East African Medical Journal Vol. 103 No. 1 January 2026
MOLECULAR TESTING OF MINIMALLY INVASIVE CYTOLOGY SPECIMENS IN PRECISION ONCOLOGY: ANALYTICAL CHALLENGES AND CLINICAL IMPLICATIONS: A SCOPING REVIEW

Munyoki Nyamai, School of Health Sciences, Department of Medical Laboratory and Pharmaceutical Sciences, Murang'a University of Technology, P.O Box 75-10200, Nebert Mchidi, School of Health Sciences, Department of Nursing, Murang'a University of Technology, P.O Box 75-10200, Damaris, Katsutsu, School of Biomedical Sciences, Department of medical laboratory sciences, Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000 – 00200, Nairobi.

Corresponding Author: Munyoki Nyamai, Murang'a University of Technology, P.O Box 75-10200. Email: munyokinymai@gmail.com

MOLECULAR TESTING OF MINIMALLY INVASIVE CYTOLOGY SPECIMENS IN PRECISION ONCOLOGY: ANALYTICAL CHALLENGES AND CLINICAL IMPLICATIONS: A SCOPING REVIEW

M. Nyamai. N. Mchidi and D. Katsutsu

ABSTRACT

Background: **The increasing use of molecular testing in oncology has amplified reliance on diagnostic material obtained through minimally invasive procedures. In numerous clinical scenarios, cytological specimens represent the only available substrate for molecular and genomic analysis. Despite their growing clinical relevance, published studies addressing molecular testing in minimally invasive cytology remain methodologically diverse and analytically heterogeneous, complicating interpretation and comparison.**

Objective: **This scoping review sought to systematically identify molecular testing methodologies applied to minimally invasive cytology specimens, describe patterns of specimen utilization, classify reported clinical applications, evaluate laboratory and technical factors affecting analytical feasibility and reliability, and highlight recurrent methodological limitations and knowledge gaps within the literature.**

Methods: **The review followed the Arksey and O'Malley scoping review framework and was reported according to PRISMA-ScR guidance. A comprehensive search of major biomedical databases was conducted to identify studies describing molecular or genomic analyses performed on minimally invasive cytological specimens. Following duplicate removal, records underwent structured title, abstract, and full-text screening using predefined eligibility criteria. Relevant study characteristics and methodological data were extracted using a standardized charting approach.**

Results: **Two hundred studies met eligibility criteria and were included. The literature demonstrated substantial variability in molecular platforms,**

specimen preparation techniques, and clinical contexts. Next-generation sequencing and PCR-based assays were most commonly reported, with many studies employing multiple analytical approaches. Fine-needle aspiration cytology and cell block preparations predominated. Analytical feasibility was consistently influenced by specimen adequacy, cellularity, nucleic acid yield, and pre-analytical variability. Frequent methodological limitations included retrospective designs and inconsistent reporting practices.

***Conclusion*: The evidence reflects expanding integration of minimally invasive cytology into molecular diagnostic workflows across oncologic applications. However, heterogeneity in study design, laboratory practices, and reporting standards limits comparability and definitive assessment of analytical performance. Standardization efforts and prospective validation studies are needed to strengthen the evidence base.**

INTRODUCTION

The integration of molecular diagnostics into oncology has transformed approaches to cancer classification, diagnosis, and therapeutic decision-making. Precision oncology relies on the identification of genomic alterations and predictive biomarkers to guide tumor characterization and the selection of targeted therapies[1]. Evidence increasingly shows that tumors with similar morphological features may exhibit distinct molecular profiles with important clinical consequences[2]. Consequently, molecular profiling is now central to contemporary oncologic practice and has created a sustained demand for analytical approaches capable of generating reliable genomic data from limited or minimally invasive specimens[3]. This requirement is particularly relevant in advanced disease and in anatomically challenging sites where surgical biopsy is either impractical or unsuitable for repeated sampling[4].

Minimally invasive cytology provides a practical and widely used source of diagnostic material in this setting. Cytological specimens obtained through fine-needle aspiration, exfoliative techniques, effusion analysis, brushings, washings, and liquid-based preparations are routinely applied across a broad range of tumor types[5]. These approaches offer clear advantages, including reduced procedural risk, rapid specimen acquisition, and the feasibility of repeated sampling for ongoing clinical assessment[6]. In many clinical contexts, especially in metastatic disease, cytological material may represent the only accessible substrate for both diagnostic evaluation and molecular analysis[7].

Despite these strengths, the application of cytology to molecular testing has historically been approached with caution. Concerns have focused on specimen adequacy, tumor cellularity, nucleic acid yield, and the effects of fixation and processing on molecular integrity[8]. Cytological preparations differ from histological specimens in cellular composition, preservation methods, and processing workflows, all of which influence downstream analytical performance. Tumor fraction and specimen adequacy remain consistently identified as critical determinants of successful molecular testing[9].

Recent advances in molecular pathology have expanded the feasibility of cytology-based molecular analysis. High-sensitivity platforms, including next-generation sequencing and digital polymerase chain

reaction, enable genomic interrogation from low-input or partially degraded nucleic acids[10]. When pre-analytical handling and laboratory workflows are appropriately optimized, cytological specimens can yield clinically actionable molecular information[11].

