Deep Learning-based Histopathological Image Classification of Colorectal Cancer: A Brief Survey of Recent Trends

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ABSTRACT

Early diagnosis is beneficial for treating *Colorectal Cancer* (CRC) and can improve its curability. The traditional methods of CRC diagnosis generally rely on pathologists, but with the increasing number of CRC patients, manual diagnosis has many shortcomings. In recent years, *Deep Learning* (DL) has attracted wide attention in various fields. It has higher precision in many complex tasks than traditional machine learning techniques. In particular, DL is widely used in medical image classification, including histopathological images of colorectal cancer. This review summarizes multiple papers on DL for histopathological CRC image classification from 2014 to 2022. These papers discuss the task of deep neural networks and present their challenges and potential development directions for histopathological colorectal cancer image classification.

CCS CONCEPTS

• **General and reference**; • **Surveys and overviews**; • **Networks**; • **Network performance evaluation**; • **Applied computing**; • **Bioinformatics.**;

KEYWORDS

Histopathological image, Colorectal cancer, Deep learning, Deep neural network

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1 INTRODUCTION

CRC is a rapidly spreading cancer globally and ranks as the second and third most common cancer among males and females, respectively [3]. The rising incidence and mortality rates, as shown in Fig. 1 [14], are a cause for concern. Early diagnosis is essential for effective CRC treatment and improved chances of a cure [32][13][14]. Traditional CRC diagnosis relies on pathologists who manually examine processed histopathological images on slides through microscopes [26]. However, as the number of CRC cases increases, this method faces several challenges. Firstly, manual diagnosis can be influenced by subjective factors [21], impacting the accuracy of CRC analysis. Pathologists, despite their experience, may have varying observations of colorectal tissue, leading to inconsistent diagnoses. Secondly, there is a scarcity of qualified pathologists due to rigorous training requirements [35]. Manual CRC diagnosis is time-consuming and inconvenient. Additionally, the increasing CRC incidence and the limited number of pathologists have led to excessive workloads, potentially affecting diagnostic accuracy [38].

With the development of computer vision technology in recent years, automated analysis by computer vision has started to assist pathologists in improving diagnostic accuracy in a consistent and objective manner [16]. Meanwhile, DL has gained widespread attention in various fields due to its high accuracy in complex tasks compared to traditional machine learning technology [4]. Particularly in medical image classification, DL has been widely applied [38]. For instance, DL has been applied to breast cancer and glaucoma diagnosis [16]. Paper [33] proposes a *Convolutional Neural Network* (CNN)-based method to distinguish between normal and abnormal blood cell images for the treatment of patients with acute leukemia. Deep learning-based methods can improve the efficiency and accuracy of diagnosis and obtain objective results [15] by reducing errors caused by subjective factors of the pathologists. Many studies have demonstrated the applicability of deep learning in actual medical scenarios [6].

However, the number of existing reviews on histopathological image analysis of CRC is limited and often lacks comprehensive content. For instance, Work [3] aims to review *Artificial Intelligence* (AI) in CRC image classification but lacks a thorough analysis of deep learning and dataset introductions. Similarly, paper [1] briefly introduces DL-based image classification for colorectal lesions without delving into relevant datasets. Work [6] focuses on DL models for colon cancer region classification in sparsely

