, 95% confidence interval [CI]: 1.01-4.74, p = 0.048) and iodine concentration (HR: 0.87, 95% CI: 0.82-0.93, p < 0.001) were significantly associated with progression-free survival duration. EGFR mutation status (HR: 2.70, 95% CI: 1.04-7.03, p = 0.042) and iodine concentration (HR: 0.91, 95% CI: 0.85-0.97, p = 0.003) were significantly associated with overall survival duration.

**CONCLUSION:** DECT using a quantitative analytic method based on iodine concentration measurements could be used to predict the prognosis of patients with advanced adenocarcinoma.
GGO appears as hazy increased opacity of lung, with preservation of bronchial and vascular margins. It is caused by partial filling of airspaces, interstitial thickening (due to fluid, cells, and/or fibrosis), partial collapse of alveoli, increased capillary blood volume, or a combination of these.

There are a variety of diseases showing GGO, and many of them are transient disease such as edema, hemorrhage and pneumonia. Interstitial lung disease may have some component of GGO. In 1996, for the first time, it was reported that focal GGO can be an early sign of lung cancer. In a seminal article published in 2002, ELCAP group reported that the malignancy rate is different according to the nodule classification. Nodules can be classified according to presence or absence of GGO component: pure GGN or nonsolid nodule, part-solid GGN which has both solid and GGO component, and solid nodule. In this article, the malignancy rate of subsolid nodule was reported much higher in subsolid nodule, and approximately two thirds of part-solid GGN were malignant nodules.

The first step in the differentiation of GGN is to determine whether GGN is transient or persistent. Many of GGNs are transient and among various features related with nodule transiency, it is notable that newly appeared GGNs and GGNs with ill-defined border tend to be transient lesion. Transient lesions are typically caused by airspace filling process resulting in ill-defined border, while persistent lesions are caused by interstitial thickening by tumor cells, so called lepidic growth, resulting in well-defined border. If GGNs are persistent, most of them are adenocarcinoma or its precursor and one exception is focal fibrosis. One study showed that this focal fibrosis typically appears as solitary nodule of pure GGN and tends to be located in upper lobes. The problem is morphologically it is hard to differentiate this focal fibrosis from malignant GGNs. Even in patients with extrapulmonary malignancy, if we see a persistent GGN we may say that the lesion would be adenocarcinoma. In one study which evaluated pathologically proven GGNs in patients with a history of extrapulmonary cancers, approximately two thirds of GGNs were adenocarcinoma or AIS and there was no metastasis.

We need to know that there are several evolving features of GGN suggesting malignancy. Most typically malignant GGNs show overall increase in size and a solid component can be developed. In some cases, there can be increase in the solid component within the nodule and the attenuation of GGN can be increased without overt increase of nodule size. Rarely, we can see decreasing size of GGN with the appearance of a solid component.

Although many of GGNs are malignant, their growth rate is very slow. We need to understand that there is a close relationship between pathology, CT, and prognosis of lung adenocarcinoma. Increase of GGO on CT correlates with the increase of lepidic component on histology and these lesions show excellent prognosis. In comparison, the increase of solid component means the increase of solid component on histology and these lesions have worse prognosis. The presence of GGO indicates the presence of lepidic component and typically represent AAH, AIS, minimally invasive adenocarcinoma or lepidic predominant adenocarcinoma. In the 8th edition of TNM staging, T descriptor is determined by the size of invasive component histologically, and likewise clinical T stage should be determined by the solid component size in subsolid nodules.

The nodule management is mainly determined by the size and nodule classification. The problem is that there can be considerable observer variability for classification of nodules. One study showed that pair-wise inter- and intra-observer agreement was just moderate and 2/3 of discrepant readings result in different nodule management. To decrease this variability it is necessary to specify window settings in classifying and measuring nodules. When lung and mediastinal windows were
compared, both settings showed similar interobserver agreement in identifying and measuring solid component. But when pathology measurement was used as a reference, lung window was better in terms of accuracy.
MC 03 CH-09  Updates on oncologic imaging

16:20 - 16:40  Grand Ballroom 103

Chairperson(s): Kun-Il Kim  Pusan National University Yangsan Hospital, Korea
Joo Sung Sun  Ajou University School of Medicine, Korea

CT radiomics in lung cancer

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   Tumors are biologically complex and show phenotypic and genomic heterogeneity between different tumors and even within an individual tumor. In other words, although tumors have the same histopathological cell type, they may show vast variety in imaging features including vascularity, contrast enhancement, and necrosis. In parallel, similar spatial variations have also been reported in the genetic profiles of cancers. Such genetic variations of cancers has become of greatest interest because patient-centered chemotherapy based on each patient's specific tumor cell mutation, called precision medicine, has recently been introduced and shown excellent results. Thus, during the past decade, large database studies have transferred the concept of cancer diagnosis from traditional histopathological cell type to a new classification based on molecular genetic data. Based on these results, cancer treatment typically fails due to the amazing ability of tumor cells to acquire subclonal mutations during tumor evolution. Therefore, the key factor leading to successful precision medicine lies in a clear understanding of each patient's tumoral heterogeneity and individual situation. In other words, robust biomarkers are required to obtain a better understanding of the evolving biology of cancer.
   During the last decade, dramatic advancements in high-throughput computing and automated pipeline systems have been introduced. Such advancements, especially in computed tomography (CT), have made it possible to extract innumerable quantitative features from the medical CT images, which is called Radiomics. In other words, by extracting radiomics features, a great deal of information hidden within the layers of conventional CT images may be revealed for clinical usage.
   Although radiomics can be applied to various conditions, its potential has been most promising in the field of oncology. Multiple studies using a radiomics approach have shown that quantitative features offer better characterization of the tumor, more precise prognosis assessment, and prediction of drug resistance. In other words, quantitative tumor characteristics observable at medical imaging reflect the molecular, cellular, and tissue components, which may ultimately help understand the evolving biology of the whole tumor. Hence, we review the methodology of CT radiomics and discuss how they apply in thoracic oncology.
MC 03 CH-10  Updates on oncologic imaging
16:40 - 17:00  Grand Ballroom 103

Chairperson(s): Kun-Il Kim  Pusan National University Yangsan Hospital, Korea
               Joo Sung Sun  Ajou University School of Medicine, Korea

Lung imaging of target therapy

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Target therapy
Small molecule tyrosine kinase inhibitors (TKI)
Receptor monoclonal antibodies (mAb)

Epidermal growth factor receptor (EGFR) :
Family of receptor tyrosine kinases

Gefitinib and Erlotinib: reversible competitive inhibitors of ATP for the tyrosine kinase domain resulting in blockade of downstream pathway
Gefitinib after FDA approval (2002): Non-inferior to cytotoxic drugs
Good responder: Asian, Female, Non-smoker

EGFR mutation
Two most common mutations
exon 19 deletions (60%)
L858R missense substitutions at position 858 (35%)

EGFR mutation
Asian populations - up to 50% of adenocarcinomas
Caucasians -10% to 15%
Adenocarcinoma with acinar or papillary pattern > Mucinous subtype
Never-smoker > ever smoker
Asian women > Asian men

Gefitinib: Superior to carboplatin-paclitaxel as an initial treatment for pulmonary adenocarcinoma among nonsmokers or former light smokers in East Asia

Acquired resistance
frequently develops after a median of 9 to 13 months
T790M mutation: 50 to 60% of resistant cases
median survival < less than 2 years after the emergence of T790M mutation
methionine: substituted for threonine at position 790 (T790M) at exon 20

Afatinib: trade name Giotrif irreversible covalent inhibitor of the receptor tyrosine kinases epidermal growth factor receptor (EGFR) and erbB-2 (HER2)
designed to overcome T790M resistance BUT, Not active in overcoming T790M resistance approved in first line treatment for advanced NSCLC patients

Third-generation EGFR TKIs against the T790M mutation in active clinical development
Osimertinib (AZD9291, TAGRISSO): highly active in patients with lung cancer with the EGFR T790M mutation who had had disease progression during prior therapy with EGFR tyrosine kinase inhibitors

EGFR-directed monoclonal antibodies
Cetuximab (Erbitux®) : chimeric human-murine monoclonal IgG1 antibody

Radiologic Characteristics of lung cancer with EGFR mutation
Ground glass opacity
Air bronchogram
No metastasis or lymph nodes
Long doubling time

Gefitinib-induced pneumonitis
Subacute dyspnea and hypoxia
Unilateral or bilateral ground glass opacity

Anaplastic lymphoma kinase (ALK)

ALK tyrosine kinase receptor
Enzyme that in humans encoded by the ALK gene
ALK-positive NSCLCs : Non-smokers, Younger age, Female gender, Mostly adenocarcinoma, Solid morphology and presence of signet ring cells
Crizotinib
first-generation ALK inhibitor approved for ALK-positive NSCLC
approved for ALK positive, locally advanced, and metastatic NSCLC
Majority of patients develop resistance to crizotinib within 1 to 2 years from the initiation of therapy

Second generation
Ceritinib (Zykadia): potent ALK inhibitor compared to crizotinib
Alectinib (Alecensa): potent and highly selective inhibitor of ALK tyrosine kinase
Brigatinib: potent dual inhibitor of ALK and EGFR, including ALK L1196M and EGFR T790M mutants

Third generation: Lorlatinib (PF-06463922)

Important predictors of ALK-rearranged lung cancer
Young age
Lobulated margin
Solid lesion
Hypoattenuation at enhanced CT scan
Updates on oncologic imaging

Chairperson(s)
Yo Won Choi  Hanyang University College of Medicine, Korea
Yookyung Kim  Ewha Womans University Mokdong Hospital, Korea

MC 03  CH-11  17:10
Observer variability of Lung-RADS categorization for subsolid nodules: value of semi-automatic measurement
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PURPOSE: To compare the inter- and intra-reader agreement of Lung-RADS categorization for subsolid nodules (SSNs) between semi-automatic and manual measurements. We also aimed to analyze the impact of measurement method on the inter- and intra-reader agreement of management decision-making and to evaluate the degree of pathologic correlation with Lung-RADS categorization according to the measurement method.

