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Peculiarities of non-small cell lung cancer local extension radiological assessment

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Background. Purpose of the work was to investigate the diagnostic value of chest radiography and CT in assessing lung cancer local extension in the chest, in consideration of consistent patterns of non-small cell lung cancer spread in the chest.

Material and methods. 335 patients were enrolled in our study matching the inclusion criteria. The purpose was to detect how accurate and specific radiologic signs were detecting the lesions and assessing the resectability of tumour. Radiological signs of cancer resectability were analysed as well considering the NSCLC histological type, growth type and lobe localisation.

Results. Adding evaluation criteria (tumour and mediastinum contact >3 cm, tumour contact with aorta circumference >90°) and morphology as one of invasion criteria, sensitivity rises from 50% up to 85%. Combining pleural thickening sign with pleural fluid sign and adenocarcinoma morphology as one of pleural malignancy predicting signs, the sensitivity reaches 100%. The lowest sensitivity and accuracy while evaluating mediastinal invasion was determined in the case of left upper lobe tumours. The diagnostic value of CT determining mediastinal invasion was better in peripheral tumours than in the central ones: sensitivity 80%, specificity 85%, accuracy 83% in peripheral tumours and 72%, 80% and 74% in the central ones, respectively.

Conclusions. Staging lung cancer by CT and considering lung cancer histology, growing type and localisation cancer extension may be helpful while assessing local lung cancer extension more accurately and selecting patients for further investigation.

Key words: non-small cell lung cancer, local extension, radiological diagnostics

INTRODUCTION

The proper treatment of lung cancer may be achieved after precise staging by non-invasive and invasive diagnostic methods. Radiological tests are fundamental in lung cancer staging algorithm. In many countries analysis of lung cancer radiological staging possibilities is being performed for the third decade, new technologies are being implemented, however, without satisfying results.

Accurate staging has two main purposes. The first is to avoid false positive cases that may preclude palliative treatment for the patient instead of a possible radical one. The second one is to reduce false negative cases because in the event of inaccurate radiological staging unnecessary thoracotomies make an impact on increased postoperative mortality, prolongs hospital stay and delays necessary chemotherapy and radiotherapy. The dividing line lies between T3 and T4 tumours, while an operation may be performed for first ones, and for T4 lesions chemotherapy or radiotherapy have to be administered, with operation indicated only for carefully selected patients (1). T3 and T4 lesions are very different as well as radiological signs while diagnosing them (2). This is the reason why this work deals with the diagnostic accuracy of detecting various lesions. T1 and T2 lesions are detected quite accurately, whereas it is much more difficult to differentiate T3 and T4 tumours although separation of these lesions is crucial in selecting patients for surgical treatment (3).

It is predicated, that most of the lung cancer local extension signs are noticed but have a mistaken interpretation (4). Marked lesions usually are diagnosed during radiological examination and correctly interpreted. The vast problem is differentiation between contact and invasion and denoting resectability potentiality for every patient. Sometimes such lesions as pleural carcinosis (especially dry carcinosis) are not possible to denote even by newer diagnostic methods such as PET-CT (5). Watanabe (6) in his study points out that undiagnosed pleural dissemination is the cause of more than half of diagnostic thoracotomies. Furthermore, various authors point out different diagnostic value of radiological signs assessing lung cancer local extension (2, 7–15).

Besides, lately the attention is paid to the disparities of clinical behaviour and treatment of non-small cell lung cancer histological type. So in this study radiological lung cancer extension signs are correlated with histological types of non-small cell lung cancer. In our preceding article (16) we presented analysis of the disparities of different histological types of lung cancer spread in the chest. Statistically significant rela-

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tions have been established between lung cancer histological types and lung cancer extension in the chest. Based on these data this study was supplemented by more patients only with NSCLC, and comprehensive analysis of radiological signs considering lung cancer histology has been made. There are few studies in Lithuania concerning lung cancer radiological staging problems. The main methods for radiological assessment in Lithuania are radiography and CT meanwhile PET is not available in Lithuania currently.

