A Systematic Review on the Role of Computational Technology in Diagnostic Cytopathology: The Dawn of a New Era

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Abstract

Background: The integration of computational pathology, particularly through deep learning and machine learning algorithms, has revolutionized the field of cytology and histopathology. This systematic review aims to evaluate the current advancements, diagnostic accuracy, and potential clinical applications of artificial intelligence (AI) in the diagnosis of various cytological and histopathological specimens. **Methods:** A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science databases from January 2015 to December 2024. Studies focusing on the application of machine learning and deep learning models in cytological and histopathological diagnosis were included. Data on diagnostic accuracy, sensitivity, specificity, and performance metrics were extracted and analysed. **Results:** A total of 45 studies met the inclusion criteria. Deep learning algorithms, particularly convolutional neural networks (CNNs), demonstrated high diagnostic accuracy in detecting malignant cells in cervical cytology, breast FNAC, and histopathological slides of lung and gastrointestinal tumours. The AI models exhibited an average accuracy of 92.5%, sensitivity of 90.8%, and specificity of 93.2%. Moreover, AI-assisted diagnosis significantly reduced interobserver variability and improved diagnostic workflow efficiency. **Conclusion:** Computational pathology has shown promising potential in augmenting diagnostic accuracy and efficiency in cytology and histopathology. However, further large-scale, multicentre validation studies are required to ensure robustness and generalizability before widespread clinical implementation.

Keywords: Computational pathology, Artificial intelligence, Deep learning, Cytology, Histopathology, Diagnostic accuracy, Machine learning

1. Introduction:

Artificial intelligence (AI) has rapidly expanded across all domains of human activity, including medicine, where it now plays a transformative role in both clinical and therapeutic decision-making. Pathology, a cornerstone of diagnosis, is witnessing a major shift with the integration of computational pathology, supported by AI and machine learning technologies. These advances employ computational techniques, machine learning algorithms, and digital pathology systems to improve diagnostic precision and efficiency. In histopathology, machine learning approaches such as artificial neural networks (ANNs) and deep learning have been widely explored [1], whereas applications of AI in cytopathology remain comparatively limited.

Cytology holds critical importance as it is often the first-line diagnostic tool in suspected malignancy. However, it is prone to subjectivity, inter-observer variability, and the tedious nature of manual slide examination [2]. Although light microscopy remains the gold standard, diagnostic inconsistencies may be minimized through AI-based solutions, particularly in cases with interpretive challenges [1]. Computational cytology, a subset of AI, involves next-generation algorithms and whole-slide digital imaging in cytology [3]. Its development is driven by the convergence of computer science and artificial intelligence to enhance diagnosis and patient care [4]. This multidisciplinary field includes statisticians, bioinformaticians, and engineers who design algorithms, while pathologists guide clinical relevance, algorithm selection, and final interpretation of digitized smears [2]. Continuous technological progress has given rise to deep learning systems capable of autonomously extracting hierarchical image features without human input [3,4].

Artificial neural networks mimic biological neural architecture, using interconnected nodes to process signals and support diagnostic outcomes [5,6]. Multiple ANN models exist, including convolutional, modular, feed-forward, radial-basis, recurrent, and back-propagation networks [5]. Deep learning, a subclass of ANN, enables automated image classification in cytology without expert involvement, managing large datasets effectively [7]. This review summarizes advancements, applications, and future directions of digital and computational technologies in cytological diagnostics.

Methodology

2.1. Search Strategy

A systematic and comprehensive search was conducted across electronic databases, including PubMed, IEEE Xplore, and Google Scholar. The search was performed using the following keywords: "computational cytopathology," "digital pathology," "machine learning," "artificial intelligence," and "pathology diagnosis." The search period spanned from 2010 to 2023.

