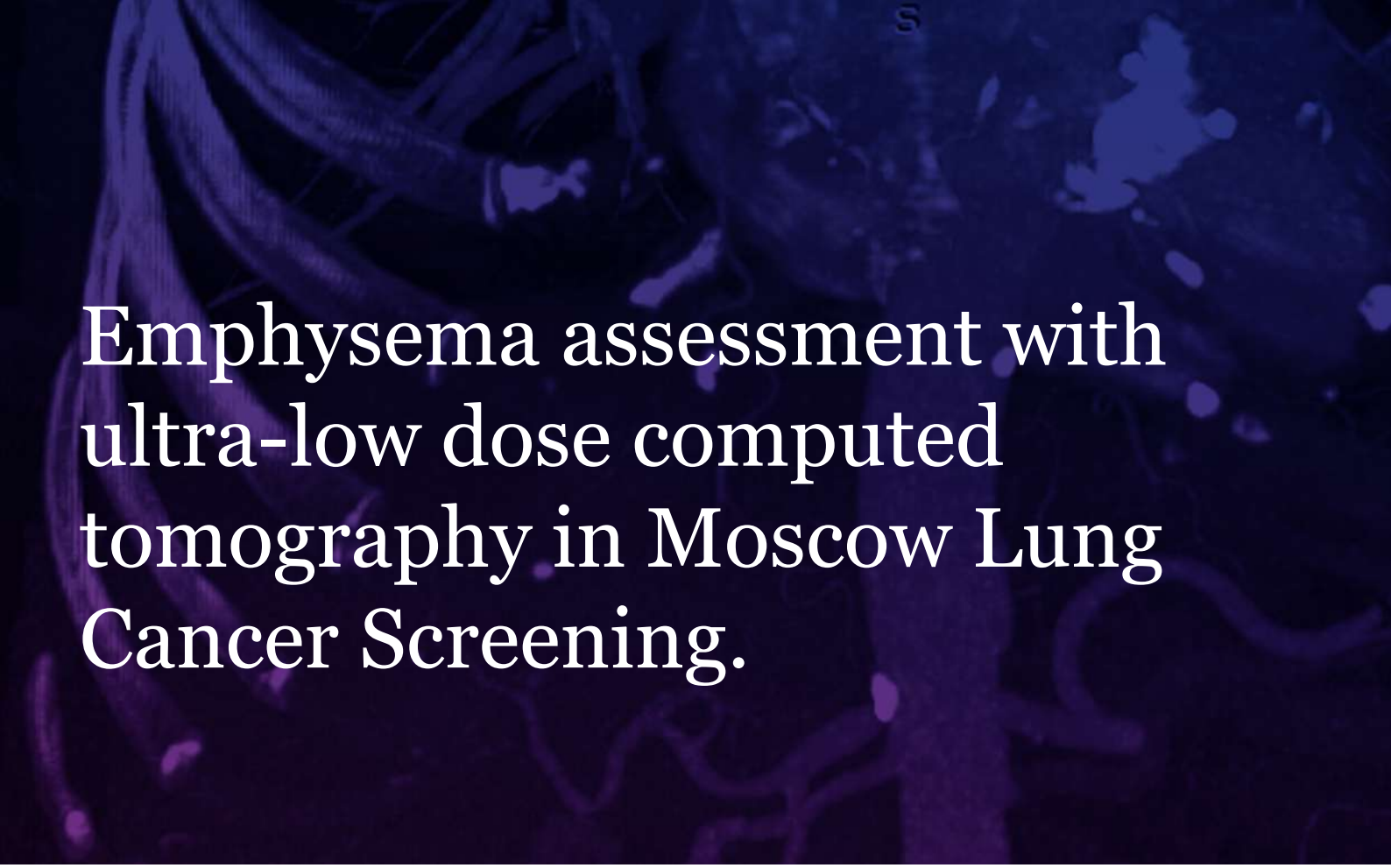

Emphysema assessment with ultra-low dose computed tomography in Moscow Lung Cancer Screening.

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Introduction

Lung cancer is one of the most common oncological diseases and a leading cause of cancer death in the world [1]. According to the literature, lung cancer mortality in both sexes is the most frequent cause of cancer death through the years [2-6].

In Russia, such diseases as coronary heart disease (CHD), lung cancer and chronic obstructive pulmonary disease (COPD) are the most common causes of death. CHD has 1st, lung cancer - 6th and COPD - 10th places respectively in the distribution of disease and death according to WHO and the Institute for Health Metrics and Evaluation (IHME). Early detection and treatment of these conditions can influence the progression of the diseases and decrease the morbidity and mortality rates. In Russia, lung cancer has the first place in the cancer mortality rate among men [7-8]. Advanced lung cancer accounts for 70% of all the diagnosed cases of lung cancer in Russia and leads to death in 50% of cases within the 1st year. [10]. In 2017, the crude mortality rate for lung cancer was 34,18/100 000 (59,66 for males and 12,15 for females), the rate in Moscow was lower than in other Russian regions and reached 26,13/100 000 (40,46 for males and 13,82 for females) [9].