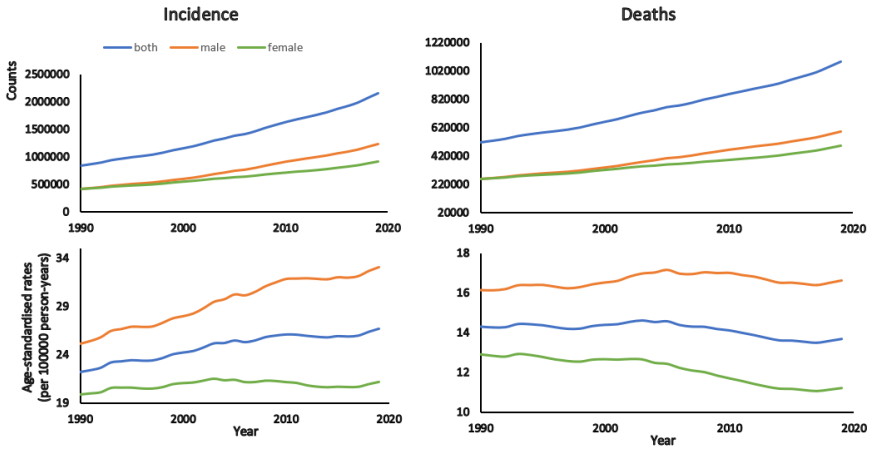

Figure 1: Global temporal patterns of colorectal cancer burden, 1990–2019

annotated histopathological data but lacks a well-structured organization. In work [22], colon cancer is divided into five classes, with a focus on deep-learning tasks, but it doesn't provide a detailed analysis of the network performances mentioned. In [32], gland segmentation and tumor classification in CRC are briefly mentioned, but the processes and networks used for histopathological image analysis of CRC are not discussed. In contrast, our survey provides a comprehensive analysis of neural network tasks, shedding new light on related research. We also introduce commonly used public datasets and offer a detailed description of the classification task. Additionally, we present a summary table summarizing relevant works.

To illustrate the recent trend and potential direction of histopathological image classification of CRC based on DL, we conduct this survey. Our study provides a summary of 42 academic papers published between 2014 and 2022, which collectively encompass a significant portion of the literature about the classification task for CRC. These papers are collected from popular academic datasets or search engines, which mainly include IEEE, Springer, Elsevier, and Google Scholar. We use "Colorectal Cancer Histopathology Image" AND ("analysis" OR "classification" OR "identification" OR "detection" OR "feature Extraction") AND ("Deep Learning" OR "Deep Neural Network" OR "Convolutional neural network" OR "Artificial Neural Networks") as the searching keywords. The structure of this paper is as follows: In Section 2, we briefly introduce the commonly used public datasets. In Section 3, We summarized the papers according to the classification task. In Section 4, the challenges and potential directions of CRC are talked about. Finally, in Section 5, the conclusion and future work of this paper is provided.

2 DATASETS

In this section, we introduce the commonly used public datasets at first. Then, the above-mentioned datasets are described. Datasets are critical in developing histopathological image classification of CRC technology. The image data capacity and quality in the datasets can directly affect the performance of the DL model. Through the investigation of relevant papers, the most widely used datasets are the Warwick-QU datasets [42][30](The Warwick-QU dataset also called GLAS challenge dataset [40] at some point), *the Kather CRC histology datasets* (KCHD) [39], *the Cancer Genome Atlas* (TCGA) dataset [29], and *the Colorectal Histology-Image Dataset* (COHID) [5]. The base information of these datasets is provided in Table 1.

2.1 Warwick-QU Datasets

The Warwick-QU dataset, about the field of colorectal cancer, was collected by a team of pathologists from the University Hospitals Coventry and Warwickshire in the United Kingdom. This dataset, which will be used in the GLAS Challenge, comprises 165 BMP format images with a resolution of 20 ×, obtained through a Zeiss MIRAX MIDI scanner with a pixel density of 0.62005 μm/pixel. The dataset is split into a training set, consisting of 37 benign and 48 malignant images, and a testing set, containing 37 benign and 43 malignant images.

2.2 Kather CRC Histology Datasets

KCHD comprise textures from human colorectal cancer histology images. It consists of two archives. The first, "Kathertexture2016imagetiles5000.zip" contains 5000 histology images, each at a resolution of 150 × 150 pixels (74 × 74 μm), representing eight distinct tissue types. This dataset is balanced with an equal number of images in each class. The second archive, "Kathertexture2016largerimages10.zip," contains ten larger histology images, each measuring 5000 × 5000 pixels, displaying a mix of multiple tissue types. All images in both archives are RGB with a pixel size of 0.495 μm, scanned at a 20 × magnification using an Aperio ScanScope. It's important to note that these histopathological specimens are anonymized images of human colorectal adenocarcinomas (primary tumors) preserved in formalin and embedded in paraffin.