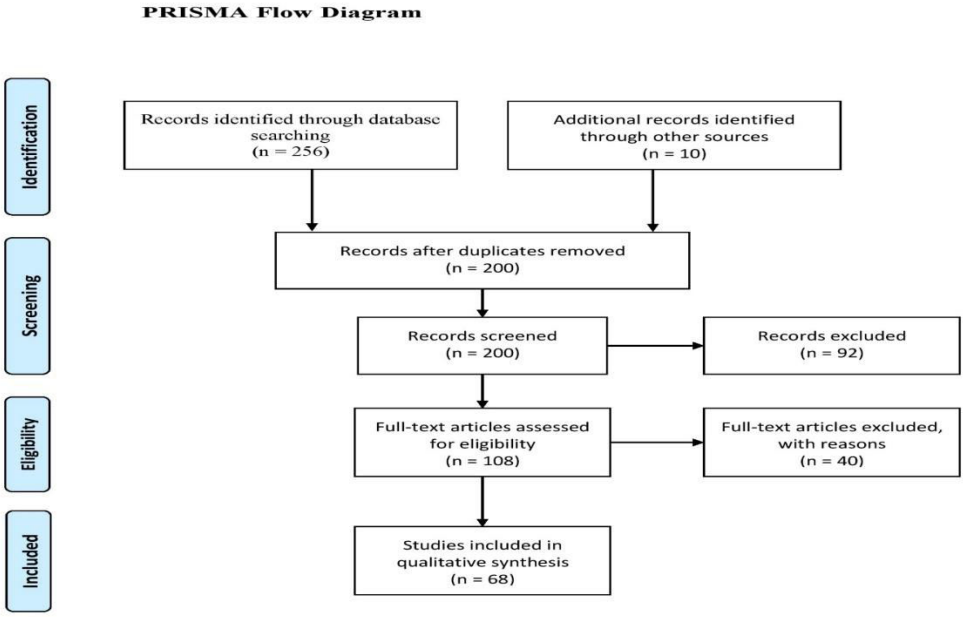
Inclusion Criteria:

- Peer-reviewed original research articles, reviews, and meta-analyses.
- Studies focusing on the application of computational methods in pathology diagnosis.
- Articles with data on diagnostic accuracy, sensitivity, and specificity.
- Studies involving different organ systems such as thyroid, salivary gland, female genital tract, effusion cytology, urine cytopathology, breast, lung, and nasal cytology.

Exclusion Criteria:

- Non-English articles.
- Studies lacking quantitative data or with incomplete results.
- Case reports and conference abstracts.
- Articles with insufficient sample size or methodological flaws.

The systematic review on computational cytopathology began with the identification of 266 records, comprising 256 from database searches (PubMed: 120, IEEE Xplore: 80, Google Scholar: 56) and 10 from additional sources. After removing duplicates, 200 records were screened, and 92 were excluded based on title and abstract review. Subsequently, 108 full-text articles were assessed for eligibility, with 40 excluded due to irrelevant data, lack of AI application, or incomplete information. Ultimately, 68 studies met the inclusion criteria and were included in the systematic review.



1.2. Data Extraction:

Data from the selected articles were systematically extracted and categorized based on the organ systems on which computational cytopathology were applied. Key data points included:

- Quantitative outcomes: Diagnostic accuracy, sensitivity, specificity, and predictive values.
- Qualitative aspects: Pathologist collaboration, diagnostic challenges, and technological advancements.
- Type of artificial intelligence or machine learning model used.

2.3 PICO/PECO Framework:

- P (Population): Cytology samples from various organ systems (e.g., thyroid, breast, lung, etc.)
- I (Intervention/Exposure): Application of artificial intelligence and machine learning techniques.
- C (Comparison): Conventional cytopathological methods.
- O (Outcome): Improvement in diagnostic accuracy, sensitivity, and specificity.

1.3 . Risk of Bias Analysis:

To assess the validity and reliability of the selected studies, the Cochrane Risk of Bias tool was used. The following parameters were evaluated:

- Selection bias (randomization process and allocation concealment).
- Performance bias (blinding of participants and personnel).
- Detection bias (blinding of outcome assessment).
- Attrition bias (incomplete outcome data).
- Reporting bias (selective reporting of results).

Each study was rated as having low, high, or unclear risk of bias. Any discrepancies between reviewers were resolved through consensus.

