**Unveiling Thymoma Typing through Hyperspectral Imaging and Deep Learning**

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**Abstract**：Thymoma, a rare tumor from thymic epithelial cells, presents diagnostic challenges due to the subjective nature of traditional methods, leading to high false-negative rates and long diagnosis times. This study introduces a thymoma classification technique that integrates hyperspectral imaging with deep learning. We initially capture pathological slice images of thymoma using a hyperspectral camera and delineate regions of interest to extract spectral data. This data undergoes reflectance calibration and noise reduction. Subsequently, we transform the spectral data into two-dimensional images via the Gramian Angular Field (GAF) method. A variant residual network is then utilized to extract features and classify these images. Our results demonstrate that this model significantly enhances classification accuracy and efficiency, achieving an average accuracy of 95%. The method proves highly effective in automated thymoma diagnosis, optimizing data utilization and feature representation learning.

**Keywords：**Thymoma, Hyperspectral Imaging, Residual Neural Network, Assisted Diagnosis

1. **Introduction**

Thymoma, a rare neoplasm originating from the epithelial cells of the thymus, represents the most prevalent tumor in the anterior mediastinum. It may manifest either as an asymptomatic incidental finding during thoracic radiographic evaluations or demonstrate clinical signs and symptoms in alignment with local mediastinal afflictions or distinctive paraneoplastic syndromes[1]. The World Health Organization categorizes thymomas into eight primary subtypes—A, AB, B1, B2, B3, C, micronodular thymoma with lymphoid stroma, and metaplastic thymoma—and identifies three infrequent subtypes: microscopic thymoma, sclerosing thymoma, and lipofibroadenoma[2]. Prognostically, the pivotal indicator is the achievement of complete surgical resection, with the integrity of surgical margins being imperative to both inhibit recurrence and minimize unnecessary excision of healthy tissue[3,4]. At present, the edge assessment technique for thymoma mainly relies on intraoperative frozen section analysis, but this method has some limitations, such as requiring experienced pathologists, having a false negative probability, difficulty in examining the entire extraction area, and requiring at least 30 minutes of examination time [5,6]. Traditional diagnostic methods include tumor classification and determination of gene mutation status, which mainly rely on the subjective judgment of pathologists and may result in inconsistencies and errors [7,8].

In recent years, with the exponential growth of computational technology, deep learning—an advanced form of artificial intelligence utilizing neural networks for autonomous data feature extraction and learning—has found extensive application across various sectors including image recognition, natural language processing, and medical diagnostics. Pioneering models by researchers such as Wei Liu have leveraged preoperative CT imaging to develop cutting-edge thymoma risk stratification models that not only identify pathological lesions and segment regions of interest (ROI) but also discern thymoma risk on arterial phase CT images with superior diagnostic efficacy compared to baseline models. Concurrently, Yuhua Yang and colleagues have devised a synergistic model integrating deep transfer learning, radiomics, and clinical radiographic features, which has demonstrated exceptional diagnostic accuracy in distinguishing thymomas from thymic cysts. These models show great promise as auxiliary tools in clinical decision-making, particularly when endoscopic biopsy entails significant risks. Despite their advances, current algorithms tend to focus predominantly on radiomic or two-dimensional depth features, necessitating manual tumor segmentation by radiologists and hence limiting their practical utility. This not only escalates radiologists' workload but also amplifies model vulnerability to annotation noise, which can lead to overfitting or underfitting and diminish accuracy in processing ambiguous pathological features. Moreover, the inherent limitations of CT imaging in capturing subtle chemical and molecular details call for the development of more robust, effective, and consistent diagnostic tools to bolster the reliability and precision of traditional methods.

Hyperspectral imaging technology (HSI), which has matured significantly over recent decades, has emerged as a crucial instrument in both remote sensing and medical domains. Distinguished from traditional imaging modalities, HSI captures a continuous spectral range from visible to infrared light, rendering intricate chemical and molecular information of materials[11]. Utilizing the differential characteristics of materials in light reflection, absorption, and transmission, HSI reveals unique spectral signatures that are pivotal in medical diagnostics[12], surgical interventions, and pathological research. Especially in pathology, where HSI serves as a non-invasive analytical tool, it enables profound examination of tissue specimens, enhancing the capabilities of conventional microscopy by providing deeper insights into the structural and biochemical properties of tissues[13]. Advances in computer-aided diagnostic technologies have prompted researchers to explore the integration of HSI with deep learning techniques for disease diagnostics. Innovative approaches by Jing Song[14] have introduced methods for identifying ALK-positive lung cancer using microscopic HSI, exhibiting superior accuracy over traditional methods. Similarly, Lixin Liu[15] has employed a random forest model to process hyperspectral data, effectively classifying various skin cancer types. Despite these advancements, rapid and accurate thymoma diagnosis and classification continue to confront significant challenges such as model sensitivity to data noise, feature extraction complexity, and classification accuracy improvement.

