Predicting tumor response to chemo-immunotherapy using attention-enhanced deep learning models and shear wave elastography

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Abstract

Personalized cancer therapy demands precise tools for predicting tumor response to treatment, as tumor heterogeneity often results in varied therapeutic outcomes. In this study(1), we introduced a novel deep learning-based framework that leverages shear wave elastography (SWE) imaging and convolutional neural networks (CNNs) augmented with attention mechanisms to predict the therapeutic response of tumors. Tumor stiffness, a mechanical property quantifiable through SWE, has been increasingly recognized as a critical biomarker for predicting treatment outcomes. However, its predictive potential remains underexplored in the context of chemo-immunotherapy, particularly when combined with advanced AI methodologies. Addressing this gap, we developed the Prognose-CNNattention model, specifically designed to utilize SWE imaging data to categorize tumors as responsive, stable, or non-responsive to therapeutic interventions.

The study leveraged a dataset comprising 1,365 SWE images obtained from 630 murine tumors across a variety of cancer types, including breast adenocarcinoma (4T1, E0771), melanoma (B16F10), fibrosarcoma (MCA205), and osteosarcoma (K7M2). Tumors underwent pre-treatment with mechanotherapeutic agents to modulate their stiffness before initiating chemo-immunotherapy. The Prognose-CNNattention model achieved a remarkable predictive performance, with an area under the curve (AUC) of 0.96 and an accuracy of 87%, significantly outperforming conventional CNN architectures and pre-trained models such as Xception, VGG16, Inception-v3, and ResNet50. These results underscore the capability of attention mechanisms to enhance predictive accuracy by focusing on salient features within the imaging data, particularly long-range spatial relationships that conventional CNNs might overlook.

The framework also integrated an automated segmentation module, termed Auto-Prognose-CNNattention, combining SWE and B-mode ultrasound images to delineate tumor regions of interest. This fully automated pipeline significantly streamlined the predictive workflow

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by eliminating the need for manual tumor segmentation. Utilizing a U-Net-based architecture for segmentation, the system achieved high concordance with manual annotations, as evidenced by Dice scores ranging from 0.79 to 0.81 across various tumor types. The integration of segmentation and classification in a unified pipeline demonstrated slightly reduced predictive performance compared to the Prognose-CNNattention model alone but remained robust, offering a practical solution for real-world applications where manual annotations are often impractical.

This research contributes significant advancements to the field of predictive oncology. First, it demonstrates that tumor stiffness, quantified through SWE imaging, can serve as a reliable non-invasive biomarker for predicting therapeutic outcomes, providing actionable insights before treatment initiation. Second, it highlights the transformative potential of attention-enhanced CNNs in medical imaging. The inclusion of attention mechanisms within the model architecture enabled it to identify and focus on critical regions of interest, such as areas of high stiffness, while also considering global image context. This approach markedly improved the interpretability and diagnostic performance of the model, making it a valuable tool for clinical decision-making.

The study also addresses the challenges associated with tumor heterogeneity, both across and within tumor types. By analyzing SWE data from diverse tumor models collectively, the findings suggest that the biomarkers identified through this approach are broadly applicable, independent of specific tumor types. This generalizability is particularly important for clinical translation, as it indicates that the model can potentially be adapted to a wide range of cancer settings.

Furthermore, the automated segmentation and classification framework was rigorously evaluated for robustness and reproducibility. Assessments of inter- and intra-user variability revealed consistent performance across different evaluators, including laboratory experts and radiation oncologists. This consistency underscores the reliability of the framework in practical applications, where variability in human interpretation can significantly impact outcomes. By reducing dependence on manual input, the automated pipeline enhances the reproducibility of tumor response predictions, a critical factor for clinical adoption.

The clinical implications of this work are profound. SWE imaging is already an established tool in oncology for assessing tumor stiffness and staging. Integrating it with AI-driven predictive frameworks could revolutionize its utility, transforming it from a diagnostic modality to a prognostic tool. The ability to predict tumor response to therapy using non-invasive imaging techniques has the potential to significantly improve patient outcomes. By enabling early and accurate identification of non-responsive tumors, clinicians can avoid ineffective treatments and explore alternative therapeutic strategies, thereby minimizing patient exposure to unnecessary side effects and optimizing resource utilization.

Additionally, the study lays a foundation for future clinical trials aimed at validating the proposed framework in human patients. Early collaborations with oncology centers have shown promising preliminary results, with ongoing efforts to adapt the model for human tumors. Transfer learning techniques are being employed to fine-tune the model on smaller datasets of human SWE images, leveraging the extensive preclinical data to bridge the gap between laboratory research and clinical practice. These efforts are expected to accelerate the clinical translation of this technology, bringing it closer to integration into standard diagnostic and treatment workflows.

The research also acknowledges the limitations of its preclinical focus. While the use of murine models offers a controlled environment for developing and validating predictive methodologies, the mechanical and biological properties of human tumors present additional complexities. Addressing these challenges will require extensive validation studies and iterative refinement of the model. The incorporation of additional data modalities, such as genomic and molecular biomarkers, could further enhance the predictive power of the framework, paving the way for a more holistic approach to personalized cancer therapy.

In conclusion, this study presents a comprehensive and innovative approach to predicting tumor response to therapy, combining the strengths of SWE imaging and advanced AI methodologies. The Prognose-CNNattention model, with its attention-enhanced architecture, sets a new benchmark for predictive performance in this domain. The integration of automated segmentation further enhances its practicality, offering a scalable solution for clinical settings. By providing early and accurate predictions of therapeutic outcomes, this framework supports the development of personalized treatment strategies, ultimately improving patient care. Future directions will focus on validating the model in clinical trials, exploring its applicability to other imaging modalities, and integrating additional biomarkers to create a robust, multi-dimensional prognostic tool.

(1) Voutouri, C., Englezos, D., Zamboglou, C. et al. A convolutional attention model for predicting response to chemo-immunotherapy from ultrasound elastography in mouse tumor models. Commun Med 4, 203 (2024). https://doi.org/10.1038/s43856-024-00634-4