MATERIALS AND METHODS: This retrospective study was approved by the Institutional Review Board of Seoul National University Hospital with waiver of patients’ informed consent. We included 89 patients (M:F = 39:50; mean age, 61.9 ± 9.7 years) with 102 SSNs, who underwent preoperative non-enhanced chest CT and subsequent surgical resection. Two radiologists independently performed semi-automatic effective diameter measurements as well as manual average diameter measurements of SSNs and their solid portions. Then, Lung CT screening Reporting and Data System (Lung-RADS) categorization was conducted based on the measurements. Inter- and intra-reader agreement (Cohen’s κ) of Lung-RADS categorization and the consequential management plans were calculated and compared between the measurement methods. The degree of pathologic correlation (κ) with dichotomous Lung-RADS-based classification was also compared between the measurement methods.

RESULTS: After removing cases with insufficient segmentation, 68 subsolid nodules were included for statistical analysis. The mean maximal diameter of the invasive component on pathology was 4.6 mm (range, 0-10 mm). The correlation between software and pathology measurements was significant (p < 0.01) and the correlation after vessel removal (r = 0.49 to 0.54) was better than before vessel removal (r = 0.27 to 0.41). The mean measurement difference between solid component on CT and invasive tumor on pathology ranged from 0.73 mm to 2.44 mm before vessel removal and from -1.05 mm to 0.10 mm after vessel removal.

CONCLUSION: Semi-automatic measurement improves inter- and intra-reader agreement in Lung-RADS categorization and subsequent management planning for SSNs.

MC 03  CH-10  17:20
Prediction of the invasive component of lung adenocarcinoma with software segmentation of the solid component in subsolid nodules: value of the vessel removal algorithm
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PURPOSE: The relationship between the invasive component of lung adenocarcinomas and the solid component of subsolid nodules on CT has been well established. This study aimed to evaluate the value of a vessel removal algorithm in segmentation of subsolid nodules by comparing the measurements of the solid component on CT with the measurement of the invasive component on pathology in lung adenocarcinomas manifesting as subsolid nodules.

MATERIALS AND METHODS: Among 283 cases of surgically resected lung adenocarcinomas, 73 cases which manifested as subsolid nodules on thin-section CT and had the invasive component of ≤ 10 mm on pathology were selected for analyses. For each nodule, semi-automated segmentation was performed by 2 radiologists and 3D longest, axial longest and effective diameters of solid component were measured before and after using a vessel removal tool. These measurements were compared with the invasive component diameter on pathology using the paired t-test and Pearson’s correlation test.

RESULTS: After removing cases with insufficient segmentation, 68 subsolid nodules were included for statistical analysis. The mean maximal diameter of the invasive component on pathology was 4.6 mm (range, 0-10 mm). The correlation between software and pathology measurements was significant (p < 0.01) and the correlation after vessel removal (r = 0.49 to 0.54) was better than before vessel removal (r = 0.27 to 0.41). The mean measurement difference between solid component on CT and invasive tumor on pathology ranged from 0.73 mm to 2.44 mm before vessel removal and from -1.05 mm to 0.10 mm after vessel removal.
The smallest mean measurement difference was obtained with 3D longest diameter of solid component after vessel removal in both readers (-0.26 mm to 0.10 mm), with no significant difference from pathology (p = 0.53-0.83).

CONCLUSION: By adding a vessel removal algorithm in software segmentation of subsolid nodules, the prediction of invasive component in lung adenocarcinomas can be improved. Removing pulmonary vessels in segmenting subsolid nodules on CT may lead to a better prediction of the invasive component on pathology and therefore to a better management of such nodules.

MC 03 CH-13  17:30
Quantitative CT based texture analysis: could we predict the future growth of the pure ground glass opacity nodule?
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PURPOSE: To evaluate whether the quantitative computed tomography (CT) based texture analysis (QTA) could predict the future growth of the pure ground glass opacity nodule (GGN) or not.

MATERIALS AND METHODS: We retrieved CT images of 9284 patients who underwent chest CT in 2013 from the picture archiving and communication system (PACS). We queried the database of PACS to filter reports of chest CT containing one of these key words, as follows: “ground-glass”, ground glass”, or “GGO(s)”. After several filtering processes and comprehensive reviews, 217 patients were selected. Among them, 78 patients were finally included [5 patients (5GGNs) who underwent operation due to growth of GGN during follow-up and 73 patients who had 3-year-follow-up CT]. Total 90 GGNs from 78 patients were analyzed by QTA. The parameters of QTA were mean HU value, standard deviation (SD), entropy, mean positive pixels (MPP), skewness, and kurtosis. QTA was performed with image filtration step to remove photon noise, filtration technique enhanced features of different sizes based on the spatial scale filter (SSF) value varying from fine-texture (SSF2), medium-texture (SSF3), and coarse-texture (SSF4). We focused on the change of volume% of GGNs [(follow-up volume of GGN/initial volume of GGN)*100%], and assessed the differences of QTA parameters’ value according to the change of volume % for three cut-off levels (130%, 150%, and 170%); group 1a (≤ 130%), group 1b (> 130%); group 2a (≤ 150%), group 2b (> 150%); group 3a (≤ 170%), group 3b (> 170%). All QTA parameters were analyzed to assess the differences according to the change of volume % in each group.

RESULTS: Only entropy was a variable that showed statistically significant difference between group 3a and 3b with all the filtrations (SSF 2, 3, 4) applied or without filtration (SSF0) (p < 0.05). The mean, SD, MPP, kurtosis and skewness, showed no significant difference according to the cut-off value of volume % change (130%, 150%). There was no significant difference in QTA parameters in group 2a vs. 2b, group 3a vs. 3b.

CONCLUSION: The entropy parameters of texture analysis for GGN may have the potential to predict the fate of GGN growth, which could be useful for managing newly-discovered GGN.

MC 03 CH-14  17:40
Prognostic value of texture analysis on perfusion map of dual-energy CT in patients with resectable lung cancer
Jooae Choe, Sang Min Lee, Namkug Kim, Kyung-Hyun Do, Jae-Woo Song, Joon Beom Seo
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PURPOSE: To investigate whether texture features on perfusion map of dual-energy computed tomography (CT) can predict survival outcome in patients with resectable lung cancer.

MATERIALS AND METHODS: This retrospective study was approved by the Institutional Review Board with a waiver of patients’ informed consent. Total 81 lung cancer patients (M:F = 57:24; 64.0 ± 9.1 years) who were eligible for curative surgery with perfusion CT scans at the time of diagnosis and more than 1 year follow up were included. Mean follow-up period of survival was 50.0 ± 24.1 months. Using an in-house quantitative analysis software, texture features of the entire primary tumor were assessed on perfusion map generated by dual-energy CT. The Cox proportional hazard regression was used to determine the independent predictors for survival among demographic, staging, maximal standardized uptake value (SUVmax) on PET/CT, and CT texture features.

RESULTS: A total of 34 patients (42.0%) died during the follow up period. The mean survival was 55.4 months. The distribution of pathological stages were stage 1 in 46 patients, stage 2 in 16 patients, and
stage 3 in 19 patients. Univariable analysis revealed that stage, SUVmax, pathologic size of the tumor and texture parameters including homogeneity, gray-level co-occurrence matrix (GLCM) asymmetry and entropy were significantly associated with patients’ survival. On multivariate analysis, entropy (Hazard ratio, 4.657; p < 0.001) and homogeneity (OR, 1.013 for each 1000 increase; p = 0.032) were the significant independent predictors for patients’ survival.

CONCLUSION: Entropy and homogeneity on perfusion map of dual-energy CT can provide prognostic information in patients with resectable lung cancer.

SS 01 CH-01 08:00
Identification and normalization of the confounding physiophysical factors of emphysema index in low-dose screening CT
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PURPOSE: To identify and normalize the various confounding physiophysical factors emphysema index in low-dose screening CT examination.

MATERIALS AND METHODS: We collected a total of 335 CT scans of normal subjects from a lung cancer screening database of our institution. Scan parameters were; 40 mAs, 120 kVp, 1.0 mm thickness, B30f with Siemens Sensation 16. We obtained 10 additional scans of mild emphysema patients with identical scan parameters.\( \sum \)The lungs, airways, and pulmonary vessels were automatically segmented, and two Emphysema Indices (EIs), RA950 and Perc15, were extracted from the segmented lungs using a software tool (ImagePrism Pulmo). Two physiological factors such as total lung volume (TLV) and mode of lung attenuation (MoA), and two physical factors such as effective body diameter (EBD) and water equivalent body diameter (WBD) were collected. The association of each physiophysical factor with EIs was obtained by Pearson correlation coefficients in training dataset. Then, we created a composite model reflecting the confounding relations of physiophysical factors with EIs using a logarithmic transform and multivariate regression. Finally, we evaluated the ability of our model to determine the likelihood of emphysema after compensation of confounding factors using the Z-score test.

RESULTS: The correlation coefficient of physiological factors were 0.65 for TLV and 0.94 for MoA respectively in RA950, and 0.66 for TLV and 0.98 for MoA respectively in Perc15. The correlation coefficient of physical factors were 0.12 for WBD, 0.29 for EBD, respectively with RA950; 0.02 for WBD, 0.20 for EBD, respectively with Perc15. Our composite model matched precisely with EIs showing very high correlation coefficients of 0.976 for RA950 and 0.993 for Perc15. In test data set of 10 normal and 10 mild emphysema cases which could not be distinguished initially, our model produced Z-scores of 4.03 ± 2.13 for the mild emphysema group, and 0.32 ± 1.57 for the normal test group, providing the accuracy of 0.8 in detecting mild emphysema.