2.3 TCGA Datasets

TCGA is a publicly accessible resource that offers extensive genomic and clinical information on various cancer types. Developed

Table 1: The base information of CRC datasets. For short, Image Number are abbreviated as No..

Dataset	No.	Format	Resolution
Warwick-QU datasets [40]	165	BMP	20× (0.62005 μm/pixel)
KCHD [39]	5000	TIFF	150×150
TCGA datasets [29]	——	BAM VCF TXT , etc	——
COHID [5]	36500	JPEG	224×224

through a collaborative initiative between *the National Cancer Institute* (NCI) and *the National Human Genome Research Institute* (NHGRI), TCGA involves the participation of numerous research institutions and investigators across the world. The dataset encompasses genomic data, including DNA sequencing, RNA expression, DNA methylation, and proteomic data, alongside clinical data on patient demographics, treatment history, and survival outcomes. Multiple cancer types, such as breast, lung, colon, and prostate cancers, are included in the TCGA dataset, which employs diverse formats of data, such as BAM, VCF, and TXT formats, etc. The distinct types of data are preserved in different formats.

2.4 The Colorectal Histology-Image Dataset

COHID aims to provide standardized, high-quality *Hematoxylin & Eosin* (H&E) stained *whole-slide images* (WSIs) of colorectal tissues for researchers and clinicians to develop and test algorithms for automated detection, diagnosis, and grading of colorectal cancer. The dataset comprises 160 H&E stained WSIs of colorectal tissue specimens, acquired at 40x magnification and available in SVS and TIFF formats. The images represent various disease stages and grades, including both normal and cancerous tissues, and come with corresponding clinical and pathological data, such as patient age, gender, disease stage, and histological grade.

3 HISTOPATHOLOGICAL CRC IMAGE CLASSIFICATION BASED ON DEEP LEARNING

An overview of CRC histopathological diagnosis based on DL is presented in this section. In this section, we provide a brief introduction to deep learning-based CRC histopathological diagnosis. Based on different classification methods, this section is divided into two parts: non-end-to-end methods and end-to-end methods. Representative methods are introduced in each part. Table 2 compares their characteristics, advantages, and disadvantages.

3.1 Non-End-To-End

Non-end-to-end approaches generally contain several components to make the prediction. In the CRC pathology image classification task, non-end-to-end approaches usually consist of three steps. The three steps are preprocessing, feature extraction, and classification. The details are as follows.

Preprocessing. The quality of pathological images significantly impacts subsequent research and analysis. Raw image data often contains inherent noise, missing values, inconsistencies, and errors. Image preprocessing, a crucial step in image analysis, involves operations and transformations applied to images before use. It aims to remove irrelevant information, restore meaningful data, enhance pathology-related features, and reduce data redundancy, ultimately improving the reliability of processes like feature extraction, image segmentation, classification, and recognition [2].

In the context of CRC histopathologic images, preprocessing includes denoising, background removal, image enhancement, and contrast adjustment. Paper [39] employs various enhanced techniques, such as Random Translation, zooming, rotation modifications, and random horizontal flipping, to optimize runtime data. These methods prevent model overfitting and enhance generalization, resulting in exceptional performance.

Additionally, Paper [36] introduces an innovative image translation approach to address data imbalances in a dataset of colorectal polyp histopathology images. This approach mitigates biases and enhances analysis robustness, ultimately improving research outcomes.

Feature extraction. Feature extraction is crucial in analyzing CRC histopathologic images. CNNs, as demonstrated in Paper [34], can automatically extract features from images. In this study, an *Artificial Neural Network* (ANN) is used to classify eight classes of CRC tissue image patches, with 532 multi-level pathological histological features extracted using visual descriptors like local binary patterns, wavelet transform, and Gabor filters.