Beyond their role in initial diagnosis, cytology-based specimens are increasingly used for longitudinal disease monitoring. Serial sampling allows the detection of tumor evolution, including the emergence of resistance-associated mutations and clonal heterogeneity under therapeutic pressure[12]. This application is supported by advances in liquid biopsy and circulating tumor DNA technologies, which have demonstrated the feasibility of real-time genomic monitoring in clinical oncology [16,17,18]. Such approaches inform treatment modification, support adaptive therapeutic strategies, and contribute to survivorship care through ongoing molecular assessment [19,20].

The existing literature in this field is, however, characterized by substantial heterogeneity. Variations in specimen preparation techniques, analytical platforms, and reporting practices complicate cross-study comparisons and limit the development of standardized workflows[14]. These differences often reflect interactions among pre-analytical variables, specimen characteristics, and platform-specific requirements rather than intrinsic limitations of cytological material[15].

Laboratory and technical factors remain central to analytical reliability. Pre-analytical variables such as fixation methods, specimen handling, tumor fraction, and nucleic acid extraction protocols have measurable effects on assay performance and reproducibility [8]. Additional factors, including assay sensitivity thresholds and bioinformatic interpretation frameworks, further contribute to variability in analytical outcomes[10].

Existing reviews have largely focused on individual tumor types or specific molecular platforms, thereby limiting a comprehensive understanding of the broader field. A structured synthesis that maps molecular methodologies, specimen utilization patterns, clinical applications, and technical challenges across diverse study settings is therefore warranted.

Accordingly, this scoping review was undertaken to systematically characterize the evidence on molecular testing in minimally invasive cytology. The objectives were to map molecular methodologies, describe patterns of specimen utilization, classify clinical applications including diagnostic, therapeutic, and monitoring roles, examine laboratory factors influencing analytical reliability, and identify key methodological gaps relevant to precision oncology.

METHODOLOGY

This study was conducted as a scoping review to systematically examine methodological approaches, analytical strategies, and thematic trends in the literature on molecular testing using minimally invasive cytology specimens in oncology. A scoping review design was selected because the available evidence is methodologically heterogeneous, with substantial variation in study designs, specimen types, molecular platforms, and reporting practices, thereby limiting the feasibility of quantitative synthesis. Scoping reviews are particularly valuable for mapping broad and complex evidence within emerging fields of research [21]. The review followed the methodological framework proposed by Arksey and O'Malley [21] and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-

Analyses extension for Scoping Reviews (PRISMA-ScR) to enhance methodological transparency and reproducibility[23].A comprehensive literature search was conducted in PubMed/MEDLINE, Embase, Scopus, and Web of Science between 15 April and 20 October 2025. The search strategy incorporated both controlled vocabulary and free-text terms related to cytology, minimally invasive sampling, molecular diagnostics, and oncology. Retrieved records were imported into reference management software, and duplicate entries were removed through automated detection followed by manual verification.Study selection was undertaken in two sequential stages comprising title and abstract screening followed by full-text assessment. Two reviewers independently screened studies using predefined eligibility criteria, and disagreements were resolved through discussion and consensus. The study selection process is summarized in Figure 1.Eligibility criteria were developed using the Population–Concept–Context framework recommended for scoping reviews[22]. Studies were included if they reported primary data on molecular or genomic analyses performed on human-derived minimally invasive cytology specimens in oncologic settings. Eligible specimen types included fine-needle aspiration cytology, cell block preparations, liquid-based cytology, effusions, brushings, and washings. Studies involving non-neoplastic conditions, histology-only specimens, non-human data, or insufficient methodological detail were excluded.

Database Search Strategies

Data charting was conducted using a standardized extraction framework developed prior to analysis. Extracted variables included study characteristics, specimen types, molecular methodologies, clinical applications, and laboratory or technical factors influencing analytical performance. Data extraction was completed by one reviewer and independently verified by a second reviewer to ensure consistency and accuracy.Evidence synthesis followed a descriptive and thematic approach consistent with scoping review methodology[22]. The analysis aimed to map patterns in study design, specimen utilization, analytical methodologies, clinical applications, and methodological limitations across the available evidence base.

Search Strategy 1 – Broad Cytology + Molecular Oncology Query (PubMed/MEDLINE)

```
("cytology"[Title/Abstract] OR "fine needle aspiration"[Title/Abstract]
OR "fine-needle aspiration"[Title/Abstract] OR "FNA"[Title/Abstract]
OR "cell block"[Title/Abstract] OR "liquid-based cytology"[Title/Abstract]
OR "effusion"[Title/Abstract] OR "brushings"[Title/Abstract]
OR "washings"[Title/Abstract])
AND
("molecular"[Title/Abstract] OR "genomic"[Title/Abstract]
OR "next generation sequencing"[Title/Abstract]
OR "next-generation sequencing"[Title/Abstract]
OR "NGS"[Title/Abstract] OR "PCR"[Title/Abstract]
OR "digital PCR"[Title/Abstract] OR "FISH"[Title/Abstract]
OR "RNA"[Title/Abstract] OR "methylation"[Title/Abstract])
AND
("cancer"[Title/Abstract] OR "neoplasm"[Title/Abstract]
OR "tumor"[Title/Abstract] OR "oncology"[Title/Abstract])
```

Search Strategy 2 – Specimen-Focused Molecular Cytology Query

```
("fine needle aspiration"[Title/Abstract] OR "fine-needle
aspiration"[Title/Abstract]
OR "FNA cytology"[Title/Abstract] OR "cytology specimen"[Title/Abstract]
OR "cell block"[Title/Abstract])
AND
("molecular testing"[Title/Abstract] OR "molecular analysis"[Title/Abstract]
OR "next generation sequencing"[Title/Abstract]
OR "PCR"[Title/Abstract] OR "FISH"[Title/Abstract]
OR "mutation analysis"[Title/Abstract])
AND
("malignancy"[Title/Abstract] OR "cancer"[Title/Abstract]
OR "carcinoma"[Title/Abstract] OR "neoplasm"[Title/Abstract])
```

