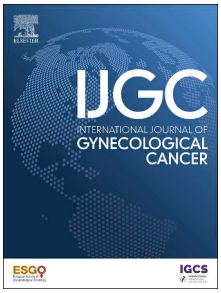
ORIGINAL RESEARCH

Electronic nose-based volatile organic compound profiling in gynecologic oncology: current evidence and diagnostic accuracy



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ABSTRACT

Objective: Volatile organic compounds profiling has emerged as a promising approach for cancer detection. Electronic noses are portable sensor-based devices capable of recognizing volatile organic compound patterns in various biological matrices, offering a rapid, non-invasive, and cost-effective diagnostic alternative. The aim of this systematic review was to evaluate the diagnostic performance of electronic noses in gynecologic oncology and to delineate their technical characteristics.

Methods: This review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and was registered in International Prospective Register of Systematic Reviews (CRD420251122293). PubMed, Scopus, and Google Scholar were searched up to August 2025. Eligible studies included prospective investigations evaluating volatile organic compound analysis through electronic noses in ovarian, cervical, endometrial, and vulvar cancers, as well as high-grade squamous intraepithelial lesions, using histopathology as the reference standard. Diagnostic performance parameters were extracted, and the risk of bias was assessed with Quality Assessment of Diagnostic Accuracy Studies 2. No meta-analysis was performed due to study heterogeneity.

Results: Fifteen studies with a total of 1224 patients were included. Among them, 562 (45.9%) had gynecologic malignancies, and 662 (54.1%) served as controls. Ten studies (66.7%) investigated ovarian cancer, 4 (26.7%) cervical cancer, and 1 (6.7%) high-grade squamous intraepithelial lesions of the cervix; no studies evaluated endometrial or vulvar cancers. Biological matrices analyzed included breath (33.3%), urine (20%), tissue (20%), plasma (6.7%), genitourinary secretions (6.7%), or combined samples (6.7%). Reported diagnostic performance ranged from 71% to 97.7% for sensitivity, from 63% to 100% for specificity, and from 71% to 95% for accuracy across all cancer types. In ovarian cancer studies, sensitivity ranged from 71% to 97.7%, specificity from 63% to 91.4%, and accuracy from 71% to 87%. In cervical cancer studies, sensitivity ranged from 88% to 93%, and specificity from 85% to 100%.

Conclusions: Electronic nose technologies show encouraging diagnostic accuracy in gynecologic oncology, particularly for cervical cancer, whereas performance in ovarian cancer remains more variable depending on the biological matrix and comparator group. Despite promising results, the lack of standardized protocols and the heterogeneity of current evidence limit immediate clinical translation. Larger, multicenter, and standardized studies are needed to validate their integration into diagnostic workflows.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Volatile organic compounds have been associated with cancer-specific metabolic alterations, and electronic noses can rapidly detect these patterns in biological samples. Preliminary studies in oncology have suggested promising diagnostic performance, but evidence in gynecologic cancers remains fragmented and heterogeneous.

WHAT THIS STUDY ADDS

This systematic review shows that electronic noses achieve encouraging diagnostic accuracy in gynecologic cancers, with sensitivity ranging from 71% to 98%, specificity from 63% to 100%, and accuracy from 71% to 95%. Diagnostic performance was particularly consistent in cervical cancer, whereas results in ovarian cancer were more variable depending on the biological matrix and comparator groups.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

Electronic noses have the potential to become rapid, non-invasive diagnostic tools in gynecologic oncology. Standardized protocols and multicenter validation studies are essential to move from feasibility to clinical translation, with implications for early detection, patient triage, and integration into precision diagnostic pathways.

