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Electronic nose technology in the diagnosis of prostate cancer

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ABSTRACT

Prostate cancer is a significant problem in modern oncourology due to its high incidence and mortality, largely due to untimely diagnosis of the disease. This article provides an overview of current diagnostic methods, including biopsy and magnetic resonance imaging, highlighting their limitations such as invasiveness and insufficient sensitivity. Given the need for more accurate and non-invasive diagnostic techniques, the potential use of an "electronic nose" — a multisensory system capable of detecting volatile organic compounds in urine samples — is explored. The literature review indicates that the use of this technique may offer high sensitivity and specificity in detecting prostate cancer, comparable to results obtained from specially trained detection dogs. The article analyzes recent clinical studies that validate the effectiveness of the electronic nose in identifying prostate cancer and describes the machine learning methodologies employed for recognizing urine samples. It is important to create uniform standards for the analysis of the gas composition of urine using the electronic nose. For the widespread implementation of this diagnostic method, it is necessary to conduct large randomized studies with the formation of a sufficient evidence base.

Keywords: prostate cancer; electronic nose; volatile organic compounds; diagnosis; machine learning.

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«Электронный нос» в диагностике рака предстательной железы

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АННОТАЦИЯ

Рак предстательной железы представляет собой значительную проблему современной онкоурологии из-за высокой заболеваемости и смертности, в значительной степени обусловленных несвоевременной диагностикой заболевания. В данной статье рассмотрены современные методы диагностики рака предстательной железы, включая биопсию и магнитно-резонансную томографию, а также их ограничения, такие как инвазивность и недостаточная чувствительность. С учетом необходимости разработки более точных и неинвазивных методов диагностики исследуется потенциал применения «электронного носа» — мультисенсорной системы, способной обнаруживать летучие органические соединения в образцах мочи. Обзор литературы показывает, что использование данной методики может обеспечить высокую чувствительность и специфичность в диагностике рака предстательной железы, аналогично результатам, полученным с помощью специально обученных собак. Статья включает анализ существующих исследований, подтверждающих эффективность «электронного носа» в выявлении заболевания, а также приведена методология машинного обучения, используемая для распознавания образцов мочи. Важное значение имеет создание единых стандартов анализа газового состава мочи с использованием «электронного носа». Для широкого внедрения данного диагностического метода необходимо проведение крупных рандомизированных исследований с формированием достаточной доказательной базы.

Ключевые слова: рак предстательной железы; «электронный нос»; летучие органические соединения; диагностика; машинное обучение.

Как цитировать

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Urologic cancers contribute substantially to global morbidity and mortality, primarily due to delayed diagnosis [1, 2]. Mortality from these conditions is projected to increase and, according to various estimates, may account for 13.1 million deaths worldwide by 2030 [3]. Prostate cancer (PCa) is the most commonly diagnosed malignant neoplasm among men globally [4]. In 2020, there were 1.4 million newly diagnosed cases worldwide, with approximately 375,000 deaths attributed to disease-related complications. In the Russian Federation, 40,785 new cases were registered in 2020, making it the second most common cancer, with 12,565 deaths reported [5]. One of the primary reasons for the persistently high incidence and mortality rates of PCa is late detection. This malignancy often progresses asymptomatically or with nonspecific symptoms; when clinical signs appear, the disease is typically locally advanced or metastatic [6].

According to the 2024 guidelines of the European Association of Urology, indications for prostate biopsy include elevated prostate-specific antigen (PSA) levels and/or the presence of a hard nodule on digital rectal examination, as well as pathologic lesions identified by contrast-enhanced pelvic magnetic resonance imaging (MRI) [7, 8]. Currently available diagnostic methods for PCa are invasive and have limited sensitivity and specificity, underscoring the need for more accurate screening tools. The limitations of existing approaches contribute to delayed diagnosis and high mortality rates. Digital rectal examination remains one of the simplest and most accessible diagnostic methods for PCa. However, it is subjective and considered a "late-stage" diagnostic tool, as stony-hard induration, indicative of PCa, are typically detectable only when the lesion is significantly enlarged or superficially located in the peripheral zone. In the PROBASE study (*n*=6537), digital rectal examination identified stony-hard induration in only 57 participants, with prostate cancer subsequently confirmed in just 3 cases, corresponding to a detection rate of 0.03% [9, 10]. In a meta-analysis by Matsukawa et al. [11], 85,798 men underwent PCa screening, with digital rectal examination abnormalities found in 4718 patients (6.6%). Beyond its low predictive value, digital rectal examination is also associated with discomfort and psychological stress for patients [12].

Interest in identification of cancer biomarkers in biological fluids emerged during the 1960s and 1970s, paralleling advances in immunology. The first study quantifying PSA levels for PCa diagnosis was conducted by Stame et al. in 1980 [13]. Since the 2000s, total PSA testing has become one of the most widely used methods for PCa screening and diagnosis and remains a recommended approach. Despite its broad clinical use, total PSA testing lacks specificity and results in unnecessary prostate biopsies in approximately two-thirds of cases [7, 14, 15]. Conversely, clinically significant PCa is sometimes detected in patients with normal total PSA levels [16]. Autopsy studies indicate that approximately 40% of men who do not undergo regular screening have PCa; this prevalence increases to 60% in individuals over 80 years of age. Notably, only 32% of these cases represent clinically significant disease (ISUP ⩾2) [17]. According to Gao et al. [18], initial biopsy confirms PCa in only 22% of cases, while more than one-third of biopsies reveal clinically insignificant process. Since PSA exists in various molecular forms in serum (including free PSA and multiple isoforms), numerous efforts have aimed to enhance diagnostic accuracy by quantifying these isoforms. Although assessing the free-to-total PSA ratio and isoform p2PSA increases cancer detection rates, these approaches lack sufficient diagnostic value and cost-effectiveness for routine PCa screening [14].