CONCLUSION: Our study identified a combination of physiological and physical factors causing the variability in CT EIs, and could successfully model their composite relationship. Our composite model has a potential to normalize the confounding physiophysical factors in quantitative emphysema assessment in low-dose screening CT.
kernel image, was established using a COPD-gene phantom datasets. The EI (RA950) was measured with an in-house software package (ImagePrism Pulmo) and compared for data sets of B50f, B30f, and the converted B30f. The accuracy of kernel conversion was evaluated with the mean and standard deviation of pair-wise differences in EI. Population mean of EI was 27.19 ± 6.48% for B50f data set, 10.64 ± 6.68% for the B30f data set, and 11.52 ± 7.18% for the converted B30f data set. The pair-wise differences in EI between B30f and the converted B30f was 1.02 ± 0.85%. Our study demonstrates the feasibility of image spectrum-based kernel conversion method for normalization of kernel effect in measurement of EI. This technique has a potential to be used in evaluating the longitudinal changes of EI even when the CT images were reconstructed with different kernels.

SS 01 CH-03 08:20
Accuracy of emphysema volume and airway measurements in CT phantom study: hybrid IR, model-based IR, and virtual monoenergetic reconstruction algorithms at low- and standard dose CT
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PURPOSE: To evaluate the measurement accuracy of emphysema volume and airway wall thickness produced by various iterative reconstruction (IR) and virtual monoenergetic (VME) algorithms, using both low- and standard dose CT.
MATERIALS AND METHODS: CT images were obtained on thoracic phantom containing air columns (5, 10, 30 mm in diameter) and airway tubes (3 tubes with different angles/wall thicknesses) at both low- and standard dose CT (30 and 100 mAs at 120 kVp). Each CT scan was reconstructed using filtered back-projection (FBP), hybrid IR (iDose4 level 6), model-based IR (IMR-R1 [routine level 1], ST1 [body soft tissue level 1], SP1 [sharp plus level 1]), and VME images with 70 KeV (VME70) algorithms. The volume of each emphysema hole, and the wall area percentage (WA%) of each airway hole were measured using commercial software in all algorithms. Absolute percentage measurement errors of emphysema volume (APEvol) and airway wall thickness (APEWA%) were then calculated using reference standard and compared between algorithms.
RESULTS: APEvol across all air columns and each column was significantly lower when IMR-R1 was used for reconstruction in both low-dose and standard dose (all ps < 0.05). VME70 showed significantly lower APEvol than FBP (p = 0.003), however, it showed significantly higher APEvol than iDose4, IMR-R1, and IMR-ST1 (all ps > 0.004). There were no significant differences in the mean APEvol of all the air columns between IMR-R1 at low-dose and IMR-R1 at standard dose (all ps > 0.05). APEWA% across all airway tubes and each airway tube were significantly lower when IMR-SP1 was used for reconstruction in both low-dose and standard dose (all ps < 0.05). There were also significant differences in APEWA% between IMR-SP1 and each algorithm in all the airway tubes in both low-dose and standard dose CT. VME70 showed significantly higher APEWA% compared with each algorithm (all ps < 0.001). The mean APEWA% was significantly lower in IMR-SP1 at standard dose than in IMR-SP1 at low-dose in the airway tube with lower WA% (p = 0.046).
CONCLUSION: The measurement of emphysema volume and airway measurement via application of IMR in both low- and standard dose CT showed reliable accuracy in a phantom study. However, VME did not result in any improvement of measurement accuracy.

Analysis of diaphragmatic motion in patients with emphysema: application of image registration based local displacement technique (lung motionography)

SS 01 CH-04 08:30
Analysis of diaphragmatic motion in patients with emphysema: application of image registration based local displacement technique (lung motionography)

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PURPOSE: Limited diaphragm motion and diaphragm flattening are frequently associated features in patients with emphysema. However, difference in three-dimensional (3D) and regional diaphragmatic movement between normal population and patients with emphysema have not been well understood. The following study applied image registration based local displacement information from expiration to inspiration to assess diaphragmatic motion.

MATERIALS AND METHODS: 21 normal and 30 emphysema subjects were included in the study. A mass preserving image registration technique was used to compute displacement vectors of local lung regions at an acinar scale. Movement of diaphragm was assumed to be equivalent to movement of basal lung within 5 mm from diaphragm. 3D displacement was normalized by the cubic root of global lung volume change from expiration to inspiration CT scans. Magnitude and direction of displacement vectors were compared and correlated with LAA_A950HUinsp and LAA_A950HUexp. Diaphragm thickness was measured in the coronal plane of...
inspiratory CT after reconstruction of the images on PACS.

**RESULTS:** 3D and basal displacement were smaller in emphysema than normal subjects (p = 0.044, p = 0.026). Standard deviation of 3D displacement angle was greater in emphysema than normal subjects (p < 0.001). Direction of movement in posteromedial portion of the diaphragm was more medial toward mediastinum (p = 0.001) and posteromedial portion was thinner (p = 0.01) in emphysema patients than normal subjects. LAA-856HUexp in total lung showed significant correlation with decreased 3D and apical-basal displacement (r = -0.408, p = 0.025; r = -0.393, p = 0.031). Ventral-dorsal displacement was smaller in lower lobe predominant emphysema compared to upper lobe predominant patients (p = 0.012).

**CONCLUSION:** In emphysema patients, 3D and basal movement of diaphragm are reduced, and the movement directions are more heterogeneous. Posteromedial portion of the diaphragm is thinner and moves toward mediastinum compared to the normal subjects.

**CLINICAL RELEVANCE:** Diaphragm flattening could be explained by the image registration based lung mechanics analysis as reduced 3D and basal movement with heterogeneous direction. Thinning of the diaphragm can be a cause for more medial movement in the posteromedial portion of the diaphragm compared to the normal subjects. Air trapping may be a useful feature to explain reduced diaphragm movement in emphysema patients.

**Figure 1.** Comparison of (a,c) a healthy subject and (b,d) an emphysema patient: (a,b) Low attenuation area at inspiration (< -950HU), and (c,d) displacement vectors color-coded by the normalized displacement magnitude.

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**SS 01 CH-05 08:40**

**Lung motionography in emphysema patients based on mass preserving non-rigid image registration of inspiration-expiration CTs: correlation with PFTs and air trapping**

Lorenzo Garzelli¹, Jiwoong Choi², Margaret Park³, Ching Long Lin⁴, Eric Hoffman⁵, Philippe Grenier⁶, Jin Mo Goo⁷, Chang Huyun Lee⁸

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**PURPOSE:** Lung motion may be different between emphysema and normal subjects but the underlying mechanisms of lung motion abnormality in emphysema are not well known. The purpose of the study was to investigate whether the lung motion is different between normal and emphysema subjects and to correlate with lung function and low attenuated areas (LAAs) on CT scan.

**MATERIALS AND METHODS:** Both inspiratory and expiratory scans from 21 normal and 40 emphysema subjects were retrospectively included in our study. Institutional Review Board was approved and inform consent was waived. VIDA Apollo software (Coralville, IA) and mass preserving image registration technique were used to compute displacement vectors of local lung regions at an acinar scale. Global lung mean values of relative 3D and dorsal-basal (z axis: apical-basal, y axis: dorsal-ventral) displacement magnitudes were compared between normal and emphysema subjects and correlated with PFTs and LAAs on CT scan using unpaired t-test and Pearson's correlation test.

**RESULTS:** Global lung mean values of relative 3D and dorsal-basal displacement magnitudes were smaller in emphysema subjects (p = 0.01; p = 0.01). In emphysema subjects, 3D and dorsal-basal displacements of the whole lung were, respectively, negatively correlated with LAA-856exp (r = -0.57, p < 0.001; r = -0.60, p < 0.001), expiratory skewness (r = -0.52, p < 0.001; r = -0.57, p < 0.001) and kurtosis (r = -0.53, p = 0.001; r = -0.57, p < 0.001), and positively correlated with expiratory mean attenuation (r = 0.60, p < 0.001; r = 0.63, p < 0.001), and expiratory 15th percentile point (r = 0.53, p < 0.001; r = 0.55, p < 0.001). 3D and dorsal-basal displacement were respectively correlated with DLCO (p = 0.01; p < 0.01) and FEV1/FVC (p = 0.02; p = 0.01). There was no correlation between voxel displacements and inspiratory variables including LAA-950insp. In normal and emphysema subjects, both 3D and dorsal-basal displacements were smaller in upper lobes (all ps < 0.001).

**CONCLUSION:** Lung motion is restricted in emphysema subjects and correlates well with the presence of air-
trapping rather than LAA-950insp. Air-trapping on expiratory CT may be more robust variable explaining the acinar scale limited lung motion during respiration in emphysema subjects.

**COPD and small airways**

**Chairperson(s)**
Yu-whan Oh  
Korea University Anam Hospital, Korea  
Hyun-Ju Lee  
Seoul National University Hospital, Korea

**SS 01 CH-06 08:50**
Predictors of treatment response in COPD patients at 1-year follow-up: value of advanced CT quantification

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**PURPOSE:** To investigate predictive factors of treatment response in COPD patients at 1-year follow-up using advanced quantitative CT analyses.

**MATERIALS AND METHODS:** This retrospective study was approved by the Institutional Review Board with waiver of informed consent. 258 patients (M:F = 240:18; mean age, 66.0 years ± 8.0) were selected from Korean Obstructive Lung Disease (KOLD) cohort, who underwent baseline chest CT, initial and 1-year follow-up pulmonary function test (PFT) during treatment. Patients received combined inhalation of long-acting beta-agonist and corticosteroid. From volumetric CT data, emphysema index, airway trapping index (ATI), and small airway parameter (AWT-Pi10) using both full-width-half-maximum (FWHM) and integral-based half-band (IBHB) methods were obtained. ATI measurements were acquired by using thresholds of -856 HU on expiratory CT (ATI_-856) and by using co-registration (ATI_emphysema, ATI_hyperinflated, ATI_normal, respectively). The clinically meaningful treatment response was defined as an absolute increase of at least 0.225L on follow-up PFT. Multiple logistic regression analysis was performed to identify predictive factors of treatment response.