Search Strategy 3 – Analytical / Technical Emphasis Query

```
("cytology"[Title/Abstract] OR "FNA"[Title/Abstract]
OR "cell block"[Title/Abstract])
AND
("nucleic acid"[Title/Abstract] OR "DNA"[Title/Abstract]
OR "RNA"[Title/Abstract] OR "tumor fraction"[Title/Abstract]
OR "cellularity"[Title/Abstract] OR "specimen adequacy"[Title/Abstract]
OR "pre-analytical"[Title/Abstract])
AND
("molecular"[Title/Abstract] OR "sequencing"[Title/Abstract]
OR "PCR"[Title/Abstract] OR "NGS"[Title/Abstract])
```

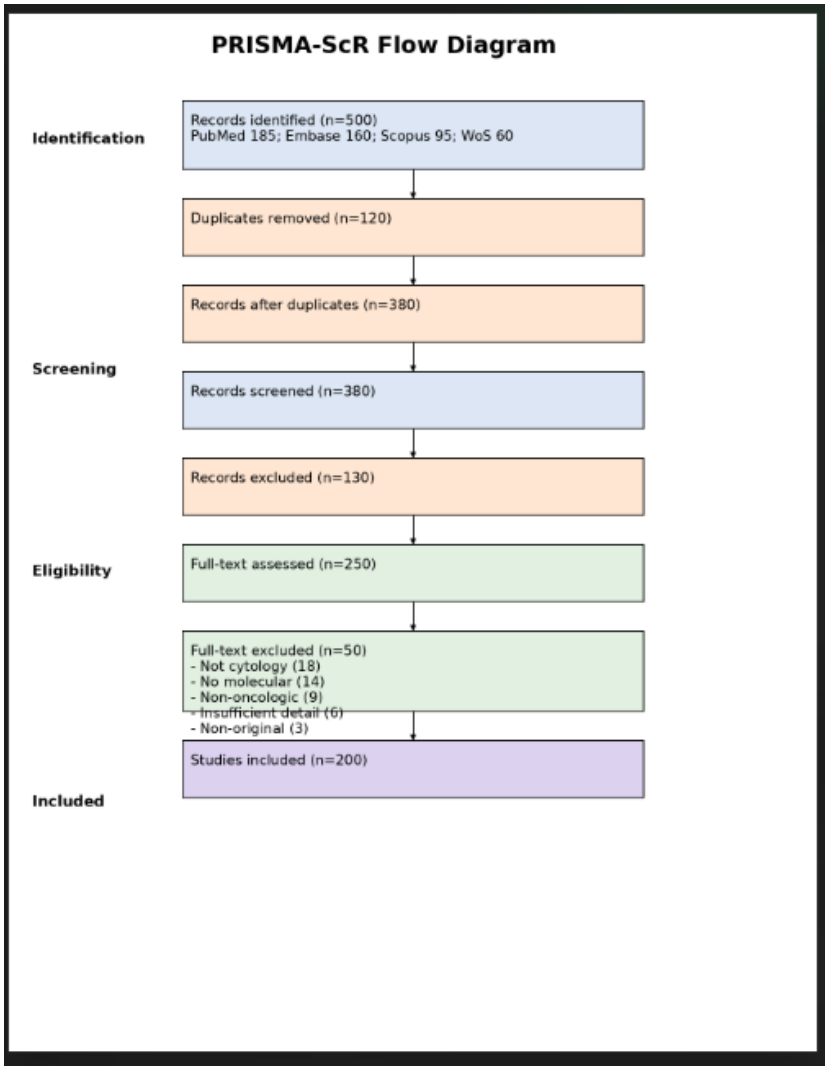

Figure 1: PRISMA-ScR Flow Diagram of Study Identification, Screening, Eligibility Assessment, and Inclusion

Flow diagram illustrating the identification, screening, eligibility assessment, and inclusion of studies in the scoping review of molecular testing in minimally invasive cytology. The figure details database retrieval, duplicate removal, exclusion criteria, full-text evaluation, and final study inclusion, reported in accordance with PRISMA-ScR guidelines for scoping reviews.

RESULTS

Overview of Study Selection

A total of 200 studies met the predefined eligibility criteria and were included in this scoping review (Figure 1). The included studies encompassed a wide range of oncologic contexts, molecular testing methodologies, and cytological specimen types, reflecting the methodological and clinical heterogeneity of cytology-based molecular diagnostics. Across the evidence base, variability was observed in study design, specimen preparation approaches, and analytical platforms.The principal findings are summarized in Tables 1,2 and figure 2,3,and 4

Characteristics of Included Studies

The included studies demonstrated diverse methodological designs and clinical

applications (Table 1). Retrospective observational studies constituted the largest proportion (n = 107), followed by method development or feasibility studies (n = 39) and prospective validation studies (n = 37). A smaller subset focused on clinical utility or outcome-based analyses (n = 17).In terms of oncologic context, lung cancer was the most frequently represented (n = 63), followed by breast (n = 20), thyroid (n = 18), head and neck (n = 17), prostate (n = 16), and pancreatic malignancies (n = 15). Geographic representation was led by studies from the United States (n = 44), Japan (n = 19), China (n = 17), Italy (n = 16), and Germany (n = 15), although reporting of study location was not uniform across all included publications.