In response to these challenges, this study introduces the integration of hyperspectral imaging technology with Gramian Angular Field (GAF) methods and variant residual networks, developing a novel pathologic classification method for thymomas. Our findings demonstrate that this approach not only enhances therapeutic outcomes for thymoma patients but also opens new avenues for personalized medicine, enabling physicians to devise more targeted treatment plans based on individual pathologic characteristics of each patient.

The specific contributions of this study are as follows:

1. A variant residual network model (Res2Net-48) was proposed, which achieved an accuracy of 94% in classifying thymoma subtypes.

2. This study included six common types of thymoma and achieved rapid and accurate pathological classification diagnosis through significant differences in hyperspectral image data, helping clinical doctors develop more effective treatment plans.

1. **Materials and Methods**
   1. **Collection of clinical samples**

Select 180 thymoma samples from Qilu Hospital in Shandong Province that have obtained complete genetic testing results, including 30 samples from each of the six different thymoma subtypes (A, AB, B1, B2, B3, and C). Collect tumor cell hotspots under a 200x magnification. Collect their medical history and record relevant clinical data. This study was approved by the hospital ethics committee.

The specific sample information is shown in Table 1:

|  |  |  |
| --- | --- | --- |
| Sample Type | number | Number of acquisitions (field of view) |
| group A | 30 | 60 |
| group AB | 30 | 60 |
| group B1 | 30 | 60 |
| group B2 | 30 | 60 |
| group B3 | 30 | 60 |
| group C | 30 | 60 |

Table 1. Sample Collection Display

**2.2 Collection device and image acquisition**

In this study, we employed the GaiaField(Pro) portable hyperspectral system (Jiangsu Shuanglihe Spectra) to capture reflective hyperspectral images of pathological slices from patients with pulmonary adenocarcinoma. This system features a universal microscopic optical path structure that allows for clear observation and collection of microscopic hyperspectral data under objectives of various magnifications. With its built-in two-dimensional translation structure, the system facilitates automatic exposure and software focusing functionalities, where the X-axis represents the image scanning axis and the Y-axis the focusing axis. The GaiaField(Pro) system operates within the visible to near-infrared spectrum (400-1000nm), featuring over 256 spectral channels (bands) with a minimum sampling interval of 1.5nm. The extensive array of spectral channels enhances the acquisition of detailed information, aiding researchers in revealing high-value data details through the analysis and inversion of continuous spectra.

The sample collection process in this research commenced with the placement of the pathological slices under the microscope for observation. Initially, we began at a low magnification (5x) and gradually increased to a higher magnification (100x) to comprehensively assess the tissue samples. Based on the specific needs of the research objectives and plan, we opted to use a 20x objective magnification for observation and data collection, which provides sufficient detail while facilitating spectral information extraction. The exposure time was set at 30 milliseconds, followed by adjustment of the slice sample's position to locate areas of high cell density. Upon identifying an appropriate target area, it was positioned at the center of the microscope's field of view. Subsequent adjustments to the microscope's coarse and fine focusing knobs ensured that the target area was clearly imaged. To optimize the quality of the hyperspectral data, we utilized the focusing functionality of the hyperspectral data collection system. Fine adjustments to the microscope's fine focus knob were made based on system feedback to ensure that the images captured were clear and precise. This repetitive process ensured data consistency and reproducibility, laying a solid foundation for subsequent spectral analysis and feature extraction.

