

Image Classification of Ischemic Stroke Blood Clot Origin Using Classical Machine Learning

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Abstract—Ischemic stroke, the predominant subtype of stroke, occurs when a blood clot obstructs an artery in the brain, leading to significant morbidity and mortality. Identifying the etiology of the ischemic stroke, whether cardioembolic (CE) or large artery atherosclerosis (LAA), is crucial for effective treatment and prevention of recurrence. This paper proposes a classical machine learning approach using XGBoost to classify ischemic stroke subtypes based on whole slide digital pathology images of blood clots. The study leverages a dataset from the Mayo Clinic's STRIP AI Kaggle competition, which includes high-resolution TIFF images stained with Martius Scarlet Blue (MSB) to differentiate thrombus components. By extracting and analyzing features from these images, the proposed method achieves superior performance outperforming previous deep learning models. The findings suggest that classical machine learning techniques can provide reliable, interpretable, and resource-efficient solutions for medical image classification, offering potential improvements in stroke diagnosis and treatment.

Index Terms—image classification, ischemic stroke, machine learning, whole slide digital pathology images, computer vision

I. INTRODUCTION

Strokes continue to be the second most common cause of death globally. More than 700,000 people in the United States suffer from an ischemic stroke every year as a result of a blood clot obstructing a brain artery. The odds of the patient surviving are decreased by a second stroke, of which 23% are recurrent. However, if medical professionals can identify the cause of a stroke, it may lessen the likelihood of more strokes since this information affects the treatment that follows a stroke episode. [1]

Ischemic stroke is one of the two main types of strokes, hemorrhagic and ischemic, specifically when there is a blockage or inhibition in the blood vessels supplying the brain, leading to a reduction or conclusion of blood inflow. [2] Two types define an ischemic stroke, thrombotic (LAA) and embolic (CE). In thrombotic stroke, the blood clot (thrombus) forms in one of the arteries that supply blood to the brain. An embolic stroke happens when a blood clot forms away from the patient's brain usually in the patient's heart and travels through the patient's bloodstream to lodge in narrower brain arteries. [3]

Identifying the source of blood clots that caused the ischemic stroke happens to be a significant challenge due to the complicated nature of the upholding pathology. Furthermore, the ischemic stroke symptoms may depend on the thrombus size, position, and components complicating the classification process. Normally, doctors perform an echocardiogram and a Doppler ultrasound for the patient to diagnose whether the stroke came originally from the large artery or if it is a cardioembolism. Additionally, lab evaluations involving blood tests, clotting factor analysis, and thorough clinical assessments are all involved in the classification process. All these usual diagnosing methods have been proven to be accurate but not very time-efficient, inspiring data scientists to improve artificial intelligence-based etiology classification so that physicians are better equipped to prescribe the correct treatment immediately.

Machine learning plays a transformative role in revolutionizing medical applications, offering innovative solutions to

enhance diagnosis, treatment, and patient care. Its ability to analyze vast and complex datasets enables the identification of patterns, correlations, and insights that may be challenging for human professionals to discern. In medical imaging, machine learning excels in tasks such as detecting anomalies in X-rays, MRIs, and CT scans, aiding radiologists in accurate and timely diagnosis. In the case of ischemic strokes, machine learning can assist in identifying the blood clot's origin by classifying whole slide digital pathology images of the thrombus.

Whole slide digital pathology imaging offers the possibility of digitally capturing and saving highly detailed microscopic-level slides in TIFF image format. Prior to creating the images, a blood clot sample is obtained from a patient, usually through a biopsy or surgical procedure. The sample may be collected from blood vessels, organs, or tissues where a clot has formed. The collected sample is immediately fixed to preserve its cellular structure. The sample is then cut into thin sections (typically 4-6 micrometers thick) using a microtome. These sections are then mounted onto glass slides. The sections are stained using various histological stains to highlight specific cellular components and structures. The pathologist or a technician captures images of the stained sections using a microscope equipped with a camera. These images can be stored digitally for further analysis, documentation, and communication. [4]