The purpose of the work was to investigate the diagnostic value of chest radiography and CT in assessing lung cancer local extension in the chest, considering consistent patterns of non-small cell lung cancer spread in the chest.

MATERIAL AND METHODS

During 1999–2007 January about 1700 patients with lung cancer were operated on in the Thoracic Surgery Department of the Institute of Oncology, Vilnius University. 335 patients were enrolled in our study (291 men and 44 women) that fitted the inclusion criteria.

The inclusion criteria were the following ones: patients with non-small cell lung cancer; radiological examination tests for staging lung cancer before operation; T3 and T4 lesions confirmed pathologically after operation (except superior sulcus tumours). Exclusion criteria: second primary tumour, chemotherapy or radiotherapy before operation or radiological examinations.

Our purpose was to detect how accurate and specific radiological signs were while detecting the lesions and assessing the resectability of tumour. The study data were collected from medical case histories, operation and pathology reports. Chest radiograms and CT views assessing lung cancer extension were retrospectively evaluated. Changes in chest radiograms and CT views were divided into two groups: lung parenchyma changes and cancer local spread signs. Lung parenchyma changes encompass lung masses, infiltration, atelectasis and hypoventilation, lung root enlargement. Nodal or plate form parietal and interlobar pleural thickening, pleural fluid, tumour contact with the chest wall and mediastinum, rib destruction were remarked as cancer local spread signs. Later on all these signs were collated with operation and pathology reports.

The study data were arranged using Microsoft Excel software, and statistical analysis was performed using SPSS (statistical package for social sciences) 13.0 software. All the significance and frequency characteristics of the variables were verified by parametric and non-parametric statistical methods.

Assessing the relations of tumour characteristics such as histological type, growing type (central or peripheral), and localisation in the lung lobes with lung cancer local spread signs cross tabulation method and logistic regression analysis were used. Radiological signs of cancer resectability were analysed as well as considering NSCLC histological type. Diagnostic value of radiologic methods was calculated applying 95% confidence interval. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated. p values <0,05 were considered to be significant.

RESULTS

Cross-tabulation method and logistic regression analysis test revealed the statistically significant ($p < 0.05$) relations between adenocarcinoma histology and pleural carcinosis with malignant pleural fluid, as well as the relation between non-differentiated carcinoma and mediastinal invasion. Squamous and non-differentiated carcinomas tend to invade chest wall more frequently than adenocarcinomas, however, the differences were not statistically significant in this case. So these peculiarities of lung cancer extension were applied as complementary factors while establishing tumour extension to the mediastinum, chest wall or pleura by radiological methods.

While evaluating mediastinal invasion various signs were used that were summarised in Table 2. It can be noticed (Fig. 1) that adding evaluation criteria (tumour and mediastinum contact >3 cm, tumour contact with aorta circumference >90°) and non-differentiated cancer morphology as one of invasion criteria, sensitivity rises from 50% up to 85%. Besides, only diagnostic thoracotomies were performed to all the patients with these signs, therefore, the latter signs denoted not only the pathological process but also unresectability in this study.

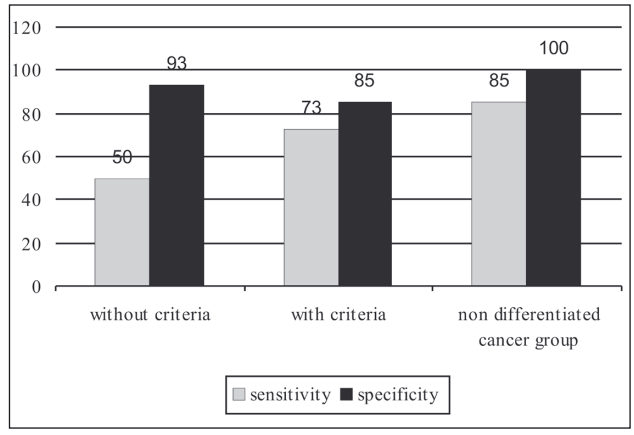


Fig. 1. CT sensitivity and specificity (%) assessing mediastinal invasion using criteria (tumour and mediastinum contact >3 cm, tumour contact with aorta circumference >90°), without them and in non-differentiated cancer group with the above evaluation criteria

The lowest sensitivity evaluating mediastinal invasion was determined in the case of left upper lobe tumours – 62.5% (Fig. 2). Accuracy was lowest in this case as well reaching only 66%. Specificity was lowest evaluating the right upper lobe tumour invasion to mediastinum – 60%. Tumours in the right lower lobe were evaluated most accurately – 91.6%.