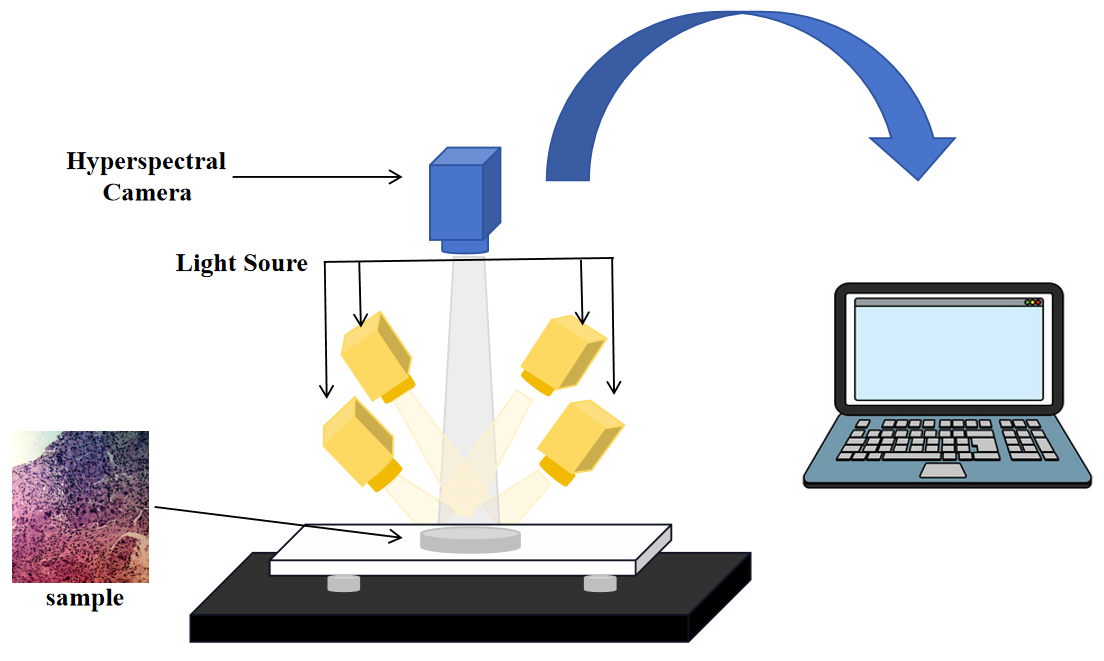


Figure 1. Image acquisition device

**2.3 Image Data Preprocessing**

**2.3.1 Reflectance calibration**

Owing to the influence of non-uniformity in the lighting source, dark current, and bias factors, hyperspectral imaging systems may output images with uneven illumination. This non-uniformity hampers subsequent data processing and analysis. Therefore, it is imperative to conduct dark and white calibration of the data to correct for these discrepancies[16], as delineated in Equation (1):

(1)

In Equation (1),represents the corrected reflectance image of the sample, denotes the original spectral reflectance image of the sample, is the dark reference calibration image, andrefers to the white reference calibration image.

**2.3.1 Savitzky Golay curve smoothing**

The Savitzky-Golay filter[15] is a type of digital filter that smooths data by fitting subsets of data points to a low-order polynomial, thereby preserving the inherent shape and features of the data, such as peaks and widths. This method is particularly suited for applications in chemistry and spectral analysis. Assume we have a dataset (Among them ) where iii ranges over the dataset, and we aim to smooth each data point yiy\_iyi​. We define a window of size 2m+12m+12m+1, where mmm represents the number of points on one side of the window. This window slides across the entire dataset to apply the smoothing process.

The smoothed value can be expressed as the weighted sum of the original data points:

= （2）

Among them, is the weight coefficient obtained by polynomial fitting. In this study, we smoothed the one-dimensional spectral data of thymoma pathological sections using a 5 window.

**2.3.2 Wavelet Threshold Denoising**

Wavelet transform has good local time-frequency feature characterization ability and multi-resolution analysis ability, and is widely used in signal denoising processing [16]. The wavelet function can be expressed as:

, （4）

Among them, parameter a represents the scaling factor, and parameter b is the translation parameter. The wavelet threshold denoising method is widely used for denoising spectral waveforms due to its wide applicability and significant denoising effect. Soft threshold denoising method is an implementation of wavelet threshold denoising, which can filter out high-frequency noise and preserve signal features. Specifically, when the absolute value of the wavelet coefficient is below the threshold, it is set to 0; When the threshold is exceeded, subtract the threshold:

, （5）

In the formula, is the wavelet coefficient after applying a threshold, t is the threshold, and is the wavelet coefficient. In this study, we used DB2 wavelets for two rounds of denoising, with each threshold set at 50% of the original wavelet coefficients, to denoise one-dimensional spectral data of thymoma pathological sections.