Keywords:
Electronic Nose; Volatile Organic Compounds; Gynecologic Oncology; Ovarian Cancer; Cervical Cancer

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INTRODUCTION

Volatile organic compounds are gaseous by-products of metabolic and biochemical processes that can be detected in various biological matrices, including exhaled breath, urine, blood, and genital tract secretions.[1,2] Changes in volatile organic compounds profiles have been associated with several pathological conditions, including malignancies, and their analysis has emerged as a promising approach for cancer detection.[3] Given their volatility and low solubility, volatile organic compounds readily diffuse into exhaled breath or accumulate in other body fluids, providing a potential non-invasive means of diagnosis.[4]

Traditionally, volatile organic compounds have been identified through gas chromatography—mass spectrometry (GC-MS), which enables precise characterization of individual compounds but is expensive, time-consuming, and not suitable for routine clinical practice.[5] In recent years, portable sensor technologies such as electronic noses (e-noses) and electronic tongues (e-tongues) have been developed to overcome these limitations.[6] These devices do not identify single compounds but instead recognize complex volatile organic compound patterns, generating a biochemical "fingerprint" that can be processed by statistical or machine learning algorithms.[7] Recent studies have shown that volatile organic compounds profiles from breath, urine, plasma, and genital secretions may allow reliable discrimination between malignant and benign conditions,[8] and electronic noses have demonstrated encouraging diagnostic performance across a wide range of cancers, with reported sensitivities and specificities often exceeding 80% to 90%.[7]

In gynecologic oncology, early diagnosis remains a major clinical challenge. Ovarian cancer, the eighth most common cancer in women worldwide, is often diagnosed at an advanced stage due to the absence of effective screening tools and nonspecific early symptoms.[9] Similarly, although cervical cancer is preventable through screening programs and human papillomavirus (HPV) vaccination, accurate and timely diagnosis of high-grade squamous intraepithelial lesions (HSIL) and early cervical cancer still represents a diagnostic challenge in several settings.[10,11]

A number of pilot and feasibility studies have investigated the diagnostic role of volatilome analysis in gynecologic cancers. For ovarian cancer, electronic nose platforms have demonstrated the potential to distinguish between malignant and benign adnexal masses, as well as between early and advanced disease.[8] In cervical cancer, volatile organic compounds collected from breath or genitourinary secretions have shown promising accuracy, with some studies reporting sensitivities and specificities above 90%.[12] Despite these encouraging findings, the clinical application of volatile organic compounds profiling remains limited by small sample sizes, methodological heterogeneity, and a lack of standardized protocols.

Given the growing body of evidence, a systematic synthesis of the available literature is warranted. The present systematic review aims to summarize and critically appraise the diagnostic performance of electronic noses compared with histology for volatile organic compounds profiling in gynecologic oncology and to delineate their technical characteristics.

METHODS

Search Strategy

The comprehensive review adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[13] and was officially registered with the International Prospective Register of Systematic Reviews (CRD420251122293), before the extraction of data began.

Eligibility Criteria

This systematic review was designed according to the PICO framework (Patient/Population, Intervention, Comparison, Outcome). Eligible studies were those investigating the application of volatile organic compounds analysis through electronic nose technology for the diagnosis of gynecologic oncology lesions, including ovarian cancer, cervical cancer, endometrial cancer, vulvar cancer, and HSIL of the uterine cervix. Studies were required to report primary diagnostic performance data—such as sensitivity, specificity, or accuracy—using histopathological confirmation as the reference standard. Exclusion criteria were non-original works (conference abstracts, narrative reviews, systematic reviews, meta-analyses, editorials, and letters), studies not involving human participants, non-English publications, and studies evaluating only non-gynecologic malignancies.

Search Strategy

Articles were sourced by searching the PubMed database, Google Scholar, and Scopus from July 1 to August 3, 2025, using the following search terms: "electronic nose," "volatile organic compounds," "VOC," "breath analysis," "cervical cancer," "endometrial cancer," "ovarian cancer," "vaginal cancer," "vulvar cancer," filtered only for the English language. The complete search strategy is reported in the supplementary material (Online Supplement A).

Study Selection

Rayyan software (Qatar Computing Research Institute, HBKU, Doha, Qatar)[14] was used independently by 2 authors (CI and NM) to screen titles and abstracts for eligibility. Duplicate publications were first removed, followed by the independent review of the titles, abstracts, and keywords (CI and NM for inclusion), and the full-text review of eligible articles. In case of discrepancies, a consensus was reached through agreement with a third author (MP).

Data Extraction

Data regarding sample size, field of application, diagnostic parameters, and technical specifications of the devices used for volatile analysis were extracted for further analysis. In accordance with the journal's guidelines, we will provide our data for independent analysis by a selected team for the purposes of additional data analysis or for the reproducibility of this study in other centers upon reasonable request.