Paper [10] introduces various feature extraction methods for normalized CRC images, particularly useful for distinguishing between epithelium and stroma in CRC histopathology images, as well as for feature selection and analysis. Textural features, as detailed in Paper [10], employ a perception-based approach to differentiate between epithelium and stroma in CRC images. Additionally, Paper [4] presents a novel method that combines sample entropy with multiscale, multi-dimensional, and fuzzy strategies to quantify color images. This approach involves quantification from windows of different sizes and tolerance variations, aiming to define the similarity of patterns between pixels. Furthermore, Paper [9] contributes to the automatic classification of microscopic colonic images by utilizing a 2-D wavelet transform for feature extraction and a neural network for classification, specifically categorizing images into normal, cancerous, or adenomatous polyp classes.

Classification. Non-end-to-end classification involves several components. For example, R-CNN entails training three modules: CNN feature extraction, SVM classification, and border correction. In paper [11], a technique for classifying colon cancer from immunohistochemical staining images is proposed. It employs three methods for extracting vital image features: gray-level co-occurrence matrix, local binary pattern, and histogram-based features. Stacking integration techniques create models for cancer classification,

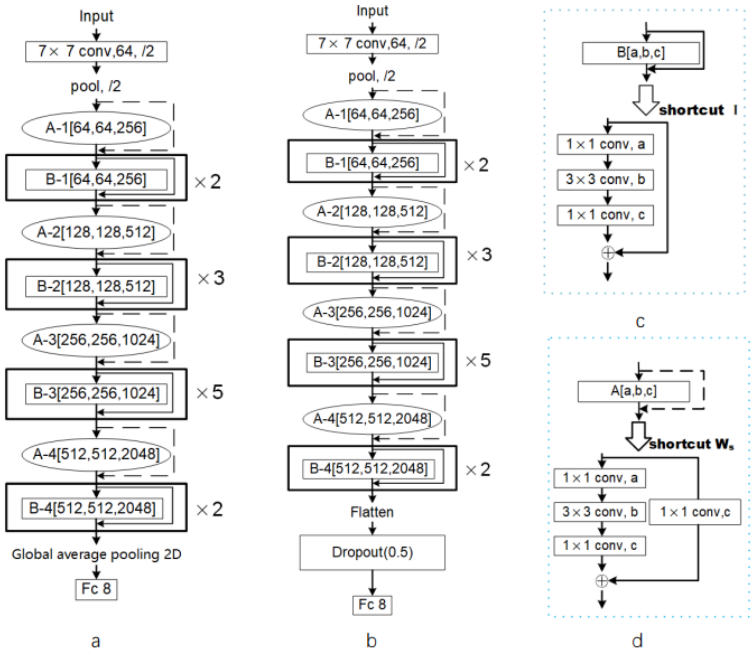

Figure 2: (a) The original ResNet-50, (b) the proposed ResNet50-fla-drop, (c) building block B consists of three stacked layers with a shortcut of identity mapping, (d) building block A consists of three stacked layers with a shortcut of linear projection mapping.

including neural networks, SVMs, and logistic regression. An automated system for accurately classifying CRC tissue regions can enhance diagnosis and reduce clinical workload. Tissue classification is challenging due to complex morphological and textural features in histopathological images.

In paper [34], an artificial neural network and SVM classify eight classes of CRC tissue patches. Paper [9] uses 2-D wavelet transforms and neural networks for colonic histopathological image classification. Parallelization across multiple GPUs offers advantages in handling memory limitations with larger batch sizes. Work [7] suggests using three GTX-1080 graph processing units for ResNet model parallelization.

3.2 End-To-End

End-to-end learning assigns the task of feature extraction to the model to do, directly input the raw data or some micro-preprocessed data, and let the model conduct feature extraction by itself. By reducing the manual preprocessing and subsequent processing, the model can be made from the original input to the final output as much as possible. It gives the model more space that can be automatically adjusted according to the data and increases the model's overall fit. In the image domain, the CNN is a very typical end-to-end architecture. In this section, we will mainly present CNN as well as some innovative networks.

ResNet. ResNet is known for its efficient training process, displaying significant performance improvements in both training and generalization errors. It offers various depths, including ResNet-18, ResNet-34, ResNet-50, ResNet-101, and ResNet-152. In the realm of target detection, Paper [41] conducts experiments with multiple CNN architectures, including AlexNet, VGG, and ResNet, finding that ResNet excels in patch-based classification.