**2.4 Convert one-dimensional data into two-dimensional data**

Although deep learning algorithms have demonstrated robust capabilities in processing one-dimensional data, current research predominantly focuses on the manipulation of two-dimensional structured datasets, particularly within the realm of computer vision, where methodologies continue to emerge and evolve. In this study, we propose a data transformation method utilizing the Gramian Angular Field (GAF) [17]information encoding strategy, which converts processed one-dimensional spectral data into two-dimensional images. Given that the spectral wavelength of the images is 256, the generated two-dimensional images have a resolution of 256×256 pixels. This ensures that the transformed images retain the same amount of information as the original one-dimensional data without any loss of spectral information.

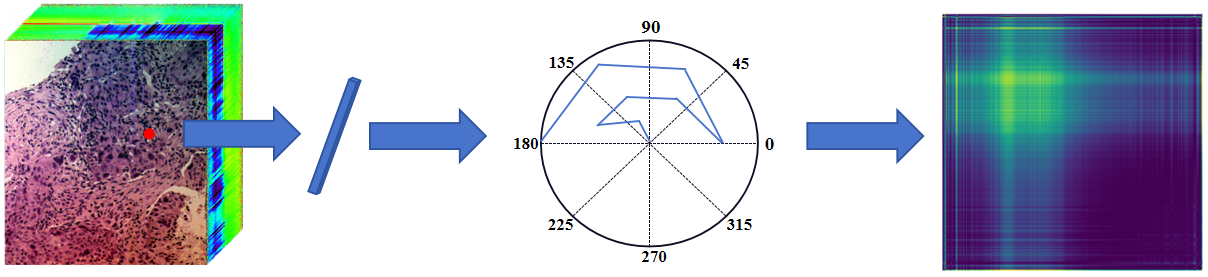


Figure 2 .Schematic diagram of data conversion

**2.5 Model Establishment**

When constructing our model, we initially attempted to employ the traditional ResNet [18]architecture. However, preliminary experiments indicated that ResNet did not perform well with our dataset. The primary limitation of ResNet lies in its constrained feature extraction capabilities when dealing with complex and high-dimensional data, which impedes its ability to discern subtle variations within the data. This limitation resulted in suboptimal accuracy when classifying thymoma pathological slices.

In response to these challenges, this study proposes an enhanced model based on Res2Net-48. Res2Net significantly improves the network’s capability for feature extraction and representation by incorporating a multi-scale feature expression mechanism. Specifically, Res2Net introduces multiple parallel scales within each residual block, allowing the network to process information across different scales concurrently. This design enables better capture of complex features within images.

**Specific structural improvements:**

Res2Net-48 introduces multiple parallel scales within each residual block, enabling the network to capture features at various scales and integrate these features through a specific connectivity scheme, thereby enhancing the diversity and robustness of feature representation. This design significantly improves the network's capability for feature extraction and classification performance without a substantial increase in computational demand. In terms of specific parameter settings, the Res2Net-48 architecture has a depth of 50 layers, with each scale having a width of 48, and each residual block containing two scales. The structure is illustrated in Figure 3.