It was determined that mediastinal invasion depends on the tumour growth type (central or peripheral) (Fig. 3).

The diagnostic value of CT determining mediastinal invasion was better in peripheral tumours than in the central ones: sensitivity 80%, specificity 85%, accuracy 83% and 72%, 80% and 74%, respectively.

It is difficult to diagnose pleural carcinosis sustaining on pleural thickening sign (Fig. 4). Neither calculating its sensitivity and specificity only in adenocarcinoma patients' group is

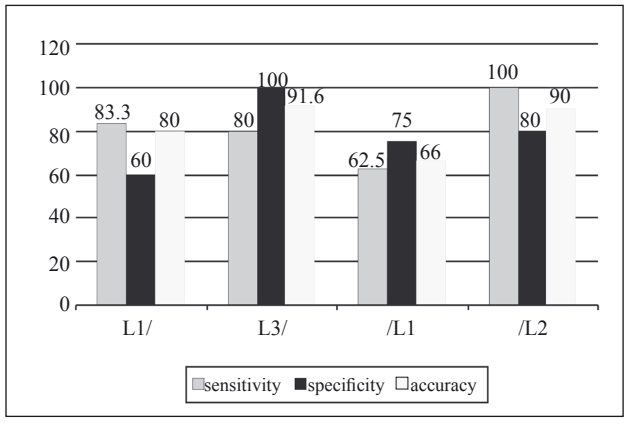


Fig. 2. CT diagnostic value (%) assessing mediastinal invasion depending on tumour lobe localisation (L1/ right upper lobe, L3/ right lower lobe, /L1 left upper lobe, /L2 left lower lobe)

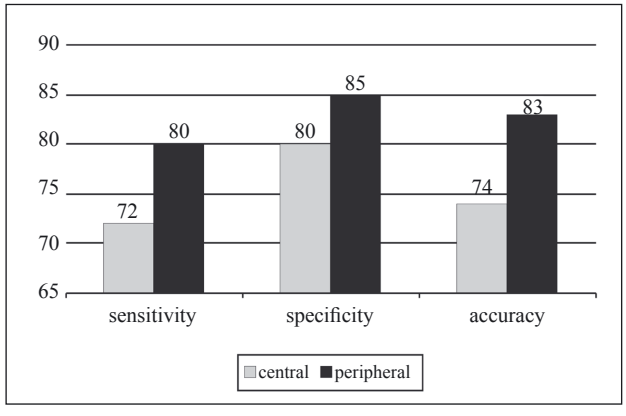


Fig. 3. CT diagnostic value (%) assessing mediastinal invasion depending on tumour growth type (central, peripheral)

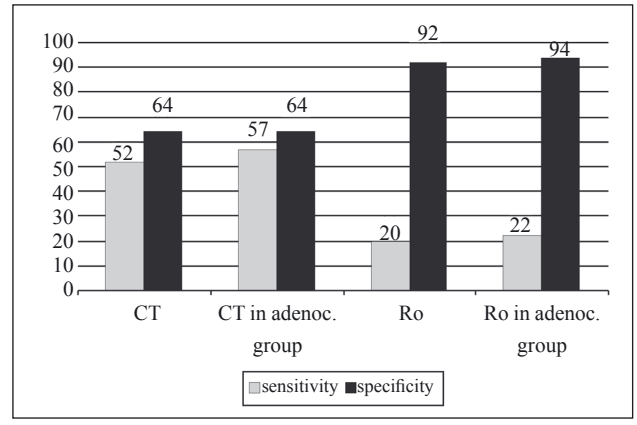


Fig. 4. Sensitivity and specificity (%) of pleural thickening sign diagnosing pleural carcinosis by CT and radiography and in the adenocarcinoma patients' group

