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Ovarian Cancer Diagnosis Using Advanced Deep Learning Models with Histopathology Images

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Abstract

The classification of ovarian cancer through advanced deep learning models presents a noteworthy challenge in the field of medical diagnosis, given potential implications for patient health and wellbeing. In this study, our focus is on automating the classification of ovarian cancer using cutting-edge deep-learning models such as VGG-19, ResNet-50, InceptionV3, and EfficientNetV2. Each model employs transfer learning, drawing insights from an extensive dataset consisting of various imaging modalities, eventually categorizing them into five clearly defined ovarian cancer conditions: (1) HGSC - High-Grade Serous Carcinoma, (2) CC - Clear-Cell Ovarian Carcinoma, (3) EC - Endometrioid, (4) LGSC - Low-Grade Serous, and (5) MC - Mucinous Carcinoma. The training dataset contains samples that are all characterized by distinct cellular morphologies, etiologies, molecular and genetic profiles, and clinical attributes, encompassing all five cancer subtypes. Our analysis demonstrates that among the models assessed, EfficientNetV2 showcases exceptional performance, achieving an impressive classification accuracy of 98.11%, precision of 99.3%, and a recall of 99.1%, outperforming the other models.

Keywords: Ovarian Cancer; Deep Learning; Convolutional Neural Networks; Classification.

Introduction

The advancement of health data analysis plays a pivotal role in transforming medical research and clinical care. By systematically examining large datasets, researchers can uncover hidden patterns, correlations, and insights that drive precision medicine and personalized treatment strategies [1]. This is particularly critical in the context of cancer [2,3], where understanding the biological behavior of malignant cells—such as their rapid proliferation, invasion of nearby tissues, and

resistance to therapy [4,5]—provides the foundation for developing targeted treatments. Analyzing data related to tumor progression and response to treatment can guide the design of more effective therapies, reduce adverse effects, and ultimately improve survival rates [6]. Furthermore, health data analysis extends beyond cancer research to address broader aspects of women's health, including pregnancy outcomes. Analyzing pregnancy-related data enables clinicians to identify risk factors for adverse outcomes, optimize prenatal care, and develop predictive models to prevent complications [7]. In gynecological oncology, integrating these analytical insights fosters a comprehensive approach to managing health conditions across a woman's lifespan, linking early detection and intervention for ovarian cancer to improved maternal and reproductive health outcomes. By bridging the fields of oncology, pregnancy, and health data analysis, researchers can unlock new opportunities for enhancing women's healthcare at multiple levels.

Ovarian cancer is the most lethal gynecological malignancy, with a five-year survival rate of only 46%. The absence of reliable screening methods significantly hampers early detection, leading to diagnosis at advanced stages in approximately 70% of cases. This delay in diagnosis results in a further decline in survival rates, with advanced-stage ovarian cancer patients facing a five-year survival rate as low as 28% [8]. Accurate diagnosis of ovarian cancer is inherently challenging, as it requires precise differentiation of subtypes based on histopathological images. Pathologists rely on these images for diagnosis; however, the increasing volume and complexity of samples can lead to errors, particularly under high workloads. Imaging plays a pivotal role in the field of ovarian cancer research and diagnosis, serving as a cornerstone for understanding disease progression, guiding treatment strategies, and improving patient outcomes. Advanced imaging techniques, such as cellular and subcellular imaging, have been widely utilized across various fields [9] to study biological processes with precision. In the context of ovarian cancer, using high-resolution pathological images enables the detailed visualization of cellular and tissue structures, aiding in the accurate differentiation of benign and malignant neoplasms. Techniques like digital pathology and multiplexed fluorescence imaging further enhance the ability to identify tumor heterogeneity, assess the tumor microenvironment, and evaluate molecular markers critical for personalized therapy. To enhance diagnostic accuracy and alleviate the burden on clinicians, researchers are actively investigating the application of computational tools, particularly advanced deep learning models, in the diagnosis of ovarian cancer. A clear distinction between benign and malignant ovarian neoplasms is crucial, as it directly influences both treatment strategies and prognostic outcomes. For benign lesions, non-invasive follow-up regimens are often recommended to reduce psychological distress and preserve ovarian function, both of which may be unnecessarily compromised by surgical interventions or biopsies [10]. In the case of malignant ovarian, precise tumor staging is essential for guiding gynecological oncologists in formulating effective treatment plans [11]. Consequently, the ability to preoperatively differentiate between benign and malignant ovarian neoplasms is of paramount importance for implementing tailored and successful therapeutic strategies.