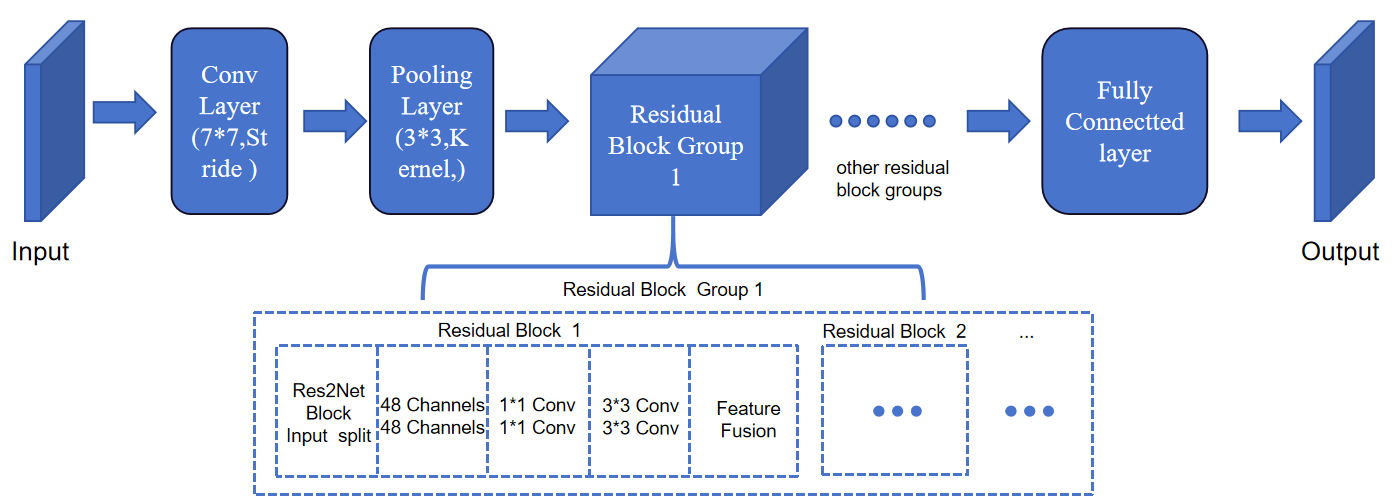


Figure 3. Model Structure Diagram

**2.6 Evaluation Criteria**

In this study, we used confusion matrices and Roc curves [19]. The horizontal axis in the confusion matrix graph represents the predicted result type of the sample, and the vertical axis represents the label type of the sample. ROC: The accuracy is closer to 1, indicating that the constructed model has better diagnostic results. The evaluation of model classification performance refers to the calculation method of standard accuracy [20] as follows:

Accuracy is equal to the proportion of correctly classified samples to the total number of samples:

Accuracy= （6）

In the formula, BP represents correctly classified samples in positive samples, BN represents correctly classified samples in negative samples, FP represents misclassified samples in positive samples, and FN represents misclassified samples in negative samples.

1. **Result**

Figure 4(a) presents results that distinctly reveal significant differences in the spectral curves of pathological slices from six types of thymoma patients within specific wavelength ranges. These differences likely reflect the chemical and molecular characteristics of six different mutational tissue states. Upon closer inspection of the curves, however, numerous spikes were observed, which may be attributed to noise within the spectral data or uncertainties during the measurement process. Moreover, the subtle features and overlaps between absorption peaks were not pronounced. This observation underscores the importance of implementing appropriate preprocessing techniques to enhance data quality and analytical precision. Accordingly, we employed two preprocessing techniques. To demonstrate the effects of preprocessing, we use spectral data from a type A thymoma patient as an example. Initially, we applied wavelet threshold transformation for noise reduction, and the processed spectral curve, as shown in Figure 4(c), significantly improved the signal-to-noise ratio with a marked effect. Subsequently, we utilized Savitzky-Golay (SG) curve smoothing, which effectively smoothed the spectral curve, reducing the impact of noise and spikes, as illustrated in Figure 4(b). This preprocessing approach significantly enhanced the quality and interpretability of the data, providing a more reliable foundation for the subsequent training of classification models.

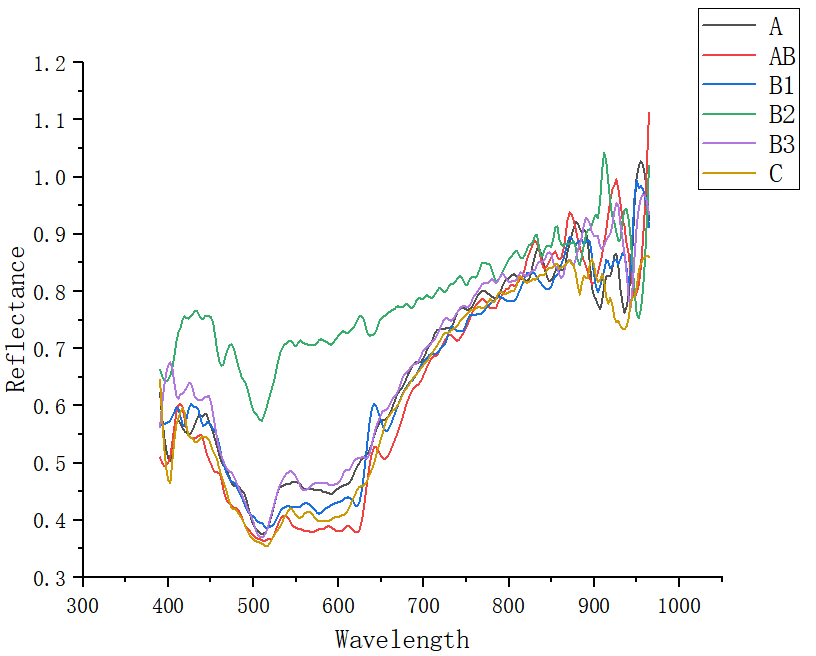


Figure 4 (a) .Spectral curves of different types of thymoma. A: Thymoma subtypes A, AB: thymoma subtypes AB, B1: thymoma subtypes B1, B2, B3, C