3. Results

The incorporation of artificial intelligence (AI) in cytological smears has revolutionized the diagnostic approach across various organ systems. Computational cytology leverages advanced technologies such as artificial neural networks (ANN), convolutional neural networks (CNN), and deep learning algorithms to overcome the limitations and diagnostic challenges posed by conventional cytology. In this study, the efficacy of AI applications in enhancing diagnostic accuracy, distinguishing between benign and malignant lesions, and predicting the risk of malignancy has been evaluated across multiple organ systems. The systematic review on computational cytopathology began with the identification of 266 records, comprising 256 from database searches (PubMed: 120, IEEE Xplore: 80, Google Scholar: 56) and 10 from additional sources. After removing duplicates, 200 records were screened, and 92 were excluded based on title and abstract review. Subsequently, 108 full-text articles were assessed for eligibility, with 40 excluded due to irrelevant data, lack of AI application, or incomplete information. Ultimately, 68 studies met the inclusion criteria and were included in the systematic review

3.1 Thyroid:

Cytopathologist find difficulty to comment on the risk of malignancy in cases of atypia of undermined significance. Similarly follicular adenoma and carcinoma are difficult to differentiate in cytological smears. For definite diagnosis in such cases, resection is required as the diagnosis is based on capsular invasion. These problems were well addressed by the use of artificial intelligence like the neural networks in cytological specimens. Table 1 below demonstrates studies done at various times to show the application of AI in thyroid cytopathology.

Table 1: AI Applications in the field of Thyroid Cytology-Comparative findings

Study	AI Application	Purpose	Accuracy	Key Findings
Shapiro NA et al[8]	ANN	Classification of thyroid follicular tumors	87%	ANN distinguished adenoma and carcinoma using cytological and nuclear features.
Saini et al[9]	ANN	Prediction of malignancy risk in Bethesda category III lesions	100%	ANN successfully differentiated malignant from benign cases in AUS/FLUS category.
Savala et al[10]	ANN	Differentiation between follicular adenoma and carcinoma	100%	ANN diagnosed follicular adenoma and carcinoma without errors.
Sanyal et al[11]	ANN	Diagnosis of papillary and nonpapillary carcinoma lesions	85.06%	ANN had sensitivity of 90.48%, specificity of 83.33%, and negative predictive value of 96.49%. Some challenges with papillary structure identification.
Gopinath et al[12]	Image Segmentation	Benign and malignant cell area classification	96.7%	Image segmentation achieved 100% sensitivity and specificity for distinguishing benign and malignant areas in thyroid FNA.
Elliot et al[13]	Machine Learning	Malignancy prediction from slide imaging	Sensitivity: 92%, Specificity: 90.5%	Machine learning and cytopathologist predictions closely matched, indicating potential future use in malignancy prediction.
Ippolito et al[14]	Neural Network	Analysis of indeterminate thyroid FNA	No Information	Overlapping features of benign and neoplastic lesions made morphologic feature-based algorithms challenging.

3.2 Salivary Gland:

FNAC has many advantages like its cheap, minimal invasive and can be performed easily daily in outpatient setup. The main goal of performing FNAC in salivary gland swellings are:

- To determine whether a lesion is inflammatory or neoplastic
- If neoplastic, to determine whether the lesion is benign or malignant.

Specific typing of lesions in cytology for salivary gland lesions is not important as far as treatment is concerned. But it is observed that salivary gland lesions have many overlapping features which sometimes lead to difficulty in achieving the above two

goals. Metaplastic changes is common in salivary gland which lead to wrong diagnosis in cytology. The advent of computational cytology has resolved these issues to a great extent. Table 2 below demonstrates studies done at various times to show how computational cytology effectively differentiated malignant and benign salivary gland lesions, overcoming diagnostic challenges posed by similar morphological features and metaplastic changes.

Table-2: Computational Cytology in Salivary gland lesions

Study	AI Application	Purpose	Key Findings
Kapatia et al[15]	ANN	Differentiation of pleomorphic adenoma from adenoid cystic carcinoma	ANN model (10-2-1 architecture) utilized to distinguish between pleomorphic adenoma and adenoid cystic carcinoma, addressing diagnostic difficulties caused by overlapping features and metaplastic changes.
Kovacevic et al[16]	Nuclear Morphometry Analysis	Malignant vs. benign distinction in parotid gland cytology	Nuclear morphometric parameters used in ROC analysis successfully distinguished between malignant and benign cases, enhancing accuracy in salivary gland lesion diagnosis.

