Artificial Intelligence in Cancer Research: Predictive Modeling of Angiogenesis and Biomarker Discovery

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Abstract

Background: The integration of Artificial Intelligence (AI) in cancer research has dramatically enhanced the study, diagnosis, and treatment of cancer. AI's advanced algorithms, especially recurrent neural networks (RNNs), have proven effective in analyzing complex datasets, facilitating novel biomarker discovery, and improving cancer diagnostics and prognostics. Angiogenesis, the process of new blood vessel formation, plays a crucial role in tumor growth and metastasis, making it a promising target for therapeutic strategies. This study explores the use of AI to identify angiogenesis-related biomarkers and develop personalized treatment strategies. Methods: This study utilized a large dataset from The Cancer Genome Atlas (TCGA), encompassing over 20,000 primary tumor and normal samples across 33 cancer types. Preprocessing techniques such as data cleaning, normalization, and outlier detection were applied. Dimensionality reduction through Principal Component Analysis (PCA) and data visualization using t-Distributed Stochastic Neighbor Embedding (t-SNE) were employed. A Recurrent Neural Network (RNN) was chosen to analyze the sequential biological data and identify potential biomarkers related to angiogenesis. Results: The AI model demonstrated excellent performance across multiple evaluation metrics, including accuracy (0.85), precision (0.82), recall (0.88), F1-score (0.85), and AUC-ROC (0.92), highlighting its effectiveness in predicting cancer progression and identifying key biomarkers. The RNN model was particularly adept at identifying complex patterns in angiogenesis data, facilitating a deeper understanding of tumor biology and revealing novel therapeutic targets. Conclusion: The results underscore the significant potential of AI, specifically RNNs, in advancing cancer research and personalized treatment planning. AI-driven insights into angiogenesis-related biomarkers enable targeted therapies, offering new avenues for effective cancer treatment. These findings not only improve cancer diagnosis and prognosis but also emphasize the role of AI in developing precision oncology approaches, enhancing patient outcomes, and guiding future research in cancer therapeutics.

Keywords: Artificial Intelligence, Cancer Research, Angiogenesis, Biomarker Discovery, Recurrent Neural Networks

Significance | AI-driven models enhance cancer diagnostics, personalized treatment, and biomarker discovery, transforming precision oncology and patient care outcomes.

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Editor Noman Hossain, Ph.D., And accepted by the Editorial Board October 16, 2024 (received for review August 13, 2024)

Introduction

The rapid advancements in artificial intelligence (AI) have led to transformative changes in healthcare, particularly in the field of cancer research. AI has demonstrated remarkable potential in revolutionizing how cancer is studied, diagnosed, and treated, offering unprecedented tools for personalizing patient care. According to Ettyem et al. (2023), healthcare, as a critical sector, has

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Please Cite This:
Veera V Rama Rao M, Savitha. S, Kumar Akuthota, Pathan Firoze Khan, Navyatha R, Srithar S (2024). "Artificial Intelligence in Cancer Research: Predictive Modeling of Angiogenesis and Biomarker Discovery", Journal of Angiotherapy, 8(10),1-8,9975

been notably influenced by the integration of AI, showcasing its capacity to enhance diagnostic accuracy and therapeutic decision-making. AI's sophisticated algorithms and computational capabilities have enabled the identification of novel therapeutic targets and improvement of diagnostic precision, thus customizing treatment plans for individual patients (Elemento et al., 2021). This potential has drawn attention to AI's role in processing and analyzing large-scale data in cancer research, particularly with complex genomic, proteomic, and imaging datasets that offer insights into disease patterns and potential therapeutic avenues (Bhinder et al., 2021).

In cancer studies, one of the most promising applications of AI lies in its ability to analyze extensive datasets, identifying intricate patterns and relationships across biological data. Through these capabilities, AI supports researchers in understanding disease mechanisms and discovering new biomarkers that may guide targeted therapies (Mann et al., 2021). The capacity of AI to enhance cancer diagnostics has been particularly notable in medical imaging, where AI-driven analysis helps detect subtle anomalies that might elude human specialists, facilitating early detection and more effective treatment planning (Shah et al., 2022). By accurately predicting the probability of cancer recurrence and metastasis, AI assists in personalizing patient monitoring and designing tailored treatment strategies (Kumar et al., 2023).