**RESULTS:** Treatment responders were 41 patients (15.9%). The mean increase in FEV1 was 0.38 ± 0.17 L. Univariate analysis showed that age, initial 6-minute walk distance (6MWD), initial DLCO, emphysema index, ATI_emphysema and Pi10_IBHB were significantly different between patients with and without treatment response (p = 0.008, 0.001, 0.002, 0.004, 0.001 and < 0.001, respectively). Multivariate analysis revealed that 6MWD and Pi10_IBHB were independent variables predictive of FEV1 increase (p = 0.001 and < 0.001, respectively). The adjusted odds ratio was 1.008 (95% CI, 1.003-1.012) and 5.439 (95% CI, 2.069-14.301) respectively. Receiving operating characteristic curve showed that area under the curve of these two variables was 0.715.

**CONCLUSION:** Accurate measurement of Pi10 by IBHB methods may help predict treatment outcome of COPD at 1-year follow-up.

**SS 01 CH-07 09:00**
Cross-volume and cross-time CT image matching assessment provides multiscale characterization of individual asthmatic lung responses to bronchodilator

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**PURPOSE:** To investigate multiscale asthmatic lung responses to inhaled BD, by quantitative CT imaging and image matching of pre- and post-BD inspiration-expiration CT pairs.

**MATERIALS AND METHODS:** We collected full inspiratory and full expiratory MDCT image data sets and PFT results serially acquired before and after BD inhalation from 52 (15 to date) never-smoking asthmatic patients (to date; all female, age = 64.0 ± 11.1). VIDA Apollo software (Coralville, IA) was used for segmentation and measurement of individual CT images. Mass preserving non-rigid image registration was adapted for cross-volume and cross-time CT image matching. 3D-1D coupled entire conducting airway models were generated to link central airways to the lung periphery. Relative regional air volume change (RRAVC) map is adapted to compare local contributions to the expiration-to-inspiration global lung inflation.
between pre- and post-BD. Excessive regional changes were assessed on inspiration and expiration. Paired t-test was used to evaluate pre- and post-BD changes.

**RESULTS:** After BD inhalation, air volume on expiration significantly decreased in the lower lobes (p < 0.05), reflecting that the lower lobes are the main sites of global lung function improvement (FEV1, FVC, and FEV1/FVC). In the upper lobes, no significant air volume changes were found. Localized coupled responses of regional excessive inflation and deflation were depicted (Fig. 1), rather than mere decrease of regional air-trapping. The regional dependency of RRAVC map (air volume change increasing gradually toward dorsal and basal regions) becomes more prominent in the post-BD maps compared to the pre-BD (Fig. 1A), which is less noticeable in the severe asthmatics than the non-severe. While it is variable between subject, BD induced regional hyper- and hypo-inflation on inspiration and hyper- and hypo-deflation on expiration tend to form paired patchiness (Fig. 1B). Wide hyper-deflated regions in Figure 1C demonstrates improved expiration in the lower lobes. Intersubject variability is observed for excessively inflated and deflated regions and their correspondence to the RRAVC defect regions, suggesting in-depth regional characterization of asthmatic lungs.

**CONCLUSION:** The multiscale cross-volume and cross-time CT image matching assessment elucidated the characterization of lung function improvement by BD in asthmatic patients, showing local lung responses linked to the sublobes, the lobes, and the global lung.

**SS 01 CH-08 09:10**

CT assessment of airway and visceral fat in asthma patients: preliminary report

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**PURPOSE:** To investigate whether visceral fat area (VFA) on fat amount CT is associated with bronchial measurements in chest CT and to compare clinical characteristics and pulmonary function tests (PFT) between patients with visceral obesity (VO) and without visceral obesity (NO).

**MATERIALS AND METHODS:** Fifty two consecutive asthma patients, who were diagnosed with objective measurement of airflow limitation, were prospectively enrolled. We investigated clinical characteristics including age, body mass index (BMI), asthma diagnosed age, current smoking, uncontrolled symptom, and PFT including forced expiratory volume in 1 second (FEV1), FEV1 predicted (FEV1pred), forced vital capacity (FVC), FVCpred, forced expiratory flow at 25-75% (FEF 25-75%) and FEV1/FVC. Both chest CT and fat amount CT scans were performed in all patients. With dedicated postprocessing software, we evaluated wall thickness, wall area, lumen diameter, and lumen area at the right upper lobar bronchus apical segmental bronchus orifice and calculated visceral and subcutaneous fat area (SFA). Visceral obesity was defined as BMI > 25 and VFA/SFA > 0.4.

**RESULTS:** There were negative correlation of VFA with lumen diameter (r = 0.31, p = 0.027), lumen area (r = 0.32, p = 0.028). Wall thickness (r = 0.01, p = 0.927) and wall area (r = 0.12, p = 0.398) did not show significant correlation. Age, BMI and asthma diagnosed age in VO was significantly greater than in NO. There was no significant difference in current smoking between two groups (p = 0.419). In PFT, decrease in FEV1 (2.3 L in NO and 2.0 in VO, p = 0.175), FEV1pre (99% and 89, p = 0.066), FVC (3.3 L and 2.9, p = 0.073), FVCpred (104 % and 89, p < 0.001) was found in VO. No significant difference was found in FEV1/FVC (0.69 L and 0.71, p = 0.408) and FEV1-75% (59% and 63, p = 0.646). Uncontrolled symptom and FEV1pre < 60% was more frequent in VO than NO without statistical significance (19% and 45%, p = 0.157 for uncontrolled symptom and 4% and 12%, p = 0.341 for FEV1pre < 60%).

**CONCLUSION:** Visceral obesity in asthma patients is associated with bronchial luminal narrowing without wall thickening. Those findings may correspond with frequent uncontrolled symptom and decrease in FEV1pre% and FVC in VO.

**SS 01 CH-09 09:20**

How much the wall thickness of small airways change at inspiration and expiration? A preliminary?study with a low-dose CT

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**PURPOSE:** To investigate the feasibility of quantifying the changes in wall thickness of small airways at inspiration and expiration CT in low-dose CT setting.

**MATERIALS AND METHODS:** Low-dose CT scans (120 kVp, 40 mAs, and 1 mm slice thickness) of 10 normal subjects were acquired with a commercial CT (Sensation 16, Siemens) at inspiration and expiration conditions. In each dataset, 2 to 5 small airways (Pi15) at 3rd to 4th generation bronchial segments were selected and matched between inspiration and expiration CT scans with visual assessment. An in-house software
(ImagePrism Pulmo) which integrates CT scanner’s point spread function into attenuation profile matching technique was used to measure the airway wall thickness with high accuracy.

**RESULTS:** Mean perimeter of airway lumen was 15 mm. Mean wall thickness of small airways was 0.61 ± 0.17mm at inspiration, and 0.75 ± 0.17 at expiration. Compared to inspiration, the measured small airway walls were 28% thicker at expiration on an average.

**CONCLUSION:** Wall thickness of small airways changes significantly depending on patient’s inspiration state. Care should be taken in interpretation of measured airway wall thickness.

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**Chest**

**08:00 - 09:30**

**203**

**Chest**

**Oct 27, Fri**

**Lung cancer screening**

**Chairperson(s)**

Chan-Sup Park  
*Myongji Hospital, Korea*

Myung hee Chung  
*The Catholic University of Korea, Bucheon St. Mary's Hospital, Korea*

**SS 18 CH-01 08:00**

**Preliminary report of a pilot study for the Korean Lung Cancer Screening (K-LUCAS) project**

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**PURPOSE:** Lung cancer screening with low-dose chest CT (LDCT) can reduce lung cancer-specific mortality according to the National Lung Cancer Screening Trial. On the basis of this result, the Korean Lung Cancer Screening (K-LUCAS) project was launched and the pilot study of K-LUCAS project was performed to evaluate the feasibility on the implementation of lung cancer screening with LDCT in 2016. The purpose of our study was to analyze clinical features and positive rate of this pilot test.

**MATERIALS AND METHODS:** The National Cancer Center and three regional cancer centers of Korea participated in this pilot study. The eligibility criteria was asymptomatic current or ex-smokers with age of 55 to 74 years and smoking history of at least 30 pack-years quitting within the last 15 years. A total of 256 participants were enrolled and underwent LDCT (CTDIvol < 3 mGy) between November 2016 and March 2017. The American College of Radiology Lung Imaging Reporting and Data System (Lung-RADS) was used to categorize initial LDCT findings.

**RESULTS:** Mean age of the participants was 63.2 ± 5.4 years and 98.8% (253/256) were male. Mean volume CT dose index was 1.67 ± 0.6 mGy and effective radiation dose was 0.95 ± 0.36 mSv. A total of 145 subjects (56.6%) were current smoker with a mean smoking history of 40 ± 9 pack years and 111 subjects (43.4%) were ex-smokers with mean smoking history of 42 ± 32 pack years. Participants were category 1 in 56.2% (n = 146), category 2 in 34.2% (n = 89), category 3 in 4.6% (n = 12), and category 4 in 3.5% (n = 9). Therefore, 8% (21/256) of participants had positive results (category
3 or 4). Lung cancer was diagnosed in 1 participant (0.39%), which was surgically confirmed as small cell lung cancer with limited stage. Other CT findings include pulmonary emphysema (n = 84, 32.8%), coronary artery calcification (n = 79, 30.9%), old pulmonary tuberculosis (n = 30, 11.7%), bronchiectasis (n = 33, 12.9%), interstitial lung disease of usual interstitial pneumonia pattern (n = 3, 1.2%) and pleural effusion (n = 2, 0.8%).