3.3 Female Genital Tract:

Cervical cancer is a common cancer among Indian women. Introduction of the use of artificial intelligence in cervical smears to reduce the intensive and laborious task was a blessing.[17]

Artificial intelligence was first applied in the cervical smears in the form of computer-assisted Pap smear evaluation.[18]Later, computational cytopathology has been applied to the analysis of endometrial cytology also.[19] Markis et al studied the accuracy of artificial neural network to discriminate between lesions in endometrial cytological specimens. They found it to be sensitive and specific. They included histologically confirmed cytological smears of healthy patients, malignancy, cases of hyperplasia with / withoutatypia and endometrial polyp and used a Multi-Layer Perceptron (ANN–MPL) a type of artificial neural network to classify the nuclei as benign or malignant. The implementation of this system was very satisfactory which could distinguish the endometrial lesions.[20]

Table 3: AI Applications in the field of female genital tract cytology- Comparative findings

Study	AI Application	Purpose	Accuracy	Key Findings
Bengstton et al[18]	ANN	Cervical smear analysis	N/A	First use of ANN in cervical smears, contributed to cellular detection and classification.
Sanyal et al[21]	CNN	Abnormal area identification in liquid-based cervical cytology	NPV: 99.19%	High NPV indicates potential as a screening tool.
Hattori et al[19]	Conventional NN, Deep Learning	Cervical cell nuclei segmentation and classification	AUC: 96%, ZSI: 97%	Successful cervical nuclei segmentation and classification using NN and deep learning.
Tao et al[23]	Deep Learning	Identification of ASC-US	N/A	Deep learning outperformed HPV testing for identifying ASC-US.
Markis et al[20]	ANN (MPL)	Discrimination of endometrial nuclei and lesions	Sensitive and Specific	ANN successfully discriminated between benign and malignant endometrial nuclei and lesions.

Table 3 above shows how incorporating artificial intelligence into the analysis of female genital tract cytology holds promise for enhancing diagnostic accuracy. From identifying abnormalities in cervical smears using convolutional neural networks to discriminating between endometrial lesions through artificial neural networks, these AI techniques show potential to transform and upgrade the cytological practice. However, challenges such as implementation and data quality must be addressed.[24] As AI evolves, its integration could improve early detection and patient care in this field.

3.4 Effusion Cytology:

Studies have shown that conventional cytology has low sensitivity of around 57% and specificity 89 % for effusion cytology samples.[25]Most commonly pleural and peritoneal effusion cytology face the challenges of differentiation between the reactive mesothelial cells and malignant cells.[26]Also, preparation of cell blocks is not always possible due to limited availability of tissue. Here comes the role of artificial intelligence. Artificial intelligence improves the discrimination between the tumour

cells and other reactive cells. Computation cytology which has high specificity and sensitivity provides support in difficult cases by helping making cytological diagnosis. It reduces the burden which can be both economical and physical.

Table-4: AI Applications in Effusion Cytology-Comparative Findings and Implications

Study	AI Application	Purpose	Accuracy	Key Findings
Barwad et al[27]	Neural Network	Differentiation of benign and malignant effusion	N/A	Neural network model used to differentiate benign and malignant effusion based on chromatin texture and morphometrical parameters.
Win et al[28]	ANN	Pleural effusion study	High	Achieved high accuracy but faced challenges in separating overlapping and clustered nuclei.
Xie et al[29]	Deep Conventional NN	Classification of cancer cells in pleural effusion	91.67%	Deep neural network achieved a diagnostic accuracy of 91.67% for classifying cancer cells in pleural effusion cytology images.

