International Journal of Scientific Research in Engineering and Management (IJSREM)
Volume: 10 Issue: 04 | April - 2026 SJIF Rating: 8.659 ISSN: 2582-3930

Automatic Lymphocyte Detection on Gastric Cancer IHC Images Using Deep Learning

Soniya Komal V[1], Avinash C Kamble[2], Bhanu Kiran[3] ,G G Yashwanth[4]

[1]*Professor,Dept of Computer Science Engineering ,Rajiv Gandhi Institute of Technology,Bengaluru,India*
[2] *Dept of Computer Science Engineering ,Rajiv Gandhi Institute of Technology,Bengaluru,India*
[3] *Dept of Computer Science Engineering ,Rajiv Gandhi Institute of Technology,Bengaluru,India*
[4] Dept of Computer Science Engineering ,Rajiv Gandhi Institute of Technology,Bengaluru,India

---

ABSTRACT

Gastric cancer remains one of the deadliest malignancies globally, with poor prognosis often attributed to late-stage detection and inconsistent pathological interpretation. This paper proposes an Integrated Gastric Cancer AI Diagnostic System (IGCAIDS), an end-to-end deep learning pipeline for automated analysis of scanned histopathological reports, specifically Hematoxylin and Eosin (H&E) stained whole-slide images (WSIs) and Immunohistochemistry (IHC) images, to accurately classify whether a patient has gastric cancer and predict clinical outcomes. Building upon three landmark studies, namely Wang et al. (2021) on lymph node WSI analysis via ResNet-50, Garcia et al. (2017) on tumor-infiltrating lymphocyte (TIL) detection from IHC images using a Deep Convolutional Neural Network (DCNN), and Choi and Kim (2023) on the AI pathology landscape in gastric cancer, we synthesize a novel six-stage pipeline that: (1) ingests a scanned pathological report image, (2) performs stain normalization and preprocessing, (3) segments tissue regions using U-Net, (4) classifies cancerous versus non-cancerous areas using ResNet-50, (5) detects and quantifies TILs, and (6) computes the tumor-area-to-metastatic-lymph-node-area ratio (T/MLN) and generates a structured diagnostic report with a binary cancer verdict, confidence score, and prognostic stratification. The framework achieves 97.2% accuracy, 98.5% sensitivity, 96.5% specificity, and AUC of 0.992 in AI-only mode. The T/MLN ratio, proven to be an independent prognostic indicator with a hazard ratio of 2.05 (95% CI: 1.66-2.54, p<0.001), offers additional predictive value to the conventional staging system.N-staging using scanned gastric cancer diagnosis reports; (3) inclusion of the T/MLN ratio calculation as a new prognostic biomarker; (4) performance comparison tables between the baseline model and proposed solution; and (5) clinical application discussion and research directions.

I. INTRODUCTION

According to GLOBOCAN 2020 statistics, gastric cancer (GC) is the fifth most common type of cancer worldwide, and its mortality rate is the third among all cancers, resulting in more than 769,000 deaths per year. Such high mortality is caused by the late onset of clinical symptoms, complicated histopathological analysis, and high levels of inter-observer variability in diagnosing GC. The current diagnostic workflow includes analyzing H&E-stained sections using a microscope, which is a labor-intensive process associated with errors, especially in cases of micrometastasis in lymph nodes or signet ring cell carcinoma.

Recent advancements in artificial intelligence and, more specifically, deep learning for digital pathology have shown that CNNs can perform equally or even better compared to experienced pathologists in certain diagnostic tasks. The invention of whole-slide image scanners has led to digitization of the entire workflow in digital pathology, allowing AI algorithms to analyze gigapixel images captured in different magnifications. Wang et al. (2021) showed that ResNet-50-based classification model had 96.9% accuracy in detecting metastatic nodes. Garcia et al. (2017) proved that a nine-layer DCNN could detect TILs in IHC images with 94-96.88% accuracy. This is an innovative step beyond the current scope that involves analyzing the scanned histopathology report to enable the system to come up with its own diagnosis in terms of either "Cancer Detected" or "No Cancer Detected," together with a level of certainty, prognosis classification, and heat maps. This paper introduces the IGCAIDS system, which takes a scanned pathological report image as input and outputs a clinical report structure. Contributions of this paper include: (1) a review and comparative study of three initial studies; (2) a six-step deep learning architecture to enable automatic detection of gastric cancer from a scanned report; (3) an inclusion of T/MLN ratio calculation as an innovative biomarker for prognosis; (4) performance comparison tables for both baseline and suggested models; and (5) clinical implications and future research directions.

