Available online at www.HighTechJournal.org

HighTech and Innovation Journal

ISSN: 2723-9535

Vol. 3, No. 3, September, 2022

Sensor Technology for Opening New Pathways in Diagnosis and Therapeutics of Breast, Lung, Colorectal and Prostate Cancer

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Received 20 March 2022; Revised 19 July 2022; Accepted 08 August 2022; Published 01 September 2022

Abstract

This study analyzes the interaction between sensor research and technology and different types of cancer (breast, lung, colorectal, and prostate) with the goal of detecting new directions for improving diagnosis and therapeutics in medicine. This study develops an approach to computational scientometrics based on data from the Web of Science from the 1991 to 2021 period. The results of this analysis show the vital role of biosensors and electrochemical biosensors applied in breast cancer, lung cancer, and prostate cancer research. Instead, scientific research of optical sensors is developing main technological trajectories in breast, prostate, and colorectal cancer for improving diagnostics. Finally, oxygen sensor research has a main technological development in breast and lung cancer for new applications in breath analysis directed to treatment processes. Preliminary results presented here clearly illustrate the evolutionary paths of sensor research and technologies that have great potential for developing incremental and radical innovations in cancer diagnosis and therapies. These conclusions are, of course, tentative. There is a need for much more detailed research based on other aspects and factors for detecting stable technological trajectories that can foster the technology transfer of new sensor in cancer research for improving diagnosis and therapeutics, reducing, whenever possible, world-wide mortality of cancer in society.

JEL Classification: I10, O30, O31, O32; O33.

Keywords: Sensor Technology; Sensor Research; Technological Trajectories; New Technology; Diagnosis; Biosensor; Cancer; Lung Cancer; Prostate Cancer; Breast Cancer; Colorectal Cancer.

1. Introduction and Goal of Investigation

The research field of sensors is undergoing a significant change that supports the evolution of science and technology in society [1-4]. The goal of this study is an exploratory analysis to detect sensor technologies applied in cancer research having a high potential growth for improving diagnosis and treatment and reducing, whenever possible, mortality between countries. The vast literature on these topics shows the main applications of sensors in cancer research [5-11].

As far as breast cancer is concerned, Wu et al. (2022) [12] designed a dual-aptamer functionalized gold for the classification of breast cancer based on Förster resonance energy transfer, which is potentially useful for quantitative classification of different subtypes of breast cancer. Lu et al. (2022) [13] argue that phthalates can penetrate the environment and enrich various aquatic organisms through the food chain, which is involved in promoting the growth of breast cancer. It is of current interest to develop new sensors for phthalates. Results show that guest-induced reassembly brings forth significant fluorescence change, which is a promising way of designing new fluorescent probes

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http://dx.doi.org/10.28991/HIJ-2022-03-03-010

for the analysis of phthalates in the environment and food. Pothipor et al. (2022) [14] show that a dual-mode electrochemical biosensor has been successfully developed for simultaneous detection of two different kinds of breast cancer biomarkers. The experimental results suggest that this label-free biosensor exhibits good linear responses to the concentrations of both target analytes within the limits of detection. This assay strategy has great potential to be further developed for the simultaneous detection of a variety of microRNAs and protein biomarkers for point-of-care diagnostic applications. Kim et al. (2022) [15] maintain that mechanophores are molecular motifs that respond to mechanical perturbance with targeted chemical reactions toward desirable changes in material properties. Taking advantage of the strengths of mechanophores and high-intensity focused ultrasound, mechanochemical dynamic therapy can provide noninvasive treatments for diverse cancer types [16]. About prostate cancer, Bax et al. (2022) [17] argue that diagnostic protocol is affected by poor accuracy and high false-positive rate and propose an electronic nose for non-invasive prostate cancer detection. The approach proved to be effective in mitigating drift on 1-year-old sensors by restoring accuracy from 55% to 80%, achieved by new sensors not subjected to drift. The model achieved, on double-blind validation, a balanced accuracy of 76.2%. Prema et al. (2022) [18] examine the biological synthesis of gold nanoparticles using green tea and their cytotoxicity against human prostate cancer cells. The findings suggest that the biosynthesized reduced prostate cancer cell proliferation and exert their anti-proliferative action on the prostate cancer cell line by inhibiting growth, decreasing DNA synthesis, and triggering apoptosis (cf., [19-27] for sources of innovations and other groundbreaking pathways in biomedicine and nanomedicine).