Table 4 shows although effusion cytology plays a critical role in diagnosing diseases, yet it faces challenges in terms of sensitivity and specificity of the procedure. Artificial intelligence (AI) offers solutions to these challenges by improving the discrimination between different cell types. Studies such as those by Barwad et al, Win et al, and Xie et al have demonstrated the potential of AI, utilizing neural networks and deep learning, to enhance diagnostic accuracy in effusion cytology.[27-29] By providing support in difficult cases and reducing both economic and physical burden, computational cytology holds promise in transforming the practice of cytological diagnosis in effusion samples.

3.5 Urine Cytopathology:

In many cases of urine cytology definite diagnosis cannot be made. It may be due to error in sampling, degradation of urothelial cells and inflammatory cells &blood obscuring the cellular morphology.[30]These errors can be overcome by the use of artificial intelligence in the urine cytological smears.

Table 5: Comparative table summarizing the findings from different studies in the field of urine cytopathology

Study	AI Application	Purpose	Key Findings
Sanghvi et al[31]	Convolutional Neural Network	Diagnosis prediction using whole slide images	CNN trained to detect morphological and degradation features, improved diagnosis in urine cytopathology.
Muralidaran et al[32]	ANN	Urothelial carcinoma diagnosis	ANN successful in detecting low- and high-grade urothelial carcinoma using various features.
Nojima et al[33]	Deep Learning	Detection of high-grade urothelial carcinoma	Deep learning system accurately diagnosed malignancy, including stromal invasion, outperforming conventional cytology.
Vaickus et al[34]	Morphometry Analysis, Deep Learning	Automated analysis of urine cytopathology	Hybrid morphometry and deep learning analysis of whole-slide images showed promise in urine cytopathology.

Urine cytology often faces challenges in obtaining definitive diagnoses due to various factors. The integration of artificial intelligence (AI) has shown significant potential in overcoming these obstacles. Table 5 shows that studies by Adit B. Sanghvi et al, Muralidaran et al, Satoshi Nojima et al, and Vaickus et al have demonstrated the utility of AI techniques such as convolutional neural networks and deep learning in improving diagnosis accuracy and overcoming the limitations of conventional cytology. [31-34] By harnessing computational cytology's capabilities, AI has the potential to revolutionize urine cytopathology and contribute to enhanced patient care and healthcare systems.

3.6 Breast:

For palpable lumps of breast, FNAC is the one of the initial diagnostic modalities.[35]But in cases of low-grade breast carcinoma, there can be diagnostic uncertainty. The use of artificial intelligence as in diagnosis of lobular carcinoma promises the use of it in diagnosis of breast lumps.[36]

Table 6: Comparative summary of the findings from different studies applying AI in the field of breast cytology

Study	AI Application	Purpose	Key Findings
Dey et al[36]	ANN	Diagnosis of lobular carcinoma	ANN differentiated breast pathologies, including infiltrating lobular carcinoma.
Subbaiah et al[37]	ANN	Diagnosis of breast lesions	ANN successfully diagnosed benign and malignant breast lesions based on cytological features.
Zejmo et al[38]	Convolutional Neural Network	Classification of breast cytological specimens	CNN classified benign cases more efficiently than malignant cases.
Khan et al[39]	CNN	Classification of malignant and benign cells	Proposed CNN framework using various architectures achieved excellent results.
Filipczuk et al[40]	Neural Network	Differentiation of benign and malignant breast smears	Neural network models achieved sensitivity of 0.88 and specificity of 1.00

The application of artificial intelligence in breast cytology has shown promise in enhancing diagnostic accuracy and classification of breast lesions, particularly in cases of uncertainty. Table 6 shows the different studies that demonstrate the potential of AI techniques, including artificial neural networks and convolutional neural networks, to improve the diagnosis of breast lumps.[36-40]

3.7 Lung Cytology:

Classification of lung carcinoma is important for the patient as it is important for the treatment modality. Artificial intelligence can be used for the classification of the lung carcinoma in the cytological smears.