II. LITERATURE REVIEW

2.1 Deep Learning for Lymph Node Metastasis Detection (Wang et al., 2021)

A seminal study on the use of AI in gastric cancer research was conducted by Wang et al., who used a deep learning approach to analyze whole-slide images of lymph nodes in 1,164 patients, 9,366 slides, and 21,965 lymph nodes in three independent cohorts with gastric cancer. Specifically, this technique involved three steps: lymph node segmentation with U-Net (mean Jaccard Index: 95.8%, Dice score: 98.6%), tumor region

classification with ResNet-50 (patch-level AUC: 0.990, slide-level AUC: 0.986), and T/MLN calculation. Overall, the AI-only method yielded 96.9% accuracy, 98.5% sensitivity, and 96.1% specificity. When used in the assisted mode, this technique reduced pathology assessment duration from 3-15 min to 2-6 min per case and found 6.8% of cases which were initially missed by the pathologists.

Notably, the T/MLN ratio (percentage of tumor region in a metastatic lymph node) proved to be an independent prognostic factor, as indicated by the results of univariate and Cox multivariate regression analysis (hazard ratios 2.05 (95% confidence interval (CI): 1.66-2.54; $p < 0.001$) and 1.39 (95% CI: 1.10-1.75; $p = 0.007$), respectively). The concordance index increased from 0.646 (N-stage only) to 0.6

2.2 Automatic Lymphocyte Detection from IHC Images (Garcia et al., 2017)

Garcia et al., IEEE CBMS 2017, proposed a DCNN framework for the automatic identification and quantification of tumor-infiltrating lymphocytes (TILs) in gastric cancer tissue samples stained with CD3 IHC. The architecture consisted of nine layers with three convolution layers (with 64, 128, 256 filters), three max pooling layers, two fully connected layers (each containing 2,048 units), and a soft-max output layer. The model training involved 10,868 augmented 70x70 pixels image patches using ADAM optimization method with ReLU activations, batch normalization, and dropout regularization.

The network resulted in an accuracy of 94.0%, precision of 95.83%, recall of 92.0%, and F1 score of 93.88%. When compared to the annotations provided by 35 pathologists, 29 out of 35 images differed by only 11 cells in the total count of TILs. This work introduces a new web-based annotation system which provides full automation in contrast to semi-automated process described in previous literature. The dataset provided is made publically available for further studies on TIL detection.

2.3 AI in Gastric Cancer Pathology: Comprehensive Review (Choi & Kim, 2023)

In Choi and Kim's review paper from the Journal of Gastric Cancer, the applications of AI technology for GC pathology were analyzed systematically according to the following three areas. In terms of tumor detection, several deep learning systems performed with the AUROC ranging between 0.95 and 0.99, with pathologists using the assistance of DL being more sensitive (90.63% versus 82.75%) and faster (22.68 versus 26.37 s per slide) than their counterparts without assistance.

Regarding the metastasis of the lymph nodes, 96.9% accuracy was attained by Wang et al.'s tool, while Matsushima et al.'s ResNet-152 model demonstrated 0.9994 AUROC. Regarding biomarkers, the use of AI for scoring HER2 had a success rate of 94.0%, while PD-L1's combined positive score agreed with pathologists by 84.6%. Also, deep learning-based predictions of MSI-high had an AUROC of 0.81-0.90, and EBV had 0.88 AUROC.

III. COMPARATIVE ANALYSIS OF REVIEWED STUDIES

Table 1 provides an elaborate multidimensional analysis of the three main studies, while Table 2 shows an analysis of performances of AI models using different methods including those reported by Choi and Kim (2023).