Risk of Bias

The risk of bias was assessed independently by 2 reviewers (CI and NM) using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool.[15] The risk of bias was assessed for the

following domains: patient selection, index test, reference standard, and flow and timing.

RESULTS

The search strategy initially identified 575 studies, of which 15 (2.6%) met the inclusion criteria for the systematic review (Fig. 1). Included articles are listed in Online Supplement B, which summarizes the main study characteristics, including sample size, type of electronic nose, and biological matrix analyzed. Excluded articles are listed in the supplementary material (Online Supplement C).

All the included studies in gynecologic oncology (15/15, 100%) were prospective. Among the 1224 patients enrolled, 562 (45.9%) were diagnosed with gynecologic malignancies, whereas 662 (54.1%) served as controls, either healthy individuals or patients with benign conditions. Of the total, 10 studies (66.7%) investigated volatilome analysis for the diagnosis of ovarian cancer, 4 (26.7%) focused on cervical cancer, and 1 (6.7%) on HSIL of the uterine cervix. No studies were identified that evaluated volatilome analysis for the diagnosis of endometrial or vulvar cancers.

Regarding the biological matrices examined, 5 studies (33.3%) investigated breath, 3 (20%) analyzed specific tissues (ovary, myometrium, fallopian tubes), and 3 (20%) focused on urine. One study (6.7%) investigated plasma alone, 1(6.7%) simultaneously analyzed breath, urine, venous blood, and plasma, and 1 (6.7%) considered genitourinary secretions (Online Supplement B).

When considering all lesion types combined (ovarian cancer, cervical cancer, and HSIL), diagnostic performance data (sensitivity, specificity, and accuracy) were reported in 14 studies (93.3%). Sensitivity ranged from 71% to 97.7%, specificity from 63% to 100%, and accuracy from 71% to 95%. In ovarian cancer studies, sensitivity ranged from 71% to 97.7%, specificity from 63% to 91.4%, and accuracy from 71% to 87%. In cervical cancer studies, sensitivity ranged from 88% to 93% and specificity from 85% to 100%. Accuracy was reported in 2 studies (50.0%) and was consistently 89% (Tables 1 and 2[6,8,12,16-27]; Fig. 2). Median sensitivity and specificity were 85.4% and 85.3% for ovarian cancer, and 91.6% and 92.0% for cervical cancer/HSIL, respectively.

Electronic noses are portable sensor-based devices designed to detect and discriminate complex mixtures of volatile organic