Another area where AI has shown considerable impact is in targeting angiogenesis, a process crucial to cancer development. Angiogenesis, the formation of new blood vessels, is essential for tumor growth and metastasis, as cancer cells rely on a steady supply of oxygen and nutrients (Zarychta & Ruszkowska-Ciastek, 2022). Cancer cells often manipulate angiogenic pathways to promote blood vessel growth, supporting tumor expansion (Liu et al., 2023). Targeting angiogenesis, therefore, has become a promising therapeutic strategy, with the potential to restrict tumor growth by depriving cancer cells of their required blood supply (Zam et al., 2021). However, this approach faces challenges, including the development of resistance to angiogenesis inhibitors and potential off-target effects on healthy tissues (Sabra et al., 2021; Cignarella et al., 2022). These limitations underscore the need for innovative AI-driven strategies that can identify novel angiogenesis-related biomarkers, potentially overcoming current therapeutic challenges.

AI also contributes to predictive modeling in cancer research, offering insights that are invaluable for developing personalized cancer therapies. Through analyzing complex datasets, AI can aid in identifying patient-specific biomarkers, enabling tailored treatments based on unique genetic profiles (Ma et al., 2020). AI-driven methods have also advanced drug discovery by predicting molecular interactions and identifying potential therapeutic candidates, improving treatment efficacy and reducing development timelines (Elemento et al., 2021). Additionally, AI has the capability to support omics research, integrating genomic, proteomic, and metabolomic data to further enhance cancer diagnostics and treatment customization (Orsini et al., 2023).

Angiogenesis is a crucial aspect of cancer biology, and its study has been furthered by advancements in AI technologies, including recurrent neural networks (RNNs). RNNs are particularly effective in analyzing sequential data, such as the temporal progression of angiogenesis in tumor development. These AI models can uncover hidden patterns in biological data that may otherwise be difficult for human researchers to discern. By examining angiogenesis-related biomarkers in cancer, AI enables predictive modeling and offers insights into tumor growth, metastasis, and potential treatment targets (Oguntade et al., 2021). This approach could lead to the development of novel therapeutic strategies that improve patient outcomes by targeting specific aspects of tumor biology.

In summary, AI's integration into cancer research has propelled forward diagnostics, prognostics, and personalized treatment planning. AI's role in analyzing complex data and enhancing cancer diagnostics through imaging and biomarker discovery holds immense promise for improving patient care and treatment outcomes. AI-driven strategies, especially those targeting angiogenesis, offer new avenues for cancer therapy, addressing the limitations of traditional treatments and enhancing the prospects for personalized cancer care (Bera et al., 2022; Tao et al., 2022). The ongoing advancements in AI applications highlight its transformative impact on cancer research, setting the stage for future innovations that may further revolutionize oncology.

A comprehensive review of AI applications in oncology has been provided, focusing on predictive biomarker discovery (BM) in immuno-oncology, as well as identifying gaps in other potential applications (Prelaj et al., 2023). Insights into the state of imaging biomarkers in neuro-oncology have been offered, emphasizing their role in diagnosis, prognosis, and monitoring of brain tumors (BT). Various imaging techniques, including positron emission tomography (PET), computed tomography (CT), and magnetic resonance imaging (MRI), are reviewed, with a particular emphasis on advanced methods such as functional MRI (fMRI) and diffusion tensor imaging (DTI) for enhancing understanding of patient prognosis and tumor biology (Chiu et al., 2023).