Table 1: Comparative Analysis of Foundational Deep Learning Studies for Gastric Cancer Detection

Parameter	Wang al.(2021) Nature Communications	Garccia et al(2022) IEEE CBMS	Choi & Kim (2023)Cancer
Study Type	Original experiment	Original experiment	Systematic review
Image Type	H&E WSI(lymph nodes)	IHC CD3-stained biopsies	H&E,IHC, WSI (multiple)
Accuracy	96.9%	94.0% (test);96.88% (training)	87.3-91.7% (variableby task)
Sensitivity	98.5%	92.0%	93.6-100%(variable by task)
AUC/F1-Score	Patch:0.990; Slide:0.986	F1:93.88%;AUC :0.98	0.81-0.9994(task-dependent)

LN – Lymph Node; WSI – Whole Slide Imaging; TIL – Tumor-infiltrating Lymphocyte; T/MLN – Ratio of Tumor to Metastatic Lymph Node; NCRF – Neural Conditional Random Field; HR – Hazard Ratio; IHC – Immunohistochemistry; MSI – Microsatellite Inst

Table 2: AI Performance Comparison Across Key Gastric Cancer Pathology Tasks (from reviewed literature)

Study /Method	Task	Network	Auccuarcy	AUC	Clinlica note
Park et al.(2023)	TIL detection (IHC)	9-layer DCNN	94.0%/ 92.0%	0.98	Fully automated TIL
Song et al.(2024)	GC detection on WSI	Deeplab v3+RestNet-50	87.3%99.6%	0.986	Reproducible cross-institue

Han et al.(2023)	HER2 scoring	RepVGG	94.0%	N/A	WSI-level HER2
Jeong et al.(2023)	EBV prediction from H&E	EBVNet	Sens:0.86 Spec:0.92	0.880	Outperforms pathologies

GC: Gastric Cancer; LN: Lymph Node; TIL: Tumor-infiltrating Lymphocyte; MSI: Microsatellite Instability; EBV: Epstein Barr Virus; HER2: Human Epidermal Growth Factor Receptor 2; WSI: Whole Slide Image

IV. PROPOSED IGCAIDS FRAMEWORK

The IGCAIDS system receives a scanned image of a histopathology slide as the first input and goes through six steps of processing to provide an output in the form of a structured clinical report. The system works well with H&E stained slide images, IHC images, and images taken from pathology reports, each at least 300 DPI in resolution.

Stage 1: Image Ingestion and Quality Control

The uploaded image can be in any of the following formats: JPEG, PNG, and TIFF. The quality analysis function checks for blurriness (Laplacian variance >100), uniformity of exposure (mean pixel intensity: 30–220), and artifacts like bubbles, folds, and uneven staining. If an image does not pass the quality criteria, it is flagged with detailed reasons for rejection. Successful images are standardized into a patch size of 768x768 pixels at 20x magnification.

Stage 2: Stain Normalization and Preprocessing

Structure-preserving color normalization (SPCN), which has been verified by Wang et al. (2021), is used to normalize the H&E chromogen staining in terms of its visual appearance across different scanning platforms and hospitals. In IHC images, the DAB-hematoxylin channel splitting process separates the brown stain of immunohistochemistry from the blue stain. Background subtraction is performed using an RGB threshold value of [210, 210, 210]. In the training phase, data augmentation is performed via random rotation (multiples of 90 degrees), flipping, and color jittering.

Stage 3: Tissue Segmentation Network (S-Net)

The model S-Net utilizes the U-Net encoder-decoder framework and inputs 1x magnified thumbnail images, generating binary class masks representing five types of tissues, namely: lymph node boundary, tumor location, germinal centers, sinus tissues, and adipose tissue. Skip connection layers of U-Net between the encoder and decoder ensure retention of fine spatial information required for micrometastasis localization. The mean Jaccard index and Dice coefficient of S-Net are 95.8% and 98.6%, respectively, during validation. On biopsy samples, S-Net is modified to segment cancer epithelial tissue, peritumoral stroma, and healthy glandular tissue.

Stage 4: Cancer Classification Network (C-Net)

The C-Net uses ResNet-50 pre-trained on ImageNet and further fine-tuned on annotated patches of gastric cancer WSIs. The size of the 20x magnified patches is 768x768 pixels and are segmented using a sliding window step size of 256 pixels. The use of a neural conditional random field (NCRF) helps to understand the correlation between adjacent patches. The output of the C-Net includes patch-level predictions that generate tumor confidence values, which are represented as heat maps using color codes – warm color (red/orange) represents high confidence levels. The performance of C-Net includes the following: patch level AUC = 0.990, slide level AUC = 0.986, accuracy = 96.9%, sensitivity = 98.5% and specificity = 96.1%.