Currently, in cases of suspected PCa, contrast-enhanced pelvic MRI is recommended prior to prostate biopsy for staging purposes [8]. MRI demonstrates a high negative predictive value—approximately 90%—with minimal variability across centers. In contrast, its positive predictive value is comparatively low: reported rates are 17%, 46%, and 75% for lesions with Prostate Imaging Reporting and Data System (PI-RADS) scores of 3, 4, and 5, respectively. However, studies comparing MRI findings with histopathological data following radical prostatectomy reveal that 8% to 24% of clinically significant PCa (ISUP ⩾2) may go undetected by imaging, including prostate MRI [19]. This discrepancy may result from technical or interpretive limitations and the presence of rare histologic subtypes, such as cribriform PCa [20].

Ongoing efforts to reduce diagnostic invasiveness led to a 2022 study by Meissner et al. [21], where 25 patients underwent robot-assisted radical prostatectomy without prior prostate biopsy. All patients demonstrated PI-RADS ⩾4 lesions on contrast-enhanced prostate MRI and underwent Ga68-PSMA positron emission tomography/computed tomography (PET/CT), which revealed reliable evidence of pathological radiopharmaceutical uptake in the prostate (SUV_{max} ⩾9.0). Histologic examination of resected specimens confirmed clinically significant PCa (ISUP ⩾2) in all patients. These findings suggest the feasibility of radical prostatectomy without preoperative biopsy, although further studies with larger, ethics committee–approved cohorts are needed [21].

Thus, there is a critical need to develop novel diagnostic tools for earlier and more accurate PCa detection that meet criteria for noninvasiveness. In recent years, several potentially promising biomarkers and test systems have been investigated, including prostate cancer antigen 3 (PCA3) and the prostate health index (PHI), both FDA-approved, as well as commercial tests such as the 4Kscore panel (total PSA, free PSA, intact PSA, and human kallikrein-related peptidase 2), and molecular

diagnostic assays such as SelectMDx, ConfirmMDx, MiPS, and the Stockholm3 test [22–27].

PCA3 was identified in the late 1990s through collaborative research of Radboud University and Johns Hopkins Hospital. It is a long non-coding RNA mapped to chromosome 9q21–22 within intron 6 of the *PRUNE2* gene, which is overexpressed in prostate cancer cells. PCA3 mRNA levels are measured in urinary sediment collected after digital rectal examination. Although PCA3 is a reliable tool for prostate cancer detection, studies report no significant correlation with tumor aggressiveness or clinical stage [27].

In 2012, the U.S. Food and Drug Administration (FDA) approved the use of the prostate health index for early detection of PCa. The prostate health index is a composite score calculated by multiplying the ratio of [–2]proPSA to free PSA by the square root of total PSA. In a large prospective multicenter study including 892 men with total PSA levels between 2 and 10 ng/mL, the prostate health index demonstrated sensitivity ranging from 80% to 95% and superior specificity compared with total or free PSA testing alone [24].

Also in 2012, a group led by Vickers introduced the 4Kscore test to assess the likelihood of clinically significant PCa. This test measures four kallikrein biomarkers in serum (total PSA, free PSA, intact PSA, and human kallikrein-related peptidase 2) and incorporates clinical variables, including patient age, digital rectal examination findings, and prostate biopsy history [26]. In a systematic review by Zappala et al. [28], the diagnostic accuracy of the 4Kscore was 81%; however, there remains insufficient evidence to support the routine use of the 4Kscore in diagnosing clinically significant PCa. Despite promising data for these and other diagnostic tools—including the Stockholm3, SelectMDx, ConfirmMDx, and MiPS tests—their adoption is currently limited by lower cost-effectiveness compared with traditional diagnostic methods [8, 22–27].

Given the limited diagnostic accuracy of the aforementioned methods, there remains a pressing need for a more specific, noninvasive, and accessible approach to diagnosing and screening for PCa [29].

This review aimed to present the methods and recent findings of studies utilizing *electronic nose* technology for the detection of prostate cancer.

This review was based on a sources search using the PubMed, Medscape, and eLibrary databases with the following keywords: *prostate cancer*, *volatile organic compounds*, and *electronic nose*. The analysis focused on studies conducted by research teams from Russia, the United States, Europe, and China, primarily published between 2020 and 2024.

The use of urine in disease detection has a long-standing history in medicine [29]. As a renal filtrate, urine reflects systemic metabolic processes and is readily available in large volumes, requiring no invasive collection procedures. Urine has the potential to provide valuable information not only about diseases of the urinary and male reproductive systems but also about disorders of distant organ systems, owing to the presence of characteristic volatile organic compounds (VOCs) [30, 31]. VOCs are naturally occurring chemical compounds with low boiling points [32]. These compounds are produced through oxidative stress and lipid peroxidation of cellular membranes and are excreted in feces, urine, and sweat [33–36]. The disease-specific release of VOCs has been validated in numerous studies employing specially trained scent detection dogs [1,37–42]. However, despite high sensitivity, specificity, and diagnostic accuracy in detecting cancer, particularly PCa, the integration of canine olfactory detection into clinical practice is accompanied by several limitations. These include the high cost and duration of training, susceptibility to fatigue and boredom, and difficulty incorporating animals into standardized clinical protocols [43, 44].

