Letter to the Editor

Robust Feature Attribution in Radiomics: A Call for Multi-faceted Methodologies

From:
Souichi Oka,
Yoshiyasu Takefuji

From the Science Park Corporation, 3-24-9 Iriya-Nishi Zama-shi, Kanagawa 252-0029, Japan (S.O.); Faculty of Data Science, Musashino University, 3-3-3 Ariake Koto-ku, Tokyo 135-8181, Japan (Y.T.).

Letter to the Editor,

Chen et al. (2025) conducted a multi-institutional radiomics study to differentiate glioblastoma from solitary brain metastasis using contrast-enhanced T1-weighted magnetic resonance imaging features extracted from the brain–tumor interface (BTI) (1). Their study focused on a 10 mm BTI region and employed a multi-step feature selection process. This process included intraclass correlation coefficient filtering, hypothesis testing, minimum redundancy maximum relevance, and finally Least Absolute Shrinkage and Selection Operator (LASSO) regression, which was used to identify ten radiomic features for model development. These features were then used to train nine machine learning (ML) algorithms. Logistic regression (LR) was selected as the best-performing model, achieving an area under the curve of 0.808 on the test set. To interpret the model's predictions, they applied SHapley Additive Explanations (SHAP) to quantify the contribution of each feature.

Although this approach is widely used in radiomics-based ML, it raises important concerns regarding the reliability of feature attribution and interpretability. LASSO regression, as a linear and parametric method, may exclude features that capture nonlinear or interaction effects, introducing bias into the selected feature set. This bias can influence the LR model and propagate into SHAP-based explanations. Since SHAP is model-dependent, it reflects and amplifies these biases, resulting in importance scores that do not necessarily correspond to biological or causal relevance. The assumption that predictive accuracy confirms feature relevance is flawed and widely challenged. Numerous studies have documented the disconnect between high predictive performance and meaningful attribution, underscoring the need for rigorous, model-independent frameworks that support reproducible biomarker discovery and clinically meaningful interpretation (see Supplementary Material) (2).

First, LASSO, being a linear and parametric method, inherently eliminates nonlinear features, introducing critical biases (3). It tends to select only one variable from highly correlated groups, potentially overlooking other important predictors. Its tendency to shrink coefficients to zero can oversimplify the model by excluding genuinely relevant variables. Moreover, LASSO is sensitive to its regularization parameter; improper tuning can significantly affect performance and introduce configuration-specific biases.

Second, their reliance on LR presents a notable methodological limitation (4). LR is a linear model that assumes a direct relationship between predictors and the log-odds of the outcome. It is also parametric, relying on a fixed number of parameters and a predefined functional form. This combination of linearity and parametric assumptions makes LR less suitable for complex domains like radiomics, where relationships between features and biological outcomes are often nonlinear and data distributions rarely conform to simple mathematical structures.

Additionally, SHAP values, a widely used method in explainable AI for interpreting feature importance, inherit and often amplify biases from the underlying model (5). Because SHAP relies on model outputs, it remains vulnerable to embedded biases, which can lead to misleading interpretations and compromise analytical reliability. The pipeline used by Chen et al., combining LR with SHAP, exemplifies this issue. The assertion that this approach successfully identifies predictive features warrants careful scrutiny, as compounded biases from both LR and SHAP may significantly undermine interpretability.

Evaluating feature importance remains challenging due to the lack of definitive ground truth. Differences in algorithmic design and assumptions lead to inconsistent feature rankings across models, complicating interpretation. This highlights the need for careful methodological scrutiny. In radiomics, where biological relevance is often unclear, it is essential to validate whether model-derived feature contributions truly reflect causal biological relationships.

To overcome methodological pitfalls and improve interpretability in health risk assessment, a more robust, multi-faceted analytical framework is essential. This should reflect the complexity of biomedical data and incorporate methods suited to non-linear relationships. Unsupervised techniques such as Feature Agglomeration and, where applicable, Highly Variable Gene Selection, offer model-independent insights (6,7). Additionally, non-parametric statistics like Spearman's rho and Kendall's tau can detect monotonic associations without assuming linearity, enhancing both precision and interpretability (8). These approaches are particularly valuable in translational biomarker research, where clarity and reproducibility are critical for clinical decision-making and stakeholder communication.

In conclusion, despite their utility in feature selection and prediction, techniques like LASSO, LR, and SHAP carry inherent biases and limitations, especially in complex domains such as medical diagnosis. Addressing these challenges requires a multi-faceted analytical framework that integrates rigorous statistical methods with ML. Such an approach enhances interpretability and supports more reliable, clinically meaningful insights.

FUNDING SOURCES

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Souichi Oka: Writing – original draft, Conceptualization. **Yoshiyasu Takefuji**: Writing – review & editing, Supervision, Project administration.

DATA AVAILABILITY

No new data were generated or analyzed in support of this research.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

ACKNOWLEDGMENTS

We extend our sincere gratitude to Takuma Yamazaki and Nobuko Inoue of Science Park, Inc., for their invaluable assistance with the extensive literature review.

APPENDIX A. SUPPORTING INFORMATION

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.acra.2025.07.048.

REFERENCES

1. Chen Y, Guo W, Li Y, et al. Differentiation of glioblastoma and solitary brain metastasis using brain-tumor interface radiomics features based on MR images: a multicenter study. Acad Radiol 2025; 32:4164–4176. https://doi.org/10.1016/j.acra.2025.04.008
2. Fisher A, Rudin C, Dominici F. All models are wrong, but many are useful: Learning a variable's importance by studying an entire class of prediction models simultaneously. J. Mach Learn Res 2019; 20:177. https://doi.org/10.48550/arXiv.1801.01489
3. Wüthrich K, Zhu Y. Omitted variable bias of Lasso-based inference methods: a finite sample analysis. Rev Econ Stat 2023; 105:982–997. https://doi.org/10.1162/rest_a_01128
4. Kepplinger D. Robust variable selection and estimation via adaptive elastic net S-estimators for linear regression. Comput Stat Data Anal 2023; 183:107730. https://doi.org/10.1016/j.csda.2023.107730
5. Huang X, Marques-Silva J. On the failings of Shapley values for explainability. Int J Approx Reason 2024; 171:109112. https://doi.org/10.1016/j.ijar.2023.109112
6. Zhang J, Wu X, Hoi SCH, Zhu J. Feature agglomeration networks for single stage face detection. Neurocomputing 2020; 380:180–189. https://doi.org/10.1016/j.neucom.2019.10.087
7. Xie Y, Jing Z, Pan H, et al. Redefining the high variable genes by optimized LOESS regression with positive ratio. BMC Bioinform 2025; 26:104. https://doi.org/10.1186/s12859-025-06112-5
8. Okoye K, Hosseini S. Correlation tests in R: Pearson Cor, Kendall's Tau, and Spearman's Rho. In: Okoye K, Hosseini S, editors. R Programming: Statistical Data Analysis in Research Springer Nature; 2024. p. 247–277. https://doi.org/10.1007/978-981-97-3385-9_12

https://doi.org/10.1016/j.acra.2025.07.048