Purpose

To describe the CT imaging findings of lung adenocarcinoma in a series of patients submitted to surgical resection and to correlate the radiological features with the pathological subtypes.
Materials and Methods

This retrospective study included 204 consecutive patients with lung adenocarcinomas who underwent thoracic surgery between June 2011 and December 2014 at our institution. Patients were identified through a search of the lung cancer surgical registry database of the department of thoracic surgery. A total of 189 patients (126 men and 63 women, mean age 65.8 years) who had undergone chest CT for preoperative staging at our institution were finally enrolled, representing a total of 197 tumors. Eighteen of the 189 patients were treated with neoadjuvant therapy before surgery.

Preoperative images were acquired either with a 6-detector row PET/CT or a 64-channel multidetector CT machine. Images were reconstructed with a section thickness of 2.5-5 mm for CT/PET and 1-1.25 mm for 64-detector row CT with both soft tissue and chest algorithm. Studies were performed with or without iodinated contrast material.

Two radiologists reviewed CT images at diagnosis recording the following lesion features: type (nodule, mass or consolidation), size (longest diameter), attenuation (pure ground glass, part-solid or solid opacity), borders (smooth, irregular, lobulated or spiculated), and internal density (homogeneous, bubble-like, air-bronchogram or cavitation). In the case of part-solid nodules both total and solid component diameters were measured.

All tumors were surgically resected (lobectomy, segmentectomy or pneumonectomy).

Radiological features were correlated with the following histopathological findings: histologic subtype according to IASCL / ATS / ESR International Multidisciplinary Lung Adenocarcinoma Classification Table 1 on page 4, cell differentiation grade (well, moderately or poorly differentiated), pleural invasion, and lymph node metastases. Regarding the histologic subtype in each tumor, the most predominant pattern was chosen (e.g. lepidic predominant); the tumor was classified as mixed when there was no predominant subtype. Tumors were stratified as preinvasive (adenocarcinoma in situ (AIS)), minimally invasive (MIA) and invasive adenocarcinoma (lepidic, acinar, papillary, micropapillary, solid, or mixed adenocarcinomas). Finally, tumors were staged according to the Seventh Edition TNM staging for lung cancer.

To compare the radiologic and pathological findings Chi-square and likelihood ratio tests were used for statistical analysis. A p value of < 0.05 was considered statistically significant. Statistical analysis was performed with SPSS software (version 15.0).
Table 1: IASCL / ATS / ESR International Multidisciplinary Lung Adenocarcinoma Classification of lung adenocarcinomas (1)

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Results

Among the 197 primary lung tumors, 149 lesions (75.1%) manifested as solid opacities on CT (103 nodules and 46 masses), 36 (18.3%) as part-solid opacities (30 nodules and 6 masses), 7 (3.6%) as pure ground glass nodules, and the remaining 6 lesions (3%) as lobar consolidations Fig. 1 on page 7. Tumor sizes ranged from 8 to 102 mm in diameter (mean 28.2 mm). Twenty tumors showed smooth borders (10.2%), 39 had irregular margins (19.8%), 41 were lobulated (20.8%) and 91 were spiculated (46.2%). Regarding internal density, homogeneous pattern was the most common (54.3%), followed by air-bronchogram (26.9%), bubble-like (9.1%) and cavitation (6.6%). Pleural effusion was seen in 2 patients.

Regarding histopathological study, the vast majority of lesions were invasive adenocarcinomas, whereas 3 tumors were preinvasive adenocarcinomas and 1 lesion was a minimally invasive adenocarcinoma Fig. 2 on page 8. Among the 197 lesions, the most frequently observed histologic subtype was acinar predominant pattern in 90 cases (45.7%), followed by papillary in 23 cases (11.7%), solid in 20 cases (10.2%) lepidic in 13 (6.6%), mucinous in 12 (6.1%), and 15 tumors (7.6%) showed a mixed pattern. One micropapillary predominant adenocarcinoma was detected. In terms of histologic cell differentiation, 50 tumors were well differentiated (25.4%), 95 moderately (48.2%) and 25 poorly differentiated (12.7%). Lymph node metastases were pathologically detected in 20 patients after surgery (10.1%). Finally, pleural invasion was detected in 106 cases (54.6%).

Radiological and pathological findings are summarized in Table 2 on page 7.

Correlation between CT and histopathological findings:

- Internal density: Most lesions with bubble-like internal density (64.7%) corresponded to moderately differentiated adenocarcinoma (p=0.002), particularly in the acinar subtype (64.7%) (p=0.016) Fig. 3 on page 9 a. Those tumors with air-bronchogram corresponded to well or moderately differentiated adenocarcinomas (97, 9%) Fig. 3 on page 9 b, and only one of them (2%) to a poorly differentiated adenocarcinoma. (p=0.002).