Table 1

Characteristics of Included Studies (N = 200)

Study Characteristic	**Category**	**Number of Studies (n)**
Study Design	Retrospective observational	107
	Method development / feasibility	39
	Prospective validation	37
	Clinical utility / outcomes	17
Oncologic Context	Lung	63
	Breast	20
	Thyroid	18
	Head & Neck	17
	Prostate	16
	Pancreatic	15
Geographic Representation of Studies	United States	44
	Japan	19
	China	17
	Italy	16
	Germany	15

Descriptive characteristics of studies included in the scoping review. Values represent frequencies of reported study attributes across the evidence base. Categories are presented for mapping purposes and do not imply comparative methodological weighting.

Molecular Testing Methodologies

A broad spectrum of molecular testing approaches was reported across the included studies (Figure 2). Next-generation sequencing (NGS) was the most frequently described methodology (n = 90), followed by polymerase chain reaction (PCR)-based assays (n = 42). RNA-based panels or transcriptomic assays were reported in 23 studies, while fluorescence in situ hybridization (FISH) was utilized in 20 studies. Less frequently reported methodologies included methylation or epigenetic assays (n = 13) and digital PCR (n = 12).Many studies employed more than one molecular technique, reflecting the complementary use of targeted and high-throughput platforms in cytology-based molecular diagnostics.

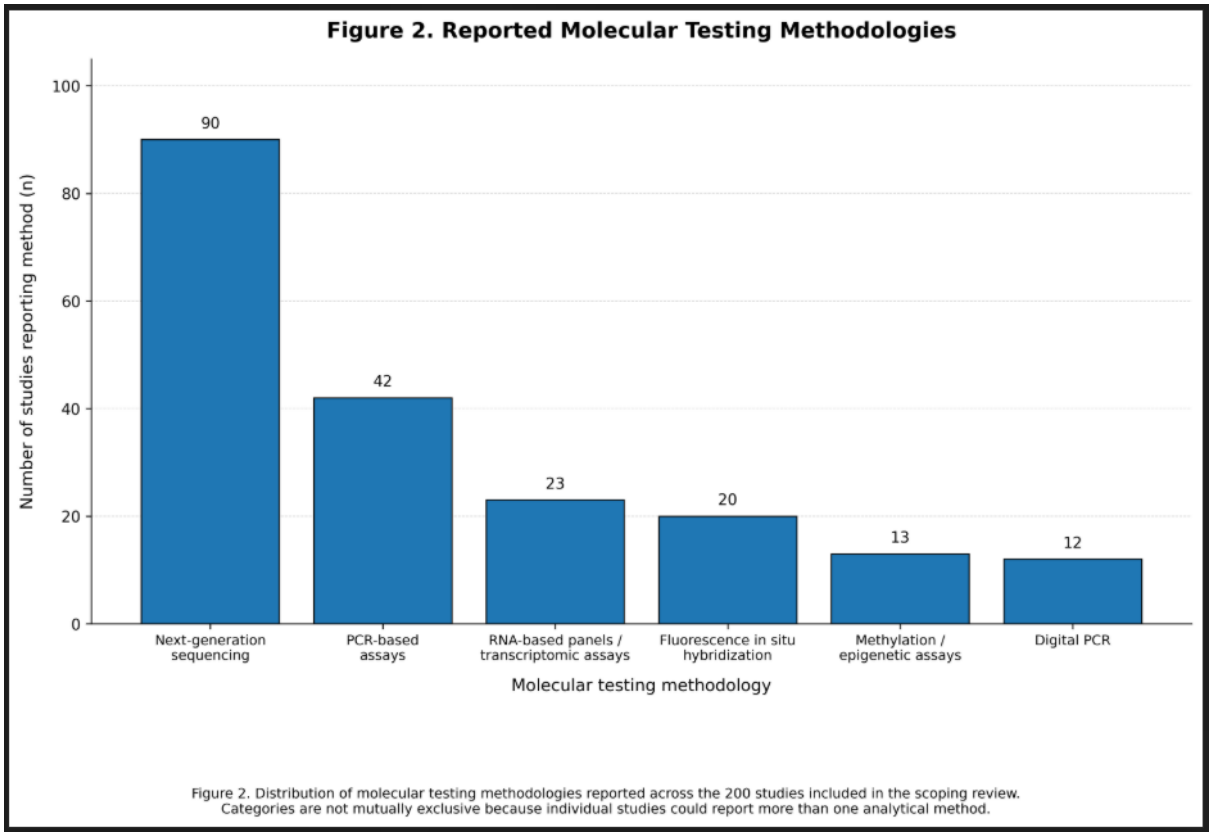

Figure 2: Reported Molecular Testing Methodologies

Reported molecular testing methodologies across included studies. Frequencies reflect the number of studies reporting each analytical approach. Multiple molecular techniques may have been utilized within individual studies.

Cytological Specimen Types Used for Molecular Analysis

Multiple cytological specimen types were utilized for molecular analysis (Table 2). Fine-needle aspiration (FNA) cytology was the most commonly reported specimen type (n = 72), followed by cell block preparations (n = 57) and liquid-based cytology (n = 35). Effusion cytology samples (n = 21) and brushings or washings (n = 15) were less frequently represented.The use of multiple specimen types within individual studies was common, reflecting variability in clinical sampling approaches and laboratory workflows.