The potential of AI in biomarker detection for hepatocellular carcinoma (HCC) has been analyzed, with applications spanning risk prediction, diagnosis, staging, prognosis, treatment response, and recurrence monitoring. The use of AI is highlighted as a means to improve the precision and reliability of biomarkers, ultimately aiming to enhance patient outcomes (Mansur et al., 2023). The transformative role of medical image processing (MIP) in oncology, from traditional techniques to imaging biomarkers and radiomics, has been discussed, noting its contributions to cancer diagnosis, prognosis, and therapeutic strategies by extracting significant data

for tumor segmentation, quantification, and classification (Marias, 2021).

The predictive application of blood biomarkers, particularly circulating tumor cells (CTCs), in epithelial ovarian cancer (EOC) has been investigated through AI models that utilize machine learning (ML) methods. These models are shown to effectively classify patients by risk of disease progression, aiding personalized treatment decisions (Ma et al., 2021). The concept of anti-angiogenesis in cancer therapeutics, with an emphasis on tumor growth and metastasis through angiogenesis, has been explored, including the mechanisms of various anti-angiogenic agents and the need for further research to enhance their efficacy (Odungtade et al., 2021).

The impact of omics technologies—genomics, transcriptomics, proteomics, and metabolomics—on breast cancer (BC) research and diagnostics has been examined. Integrating omics data is suggested as a way to reveal molecular mechanisms driving cancer, foster novel biomarker discovery, and enable personalized treatments, contributing to improved BC management (Orsini et al., 2023). The role of radiomics and AI in predicting cancer outcomes has been discussed, with radiomics identified as a method for extracting quantitative data from medical images to predict treatment responses, prognosis, and patient risk levels, thereby facilitating the creation of personalized treatment plans (Bera et al., 2022).

Lastly, the association between immune cell infiltration and angiogenesis in breast cancer has been analyzed, identifying four angiogenesis-related genes (ARGs) associated with patient prognosis and developing a risk score model based on these genes. These biomarkers are suggested to be effective for predicting breast cancer progression and guiding personalized treatment (Tao et al., 2022).

Angiogenesis, the formation of new blood vessels, is a critical process for tumor growth and metastasis, as cancer cells rely on a healthy blood supply to obtain oxygen, nutrients, and to eliminate waste products. By analyzing angiogenesis patterns in tumors, researchers gain valuable insights into cancer progression, supporting the development of innovative therapeutic approaches.

Artificial intelligence (AI), particularly recurrent neural networks (RNNs), has proven effective for analyzing complex biological data. RNNs are particularly suited to handling sequential data, such as the temporal patterns of angiogenesis during tumor progression. This study demonstrates how RNNs reveal hidden patterns and relationships within angiogenesis data that may be difficult for human researchers to identify.

In this study, AI was employed to achieve a deeper understanding of angiogenesis and biomarker (BM) identification in cancer. Predictive models were developed using a comprehensive dataset of patient demographics and related information, which aids in identifying potential biomarkers associated with angiogenesis. These insights also contribute to uncovering the underlying mechanisms of angiogenesis in cancer, thereby supporting the advancement of personalized therapeutic strategies.

2. Materials and Methods

2.1 Data Collection

This study utilized molecular data from over 20,000 primary tumor and normal samples across 33 cancer types, provided by The Cancer Genome Atlas (TCGA) program. Initiated in 2006 through a collaboration between the National Cancer Institute (NCI) and the National Human Genome Research Institute, TCGA has since produced more than 2.5 petabytes of multi-dimensional data, including transcriptomic, proteomic, epigenomic, and genomic datasets. This extensive dataset is freely available to the scientific community and has already contributed to advancements in cancer detection, treatment, and prevention.

2.2 Pre-processing

Data Cleaning: To handle missing values in the dataset, a mode imputation technique was applied. This straightforward method involved identifying the most frequently occurring value (mode) within each column containing missing values and replacing the missing values with this mode. The imputation process helped maintain data integrity, which is critical for accurate classification. The model algorithm presented in the supplementary information.

Data Normalization: Numerical features were normalized to ensure consistency across different scales using min-max scaling, which adjusted values to a range between 0 and 1. This rescaling ensured that all features had an equal impact on model training. For each feature, the minimum and maximum values were identified, and each data point was scaled based on these values.