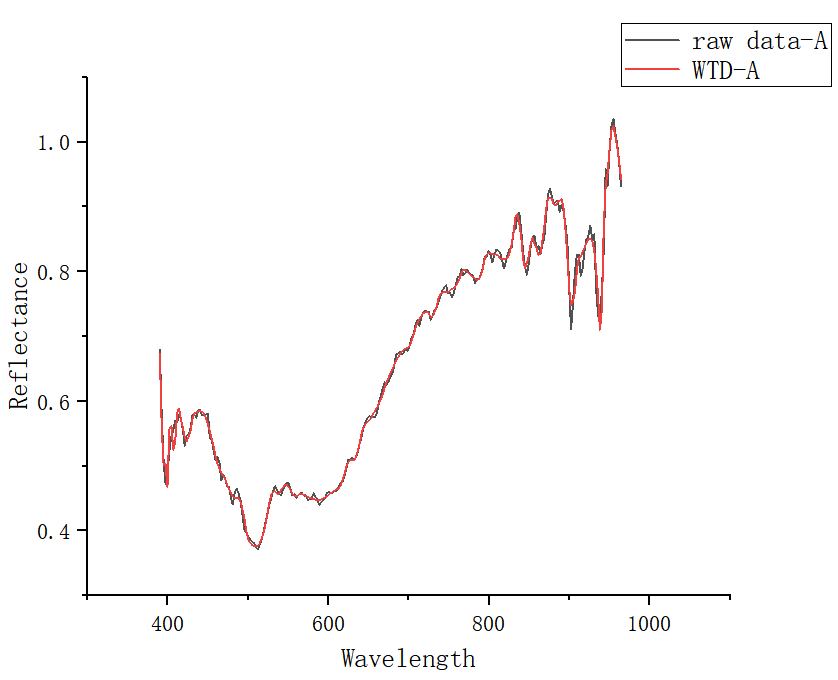


Figure 4 (B) shows the curves before and after wavelet threshold denoising (WTD) processing.

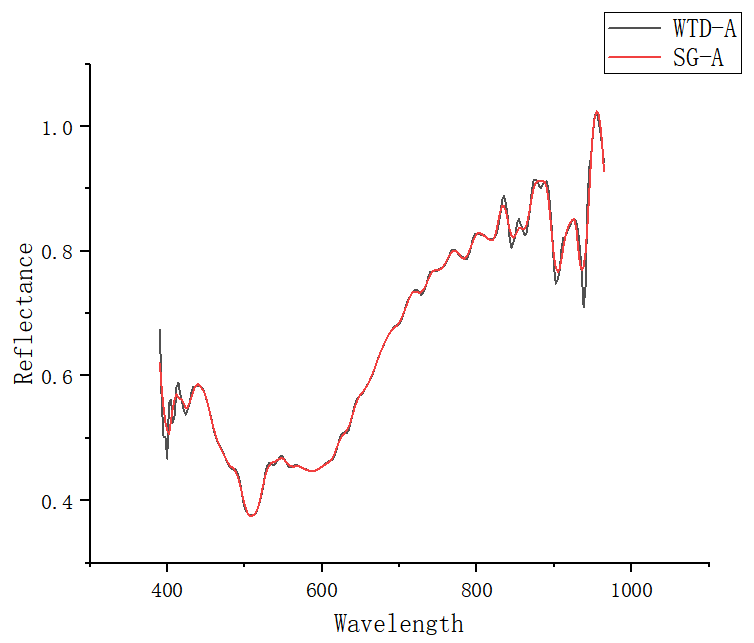


Figure 4 (c) SG smoothed curve graph

Due to the previously verified results where the sole use of the ResNet model yielded suboptimal accuracy levels, as demonstrated in Table 2, this study employed the Res2Net-48 model. This model represents a substantial enhancement over the foundational ResNet framework, making it particularly apt for our intricate spectral data analysis endeavors. The outcomes of the model's multi-classification tasks, assessed via ROC curve analyses, indicate that the AUC values for all classes are above 0.95, affirming its high classification accuracy across diverse tasks, as shown in Figure 5(a). Notably, categories 0, 3, and 4 achieved AUC values of 0.96, while categories 1, 2, and 5 reached AUC values of 0.95, illustrating the model's exceptional efficacy in these specific categories. Both the micro-average and macro-average AUC values stand at 0.96, further confirming the model's robustness and consistency in comprehensive classification efforts.