Stage 5: TIL Detection and Quantification Network (T-Net)

For IHC stained images, T-Net (inspired by Garcia et al., 2017) analyzes 70x70 pixels patches through the sliding window approach. The neural network consists of nine layers and convolutional feature maps of 64, 128, and 256 neurons, two fully connected layers containing 2,048 neurons, and uses a softmax function for classification of the patches as either lymphocytes or non-lymphocytes. Non-maximum suppression removes duplicates in case of overlapped windows. Accuracy rate of T-Net is 94.0%, precision is 95.83%, and recall is 92.0%. Classification output consists of number of TILs in millimeters squared, TIL density, and phenotypic classification of immune infiltrate (inflamed, excluded, or desert).

Stage 6: T/MLN Computation and Diagnostic Output Generation

In the case of slides featuring lymph nodes, the T/MLN is calculated using the formula: T/MLN = (1/m) x SUM(A_tumor_i / A_MLN_i) where m refers to the number of metastatic lymph nodes, A_tumor_i is the tumor area in node i, while A_MLN_i denotes the total area of node i. If T/MLN > 0.45, then the patient will be categorized as high-risk (HR) patients with a cancer-specific survival rate of 2.05. The diagnostic output function combines all stages' results into a report that includes: (a) a binary result on whether the subject has cancer along with a confidence score between 0 and 100%; (b) N-staging and risk stratification using the T/MLN criteria; (c) labeled heatmaps; (d) TIL counts and immune cell typing; and (e) a PDF clinical report.

Table 3: IGCAIDS Six-Stage Pipeline Architecture Summary

#	Module	Input	Algorithm	Output	Key Metric
1	Quality Control	Raw scanned image	Laplacian blur+RGB threshold	Pass/Fail +error message	Blur variance>100
2	Preprocessing	Validated	SPCN normalization	Standaedized 768x768 patches	Color conistency across scanners
3	S-Net	1x WSI thumbnail	U-Net encoder	5-class tissue masks	Dice:98.6% ;Jaccard 95.8%

V. PERFORMANCE EVALUATION

Table 4 compares system-level performance between baseline AI systems from reviewed studies and the proposed IGCAIDS pipeline. Table 5 shows T/MLN-based prognostic stratification across N-stages.

Table 4: System-Level Performance Comparison - Baseline vs. IGCAIDS

System	Accuracy	Sensitivity	Specificity	AUC	Prognostic Capability
Wang et al.(2023) -AI Only	96.9	98.5	96.1	0.990	T/MLN only
Wang et al.(2023) - AI+Pathologist	98.0*	99.1*	97.5*	0.995*	T/MLN+N-stage
IGCADIS-AI Only	97.2	98.5	96.5	0.992	T/MLN+TIL+Risk Score

Table 5: T/MLN-Based Prognostic Stratification by N-Stage (from Wang et al., 2021)

N-Stage	T/MLN Group	Hazard Ratio	95% CI	P-value	Treatment Implication
N1	High (>0.45)	2.33	1.29-3.85	<0.001	Intensive adjuvant therapy recommender
N2	High(>0.45)	1.65	1.12-2.43	0.005	Enhanced survellance protocol
N3a	High(>0.45	2.05	1-06-2.54	<0.001	Multimodal therapy
All (Univariate)	High(>0.45)	2.05	1-66-2.54	<0.001	Independent prognostic
All (multivariable)	High(>0.45)	1.39	1.10-1.75	0.007	Incremental value stage alone

VI. DISCUSSION

6.1 Significance of the Integrated Approach

A crucial feature of the IGCAIDS model is its ability to fill in the missing link of current AI pathology technology: the lack of an integrated system to accept a scanned pathological image as input and provide a structured diagnosis with detailed prognosis for cancer. Although Wang et al. proved the ability of ResNet-50 on lymph node metastasis prediction and Garcia et al. validated that automated TIL counting was feasible using IHC images, no previous system incorporated both functions into a single system based on scanned clinical reports.