After acquiring the blood clot digital pathology images, machine learning can utilize the components that form the thrombus, their respective percentages, and any distinctive features as the main differentiator between ischemic stroke subtypes. A thrombus is a blood clot that forms within a blood vessel and remains attached at its site of origin. The components of a thrombus can vary depending on the circumstances of its formation and the specific conditions of the individual. Generally, a thrombus is composed of red blood cells (RBCs), platelets, fibrin, and white blood cells (WBCs). Determining the thrombus components might come in handy as it is an important factor during classification. [5]

Although image-based deep learning models have significantly facilitated rapid stroke diagnosis, accurate outcome predictions remain challenging. This study proposes the use of classical machine learning techniques in categorizing the two main subtypes of ischemic strokes: CE and LAA. This endeavor aligns with the mission of the Mayo Clinic's Neurovascular Research Laboratory [6], which advocates for the development of AI-based stroke cause research and classification systems to support healthcare practitioners in making informed treatment decisions, ultimately striving to save the lives of stroke survivors.

II. RELATED WORK

Machine learning has made significant strides in aiding medical diagnosis. Early systems faced limitations due to insufficient processing power and data. However, with advanced computational technologies and the availability of extensive medical datasets, machine learning has become a powerful tool in healthcare. Modern algorithms, particularly

deep learning models, excel in analyzing complex medical data, such as imaging and genetic information. This has led to breakthroughs in diagnosing conditions like cancer, diabetic retinopathy, and cardiovascular diseases. [7], [8] Machine learning enhances diagnostic accuracy, speeds up the diagnostic process, and supports physicians in making more informed decisions, ultimately improving patient care and outcomes. [9] The following are papers that served as the foundation for this study's conceptual framework, guiding it and paving the way for its contributions and insights.

In 2019, Staessens et al. [5] provided guiding information on thrombus handling, procedures, and analysis to facilitate and standardize this emerging research field. The recent arrival of endovascular procedures has created the unique opportunity to collect and dissect blood clots removed from cerebral arteries, instigating a new subfield in stroke research. Insights into thrombus characteristics and composition could play an important part in ongoing measures to improve ischemic stroke therapy.

An article by Mainali, Darsie, and Smetana [10] reviews machine learning technology's application in stroke diagnosis and outcome prediction, emphasizing the rapid diagnostic capabilities of image-based models and the complexity of prognostication due to patient-specific factors requiring clinical oversight. Over the past decade, 13 companies have developed automated stroke diagnostic software with excellent evaluation metrics. The authors analyzed 54 studies using various machine learning approaches, from classical algorithms to deep convolutional neural networks (CNN) models, leveraging diverse data sources such as medical records and imaging. Despite advancements, the intricate nature of stroke diagnosis and prognosis necessitates comprehensive data and clinician awareness of machine learning limitations to avoid misdiagnosis. Thus, machine learning tools should support but not replace clinical decision-making.

Fitzgerald et al. [11] discussed the histopathological composition of acute ischemic stroke (AIS) clots, emphasizing the importance of characterizing thromboemboli features through quantitative histomorphometry and diagnostic imaging. Accurately identifying clot composition prior to intervention can significantly impact the success of revascularization strategies. The main focus is on the correlation between clot composition, diagnostic imaging, stroke etiology, and revascularization outcomes. Additionally, the authors explore the impact of various pathology image stains on thrombus image features, enhancing the analysis and characterization of clots.

In a recent study, Patel et al. [12] introduced an unexplored histomics pipeline for quantifying the complex structure and WBC heterogeneity in AIS clots, aiming to classify cryptogenic cases. By analyzing histomic features of stroke blood clots retrieved by mechanical thrombectomy (MT), the study leverages a dataset of 107 thrombi from AIS patients to extract features related to RBC and FP components using computational image analysis techniques. Additionally, high-resolution approaches are employed for WBC segmentation, with quality control measures ensuring data reliability. Results indicate

that features extracted from RBC/FP regions can effectively differentiate between different stroke etiologies, particularly distinguishing between LAA and CE clots, potentially offering improved diagnostic capabilities compared to current methods.