In lung cancer, Joshi et al. (2022) [28] argue that proper and early diagnosis of cancers provide basic aspects to efficient treatment and better prognosis and report a simple and label-free method of detection of two antigens: carcinoembryonic antigen (CEA) and cytokeratin-19 fragment (CYFRA 21-1) that are the biomarkers of many cancers including lung cancer. The responses of the sensors ranged from 10.96 to 26.48% for 0.25 pg/mL to 20 ng/mL CEA and it varied from 17.66 to 26.68% for 0.25 pg/mL to 20 ng/mL CYFRA 21-1. Kaya et al. (2022) [29] review the recent advances and improvements (2011–2021 period) in nanomaterials based on electrochemical biosensors for the detection of the lung and colon cancer biomarkers [30]. In colon cancer, Jiang et al. (2022) [31] point out that Transient receptor potential vanilloid 1 (TRPV1) acts as cellular sensor and is implicated in the tumor microenvironment cross talk and the functional role of TRPV1 in colorectal cancer (CRC). The study reveals an important role for TRPV1 in regulating the immune microenvironment during colorectal tumorigenesis and might be a potential target for CRC immunotherapy. Welz et al. (2022) [32] point out that the intestinal epithelium undergoes constant self-renewal from intestinal stem cells. Together with genotoxic stressors and failing DNA repair, this self-renewal causes susceptibility toward malignant transformation. The study shows that X-box binding protein 1 is a stress sensor involved in coordinating epithelial DNA damage responses and stem cell function.

In this context of the evolution of science and technology towards manifold fields of research, the motivation of this study is to clarify the role of sensor research and technology for main typologies of cancer, describing the networks of interconnection of sensors with technologies and scientific fields related to cancer under study (cf., [33, 34]). Proposed methodology can indicate new directions of sensor research and technologies for diagnosis and treatments of cancer and help R&D managers and policymakers to allocate with efficiency financial resources to support scientific and technological development in these critical fields for society [35-41].

The balance of the paper proceeds as follows. First, it describes the data and methodology, applying a novel information processing approach of computational scientometrics, to generate maps of science that can explain the scientific interaction of sensor research and technologies in studies concerning specific typologies of cancer. We then show the results and conclude with a discussion on new directions of the evolution of sensor research and technology in cancer and limitations of the paper to be solved with future studies.

2. Study Design

First, this study focuses on main typologies of cancer that have the highest estimated age-standardized incidence and mortality rate worldwide as indicated in Table 1 and Figure 1 based on data by World Health Organization-Cancer Today (2020) [42].

Table 1. Estimated age-standardized incidence and mortality rates in 2020, worldwide, both sexes, all ages [42]

Cancer	Incidence	Mortality
Breast	47.8	13.6
Prostate	30.7	7.7
Lung	22.4	18
Colorectum	19.5	9
Cervix uteri	13.3	7.3
Stomach	11.1	7.7
Liver	9.5	8.7
Corpus uteri	8.7	1.8
Ovary	6.6	4.2
Thyroid	6.6	0.43