Table 2

Cytological Specimen Types Used for Molecular Analysis

Cytology Specimen Type	**Number of Studies Reporting Specimen (n)**
Fine-Needle Aspiration Cytology (FNA Cytology)	72
Cell Block Preparations	57
Liquid-Based Cytology	35
Effusion Cytology Samples	21

Brushings / Washings	15

Reported cytological specimen types used for molecular analysis across included studies. Values indicate frequencies of studies reporting each specimen category. Classifications are presented for descriptive mapping and do not imply relative analytical performance or utilization prevalence.

Clinical Roles of Cytology-Based Molecular Testing

The clinical roles of molecular testing performed on minimally invasive cytology specimens were diverse (Figure 3). Predictive biomarker assessment was the most frequently reported application (n = 73), followed by diagnostic classification or refinement (n = 65). Treatment selection or stratification was described in 44 studies, while disease monitoring or surveillance applications were reported in 18 studies.These findings indicate that cytology-based molecular testing is applied across multiple stages of the diagnostic and therapeutic continuum in oncology.

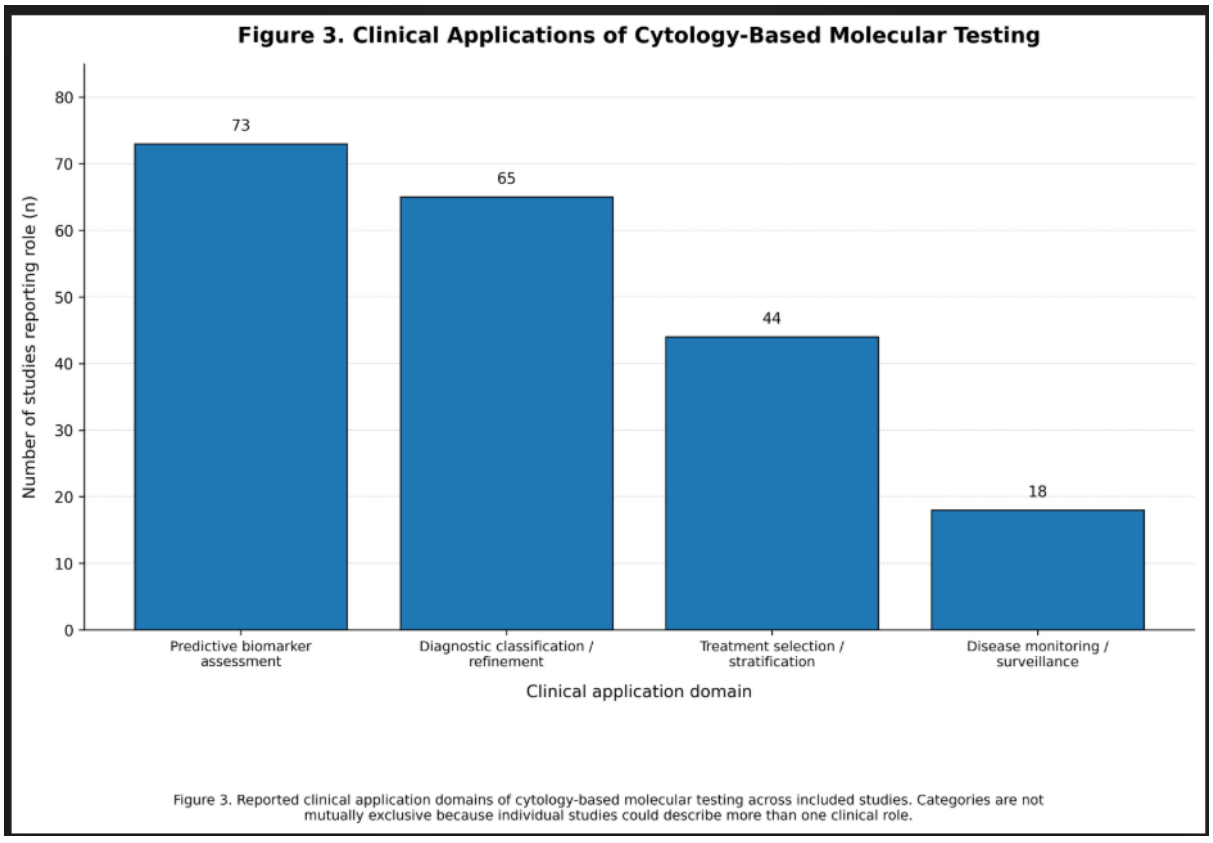

Figure 3: Reported Clinical Roles of Cytology-Based Molecular Testing

Reported clinical roles of cytology-based molecular testing across included studies. Values represent frequencies of studies describing each application domain. Categories are presented for descriptive mapping and should not be interpreted as indicators of clinical effectiveness, priority, or comparative utility.

Laboratory and Technical Considerations

Recurrent laboratory and technical factors influencing molecular analysis were

identified across the included studies (Figure 4). The most frequently reported challenges included low cellularity or specimen adequacy constraints (n = 50) and limited nucleic acid yield (n = 47). Variability in fixation and specimen preparation was described in 41 studies, while assay sensitivity limitations were reported in 28 studies. Tumor fraction variability (n = 25) and bioinformatic or interpretative challenges (n = 9) were also noted.

These factors were frequently described in combination within individual studies, highlighting the multifactorial nature of analytical variability in cytology-based molecular testing.

