AI-Driven Survival Prediction in Cancer: The Role of Artificial Neural Networks

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Abstract. Accurate survival prediction in oncology is critical for informing treatment strategies and improving patient outcomes. Traditional statistical models like the Cox proportional hazards model often underperform when applied to complex, high-dimensional datasets such as genomics and histopathology. This review explores the emergence of artificial neural networks (ANNs), particularly deep learning architectures, as advanced tools for survival analysis. This paper highlights multiple ANN-based models across cancer types—including breast, lung, and brain—that utilize multimodal data inputs such as gene expression, histopathology images, and longitudinal clinical records. Methods discussed include fully connected neural networks, convolutional neural networks (CNNs), long short-term memory (LSTM) networks, and ensemble learning strategies. This paper further examines architectures such as PASNet and MDNNMD, and models trained on datasets like TCGA. Despite improved performance over conventional methods, challenges persist in clinical adoption due to interpretability, generalizability, and data privacy. Future prospects include expert systems, domain adaptation, federated learning, and multimodal integration. This paper concludes that while ANN-based survival models show great promise, interdisciplinary efforts are required to translate these innovations into scalable, secure, and explainable clinical applications.

1 Introduction

In the era of oncology treatment, accurate survival prediction plays a critical role in guiding therapeutic decisions, directing clinical monitoring, and developing long-term care strategies. Traditionally, cancer survival prediction has relied on statistical methods such as Cox proportional risk models and Kaplan-Meier estimators [1]. Although these tools have been foundational models for decades, they often fall short when faced with complex, high-dimensional, multimodal data such as gene expression profiles, histopathologic images, and longitudinal clinical records. As a result, there is a growing trend towards developing more flexible and robust modeling frameworks, especially those with regard to Artificial Intelligence (AI) and Machine Learning (ML), as a way to improve accuracy.

Artificial Neural Networks (ANNs), and deep learning architectures more broadly, have become transformative tools in the field of healthcare data analytics. These models are

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capable of learning complex nonlinear relationships from large, high-dimensional datasets without relying on manual feature engineering. In oncology, ANNs have been increasingly used to model cancer progression, classify histomorphology, and predict survival outcomes. Of greater interest is their ability to integrate various data sources, including digitized full-slice histological images, multi-omics profiles, and structured clinical variables, making them optimal for modeling survival in heterogeneous patient populations. Recent studies have demonstrated the great potential of deep learning models for survival prediction. For example, Zhu et al. reviewed multiple neural network architectures for cancer prognosis modeling, including Convolutional Neural Networks (CNNs) and fully connected networks [2]. Their analysis highlights the effectiveness of integrating feature extraction from multi-omics data, enabling the construction of models that outperform traditional statistical methods. Similarly, Wulczyn et al. showed how histopathology sections from the Cancer Genome Atlas (TCGA) could be used to predict disease-specific survival for 10 cancer types. Their approach bypasses manual region-level annotations by learning global survival labels, which improves risk stratification and adds prognostic value based only on clinical stage, age, and gender [3]. These advances are part of a broader trend in computational pathology and translational oncology to move from rule-based interpretation to data-driven decision-making.

ANN is not only capable of replicating human-level diagnostic tasks, such as metastasis detection and tumor grading but also develops entirely new prognostic patterns that are undetectable by traditional assessment methods. This capability has important implications for stratifying patients within the same tumor stage, improving early detection of aggressive disease, and potentially uncovering unknown prognostic biomarkers. It is worth mentioning, however, that despite these encouraging advances, the application of ANN-based survival prediction models in routine clinical practice remains limited. Challenges such as small sample size, data heterogeneity, overfitting, interpretability, and the need for external validation remain. For instance, a study on non-small cell lung cancer (NSCLC) patients demonstrated that a deep learning survival neural network achieved a concordance index (C-index) of 0.739, outperforming the traditional tumor-node-metastasis (TNM) staging system, which had a C-index of 0.706—an improvement of approximately 3.3% [4]. However, even such improvements must be critically weighed against concerns regarding transparency, generalizability, and clinical interpretability. Overcoming these limitations requires larger and better datasets, clear regulatory provisions, interdisciplinary collaboration, and continued methodological innovation. Therefore, this paper aims to provide an overview of the current state of the art in the application of artificial neural networks to survival prediction, and point out key challenges and future research directions. By situating artificial neural network approaches within the evolving precision medicine paradigm, this review emphasizes their potential to significantly improve cancer prognosis and private treatment of patients.