**CONCLUSION:** Even though the size of our study population was small, positive rate was only 8% which was similar to or even lower than the results of other lung cancer screening studies. Lung-RADS seems to be applicable in Korea where pulmonary tuberculosis is endemic.

**SS 18 CH-02  08:10**

Size-specific dose estimation in the Korean Lung Cancer Screening (K-LUCAS) project: does a 32-cm diameter phantom represent a standard sized patient?

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**PURPOSE:** Reference phantom-based radiation dose estimates have potential errors caused by the lack of body size consideration in the CT radiation dose calculation. The purpose of this study was to evaluate body size specific radiation dose of low-dose chest CT examination for the Korean Lung Cancer Screening (K-LUCAS) project.

**MATERIALS AND METHODS:** We collected participant-specific CT scan parameters and radiation dose output of 252 participants in the pilot study of the K-LUCAS between November 2016 and March 2017. A 32-cm diameter reference phantom-based radiation dose estimates (volume CT dose index, CTDIvol) were compared with size-specific dose estimates (SSDE), which were recalculated from CTDIvol using conversion factors based on participant’s body size (anterior-posterior plus lateral dimensions at mid-liver level) from the American Association of Physicists in Medicine Report 204. This comparison was subsequently assessed according to the BMI levels (underweight [BMI < 18.5 cm/m²], normal weight [18.5 ≤ BMI < 23 cm/m²], overweight [23 ≤ BMI < 25 cm/m²], and obese [BMI ≥ 25 cm/m²]).

**RESULTS:** The SSDE was higher than CTDIvol in all participants (2.22 ± 0.75 mGy vs. 1.67 ± 0.60 mGy, p < 0.001). The ratio of SSDE to CTDIvol increased in the lower BMI groups: 1.26 for obese participants (n = 103), 1.37 for overweight (n = 70), 1.43 for normal weight (n = 75), and 1.53 for underweight (n = 4). Although CTDIvol of overweight/obese participants was significantly higher than that of normal/underweight participants (1.76 ± 0.65 mGy vs. 1.46 ± 0.43 mGy, p < 0.001), the SSDE was not different between these two BMI groups (2.27 ± 0.79 mGy vs. 2.10 ± 0.62 mGy, p = 0.055).

**CONCLUSION:** CTDIvol based on a 32-cm diameter phantom does not represent the radiation exposure to a standard sized patient. The use of a 32 cm diameter phantom-based dose calculation can lead to significant errors in the dose assessment when body size is not considered.

**SS 18 CH-03  08:20**

Optimization of a chest CT protocol for the detection of ground glass opacity nodules: feasibility study with a computer assisted detection system and a lung cancer screening phantom

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**PURPOSE:** To optimize computed tomography (CT) parameters for the detection of ground glass opacity nodules (GGNs) by using computer assisted detection (CAD) system and a lung cancer screening phantom.

**MATERIALS AND METHODS:** A lung cancer screening phantom containing 15 artificial ground glass nodules (>600 HU, from 2 mm to 12 mm) in the left lung was examined with a 256 row multi-detector CT scanner. Three tube voltages of 120, 100, and 80 kVp were used in combination with five tube currents of 400, 200, 100, 50, and 25 mA; three slice thickness of 0.625, 1.25, and 2.5 mm; and four different reconstruction algorithms of filtered back projection and iterative reconstruction (ASIR-V) of 30, 60, and 90. For each protocol, the accuracy of the CAD system was evaluated for the 6 target GGNs that were 6, 10, or 12 mm in size. The cutoff size of the CAD system was set to 5 mm to minimize the false positives.

**RESULTS:** Among the 180 combinations of tube voltage, tube current, slice thickness, and reconstruction algorithms, 80 kVp, 200 mA, and 1.25 mm slice thickness with an ASIR V of 90 had the best performance in the detection of GGNs with 6 true positives and no false positives. For 80 kVp, 400 mA, and 1.25 mm slice thickness with ASIR V of 90, there were 5 true positives and 1 false positive; and 100 kVp, 100 mA, and 1.25
mm slice thickness with ASIR V 90 had 4 true positives and 1 false positive; while 100 kVp, 50 mA, and 1.25 mm slice thickness with ASIR V 90 had 4 true positives and 1 false positive; and 120 kVp, 25 mA, and 1.25 mm slice thickness with ASIR V 90 had 4 true positives and 3 false positives. Other combinations had fewer than 3 true positives. In particular, any combinations with a 0.625 mm slice thickness had 0 true positives and at least 1 false positive result.

**CONCLUSION:** Chest CT at a low voltage with a thin slice thickness and a high iterative reconstruction algorithm might improve the detection rate of a CAD system for small GGNs in lung cancer screening. However, too thin slices could hamper the CAD system.

**SS 18 CH-04 08:30**

*Accuracy of part-solid ground-glass nodule volumetry in chest CT with iterative reconstruction: an anthropomorphic chest phantom study*

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**PURPOSE:** To evaluate the accuracy of volume assessment of solid component and non-solid component in part-solid ground-glass nodule (GGN) in chest CT with application of variable iterative reconstruction (IR) according to nodule size, nodule density and CT tube currents, using artificial lung nodules.

**MATERIALS AND METHODS:** Four part-solid ground-glass nodules (non-solid portion: 20 mm diameter, -650 HU density; solid component: 3, 5, 7, 9 mm diameters; +50 HU density) and four solid nodules were randomly placed inside a thoracic phantom. Scans were performed with tube current-time product to 10, 30 and 100 mAs. Images were reconstructed with filtered back projection (FBP), hybrid iterative reconstruction (iDOSE4), model-based iterative reconstruction (IRM R1, SP1, ST1). We compared volume estimates to a reference standard and calculated the absolute percentage error (APE).

**RESULTS:** The APE of all nodules were significantly lower when model-based reconstruction was used than with FBP (p < 0.05). Model-based IR showed a significantly lower APE than FBP in solid component of part-solid ground-glass nodules (p < 0.05), and the difference was more pronounced at the part-solid ground-glass nodules with inner smallest solid component and at the lowest tube current (p < 0.05). The effect of IR was most pronounced for part-solid ground-glass nodules with inner smaller solid component in the lowest CT tube current.

**CONCLUSION:** Lung nodule volumetry for solid component in part-solid ground-glass nodule by application of model-based IR showed reliable accuracy in a phantom study. Lung nodule volumetry can be reliably applicable to part-solid ground-glass nodules even with inner small portion of solid component.

**SS 18 CH-05 08:40**

*Automatic detection of malignant pulmonary nodules on chest radiographs using a deep convolutional neural network: detection performance and comparison with human experts*

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**PURPOSE:** To evaluate the performance of a deep learning-based automatic detection (DLAD) algorithm in detecting malignant pulmonary nodules on chest radiographs (CPAs) and its comparison with human experts.

**MATERIALS AND METHODS:** A DLAD algorithm was developed using a 25-layer deep convolutional network in a novel semi-supervised manner with 41,792 cases. For this observer performance test, 181 CPAs not used in the development of DLAD were included: 119 CPAs with 147 pathologically- or clinically-confirmed malignant lung nodules (mean size, 2.50 cm ± 1.60) and 62 normal CPAs. Reference for the nodules was established via CT taken within a week. Nineteen readers including 3 non-radiology physicians, 6 radiology residents, 5 board-certified radiologists, and 5 thoracic radiologists independently reviewed each CPA to detect lung nodules on a five-point confidence scale without DLAD (test 1). After test 1, each reader was allowed to change their decision by reviewing the results of test 1 and that of DLAD (test 2). The detection performances of DLAD, human experts (test 1), and human experts using DLAD (test 2) were evaluated and compared using jackknife free-response receiver operating characteristic (JAFROC) figure of merits (FOMs) on a per-nodule basis.
RESULTS: DLAD alone exhibited a FOM of 0.857, which was significantly higher than that of 16 of 19 readers (all ps < 0.05). The mean FOM of the 19 readers using DLAD were significantly higher than that without DLAD (0.825 vs. 0.713, p = 0.002). All readers showed improved detection performances for malignant pulmonary nodules using DLAD (mean FOM increase of 0.044 [range, 0.007-0.193]) with significant differences in 15 readers (p < 0.05). On subgroup analysis, FOMs of the four reader groups (non-radiology physicians, radiology residents, board-certified radiologists, and thoracic radiologists) were 0.678, 0.784, 0.808, and 0.820, respectively, and their detection performances significantly improved with DLAD (0.814, 0.817, 0.827, 0.841; all ps < 0.005).

CONCLUSION: DLAD showed better performance than most experts in detecting malignant pulmonary nodules on CPAs and enhanced the performance of human experts when used in conjunction.

SS 18 CH-06  08:50
Potential of grid-like software on bedside chest radiograph in improving image quality and dose reduction: an observer preference study between non-grid, grid-like, and grid images
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PURPOSE: Applying an anti-scatter grid improves image quality of bedside chest radiography but impedes workflow in installing and aligning the grid. This study aimed to compare the observer preference of image quality and radiation dose between non-grid, grid-like, and grid images.

MATERIALS AND METHODS: After IRB approval and obtaining informed consent, 38 patients were enrolled in this study. Each patient underwent two bedside chest radiography examinations with and without grid. A grid-like image was generated from a non-grid image by applying SimGrid software (Samsung Electronics Co. Ltd.) which uses de-scattering image processing technology. Two readers recorded the preference for 10 anatomic landmarks and overall appearance on a five point scale for a pair of non-grid and grid-like images and then a pair of grid-like and grid images respectively which were presented in a randomized order. Dose area product (DAP) was also recorded. Wilcoxon’s rank sum test was used to assess the significance of preference.