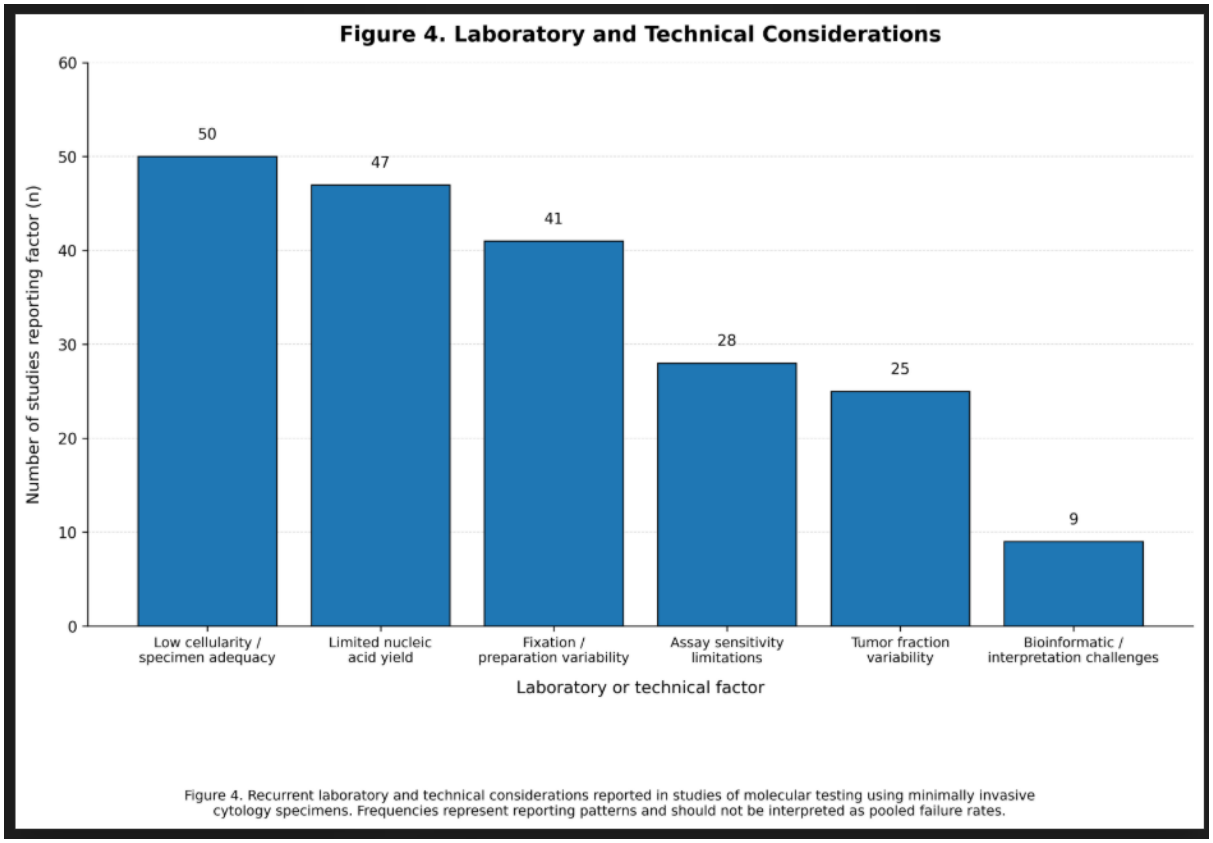

Figure 4: Reported Laboratory and Technical Considerations

Reported laboratory and technical considerations influencing molecular analysis of cytological specimens across included studies. Values represent frequencies of studies describing each factor. Categories are presented for descriptive synthesis and do not quantify assay failure rates or relative analytical impact.

DISCUSSION

This scoping review examined the methodological and analytical landscape of molecular testing performed on minimally invasive cytology specimens across diverse oncologic applications. The findings indicate that the field is characterized by substantial variability in analytical platforms, specimen preparation strategies, and reporting practices. Such heterogeneity is expected in an evolving diagnostic domain but limits reproducibility and comparability across studies[24].

The prominence of next-generation sequencing within the literature reflects its increasing integration into precision oncology workflows[25]. However, its frequent use does not imply universal applicability. Implementation is influenced by factors such as nucleic acid input requirements, assay validation complexity, and sensitivity to pre-analytical variation [26].

In contrast, targeted molecular techniques, including polymerase chain reaction and hybridization-based assays, remain relevant in settings where focused diagnostic questions or resource constraints shape methodological selection[26].

The analytical reliability of cytology-derived material remains an area of active evaluation. While several studies demonstrate the feasibility of genomic testing on cytological specimens, others report reduced sensitivity or assay failure associated with low cellularity, limited tumor fraction, or compromised nucleic acid quality[26]. These differences are largely attributable to variability in laboratory workflows and analytical thresholds rather than intrinsic limitations of cytological material[29] .

Comparisons between cytological and histological specimens further illustrate unresolved methodological challenges. Some studies report comparable analytical performance under optimized conditions, while others describe variability related to specimen architecture, preservation effects, and tumor cell representation[30]. These inconsistencies suggest that cytology and histology are not universally interchangeable and that equivalence depends on standardized adequacy criteria and validated protocols[31].

From a clinical perspective, cytology-based molecular testing is frequently driven by necessity. In advanced malignancies or anatomically inaccessible lesions, minimally invasive specimens may represent the only available material for genomic analysis[32]. Beyond initial diagnosis, their role is expanding into longitudinal disease monitoring. Serial sampling enables detection of tumor evolution, including resistance mutations and clonal heterogeneity under therapeutic pressure[33]. This supports treatment modification and contributes to survivorship care through ongoing molecular assessment[34].