Inspired by the promising results of canine detection of PCa, researchers have explored instrumental alternatives such as the electronic nose to replicate these findings [37–40, 43–45]. An electronic nose is a multisensor system comprising an array of selective or non-selective sensors with cross-sensitivity, trained for pattern recognition of diverse vapor and gas mixtures. Unlike conventional sensors, modern electronic nose devices can identify specific gases even at minimal concentrations due to their use of non-selective sensor [46]. Similar to mammalian olfactory systems, the software component of electronic nose comprises a sensor network (gas sensor matrix and transmission pathways) and a data processing unit, which identifies and classifies each detected odor by creating unique digital signatures of chemical compounds [47–52]. Each sensor contains a metal oxide film and a measurement transducer that adsorbs VOCs on its surface. This interaction alters the resonant frequency due to a change in sensor surface mass, a relationship described by the Sauerbrey equation [53]. Sensor-VOC interactions are governed by weak forces such as van der Waals, dipole-dipole, and hydrogen bonds. The frequency shift relative to baseline constitutes the sensor response. The final result is a sensor response pattern from all sensors. The matrix containing all measurements is then extracted using specialized software [54].

Prior to its diagnostic application in oncology, the electronic nose undergoes a machine learning phase, where VOC patterns from cancer and control groups are analyzed to create a database of “urinary profiles” for comparison with new samples. The machine learning process involves data acquisition, modeling, training, and evaluation standardization (Fig. 1) [47, 54]. Major advantages of the electronic nose include rapid analysis, ease of use, low cost, and compact design (Fig. 2) [49, 50].

The first published study using the electronic nose for PCa detection in urine samples was conducted by D'Amico et al. in 2012. This pilot study including 21 patients demonstrated promising results and served as a foundation for further research [55] (Table 1).

The ability of the electronic nose to distinguish PCa from benign prostatic hyperplasia (BPH) based on urinary VOC profiles was evaluated by Roine et al. [56]. The study included 50 patients with PCa scheduled for robot-assisted radical prostatectomy and 15 patients with BPH scheduled for transurethral resection of the prostate. The electronic nose demonstrated a sensitivity of 78% and specificity of 67% for PCa detection, with an area under the curve (AUC) of 0.77. A study limitation was the potential underdiagnosis of PCa, as the peripheral zone—where PCa most frequently arises—is not resected during transurethral procedures.

The importance of proper sample collection for reliable PCa diagnosis was supported in a prospective study by Asimakopoulos et al. [54], where urine samples from 41 patients were collected prior to prostate biopsy. Each patient provided both a first-void and midstream urine sample, which were immediately analyzed using an electronic nose. First-void urine more accurately indicated the presence of PCa compared with midstream urine. The electronic nose correctly detected PCa in 10 of 14 cases — sensitivity 71.4% (95% confidence interval, CI 42%–92%)—and correctly excluded it in 25 of 27 patients — specificity 92.6% (95% confidence interval, CI 76%–99%).

Solovieva et al. [57] analyzed urinary VOC patterns associated with PCa using electronic nose technology. The study included 89 urine samples (43 patients with confirmed PCa and 46 control group patients). The authors compared various machine learning approaches for the electronic nose, with the logistic regression model demonstrating the best performance. The sensitivity of PCa detection using this model was 100%, with a specificity of 93%. The limitation of this study was the relatively small patient sample size. To obtain more accurate and reliable results for the application of the logistic regression model in diagnosing PCa using electronic nose, large-scale multicenter studies with a greater number of patients are necessary.

Urinary VOC detection across three different void fractions was assessed by Capelli et al. [44], who included 132 PCa patients and 60 controls. Sensitivity in detecting PCa using the electronic nose was 81% for the first-void, 75% for midstream, and 27% for terminal fractions. Catheterized samples yielded 91% sensitivity. However, the authors do not describe the specificity or accuracy of the study. These findings support earlier results by Asimakopoulos et al. [54], who first identified a stronger association between first-void urine and PCa detectability.

In 2022, Filianoti et al. [58] assessed the electronic nose's ability to differentiate between urine samples from PCa patients and healthy individuals. The method demonstrated 82.7% sensitivity and 88.5% specificity. However, the authors acknowledged potential confounders such as diet, medications, smoking, alcohol consumption, and chronic kidney disease, which were not taken into account.