Table 2 ResNet model result display

|  |  |  |  |
| --- | --- | --- | --- |
| Model | Accuracy(%) | | |
| Train(%) | Test(%) | Overall(%) |
| ResNet-34 | 75 | 72 | 73 |
| ResNet-50 | 79 | 77 | 78 |

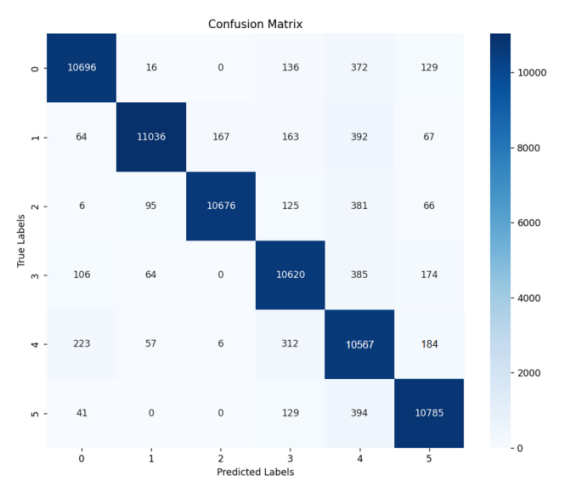
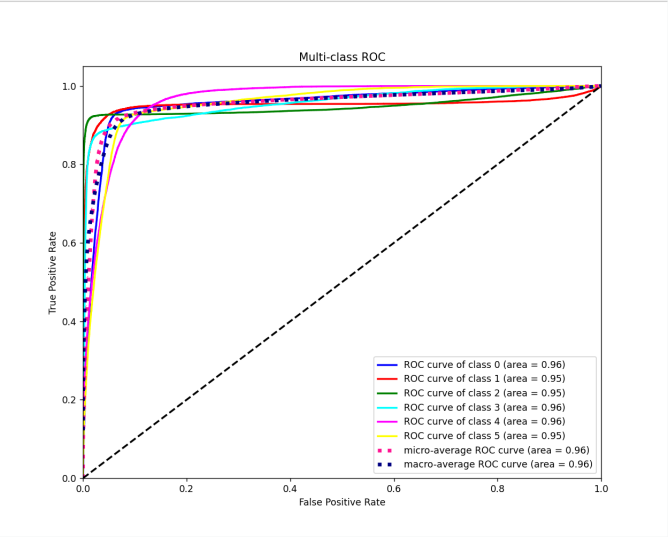


Figure 5 (a) ROC curve Figure 5 (b) Confusion matrix

The confusion matrix analysis reveals the detailed classification performance of the model, with a high number of correct classifications for most categories, as shown in Figure 5 (b), especially for Class 0, Class 1, Class 2, and Class 3, with correct classifications of 10696, 11036, 10676, and 10620, respectively. However, there is a certain degree of confusion between class 4 and class 5 in the model, with 312 samples misclassified as class 4 and 184 samples misclassified as class 5. The relatively low number of misclassifications between other categories indicates that the model's classification performance is relatively stable in these categories.

Overall, the model performs well in handling complex multi class classification tasks, with high classification accuracy and stability. Although there is some confusion between certain categories, the overall performance is still satisfactory. This indicates that the model is suitable for most multi class classification tasks, but in future optimizations, further improvements can be made to address misclassification issues between specific categories to enhance overall classification performance.

1. **Discussion**

In this study, we innovatively applied the variant model Res2Net-48, which significantly enhanced the classification and diagnosis of thymoma pathological slices by extracting features from hyperspectral data. Our approach utilized the Gramian Angular Field (GAF) technique to transform hyperspectral data into two-dimensional images, combined with the multi-scale feature expression capability of the variant model, achieving high accuracy in thymoma classification. The foundation of the research was the construction of a comprehensive dataset covering six types of thymoma pathology. The hyperspectral imaging captured a wide range of wavelengths from 400nm to 1000nm, securing rich spectral information. Given the scarcity of clinical samples and the challenges in obtaining samples that meet the criteria, we adopted a small sample analysis approach, manually delineating regions of interest and extracting one-dimensional spectral data. Subsequent steps such as reflectance calibration, wavelet threshold denoising, and Savitzky-Golay curve smoothing were employed to enhance data quality, ensuring consistency and accuracy in the model input data.