RESULTS: As for overall image quality, both readers preferred grid-like images to non-grid images significantly (p < 0.001); there was discrepancy in preference of grid images to grid-like images between two readers (p = 0.317, 0.034, respectively). As for anatomic landmarks, both readers preferred grid-like images to non-grid images (p < 0.005) in all landmarks; significant preference of grid-images to grid-like images was observed in proximal airways by two readers and in retrocardiac lung and thoracic spine by one reader. DAP was 1.53 ± 0.16 dGy*cm² in images with grid and 1.24 ± 0.13 dGy*cm² in images without grid.

CONCLUSION: SimGrid software improved image quality of non-grid images significantly to an almost similar level of grid images with relatively lower level of radiation exposure.

SS 18 CH-07  09:00
The impact of virtual monoenergetic reconstruction algorithms on spectral CT in reducing beam hardening artifacts of contrast media in the subclavian vein
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PURPOSE: As the lower neck area contains important structures such as lymph nodes, beam hardening artifacts (BHA) around subclavian veins (SCV) can affect the evaluation. Our aim was to investigate the clinical value of virtual monoenergetic images (VME) from spectral CT for reducing BHA of contrast media in SCV.

MATERIALS AND METHODS: A total of 101 consecutive patients, who underwent chest CT, were retrospectively included in this study. The same contrast media and injection protocols were applied to the whole study population (at a rate of 3 ml/sec via 20 gauge cannula into right or left antecubital vein using a power injector). Data acquired with spectral CT were subsequently used to calculate VME image data sets ranging from 70 to 200 keV (at 10-keV intervals per patient). Readers’ subjective image quality scores were recorded in conventional 120 kVp polychromatic images (COV) and VMEs with energy levels from 70 keV (VME70), 100 keV (VME100), 130 keV (VME130), and 200 keV (VME200). Image noise, differences in image attenuation, contrast-to-noise ratio (CNR), and signal-to-noise ratio (SNR) were also obtained in each algorithm. Comparisons between COV and VMEs were performed using the Kruskal-wallis test with Bonferroni correction.

RESULTS: The best subjective image quality score was shown in VME130. Also, subjective image quality was rated significantly better in VME130 when compared with COV and other VMEs (Table 1, all ps < 0.001). Interobserver agreement was good (ICC, 0.626). Image
noise and differences in image attenuation were lowest in VME130, and were significantly lower in VME 130 than in COV (Tables 2, 3; all ps < 0.001). There were no significant differences in image noise between VME100, VME130, and VME200 (all ps > 0.999). As the energy level increased, both SNR and CNR decreased (Figs. 1, 2). Both SNR and CNR were highest in VME70 (Tables 4, 5). SNR of VME100 was not significantly different than those of VME70 and COV.

CONCLUSION: The VME130 offered the best image quality, the lowest image noise, and the lowest difference in image attenuation among COV and other VMEs. Therefore, VME130 will help evaluate the structures around SVC that are limited by BHA.

SS 18 CH-08  09:10
The value of iterative metal artifact reduction (iMAR) for detection of ground-glass opacity nodule (GGN): a pilot phantom study
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PURPOSE: To investigate the relationship between the ground-glass opacity nodules (GGN) and different reconstruction algorithm with or without iterative metal artifact reduction (iMAR) algorithm.

MATERIALS AND METHODS: The anthropomorphic chest phantom containing 26 GGNs (LSCT001; Kyoto Kagaku Co., Kyoto, Japan) used in this study. CT scan was performed with 256 channel multidetector CT (SOMATOM Definition Flash, Siemens Medical Solutions, Forchheim, Germany) with 100 kVp and Care Dose 4D modulation. All CT images were reconstructed with filtered back projection (FBP) and iterative reconstruction (ADMIRE) with or without iMAR algorithm. Two board-certified chest radiologists analyzed following factors: contrast-to-noise ratio (CNR), signal-to-noise ratio (SNR) and diagnostic confidence.

RESULTS: CNR was significantly higher in ADMIRE than FBP regardless of whether iMAR algorithm was added or not (11.6 ± 1.7 vs. 7.0 ± 0.6, p = 0.01; 8.9 ± 0.9 vs. 8.2 ± 0.8, p = 0.03, respectively). Additionally, even if iMAR was added, there was no significant different in CNR between the same algorithm. SNR was statistically higher in ADMIRE-iMAR than FBP-iMAR (-45.5 ± 4.2 vs. -34.6 ± 2.9, p < 0.01). However, SNR in other groups; ADMIRE and FBP, ADMIRE and ADMIRE-iMAR, FBP and FBP-iMAR was not significantly different. Diagnostic confidence was higher with ADMIRE-iMAR than FBP-iMAR (-45.5 ± 4.2 vs. -34.6 ± 2.9, p < 0.01). However, SNR in other groups; ADMIRE and FBP, ADMIRE and ADMIRE-iMAR, FBP and FBP-iMAR was not significantly different. Diagnostic confidence was higher with ADMIRE than FBP (2.88 ± 0.08 vs. 2.62 ± 0.12, p < 0.01). However, there was no significant different in diagnostic confidence between ADMIRE-iMAR and FBP-iMAR (2.73 ± 0.10 vs. 2.73 ± 0.12, p = 1).

CONCLUSION: In high quality CT with making relatively low metallic artifact, adding the iMAR algorithm does not improve value in ADMIRE and FBP reconstruction.

CLINICAL RELEVANCE: iMAR algorithm may make an influence to patients without metal artifact with reducing noise level.
Application of kernel conversion between different reconstruction kernels at CT using convolutional neural network: feasibility in radiomics
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PURPOSE: To assess the feasibility of CT kernel conversion between different reconstruction kernels using convolutional neural network (CNN) in terms of radiomics.

MATERIALS AND METHODS: Total 38 patients (M:F = 19:19; 63.8 ± 10.2 years) with pulmonary nodule or mass underwent contrast enhanced chest CT using single CT machine. All of the chest CT was reconstructed in both B30f and B50f kernels from each patient’s sinogram. CNN can learn an end-to-end mapping between the CT scans with different reconstruction kernels. CNN were used to generate the kernel converted images, from B30f to B50f and from B50f to B30f. We evaluated the difference of 26 texture features of nodules or masses between the generated image and ground truth image of both B30f and B50f using paired t-test.

RESULTS: From 38 scans, 76 original and 76 kernel converted image sets were obtained. The differences (= Δ of texture feature measurements in two different sets) of texture features between original B30f and converted B30 (group 1) and between original B50f and converted B50 (group 2) were significantly smaller than those between original B30f and original B50f (group 3). While the difference of 8 parameters were significantly greater in group 3 compared to group 1, 18 parameters were significantly greater in group 3 compared to group 2. And 2 parameters were significantly greater in group 1 compared with group 2. In terms of texture features, 18 parameters including mean attenuation, standard deviation (SD), energy, entropy, run-length and gray level co-occurrence matrix (GLCM) were significantly different between original B30f and original B50f (p ≤ 0.001). And 10 parameters including mean attenuation, SD, energy and entropy were significantly different (p < 0.001) between original B30f and converted B30f images. In original B50f and converted B50f images, 7 parameters including mean attenuation were significantly different (p ≤ 0.003).

CONCLUSION: Kernel conversion using CNN has potential to reduce differences of reconstruction kernel and decrease variability in the values of radiomics features, although it still needs to be improved.
was designated when blood transfusion, vascular embolization, or cardiopulmonary resuscitation were required to manage patients with the diagnosis.

RESULTS: Hemoptysis occurred in 5.78% of all PTNB procedures, while severe hemoptysis occurred in 0.18%. Female sex, history of anti-platelet or anti-coagulative drugs, prolonged activated partial thromboplastin time, subsolid nodules, caviary nodules, and long pleurato-target distance were independent risk factors for hemoptysis, while mPAD enlargement (greater than 29.5 mm) was not a significant risk factor. Regarding severe hemoptysis, however, mPAD enlargement was an independent risk factor in combination with subsolid and caviary target nodules.

CONCLUSION: mPAD enlargement was not a significant risk factor for PTNB-related hemoptysis. However, it was a significant risk factor for severe PTNB-related hemoptysis.

SS 24 CH-02 16:10
Life-threatening hemoptysis after percutaneous needle lung biopsy: re-analysis of risk factor
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PURPOSE: To retrospectively evaluate the predictive factor of a life-threatening hemoptysis after percutaneous needle lung biopsy.

MATERIALS AND METHODS: We included 111 patients consecutive patients (M:F = 57:54; mean age, 64.7 years) who complaint of hemoptysis after cone-beam CT-guided percutaneous needle lung biopsy from January 2014 to January 2017. The life-threatening hemoptysis was defined as a hemoptysis causing oxygen desaturation greater than 10% of baseline on continuous arterial oxygen saturation monitoring or hemodynamic instability. Two radiologists evaluated conventional CT findings for lesion characteristics on pre-procedural CT scan, along with open bronchus sign which was defined as a bronchiolar dilatation within the lesion connecting to proximal bronchus with preserved luminal patency. Those readers evaluated vulnerable vessel and bronchus signs on intra-procedural 3D cone beam CT which was performed for confirming the location of needle tip before firing: vulnerable vessel or bronchus sign, a pulmonary vessel or bronchus 1 mm or larger in diameter bi-dimensionally placed on the expected course of biopsy gun (active needle part, 22 mm in length) when fired. Other characteristics of biopsy procedures and pathology reports of biopsy specimen were reviewed. Risk factors for life-threatening hemoptysis were assessed by using uni- and multivariate logistic regression analysis.

RESULTS: 17 patients (15.3%; 95% CI, 9.7-23.2%) had life-threatening hemoptysis. The open bronchus sign, vulnerable bronchus sign, vulnerable vessel sign, nodule consistency (solid or ground-glass nodule), and non-diagnostic result of biopsy specimen were significant risk factors (p = 0.002, p = 0.013, p = 0.004, p = 0.007, and p = 0.05, respectively), whereas a number of biopsy was not. Multivariate analysis revealed non-diagnostic result (OR, 0.388, 95% CI, 0.095-0.036; p = 0.005) and vulnerable vessel sign (OR, 0.216, 95% CI, 0.062-0.752; p = 0.016) were significant risk factors for life-threatening hemoptysis.