The accuracy of PCa diagnosis using electronic nose to analyze urine samples was investigated by Taverna et al. [38] in 2022. A blinded prospective study included 174 patients: 88 (50.6%) in the prostate cancer group and 86 (49.4%) in the control group. According to sensitivity test, the electronic nose achieved 85.2% sensitivity (13 false negatives out of 88) and 79.1% specificity

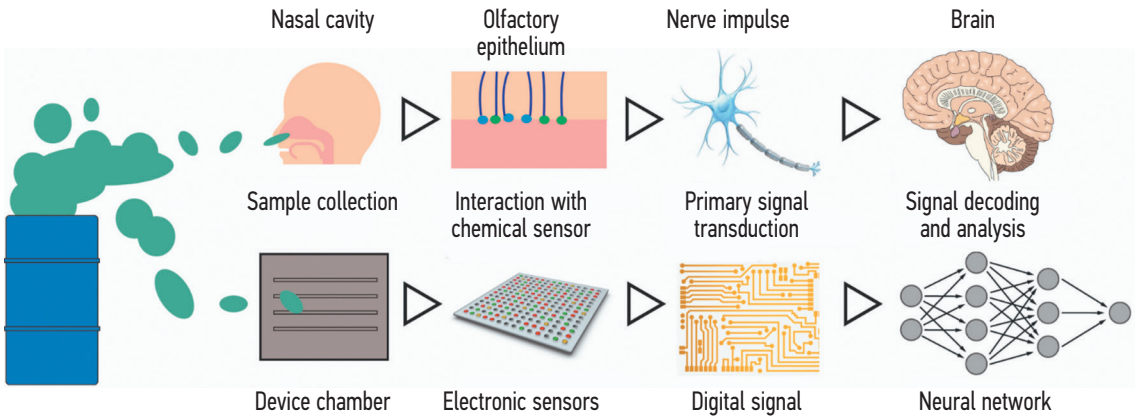

Fig. 1. Algorithm for odor recognition using an electronic nose (comparative diagram of biological and electronic noses). Photo: Marianna Yerknapeshyan / Scientific Russia. Information sourced from the portal "Scientific Russia" (https://scientificrussia.ru/).
Рис. 1. Алгоритм распознавания запахов с помощью «электронного носа» (сравнительная схема биологического и электронного носа). Фото: Марианна Еркнапешян / Научная Россия. Информация взята с портала «Научная Россия» (https://scientificrussia.ru/).

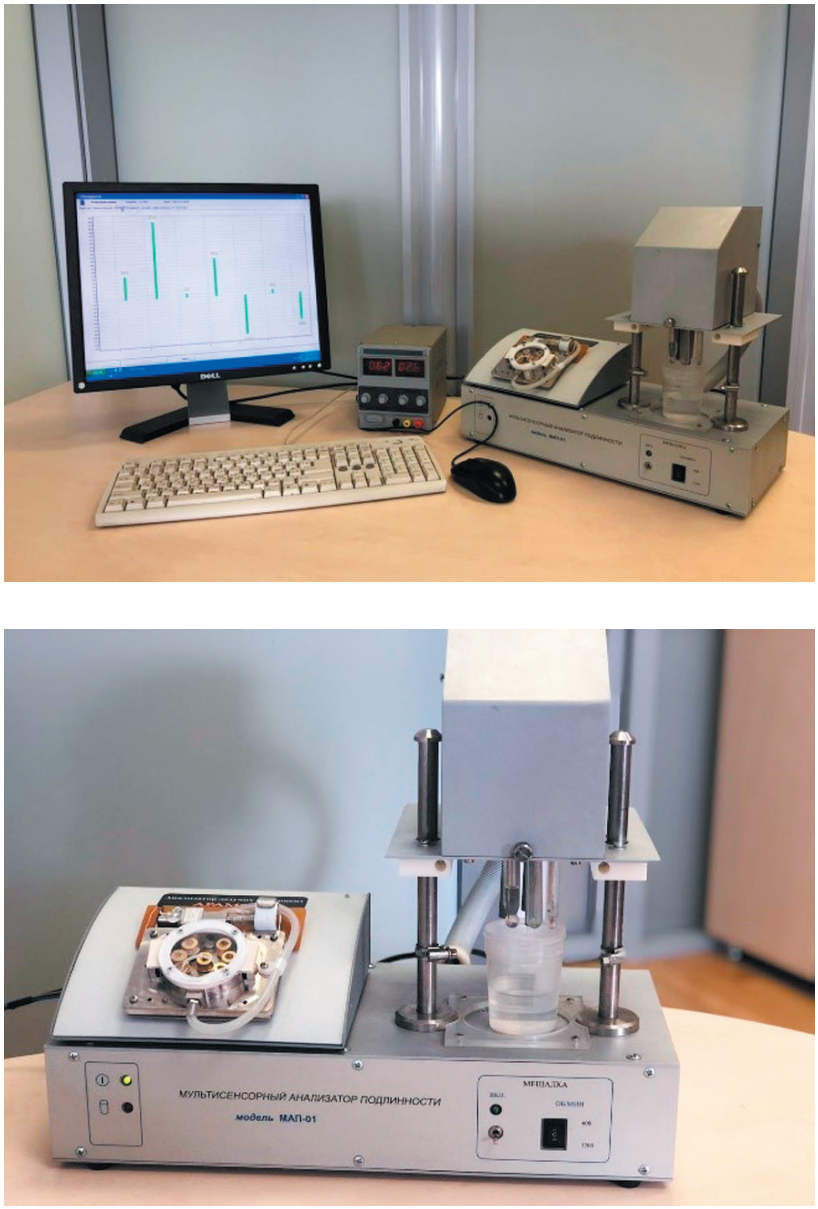

Fig. 2. Electronic nose "Aramos 7". Photo source: NPO "Pribor" (Saint Petersburg).
Рис. 2. «Электронный нос» Арамос 7. Источник фото: НПО «Прибор» (Санкт-Петербург).

(18 false positives out of 86). Notably, PCa could not be ruled out even in cases with PSA <2.5 ng/mL, negative digital rectal examination, and no family history of PCa.