To fully leverage the characteristics of the sample data, we employed the Gramian Angular Field (GAF) method to convert one-dimensional spectral data into two-dimensional images. This method enabled the Res2Net-48 model to better capture and interpret complex patterns in hyperspectral data, significantly improving classification performance. The results showed that our model achieved an average accuracy of 95% in multi-class classification tasks, demonstrating its exceptional ability in thymoma classification. Nakajo et al. [21] built a predictive model using CT images, combining 107 radiomic features and 1024 deep learning features, and employed six different machine learning algorithms to predict pathological risk subtypes. Among these algorithms, the logistic regression model showed the highest AUC and accuracy, with predictive values for thymoma at 90% and 81%, respectively. Lan Shang et al. [22] used a multiclassifier machine learning (ML) model based on non-enhanced CT radiomic features to classify anterior mediastinal cysts (AMC) from thymomas and high-risk from low-risk thymomas, achieving optimal accuracies of 87% and 92%. As shown in Table 3, compared to these classification methods, our data processing approach exhibited higher accuracy, and the performance of the Res2Net-48 model was also superior.

Table 3 Similar research

|  |  |  |  |
| --- | --- | --- | --- |
| Name | data | method | [result](file:///F:/%E6%96%B0%E5%BB%BA%E6%96%87%E4%BB%B6%E5%A4%B9/baidu-translate-client/resources/app.asar/app.html" \l "/#) |
| Sangamithraa[23] | CT image of lung cancer | Backpropagation Network (BPN) | 90.7% |
| Jin、Zhang[24] | CT image of lung cancer | Convolutional Neural Network (CNN) | 84.6% |
| Ziyan Chen[25] | Meningioma MRI image | Residual Network (ResNet-50) | 88.9% |
| Tembhurne J V[26] | Skin cancer RGB image | Logistic Regression (LR) | 93% |

However, the classification and interpretation of subtle variations in thymoma pathological slices still pose challenges. Like all deep learning applications, we also face the risks of overfitting or underfitting, especially when dealing with highly variable biological data. Future improvements will focus on enlarging the dataset's scale and exploring more advanced machine learning techniques to enhance the model's generalization ability and diagnostic accuracy. Additionally, the adaptability of our system in various clinical settings remains a priority. Differences in imaging equipment and techniques may affect data consistency; future developments will aim to standardize the imaging process and implement domain adaptation techniques to ensure robust performance of the model across various settings.

1. **Conclusion**

This study introduces a novel classification method for thymoma pathological slices based on hyperspectral imaging technology (HSI) and residual networks (ResNet), which transforms one-dimensional spectral data into two-dimensional images using the Gramian Angular Field (GAF) technique and utilizes the enhanced Res2Net-48 model for feature extraction and classification. Compared to existing methods, our approach eliminates the need for manual segmentation, thereby reducing the workload of radiologists, while significantly improving classification accuracy and efficiency. Experimental results indicate that the model combining GAF and Res2Net-48 surpasses traditional ResNet and other two-dimensional depth feature-based methods in terms of classification accuracy, achieving an average accuracy of 95%. These findings suggest that the integration of hyperspectral imaging technology with an improved deep learning model holds substantial potential in the classification and diagnosis of thymoma, offering more detailed spectral information and enhanced feature extraction capabilities. This method not only aids in increasing the diagnostic accuracy and consistency for thymoma patients but also provides a new pathway for personalized medicine, allowing physicians to tailor treatment plans based on the specific pathological features of each patient, thus improving treatment outcomes and prognoses.

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**Ethical Statement**

This research adheres to the highest ethical standards in every phase, ensuring the protection and confidentiality of all patient data involved. Rigorous anonymization and de-identification protocols are in place to safeguard individual privacy rights.

**Data Availability**

The data supporting the findings of this study are not publicly available but can be provided by the authors upon reasonable request.

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**Disclosure**

The authors declare no conflicts of interest. The research was conducted independently and the results are presented without any external influence.

**Authors' Contributions**

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Supervision: Wei Li, WeiMing Yue

Validation:QiZe Lv,Liang Ke

Visualization: QiZe Lv,Liang Ke

Writing – Original Draft: QiZe Lv,Liang Ke

Writing – Review & Editing: Wei Li, QiZe Lv,Liang Ke, WeiMing Yue

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