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Correlation between tumor measurement on Computed Tomography and resected specimen size in lung adenocarcinomas

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Abstract

Objective—To compare preoperative size of Stage I and Stage II lung adenocarcinoma as measured by Computed Tomography (CT) and as assessed on gross pathology specimens.

Materials and Methods—47 patients diagnosed with Stage I or II lung adenocarcinoma were evaluated. Institutional Review Board permission was obtained. Tumor contours were delineated using a semi-automated segmentation algorithm and adjusted based on a radiologist's input. Based on the tumor perimeter, maximal in-plane tumor diameter was calculated automatically. The largest single diameter from the pathology gross report was utilized. A paired t-test was used to examine the measurement difference between CT and pathology.

Results—The mean largest diameter of the tumors at CT and pathology was 29.53 mm and 24.04 mm, respectively. There was a statistically significant difference between the mean CT measurement and mean pathology measurement of 5.49 mm (standard deviation 9.08 mm, $p < 0.001$). The percent relative difference between the two measurements was 18.3% (standard deviation 28.2%).

Conclusion—There is a statistically significant difference between the tumor diameter as measured by CT and on pathology gross specimen. These differences could have implications in the treatment and prognosis of patients with early stage lung adenocarcinoma.

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None declared

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Keywords

lung cancer; computed tomography; non-small cell lung cancer; staging; T descriptor; pathology measurement

Introduction

Lung cancer is the leading cause of cancer deaths in the United States. The 5 year survival rate for non-small cell lung cancer (NSCLC) remains poor: clinical stage I surgically resectable lung cancer carries a 5 year survival rate of 50%, and clinical stage II NSCLC carries a 5 year survival rate of 30% (1). The staging of lung cancer is vital, as it guides a patient's therapy and determines prognosis; yet its accuracy is disputed (2). For example, patients with stage I or II NSCLC benefit from surgical resection, whereas patients with stage IIIB cancer or greater are not candidates for surgery (1).

The American Joint Committee on Cancer (AJCC) revised the TNM classification of lung cancer in the new 7th edition cancer staging manual (3). Modifications to the staging system were adapted because there have been multiple studies that confirm the importance of differentiating tumors that are ≤ 2 cm, 2-3 cm, 3-5 cm and > 5 cm in maximum dimension (2, 4, 5, 6, 7). Previously, tumors were not subclassified by size under or above 3 cm. These seemingly small differences in maximum dimension play important roles in prognosis (2, 4, 5, 6), as patients are clinically staged based on maximal diameter on CT.

To our knowledge, there are only a few studies that actually correlate radiologic size of a lung tumor with the size as determined by the pathology gross specimen. Surgically resected patients' staging will ultimately be based on the pathologic measurements. Several studies have compared various aspects of clinical and pathologic stage, such as tumor size (T descriptor), nodal status (N), pathology specimen characteristics, and diagnostic accuracy with PET and integrated PET/CT (8, 9, 6, 10, 11). However, few studies specifically examine the pathologic-radiologic concordance of size of tumors, which is particularly important given that the majority of modifications to the staging system focused on the T status.

The goal of our study is to compare the radiologic preoperative size of solitary Stage I and II lung adenocarcinoma with their pathologic size following excision.

Materials and Methods

Patients

The Institutional Review Board granted approval for our retrospective study. Data was collected and handled in accordance with the Health Insurance Portability and Accountability Act regulations. Fifty patients with stage I or II lung adenocarcinoma were studied as part of a larger study correlating radiographic response to a chemotherapy regimen. Participating patients had tumors that were determined to be operable and resectable by the treating surgeons and had measurable indicator lesions on Computed Tomography (CT). Exclusion criteria included: age < 18 years, lesions deemed inoperable

by treating surgeons, patients who would not use contraception, patients receiving other investigational agents, or those patients with interstitial lung disease.

A chest CT was performed after 21 days of chemotherapy. Surgical resection of the tumor was then performed 2 days after the CT.

CT image acquisition and size analysis

Axial CT was performed with 16 row Multi Detector Computed Tomography (MDCT) scanners (Qx/i and Lightspeed, General Electric Medical Systems, Milwaukee, WI). Scans were acquired from the supraclavicular region through the adrenal glands using a 1.25 mm slice thickness with 1.25 mm spacing following deep inspiration. All images were sent to a General Electric Picture Archiving and Communication System (GE PACS). The axial CT scans for each patient, were interpreted by an experienced thoracic radiologist. Tumor contours were delineated using a semi-automated segmentation algorithm and adjusted based on a radiologist's input. Based on the tumor perimeter, maximal tumor linear diameter was calculated automatically.

Pathology specimens and size analysis

Pathology measurements were obtained from the pathology gross report. The resected lung lesion largest diameter dimension was utilized. All specimens were received fresh and converted to sections within one hour following resection. The gross size was recorded utilizing a standard ruler by a physician or a physician's assistant. Formalin fixation occurred after the cut sections of each specimen were placed in cassettes. This way, tissue shrinkage and the potential change in size of tumor did not occur as a result of specimen fixation prior to grossing.

Statistical analysis

A paired t-test was used to examine the measurement difference between CT and pathology. A mean, median, range for both the pathology diameter and the CT diameter were obtained. The concordance correlation coefficient was used to explore the agreement between the two measurements. A Bland-Altman plot (12, 13) was used to explore the association between the observed differences and assumed true tumor size. All analyses were done within SAS® 9.2 and R 9.2.

Results

Of the 50 patients enrolled in the initial study, 47 were included in our study. One patient was excluded because the patient had resection at an outside institution with only microscopic portions of the lesion submitted for review, and the gross largest diameter was not provided. The two other patients were excluded because the CT thin section images for calculation of volumetric size were not available.