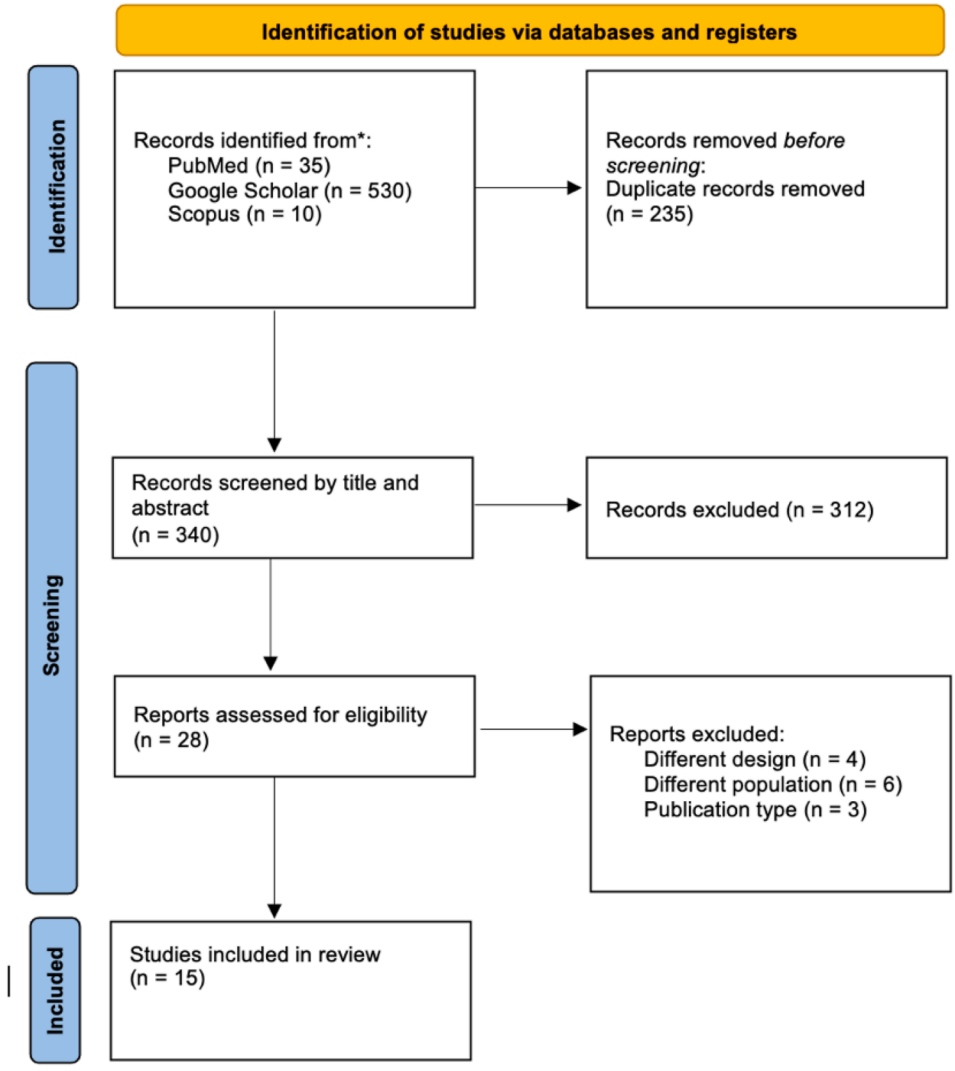

Figure 1 PRISMA flow diagram of selected studies (Abbreviations: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

Table 1 Electronic Nose Diagnostic Performance in Comparison With Histopathology as Gold Standard for Ovarian Lesions

Year	Source	Sensitivity (%)	Specificity (%)	Accuracy (%)	Biological sample	Cancer type
2009	Chilo and colleagues[16]	NA	NA	NA	Samples from tissues (ovarian cancer, myometrium, Fallopian tubes)	Ovarian cancer
2009	Chilo and colleagues[17]	84.8 (training data), 82.6 (test data)	91.4 (for training and test data)	86.4	Samples from tissues (ovarian cancer, myometrium)	Ovarian cancer
2010	Horvath and colleagues[18]	84.4	86.8	Nd	Samples from tissues (ovarian cancer, myometrium, Fallopian tubes)	Ovarian cancer
2014	Amal and colleagues[8]	71	71	71	Breath	Ovarian cancer
2015	Kahn and colleagues[19]	83.4	80.8	82	Breath	Ovarian cancer
2018	Niemi and colleagues[20]	91.2	63.1	81.3	Urine	Ovarian cancer
2020	Raspagliesi and colleagues[21]	89	86	87	Breath	Ovarian cancer
2020	Kybert and colleagues[22]	NA	NA	NA	Plasma	Ovarian cancer
2024	Angioli and colleagues[6]	86 (e-Nose 41, e-Tongue 78)	88 (e-Nose 91, e-Tongue 53)	NA	Breath, urine, venous blood, plasma	Ovarian cancer
2024	Eriksson and colleagues[23]	97.7	84.6	95	Plasma	Ovarian cancer

Abbreviations: NA, not applicable; Nd, not determined

Table 2 Electronic Nose Diagnostic Performance in Comparison With Histopathology as Gold Standard for Cervical Lesions

Year	Author	Sensitivity (%)	Specificity (%)	Accuracy (%)	Biological sample	Cancer type
2017	Zhou and colleagues[24]	92.3	88.2	89.4	Breath	Cervical cancer
2018	Rodríguez-Esquivel and colleagues[25]	93	93	NA	Genitourinary secretions	Cervical cancer
2021	Díaz de León-Martínez and colleagues[26]	91.6	100	NA	Urine	Cervical cancer
2023	Dokter and colleagues[12]	88	92	NA	Breath	HSIL
2025	Zucha and colleagues[27]	91	85	89	Urine	Cervical cancer

Abbreviations: HSIL, high-grade squamous intraepithelial lesion; NA, not applicable.