Pre-analytical and post-analytical factors remain central to analytical performance. Variables such as specimen adequacy, tumor fraction, fixation methods, and nucleic acid preservation directly influence assay outcomes[35]. Post-analytical processes, including bioinformatic pipelines and variant interpretation thresholds, further contribute to variability in reported results[36]. In many instances, these workflow-dependent factors exert greater influence on analytical success than specimen type alone.

The application of cytology-based molecular testing in African settings remains limited but highlights important contextual challenges. Access to advanced molecular platforms is often restricted, and infrastructure constraints, reagent availability, and workforce limitations affect service delivery[37]. Pre-analytical challenges, including delayed processing and variability in fixation practices, may further compromise nucleic acid integrity. Despite these constraints, minimally invasive cytology offers practical advantages due to its cost-effectiveness and feasibility. The limited representation of African studies underscores a significant evidence gap and highlights the need for context-specific research and capacity building[38].

The methodological composition of the evidence base introduces additional limitations. The predominance of retrospective and single-center studies raises concerns regarding reproducibility and potential selection bias[24]. Prospective

validation studies remain limited, and inconsistent reporting of methodological details constrains cross-study comparison.
This review is also subject to limitations inherent to scoping methodology. Formal quality assessment was not undertaken, and reported frequencies reflect patterns of evidence rather than measures of analytical validity. Restriction to English-language publications may introduce bias, and publication bias is likely, as studies reporting successful outcomes are more frequently disseminated.

Overall, cytology-based molecular diagnostics is a technically feasible but methodologically heterogeneous field. Progress will depend on improved standardization of pre-analytical workflows, clearer reporting of validation parameters, and increased adoption of prospective multi-center studies. These efforts are essential to enhance reproducibility and strengthen the role of minimally invasive cytology in precision oncology.

CONCLUSION

This scoping review demonstrates that minimally invasive cytology specimens can provide reliable material for molecular testing in precision oncology, particularly when conventional tissue biopsies are limited or unsuitable for repeated sampling. Cytology-based molecular analysis supports genomic characterization, predictive biomarker assessment, treatment selection, and longitudinal monitoring of tumor evolution and resistance mechanisms.

Despite these advances, the current evidence base remains methodologically heterogeneous. Variability in specimen preparation, fixation methods, analytical platforms, and reporting practices limits reproducibility and complicates comparison across studies. Analytical reliability was consistently influenced by factors such as specimen adequacy, tumor cellularity, nucleic acid quality, and bioinformatic interpretation frameworks.

Although many studies reported clinically actionable molecular findings, the predominance of retrospective designs and inconsistent methodological reporting reduces the strength of available evidence. In addition, disparities in access to molecular diagnostics in resource-limited settings highlight important infrastructural and implementation challenges.

Future research should emphasize standardized laboratory workflows, harmonized reporting practices, and prospective multi-center validation studies to strengthen reproducibility and support the broader integration of cytology-based molecular diagnostics into routine precision oncology practice.

Acknowledgement
The author acknowledges Nebert Mchidi for his careful and insightful review of this manuscript. His constructive feedback was instrumental in improving the clarity, structure, and overall quality of the work.

Use of Artificial Intelligence Disclosure
The author used ChatGPT (OpenAI) to assist with language editing and manuscript structuring. All content was critically reviewed and revised to ensure accuracy and integrity. The author takes full responsibility for the content of this publication.

Funding
No external funding was received for this study.