In a 2024 study, Taverna et al. [59] evaluated the feasibility of using the electronic nose to assess PCa aggressiveness (well-, moderately, and poorly differentiated) through the analysis of urine VOC profiles. The electronic nose was trained on urine samples from 329 patients in the training cohort, who were further subdivided into three groups: well-differentiated (*n*=64), moderately differentiated (*n*=131) and poorly differentiated prostate cancer (*n*=134). All patients in the training cohort (*n*=329) subsequently underwent radical prostatectomy. Following training, the test set included 120 preoperative urine samples. The overall accuracy of the electronic nose in grading tumor aggressiveness was 79.2%. The study demonstrated high accuracy in assessing PCa aggressiveness by analyzing urinary VOC profiles using an electronic nose. However, the authors noted the relatively small cohort size as a limitation. To ensure greater reliability, large-scale multicenter studies are needed [59].

In a study assessing the diagnostic accuracy of the electronic nose for PCa diagnosis, Durán Acevedo et al. [60] included 113 participants: 66 with histologically confirmed PCa and 47 controls, comprising patients with BPH, chronic prostatitis, and healthy individuals. Participants refrained from food, smoking, alcohol, and drugs for 10 hours prior to testing. The diagnostic accuracy for

Table 1. Results of sensitivity, specificity, and accuracy of prostate cancer diagnosis using an electronic nose

Таблица 1. Результаты чувствительности, специфичности и точности диагностики рака предстательной железы с помощью «электронного носа»

Authors	Experimental group (*n*)	Control group (*n*)	Sensitivity, %	Specificity, %
A. Roine et al. (2014) [56]	50	15	78%	67%
A. Asimakopoulos et al. (2014) [54]	14	27	71.4%	92.6%
S. Solovieva et al. (2019) [57]	43	46	100%	93%
L. Capelli et al. (2021) [44]	132	60	82%	87%
A. Filianoti et al. (2022) [58]	133	139	82.7%	88.5%
G. Taverna et al. (2022) [38]	88	86	85.2%	79.1%
C.M. Duran Acevedo et al. (2024) [60]	66	47	94.2%	96.6%
H. Heers et al. (2024) [61]	56	53	77%	62%

distinguishing PCa from non-malignant conditions was 95.5%. However, as this was a single-center study, multicenter studies with larger number of participants are necessary for validation.

Heers et al. [61] evaluated the effectiveness of PCa diagnosis using electronic nose technology based on midstream urine samples. The study included 56 patients with confirmed PCa and 53 controls. The reported sensitivity was 77%, and specificity 62%. The study was limited by a relatively small sample size and did not stratify PCa patients according to d'Amico risk classification for clinical significance.

Despite numerous investigations and significant advances in electronic nose technology for PCa detection, several unresolved challenges remain. Many studies fail to account for confounding variables such as comorbidities affecting metabolism (e.g., diabetes mellitus, gout, urolithiasis), age, genetic and geographic diversity, lifestyle factors including diet, drug use, and alcohol consumption within 24 hours prior to testing. The design of studies investigating prostate cancer diagnosis using electronic nose technology is heterogeneous; each study refers primarily to its own findings or to other works with inherent limitations. To date, no comprehensive databases have been developed that consolidate urinary VOC profiles characteristic of PCa. However, despite the heterogeneity of study methodologies, these issues are gradually being addressed through the development of more rigorous study designs and efforts to standardize sample preparation protocols [51, 62].

Another limitation of electronic nose implementation, despite high sensitivity, specificity, and accuracy, is sensor signal degradation over time due to oxidation, a phenomenon known as sensor drift. Sensor drift refers to unpredictable changes in sensor output over time under consistent exposure to the same VOCs under identical conditions. In the vast majority of studies, sensor drift and the reproducibility of measurements across different electronic nose devices have not been addressed. This limitation hinders their clinical applicability, and sensor drift remains one of the key challenges that must be resolved before electronic nose technology can be integrated into clinical practice [63, 64].

Bax et al. [65] developed a drift correction model using orthogonal signal correction (OSC) algorithms for PCa detection. Their approach mitigated sensor degradation effects over a 1-year operational period. They also proposed a five-step signal correction protocol (5-OSC), which restored diagnostic accuracy from 55% to 80% after one year of use. However, the long-term applicability of this correction strategy requires further evaluation before it can be implemented in routine clinical settings.

In conclusion, this review highlights the promising potential of electronic nose technology as a noninvasive

tool for early detection of PCa. However, integration into clinical screening and diagnostic guidelines will require large-scale randomized controlled trials to establish a robust evidence base. The development of standardized protocols for analyzing urinary volatile profiles using electronic nose technology is of importance [51, 54]. A major challenge is the limited accessibility of existing research data. Open-access databases containing urinary VOC profiles from PCa patients and healthy individuals, along with standardized machine learning algorithms, would significantly accelerate validation and facilitate clinical implementation of electronic nose systems [62].

ADDITIONAL INFO

Authors' contribution. M.S. Mosoyan, concept and design of the study, analysis of the data obtained, editing of the manuscript; I.E. Jagatspanyan, analysis of literature data, editing of the manuscript; A.A. Vasiliev, V.A. Makeev, collection of material, analysis of literature data, writing the text of the article. The authors have approved the version for publication and have also agreed to be responsible for all aspects of the work, ensuring that issues relating to the accuracy and integrity of any part of it are properly considered and addressed.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

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Источники финансирования. Отсутствуют.