Artificial intelligence (AI) and machine learning have revolutionized various fields by enabling advanced data analysis, pattern recognition, and predictive modeling, offering innovative solutions to complex challenges in domains such as healthcare, engineering, and environmental sciences. A recent surge has been observed in the adoption of machine learning and deep learning paradigms for addressing diverse analytical tasks. This utilization has extended across a wide range of domains, including the identification of complex patterns [12] and the prediction of dynamic phenomena such as earthquakes and weather conditions [13]. In the medical domain, machine-learning models have

been extensively employed for applications such as tumor detection [14], abnormal tissue segmentation [15], and the automated diagnosis of medical conditions [16,17] from radiological and histopathological images [18,19]. Simultaneously, significant advancements have been made in leveraging graph-based machine learning techniques, which excel at modeling complex relationships and interconnected data structures [20]. These methods have been particularly impactful in biological and biomedical research, such as analyzing molecular interactions, disease-gene associations, and the structural organization of tissues. Additionally, the application of machine learning to text-based data has enabled the extraction of valuable insights from clinical notes, medical records, and research literature, contributing to tasks such as disease classification, symptom analysis, and treatment prediction [21].

Deep neural networks, exhibiting proficiency in end-to-end learning, are being passively demonstrated to possess the capability of autonomously extracting salient characteristics from ovarian cancer histopathology imagery. This is particularly evident in the successful application of deep learning algorithms for the classification of ovarian tissue specimens. Types of convolutional neural networks are employed to classify histopathological images. Xu et al. [22] introduced deep convolutional activation features trained with ImageNet knowledge and applied a CNN model to extract features from tumor digital histopathology datasets. CNN features are superior to manual features, achieving state-of-the-art results in classification and segmentation tasks for types of cancer. Panigrahi et al. [23] observed the effectiveness of machine learning and deep learning algorithms in analyzing histopathological images. Deep learning outperformed traditional machine learning in handling complex tasks. The increasing use of artificial intelligence techniques in research reflects the need for unsupervised learning methods. Deep learning models can automatically extract features from data, reducing the need for human intervention. Ovarian cancer may be diagnosed earlier if a biomarker and machine learning algorithm are used together [24].

In this study, a meticulous investigation into the potential of deep learning for ovarian cancer detection and classification is undertaken. A formidable arsenal of well-regarded models is leveraged, including the established VGG19, the robust ResNet50, the versatile Inception V3, and EfficientNetV2. These intricately architected models, renowned for their prowess in understanding visual patterns, are incorporated to enrich the domain of ovarian cancer detection. Their success in various image analysis tasks establishes them as reliable tools for navigating the complexities of ovarian cancer identification. Through meticulous evaluation of this ensemble of powerful deep learning models, their adaptability to diverse scenarios is appraised. The findings aim to offer valuable guidance for both medical imaging novices and veterans, ultimately facilitating the precise and effective detection of ovarian cancer.

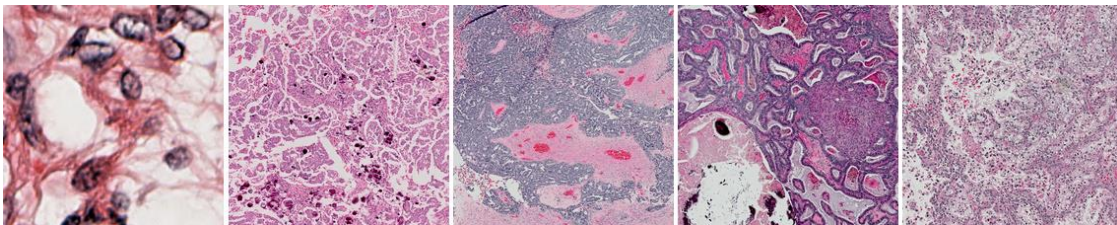


Figure 1 Representative Ovarian Cancer Coherence Histopathology Images (Left to right: MC, LGSC, HGSC, EC, CC) [26]

Methods

Histopathology Dataset

We conducted our experiment using a new dataset of histopathology images from Kaggle [26] sourced from publicly available data released in 2023. The dataset contains a substantial collection of 34000 histopathology images, 90% of which will be used as training, and other 9% for validation, and 1% for testing. This dataset truly stands out because it includes exceptionally high-resolution images. Within this dataset, a variate array of ovarian cancer has been grouped into five classes:

1. The HGSC class represents cases of high-grade serous carcinoma.
2. The CC class corresponds to instances of clear-cell ovarian carcinoma.
3. The EC class indicates the presence of endometrioid carcinoma.
4. The LGSC class, signifying cases where the low-grade serous exhibits typical characteristics.
5. The MC class, evidencing cases of mucinous carcinoma.