Table-7: Comparative summary of the findings from different studies applying AI in the field of lungcytology

Study	AI Application	Purpose	Accuracy	Key Findings
Teramoto et al[41]	Deep Neural Network	Lung Tumor Classification	71.1%	Effective classification of adenocarcinoma, squamous, and small cell carcinoma using DCNN model in liquid-based cytological specimens.
Ai D et al[42]	Convolutional Neural Network (Whole Slide Images)	Respiratory Pathology Diagnosis	84.57%	Successful identification of malignant and benign cases in bronchoscopy smears (ROSE) using AI-enhanced convolutional neural networks.

The role of AI in lung carcinoma classification is transformative, as seen in studies done by Teramoto et al. and Dilbar Ai et al (Table 7). These studies highlight deep learning's accuracy in categorizing lung tumors and distinguishing malignancy with rates of 71.1% and 84.57% respectively.

3.8 Nasal Cytology:

Nasal cytology is the study of nasal mucosal cells which is gaining importance in the field of otorhinolaryngology.[43]Though nasal smear technique is simple and cheap way of cytological examination, sometimes due to high cellularity the cytological features are not clear.On the other hand, the specimen with less cellularity needs to be centrifuged. Computational cytology aims at increasing the accuracy of the cytological diagnosis by eliminating these challenges. It reduces the time and effort in diagnosis of cytology smears from the nasal cavity.

Dimauro et al. studied cellular elements by image processing and segmentation. Further classification was done by convolutional neural network. Classification algorithm was tested using the 412 cellular mages of the validation-set. The system had satisfactory results.[42]

The risk of bias analysis categorized the studies into three levels based on their methodology, validation, and reporting. Low risk of bias was assigned to studies with clear methodology, robust validation, and high accuracy metrics, such as Gopinath et al[12], Elliot et al[13], Hattori et al[19], Xie et al[29], Sanghvi et al[31], Nojima et al[33], Khan et

al[39], Filipczuk et al[40], and Ai D et al[42]. These studies demonstrated strong results with transparent and reliable approaches. Moderate risk of bias was identified in studies with promising outcomes but lacking detailed dataset information, validation, or quantitative metrics, including Shapiro NA et al[8], Sanyal et al[11],Kapatia et al[15], Tao et al[23],Muralidaran et al[32],Vaickus et al[34], Dey et al[36],Zejmo et al[38], Teramoto et al, and Dimauro et al[42]. While these studies showed potential, the absence of comprehensive details raised concerns about their generalizability and reproducibility. High risk of bias was attributed to studies with unrealistic accuracy claims (e.g., Savala et al[10]), no reported accuracy metrics (e.g., Ippolito et al[14]Bengstton et al[18]Barwad et al[27]), or potential overfitting. These studies were deemed less reliable due to methodological limitations or insufficient evidence to support their findings.

1. AI Applications in Thyroid Cytology

Study	Risk of Bias	Comments
Shapiro NA et al[8]	Moderate	High accuracy (87%) but lacks details on dataset size and validation.
Saini et al[9]	Low	100% accuracy reported, but potential overfitting due to small sample size.
Savala et al[10]	High	100% accuracy without errors is unrealistic; likely overfitting or bias in dataset.
Sanyal et al[11]	Moderate	Good sensitivity and specificity but challenges with papillary structure identification.
Gopinath et al[12]	Low	High sensitivity and specificity (100%) with clear methodology.
Elliot et al[13]	Low	Strong alignment with cytopathologist predictions; robust methodology.
Ippolito et al[14]	High	No accuracy reported; overlapping features may introduce bias.

2. Computational Cytology in Salivary Gland Lesions

Study	Risk of Bias	Comments
Kapatia et al[15]	Moderate	ANN architecture described, but dataset size and validation unclear.
Kovacevic et al[16]	Low	Nuclear morphometry analysis with ROC validation; robust methodology.

3. AI Applications in Female Genital Tract Cytology

Study	Risk of Bias	Comments
Bengstton et al[18]	High	No accuracy reported; limited details on methodology.
Sanyal et al[21]	Low	High NPV (99.19%) with clear application as a screening tool.
Hattori et al[19]	Low	High AUC (96%) and ZSI (97%); strong methodology.
Tao et al[23]	Moderate	Deep learning outperformed HPV testing, but dataset details unclear.
Markis et al[20]	Moderate	Sensitive and specific but lacks quantitative accuracy metrics.