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REFERENCES | СПИСОК ЛИТЕРАТУРЫ

1. Wood S, Knowles M, Thompson D, et al. Proteomic studies of urinary biomarkers for prostate, bladder and kidney cancers. *Nat Rev Urol*. 2013;10:206–218. doi: 10.1038/nrurol.2013.24

2. Richards MA. The size of the prize for earlier diagnosis of cancer in England. *Br J Cancer*. 2009;101:125–129. doi: 10.1038/sj.bjc.6605402

3. Siegel RL, Miller KD, Jemal A. Cancer statistics. *Cancer J Clin.* 2018;68(1):7–30. doi: 10.3322/caac.21442

4. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *Cancer J Clin*. 2021;71(3):209–249. doi: 10.3322/caac.21660S

5. Kaprin AD, Starinsky BB, Shakhzadova AO, editors. *Malignant neoplasms in Russia in 2020 (morbidity and mortality)*. Moscow: P.A. Herzen MNIOI. Branch of NMRC Radiology of the Ministry of Health of Russia; 2021. 252 p. (In Russ.)

6. Nicholson BD, Hamilton W, O'Sullivan J, et al. Weight loss as a predictor of cancer in primary care: a systematic review and meta-analysis. *Br J Gen Pract*. 2018;68(670):e311–e322. doi: 10.3399/bjgp18X695801

7. Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer — 2020 update. Part 1: screening, diagnosis, and local treatment with curative intent. *Eur Urol*. 2021;79(2):243–262. doi: 10.1016/j.eururo.2020.09.042

8. European Association of Urology. *Prostate cancer*. 2024. Available from: https://uroweb.org/guideline/prostate-cancer/

9. Arsov C, Albers P, Herkommer K, et al. A randomized trial of risk-adapted screening for prostate cancer in young men — results of the first screening round of the PROBASE trial. *Int J Cancer*. 2022;150(11):1861–1869. doi: 10.1002/ijc.33940

10. Krilaviciute A, Becker N, Lakes J, et al. Digital rectal examination is not a useful screening test for prostate cancer. *Eur Urol Oncol*. 2023;6(6):566–573. doi: 10.1016/j.euo.2023.09.008

11. Matsukawa A, Yanagisawa T, Bekku K, et al. Comparing the performance of digital rectal examination and prostate-specific antigen as a screening test for prostate cancer: A systematic review and meta-analysis. *Eur Urol Oncol*. 2024;7(4):697–704. doi: 10.1016/j.euo.2023.12.005

12. Romero FR, Romero AW, Filho TB, et al. Patients' perceptions of pain and discomfort during digital rectal exam for prostate cancer screening. *Arch Esp Urol*. 2008;61(6):850–854. doi: 10.4321/S0004-06142008000600019

13. Rao AR, Motiwala HG, Karim OM. The discovery of prostate-specific antigen. *BJU Int*. 2007;101(1):5–10. doi: 10.1111/j.1464-410X.2007.07138.x

14. Bax C, Taverna G, Eusebio L, et al. Innovative diagnostic methods for early prostate cancer detection through urine analysis: A review. *Cancers*. 2018;10(4):123. doi: 10.3390/cancers10040123

15. Blute ML Jr, Abel EJ, Downs TM, et al. Addressing the need for repeat prostate biopsy: new technology and approaches. *Nat Rev Urol*. 2015;12(8):435–444. doi: 10.1038/nrurol.2015.159

16. Pepe P, Panella P, Savoca F, et al. Prevalence and clinical significance of prostate cancer among 12,682 men with normal digital rectal examination, low psa levels (⩽4 ng/ml) and Percent free PSA cutoff values of 15 and 20 %. *Urol Int*. 2007;78(4):308–312. doi: 10.1159/000100833

17. Zlotta A, Egawa S, Pushkar D, et al. Prevalence of prostate cancer on autopsy: cross-sectional study on unscreened Caucasian and Asian men. *J Natl Cancer Inst*. 2013;105(14):1050–1058. doi: 10.1093/jnci/djt151

18. Gao Q, Su X, Annabi MH, et al. Application of urinary volatile organic compounds (VOCs) for the diagnosis of prostate cancer. *Clin Genitourin Cancer*. 2019;17(3):183–190. doi: 10.1016/j.clgc.2019.02.003

19. Barrett T, de Rooij M, Giganti F, et al. Quality checkpoints in the MRI-directed prostate cancer diagnostic pathway. *Nat Rev Urol*. 2023;20(1):9–22. doi: 10.1038/s41585-022-00648-4

20. Grizzi F, Bax C, Hegazi MA, et al. Early detection of prostate cancer: The role of scent. *Chemosensors*. 2023;11(7):356. doi: 10.3390/chemosensors11070356

21. Meissner VH, Rauscher I, Schwamborn K, et al. radical prostatectomy without prior biopsy following multiparametric magnetic resonance imaging and prostate-specific membrane antigen positron emission tomography. *Eur Urol*. 2022;82(2):156–160. doi: 10.1016/j.eururo.2021.11.019

22. Sanda MG, Feng Z, Howard DH, et al. Association between combined TMPRSS2: ERG and PCA3 RNA urinary testing and detection of aggressive prostate cancer. *JAMA Oncol*. 2017;3(8):1085–1093. doi: 10.1001/jamaoncol.2017.0177