At the heart of ResNet lies the structured residual block, which employs skip connections to directly link the input to the weight layer. This approach accelerates learning without increasing computational complexity, as it involves a simple additive operation. Consequently, papers [16][28][31][24][19], and [25] utilize a ResNet model with 50 layers. Specifically, Paper [16] applies ResNet, DenseNet, and Inception V3 models for classifying colorectal tissues, with ResNet demonstrating exceptional performance in data feature extraction. Paper [28] employs the ResNet-50 model for classifying CRC histopathological images and enhances accuracy through transfer learning and fine-tuning techniques.

In Paper [12], a DL approach based on the ResNet-18 architecture is proposed for the classification of histopathological tissues and images based on a pre-trained CNN.

Additionally, Paper [18] introduces a modified residual network, ResNet-50-fla-drop(see Fig. 2 (a)), which differs from ResNet-50 primarily in the layers near the output end. ResNet-50-fla-drop omits global average pooling layers in favor of flat layers, preserving more features for the subsequent 8-way fully connected layer (Fc-8). It also incorporates a dropout rate (0.5 dropout rate) before the fully connected layer to mitigate overfitting. Fig. 2(c) and Fig. 2 (d) show two types of building blocks—blocks A and B used in ResNet. Comparative experiments between the original ResNet-50 and the modified ResNet-50-fla-drop reveal that ResNet-50-fla-drop achieves superior classification accuracy.

DenseNet. DenseNet continuously connects each layer to the input of the next layer through the feature graph [16]. While ResNet uses a similar technique, the greatest difference is that ResNet has a structure that adds feature maps, whereas DenseNet has a stacked structure. The structure can stack information from the preceding layer and efficiently transfer it to the subsequent layers, thus improving the vanishing gradient and strengthening feature propagation and feature reuse without relearning the same features, thereby reducing the number of parameters. Paper [21] applies transfer learning from the CNN architecture. Moreover, it modifies the structure of the CNN to extract features from images and input them into famous machine learning methods: Naive Bayes, Multilayer Perceptron, k-Nearest Neighbors, Random Forest, and Support Vector Machine. This method combines 18 feature extractors with six conventional classifiers for 108 supervised image classification experiments. The best result of the experiment was the DenseNet169 with Support Vector Machine. In paper [16] and paper [25], the DenseNet-121 model is proposed. Its fully connected layer is cut and replaced with a dense layer containing 1024 neurons with a ReLU activation function and an output layer containing eight neurons with a softmax activation function.

Inception. Inception V1 uses the Inception module to address gradient vanishing and overfitting [16]. As network depth increases, the number of parameters and computational demands grow substantially. In order to address these challenges, Inception V2 was introduced, offering solutions that reduce computational costs through the implementation of three key modules. These modules involve the replacement of 5×5 convolutions with two 3×3 convolution operations, the substitution of 3×3 convolutions with 1×3 and 3×1 convolutions, and the widening of the Inception module to overcome representational bottlenecks. While Inception V3 shares architectural similarities with Inception V2, notable modifications were implemented, such as replacing the original 7×7 convolutions with three 3×3 convolutions, updating the optimizer to RMSProp, and introducing batch normalization in the final fully connected layer, along with label smoothing.

Paper [35] introduces an innovative AI approach based on weakly labeled supervised deep learning for CRC diagnosis, marking the first general clinical application in this context. This approach utilizes the Inception V3 architecture with weight initialization through transfer learning. Supervised learning of weak markers enables the training of diverse datasets without precise object-level labeling. Transfer learning, a highly effective and efficient DL technique for image classification, leverages previously acquired knowledge from available images for medical image classification. This study holds significant practical value in enhancing the accuracy and efficiency of colorectal cancer diagnosis and treatment.