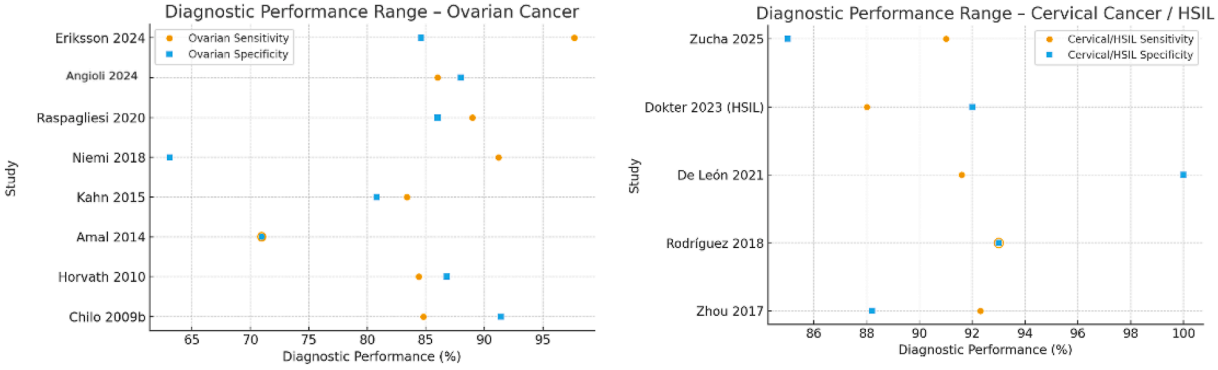

Figure 2 Diagrams of diagnostic performances for ovarian and cervical cancer (including HSIL). (Abbreviations: HSIL, high-grade squamous intraepithelial lesion).

compounds.[1] Unlike gas chromatography—mass spectrometry, which identifies individual molecules, electronic noses capture global volatile organic compounds patterns, generating a biochemical "fingerprint" characteristic of a specific condition.[21] The core technology relies on an array of partially selective sensors—commonly metal oxide semiconductors, conducting polymers, quartz crystal microbalances, or nanomaterial-based sensors—that interact with volatile organic compounds, inducing changes in electrical resistance, frequency, or other measurable properties.[2] These sensor responses are then processed by advanced computational methods, such as principal component analysis, discriminant function analysis, or machine learning algorithms, to classify samples.[4]

The advantages of electronic noses include portability, relatively low cost, and rapid output without the need for labor-intensive sample preparation, making them suitable for potential translation into clinical diagnostics (Fig. 3). Electronic nose technologies operate through arrays of partially selective chemical sensors that detect global variations in volatile organic compounds mixtures; the resulting signal patterns are subsequently analyzed using multivariate statistical methods or machine learning algorithms. Across the included studies, sample collection and handling procedures—such as breath collection modality, urine or plasma processing, and storage conditions—were heterogeneous and often incompletely detailed, representing a source of methodological variability.

The methodological quality of the included studies was evaluated using the QUADAS-2 tool,[15] which considers 4 domains: patient selection, index test, reference standard, and flow and timing. As the majority of studies were designed prospectively, the overall risk of bias was judged to be moderate to low. The prospective design contributed to reducing the risk of selection bias and ensured greater consistency in the application of both the index test and the reference standard. However, some methodological limitations were identified. In particular, variability in patient recruitment strategies and incomplete reporting of reference standards across different studies introduced potential concerns in the domains of patient selection and reference standards. Moreover, in a minority of cases, insufficient information regarding follow-up procedures and the flow of participants through the study raised the possibility of bias in the flow and timing domain (Online Supplement D).