23. Haese A, Trooskens G, Steyaert S, et al. Multicenter optimization and validation of a 2-gene mRNA urine test for detection of clinically significant prostate cancer before initial prostate biopsy. *J Urol*. 2019;202(2):256–263. doi: 10.1097/JU.0000000000000293

24. McKiernan J, Donovan MJ, Margolis E, et al. A prospective adaptive utility trial to validate performance of a novel urine exosome gene expression assay to predict high-grade prostate cancer in patients with prostate-specific antigen 2–10 ng/ml at initial biopsy. *Eur Urol*. 2018;74(6):731–738. doi: 10.1016/j.eururo.2018.08.019

25. Becerra MF, Venkatasai SA, Bhattu AS, Punnen S. Serum and urine biomarkers for detecting clinically significant prostate cancer. *Urol Oncol: Semin Orig Investig*. 2021;39(10):686–690. doi: 10.1016/j.urolonc.2020.02.018

26. Vickers AJ, Cronin, AM, Roobol MJ, et al. A four-kallikrein panel predicts prostate cancer in men with recent screening: Data from the European Randomized Study of Screening for Prostate Cancer, Rotterdam. *Clin Cancer Res*. 2010;16(12):3232–3239. doi: 10.1158/1078-0432.CCR-10-0122

27. Galasso F, Giannella R, Bruni P, et al. PCA3: a new tool to diagnose prostate cancer (PCa) and a guidance in biopsy decisions. Preliminary report of the UrOP study. *Arch Ital Urol Androl*. 2010;82(1):5–9.

28. Zappala SM, Scardino PT, Okrongly D, et al. Clinical performance of the 4Kscore Test to predict high-grade prostate cancer at biopsy: A meta-analysis of us and European clinical validation study results. *Rev Urol*. 2017;19(3):149–155. doi: 10.3909/riu0776

29. Jordaens S, Zwaenepoel K, Tjalma W, et al. Urine biomarkers in cancer detection: A systematic review of preanalytical parameters and applied methods. *Int J Cancer*. 2023;152(10):2186–2205. doi: 10.1002/ijc.34434

30. Schmidt K, Podmore I. Current challenges in volatile organic compounds analysis as potential biomarkers of cancer. *J Biomark*. 2015;2015:981458. doi: 10.1155/2015/981458

31. Hanna GB, Boshier PR, Markar SR, et al. Accuracy and methodologic challenges of volatile organic compound-based exhaled breath tests for cancer diagnosis: a systematic review and meta-analysis. *JAMA Oncol*. 2019;5(1):e182815. doi: 10.1001/jamaoncol.2018.2815

32. Kusano M, Mendez E, Furton KG. Comparison of the volatile organic compounds from different biological specimens for profiling potential. *J Forensic Sci*. 2013;58(1):29–39. doi: 10.1111/j.1556-4029.2012.02215.x

33. Gallagher M, Wysocki C, Leyden J, et al. Analyses of volatile organic compounds from human skin. *Br J Dermatol*. 2008;159(4):780–791. doi: 10.1111/j.1365-2133.2008.08748.x

34. Ashley DL, Bonin MA, Cardinali FL, et al. Determining volatile organic compounds in human blood from a large sample population by using purge and trap gas chromatography/mass spectrometry. *Anal Chem*. 1992;64(9):1021–1029. doi: 10.1021/ac00033a011

35. Phillips M, Herrera J, Krishnan S, et al. Variation in volatile organic compounds in the breath of normal humans. *J Chromatogr B Biomed Sci Appl*. 1999;729(1–2):75–88. doi: 10.1016/S0378-4347(99)00127-9

36. Costello BL, Ratcliffe N.M. Volatile organic compounds (VOCs) found in urine and stool. In: *Volatile biomarkers*. Amsterdam: Elsevier; 2013. P. 405–462. doi: 10.1016/B978-0-44-462613-4.00022-2

37. Balseiro SC, Correia HR. Is olfactory detection of human cancer by dogs based on major histocompatibility complex-dependent odour components? A possible cure and a precocious diagnosis of cancer. *Med Hypotheses*. 2006;66(2):270–272. doi: 10.1016/j.mehy.2005.08.027

38. Taverna G, Grizzi F, Tidu L, et al. Accuracy of a new electronic nose for prostate cancer diagnosis in urine samples. *Int J Urol*. 2022;29(8):890–896. doi: 10.1111/iju.14912

39. Boedeker E, Friedel G, Walles T. Sniffer dogs as part of a bimodal bionic research approach to develop a lung cancer screening. *Interact Cardiovasc Thorac Surg*. 2012;14(5):511–515. doi: 10.1093/icvts/ivr070

40. Taverna G, Tidu L, Grizzi F, et al. Olfactory system of highly trained dogs detects prostate cancer in urine samples. *J Urol*. 2015;193(4):1382–1387. doi: 10.1016/j.juro.2014.09.099

41. MacGregor M, Shirazi SH, Chan KM, et al. Cancer cell detection device for the diagnosis of bladder cancer from urine. *Biosens Bioelectron*. 2020;171:112699. doi: 10.1016/j.bios.2020.112699

42. Chan KM, Gleadle JM, Gregory PA, et al. Selective microfluidic capture and detection of prostate cancer cells from urine without digital rectal examination. *Cancers*. 2021;13(21):5544. doi: 10.3390/cancers13215544

43. Lippi G, Cervellin G. Canine olfactory detection of cancer versus laboratory testing: myth or opportunity. *Clin Chem Lab Med*. 2012;50(3):435–439. doi: 10.1515/cclm.2011.672