Deep Learning Models

Four prominent deep learning models – VGG19, ResNet50, Inception V3, and EfficientNetV2 – were leveraged to achieve high accuracy and effectiveness in ovarian cancer detection and classification. These models, recognized for their unique strengths and intricate architectures, have become established powerhouses in image analysis and classification tasks.

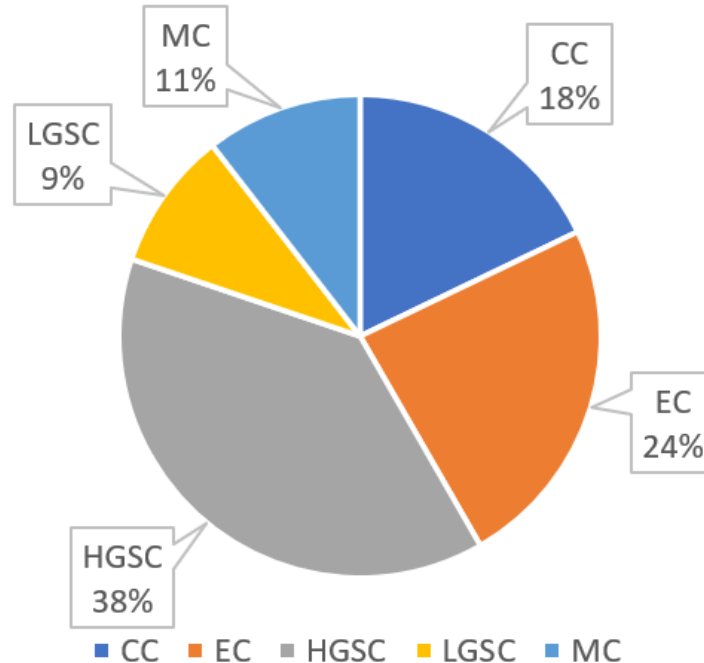


Figure 2 Percentage of five types of ovarian cancer.

To facilitate ovarian cancer classification within histological images, fine-tuning of pre-trained deep learning models was undertaken. This process involved replacing the final classification layers with a bespoke layer designed for multi-class classification, enabling the models to specialize in differentiating between various ovarian cancer subtypes. Subsequently, the entirety of the network, encompassing both the pre-trained and newly incorporated layers, was subjected to a training regimen aimed at optimizing parameters specifically for the task of classifying images into five distinct subtypes of ovarian cancer. This fine-tuning procedure is considered crucial in the development of accurate and versatile models.

Pre-trained models

A pre-trained VGG-19 deep learning model with a 19-layer architecture was employed. This architecture comprised 16 convolutional layers and three fully connected layers. The convolutional layers utilized 3x3 filters with a stride and padding of one pixel. This selection of compact kernel sizes aimed to restrict the number of parameters while guaranteeing thorough image coverage. A 2x2 max pooling operation with a stride of two was implemented within the VGG-19 model. Notably, this model achieved second place in classification and first place in positioning tasks at the 2014 ILSVRC competition, encompassing a total of 138 million parameters. The success of VGG-19 served to substantiate the notion that deep convolutional neural networks, facilitating a hierarchical interpretation of visual data, could yield superior performance. ResNet50, a prominent member of the Residual Network (ResNet) family, was employed in this investigation due to its celebrated architectural depth and ingenious structure. This model features a total of 50 layers and is characterized by the incorporation of residual blocks. These residual blocks revolutionized deep neural networks by introducing skip connections. These skip connections bypass one or more layers within the network, enabling ResNet50 to be trained at significant depth while mitigating the vanishing gradient problem. This groundbreaking structural innovation empowers ResNet50 to effectively capture intricate features within ovarian histology images, even in the presence of complex and noisy data. Essentially, the depth of this architecture facilitates the extraction of fine-grained image details, rendering it suitable for tasks like medical image analysis and classification of ovarian cancer subtypes. ResNet50 boasts 60.8 million parameters, contributing to its proficiency in recognizing subtle image variations. This characteristic, combined with its structural resilience and architectural depth, positions ResNet50 as a compelling choice for tackling intricate challenges in ovarian cancer diagnosis through image analysis and classification. The Inception V3 architecture, developed by Google researchers, is a multi-branch network recognized for its versatility. This 48-layer model leverages factorized convolutions, employing filters of varying sizes to capture features across different scales. The pre-trained Inception V3 model, boasting over 20 million parameters, was trained on a large dataset by hardware industry experts. The architecture incorporates both symmetrical and asymmetrical building blocks, each containing convolutional layers, average and max pooling layers, concatenation layers, dropout layers, and fully connected layers. Batch normalization is implemented before the activation layer in each block. Softmax classification is employed for the final output layer. EfficientNetV2 is presented as the embodiment of both computational efficiency and cutting-edge precision within the realm of deep learning models. Leveraging the achievements of its predecessor, EfficientNet, this model achieves optimized utilization of model parameters while concurrently delivering superior performance. EfficientNetV2 surpasses EfficientNet in its ability to expedite the training process and enhance parameter efficiency. This network's architecture is meticulously crafted through a combination of