CONCLUSION: Non-diagnostic result of biopsy specimen and vulnerable vessel sign were predictive factors for life-threatening hemoptysis after percutaneous needle lung biopsy.

CLINICAL RELEVANCE: Life-threatening hemoptysis is potentially avoided by performing accurate acquisition of lung pathology, along with evaluating a potential pulmonary vascular injury before firing.

SS 24 CH-03 16:20
Time-dependent analysis of incidence, risk factors and clinical significance of pneumothorax after percutaneous lung biopsy
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PURPOSE: To evaluate the time-dependent incidence, risk factors, and clinical significance of percutaneous lung biopsy (PLB)-related pneumothorax in 3251 patients.

MATERIALS AND METHODS: From January 2012 to November 2015, 3251 patients underwent 3354 Cone-beam CT-guided PLBs for lung lesions. Cox proportional-hazards, logistic and linear regression analyses were performed to identify time-dependent risk factors of PLB-related pneumothorax, risk factors of drainage catheter insertion and those of prolonged catheter placement, respectively.

RESULTS: Pneumothorax occurred in 915 out of 3354 PLBs (27.3%), with 25.1% (230 of 915) occurring during follow-ups. Older age (Hazard ratio [HR] = 1.009; p = 0.0024), emphysema (HR = 1.624; p < 0.0001), smaller target (HR = 0.922; p < 0.0001), deeper location (HR = 1.175; p < 0.0001), multiple pleural passages (HR = 1.576; p < 0.0001), and longer puncture time (HR = 1.036; p < 0.0001) were significant risk factors for
the earlier occurrence of PLB-related pneumothorax, while presence of hemoptysis (HR = 0.503; \(p = 0.0001\)) showed a protective effect against the earlier development of pneumothorax. Seventy-five cases (8.2% of pneumothorax) underwent chest drainage catheter placement. Mean duration of catheter placement of these cases was 3.2 ± 2.0 days. Emphysema (odds ratio [OR] = 2.400; \(p = 0.0019\)) and longer puncture time (OR = 1.053; \(p = 0.0146\)) were assessed to be significant risk factors for catheter insertion, and older age (Parameter estimate = 1.0139; \(p = 0.0124\)) was a predictive factor for prolonged catheter placement.

**CONCLUSION:** PLB-related pneumothorax occurred in 27.3% of all PLBs, among which 25.1% developed during follow-ups, and 8.2% of PLB-related pneumothorax required drainage catheter placement. Smaller target size, emphysema, deeply-located lesions were significant risk factors of PLB-related pneumothorax. Emphysema and older age were related with drainage catheter insertion and prolonged catheter placement, respectively.

**SS 24 CH-04 16:30**

Image guided biopsy of thoracic masses and minimizing risk of pneumothorax: 26 years’ experience in a remote cancer center

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**PURPOSE:** To determine role, accuracy and reliability of image guidance of thoracic biopsy and to know the efficacy of uses of different techniques to minimize the risk of pneumothorax.

**MATERIALS AND METHODS:** Needle biopsies were performed in 1770 patients from February 1989 to December 2015 using fluoroscopy, ultrasound (US) and CT as Image guidance. US guidance was used for peripheral lesions. Fluoroscopic and CT guidance were used for both peripheral and central lesions. After reviewing the patient, skiagram, CT and coagulation profile, a plan was formulated for safest approach. A needle was guided to the lesion with an Image technique and materials were obtained for aspiration biopsy or core biopsy. Several techniques were applied to minimize the risk of pneumothorax. Immediately after the technique, puncture site was put on dependant position to reduce the risk of pneumothorax. Other techniques included selection of appropriate image guidance, accurate and delicate performance of needle manipulation, extra pleural approach, widening of extrapleural space by saline injection, transsternal approach, pathway through non-aerated lung, minimizing pathway of normal aerated lung, avoiding fissure and bullae, limited no of pleural puncture, use of small bore needle etc. All patients underwent chest radiography to detect a pneumothorax.

**RESULTS:** There were 1380 male and 390 female in the range of 12 to 91 years. Fluoroscopy, US and CT as guidance were used in 170 (9.60%), 310 (17.51%) and 1290 (72.88%) cases respectively. The diameter of masses ranges from 1.2 cm to 12 cm. Procedure time was significantly less under US guidance. 164 cases (9.26%) needed repeat biopsy. Results obtained in 1540 cases (87%). Malignant cases were 1172 (76.10%). Complications included hemoptysis (7) and pneumothorax in 40 (2.26%). There was no pneumothorax in US guided biopsy. Pneumothorax occurred in 10 cases following fluoroscopic guidance and 30 cases in CT guidance. Only three cases of pneumothorax required placement of a chest tube, rest were small and resolved spontaneously. Incidence of pneumothorax dropped significantly after starting meticulous planning using several techniques.

**CONCLUSION:** Image guided biopsy is a safe and reliable method in tissue diagnosis of thoracic lesions. Morbidity is very low and accuracy is very high. Most common complication is pneumothorax. Risk of pneumothorax can be significantly minimized by meticulous planning using several techniques.

**SS 24 CH-05 16:40**

Risk of pleural recurrence after percutaneous transthoracic needle biopsy in stage I non-small cell lung cancer: a large center experience

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**PURPOSE:** To determine whether percutaneous transthoracic needle biopsy (PTNB) increase the risk of (a) isolated pleural recurrence and (b) concomitant pleural seeding and metastasis in stage I non-small cell lung cancer (NSCLC).

**MATERIALS AND METHODS:** In this institutional review board-approved retrospective study, medical records of total of 830 consecutive patients with stage I NSCLC who underwent curative resection between 2004 and 2010 were reviewed. Median duration of follow-up was 1843 days (interquartile range, 1006-2734). Multiple logistic regression analyses were performed to identify risk factors of pleural recurrence.

**RESULTS:** Of 830 patients, 540 patients (65.1%) underwent PTNB before surgery, while 290 patients (34.9%) underwent non-PTNB procedures including bronchoscopic biopsy or exploratory thoracotomy. An isolated pleural recurrence was found in 26 patients (3.1%, [95% CI, 2.1-4.6%]) (20 in PTNB group, 6 in...
non-PTNB group). There was no significant association between PTNB and isolated pleural recurrence (p = 0.197). Concomitant pleural recurrence occurred in 42 patients (5.1%, [95% CI, 3.8-6.8%]) (34 in PTNB group, and 8 in non-PTNB group). Subpleural location (p = 0.007), tumor consistency (solid, part-solid, nonsolid) (p = 0.046), PTNB (p = 0.027), pathologic T stage (p < 0.001), microscopic pleural invasion (p < 0.001) and microscopic lymphatic invasion (p = 0.019) were associated with concomitant pleural recurrence. The most significant factor of pleural recurrence was only microscopic pleural invasion (odds ratio [OR], 4.28; 95% CI, 2.20 to 8.29) (p < 0.001) on multiple logistic analysis. Among 540 patients undergoing PTNB, transfissural approach did not have significant association with pleural recurrence (p = 0.220), while the most sole significant factor was microscopic pleural invasion (OR, 3.40; 95% CI, 1.54 to 7.51) (p = 0.002).

**CONCLUSION:** PTNB did not increase the risk of isolated or concomitant pleural recurrence in early stage NSCLC. Higher incidence of concomitant pleural seeding in PTNB group was presumably attributed to peripheral lung cancer, potentially accompanying microscopic pleural invasion.

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**SS 24 CH-06** 16:50

**Cone-beam CT virtual navigation-guided percutaneous needle biopsy of suspected pleural malignant disease: initial experience**

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**PURPOSE:** To evaluate the diagnostic performance of cone-beam computed tomography (CBCT) virtual navigation-guided percutaneous pleural biopsy for suspected malignant pleural disease.

**MATERIALS AND METHODS:** From December 2010 to December 2016, 63 CBCT-guided biopsies were performed in 59 patients (M:F = 31:28; mean age, 63.36 years) with suspected malignant pleural disease using a coaxial system with 18- or 20-gauge cutting needles. Procedural details, diagnostic performance, radiation exposure and complication rates were investigated.

**RESULTS:** Mean diameter perpendicular to the pleura of 51 focal and 12 diffuse pleural lesions was 1.53 cm ± 0.76. Mean distance from the skin to the target was 3.40 cm ± 1.51. Mean number of CT acquisitions and biopsies were 3.21 ± 0.57 and 3.05 ± 1.54. Total procedure time and coaxial introducer indwelling time were 11.87 min ± 5.59 and 8.78 min ± 4.95, respectively. Mean dose area product was 12013.61 mGy cm² ± 7969.59. There were 48 malignant, 10 benign, and 5 indeterminate lesions. Sensitivity, specificity, and diagnostic accuracy were 93.8% (45/48), 100% (10/10) and 94.8% (55/58), respectively. Positive and negative predictive values for malignancy were 100% (45/45) and 76.9% (10/13), respectively. Four patients (6.8%) with benign pathology result on initial biopsy but still having a high suspicion of malignancy underwent repeat biopsy and three of them finally revealed to have malignant pleural disease. There were three cases with minimal pneumothorax and no grave procedure-related complications.

**CONCLUSION:** CBCT-guided biopsy is an accurate and safe diagnostic technique for suspected malignant pleural lesion with reasonable radiation exposure and procedure time.

