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## **Discussion Letter**

Reply to "Radiomics and Clinical Data for the Diagnosis of Incidental Pulmonary Nodules and Lung Cancer Screening: Correspondence"



To the Director,

We appreciate the ideas in the letter concerning the recently published article. Although many points were already discussed in the article, we will review them below. Our experimental study presents the results obtained with 97 PNs from 93 patients (training group). Although the number of cases is limited, it represents the consecutive cases collected from surgery for a pulmonary nodule at a referral hospital. As we mentioned previously, this is an aspect that can be improved with the incorporation of multicenter cases.

It is worth noting that our radiomic model, while currently demonstrating moderate accuracy, is a work in progress. In a group with an imbalance of cases, the area under the curve (AUC) is a more reliable measurement method. Our study shows a significant improvement in AUC when an integrative model, incorporating radiomic and clinical data, is employed. However, our model is optimizable. We are actively working on alternative representation spaces of the visual content and expanding the cohort to a multicenter study.

Regarding the features collected by the convolutional network, we used the 21 GLCM features available in the Pyradiomics library.<sup>2</sup> These features, such as 'Autocorrelation,' 'JointAverage,' 'ClusterProminence,' 'ClusterShade,' 'ClusterTendency,' 'Contrast,' 'Correlation,' 'DifferenceAverage,' 'DifferenceEntropy,' 'Difference-Variance,' 'JointEnergy,' 'JointEntropy,' 'Imc1,' 'Imc2,' 'Idm,' 'Idmn,' 'Id,' 'Idn,' 'InverseVariance,' 'MaximumProbability,' 'SumEntropy,' are known to be effective in characterizing the texture of medical images, which is crucial in our study of pulmonary nodules.

Considering the importance of exploring different scenarios and increasing the number of benign cases, in the next phase of the study, we will also incorporate cases of benign pulmonary nodules that have not been surgically intervened. This includes cases where the pulmonary nodules disappear during follow-up, or a non-surgical biopsy yields negative results.

Blood biomarkers are another interesting point that could be incorporated into integrative radiomic models. However, it is essential to consider that although there are many ongoing studies oriented toward lung cancer, in the specific case of diagnosing pulmonary nodules, there are no blood markers that have demonstrated effectiveness in a clinical phase. Therefore, it is not currently available to be applied in radiomic models.

The association of radiomic characteristics with genetic or molecular alterations, called radiogenomics, is another relevant point. However, it is primarily oriented toward treatments and prognosis of advanced and locally advanced stages of lung cancer. In addition, systematic molecular studies are not conducted in clinical practice to diagnose pulmonary nodule malignancy and are costly tests. We aimed to use a model that incorporates data already available for a patient with a pulmonary nodule (whether incidental or from lung cancer screening), such as clinical data, pulmonary function tests, and chest CT images. This approach makes it useful for most of this patient group without requiring additional tests or costs.

In conclusion, these discussions are crucial as they address recurring aspects such as the selection of the most representative radiomic features and the need for a larger number of cases. Importantly, data sharing is a cornerstone of our efforts. Our group has taken a significant step toward a multicenter study, recognizing that this will not only provide greater heterogeneity in the sample and increase the number of cases but also allow for external validation of the model.

## **Conflict of interests**

The authors state that they have no conflict of interests.

## References

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