scaling techniques (width, depth, resolution) and a process known as neural architecture search.

Customized network

To address the challenge of accurately classifying ovarian cancer subtypes in histological images, we employed a multifaceted deep-learning approach. We utilized pre-trained models like VGG19, ResNet50, Inception V3, and EfficientNetV2 as a foundation. These models were then fine-tuned to leverage their image recognition capabilities for ovarian cancer specifically. This fine-tuning involved replacing the final classification layers with a custom-designed fully connected layer tailored for the task of differentiating between multiple ovarian cancer subtypes. This new layer essentially reshaped the pre-trained models into specialized tools for ovarian cancer diagnosis. Following this adaptation, the entire network, encompassing both pre-trained sections and the newly added layer, underwent extensive training. During this training, the models learned from the provided ovarian cancer image dataset, refining their internal parameters to achieve accurate classification of five different subtypes: (1) HGSC - High-Grade Serous Carcinoma, (2) CC - Clear-Cell Ovarian Carcinoma, (3) EC - Endometrioid, (4) LGSC - Low-Grade Serous, and (5) MC - Mucinous Carcinoma.

Experiments

Parameter adjustment

We developed the deep learning model for ovarian cancer diagnosis using Keras, a popular deep learning framework. We conducted all experiments on a computer with a 4-core i7-6700 processor (3.4 GHz), 16GB of RAM, and a powerful NVIDIA GeForce RTX 2090 graphics card. Our approach involved using a fixed margin of 0.2 during training, randomly selecting data samples, and running the training process for 100 training epochs. We trained the model on a publicly available dataset of ovarian cancer dataset, classifying it into five distinct categories.

During preprocessing, we normalized the images and ensured they all had consistent dimensions. To ensure robust evaluation, we divided the dataset. 80% of the images were used for training and validating the model, while the remaining 20% were used for independent testing.

Performance Metrics

To assess how well our model classifies ovarian cancer subtypes, we employed a set of standard metrics based on the model's predictions. These metrics include True Positives (TP), True Negatives (TN), False Positives (FP), and False Negatives (FN). True Positives (TP) represent the number of images where the model correctly identified a specific ovarian cancer subtype. In other words, TP reflects the model's ability to accurately diagnose cancer when it's present. True Negatives (TN) represent the number of images the model correctly classified as not containing any cancer subtype. This indicates the model's ability to identify healthy tissue. False Positives (FP) represent the number of images the model incorrectly classified as having a specific cancer subtype when it was healthy tissue. FP reflects the model's tendency to make false alarms. False Negatives (FN) represent the number of images where the model missed a cancer subtype and classified it as healthy tissue. FN signifies the model's potential to overlook actual cases of cancer. By analyzing these metrics together, we gain a comprehensive understanding of the model's performance in differentiating between various ovarian cancer subtypes and healthy tissue.