Krishnan, Nikesh, Gnanasekar, and Krishnan [13] proposed a novel two-stage approach for identifying the origin of blood clots in ischemic stroke patients as either CE or due to LAA, utilizing whole-slide digital pathology images and advanced computer vision models. The dataset, sourced from the STRIP AI background clot dataset, underwent preprocessing including patch extraction, Otsu's thresholding technique for quality filtering, and augmentation using the Albumentations library. Two key models were developed: a background classifier based on MobileNetV3 architecture and a blood clot classifier employing transfer learning with various state-of-the-art (SOTA) models. Training involved the use of schedulers for improved generalization. The SwinTransformerV2 model's swinv2 tiny window16 256 variant emerged as the top-performing model among their experimented models, exhibiting the highest accuracy, precision, recall, and F1 score, thus selected to build the proposed system for blood clot origin classification in ischemic stroke cases.

In 2023, Prasad and Shukla [14] published a study focusing on utilizing machine learning techniques, specifically CNNs and CatBoost classifiers, to classify blood clots into CE and LAA categories, aiming to enhance stroke treatment strategies. After preprocessing the Mayo Clinic dataset, including down-sizing images and applying data augmentation methods, two classifiers are developed. The CNN model, with its ability to extract complex features, outperforms the CatBoost classifier in terms of accuracy, precision, and recall, demonstrating superior performance in classifying TIFF images of blood clots. The study suggests potential avenues for future research, including feature selection and optimization techniques to further improve classifier performance and exploring hybrid classifiers to enhance classification accuracy.

In a paper written by Azatyan [15], an innovative approach utilizing Artificial Intelligence (AI) to differentiate between two major AIS etiology subtypes is presented. The dataset, consisting of 754 very high-resolution TIFF images, undergoes preprocessing steps including pruning, rotation, resizing, and augmentation to mitigate challenges associated with large file sizes and limited generalizability. Four deep learning architectures, namely EfficientNet B4 and B5 with Noisy Student weights, as well as Swin Large with varying window parameters, are employed in building the final solution. Successive modifications are made to each model architecture, including the addition of linear layers and dropout, followed by softmax function application for probability transformation. Evaluation metrics are based on a custom loss function, weighted multi-class logarithmic loss (WMCLL), tailored for neural network training, facilitating better convergence and optimization. The ensemble approach, aggregating probabilities from the five models, enhances prediction accuracy, resulting in WMCLL scores of 0.69682 and 0.67188 on public and private leaderboards, respectively, underscoring the effectiveness of the pro-

posed methodology in stroke blood clot origin classification.

Rao, Puligundla, Ekkala, and Chebrolu [16] addressed the critical issue of ischemic strokes aiming to classify the origin of blood clots, specifically between CE and LAA, using whole slide digital pathology images. The proposed approach involves a stacked deep learning model combining EfficientNet-B0, ResNet-152, and VGG19 pre-trained on ImageNet, with experiments conducted on the Mayo Clinic - Strip AI dataset. Through preprocessing steps including tiling, filtering, and color normalization, the model achieves optimal performance, as evidenced by its weighted multi-class logarithmic loss. Experimental results demonstrate that the proposed stacked model outperforms individual models and achieves the lowest loss value, providing a promising tool for accurate stroke etiology classification and guiding post-stroke therapeutic management effectively.

III. METHODOLOGY

This section outlines the methodology proposed for identifying the origin of blood clots in ischemic stroke using classical machine learning techniques.

A. Dataset

In this study, the dataset comprises high-resolution whole-slide digital pathology images, each depicting a blood clot from a patient who endured an ischemic stroke. These pictures are in TIFF format, which is a standard format for digital pathology images. The slides are sourced from the Mayo Clinic as part of STRIP AI's Kaggle competition [1]. The dataset images are divided into training and test sets, showcasing blood clots with known origins and labeled as either CE or LAA. Specifically, the dataset includes 547 images associated with CE etiology and 207 images associated with LAA etiology. Additionally, CSV files are included in the dataset, containing annotations such as image_id, center_id, patient_id, image_num, and label for each image. All of the dataset images' resolutions are presented in Fig. 1.