DISCUSSION

Summary of Main Results

This systematic review reports the application of electronic nose technology in gynecologic oncology and summarizes its diagnostic performance compared with histology. Electronic noses achieve clinically relevant overall diagnostic performance, with sensitivity ranging from 71% to 97.7%, specificity from 63% to 100%, and accuracy from 71% to 95%. By lesion type, cervical cancer studies showed higher and more consistent performance: exhaled-breath and genitourinary secretion electronic nose analyses reported sensitivity ranging from 88% to 93% and specificity from 85% to 100%, with accuracy of approximately 89%. For ovarian cancer, results were more variable and depended on the biological matrix and comparator: performance was high when compared with tumor-free controls (eg, sensitivity 79%-98%, specificity 95%-100%, accuracy 89%-98%), but specificity dropped when benign adnexal masses were included (eg, 89% sensitivity and 86% specificity in breath; urine sensitivity of approximately 91% with specificity of 51%-63%).

Results in the Context of Published Literature

Current detection strategies for gynecologic cancers vary markedly across tumor types. Cervical cancer screening relies on Pap smears and HPV testing, which are highly effective but limited by incomplete population coverage, variable adherence, and occasional false-negative results.[28] In contrast, ovarian cancer lacks an established screening tool; serum biomarkers such as CA125 and HE4, as well as pelvic imaging, show suboptimal performance for early-stage disease. In this context, electronic nose technologies could serve as complementary tools by offering rapid, non-invasive assessment of disease-related volatilomic patterns, potentially improving early detection and supporting triage within existing diagnostic pathways.[29]

In ovarian cancer, multiple investigations have demonstrated the feasibility of detecting disease-specific patterns in different volatile organic compound biological matrices. Horvath and

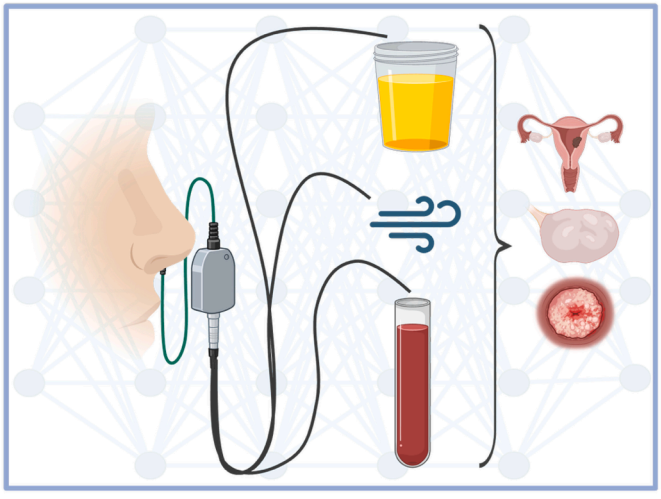

Figure 3 Electronic nose matrix analysis for gynecologic oncology lesions detection.

colleagues[18] reported that an electronic nose could distinguish ovarian carcinoma tissue from controls with an overall sensitivity of 84.4% and specificity of 86.8%. Kahn and colleagues[19] further advanced the field by employing dynamic nanoparticle-based flexible sensors, which discriminated exhaled breath samples of ovarian cancer patients with an accuracy of 82%, independent of smoking status or comorbidities. More recently, Angioli and colleagues[6] combined electronic nose and electronic tongue platforms to analyze breath, urine, and plasma, reporting high diagnostic power and suggesting complementarity with established biomarkers such as CA125 and HE4. Similarly, Kybert and colleagues[22] confirmed that plasma volatile organic compound signatures from ovarian cancer patients could be distinguished from benign and healthy samples using a combined sensor approach.

In cervical cancer, Zhou and colleagues[24] demonstrated that proton transfer reaction-MS of exhaled breath could differentiate cervical cancer patients from healthy controls with a sensitivity of 92.3% and specificity of 88.2%. Rodríguez-Esquivel and colleagues[25] identified volatile organic compounds from genitourinary secretions with a diagnostic accuracy of 89%, whereas Zucha and colleagues[27] confirmed the diagnostic value of urine volatile organic compound profiling, achieving 91% sensitivity and 85% specificity. In addition, machine learning-based algorithms applied to electronic nose data showed potential in detecting HSIL of the cervix, with sensitivities above 88%.[12]