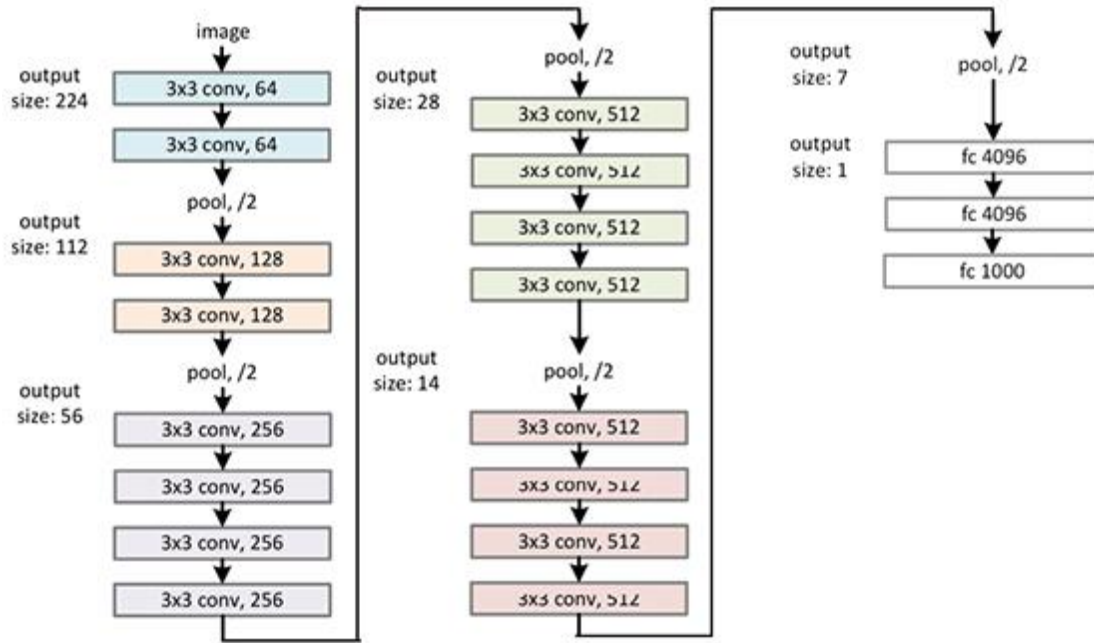


Figure 3 The Architecture of VGG19 [27]

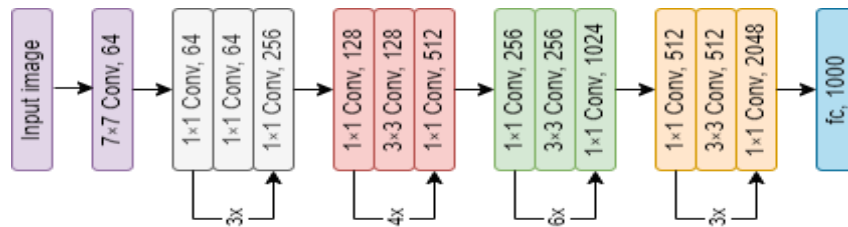


Figure 4 ResNet50 [28]

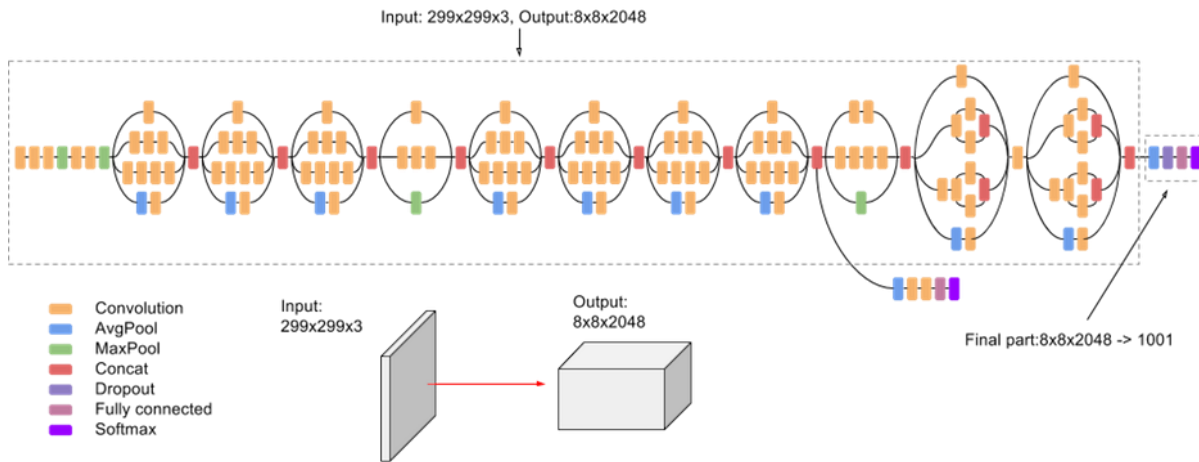


Figure 5 Inception V3 [29]

This allows us to evaluate the model's effectiveness not just in making correct diagnoses but also in identifying its limitations.