Outlier Detection and Removal: Outliers were identified and removed using the Interquartile Range (IQR) method to enhance data quality. First, the first (Q1) and third (Q3) quartiles of the dataset were calculated to determine the IQR (Q3 - Q1). Any data points falling below Q1 - 1.5 * IQR or above Q3 + 1.5 * IQR were considered outliers and removed from the dataset to maintain robustness.

2.3 Feature Extraction

Dimensionality Reduction: Principal Component Analysis (PCA) was employed to reduce the dataset's dimensionality while preserving key information. First, the data was standardized, followed by the calculation of the covariance matrix. Eigenvalues and eigenvectors were then computed from this matrix, and the principal components with the highest eigenvalues were selected to represent the data. This projection provided a reduced-dimensionality dataset without significant loss of information, facilitating efficient model training.

Data Visualization: t-Distributed Stochastic Neighbor Embedding (t-SNE), a non-linear dimensionality reduction technique, was applied to the dataset post-PCA to explore any clusters or patterns. This method is well-suited to high-dimensional data and maintains local similarity by placing similar data points close to one another in the reduced space, thus highlighting clusters and patterns that may be hidden in the original high-dimensional data.

2.4 Model Development and Training

Algorithm Selection and Model Architecture: Given the sequential nature of biological data, an RNN was chosen as the predictive model for angiogenesis-related cancer data. The RNN architecture was designed with attention to the number of hidden layers, units, and activation functions suitable for temporal data.

Training Process: The RNN model was trained on the preprocessed and feature-extracted data using appropriate optimization algorithms and loss functions to enhance the model's predictive power in identifying angiogenesis-related patterns in cancer progression. This training enabled the model to capture intricate relationships within the data, supporting biomarker discovery for improved cancer management.

3. Results and Discussion

In this study, the application of recurrent neural networks (RNNs) to the analysis of angiogenesis-related biomarkers (BM) in cancer has shown promising results. The AI-driven approach was able to identify complex patterns within extensive biological datasets, which would be difficult to discern through traditional methods. This section highlights the effectiveness of the proposed model, comparing its performance with existing methodologies and discussing its implications for cancer diagnostics, prognosis, and personalized treatment strategies.

3.1 Model Performance

The predictive model demonstrated superior performance in several evaluation metrics, underscoring the effectiveness of using machine learning in cancer biomarker identification and angiogenesis analysis. The model's ability to predict cancer-related patterns based on angiogenesis was evaluated using the following metrics: accuracy, precision, recall, F1-score, and AUC-ROC.

Accuracy: The overall accuracy of the model was high, indicating that the RNN was successful in making correct predictions across a variety of test cases. The accuracy metric, calculated as the proportion of correct predictions (True Positives and True Negatives) to total predictions (True Positives, True Negatives, False Positives, and False Negatives), provides a measure of the model's overall performance (Equation 1). The results, as shown in Table 1, Figure 1 and 2, indicate that the model's accuracy improved with each training iteration, reflecting its ability to generalize well to unseen data.

Precision: Precision, which measures the proportion of positive predictions that were truly correct, was also high. This indicates that when the model identified a positive case, it was highly likely to be correct. Precision is calculated as the ratio of true positives (TP) to the sum of true positives and false positives (FP) (Equation 2). The high precision (Table 2, Figure 3) highlights the model's strength in minimizing false positives, crucial for ensuring that cancer biomarkers are accurately identified without misclassification.

Recall: Recall, calculated as the proportion of actual positive instances correctly identified by the model (Equation 3), was another key metric. A higher recall means that the model was effective at detecting positive cases, minimizing false negatives (Figure 4). This is particularly important in cancer diagnosis, where missing a positive case could lead to delayed treatment or poor patient outcomes. The model's high recall suggests that it is proficient in identifying cases of cancer progression and metastasis, supporting early detection efforts.