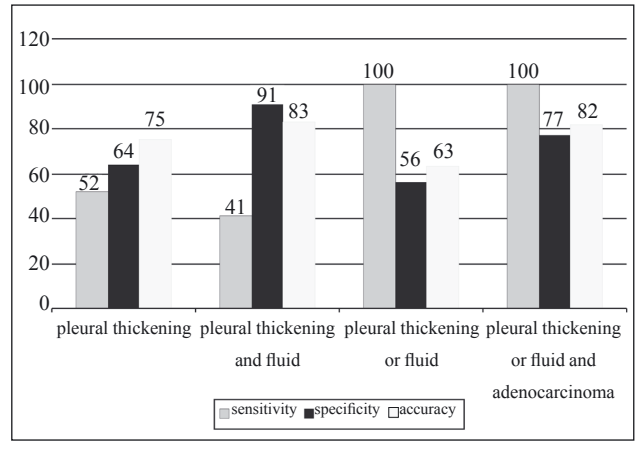


Fig. 5. Diagnostic value (%) of CT determining pleural carcinosis combining radiological signs of pleural thickening, pleural fluid and adenocarcinoma morphology

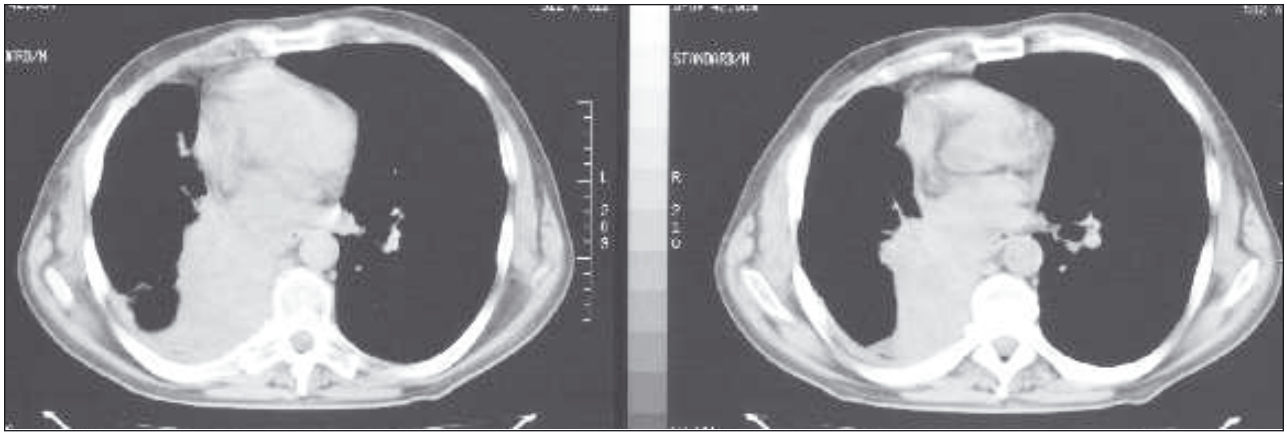
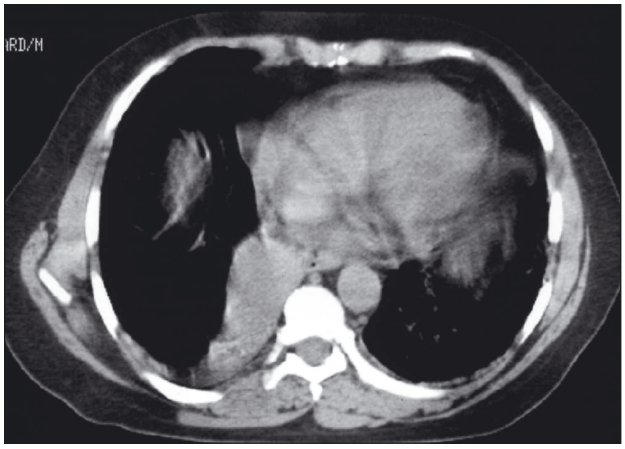