2 Method

The use of neural network-based deep learning frameworks for survival prediction in cancer has evolved significantly over the past decade. These methods are now applied across a variety of cancer types, incorporating diverse data modalities including clinical records, genomic profiles, and medical imaging. This section outlines specific deep learning techniques used in different cancer types for survival analysis, highlighting the design, workflow, and innovative features of each model.

2.1 Breast Cancer

2.1.1 ANN

Zhu et al. reviewed several ANN-based models that directly use clinical and gene expression data to predict breast cancer outcomes. One notable implementation, the Multimodal Deep Neural Network by integrating Multi-dimensional Data (MDNNMD), incorporated gene expression, Copy Number Alteration (CNA), and clinical data through parallel neural network streams. These separate streams were fused in a late fusion model to generate a final prognosis prediction score. Feature selection was achieved using minimum redundancy maximum relevance (mRMR) to address the high-dimensional input space [2]. This architecture proved superior in specificity (0.95–0.99) but showed lower sensitivity due to class imbalance.

Another example of ANN use was Pathway-associated Sparse Deep Neural Network (PASNet), which incorporated biological pathway information to guide ANN architecture. Hao et al. developed PASNet using 4359 gene inputs mapped into 574 biologically meaningful pathway nodes [5]. This biologically informed architecture improved interpretability and achieved an Area Under Curve (AUC) of 0.66 in glioblastoma survival prediction, indicating ANN's potential to integrate domain knowledge into deep learning pipelines [2].

2.1.2 CNN

Acs, Rantalainen, and Hartman reviewed how CNNshave revolutionized breast pathology [6]. CNNs trained on histopathology images from breast cancer patients have demonstrated high accuracy in scoring HER2, ER, and Ki67 biomarkers—markers essential for prognosis and therapy decisions. For instance, Bejnordi et al. developed a CNN that achieved an AUC of 0.994 in detecting lymph node metastasis, outperforming pathologists [7]. Such CNNs use slide-level labels and often require no region-specific annotation, increasing scalability in digital pathology. In another study, Romo-Bucheli et al. trained CNNs to assess tubule formation on histopathology slides and linked these structural patterns to Oncotype DX categories, offering new prognostic biomarkers through image-based modelling [6].

2.1.3 LSTM

While breast cancer studies with long short-term memory (LSTM) networks are less common, recent approaches integrating temporal dynamics have emerged. Giunchiglia et al. proposed an LSTM-based model for survival analysis that can handle censored data using a dynamic loss function inspired by Cox regression [8]. Though not specific to breast cancer, this model structure is adaptable to longitudinal breast cancer data, offering time-series modeling that traditional ANNs lack.

2.2 Lung Cancer

2.2.1 ANN

She et al. developed a deep learning ANN model using clinical and genomic data from non–small cell lung cancer (NSCLC) patients to predict survival outcomes. The workflow included data preprocessing, feature normalization, and fully connected neural networks

trained with dropout and L2 regularization to prevent overfitting. The resulting ANN achieved a concordance index (C-index) of 0.739, outperforming the traditional tumor-node-metastasis (TNM) staging system, which had a C-index of 0.706—an improvement of approximately 3.3%. This demonstrates that deep learning ANN models can offer better survival prediction performance compared to conventional clinical staging methods [4].