The performance observed in cervical cancer mirrors results from tumor sites where volatilome analysis has been more extensively validated. In lung cancer, several large-scale studies reported sensitivity and specificity exceeding 90% (95.6% and 91.1% in Chen and colleagues[30]; 95.3% and 97.2% in Liu and colleagues).[31,32] Similarly, in head and neck squamous cell carcinoma, Hakim and colleagues[33] and Leunis and colleagues[34] documented diagnostic accuracy between 85% and 100%. In gastric cancer, an accuracy of around 90% (sensitivity 87%, specificity 85%) has been consistently achieved,[35,36] whereas in breast cancer, sensitivity ranged from 84% to 86% and specificity ranged from 80% to 97%.[31,37] These figures closely align with the cervical cancer results summarized in this review, suggesting that when tumor-related volatile organic compound signals are strong and distinctive, electronic noses can perform with similar accuracy across multiple anatomical sites.

The higher diagnostic accuracy observed in cervical cancer may reflect biological and methodological factors. In cervical cancer (as in lung, breast, and head and neck tumors), the volatilome signature is likely facilitated by an epithelial or mucosal microenvironment directly exposed to luminal surfaces (airways, oral cavity, cervix).[7] This proximity favors the release of volatile organic compounds into exhaled breath or genital secretions, producing a more distinctive and detectable signal. In contrast, abdominal and pelvic tumors such as ovarian and colorectal cancers are located deep in the pelvis and are influenced by a more complex metabolic background, where benign and malignant conditions share overlapping volatile organic compound patterns, thereby reducing specificity.[7] In this context, electronic nose analysis may complement existing biomarkers—such as CA125, HE4, or HPV testing—by providing an additional, rapid, and non-invasive layer of discrimination within multimodal diagnostic pathways.

The variability observed in ovarian cancer parallels that described in colorectal cancer, where high sensitivities (approximately 94%-95%) were accompanied by markedly lower specificities in some series (as low as 64% in van Keulen and colleagues).[38] As in colorectal cancer, specificity in ovarian cancer is high when compared with tumor-free controls but decreases when benign lesions are included,[6] likely reflecting biological overlap in metabolic pathways between benign and malignant adnexal masses. These discrepancies may also be explained by heterogeneity in sampling matrices (breath, urine, plasma, tissue), sensor technologies (metal oxide semiconductors, quartz crystal microbalances, conducting polymers, nanomaterials), and analytical pipelines (statistical models vs machine learning algorithms). These differences in performance across sensing technologies and biological matrices highlight the need to contextualize electronic noses in relation to more established analytical approaches. Gas chromatography combined with mass spectrometry offers very high analytical specificity because it separates and identifies individual chemical compounds. However, this approach is time-consuming, requires specialized personnel, and is not suitable for rapid or point-of-care use. Although urine and plasma have shown encouraging results in some studies due to lower environmental influence and more standardized sampling, available evidence is still too limited to indicate them to be the best biological samples compared with breath or blood-based matrices.

Beyond biological differences, discrepancies across studies are also driven by methodological variation: (i) choice of comparator groups (healthy vs benign conditions), (ii) pre-analytical variability (sample collection, conditioning, patient diet, smoking, comorbidities), (iii) sensor design and calibration, and (iv) data processing algorithms. Studies that employed standardized sampling protocols, multi-matrix analysis, and advanced machine-learning methods consistently reported higher and more stable performance, particularly for cervical lesions.

In summary, our results are concordant with the broader oncology literature in showing that electronic noses achieve clinically relevant diagnostic accuracy when the volatile organic compound signature is distinctive (as in cervical cancer, lung, head and neck, breast, and gastric cancers). The discrepancies observed in ovarian cancer resemble those in colorectal cancer, where sensitivity remains high but specificity declines in the presence of benign comparators. These findings highlight the need for large, multicenter trials with standardized protocols, clinically relevant control groups, and multi-matrix/multi-sensor strategies to determine whether reduced specificity is an intrinsic limitation of ovarian cancer biology or a reflection of methodological heterogeneity.