Fig. 6. Right lower lobe tumour with atelectasis, pleural fluid. Bronchoscopy revealed squamous cell carcinoma. Diagnostic thoracotomy was performed and T4 carcinoma with mediastinal invasion was determined. No pleural malignant invasion was determined pathologically

satisfying (57%). It is impossible to diagnose pleural carcinosis in radiographs, as the sensitivity reaches only 20%. But if the changes are obvious, they are specific (92% and 94% in adenocarcinoma group).

After combining pleural thickening sign with pleural fluid sign and adenocarcinoma morphology as one of pleural malignancy predicting signs, the sensitivity reaches 100% (Fig. 5).



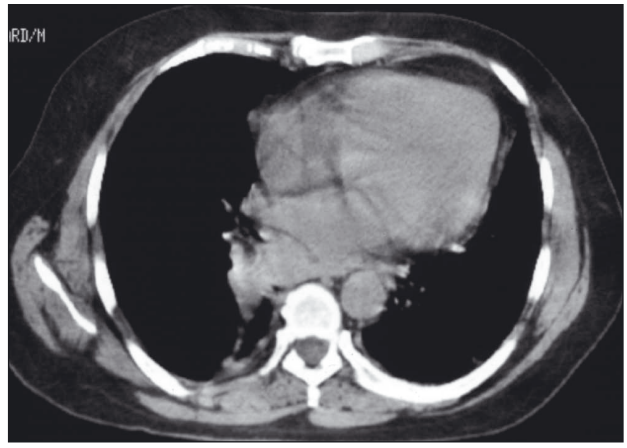


Fig. 7. Right lower lobe carcinoma with atelectasis. Little pleural thickening can be noticed (arrow). Bronchoscopy revealed central growth type adenocarcinoma. During operation tumour with pleural carcinosis was detected, no mediastinal invasion was determined

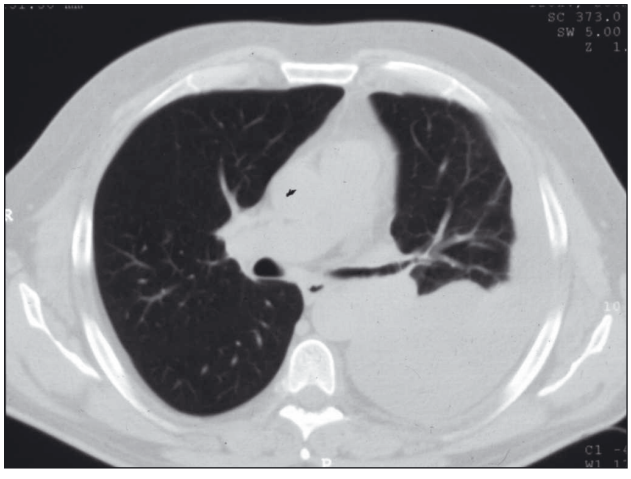


Fig. 8. CT and bronchoscopy determined left lower lobe squamous carcinoma and pleural fluid. Operation revealed T4 squamous carcinoma with pericardium invasion. No pleural carcinosis was found; pleural fluid had no signs of malignancy

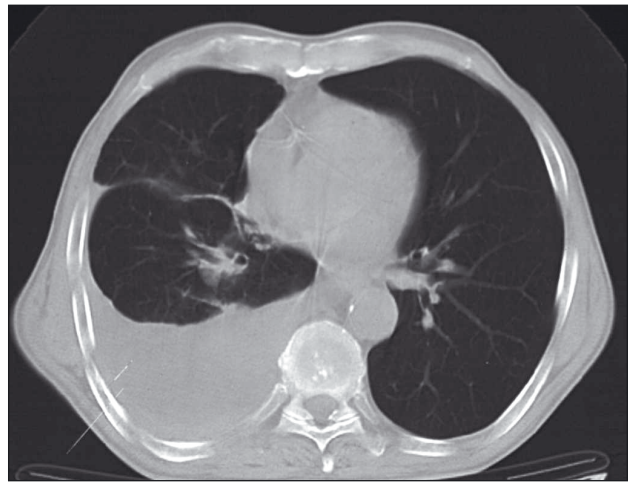


Fig. 9. Right pleural fluid, thickened interlobar pleura. Operation revealed lower lobe adenocarcinoma with pleural carcinosis and malignant pleural fluid