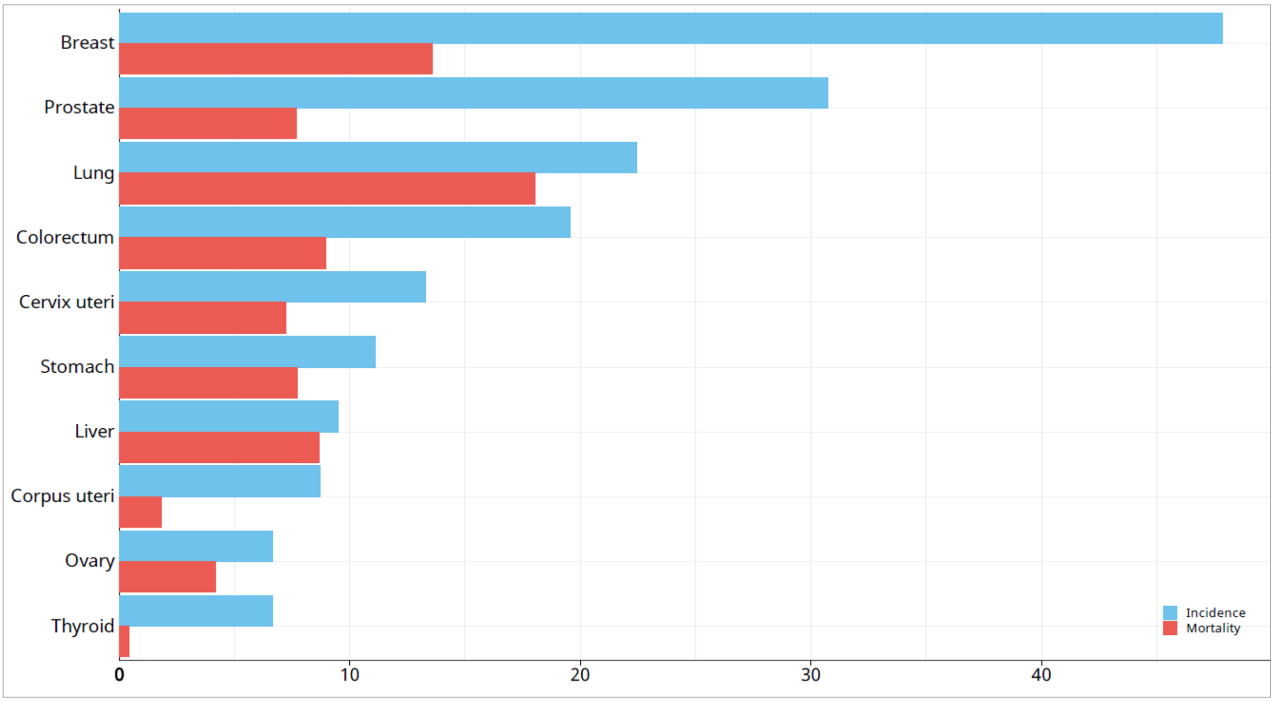

Figure 1. Estimated age-standardized incidence and mortality rates in 2020, worldwide, both sexes, all ages. Red bars indicate mortality, blue bares are incidence [42]

Considering results just mentioned of Table 1 and Figure 1, this study focuses on the investigation of sensor technology and research in the following four main types of cancer: 77874967

- Breast Cancer;
- Lung Cancer;
- Prostate Cancer;
- Colorectal Cancer.

2.1. Data Sources and Retrieval Strategy

To address the main problem of this study stated in Introduction, we used the Web of Science [43] core collection database to retrieve the articles related to sensor research and technology and cancers under study. In this paper here, we focus as said on four major types of cancer for a comparative analysis [44] including: Breast cancer (BC), Lung cancer (LC), Prostate cancer (PC) and, Colorectal cancer (CC). We used the following strategy for extracting articles related to these topics for further processing. The term "sensor" was searched with "breast cancer" in the topics of articles. We changed the "breast" to "lung" for extracting the articles related to lung cancer, "prostate" for prostate cancer and "colorectal" for colorectal cancer. The results are refined by document type = "Articles", Language = "English", Publication years = (1991-2021), Web of Science index = "SCI-EXPANDED"). We found 1,117 unique articles for breast cancer, 764 articles for lung cancer, 454 articles for prostate cancer, and 282 articles for colorectal cancer.

2.2. Data Analysis Procedure

To find the applications of sensor research and technology in cancers, we used the original keywords (DEs) provided by authors as the basis for constructing the word co-occurrences networks. According to this technique, two terms are considered co-occurrence whenever they simultaneously appear in a single document [45]. To find the relevant sensor research and technologies to each of the cancer under study, we applied the following procedure:

Keywords standardization: We tried to clean the keywords according to their meaning and structures in this step. For instance, we combined the "bio-sensor" and "biosensor" into Biosensor. Also, we changed all abbreviations and plural forms of nouns into a basic form (e.g., computers changed to computer and "AMPK" changed to "Amp-activated Protein kinase".

Network construction: We used SCI2 tool V. 1.3 for constructing the word co-occurrences network [46]. As mentioned above, we used the article's original keywords (DE tag) to create the networks. We create four different networks for breast, lung, prostate, and colorectal cancer. Also, we removed the isolated nodes after analyzing the nodes and links in the networks.

Path-finding: path-finding is a technique for choosing the shortest links between two nodes. To reduce the links of our networks and emphasize the most important nodes, we used a minimum spanning tree (MST) path-finder algorithm [47]. All the calculations are implemented by SCI2 tool [46] version 1.3. In addition, as an input parameter of the algorithm, we set the parameter Weight Attribute Measures to "SIMILARITY" and Edge Weight Attribute to "Weighted". The initial network of breast cancer contains 10,149 links, and after the algorithm the network has reduced to 2,318 edges. The lung cancer network contains 6,128 initially and has 1,539 links after applying the link reduction algorithm. After the algorithm implementation, the Prostate cancer network had 3,395 links and 850 edges. These results for colorectal cancer include 2,394 links at the first and 528 links after implementing the link reduction algorithm.