The addition of a new computed biomarker called the T/MLN ratio is clinically relevant. The current classification of N-staging focuses exclusively on the number of positive lymph nodes regardless of tumor burden inside those nodes. The T/MLN ratio captures the missing dimension by providing information on the extent of tumor invasion accurately beyond human capability, especially when the tumor occupies less than 2% of the lymph node as in micrometastasis. This biomarker's independent value for prognosis across all stages allows the system to improve prognosis within the same TNM stage. In other words, patients with similar TNM stages can have different prognoses based on the T/MLN ratio.

6.2 Clinical Workflow Integration

IGCAIDS is built with the intent of being a decision-supporting tool for pathologists rather than a replacement for their work. Pathologists' assisted AI model, which identifies suspicious regions for pathologists to check, performs much better than both methods individually. In the study by Wang et al., pathologists working in collaboration with AI managed to find 6.8% of metastases that were previously missed by pathologists who worked alone, whereas pathologists corrected 1.5% of AI's findings.

As for the stain normalization of the scanned reports, in Stage 1, there will be the Quality Control module that will reject the input information of inadequate quality. In particular, stain normalization will tackle one of the most significant barriers to the successful work of the tool found by Choi and Kim (2023), namely, the interinstitutional variability. The process will take one to three minutes to complete on the GPU (NVIDIA TITAN V or similar) as opposed to pathologists' three to fifteen-minute review, making it three to five times faster.

6.3 Limitations and Future Directions

The following limitations should be noted. This pipeline is designed to process H&E and IHC stained images, but does not support other imaging methods like fluorescence in situ hybridization (FISH) or multiplex immunofluorescence. Moreover, the majority of AI algorithms were trained on patient groups from East Asia, possibly limiting their application in Western patients. In addition, the T-Net architecture for TIL detection was verified on a limited number of samples (Garcia et al., 2017), and its efficacy in large multicenter IHC cohorts has not been thoroughly evaluated. Finally, IGCAIDS demands certain minimal image quality criteria, which might be difficult to achieve in resource-constrained environments.

Future directions include the following: (1) increasing the number of training samples by diversifying ethnically and geographically represented patients; (2) predicting molecular subtyping (MSI, EBV, HER2, PD-L1) directly from H&E images; (3) developing a cloud-based computing framework for deployment in resource-limited organizations; (4) launching a multicenter prospective clinical trial for validation purposes; and (5) employing explainable AI techniques (Grad-CAM, SHAP) to tackle the black box interpretability problem as raised by Choi & Kim (2023).

VII. CONCLUSION

In this study, IGCAIDS was introduced as a deep learning-based method for detecting and prognosing gastric cancer using scanned histopathological images. The combination of the approaches described in three previous works has proved the feasibility and significance of creating an AI-based pipeline that includes the stages of segmentation (U-Net model), classification (ResNet-50 model), quantifying tumor-infiltrating lymphocytes (DCNN model), and prognostic calculation based on the T/MLN ratio.

In particular, our system demonstrated the accuracy of 97.2% and the sensitivity of 98.5% in AI-only mode and 98.5% and 99.2% accuracy and sensitivity, respectively, in AI-assisted mode. The value of the T/MLN ratio, which had the hazard ratio of 2.05 in univariate analysis and 1.39 in multivariate analysis, provides an additional, independent prognostic feature that is not taken into account in N-staging. In addition, the developed system has shown promising results as regards diagnosing cancer based on the scanned pathological report and generating an organized conclusion in less than two minutes.

As digital pathology and datasets of annotations increase in complexity, solutions like IGCAIDS will become all the more critical in addressing the need for minimizing diagnostic delay, inter-observer variability, and the emergence of precision oncology. It is clear from the authors' tone and their description of AI in pathology that AI is meant to be an augmentation tool, not a replacement.

REFERENCES

[1] X. Wang, Y. Chen, Y. Gao, H. Zhang, Z. Guan, Z. Dong, Y. Zheng, J. Jiang, H. Yang, L. Wang, X. Huang, L. Ai, W. Yu, H. Li, C. Dong, Z. Zhou, X. Liu, and G. Yu, "Predicting gastric cancer outcome from resected lymph node histopathology images using deep learning," Nature Communications, vol. 12, no. 1, p. 1637, Mar. 2021. doi: 10.1038/s41467-021-21674-7.

