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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which include standardization of analytic software to perform texture characterization, standardization of CT acquisition (different models), and the variability of post-processing that is performed by modern scanners to limit radiation exposure to patients. Despite these limitations, it is my belief that this type of quantitative image analysis of lung nodules will likely be part of a workflow in the future and should be used as an adjunct to conventional interpretation. One example of technology that has failed to be successfully integrated into routine chest radiology reports is volumetric analysis of lung nodules, which has a track record of superiority¹ over 2-dimensional axial imaging to characterize lung nodules over time.

In this edition of the *Journal*, Qiu and colleagues² retrospectively reviewed a cohort of more than 400 patients over 3.5 years with resected clinical stage IA lung adenocarcinoma and evaluated preoperative lung nodule CT texture features (in addition to clinical characteristics) on predicting an invasive pathologic subtype. The authors developed and validated a nomogram that can predict nodules with invasive pathologic subtype that may not be suited for sublobar resection from an oncologic perspective. The CT data included total number of voxels of each nodule, attenuation and size, volume of solid component, and other texture features (variance, skewness, kurtosis, and entropy) that use histograms and mathematic equations to characterize a nodule. Of note, these features are only a few of the quantification variables that can be generated by a radiomics analysis. Patients were divided into 2 groups according to pathologic subtype (invasive vs less invasive). The less-invasive cohort included adenocarcinoma in situ, minimally invasive adenocarcinoma, and lepidic predominant phenotype. Pathologic upstaging was seen in 24 patients in the

invasive cohort. Multivariate analysis showed that smoking status, mean CT attenuation value, and entropy were independent predictors of invasive subtype. These factors were then used to create a nomogram. Applying this nomogram to an independent patient cohort is clearly necessary to further validate this study.

While the authors' nomogram may be useful in distinguishing whether a clinical stage IA nodule is more likely to be pathologically more invasive, the study does not directly address whether this will actually be useful in determining which nodules deserve sublobar resection. Altorki and colleagues³ reported that sublobar resection and lobectomy have equivalent survival for patients with clinical stage IA solid non-small cell lung cancers. The randomized Cancer and Leukemia Group B 140503 trial excluded pure ground-glass nodules but consolidation size was not considered. Japan Clinical Oncology Group 0802 evaluated segmentectomy versus lobectomy for tumors ≤ 2 cm with a consolidation to tumor ratio >0.5 . Until the survival results of these randomized trials are mature, we will not know the answer to whether sublobar resection is appropriate for these more-invasive nodules. Nonetheless, the authors provide a potential clinical tool to help surgeons predict tumor biology in the preoperative assessment of lung nodules where intraoperative frozen section has limitations.

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