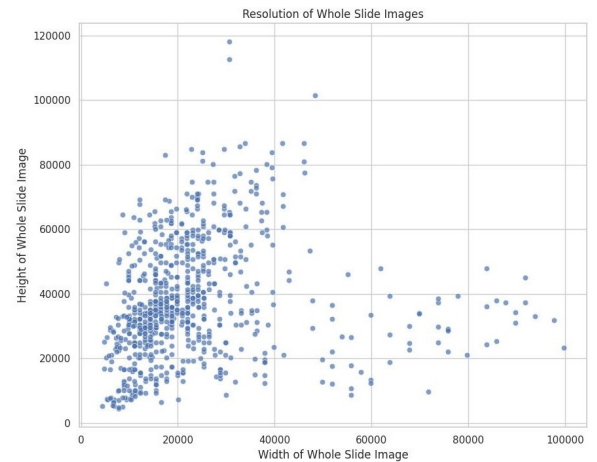


Fig. 1. Graphical representation of dataset image resolution in pixels.

With the help of an expert pathologist, it was identified that the digital pathology image dataset was stained using the Martius Scarlet Blue (MSB) staining method. The MSB technique has been used a lot for the characterization of clot composition, as it seems to be an optimal histology stain for the identification of the major components of ischemic stroke clots. [17] MSB staining allows for distinctive color separation, causing RBCs to appear as yellow fragments, fibrin/platelets as reddish violet/pink fragments, and WBCs as purple spots distributed all over the thrombus. This information was not provided by the dataset source [1], however, it is crucial for the extraction of distinctive features, making it easier for the components to be pinpointed in the images as can be seen in Fig. 2.

B. Preprocessing

1) *Tiling*: The large size of the images (1-2 GB on average) presented a significant challenge in the preprocessing stage. Due to memory constraints, direct processing or prediction was not possible. To overcome this hurdle, a tiling approach was implemented where the image was subdivided into smaller tiles, however, memory limitations persisted even during the tiling process. Therefore, a two-step approach was implemented using the *libvips* library [18], [19], which processes the images in chunks. First, a low-resolution thumbnail (20,000 x 20,000 pixels) of the image is created. Afterward, the tiling process is performed on the thumbnail, effectively alleviating memory constraints. Finally, the tiles are sorted based on the intensity of the tile, and only the 16 darkest tiles are picked, being the tiles with the most thrombus content.

Another key challenge associated with the dataset is the inherent class imbalance. The challenge lies in the significant class imbalance, with the majority class (CE) containing 73% of the data. To address this, a more selective tiling approach was adopted during preprocessing. This approach involves utilizing fewer tiles per image belonging to the overrepresented class, CE. While this reduces the overall data volume for the majority class, it maintains a sufficient number of tiles per image for informative representation. This strategy is particularly suitable due to the utilization of a machine learning model rather than a deep learning one, where data quantity is less critical for robust performance.

2) *Segmentation*: Classifying each pixel in the whole slide image as one of the three components of the blood clot (RBCs, WBCs, or fibrin/platelets) is the goal throughout the segmentation phase. The Hue, Saturation, and Value (HSV) color model [20], well-known for its ability to extract color information from an image pixel, was employed during this phase. As discussed in section III-A, the blood clot color observations in the dataset images show RBCs as yellowish to brown hues, WBCs as purple hues, and fibrin/platelets as reddish violet hues. After pinpointing which pixel belongs to which component, this data is combined from all of the pixels ultimately segmenting the areas in the image to the components they belong to. Following the conversion of the tiles to HSV color space, a binary mask is created per component