In two cases Figures 6 and 7 showed very similar radiogical presentation but revealed different lesions after operation that may lead to radiologist's mistakes and false diagnoses interpreting lung cancer extension signs. As it was detected in the previous study, lung adenocarcinoma causes pleural carcinosis and malignant pleural fluid more frequently, while squamous cell cancer grows directly to the adjacent organs and structures. These peculiarities may be helpful in deciding the operation possibility. With reference to this study results in case of adenocarcinoma patients even with minimal signs of pleural invasion VATS could be the method of choice instead of thoracotomy.

In figures 8 and 9 two other cases with pleural effusion are demonstrated. In spite of similar radiological signs, in the first case (Fig. 8) squamous carcinoma was determined, pleural fluid was non malignant. In the second case of adenocarcinoma (Fig. 9) pleural carcinosis was proved pathologically after operation.

In 26 patients peripheral carcinomas coming into contact with pleura were detected on CT images. Chest wall invasion was pathologically proven in 13 cases. Possible signs of chest invasion were analysed in both groups of patients (with and without invasion) and statistically significant signs were estimated.

In Table 1 signs of tumours with pathologically proven chest invasion are summarised.

All the tumours with chest wall invasion were more than 3 cm size in one dimension; pleural thickening was noticed almost in all cases as well (92.3%). Even 69% cases were interpreted correctly because of associated rib destruction. Tumour angle with pleura was not a reliable sign of chest invasion (61%). In 76.9% of patients squamous morphology cancer was determined, in spite of peripheral tumour localisation that is usually related with adenocarcinoma.

Table 1. **Signs of tumours with chest wall invasion**

Sign	Tumour contact with pleura >3 cm	Pleural thickening	Rib destruction	No adenocarcinoma morphology	Obtuse angle with pleura	Tumour size >3 cm in one dimension
Percent	84.6%	92.3%	69%	76.9%	61.5%	100%
Significance	0.02	0.164	0.001	0.02	0.058	0.041

DISCUSSION

Regardless diagnostic methods, the clinical stage of lung cancer does not always agree with the pathological stage after operation. Unfortunately, surgical treatment in such cases is confined to diagnostic thoracotomy (17). Radiological diagnosis depends on technical possibilities, selected assessment criteria and their interpretation. This study analyses lung cancer spread in different chest structures. Such lesions are collated in one stage III, a or b category, but come through with various radiologic signs and determine different prognosis. The retrospective analysis of operated patients' data was made, and all the present lesions were investigated providing possibility to work out separate lesion models and relate them with non-small cell lung cancer histological types. Non-small cell lung cancer encompasses adenocarcinoma, squamous, large cell, adenosquamous carcinomas. Their diagnosis, treatment strategy and prognosis are similar. It is accepted to distinguish NSCLC histological types in pathology reports, however, without paying attention to them during radiological examinations' interpretation or treatment. In this study talking-point questions for radiologists and surgeons are analysed: how to select patients that would benefit from operation and to avoid unnecessary diagnostic thoracotomies at the same time. In accordance with this study the selection of patients could be made for minimally invasive surgery by staging the advanced lung cancer.

After the comprehensive analysis of literature it can be noticed that different authors present different results estimating diagnostic value of radiological methods in assessing lung cancer local spread and resectability that are improved by new technologies used but not as much as desired. Sensitivity of CT determining pleural dissemination according to different authors (2, 7–10) ranges between 26% and 89%, whereas specificity does from 60% to 100%. Assessing diaphragmatic pleura Mori (9) points out the sensitivity to be 0–33%.