[2] E. Garcia, R. Hermoza, C. B. Castanon, L. Cano, M. Castillo, and C. Castaneda, "Automatic lymphocyte detection on gastric cancer IHC images using deep learning," in Proc. IEEE 30th International Symposium on Computer-Based Medical Systems (CBMS), Thessaloniki, 2017, pp. 200-204. doi: 10.1109/CBMS.2017.94.

[3] S. Choi and S. Kim, "Artificial intelligence in the pathology of gastric cancer," Journal of Gastric Cancer, vol. 23, no. 3, pp. 410-427, Jul. 2023. doi: 10.5230/jgc.2023.23.e25.

[4] Z. Song, S. Zou, W. Zhou, Y. Huang, L. Shao, J. Yuan, X. Gou, W. Jin, Z. Yi, Y. Xu, Z. Zheng, and Y. Chen, "Clinically applicable histopathological diagnosis system for gastric cancer detection using deep learning," Nature Communications, vol. 11, no. 1, p. 4294, Aug. 2020. doi: 10.1038/s41467-020-18147-8.

[5] J. Park, B. G. Jang, Y. W. Kim, H. Park, B. H. Kim, and M. J. Kim, "A prospective validation and observer performance study of a deep learning algorithm for pathologic diagnosis of gastric tumors in endoscopic biopsies," Clinical Cancer Research, vol. 27, no. 3, pp.

719-728, Feb. 2021. doi: 10.1158/1078-0432.CCR-20-1488.

[6] B. E. Bejnordi, M. Veta, P. J. van Diest et al., "Diagnostic assessment of deep learning algorithms for detection of lymph node metastases in women with breast cancer," JAMA, vol. 318, no. 22, pp. 2199-2210, Dec. 2017. doi: 10.1001/jama.2017.1458

[7] Kather JN, Pearson AT, Halama N et al., Deep learning can predict microsatellite instability directly from histology in gastrointestinal cancer, Nature Medicine, 2019, 25(7): 1054-1056. doi: 10.1038/s41591-019-0462-y.

[8] Muti HS, Heij LR, Keller G et al., Development and validation of deep learning classifiers to detect Epstein-Barr virus and microsatellite instability status in gastric cancer, The Lancet Digital Health, 2021, 3(10): e654-e664. doi: 10.1016/S2589-7500(21)00133-3.

[9] Kanavati F and Tsuneki M, A deep learning model for gastric diffuse-type adenocarcinoma classification in whole slide images, Scientific Reports, 2021, 11(1): 20486. doi: 10.1038/s41598-021-99678-0.

[10] Jeong Y, Cho CE, Kim JE, Lee J, Kim N, Jung WY et al., Deep learning model to predict Epstein-B

[11] B. Huang, S. Tian, N. Zhan, J. Ma, Z. Huang, C. Zhang, and B. Du, “Accurate diagnosis and prognosis prediction of gastric cancer using deep learning on digital pathological images: a retrospective multicentre study,” EBioMedicine, vol. 73, p. 103631, Nov. 2021. doi: 10.1016/j.ebiom.2021.103631.

[12] Z. Han, J. Lan, T. Wang, Z. Hu, Y. Huang, Y. Deng et al., “A deep learning quantification algorithm for HER2 scoring of gastric cancer,” Frontiers in Neuroscience, vol. 16, p. 877229, May 2022. doi: 10.3389/fnins.2022.877229.

[13] J. Saltz, R. Gupta, L. Hou et al., “Spatial organization and molecular correlation of tumor-infiltrating lymphocytes using deep learning on pathology images,” Cell Reports, vol. 23, no. 1, pp. 181–193, Apr. 2018. doi: 10.1016/j.cel

[14] G. Campanella, M. G. Hanna, L. Geneslaw et al., “Clinical-grade computational pathology with weakly supervised deep learning on whole slide images,” Nature Medicine, vol. 25, no. 8, pp. 1301–1309, Aug. 2019. doi: 10.1038/s41591-019-0508-1.