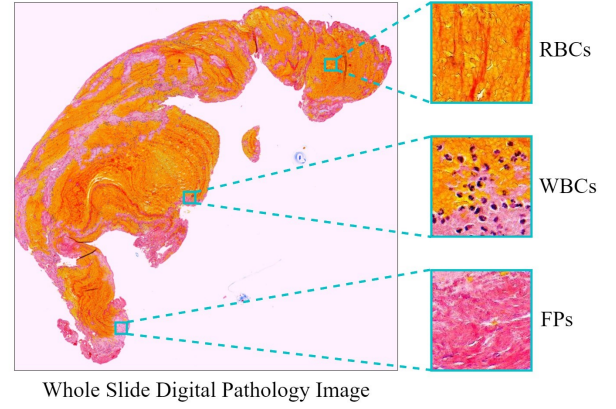


Fig. 2. Whole slide digital pathology image from the dataset, zoomed in on the components.

for each tile. Fig. 3 illustrates a tile of the whole slide image from the dataset along with its segmented components after the HSV color segmentation.

C. Feature Extraction

After the segmentation process, the tiles and their masks are transformed into the SimpleITK [21]–[23] format—a user-friendly interface layered over the Insight Segmentation and Registration Toolkit (ITK)—to be then fed to the PyRadiomics [24] feature extractor where geometric distribution, spatial distribution, and textural data are extracted. PyRadiomics is an open-source Python package that provides a comprehensive set of tools for extracting quantitative features from medical images. The features that were extracted by PyRadiomics include First Order Statistics, Shape-based (3D), Shape-based (2D), Gray Level Co-occurrence Matrix, Gray Level Run Length Matrix, Gray Level Size Zone Matrix, Neighboring Gray Tone Difference Matrix, and Gray Level Dependence Matrix. Lastly, the features are merged and stored as a CSV file to be then supplied to the machine learning model.

D. Feature Selection

Feature selection provides a method to discard redundant data, which improves learning accuracy and reduces computation time. In this study, the Mann–Whitney U test [25], [26] for non-normally distributed data is employed to select features based on a predefined P-value [27] threshold. The P-value is used to measure the statistical significance of a given feature. If the value is closer to 1, it suggests that the observed difference is likely due to chance. Conversely, if the value is closer to 0, it indicates that the observed difference is potentially significant. Given the critical role played by hyperparameter tuning in influencing the performance of machine learning models [?], this method was used to set a maximum threshold P-value for the extracted features after calculating the value of each feature.

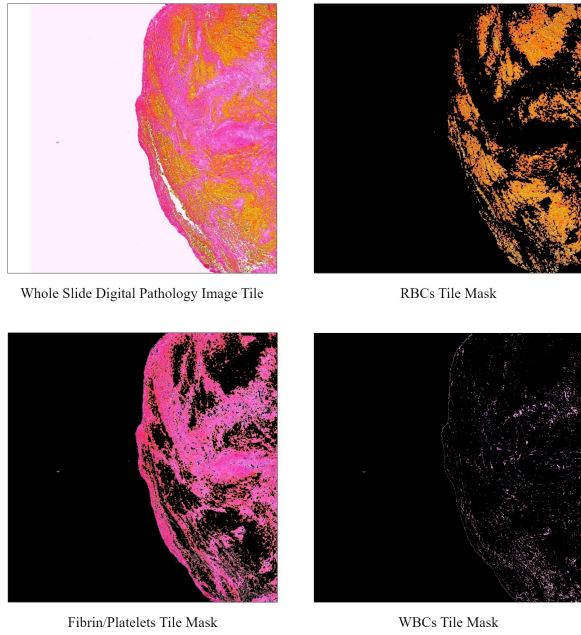


Fig. 3. Whole slide digital pathology image tile and the binary masks for each component.

E. Model

Following a comprehensive review of relevant research and exploratory experimentation, the XGBoost model [29] was identified as the most suitable choice for the study's objective. The XGBoost model incorporated three key features that significantly impacted performance and contributed to a substantial decrease in loss. Firstly, XGBoost's feature normalization was utilized to ensure a positive impact on model performance. Secondly, the Minimal Cost-Complexity Pruning (MCCP) feature [30] in XGBoost was enabled to prevent overfitting by pruning the decision tree, yielding the most significant performance improvement. Lastly, the log loss function was selected and employed during both training and evaluation within XGBoost. While the exponential loss function led to a slight increase in accuracy, it also resulted in a considerably higher loss. Given the competition's [1] focus on minimizing loss rather than maximizing accuracy, the log loss function in XGBoost was ultimately chosen as the preferred method. During the training phase, the model was trained on individual tiles as if each tile was a separate image with its own extracted features. During testing, the model classifies each tile of a test image separately, and then the final classification is based on the average of the individual probabilities of the classified tiles. The architectural representation of this methodology is demonstrated in Fig. 4.