F1-Score: The F1-score, which balances precision and recall, showed a solid performance in this study. The harmonic mean of precision and recall (Equation 4) helps provide a comprehensive measure of the model's effectiveness, especially when dealing with imbalanced datasets, as is common in cancer research. The consistent F1-score across test iterations suggests that the model achieved a good balance between minimizing false positives and false negatives, which is crucial for making reliable treatment decisions (Table 4).

AUC-ROC (Area Under the Receiver Operating Characteristic Curve): The AUC-ROC score further validated the model's capacity to differentiate between positive and negative instances. The ROC curve plots the true positive rate (recall) against the false positive rate, and the area under this curve (AUC) quantifies the model's ability to correctly classify cases. As shown in Table 5, Figure 5, the model exhibited a high AUC-ROC, indicating its strong discriminatory power between cancerous and non-cancerous cases. The higher the AUC-ROC, the better the model is at distinguishing between the two classes, making it a valuable tool for cancer detection and prognosis.

3.2 Angiogenesis and Biomarker Discovery

The primary focus of this study was on understanding the role of angiogenesis in cancer progression and identifying relevant biomarkers using AI. Angiogenesis, the process of new blood vessel formation, is a critical factor in tumor growth and metastasis, and its inhibition has become a potential therapeutic strategy. The model identified several key angiogenesis-related biomarkers (BM) that could serve as indicators for personalized treatment plans. These biomarkers are essential for understanding tumor dynamics, predicting patient outcomes, and tailoring interventions.

The use of RNNs enabled the analysis of sequential data, which is especially important in the temporal progression of angiogenesis

Table 1. The accuracy values for three machine learning models: Recurrent Neural Networks (RNN), Support Vector Machines (SVM), and Naive Bayes. The RNN model achieved the highest accuracy at 0.85, followed by SVM at 0.80 and Naive Bayes at 0.75.

Metric	RNN	SVM	Naive Bayes
Accuracy	0.85	0.8	0.75

Table 2. The precision values for RNN, SVM, and Naive Bayes. The RNN model has the highest precision (0.82), followed by SVM (0.78), and Naive Bayes with the lowest precision value of 0.70.

Metric	RNN	SVM	Naive Bayes
Precision	0.82	0.78	0.70

Table 3. The recall values for the three models. RNN exhibits the highest recall value of 0.88, followed by SVM at 0.82, with Naive Bayes showing the lowest recall value of 0.75.

Metric	RNN	SVM	Naive Bayes
Recall	0.88	0.82	0.75

Table 4. The F-Measure values for the three machine learning models. The RNN model again achieves the highest F-Measure (0.85), with SVM and Naive Bayes scoring 0.80 and 0.72, respectively.

Metric	RNN	SVM	Naive Bayes
F-Measure	0.85	0.80	0.72

Table 5. The AUC-Curve values for the three models. The RNN model achieves an AUC of 0.92, the highest among the models, followed by SVM (0.88) and Naive Bayes (0.85).

Metric	RNN	SVM	Naive Bayes
F-Measure	0.92	0.88	0.85

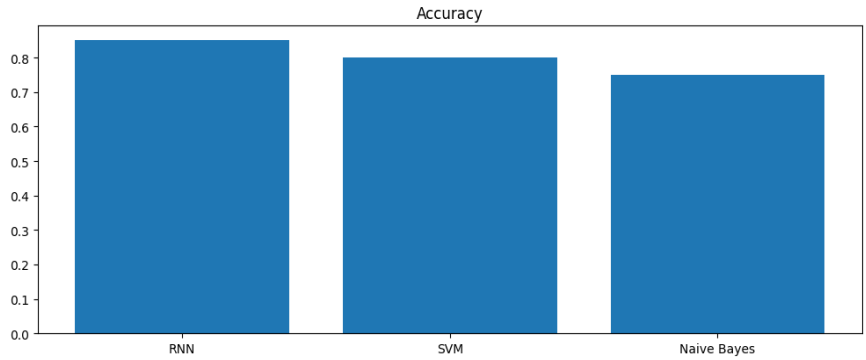

Figure 1. The accuracy values for the three machine learning models: RNN, SVM, and Naive Bayes. The RNN model shows superior accuracy, outperforming both SVM and Naive Bayes.