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN} \quad (1)$$

$$Precision = \frac{TP}{TP + FP} \quad (2)$$

$$Recall = \frac{TP}{TP + FN} \quad (3)$$

$$F_{1score} = 2 \times \frac{Precision \times Recall}{Precision + Recall} \quad (4)$$

Results

Table 1 presents a summary of the deep learning models utilized within this investigation, providing insights into their architectural complexities and parameter scales. Key details are presented, including the number of convolutional layers and the total number of parameters. VGG19, recognized for its architectural simplicity and uniformity, incorporates 19 convolutional layers and a substantial parameter count of 143 million. Conversely, ResNet50 is distinguished by its remarkable depth, featuring 50 convolutional layers while maintaining a relatively compact parameter count of 23 million. InceptionV3, lauded for its versatility, employs 48 convolutional layers and 21 million parameters, reflecting its ability to capture features at various scales. The EfficientNetV2 family, herein represented by B0, exemplifies its computational efficiency by incorporating a noteworthy 237 convolutional layers with a surprisingly modest parameter count of 25 million. This table functions as a comprehensive reference for the scale and complexity of the implemented deep learning models, paving the way for their subsequent evaluation. Tables 2 and 3 comprehensively evaluate the performance of various deep-learning models for ovarian cancer subtype detection using a range of metrics. Table 2 presents the results obtained from pre-trained models and Table 3 delves into the performance of the custom-designed model, highlighting the distinct achievements of each model variant.

Table 1. Deep Learning Models: Number of layers and parameters.

Model	Number of Convolutional Layers	Number of Parameters (Millions)
VGG19	19	143
ResNet50	50	23
InceptionV3	48	21
EfficeinNetV2	237 (B0)	25

Our evaluation revealed promising results. VGG19 achieved a high accuracy of 91.02%, demonstrating its ability to correctly classify ovarian cancer subtypes in the images. It also had a good precision score of 96.2%, meaning it made few mistakes in identifying cancer. While its recall of 90.3% indicates it might miss some cancer cases, the F1 score of 93.18 suggests a good balance between accuracy and completeness.

Table 2. Comparison of the different models: the pre-trained models (without training)

Model	Accuracy	Precision	Recall	F1 _{score}
VGG19	0.881±0.0054	0.939±0.0032	0.883±0.0034	0.902±0.0015
ResNet50	0.915±0.0046	0.961±0.0041	0.922±0.0052	0.926±0.0070
InceptionV3	0.932±0.0020	0.949±0.0019	0.924±0.063	0.941±0.0013
EfficientNetV2	0.974±0.0023	0.988±0.0074	0.988±0.0025	0.983±0.0027

Table 3. Comparison of the different models: fine-tuning the pre-trained models.

Model	Accuracy	Precision	Recall	F1 _{score}
VGG19	0.910±0.0026	0.962±0.0014	0.903±0.0075	0.931±0.0073
ResNet50	0.952±0.0070	0.981±0.0023	0.933±0.0092	0.949±0.0053
InceptionV3	0.941±0.0030	0.980±0.0029	0.930±0.0069	0.958±0.00054
EfficientNetV2	0.981±0.0019	0.993±0.0016	0.991±0.0022	0.992±0.0041

ResNet50 performed even better, achieving an impressive accuracy of 95.28 % and a very high precision of 98.12%, meaning it rarely made false alarms. The recall of 93.39% shows it was still able to identify most cancer cases, resulting in an F1 score of 94.95%. InceptionV3 also delivered good results with 94.12% accuracy and 98.03% precision, but its recall was slightly lower at 93.07%. The F1 score of 95.85 reflects a good balance between accuracy and completeness. Finally, EfficientNetV2 stood out with an exceptional accuracy of 98.11% and an incredibly high precision of 99.3%, meaning it made very few mistakes. The recall of 99.1% indicates it captured nearly all cancer cases, reflected in the outstanding F1 score of 99.23. This analysis highlights the potential of EfficientNetV2 for ovarian cancer diagnosis, where both accurate identification and avoiding missed cases are crucial.