IV. EXPERIMENTAL SETUP, RESULTS, AND ANALYSIS

This study leveraged the Kaggle platform for computational resources. Given the absence of GPU-intensive preprocessing or models, CPUs were exclusively employed to maximize available RAM. The computing environment provided 30 GB

of RAM and 73.1 GB of disk space. To optimize workflow, image tiling and feature extraction were conducted in independent notebooks and stored as Kaggle datasets. Subsequently, the primary notebook served for training and testing. In particular, test image tiling and feature extraction were performed during the testing phase within the main notebook to ensure a realistic testing scenario.

A. Hyperparameter Settings

After a series of trial and error experiments, it was determined that the optimal hyperparameters for implementing the proposed methodology were 200 estimators, a maximum depth of 4, an MCCP alpha [30] of 0.0007, and a P-value [27] of 0.07 for feature selection. These values generated the best results during the study's evaluation process.

B. Evaluation Criteria

Submissions to Kaggle's competition [1] are evaluated using a WMCLL function. The study's solution is then ranked by testing the model on a private dataset on Kaggle. Weights for each class have been added to improve this loss function, a variant of the conventional multi-class logarithmic loss. These weights highlight more significant classes by adjusting each class's contribution to the overall loss. Failed predictions are penalized by WMCLL, and the penalty is scaled based on the class weights that have been assigned. Because the loss is computed as the logarithm of predicted probabilities, accurate but confident predictions are penalized severely. The WMCLL formula is given as:

$$LogLoss = -\left(\frac{\sum_{i=1}^M w_i \cdot \sum_{j=1}^{N_i} \frac{y_{ij}}{N_i} \cdot \ln p_{ij}}{\sum_{i=1}^M w_i}\right) \quad (1)$$

where N is the number of images in the class set, M is the number of classes, \ln is the natural logarithm, y_{ij} is 1 if observation i belongs to class j and 0 otherwise, p_{ij} is the predicted probability that image i belongs to class j .

C. Results and Analysis

As can be noticed in Table 1, the results established in this study successfully surpassed previous deep learning approaches that aimed to solve the same problem with an identical dataset. The study [15] which relied on deep convolutional neural networks and visual transformers established a baseline WCMLL score of 0.67188. Another study [16] that used Stacked EfficientNet-B0, VGG19, and ResNet-152, reached a WCMLL score of 0.69312. To expand the comparison with studies that implemented similar methodologies, a study [12] has been reviewed that used a similar approach to perform feature extraction and a classical machine learning model, Naïve Bayes Classifier, but on a different dataset established accuracy results around 77%. In contrast, the solution introduced in this paper has shown a WCMLL score of 0.66588 and an accuracy of 79%.

An interpretation of the degraded accuracy achieved by the Naïve Bayes Classifier study [12] might be due to weaknesses such as downsampling the whole slide images and the staining