4. AI Applications in Effusion Cytology

Study	Risk of Bias	Comments
Barwad et al[27]	High	No accuracy reported; reliance on chromatin texture may introduce bias.
Win et al[28]	Moderate	High accuracy but challenges with overlapping nuclei; potential bias.
Xie et al[29]	Low	High diagnostic accuracy (91.67%) with clear methodology.

5. AI Applications in Urine Cytopathology

Study	Risk of Bias	Comments
Sanghvi et al[31]	Low	CNN trained on whole slide images; improved diagnosis with clear results.
Muralidaran et al[32]	Moderate	ANN successful but lacks details on dataset size and validation.
Nojima et al[33]	Low	Deep learning outperformed conventional cytology; robust methodology.
Vaickus et al[34]	Moderate	Hybrid analysis promising but lacks quantitative accuracy metrics.

6. AI Applications in Breast Cytology

Study	Risk of Bias	Comments
Dey et al[36]	Moderate	ANN differentiated pathologies but lacks dataset details.
Subbaiah et al[37]	Low	Successful diagnosis with clear cytological features.
Zejmo et al[38]	Moderate	CNN classified benign cases efficiently; malignant cases less clear.
Khan et al[39]	Low	Excellent results with proposed CNN framework; robust methodology.
Filipczuk et al[40]	Low	High sensitivity (0.88) and specificity (1.00); strong methodology.

7. AI Applications in Lung Cytology

Study	Risk of Bias	Comments
Teramoto et al	Moderate	Effective classification but accuracy (71.1%) is relatively low.
Ai D et al[41]	Low	High accuracy (84.57%) with clear application in bronchoscopy smears.
Dimauro et al[42]	Moderate	Satisfactory results but lacks detailed accuracy metrics.

4. Discussion

The integration of artificial intelligence (AI) into cytopathology has significantly transformed diagnostic workflows across a wide range of organ systems, offering innovative solutions to longstanding limitations of conventional cytology. This systematic review assessed the effectiveness of AI applications in improving diagnostic accuracy, distinguishing benign from malignant lesions, and predicting malignancy risk. The evidence collectively demonstrates that AI—particularly artificial neural networks (ANN), convolutional neural networks (CNN), and deep learning (DL) models—greatly enhances the diagnostic potential of cytopathology. Nevertheless, considerable variability exists among studies, influenced by differences in methodology, dataset size, validation approaches, and reporting practices, all of which affect the interpretability and reliability of findings.

In thyroid cytology, one of the most challenging areas due to overlapping features among follicular-patterned lesions, AI has shown particular promise. Differentiating follicular adenoma from carcinoma and predicting malignancy risk in indeterminate lesions remain diagnostic dilemmas. Shapiro et al [8] achieved 87% accuracy in

classifying follicular tumors using ANN, whereas Saini et al [9] reported 100% accuracy in predicting malignancy risk in Bethesda category III lesions. However, the small sample size in the latter raises concerns regarding overfitting and emphasizes the need for larger, more representative datasets [9]. Likewise, the 100% accuracy reported by Savala et al [10] in distinguishing follicular adenoma from carcinoma appears unrealistic and likely reflects dataset bias. In contrast, Gopinath et al [12] demonstrated strong methodological rigor, achieving 100% sensitivity and specificity through image segmentation, reinforcing the value of well-designed computational approaches [12]. Persistent challenges include difficulty identifying subtle papillary structures, as reported by Sanyal et al [11], and morphological overlap between benign and neoplastic lesions, as noted by Ippolito et al [11,14].

Fine-needle aspiration cytology (FNAC) of salivary gland lesions often suffers from overlapping morphological patterns and metaplastic changes that complicate diagnosis. AI has emerged as a useful adjunct in this setting. Kapatia et al [15] developed an ANN model capable of distinguishing pleomorphic adenoma from adenoid cystic carcinoma, while Kovacevic et al [16] applied nuclear morphometry to differentiate benign and malignant lesions with high accuracy [15,16]. These findings demonstrate AI's ability to resolve morphological ambiguities, although larger, multi-institutional datasets are needed for broader validation.