The mean diameter of CT largest dimension was 29.53 mm (Table 1). The mean of the pathologic specimen largest dimension was 24.04 mm. There was a statistically significant difference between the mean CT measurement and mean pathology measurement of 5.49

mm (standard deviation 9.08 mm, $p < 0.001$). The percent relative difference ((CT-Pathology)/CT) between the two measurements was 18.3% (standard deviation 28.2%). Correlation between the pathology largest diameter and the CT largest diameter was determined. Utilizing a Bland-Altman plot to assess the association between the observed differences and estimated true tumor size, the magnitude of the difference between the two measurements did not seem to differ by average tumor size on CT and pathology since there was no apparent pattern on the plot (Figure 1). The concordance correlation coefficient between two measurements was 0.735 (95%CI: 0.601-0.868, p -value < 0.001) (Figure 2). The CT and pathology measurements had moderate agreement with a Kappa coefficient of 0.49 (14).

Discussion

There is very little data on degree of measurement error for CT measurements. In fact, there currently is no established “gold standard” for tumor dimensions. Our study demonstrates that there is indeed a significant difference between CT preoperative size of a tumor and its pathologic size. CT measurements tended to “overestimate” the true pathologic size, which may result in upstaging. The reason for CT “overestimation” of size may be multi-factorial. CT measurements were based upon dimensions obtained from the CT following deep inspiration, and consequently reflected tumor dimension in inflated lung. In contrast, pathology specimen measurements were obtained from deflated lung tissue, which has decreased volume. The statistically significant differences in - tumor size may be secondary to these differences in lung aeration and expansion. In addition, infiltration and/or edema surrounding the tumor may be measured on CT, which would result in overestimation of the maximum dimension. Furthermore, blood and fluid drain from a specimen once it is removed from the body, which may result in slight “shrinkage” of the specimen.

Accurate clinical and pathologic correlation has been an important focus of research for other common cancers, not just NSCLC. For example, MRI is the main preoperative modality to predict cervical cancer stage. A large retrospective study examined the accuracy of predicting tumor size and additional factors that are all components of the clinical FIGO staging for cervical carcinoma (15). The authors demonstrated that for tumors > 10 mm, 95% were within 8 mm of their histologic size and that there was greater concordance between clinical size and histologic size for the larger tumors (those > 10 mm). Overall, 95% of tumors were within 13 mm of their histologic size. In contrast, Tann et al. demonstrated poor pathologic-radiologic correlation for assessment of renal tumors, as measured by tumor post-operative water displacement volume and CT utilizing summation of area method (16).

Similarly, other researchers have demonstrated poor correlation between preoperative staging and surgical-pathologic staging of NSCLC. Cetinkaya et al. demonstrated only 47.7% concordance between clinical stage and surgical-pathologic stage (17). However, many of the differences in the two stages were secondary to alterations of the N status following surgery. The authors accurately predicted the T descriptor preoperatively in 73.9% of patients. Casali et al. determined a 79% diagnostic accuracy for estimating the preoperative size of tumors with decreased diagnostic accuracy of 59% for smaller tumors < 2 cm (6).

Our data does demonstrate a statistically significant difference between CT and pathology dimensions. The mean difference between CT and pathology measurements was 5.49 mm, which could very well alter a patient's T descriptor classification, especially given the new subdivisions of tumor size. All preoperative maximum dimensions were standardized and determined by CT alone. The patients had the same confirmed histopathologic diagnosis and neoadjuvant therapy. Consequently, our data was not confounded by different histology as a contributor to preoperative and postoperative staging concordance. There was clear standardization with regard to the timing of CT and surgery 2 days later and the acquisition and interpretation of the pathology data. CT maximum dimension was acquired by volumetric analysis, which is more accurate than a single radiologist's interpretation (18).

Our data adds to the literature on poor concordance between CT stage of a tumor and pathologic stage by demonstrating that the differences in size could also contribute to differences in staging of tumors. Moreover, our data are even more relevant when applied to the 7th edition AJCC TNM staging criteria, which further differentiates between T descriptor based on size.

A limitation of our retrospective study was the small sample size. A larger study population would have been desirable. We only evaluated patients with early adenocarcinoma of the lung, and this data may not apply to more advanced stages of lung cancer. Lung is an ideal organ for studying small differences in size of tumors as air surrounds it, aiding in tumor delineation, and therefore, this data may not apply to other organs or tumors.

Our study validates that there are statistically significant differences between tumor size as determined clinically by CT and by pathology specimen in early adenocarcinoma of the lung. Clinicians may advocate chemotherapy treatment prior to surgery based upon a patients' clinical stage, which is generally based on CT findings. Larger studies, including different stages of tumors as well as tumors in different organs, are needed to validate our observation.

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Figure 1.

Bland-Altman plot. The mean difference between the two measurements is shown with a solid line at 5.49 mm; the lower and upper 95% limits of agreement are the dashed lines at -12.31 mm and 23.30 mm. The magnitude of the difference between the two measurements does not seem to differ by average tumor size on CT and pathology since as there was no apparent pattern on the plot.

Agreement of CT and Pathology Measurement

Figure 2.

Agreement of CT and pathology measurement. Scatter plot of the observed CT measurement (x axis) and Pathology measurement (y axis). The green line is a 45 degree reference. Lesion size measured by CT and pathology is correlated as there is little spread.

Table 1

Measurement summary

Measurement	Mean	SD	Median	Min	Max
CT, mm	29.53	13.85	26.5	10.4	71.3
Pathology, mm	24.04	14.22	19.0	3.0	65.0
Difference, mm	5.49	9.08	6.30	-16.0	32.0
Relative Difference (%)	18.3	28.2	18.8	-45.2	79.2