In our study the best results detecting pleural carcinosis were estimated combining pleural thickening sign with pleural fluid sign and adenocarcinoma morphology as one of pleural malignancy predicting signs; in this case the sensitivity reaches 100%.

Diagnostic value of CT determining mediastinal invasion according to different authors (11–14) ranges from 55% to 99%. In our study, while evaluating mediastinal invasion, the best sensitivity of 85% was estimated by combining mediastinal invasion radiological signs with non-differentiated cancer morphology as one of invasion criteria.

Table 2. **Chest radiography and CT signs of lung cancer local spread**

Lesion	Chest radiography criteria	CT criteria
Mediastinal invasion	Lung root enlargement Undistinguished tumour margins from mediastinum Undistinguished tumour margins from the heart	Tumour and mediastinum contact >3 cm Mediastinal fat obliteration between tumour and mediastinum Mediastinal structures dislocation Tumour interposition into mediastinum >90° and >180° tumour contact with mediastinal structures
Aorta invasion	Undistinguished tumour margins from arcus aortae	Tumour contact with aorta circumference >90° Tumour contact with aorta circumference >30% Tumour invasion into aorta wall
Pleural carcinosis	Pleural fluid Obliterated pleural sinuses Interlobar pleura thickening Pleural thickening	Nodular, plate form pleural thickening Pleural fluid Interlobar pleura thickening Strands between tumour and pleura
Chest wall invasion	Tumour flattened to the chest wall Pleural thickening Soft tissue thickening Rib destruction	Fat obliteration between tumour and pleura Tumour-pleura contact length >3 cm Tumour-pleura contact and tumour diameter ratio Obtuse angle between tumour and pleura Pleural thickening Strands between tumour and pleura Soft tissue in the tumour area Tumour with interposition into the chest wall Rib destruction

Table 3. **Factors enhancing probability of radiological signs of lung cancer invasion**

Lesion	Factors
Mediastinal invasion	Non- differentiated carcinoma
	Squamous cell carcinoma
	Central growth type
	Left upper lobe localisation
Aorta invasion	Left upper lobe localisation
	Central growth type
	Non-differentiated carcinoma
Pleural carcinosis and malignant pleural fluid	Adenocarcinoma
	Peripheral growth type
	Lower lobes localisation
Chest wall invasion	Peripheral growth type
	Squamous cell carcinoma

Sensitivity of CT in determining chest wall invasion ranges from 38% to 87%, while specificity amounts to 40–90% (2, 11, 14, 15). In our study very similar results were obtained and as one of helpful factors deciding on chest wall invasion in indeterminate cases may be non-adenocarcinoma morphology.

Toloza (18) maintains that suspecting advanced lung cancer as sensitive as possible test has to be used. In contrast, a more specific test has to be used for a patient with an early lung cancer. Therefore, in this study special attention was paid to achieving good sensitivity results combining different radiological signs with other contributory factors.

Rocha (19) determined that l/n invasion predisposition depends on tumour localisation in the lung lobe, and Ketchedjian (20) identified survival differences in case of central and peripheral lung cancer. Almost 50% of central tumours had metastases in l/n, while in peripheral cancers they were rare. These factors were taken into account in this work as well, and it was determined that mediastinal invasion was more accurately detected in peripheral than in central cancers (74% vs. 85%). The lowest diagnostic accuracy of CT appeared to be in the left upper lobe tumours that may result from anatomical features of this area.

So this study points out that cancer histology, growth type and lobe localisation make influence on the false results and mistaken interpretation of radiological images, therefore it is recommended to take into account radiological signs and cancer morphology combinations while assessing lung cancer extension that makes interpretation of radiological signs more accurate.

With reference to various authors and our results, radiological criteria for evaluating lung cancer local spread were summarised in Table 2 as practical recommendations, whereas Table 3 summarised various factors increasing the interpretation accuracy of radiological signs of lung cancer extension analysed in this study.

CONCLUSIONS

1. While staging lung cancer with CT we recommend taking into consideration cancer histological type if it is available at the time. Considering lung cancer histology, growing type and localisation, cancer extension may be diagnosed more accurately.