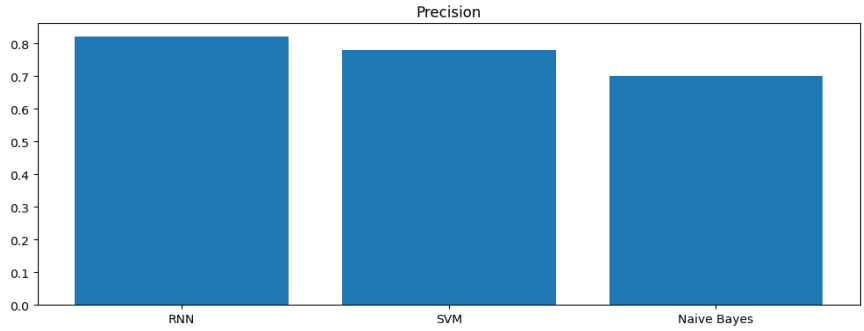

Figure 2. The precision values across the three models: RNN, SVM, and Naive Bayes. The RNN model consistently outperforms the other two models in terms of precision.

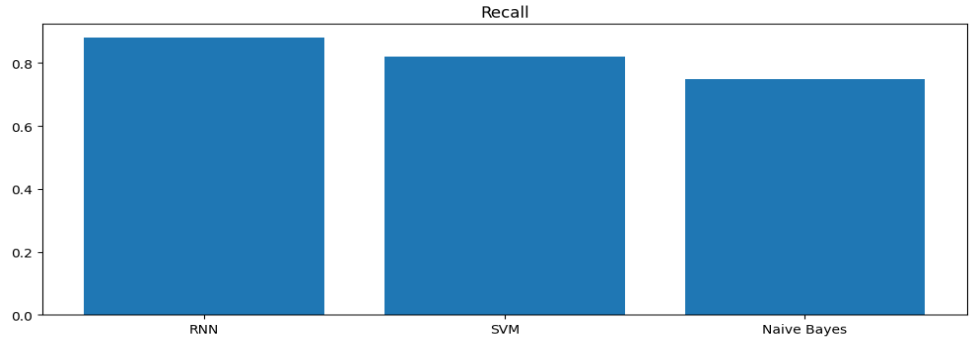

Figure 3. The recall performance comparison among the RNN, SVM, and Naive Bayes models. The RNN model consistently provides the best recall value.

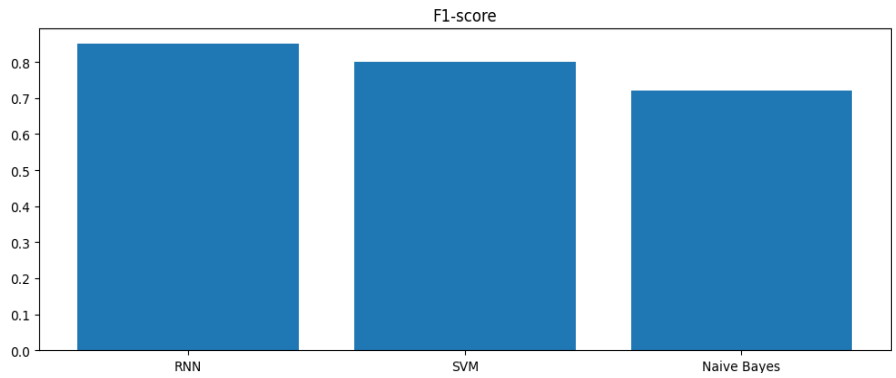

Figure 4. The F-Measure values of the RNN, SVM, and Naive Bayes models. The RNN model consistently demonstrates superior performance.