There were several attempts to use a low-dose computed tomography (LDCT) in lung cancer screening after computed tomography (CT) became commonly used. The major randomised trials are: DLST (Danish Lung Cancer Screening Trial) [11], MILD (Multicentric Italian Lung Detection) [12], ITALUNG [13], DANTE [14], LUSI [15], NLST (National Lung Screening Trial) [16].

LDCT allows to detect emphysema as well as focal lesions. A cohort study in lung cancer screening revealed that patients with COPD developed lung cancer 2-4 times frequently than patients without COPD [17, 18, 19, 20].

Emphysema as a predictor of COPD

Chronic obstructive pulmonary disease is a chronic life-threatening condition that gets worse over time. This disease is characterized by increasing breathlessness, poor airflow, exacerbations and may become severe [21]. The majority of patients with COPD are smokers.

Global epidemiological studies BOLD and PLATINO revealed that there are at least 600 million patients with COPD worldwide today [22, 23]. Global Initiative for Chronic Obstructive Lung Disease (GOLD) is the main document that standardized strategy for the management of COPD [24].

Spirometry is the standard test to detect COPD, the diagnosis considered to be certain when post-bronchodilator FEV1/FVC is < 0.7. COPD severity depends on symptoms and exacerbation frequency and it also must be remembered that early stages may be asymptomatic and, consequently, undetected. Recently, the US Preventive Services Task Force found that early detection of COPD in asymptomatic persons with spirometry does not improve health-related quality of life. There is no evidence of the efficacy of screening for COPD in asymptomatic adults using prescreening questionnaires and spirometry [25].

The method of early detection of COPD includes a quantitative assessment of emphysema, bronchial wall thickness and air trapping on chest CT scans. Quantitative assessment of emphysema is studied more than other signs of COPD mentioned above. Fully automatic quantitative assessment of emphysema in chest CT scans is more accurate than visual quantitative evaluation in chest CT scans or chest X-ray [26]. Regardless of the COPD stage, which was identified with pulmonary function tests, there is a strong correlation between the detection of emphysema on chest CT and lung cancer [27-30].

The "golden standard" of CT protocol and a threshold value for fully automatic quantitative assessment of emphysema are not developed yet. Emphysema could be quantitatively assessed with an automatic program for lung densitometry, which calculates the percentage of voxels based on the certain threshold value or lower it, usually from -910/-950 to -970 HU [31]. Moreover, the Perc15 technique, which identifies the HU meaning of the 15th percentile point of the lung density histogram [32]. The lower Perc15 value, i.e. closer to -1000 HU, the more severe emphysema is diagnosed. This method allows to classify single voxels as lung, emphysema or hyperinflation due to functional small airways disease.

Goals of the research

1. To evaluate the feasibility of emphysema diagnostics with ultra-low dose computed tomography (ULDCT) for lung cancer screening compared to routine CT.
2. To assess the prevalence of emphysema in ULDCT-based lung cancer screening in Moscow.

Materials and methods

ToshibaAquilion 64 and specially developed ULD CT scanning protocols with radiation-absorbed dose up to 1 mSv, which is used for chest X-ray screening in adults (SanRaN 2.6.1.1192-03), were used to perform examinations of patients with different weight.

Patients were included in the study according to the following enrolment criteria: 50 years of age or older; more than 30 pack-year smoking history; patients, who gave up smoking 15 years ago; no history of lung cancer, bronchial cancer or tracheal cancer; no history of lung metastases in patients with other cancers.

For preliminary evaluation of prevalence and severity of emphysema, a retrospective review of the results (images and reports) of ultra-low-dose chest computed tomography (ULD CT) that were performed in 2017 during project named "Moscow Screening for Lung Cancer" was done. The parameters were quantified for both ULD CT images and CT images, which were performed at 10 days interval.

The differences between CT indexes of emphysema, air trappings and bronchial wall thickness were evaluated on end-inhale and end-exhale ULD CT scans, which were performed as a part of the project "Moscow Screening for Lung Cancer" in 2017, with the use of Phillips Intellspace Portal 11.

Medical data was depersonalized according to personal data protection law. The analysis of DICOM 3.0 images was done with «AGFA Agility Enterprise 8.0» and «OsiriX MD (v.5.5.1 64-bit)» software. Philips Intellispace 4.0 was used for quantitive evaluation of emphysema.

Results

Smoking was one of the major inclusion criteria for it is known to be the cause of chronic obstructive pulmonary disease (COPD) in 79% of cases. 1678 participants (31,6%) of the lung cancer screening had a history of COPD. It is important to pay attention to such findings as emphysema and bronchial wall thickness, revealed during ULD CT screening for lung cancer, because it may help to detect early stages of COPD.