Visualizations: We utilized Gephi software [48] version 0.9.2 to visualize the networks. The nodes indicate the original keywords and links show the co-occurrences among them. The size of nodes are based on the Betweenness centrality (BC). This index represents the importance of a node in making the connection between other network nodes and is responsible for sustaining the network integration. Equation 1 shows how this index can be measured [36]:

$$BC(v) = \sum_{s,t \in V} \frac{\sigma_{st} v}{\sigma_{st}} \tag{1}$$

Here, BC(v) represent the Betweenness centrality value of node v, and σ-st counted the shortest paths shortest between node s and node t (cf., [34]). We implemented Betweenness Centrality (BC) measures to show the bridge nodes that facilitate the linkage of entities in the networks. Additionally we used BC value as a threshold for identifying the group of the path in each network. For this purpose, nodes with BC value greater than 0.1 has considered as a hub for identifying the groups in each network.

3. Results

3.1. Breast Cancer

Breast cancer is seriously threatening women health in the world [49, 50]. As mentioned earlier, the breast cancer sample contains 1,117 articles, and it is the most extensive dataset in our analysis. This network contains 2,319 nodes (keywords) and 2,318 links. Also, this network includes 149 sensors that are interconnected to the other nodes. Figure 2 shows the breast cancer co-word network.

