Letter to the Editor

Radiomics: a potential biomarker for N2 malignancy in clinical stage I lung adenocarcinoma

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We read with interest the comment by Dr. Cerfolio and Dr. Moore (1) regarding the clinical applicability and methodology of our recently proposed radiomics approach in identifying N2 adenopathy in patients with clinical stage I lung adenocarcinoma (2). We appreciate the stated opinions and kindly request the acceptance of our response.

As the importance of PET/CT has been validated previously in the assessment of lymph node status, it is reasonable for Robert *et al.* to ask for PET/CT to be conducted as part of preoperative work-up. In our study, only clinical stage I patients with negative findings of N2 adenopathy in preoperative CT scans were included. And, these patients were considered at low risk for N2 metastasis and were not required for routine PET/CT workup. Considering the relatively high expense of PET/CT and relatively low incidence of N2 disease, controversy remained in its routine application in clinical stage I NSCLC as previously reported (3-5). We thank the authors for the suggestion on inclusion of PET/CT data. Further studies with PET/CT would be of merit.

We agreed with the difference in lymph node dissection type may lead to significant bias in pathologic N2 reference. In our study, we performed systemic lymph node dissection if lesions indicated a malignancy of invasive adenocarcinoma or higher. As for single or multiple N2 stations, that's an important question as increasing evidence have been reported that multiple N2 involvement would impact the survival (6). However, the scope of this study is to find out whether the usage of radiomic feature could predict the N2 status and did not further analyze if multiple N2 stations were involved given the limited cases of multiple N2 disease in clinical stage I lung adenocarcinoma. The limited number of cases would lead to suboptimal performance for such an artificial intelligence method. And, the preoperative evaluation of N2 would give a hint for further invasive assessment or more precise radiologic work-up or a complete thoracic lymphadenectomy, thus our proposed manner would at least provide evidence for preoperative lymph node status that was misinterpreted by normal CT scan.

Least absolute shrinkage and selection operator (LASSO) regression model is a particular type of linear regression well-fitted for selecting radiomic features with high levels of multicollinearity in building a radiomic signature. And the features were selected for our signature construction by using LASSO regression to eliminate the possibility of overfitting, which resulted in five radiomic features eventually. Using the selected five radiomic features, the signature managed to achieved a similar performance in a hold-out external validation dataset, which was unseen during model development. The external validation showed evidence of less possibility of overfitting. However, further

geographically and temporally external validation would be needed to guarantee the model's generalizability.

We agreed with the suggestion of clear explanation for clinical parameters inclusion. The clinical data was included from the result of univariate analysis, which was described in the supplementary Tables S2,S3 (2). It is indicated that the incorporation of CEA and tumor size into the radiomics model would improve the prediction accuracy of occult N2 adenopathy in early-stage lung adenocarcinoma.

In conclusion, we believe that the application of CT radiomics combining clinical data of tumor size and serum CEA would discriminate occult N2 lymph node metastasis in early-stage lung adenocarcinoma. Again, we appreciated the opinions and suggestions raised by Dr. Cerfolio and Dr. Moore to our work.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

1. Cerfolio RJ, Moore WH. Can CT radiomics differentiate benign from malignant N2 adenopathy in non-small cell lung cancer. Transl Lung Cancer Res 2020. doi: 10.21037/tlcr-20-477.
2. Yang M, She Y, Deng J, et al. CT-based radiomics signature for the stratification of N2 disease risk in clinical stage I lung adenocarcinoma. Transl Lung Cancer Res 2019;8:876-85.
3. Jie Y, Meng X, Gu A, et al. Metabolic volume parameters based on different thresholds with baseline 18F-FDG PET/CT as prognostic factors for survival in stage III non-small cell lung cancer. Transl Cancer Res 2017;6:732-45.
4. Lin JT, Yang XN, Zhong WZ, et al. Association of maximum standardized uptake value with occult mediastinal lymph node metastases in cN0 non-small cell lung cancer. Eur J Cardiothorac Surg 2016;50:914-9.
5. Kozower BD, Meyers BF, Reed CE, et al. Does positron emission tomography prevent nontherapeutic pulmonary resections for clinical stage IA lung cancer? Ann Thorac Surg. 2008;85:1166-9.
6. Asamura H, Chansky K, Crowley J, et al. The International Association for the Study of Lung Cancer Lung Cancer Staging Project: Proposals for the Revision of the N Descriptors in the Forthcoming 8th Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 2015;10:1675-84.