2. Chest radiography lacks sensitivity determining various lesions, so chest CT must be performed for every patients assessing lung cancer extension.

3. More than 3 cm tumour contact with mediastinum, and more than 90° tumour contact with aorta circumference in CT views were radiological signs of mediastinal invasion in this study. In case of squamous and undifferentiated carcinoma these signs were also predictors of unresectability.

4. The lowest CT accuracy was estimated assessing the local spread of advanced cancer in the left upper lobe. So it is recommended to pay special attention in evaluating cancer of this localisation and possibly use minimally invasive surgery for precise staging.

5. Combining pleural thickening sign with pleural fluid sign and adenocarcinoma morphology as one of pleural malignancy predicting signs, the sensitivity reaches 100%.

6. Tumour size more than 3 cm in one dimension and non-adenocarcinoma morphology could be helpful determining chest wall invasion, in addition to other radiological signs of invasion.

7. Accuracy of CT determining mediastinal invasion was better in peripheral tumours than in central ones: 83% and 74%, respectively.

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Rūta Briedienė

RADIOLOGINIŲ POŽYMIŲ YPATUMAI VERTINANT NESMULKIALĄSTELINIO PLAUČIŲ VĖŽIO VIETINĮ IŠPLITIMĄ

S a n t r a u k a

Tyrimo tikslas. Ištirti rentgeninio ir KT tyrimo metodų diagnostinę vertę nustatant plaučių vėžio vietinį išplitimą krūtinės ląstoje ir atsižvelgiant į nesmulkialąstelinio plaučių vėžio histologinį tipą.

Medžiaga ir metodai. Į tyrimą įtraukti 335 pacientai (291 vyras ir 44 moterys), kurie atitiko įtraukimo ir neįtraukimo kriterijus. Tyrimui atrinkome pacientus, sergančius nesmulkialąsteliniu vietiškai išplitusiu (T3 ir T4 pažeidimai) plaučių vėžiu, kurie buvo operuoti, o pažeidimai patvirtinti patologinio anatominio tyrimo metu. Siekiant išanalizuoti radiologinius naviko rezektabilumo požymius, į tyrimą įtraukti pacientai, kuriems nustatyti išplitę T3 bei T4 navikai, pašalinti tiek radikaliai, tiek neradikaliai. Vertinome, kaip tiksliai šie pažeidimai buvo nustatyti (arba ne) rentgeniniu ir KT tyrimo metodais.

Rezultatai. KT tyrimo tikslumas, nustatant tarpuplaučio pažeidimą, yra mažiausias, kai vertinami kairio plaučio viršutinės skilties navikai – 62,5%. KT tyrimu periferinių navikų vietinis išplitimas nustatomas tiksliau nei centrinių – 83% ir 74%. Atsižvelgus į nesmulkialąstelinio plaučių vėžio histologinį tipą, naviko augimo pobūdį ir lokalizaciją plautyje, galima individualizuoti ligą ir tiksliau nustatyti vietinio išplitimo požymius. Mažiausiai tiksliai nustatomas vėžio išsisėjimas pleuroje remiantis pleuros sustorėjimu. Nustatant diseminaciją pleuroje, kai yra keli požymiai – skystis pleuros ertmėje, pleuros sustorėjimas ir liaukinis vėžio tipas, KT jautrumas siekia 100%. Rentgeninio tyrimo jautrumas nėra pakankamas vertinant visus vėžio vietinio išplitimo požymius.

Išvados. Vertinant pacientų, kuriems įtariamas ar nustatytas plaučių vėžys, rentgenogramas ir KT vaizdus ir atsižvelgiant į histologinį tipą, augimo pobūdį ir lokalizaciją plaučio skiltyje, galima tiksliau nustatyti vietinio išplitimo požymius ar atrinkti pacientus tolimesniems tyrimams.

Raktažodžiai: nesmulkialąstelinis plaučių vėžys, vietinis išplitimas, radiologinė diagnostika