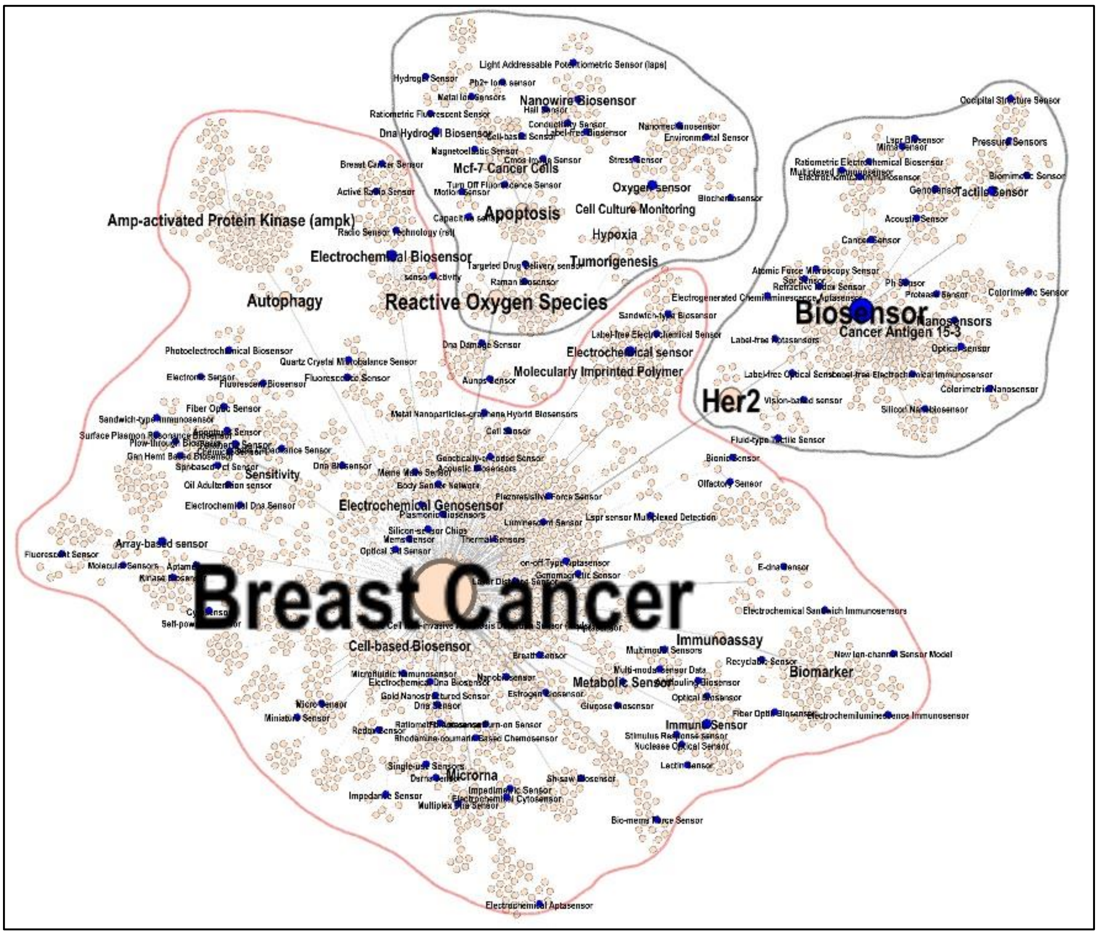

Figure 2. Co-word analysis map of breast cancer

Based on the Betweenness centrality value, we found three sub-groups in this network. Table 1A in Appendix I shows the most important information about these groups. Also, there are 149 sensors interconnected in this network.

Group 1 related to breast cancer has five hot topics: Autophagy, Immunoassay, Electrochemical Biosensor, Tumorigenesis, and Microrna, which have a high co-occurrence with Electrochemical Biosensor, Electrochemical Sensor, Oxygen Sensor, Immuno sensor, and Array-based Sensor.

Group 2 based on Biosensor has some hot topics, including HER2, Cancer antigen, Nanoparticle, Tactile Sensor, and Signal Amplification, which are significantly related to Optical sensor, Colorimetric Sensor, Colorimetric Nanosensor, Ph. Sensor, and Refractive Index Sensor.

Group 3, led by Reactive Oxygen Species, is related to Apoptosis, Mcf-7 Cancer Cells, Circulating Tumor Cell, DNA Hydrogel Biosensor, and Carbon Dot. In this domain, Raman Biosensor, DNA Hydrogel Biosensor, Light Addressable Potentiometric Sensor (laps), Capacitive Sensor, and Label-free Biosensor are sensors included in this group of connections (see Table 1A in Appendix I for details about groups, core keywords and related sensors in the breast cancer network).

3.2. Lung Cancer

Lung cancer is the second cancer were analyzed. This network contains 1,540 nodes (keywords) and 1,539 links. Also, this network includes 121 sensors that interconnected to other nodes. Figure 3 shows the lung cancer co-word network.