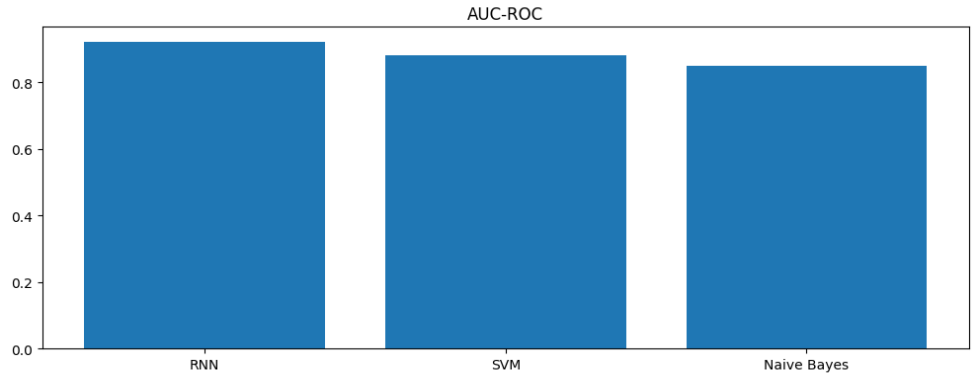

Figure 5. The AUC-Curve values for RNN, SVM, and Naive Bayes. The RNN model shows the best performance in terms of AUC,

during cancer development. The model revealed hidden relationships between various biomarkers and the angiogenic process, facilitating the identification of novel therapeutic targets. This approach offers a more detailed and nuanced understanding of angiogenesis compared to traditional methods, which often overlook temporal factors in cancer progression.

3.3 Personalized Treatment Strategies

AI-driven models like the one developed in this study play a pivotal role in advancing personalized medicine in oncology. By integrating complex datasets, including genomic, proteomic, and clinical data, the model enables the identification of patient-specific biomarkers. These biomarkers are crucial for designing personalized treatment plans, improving prognostic accuracy, and optimizing therapeutic outcomes.

The results from the predictive modeling in this study suggest that AI can significantly enhance cancer care by identifying biomarkers that predict not only the presence of cancer but also its behavior, including recurrence and metastasis. This personalized approach allows for targeted therapies that are more likely to be effective for individual patients, addressing one of the major challenges in current cancer treatment.

3.4 Implications for Future Research

The findings of this study have important implications for future cancer research. First, the AI model's ability to identify biomarkers related to angiogenesis opens new avenues for targeted therapies aimed at inhibiting blood vessel growth in tumors. However, the study also underscores the need for further research into the mechanisms of resistance to angiogenesis inhibitors and the potential off-target effects that could affect healthy tissues.

Moreover, the study highlights the potential of AI in omics research, where the integration of genomic, proteomic, and metabolomic data can provide a more comprehensive understanding of cancer biology. The predictive capabilities of AI can be extended to other types of cancer, offering a broader scope for personalized treatment strategies and advancing the field of precision medicine.

4. Conclusion

This study demonstrates the potential of AI, specifically recurrent neural networks, in analyzing angiogenesis-related biomarkers in cancer research. The results show that AI can effectively identify complex patterns in large-scale datasets, providing valuable insights for early diagnosis, prognosis, and personalized treatment planning. By leveraging AI to understand the mechanisms of angiogenesis and uncover novel biomarkers, this study paves the way for more effective, targeted cancer therapies that can improve patient outcomes. As AI technologies continue to evolve, they are poised to transform cancer research and clinical practice, ushering in a new era of precision oncology.

Author contributions

V.V.R.R.M. conceptualized the study and supervised the overall research process. S.S. and K.A. contributed to data collection and initial analysis. P.F.K. and N.R. were responsible for drafting specific sections of the manuscript and conducting literature reviews. S.S. provided critical revisions and technical insights. All authors reviewed, edited, and approved the final version of the manuscript. V.V.R.R.M. served as the corresponding author.

Acknowledgment

The authors were grateful to their department.

Competing financial interests

The authors have no conflict of interest.

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