Strengths and Weaknesses

This systematic review has several strengths. To our knowledge, it represents the first comprehensive synthesis specifically dedicated to the diagnostic performance of electronic nose technologies in gynecologic oncology. The search strategy was broad and systematic, conducted according to PRISMA guidelines, and all included studies were prospective, thereby reducing the risk of selection bias. The review also covered multiple biological matrices, highlighting the versatility of electronic nose platforms across breath, urine, plasma, tissue, and genitourinary secretions.

Importantly, diagnostic performance was consistently reported, allowing a comparative analysis across different lesions.

Nevertheless, some limitations must be acknowledged. The overall number of included studies was small, with a total sample size of 1224 patients, and most studies were single-center, exploratory, or pilot in design. Considerable heterogeneity was present in terms of devices, sensor types, and analytical algorithms, which precluded formal meta-analysis. Reporting of accuracy parameters was inconsistent. Moreover, though data were available for ovarian and cervical cancers, no eligible studies addressed endometrial or vulvar malignancies. Finally, the absence of standardized sampling protocols and external validation cohorts limits the generalizability and clinical translation of current findings.

Implications for Practice and Further Research

The results of this review indicate that electronic nose technology has the potential to become an important complement to current diagnostic strategies in gynecologic oncology. These devices may provide non-invasive, rapid, and cost-effective tools for the early detection of ovarian and cervical cancer. In practical terms, electronic nose technologies are most plausibly suited for clinic-based, point-of-care screening, analyzing non-invasive samples such as breath, urine, or cervicovaginal secretions. Though home-based volatilomic testing remains speculative, integration as an adjunct tool in cervical cancer screening may be feasible. In this setting, electronic noses would not replace Pap smears or HPV testing, but could support triage by rapidly identifying individuals at higher risk, thereby improving workflow efficiency and potentially enhancing detection in under-screened populations. Although the diagnostic performance reported across studies is encouraging, the clinical applicability of electronic nose technology is currently limited by substantial variability in patient-related and environmental factors. Differences in diet, microbiome composition, medication use, comorbidities, and smoking habits, as well as region-specific environmental volatile organic compound backgrounds, can influence volatilome signatures and contribute to heterogeneity across studies. These elements highlight the need for standardized sampling workflows, harmonized analytical pipelines, and multi-centric validation involving diverse populations. Advanced machine-learning approaches and calibration strategies specifically designed to mitigate external variability will also be essential to support future clinical translation. To date, *ex vivo* applications should be interpreted as proof-of-concept studies rather than alternatives to histopathology. Their aim is to characterize volatile organic compound signatures under controlled conditions and support the development of non-invasive diagnostics. Notably, in the future, *ex vivo* analysis may have potential value in selected scenarios where frozen-section accuracy is limited, such as intraoperative assessment of cervical cancer lymph nodes.[39]

Future research should prioritize a structured roadmap, beginning with the standardization of volatile organic compounds sampling protocols and pre-analytical procedures to reduce inter-study variability. The development of artificial intelligence-driven classifiers capable of handling multidimensional volatilomic data will be essential for improving diagnostic robustness and enabling real-time interpretation. Supervised learning models—such as support vector machines, random forests, and neural networks—can be trained on labeled volatile organic compounds datasets to refine feature extraction, reduce sensor noise, and optimize diagnostic classification. Robust training requires sufficiently large and diverse datasets, standardized sampling and measurement pipelines, and appropriate cross-validation to prevent overfitting. These approaches may contribute to more reliable and generalizable electronic nose-based diagnostic tools.[40] Finally, multi-centric prospective validation is required to assess generalizability across populations and settings. In parallel, the incorporation of volatile organic compound analysis into digital surgery platforms may expand the role of these tools in intraoperative decision-making, where imaging, robotics, and computational guidance are increasingly integrated.[41]

CONCLUSIONS

Electronic nose technology demonstrates encouraging diagnostic performance for gynecologic oncology lesions, with overall sensitivity ranging from 71% to 97.7%, specificity from 63% to 100%, and accuracy from 71% to 95%. Although current evidence is limited by small sample sizes, methodological heterogeneity, and the absence of standardized protocols, the results highlight the potential of electronic noses as non-invasive diagnostic tools. Larger, multicenter, and standardized trials are needed to confirm these findings and to define their role in clinical practice.

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Supplemental material Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijgc.2025.102866.

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