VGG. In the VGG models, the most widely used structure is the VGG-16 structure. Paper [25] proposes a VGG-like model with 12 convolution layers and 2 fully connected layers, as well as a VGG-16 model with 13 convolutional layers and 3 fully connected layers. The analysis of histological samples is critical for the early diagnosis of CRC. Conventional visual assessment is time-consuming and highly unreliable due to the subjective nature of the evaluation. On the other hand, automated analysis is extremely challenging because of the variability in the architectural and coloring characteristics of the histological images. In paper [5], a DL technique based on CNN is proposed to distinguish healthy tissue and benign lesions.

AlexNet. AlexNet is a pre-trained convolution neural network. Its architecture contains eight layers and classifies objects into 1000 classes. The input is a 227×227 pixel image with 32-bit RGB color space. In paper [23], the last layer of the network is improved, and the size of the original image is adjusted to facilitate the classification of objects in the CRC datasets. Paper [25] cuts and replaces the full-connection layer with a dense layer containing 1024 neurons with ReLU activation functions and an output layer containing eight neurons with softmax activation functions. The authors compare their approach with other networks in terms of performance and report good results.

Other Networks. This section provides a brief overview of lesser-known network architectures. For instance, MobileNet is a lightweight network with only 3 million parameters, while the initial space network employs separable convolution to significantly reduce computational complexity. In Paper [27], MobileNet demonstrates superior performance and the highest average accuracy among various classifiers.

In Paper [8], constraints pertaining to the training data for CRC are effectively mitigated through the implementation of a conditional sliding window algorithm. Notably, this algorithm exhibits versatility by extending its applicability to the generation of diverse histopathological data. The proposed CNN 7-5-7 architectural configuration surpasses the performance of the original data model, offering stable performance in distinguishing between benign and malignant classes of CRC.

Furthermore, Paper [37] introduces a new *Deep Convolutional Neural Network* (DCNN) based model for the segmentation and classification of CRC *Immunohistochemistry* (IHC) images. The DCNN architecture comprises alternating convolutional and max-pooling layers, followed by fully connected layers and a final classification layer. These layers work in tandem to extract and combine relevant image features from training samples.

The Growing Hierarchical Neural Networks (GHNN) proposed in paper [20] proposedcan autonomously detect local features without the need for advanced feature extraction techniques, and in addition, its dynamic data-dependent adjustment of neuronal counting and localization enhances generalization, providing transparent and compact knowledge representation.

4 CHALLENGE AND POTENTIAL DIRECTION

A substantial volume of data is necessary for training a CNN in order to avoid overfitting caused by small datasets with limited variability. Inaccurate predictions of new data would result from this overfitting.

Moreover, the accessibility of histopathological medical data presents a formidable challenge, as obtaining such data without the requisite ethical permissions remains a complex endeavor. This ethical hurdle underscores the importance of adhering to ethical guidelines in the acquisition of medical data, emphasizing the need for stringent ethical review and compliance in research.

Table 2: An overview of the characteristics, advantages, and disadvantages of an end-to-end and non-end-to-end approach

aspect	Non-End-To-End Method	End-To-End Method
Features	Consists of preprocessing, feature extraction, classification stages.	Models extract features directly from raw or preprocessed data.
Advantages	- Modular approach allows flexibility and specific tuning at each stage. - Can address image quality issues through preprocessing. - Well-established techniques for complex image features.	- Streamlined process with potential for better integration. - Can learn hierarchical features directly from data. - Often leads to high accuracy with deep models.
Disadvantages	- Can be more complex and time-consuming due to multiple stages. - Subject to challenges related to the consistency of preprocessing. - Potential for error accumulation at each stage.	- May require larger datasets and computational resources. - Limited transparency in feature extraction for some models. - Less interpretability compared to traditional methods.

Table 3: The summary of representative methods. For short, reference, network, accuracy, precision, dice similarity index ,$F1$-score value, average accuracy, class balanced accuracy, geometric average of recall, balanced accuracy, silhouette, Davis-Bouldin, stability, 95%confidence interval, Matthews correlation coefficient, intersection over union, the surgical pathology files of the Medical Center Manila Hospital, Netherlands Cancer Institute dataset, and Vancouver General Hospital dataset are abbreviated as Ref, Net, Ac, Pre, Dice, $F1$, AvAc, CBA, MAvG, BAC, Sil, Dav, SD, 95%CI, MCC, IoU, MCMHD, NKI Dataset, and VGH Dataset.