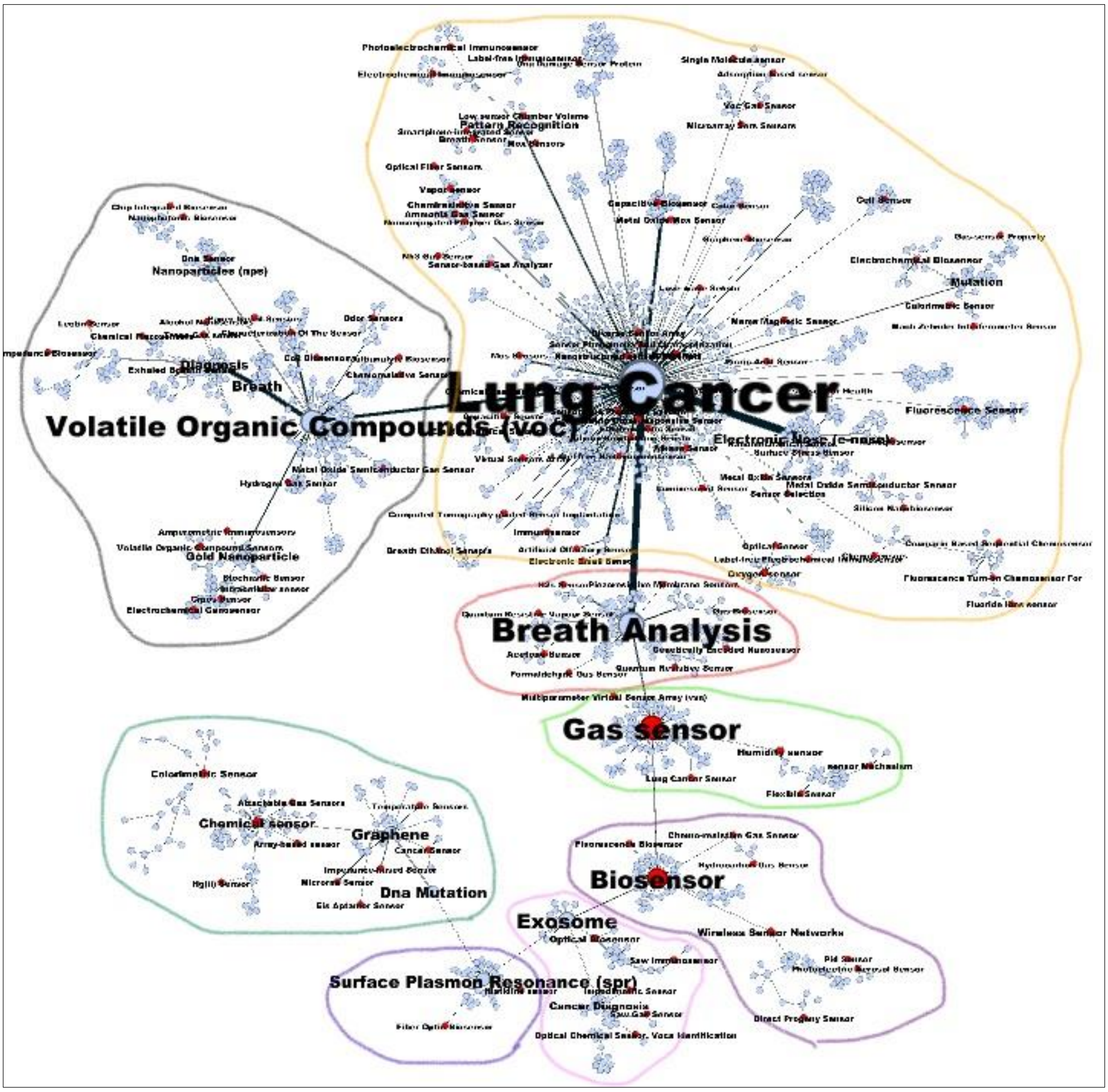

Figure 3. Co-word analysis map of lung cancer

Figure 3 shows that network of lung cancer has eight path groups. All nodes with a value of Betweenness centrality greater than 0.1 are considered the head of a group. Top keywords and all sensors included in these categories are in Table 2A of Appendix I.

Group 1, based on central node of lung cancer, is related to five hot topics: Electronic Nose (e-nose), Pattern Recognition, Mutation, Nrf2 (Nuclear factor-erythroid factor 2-related factor 2), and Calix [4] arene. It is also illustrated that 69 sensors are interconnected to this path. The oxygen sensor, Electrochemical Biosensor, Cell Sensor, Metal Oxide Semiconductor Sensor, Chemiresisitve Sensor, Breath Sensor, Electrochemical Immunosensor, and Capacitive Biosensor are sensors that are involved in the creation of linkage path among nodes.

Group 2, led by Volatile Organic Compounds (VOC), has 23 related sensors including, Exhaled Breath Sensor, DNA Sensor, Volatile Organic Compound Sensors, Cmos Sensor, Electrochemical Genosensor, etc. The topics related to this group of nodes are Breath, Diagnosis, Gold Nanoparticle, Nanoparticles, and Exhaled Breath.

Group 3, connected to Breath analysis, has eight interconnected sensors, including Piezoresistive Membrane Sensors, H2s Sensor, Formaldehyde Gas Sensor, Quantum Resistive Vapor Sens Quantum Resistive Sensor, Acetone Sensor, and Genetically Encoded Nanosensor. The most frequent keywords involved in this path group are: Real-Time, Diabetes, Non-invasive, Formaldehyde, and Sno2.

Group 4 with the head of Gas sensor is related to important keywords: Humidity sensor, Health Monitoring, Reduced Graphene Oxide, and Acetone. Six sensors of gas, lung cancer, sensor, multiparameter virtual sensor array, humidity sensor, sensor mechanism, and flexible sensor are part of this path group.

Group 5 has Biosensor as the most important technology in creating the path among different sensors. It generates a bridge with several sensors given by: Fluorescence Biosensor, Wireless Sensor Networks, Photoelectric Aerosol Sensor, Direct Progeny Sensor, Pid Sensor, Chemo-resistive Gas Sensor, Wireless Sensor Networks, Radon, Smart Home, Electrochemical Inhibitors, and Hydrocarbon Gas Sensor.

Group 6 is led by Exosome connected to the top four topic of Cancer Diagnosis, Lung-cancer Biomarker, Immunoassay, and Multi-wall Carbon Nanotubes related to six sensors of Optical Biosensor, Saw Gas Sensor, Optical Chemical Sensor, Vocs Identification, Saw Immunosensor, and Impedimetric Sensor.