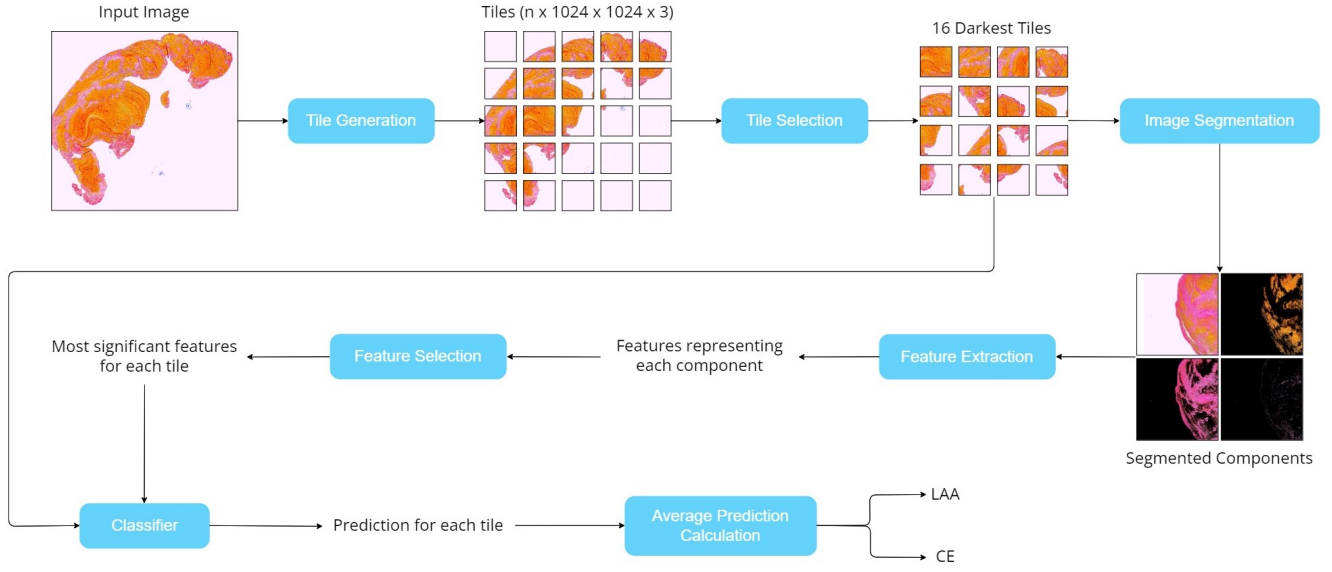


Fig. 4. Architecture of proposed ischemic stroke blood clot origin identification system.

TABLE I
COMPARATIVE RESULTS

Models	WMCLL	Accuracy
Stacked EfficientNet-B0, VGG19, and ResNet-152 [16]	0.69312	–
Deep CNNs and Visual Transformer [15]	0.67188	–
Naïve Bayes Classifiers [12]	–	0.77±0.06
XGBoost (proposed approach)	0.66588	0.79

technique used in its dataset—hematoxylin and eosin (H&E) staining. On the other hand, this introduced a solution that exploits the advantage in Kaggle’s dataset [1], which is the superior staining technique MSB. As mentioned in section III-A, MSB staining allows for distinctive color separation assisting in the extraction of distinctive features. Another reason for the higher baseline score achieved might be due to the segmentation process performed on high-resolution images. As previously explained in section III-B, the images in the dataset are not downsampled to rely on them as low-resolution images, then using them for blood clot component segmentation as was observed in the study that used Naïve Bayes classifier [12].

Despite not utilizing any deep learning methods, the suggested solution was evaluated through Kaggle’s competition [1] private dataset, and it came in fifth place on the leaderboard. Among the top rankings, this study was the only one that used a traditional machine learning methodology, demonstrating its superiority over alternative deep learning methods.

V. CONCLUSION

The study proposes a classical machine learning solution and proves its superiority, in the case of similar medical challenges, over the use of most deep learning approaches. This was done by using the XGBoost model [29] and training

it on numerically extracted features characterizing blood clot textures, bypassing the need for direct image-based training.

Classical methods are more effective with limited datasets, like in this case, and obtaining large datasets can be difficult when dealing with limited resources. On the other hand, deep learning models are more resource-intensive and less interpretable than classical models. A limitation of classical machine learning might be its need for domain expertise [31], however, this was overcome by the consultation of an expert pathologist to help identify thrombus components, understand digital pathology images, and extract discriminative features that aided the study.

Finally, an ischemic stroke is a medical emergency that needs to be treated right away to reduce brain damage and other stroke complications. Thus, the study offers an ischemic stroke blood clot origin identification system that gives doctors a dependable and quick method of diagnosing the type of ischemic stroke and determining the best treatment approach. This type of system has the potential to save lives, decrease healthcare costs, and improve overall care quality.

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