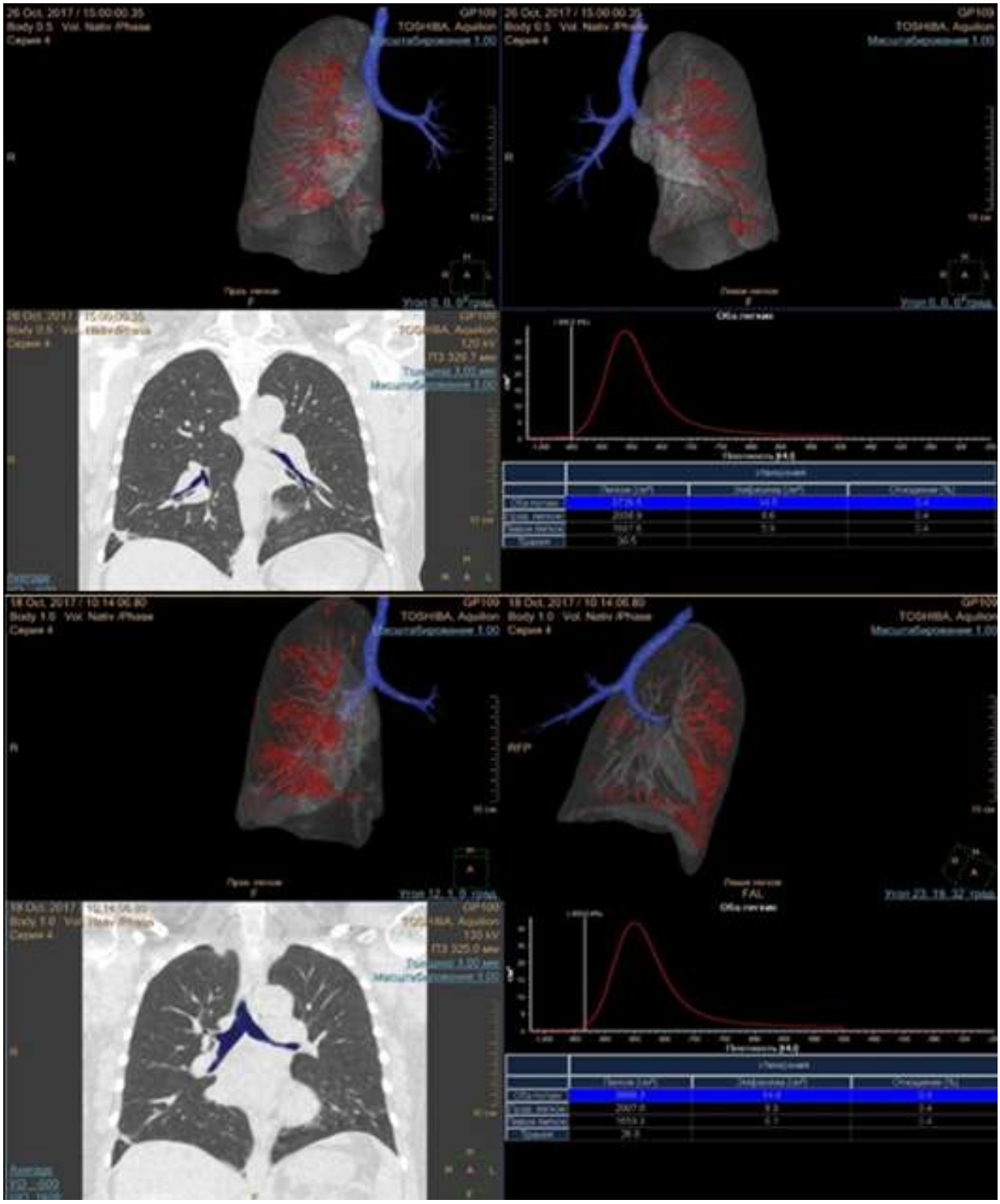
Regardless of the foci that could be classified with LungRads, incidental findings in the lungs were revealed in 68,5% (174/254) of cases. Primary LDCT reports included only 42,5% (74/174) of them.

The most frequent incidental findings on LDCT of the respiratory system included:

- thickening of the bronchial wall - 51,1% (90/174),
- emphysema - 31,65% (49/174),
- bronchiectasis - 51,1% (90/174),
- interstitial lung disease - 16,4% (29/174),
- thickening of parenchyma - 6,1% (11/174),
- pulmonary fibrosis - 22,3% (39/174).

Estimating weather emphysema was characterized in the reports the reports or not, we found that it was not mentioned in 24% of cases (12/49). Nearly half (51%, 30/49) of the radiologists did not characterized emphysema as centrilobular, panlobular, paraseptal, irregular.

Regardless of the difficulties in qualitative assessment of emphysema, ULD CT images could also be used to quantitative assessment. ULD CT and CT images (pic. 1) of the same patient, which were performed in 4 days interval end-inhale (the differences of volumes - 2,3%) are shown below. The patient has equal volumes of emphysema when threshold value for CT is -950HU and -933HU - for ULD CT.



Picture 1. *– Quantitative assessment of emphysema on CT and ULD CT images with different threshold values*

Discussion

Pulmonary emphysema can be assessed not only qualitatively, but also quantitatively on and-inhale and end-exhale ULD CT data, which allows to evaluate the prevalence of the predictor of COPD in lung cancer screening in more details. Emphysema diagnosed with ULD CT in lung cancer screening should be studied in order to detect these diseases early. Screening for the predictor of COPD in addition to screening for lung cancer will significantly improve its efficacy and diagnostic significance.

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