Group 7 is based on Surface Plasmon Resonance that includes five hot keywords of Endoscopy, Au Nps, Signal Enhancement, Erlotinib, and Tollen's Reagent, which have two sensors of Histidine sensor and Fiber Optic Biosensor in their category.

Group 8, finally, is related to Graphene, and has interaction with DNA Mutation, Chemical Sensor, Urine Headspace, Colorimetric Sensor, and Tuberculosis keywords. Chemical Sensor, Colorimetric Sensor, Cancer Sensor, Array-based Sensor, Temperature Sensors, Impedance-based Sensor, Attachable Gas Sensors, Hg(ii) Sensor, Eis Aptamer Sensor, and Microrna Sensor are the important sensing technologies in this group.

3.3. Prostate Cancer

This network contains 870 nodes (keywords) and 869 links. This network includes 72 sensors that are interconnected to other nodes.

Figure 4 shows that there are eight groups in the Prostate cancer network. The most important nodes based on the Betweenness centrality value are: Prostate cancer, Prostate-specific antigen, Activated Protein Kinase (AMPK) and Biosensor. Table 3A in Appendix I shows details of groups, core keywords of them and related sensors.

Group 1, led by Prostate cancer, is related to 5 hot topics of Gold Nanoparticle, Immunosensor, Detection, Porcine Liver Esterase, and Fluorescent Probe. 27 sensors are interconnected to this path. Immunosensor, Near-infrared Biosensor, Resonance Sensor, Fna-based Electrochemical Sensor, Impedimetric Sensor, and Aptasensor are a couple of sensors involved in the creation of linkage path among these nodes.

Group 2, led by Activated Protein Kinase (Ampk), shows Label-free Nanoimmunosensor as the only connected Sensor. The hot topics related to this group of nodes are Apoptosis, Lkb1, Lung Cancer, Mtorc1, Castrate-resistant.

Group 3, connected to Prostate Specific Antigen (PSA), has 22 interconnected sensors, including Glucose Sensor, Ph Sensor, Colorimetric Sensor, Quantum Resistive Sensor, etc. The most frequent keywords involved in this path group are Aptamer, Prostate Cancer Diagnosis, Cancer Biomarker, and Silicon Nanowire.

Group 4 with the head of Biosensor is related to important keywords of Antibody, Prostatic Carcinoma, DNA, Acoustic Wave Sensor, Cancer Metastasis. Biosensor, Optical Sensor, Acoustic Wave Sensor, Bio-mems Force Sensor are main elements of this group.

Group 5, led by Prostate, is connected to Zinc, Chromogranin A, Fluorescent Sensor, Imaging Diagnosis, and Peptide related to four sensors of Trans-rectal and Pressure Sensor Array, Chemosensor, and Fluorescent Sensor.

