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Commentary: Reading the voxels: A fortune teller's nomogram to invasiveness in stage IA lung adenocarcinoma

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In this issue of the *Journal*, Qiu and colleagues¹ report the results of a retrospective radiomic analysis of preoperative computed tomography (CT) scans showing that a nomogram comprising smoking status, mean CT attenuation values, and entropy was associated with pathological invasiveness in clinical stage IA lung adenocarcinomas. With the increasing use of chest CT lung cancer screening, smaller subsolid nodules are being increasingly identified. The ability to determine the invasiveness of these nodules has the potential to impact clinical care, and even the earliest stages of lung cancer have a substantial rate of recurrence. Radiomics is an emerging high-throughput technique that analyzes large amounts of quantitative imaging data to reveal information about tumor biology through differences in morphology, statistical models, and regional differences in tumor heterogeneity.

Other studies have also identified entropy as a predictor of invasiveness in lung cancer.^{2,3} Yoshiyasu and colleagues⁴ found that tumor volume, solid volume percentage, skewness, and entropy were associated with invasiveness. In a multicenter study, Wu and colleagues⁵ reported a radiomics model that was able to differentiate the invasiveness of part-solid lung adenocarcinomas. Wang and colleagues⁶ and Huang and colleagues⁷ also proposed radiomic signatures associated with recurrence-free survival in early-stage lung cancer.

The authors conclude that their nomogram could be useful in deciding whether patients are suitable for sublobar

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CENTRAL MESSAGE

A nomogram based on radiomic features may be useful in predicting invasiveness in lung adenocarcinoma, but the results should be validated and integrated with clinical, pathological, and genomic data.

resection. Although the authors' nomogram may be useful in distinguishing pathological invasiveness, whether this will actually be useful in determining which patients should undergo a sublobar resection is unclear. Altorki and colleagues⁸ reported that sublobar resection and lobectomy are associated with equivalent survival in patients with clinical stage IA solid non-small cell lung cancers. Until the results of the randomized CALBG 140503 and JCOG 0802 trials evaluating sublobar resection versus lobectomy are available, we will not know whether sublobar resection is appropriate for these more invasive nodules.

Although this study supports the use of radiomics to evaluate lung cancers, the specific techniques and nomogram need to be externally validated. The region of interest was determined manually by 2 thoracic surgeons. However, for radiomics to be widely adopted, the techniques must be reproducible, and automated or semiautomated methods have been reported to be superior for segmenting the tumor.⁹ There are also a wide variety of scanning techniques and parameters described in the literature, and uniform image acquisition, including whether contrast should be used and the importance of including ground-glass and perinodular areas in the regions of interest, must be established.^{5,10}

In contrast to a biopsy, which provides data from a single site within the tumor, radiomics may provide complementary information on spatial tumor heterogeneity and overall tumor

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biology. Determining the radiomic phenotype of the tumor may contribute to precision medicine. Reading the voxels and integrating radiomic features along with clinical, pathological, and genomic data may have great potential to create a complete fortune teller's nomogram to distinguish the invasiveness of early-stage lung adenocarcinomas and guide treatment decisions.

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Commentary: Looking into tumor biology through the lens of radiomics

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Radiomics is an expanding field, particularly in chest imaging, which can discriminate quantitative features from medical images and potentially predict tumor biology of subsolid nodules. In direct contrast to conventional visual inspection by a skilled chest radiologist, this quantitative modality is particularly well suited to the evaluation of lung nodules and can reproducibly extract a substantially greater number of nodule features beyond the naked eye. Since lung cancer screening with low-dose computed

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CENTRAL MESSAGE

Radiomics enhances the characterization of lung nodules beyond the naked eye and may provide a window into tumor biology that enriches the armamentarium of noninvasive predictive tools.

tomography (CT) of the chest has been associated with improved lung cancer-specific mortality in multiple randomized studies, the enthusiasm to implement radiomics to aide in the interpretation of newly detected lung nodules has great interest. There are significant limitations to translate this technology into the daily workflow of radiologists,

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