2.2.2 CNN

CNN models have also been successfully applied to histopathology-based lung cancer prognosis. Coudray et al. used CNNs trained on whole-slide images to differentiate between lung adenocarcinoma and squamous cell carcinoma, achieving AUCs exceeding 0.97 [6]. These models were later extended to predict common genetic mutations such as KRAS and TP53 directly from image data, suggesting CNN's broader utility in linking morphology with survival and genetic profiles.

2.2.3 LSTM

While LSTM application is still growing in lung cancer prognosis, Vale-Silva and Rohr developed a multimodal model that incorporates LSTM layers to capture sequence dependencies within temporal clinical data. Their model combined patient demographics, lab data, and gene expression, and it used attention mechanisms alongside LSTM to prioritize features relevant to long-term survival. Their approach achieved a C-index of 0.784, showing robust performance across validation datasets [9].

2.3 Brain Tumors

2.3.1 CNN

Chato and Latifi applied CNNs to MRI scans for survival prediction in brain tumor patients. Their workflow included segmentation of tumor regions from MRI images, followed by patch extraction and training a CNN for binary classification of long versus short survival. They demonstrated that CNNs could extract latent spatial features that manual radiomic features often overlook, leading to better generalizability in clinical settings [10].

2.3.2 RNN-Surv

Giunchiglia et al. also applied their RNN-Surv model to brain tumor datasets. This LSTM-based architecture outperformed traditional Cox regression on censored survival data, especially in time-to-event forecasting [8]. The key innovation was modeling time-variant dependencies, which are critical in diseases like glioblastoma where prognosis can change rapidly over months.

2.4 Multicancer Models

2.4.1 CNN with Cox Integration

Wulczyn et al. developed a weakly supervised CNN model trained on 9,086 whole-slide histopathology images from 10 TCGA cancer types [3]. Their pipeline used random patch sampling, MobileNet-inspired CNNs, and Cox proportional hazards output layers. Despite

minimal supervision, the model achieved a hazard ratio of 1.58 ($p < 0.0001$) after controlling for stage, age, and sex, and improved C-index by 3.7% over traditional models. This study demonstrated CNN's capability to generalize across multiple tumor types using a unified architecture.

2.4.2 Ensemble Deep Learning Models

In cancer survival prediction, ensemble deep learning models have shown promise in enhancing predictive performance and robustness. For instance, Mobadersany et al. developed a model called Genomic Survival Convolutional Neural Network (GSCNN), which integrated histopathology images and genomic information through an ensemble of CNN architectures combined with Cox regression for survival analysis of glioma patients [11]. Their ensemble strategy allowed for capturing complementary features across modalities, achieving a median concordance index (C-index) of 0.801, outperforming models based only on clinical or genomic data. Their model demonstrated superior generalizability and resilience to overfitting compared to single neural network models, illustrating how ensemble methods can improve predictive stability, particularly in the high-dimensional, heterogeneous datasets typical of cancer research.

2.4.3 Multimodal Learning

Vale-Silva and Rohr explored the integration of heterogeneous data sources using deep neural networks. They trained multimodal models incorporating gene expression, clinical metadata, and longitudinal features [9]. The architecture combined CNNs (for gene and histology embeddings) and LSTMs (for temporal data), showcasing the advantage of modeling spatial and temporal complexity in cancer survival data.

3 Discussion

Despite significant advancements, several limitations and challenges hinder the full clinical translation of ANN-based survival models in oncology. Addressing these challenges is crucial to enhance model reliability, interpretability, and applicability in diverse healthcare environments.

One major challenge is interpretability. ANN models, particularly deep learning architectures with multiple hidden layers, are often referred to as "black boxes" due to the difficulty in understanding how specific inputs influence predictions. This opacity raises concerns in clinical settings, where decisions affecting patient care must be explainable to clinicians and patients. Although techniques such as saliency maps, SHapley Additive exPlanations (SHAP) values, and attention mechanisms have been introduced to interpret neural network outputs, they are often complex themselves and not yet standardized in clinical practice [12, 13]. To ensure trust and widespread adoption, future research must prioritize explainable AI models that provide intuitive and clinically relevant justifications for their survival predictions.