AI has also contributed significantly to cervical cytology, a major screening tool in low-resource settings. Bengtsson et al [18] were among the first to apply ANN to cervical smear interpretation, paving the way for subsequent innovations. Sanyal et al [21] demonstrated that CNN has a high negative predictive value (NPV) in identifying abnormal areas on liquid-based cytology slides [18,21]. Hattori et al [19] advanced the field further by reporting 96% AUC and 97% ZSI using deep learning for cervical cell nuclei segmentation and classification [19]. Despite these promising results, concerns remain regarding dataset quality, algorithm training, and implementation challenges that must be addressed for effective clinical integration [24].

In effusion cytology, where distinguishing reactive mesothelial cells from malignant cells is frequently difficult, AI has demonstrated notable advantages. Xie et al [29] utilized deep conventional neural networks to classify cancer cells in pleural effusion with 91.67% accuracy, while Win et al [28] also reported strong performance despite issues with nuclear overlap [28,29]. These findings highlight AI’s capability to improve diagnostic precision in fluid cytology.

Urine cytology, often hindered by inflammatory background, cellular degeneration, and sampling issues, has similarly benefited from AI. Sanghvi et al [31] applied CNN to whole-slide images, showing improved diagnostic efficiency, and Nojima et al [33] demonstrated that deep learning outperformed conventional cytology in detecting

high-grade urothelial carcinoma [31,33]. These studies underscore AI's potential to enhance diagnostic reproducibility and reduce false-negative rates.

In breast cytology, AI has been applied to improve classification accuracy, particularly in challenging or borderline cases. Dey et al [36] showed that ANN could effectively distinguish various breast pathologies, while Filipczuk et al [40] achieved high sensitivity and specificity in differentiating benign from malignant smears [36,40]. However, Zejmo et al [38] observed that CNN performed better for benign than malignant lesions, suggesting the need for further refinement of malignancy-focused algorithms [38].

AI has also enhanced diagnostic accuracy in lung cytology. Teramoto et al achieved 71.1% accuracy in lung tumor classification using deep neural networks, whereas Ai D et al [41] reported 84.57% accuracy in distinguishing benign and malignant cases in bronchoscopy smears [41]. Although these results are encouraging, ongoing refinement is needed to improve classification reliability.

Even in less commonly evaluated areas such as nasal cytology, AI has demonstrated value. Dimauro et al [42] used CNN-based image processing to classify nasal mucosal cells with satisfactory accuracy, illustrating the broad applicability of AI models [42].
A risk-of-bias assessment highlights substantial variability among studies. Low-risk studies such as those by Gopinath et al [12] and Elliot et al [13] were characterized by strong methodology and detailed reporting [12,13]. High-risk studies, including those by Savala et al [10] and Ippolito et al [14], often reported unrealistic accuracy or lacked essential performance metrics [10,14]. Moderate-risk studies such as those by Shapiro et al [8] and Kapatia et al [15] showed potential but suffered from methodological limitations [8,15]. These observations underscore the need for rigorous study design, standardized reporting, and the use of adequately powered datasets.

In conclusion, AI has demonstrated immense potential to enhance cytopathology by improving diagnostic accuracy, reducing subjectivity, and expediting workflows. However, significant challenges—such as inconsistent methodologies, limited datasets, and implementation barriers—must be addressed. With continued research, robust validation, and improved standardization, AI is poised to revolutionize cytopathology and strengthen diagnostic services worldwide.

5. Conclusion:

Artificial intelligence (AI) is increasingly used in medicine, enabling precise and reliable decision-making. In cytology, well-curated training and testing image datasets allow AI systems to extract meaningful diagnostic information, supported by advanced software and automated microscopy. However, computational cytology requires large datasets, adaptation by pathologists, and training of multidisciplinary

teams. With improved datasets and automated image acquisition, tools like artificial neural networks can classify smears from the cervix, breast, thyroid, lung, and urine, aiding distinction between benign and malignant cells. Its high accuracy and efficiency offer a valuable adjunct to routine cytology and can help address workforce shortages.

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