REFERENCES

1. Malone ER, Oliva M, Sabatini PJB, Stockley TL, Siu LL. Molecular profiling for precision cancer therapies. Genome Med. 2020;12(1):8. doi:10.1186/s13073-019-0703-1.
2. Chakravarty D, Johnson A, Sklar J, et al. The molecular landscape of cancer and implications for precision oncology. Nat Med. 2021;27(3):486–498. doi:10.1038/s41591-021-01227-z.
3. Garraway LA. Genomics-driven oncology: framework for precision medicine. Cancer Discov. 2020;10(4):496–505. doi:10.1158/2159-8290.CD-20-0120.
4. Meric-Bernstam F, Brusco L, Daniels M, et al. Incidental germline variants in tumor-only sequencing. J Clin Oncol. 2021;39(21):2311–2321. doi:10.1200/JCO.20.03650.
5. Kim H, Chung JH, Lee SH. Biomarker testing of cytology specimens. J Pathol Transl Med. 2022;56(6):309–318. doi:10.4132/jptm.2022.09.27.
6. VanderLaan PA. Molecular testing of cytology specimens. J Am Soc Cytopathol. 2022;11(5):261–273. doi:10.1016/j.jasc.2022.06.003.
7. Pisapia P, Pepe F, Sgariglia R, et al. Next generation sequencing in cytology. Cytopathology. 2021;32(5):588–595. doi:10.1111/cyt.13011.
8. Roy-Chowdhuri S, Dacic S, Ghofrani M, et al. Pre-analytical variables in cytology: lessons learned from next-generation sequencing. Arch Pathol Lab Med. 2020;144(10):1227–1237. doi:10.5858/arpa.2019-0568-RA.
9. Jain D, Allen TC, Aisner DL, et al. Molecular cytopathology: a review of current applications and future directions. Arch Pathol Lab Med. 2020;144(10):1189–1203. doi:10.5858/arpa.2019-0112-RA.
10. Fassunke J, Haller F, Hebele S, et al. Utility of next-generation sequencing in diagnostics. Virchows Arch. 2017;468(1):1–12. doi:10.1007/s00428-015-1856-5.
11. Wei S, Talarchek J, Gong Y, et al. RNA next-generation sequencing in cytology specimens. Cytopathology. 2023;34(2):145–153. doi:10.1111/cyt.13175.
12. Ignatiadis M, Lee M, Jeffrey SS. Circulating tumor cells and DNA in precision oncology. Nat Rev Clin Oncol. 2021;18(8):499–512. doi:10.1038/s41571-021-00497-5.
13. Wan JCM, Massie C, Garcia-Corbacho J, et al. Liquid biopsies in cancer management. Nat Rev Cancer. 2017;17(4):223–238. doi:10.1038/nrc.2017.7.
14. Lindeman NI, Cagle PT, Aisner DL, et al. Molecular testing guideline for lung cancer. J Thorac Oncol. 2018;13(3):323–358. doi:10.1016/j.jtho.2017.12.001.
15. Rolfo C, Mack PC, Scagliotti GV, et al. Liquid biopsy for NSCLC. J Thorac Oncol. 2018;13(9):1248–1268. doi:10.1016/j.jtho.2018.05.030.
16. Heitzer E, Haque IS, Roberts CES, Speicher MR. Liquid biopsy perspectives. Nat Rev Genet. 2019;20(2):71–88. doi:10.1038/s41576-018-0071-5.
17. Siravegna G, Marsoni S, Siena S, Bardelli A. Integrating liquid biopsies. Nat Rev Clin Oncol. 2017;14(9):531–548. doi:10.1038/nrclinonc.2017.14.
18. Abbosh C, Birkbak NJ, Wilson GA, et al. ctDNA and tumor evolution. Nature. 2017;545(7655):446–451. doi:10.1038/nature22364.
19. Dawson SJ, Tsui DWY, Murtaza M, et al. Circulating tumor DNA monitoring. N Engl J Med. 2013;368(13):1199–1209. doi:10.1056/NEJMoa1213261.
20. Tie J, Kinde I, Wang Y, et al. ctDNA in colorectal cancer monitoring. Sci

Transl Med. 2015;7(302):302ra133. doi:10.1126/scitranslmed.aac8612.
21. Arksey H, O'Malley L. Scoping studies framework. Int J Soc Res Methodol. 2005;8(1):19–32. doi:10.1080/1364557032000119616.
22. Peters MDJ, Godfrey CM, Khalil H, et al. Guidance for scoping reviews. Int J Evid Based Healthc. 2015;13(3):141–146. doi:10.1097/XEB.0000000000000050.
23. Tricco AC, Lillie E, Zarin W, et al. PRISMA-ScR checklist. Ann Intern Med. 2018;169(7):467–473. doi:10.7326/M18-0850.
24. Ioannidis JPA. Contradicted clinical research findings. JAMA. 2005;294(2):218–228. doi:10.1001/jama.294.2.218.
25. Goodwin S, McPherson JD, McCombie WR. Next-generation sequencing decade. Nat Rev Genet. 2016;17(6):333–351. doi:10.1038/nrg.2016.49.
26. Roy-Chowdhuri S, Stewart J. Preanalytic variables in cytology. Arch Pathol Lab Med. 2016;140(11):1199–1208. doi:10.5858/arpa.2016-0116-RA.
27. Lindeman NI, Cagle PT, Beasley MB, et al. Molecular testing guideline update. J Thorac Oncol. 2013;8(7):823–859. doi:10.1097/JTO.0b013e318290868f.
28. Pisapia P, Malapelle U, Troncone G. Cytology and NGS feasibility. Cancers (Basel). 2019;11(3):292. doi:10.3390/cancers11030292.
29. Jain D, Roy-Chowdhuri S. Molecular cytopathology overview. Arch Pathol Lab Med. 2018;142(3):321–326. doi:10.5858/arpa.2016-0629-RA.
30. Roy-Chowdhuri S, et al. Cytology versus histology testing. Cancer Cytopathol. 2018;126(6):400–409. doi:10.1002/cncy.21970.
31. College of American Pathologists. Molecular testing standards. Arch Pathol Lab Med. 2018;142(3):321–346. doi:10.5858/arpa.2017-0001-SA.
32. VanderLaan PA. Cytology molecular applications. J Am Soc Cytopathol. 2017;6(4):178–187. doi:10.1016/j.jasc.2017.03.002.
33. Wan JCM, et al. ctDNA clinical applications. Nat Rev Cancer. 2017;17(4):223–238. doi:10.1038/nrc.2017.7.
34. Dawson SJ, et al. ctDNA and treatment monitoring. N Engl J Med. 2013;368(13):1199–1209. doi:10.1056/NEJMoa1213261.
35. Srinivasan M, Sedmak D, Jewell S. Fixation effects on nucleic acids. Am J Pathol. 2002;161(6):1961–1971. doi:10.1016/S0002-9440(10)64472-0.
36. Jennings LJ, Arcila ME, Corless C, et al. NGS interpretation guidelines. J Mol Diagn. 2017;19(1):4–23. doi:10.1016/j.jmoldx.2016.09.002.
37. Abayomi EA, Somers A. Molecular pathology in Africa. Afr J Lab Med. 2017;6(1):1–6. doi:10.4102/ajlm.v6i1.455.
38. Bates I, Maitland K. Diagnostics in resource-limited settings. Lancet Glob Health. 2015;3(10):e577–e578. doi:10.1016/S2214-109X(15)00190-1.