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**SS 24 CH-07** 17:00

**LOGIS (LOcalization of Ground-glass-opacity and pulmonary lesions for mInimal Surgery) registry: design and rationale**

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**PURPOSE:** An optimal pulmonary localization technique for video-assisted thoracic surgery (VATS) of small lung nodules has not yet been established. The LOcalization of Ground-glass-opacity and pulmonary lesions for mInimal Surgery (LOGIS) registry aims to establish a multicenter database and investigate the usefulness and safety of localization techniques for small pulmonary lesions in individuals undergoing VATS.

**MATERIALS AND METHODS:** The LOGIS registry is a large-scale, multicenter cohort study, aiming to enroll 825 patients at 10 institutions. Based on the inclusion
and exclusion criteria, all study participants with pulmonary lesions indicated for VATS will be screened and enrolled at each site. All study participants will undergo preoperative lesion localization by the hook-wire or Lipiodol localization methods according to site-specific methods. Within a few hours of marking, thoracoscopic surgery will be done under general anesthesia by experienced thoracoscopic surgeons. The primary endpoints are the success and complication rates of the two localization techniques. Secondary endpoints include procedure duration, recurrence rate, and all-cause mortality. Study participant enrollment will be completed within 2 years. Procedure success rates and incidence of complications will be analyzed based on computed tomography findings. Procedure duration, recurrence rate, and all-cause mortality will be compared between the two techniques. The study will require 5 years for completion, including 6 months of preparation, 3.5 years for recruitment, and 1 year of follow-up endpoint assessment.

CONCLUSION: The LOGIS registry, once complete, will provide objective comparative results regarding the usefulness and safety of the Lipiodol and hook-wire localization techniques.

SS 24 CH-08 17:10
CT-guided localization of small pulmonary nodule: value of specimen CT scanning of excised tissue to immediately confirm complete resection
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PURPOSE: We previously described pleural marking method of computed tomography (CT)-guided localization of small pulmonary nodules prior to video-assisted thoracoscopic surgery (VATS) biopsy. Therefore, we had a need to prove that the pleural marking method was appropriate. The purpose of this article is to reveal usefulness of specimen CT scanning for determining the presence of small pulmonary nodule in excised tissue by VATS after CT-guided pleural marking.

MATERIALS AND METHODS: A computer search of 7-year period from April 2010 through April 2017 revealed 51 consecutive patients referred for CT-guided localization of small pulmonary nodules. Specimen CT (n = 13) was performed as the initial evaluation to confirm complete excision. We retrospectively reviewed the clinical data, surgical findings, pathologic results associated with CT-guided localization and successful excision by VATS.

RESULTS: Fifty-one consecutive patients underwent CT-guided pleural marking localization of small pulmonary nodules (25 pure ground-glass opacity nodules, 25 solid nodules, and 1 part-solid nodule). The mean size of the nodules was 9.5 mm. Histological assessment demonstrated lung cancer in 22 patients (43%), metastasis in 16 (31%), inflammatory disease in 11 (22%), and hamartoma in 2 patients (4%). The 13 specimen CT scans performed, 11 CT scans showed complete excision of pulmonary nodule. In one case, the specimen CT revealed excisional tissue without pulmonary nodule. Therefore, immediate re-excision was performed. Subsequent specimen CT couldn’t show the nodule in excised tissue because of large hematoma due to previous operation. Only frozen pathologic result could demonstrate successful re-excision of small pulmonary nodule.

CONCLUSION: CT-guided pleural localization for small pulmonary nodule is the efficient method of guide for VATS biopsy. Also, the specimen CT may be useful for immediately determining the presence or absence of the targeted lesion in tissue after VATS biopsy for small pulmonary nodule.

SS 24 CH-09 17:20
Re-biopsy for advanced non-small cell lung cancer after EGFR tyrosine kinase inhibitor therapy: CT characteristics of patients with T790M mutation and the use of various re-biopsy procedures
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PURPOSE: Re-biopsy for mutation analysis of non-small cell lung cancer (NSCLC) after EGFR-tyrosine kinase inhibitor treatment is important to determine further chemotherapy regimen. There have been no studies about the radiologic characteristics of NSCLC with T790 mutation and the use of the various re-biopsy procedures.

MATERIALS AND METHODS: Between January and December 2016, 78 patients underwent re-biopsy for mutation analysis of NSCLC, and among them, 76 were assessed with adequate specimen. Patients’ treatment course, serial CT scans and pathologic reports were retrospectively reviewed. Re-biopsy methods are varied: EBUS or BFS-guided (n=27), CT-guided (n=18), fluoroscopy-guided (n=5) biopsies, US-guided supravacuicular lymph node (n=6) or other sites (n=6) biopsies and pleural fluid analysis (n=14). CT images obtained at the time of initial biopsy and re-biopsy were compared between patients with and without T790M mutation. Re-biopsy associated complications were assessed.

RESULTS: Among 76 patients, 40 (52.6%) presented
T790M mutation on re-biopsy. Progression free survivals between patients with and without T790M mutation were not statistically different (322 and 389 days, respectively). On initial CT, pleural retraction (odds ratio [OR], 4.1; p=0.03) and the presence of pleural metastasis (OR, 3.4; p=0.03) were significant factors that related to the positive T790M mutation by multivariate logistic analysis. Pleural retraction (OR, 26.8, p=0.03) and pleural metastasis (OR, 11.4; p=0.004) are also shown as significant factors that related to the positive T790M mutation on CT obtained at the time of re-biopsy. Three patients developed pneumothorax, and two were managed by chest tube insertion. One patient who was negative T790M mutation on pleural fluid analysis finally diagnosed as positive T790M mutation by following CT-guided biopsy.

CONCLUSION: Pleural retraction and pleural metastasis were significantly associated factors to positive T790M mutation in NSCLC patients who underwent re-biopsy. Negative T790M on pleural fluid analysis could not give a guarantee for true negative, and further core biopsy might be recommended.

SS 24 CH-10 17:30
Repeat biopsy of patients with acquired resistance to EGFR TKIs: implications of biopsy-related factors on T790M mutation detection
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PURPOSE: Identification of the T790M resistance mutation through repeat biopsy is essential to determine the eligibility of candidates for third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs). We aimed to find potential predictors of non-diagnostic repeat biopsy specimen acquisition for mutational analysis and detection of the T790M mutation.

MATERIALS AND METHODS: We retrospectively reviewed 90 advanced non-small cell lung cancer patients harboring EGFR mutations who underwent repeat cone-beam CT-guided transthoracic needle biopsy. Clinical characteristics as well as repeat biopsy-related factors were compared between patients with and without diagnostic biopsy specimen acquisitions and between patients with and without the T790M mutation. After univariate analysis, multivariate logistic regression analysis was performed to reveal independent predictors.

RESULTS: Appropriate biopsy specimens were obtained in 90% (81/90) of patients, of which 62% (50/81) possessed the T790M mutation. None of the analyzed variables were significantly associated with non-diagnostic biopsy specimen acquisition. For T790M mutation detection, duration of EGFR TKI treatment (p = 0.066), duration of total chemotherapy treatment (p = 0.026), tumor size (p = 0.066), and metastatic lesion as a biopsy target (p = 0.029) showed P values less than 0.10. Multivariate analysis revealed that smaller target tumor size (OR, 0.765; 95% confidence interval: 0.600, 0.975; p = 0.031) was an independent predictor of T790M mutations. Metastatic lesions as biopsy targets (OR, 4.194; 95% confidence interval: 0.997, 17.637; p = 0.050) showed marginal statistical significance.

CONCLUSION: Detection of the T790M mutation at repeat biopsy may be associated with smaller target tumor size and selection of metastatic lesions as biopsy targets.
CT and found out higher pleural plaque volume tended to exhibit a restrictive pattern. However, pleural plaques alone were not found to be significantly associated with pulmonary function.

SS 24  CH-12  17:50
Long-term follow-up observational study of effects of Sirolimus in lymphangioleiomyomatosis patients on lung cysts and pulmonary function
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PURPOSE: To retrospectively determine whether Sirolimus (SR) has beneficial effects on lung cysts and pulmonary function (PF) in lymphangioleiomyomatosis (LAM) and to investigate natural course of LAM in the long-term follow up (FU).

MATERIALS AND METHODS: From May 2001 to December 2016, 73 patients with biopsy proven LAM were identified. Among these, 38 (52%) underwent SR therapy. For quantitative analysis of lung cysts, 171 chest CT images from 69 patients (including 38 with SR therapy) who had at least two chest CT scans during follow-up (initial, last, and/or at the time of initiating SR) were analyzed using computer aided system, and the cyst score (CS) was computed. For qualitative analysis, two radiologists recorded CS in all CT images, and evaluated changes of lung cysts between CT scans. Then the CS from both quantitative and qualitative analysis of the last CT scans was compared with those of CT scans done on SR therapy and/or initial CT scans. For PF evaluation, PF tests done on initial, SR therapy, and the last FU from 65 patients (including 35 with SR therapy) were evaluated and compared.

RESULTS: In patients with SR therapy, total FU period was 116 ± 38 months and FU period after SR therapy to the last FU was 42 ± 39 months. In both quantitative and qualitative analysis of lung cysts, CS at the last CT were significantly aggravated with initial CS (all p > 0.05), but not significantly different from CS at the time of initiating SR in patients with SR therapy (Table 1, all ps < 0.05). Both readers evaluated that 62.2% and 64.8% of patients showed stable or improvement of lung cysts after SR therapy (Table 2). The last PT test result was significantly aggravated than initial study (all ps < 0.05), but no significantly different from study at the time of initiating SR (all ps > 0.05) (Table 3). In patients without SR therapy, both CS and PF showed interval aggravation between initial and the last studies (FU period, 60 ± 44 months), but there were no significant differences (all ps > 0.05).

CONCLUSION: The present study proved the benefits of Sirolimus on lung cysts and lung function compared between pre- and post-Sirolimus therapy through long-term follow-up in the largest LAM population. SR therapy underwent 52% of patients with LAM. SR therapy slowed down lung function decline and increase in cystic lesions during the long-term FU period.