Another significant limitation of artificial neural network survival models is their limited applicability and generalizability across different clinical settings. Many models are trained on carefully selected datasets, often from large academic institutions or genomic consortia like TCGA, that do not reflect the variability in real-world clinical settings, including differences in imaging protocols, genetic backgrounds, comorbidities, and treatment options. As a result, these models often perform poorly when applied to heterogeneous datasets, requiring external validation across institutions, ethnic groups, and healthcare systems step

that is often overlooked. In addition, while retraining or fine-tuning models using local data can enhance adaptability, this requires significant resources and technical expertise that are not universally available. Generalizability remains an open question, as most studies rely on retrospective data and rarely include prospective validation. The performance of ANN models typically deteriorates when dealing with out-of-distribution data, thus limiting their reliability in clinical trials and real-world applications. Although adaptive strategies in areas such as adversarial training and transfer learning are being investigated to address this challenge, their successful implementation in survival analysis for various cancer types and stages remains an open and active area of research.

Data privacy and security also pose substantial barriers to deploying ANN models in healthcare. Patient data, especially genomic and histopathologic information, is highly sensitive. The need to compile large, multicenter datasets for training robust models conflicts with strict data protection regulations such as HIPAA in the U.S. and GDPR in Europe. Traditional centralized data aggregation approaches raise serious privacy concerns and increase the risk of data breaches. Innovative solutions such as federated learning offer a promising pathway, allowing model training across multiple institutions without sharing raw data.

Looking ahead, several future prospects offer exciting avenues to overcome these limitations. One promising direction is the development of expert systems that combine ANN predictions with rule-based clinical knowledge. By integrating structured domain knowledge, such systems could enhance interpretability and clinical alignment. For example, an expert system could adjust ANN outputs based on known prognostic factors like tumor grade or performance status, improving trust among clinicians.

Another important advancement is domain adaptation. Deep learning models can be pre-trained on large, related datasets and fine-tuned on smaller, local datasets to account for population-specific characteristics. Transfer learning approaches, particularly those leveraging unsupervised pretraining on histopathology images or genomic data, have demonstrated improved model robustness with minimal new data. This approach could facilitate the deployment of survival prediction models in resource-limited settings where labeled data is scarce.

Furthermore, federated learning has the potential to revolutionize collaborative oncology research. Instead of sharing patient data, hospitals and research institutions can collaboratively train models while retaining data locally. Early studies show that federated models can achieve performance comparable to centralized models while preserving data privacy. As communication protocols and security mechanisms mature, federated learning could become a standard for multicenter model training, enabling large-scale, privacy-preserving AI studies.

Finally, the integration of multi-modal data sources—including radiology, pathology, genomics, and longitudinal clinical records—is likely to further enhance survival prediction accuracy. Future ANN architectures that can simultaneously process these heterogeneous data types, possibly through hybrid CNN-LSTM frameworks or attention-based fusion models, will offer a more comprehensive view of the patient's disease trajectory.

4 Conclusion

Artificial neural networks have opened a new frontier in survival prediction, offering superior performance over traditional statistical approaches by learning complex, nonlinear relationships from heterogeneous and high-dimensional data. Their application across a range of cancers, from breast and lung to brain tumors, demonstrates their flexibility and transformative potential. Nevertheless, challenges such as model interpretability, clinical applicability, data privacy, and the need for rigorous external validation remain significant

barriers to widespread clinical adoption. Future directions point toward the integration of expert systems, domain adaptation techniques, and federated learning frameworks to improve model robustness, generalizability, and patient data security. As the field progresses, collaboration between clinicians, data scientists, and regulatory agencies will be essential to translate these technological advances into routine clinical care. Ultimately, ANN-based survival prediction holds the promise of enabling truly personalized cancer treatment and improving patient outcomes on a global scale.

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