Analysis revealed significant differences in how well the models classified ovarian cancer subtypes. EfficientNetV2 achieved the highest accuracy, 98.11%, meaning it correctly identified the most cancer classes. VGG19 had the lowest accuracy, 91.02%. In terms of precision, EfficientNetV2 again performed best at 99.3%, indicating it made the fewest mistakes when identifying cancer. VGG19 had the lowest precision 96.2%. When it comes to recall, EfficientNetV2 was also the leader at 99.1%, meaning it missed the fewest cancer cases. ResNet50 and InceptionV3 had identical recall scores. Finally, the F1 score combines precision and recall. EfficientNetV2 had the highest F1 score 99.23, showing a great balance between accuracy and completeness. VGG19 had the lowest F1 score, 93.18. Among the models scrutinized, EfficientNetV2 emerged as the clear standout, consistently delivering the highest accuracy, precision, and recall scores, culminating in an exceptional F1 score of 99.23.

Analysis of Variance

An evaluation of potential statistically significant differences between the models' classification performance metrics (accuracy, precision, recall, and F1 score) can be achieved through the utilization of statistical methods. One such method is the Analysis of Variance (ANOVA), specifically designed for the comparison of multiple groups concurrently. ANOVA facilitates the investigation of whether substantial disparities exist within the means of the various models' performance. The p-values generated by ANOVA serve as indicators for ascertaining the presence of meaningful variations amongst the models concerning each metric. When these p-values fall below a predetermined threshold for significance (e.g., 0.05), a conclusion can be drawn that statistically significant disparities are indeed present between the models.

Analysis of Variance (ANOVA) was conducted to assess potential differences among the models across all four performance metrics: Accuracy, Precision, Recall, and F1 Score. The p-value obtained for accuracy was $1.73e-03$, suggesting statistically significant distinctions exist between the models ($p < 0.05$). Similarly, the p-value for precision ($5.8e-03$) and F1 Score ($5e-03$) further confirm significant variations across the models. The p-value for recall was even lower ($4.2e-04$), highlighting a particularly noteworthy difference in the model's ability to capture true positive cases. The implemented statistical analysis revealed significant variations in performance between the models across all four evaluated metrics: Accuracy, Precision, Recall, and F1 Score. This highlights the importance of selecting an appropriate model, as the choice can significantly impact the effectiveness of classification performance.

Conclusion

An evaluation of fine-tuned deep-learning models designed for ovarian cancer subtype classification in histological images was undertaken in this study. Four established deep learning architectures including VGG19, ResNet50, InceptionV3, and EfficientNetV2 were employed, each supplemented with a bespoke fully connected layer for cancer subtype categorization. A rigorous performance assessment was conducted using a battery of metrics encompassing accuracy, precision, recall, and F1 score. This comprehensive analysis yielded valuable insights into the models' capacity for ovarian cancer subtype detection. Among the evaluated models, EfficientNetV2 emerged as the superior performer. Its exceptional and consistent results across all metrics underscored its efficacy in accurately classifying ovarian cancer subtypes. Notably, EfficientNetV2 achieved an accuracy of 98.11% and a precision of 99.3%, demonstrating its effectiveness in minimizing false positive classifications, a crucial aspect in cancer diagnosis. Furthermore, it attained a recall score of 1, signifying its ability to identify all cancerous tissue samples within the images. The model's overall performance was further solidified by an impressive F1 score of 99.23, indicative of a well-balanced trade-off between precision and recall.

Several limitations of the current approach warrant further expansion. First, the investigation predominantly employed established deep learning models (VGG19, ResNet50, Inception V3, EfficientNetV2). To address this, future research should incorporate transformers, a novel architecture demonstrating effectiveness in various deep learning tasks due to their attention mechanisms. Integration of transformers could be evaluated for potential improvements in capturing complex patterns within ovarian histology images. Additionally, for a more robust assessment of generalizability, the inclusion of a distinct ovarian cancer dataset in forthcoming experiments is crucial. This expansion would facilitate a more comprehensive evaluation of the model's performance across diverse data sources, ultimately enhancing understanding of its robustness and applicability beyond the training data.

Conflict of Interest

The authors imply no conflict of interest.

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