Ref.	Net	Dataset	Performance(%)
[5]	CNN	COHID	Ac>96
[6]	CNN	KCHD	Ac=96.68
		Warwick-QU	
[9]	ANN	MCMHD	Ac=91.11
[11]	ANN	——	Ac=88.5
[12]	ResNet-18	KCHD	Ac=88.5
[13]	DenseNet121	DigestPath	Ac=97.07±1.56 Dice=82.74±1.77 $F1$=82.79±1.79
[14]	DenseNet	TCGA	Ac=97.34
[17]	MobileNet	KCHD	AvAc=91.52 CBA=0.8898 MAvG=90.50
[18]	ResNet-50-fla-drop	KCHD	Ac=94.4
[19]	ResNet-50	KCHD	BAC=85±0.6 Sil=0.37±0.02 Dav=1.41±0.08
[21]	DenseNet169	KCHD	Ac=92.083 $F1$=92.17
[23]	AlexNet	Histo_Image-357	AcAc=89.53 SD=0.28 95%CI=(89.10,90.59)
[24]	ResNet-50	Colorectal Data	Ac=95.7 Pre=86.8 Recall=92.2 $F1$=88
		KVASIR Dataset	
[27]	MobileNet	CRC Extended CRC	AvAc=92.78
[28]	ResNet-50	KCHD	Ac=97.7
[34]	ANN	KCHD	Ac=95.32±2.16
[35]	Inception-V3	TCGA	Ac=97.98
		NCT-CRC-HE-100K	Ac=96.07
[37]	DCNN	NKI Dataset	Ac=85 MCC=86 $F1$=85
		VGH Dataset	
[38]	CN	NKI Dataset	Ac=90.34 $F1$=90.07
		VGH Dataset	Ac=94.30 $F1$=93.66
[39]	CCT	KCHD	Ac=94.75 Pre=94.8 Recall=94.75 $F1$=94.74
[40]	CNN	TCGA	Ac=94.6
[42]	CNN	Warwick-QU	Ac=89.62 Pre=94.23 $F1$=90.46 IoU=82.58

In the context of classification tasks, data imbalance denotes a circumstance where there exists a significant discrepancy in the number of instances between the minority class (comprising fewer observations) and the majority class (comprising more observations). This imbalance poses a substantial impediment to conventional machine learning algorithms, often leading to skewed predictive outcomes.

Similarly, when examining the dataset of colorectal histopathological images, one observes a notable imbalance in the distribution of data. These images exhibit a spectrum of complexities, ranging from diverse structural patterns and heterogeneous cellular compositions to variability, damage, and substantial variations in scale and resolution. These multifaceted characteristics collectively render the classification of such images an intricate and challenging task, necessitating advanced techniques and model adaptation to address their intricate nature effectively.

5 CONCLUSION

This succinct survey is dedicated to the exploration of DL technology's applications in the classification of histopathological images of CRC. Our study commences with an in-depth investigation of the publicly available datasets commonly utilized in this domain. Following this, we conduct an analysis of the pertinent literature, encompassing both non-end-to-end and end-to-end classification methodologies. In addition to this, we propose potential avenues for addressing existing challenges and advancing the state of research in this field.

The successful integration of deep neural networks in the realm of CRC histopathological image classification critically depends on the availability of more comprehensive and realistic datasets, as well as the development of effective solutions to mitigate issues related to data imbalance.

For the reader's convenience, we have thoughtfully included a comprehensive summary table Table 3) that provides swift access to crucial information pertaining to each reviewed paper. This review effectively underscores the notable advantages of DL-based approaches in the context of histopathological image classification for CRC, surpassing traditional manual diagnostic techniques. Looking ahead, our future plans include an extensive exploration of additional literature and the exploration of novel DL techniques in the context of CRC, with the aim of providing a comprehensive and up-to-date review of this evolving field.

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