- Borders: Smooth margins were more frequently observed in papillary subtype (46.2%) Fig. 4 on page 10. Acinar adenocarcinomas showed often lobulated (61.1%), spiculated (65.3%) or irregular borders (58.1%) (p=0.001) Fig. 5 on page 11.

- Attenuation: No significant difference was found between tumor attenuation (solid, part-solid or ground glass opacity) and histologic subtypes or cell differentiation grades. All 6 ground glass tumors were well or moderately differentiated Fig. 6 on page 12. Among
in situ tumors (3 AIS) two corresponded to solid nodules and one to ground glass opacity, whereas the minimally invasive tumor (1) was a part-solid nodule.

Discussion:

In 2011 the International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society proposed a new classification for lung adenocarcinoma. This classification now considers resection specimens, small biopsies, and cytology specimens (IASLC/ATS/ERS). Specific changes in this classification include the addition of both adenocarcinoma *in situ* (AIS) as a preinvasive lesion and minimally-invasive adenocarcinoma (MIA), and a new classification of the subtypes of invasive adenocarcinomas based on predominant patterns. The previously used term *bronchioloalveolar carcinoma* is no longer used. This new classification affects radiologic interpretation of computed CT scans for the diagnosis of adenocarcinoma.

Based on our results we have found that acinar and papillary adenocarcinomas are usually solid as it has been described in the literature.(2)

The acinar predominant pattern was the most common histologic subtype in our series, representing approximately a half of the patients. A similar rate was reported by Lee HY. (3)

We also found that air-bronchogram and bubble like internal density were associated with better cell differentiation, according to Yabuuchi et al study.(4)

There were no significant differences between preinvasive lesions and invasive adenocarcinomas, as both can manifest as pure ground glass opacities or as part-solid nodules, as in San Ming et al. study (5). Furthermore, recently studies had reported invasive adenocarcinomas as ground glass opacities (including Lim Hj (6) and Jin X, Zhao S-h et al. (7)).

Our study had several limitations. Some CT images were obtained with a 2,5-5 mm thickness reconstruction. The sample size of preinvasive and minimally invasive lesions was small. Finally, histologic subtypes of those patients who underwent neoadyuvant therapy could not be reported in some cases.
**Table 2:** Clinico-radiological characteristics and histopathological findings

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Fig. 1: 68-year-old male patient with adenocarcinoma manifesting as lobar consolidations. (a) Axial CT image shows a non-resolving consolidation in the right lower lobe. Pathological study demonstrated an invasive mucinous adenocarcinoma. (b) CT image eight months later shows the persistent consolidation with air-bronchogram (yellow arrow) and a new emergent one in the middle lobe despite the therapy. (c) CT image performed 16 months later demonstrates an increase in the size of the middle lobe consolidation, note cystic lucencies (red arrow). (d) Last CT image two years later shows an increase in number and size of the consolidations that were finally bilateral.

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Fig. 2: 54-year-old woman with an incidental finding on chest CT. Axial CT image shows a 8-mm solid nodule (arrow) that was confirmed as minimally invasive adenocarcinoma.

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Fig. 3: Axial chest CT images showing bubble-like and air-bronchogram internal density in well and moderately differentiated adenocarcinomas. (a) 71-year-old woman with a 22-mm solid nodule with bubble-like appearance inside the lesion (arrow). The lesion was an acinar predominant moderately differentiated adenocarcinoma. (b) Another 80-year-old female patient with an 18-mm solid nodule with air-bronchogram (arrow). Pathologic study demonstrated a lepidic predominant well differentiated adenocarcinoma.

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**Fig. 4:** 60 year-old-man. Axial 5 mm CT image of PET/CT using a lung window shows an 8 mm-nodule with smooth margins that proved to be a papillary predominant moderately differentiated adenocarcinoma (arrows).

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**Fig. 5:** Different types of margins of acinar adenocarcinoma on chest CT. (a) 73 year-old-man with a 22-mm solid nodule with lobulated borders (arrow). (b) 47 year-old-man with a part-solid nodule with irregular borders and air-bronchogram (arrow). The solid component measured 17 mm and the total diameter was 34 mm (c) 76-year-old man with a 20-mm solid nodule showing spiculated borders (arrow).

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**Fig. 6:** Axial CT images show different ground glass opacities which were all well or moderately differentiated adenocarcinomas (arrows): (a) Adenocarcinoma in situ (20 mm). (b, c) Acinar predominant adenocarcinomas (12 mm and 26 mm). (d, e)
papillary predominant adenocarcinomas (20 mm and 8 mm). (f) Solid predominant adenocarcinoma with mucin production (23 mm).

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Conclusions

Lung adenocarcinomas submitted to surgical resection commonly manifested as a solitary pulmonary solid attenuation nodule and most of them corresponded to histological invasive adenocarcinomas. Tumor margins correlated with some histologic subtypes. Internal density of the lesions correlated with tumor differentiation grade.

References