44. Capelli L, Bax C, Grizzi F, Taverna G. Optimization of training and measurement protocol for eNose analysis of urine headspace aimed at prostate cancer diagnosis. *Sci Rep*. 2021;11:20898. doi: 10.1038/s41598-021-00033-y

45. Ahmad F, Cherukuri MK, Choyke PL. Metabolic reprogramming in prostate cancer. *Br J Cancer*. 2021;125:1185–1196. doi: 10.1038/s41416-021-01435-5

46. Novikova LB, Kuchmenko TA. The analytical capabilities of the systems of artificial sense of smell and taste. Part 1. "Electronic nose". *Proceedings of the Voronezh State University of Engineering Technologies*. 2019;81(3):236–241. doi: 10.20914/2310-1202-2019-3-236-241 EDN: XHBHXS

47. Pearce TC. Computational parallels between the biological olfactory pathway and its analogue "The Electronic Nose": Part II. Sensor-based machine olfaction. *Biosystems*. 1997;41(2):69–90. doi: 10.1016/S0303-2647(96)01660-7

48. Sankaran S, Khot LR, Panigrahi S. Biology and applications of olfactory sensing system: a review. *Sens Actuator B Chem*. 2012; 171–172:1–17. doi: 10.1016/j.snb.2012.03.029

49. Hagleitner C, Hierlemann A, Lange D, et al. Smart single-chip gas sensor microsystem. *Nature*. 2001;414:293–296. doi: 10.1038/35104535

50. Francesco F, Fuoco R, Trivella MG, et al. Breath analysis: trends in techniques and clinical applications. *Microchem J*. 2005;79(1–2): 405–410. doi: 10.1016/j.microc.2004.10.008

51. Karakaya D, Ulucan O, Turkan M. Electronic nose and its applications: a survey. *Int J Autom Comput*. 2020;17:179–209. doi: 10.1007/s11633-019-1212-9

52. Cheng L, Meng Q, Lilienthal AJ, Qi P-F. Development of compact electronic noses: A review. *Meas Sci Technol*. 2021;32(6):062002. doi: 10.1088/1361-6501/abef3b

53. Sauerbrey G. Use of quartz crystals for weighing thin films and for microweighing. *Z Physik*. 1959;155:206–222. doi: 10.1007/BF01337937

54. Asimakopoulos A, Del Fabbro D, Miano R, et al. Prostate cancer diagnosis through electronic nose in the urine headspace setting: a pilot study. *Prostate Cancer Prostatic Dis*. 2014;17:206–211. doi: 10.1038/pcan.2014.11

55. D'Amico A, Santonico M, Pennazza G, et al. A Novel approach for prostate cancer diagnosis using a gas sensor array. *Procedia Eng*. 2012;47:1113–1116. doi: 10.1016/j.proeng.2012.09.346

56. Roine A, Veskimae E, Tuokko A, et al. Detection of prostate cancer by an electronic nose: A proof of principle study. *J Urol*. 2014;192(1):230–234. doi: 10.1016/j.juro.2014.01.113

57. Solovieva S, Karnaukh M, Panchuk V, et al. Potentiometric multisensor system as a possible simple tool for non-invasive prostate cancer diagnostics through urine analysis. *Sens Actuators B: Chem*. 2019;289:42–47. doi: 10.1016/j.snb.2019.03.072

58. Filianoti A, Costantini M, Bove AM, et al. Volatilome analysis in prostate cancer by electronic nose: A pilot monocentric study. *Cancers*. 2022;14(12):2927. doi: 10.3390/cancers14122927

59. Taverna G, Grizzi F, Bax C, et al. Prostate cancer risk stratification via eNose urine odor analysis: a preliminary report. *Front Oncol*. 2024;14:1339796. doi: 10.3389/fonc.2024.1339796

60. Durán Acevedo CM, Carrillo Gómez JK, Cuastumal Vasquez CA, Ramos J. Prostate cancer detection in Colombian patients through e-senses devices in exhaled breath and urine samples. *Chemosensors*. 2024;12(1):11. doi: 10.3390/chemosensors12010011

61. Heers H, Chwilka O, Huber J, et al. VOC-based detection of prostate cancer using an electronic nose and ion mobility spectrometry: A novel urine-based approach. *Prostate*. 2024;84(8):756–762. doi: 10.1002/pros.24692

62. Janfaza S, Banan Nojavani M, Khorsand B, Nikkhah M. Cancer odor database (COD): a critical databank for cancer diagnosis research. *Database*. 2017;2017:bax055. doi: 10.1093/database/bax055

63. Oh EH, Song HS, Park TH. Recent advances in electronic and bioelectronic noses and their biomedical applications. *Enzyme Microb Technol*. 2011;48(6–7):427–437. doi: 10.1016/j.enzmictec.2011.04.003

64. Biasioli F, Yeretzian C, Mark TD, et al. Direct-injection mass spectrometry adds the time dimension to (B) VOC analysis. *TrAC Trends Anal Chem*. 2011;30(7):1003–1017. doi: 10.1016/j.trac.2011.04.005

65. Bax C, Prudenza S, Gaspari G, et al. Drift compensation on electronic nose data for noninvasive diagnosis of prostate cancer by urine analysis. *iScience*. 2021;25(1):103622. doi: 10.1016/j.isci.2021.103622

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