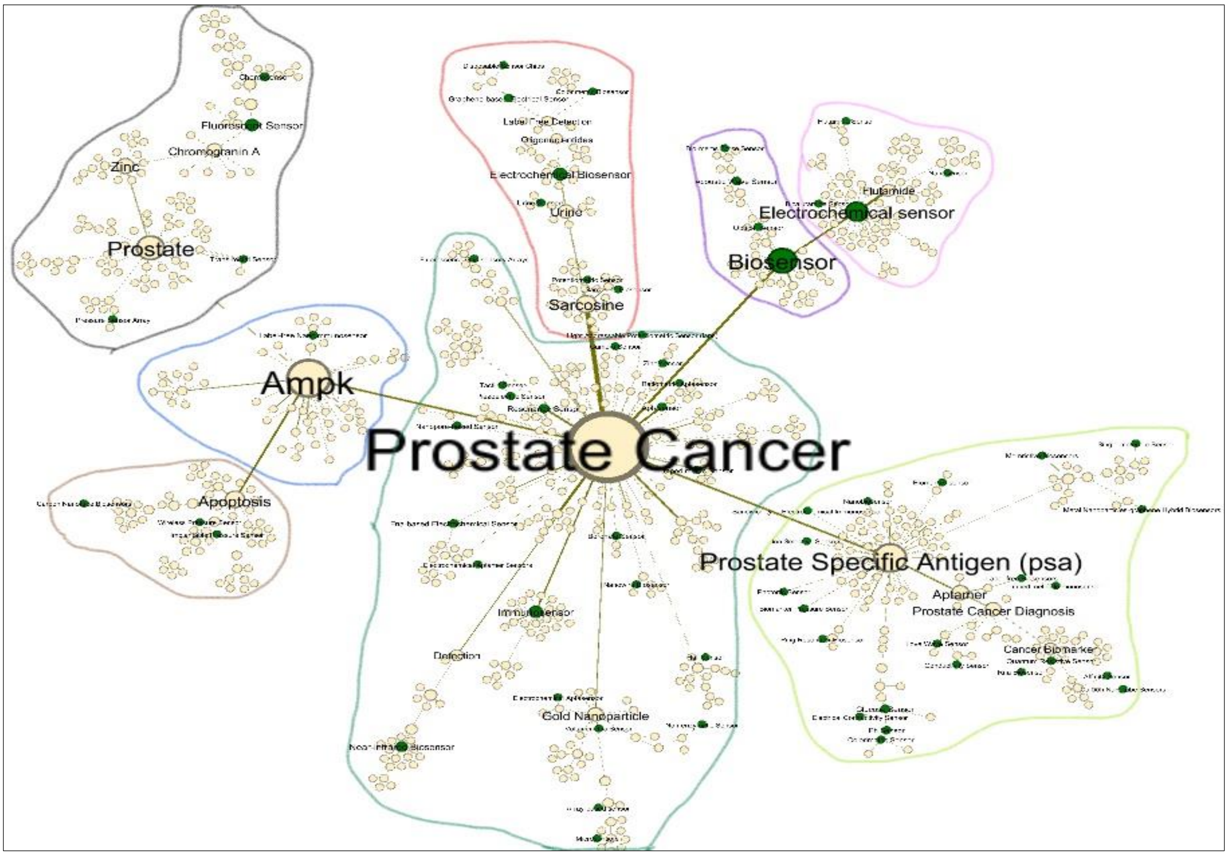

Figure 4. Co-word analysis map of Prostate cancer

Group 6 has Electrochemical Sensor that generates the path among different sensors and keywords. It is responsible for making a bridge between Nanosensor, Flutamide Sensor, Bicalutamide Sensor and most frequent keywords of Flutamide, Nanocomposite, Voltammetry, Anticancer Drug, and Electrophilicity.

Group 7, distinguished by Sarcosine, includes keywords of Urine, Electrochemical Biosensor, Oligonucleotides, Label Free Detection, and different sensors (Sarcosine Biosensor, Potentiometric Sensor, Electrochemical Biosensor, Urine Sensors, Graphene-based Electrical Sensor, Disposable Sensor Chips, and Colorimetric Biosensor) in their category.

Group 8, related to Apoptosis, has keywords of Chemotherapy, DNA Damage, DNA Repair, Rad9, and Tumor Suppressor. Three sensors of Carbon Nanotube Biosensor, Wireless Pressure sensors, and Implantable Pressure Sensor are the important sensing technologies in this group.

3.4. Colorectal Cancer

Finally, the colorectal cancer co-word network contains 529 nodes and 528 links. Figure 5 shows the co-occurrence network of keywords of this cancer and their connections with sensors.

Figure 5 shows 9 groups in the colorectal cancer network. The most important nodes based on the Betweenness centrality value are colorectal cancer, Faecal Immunochemical Test, Screening, and Biosensor. Table 4A in Appendix I shows details of these groups, core keywords of them and related sensors. Table 4A also shows that there are 31 sensors interconnected in this network.

Group 1, led by Colorectal Cancer, is related to five topics of Apoptosis, Occult Blood Test, Precision Medicine, Social Health, and Electrochemical Biosensor. Thirteen sensors are interconnected to this path. Electrochemical Biosensor, Gas Sensor Array, Nanostructured Sensors, Bifunctional Nanobiosensor, and Inductive Sensors are of technologies involved in creating linkage path among these nodes.

Group 2, led by Faecal Immunochemical Test (fit), has five topics: Inflammatory Bowel Disease, Reg3, Quality Assurance, Advance Notification, and Letter.

Group 3, connected to Screening, has two interconnected sensors including, Chemoresistive Sensors and Nucleic Acid-sensor. The most frequent keywords involved in this path group are Chemoresistive Sensors, Blood, Tumor Marker, Tissue Microarray, Faecal Occult Blood Test.

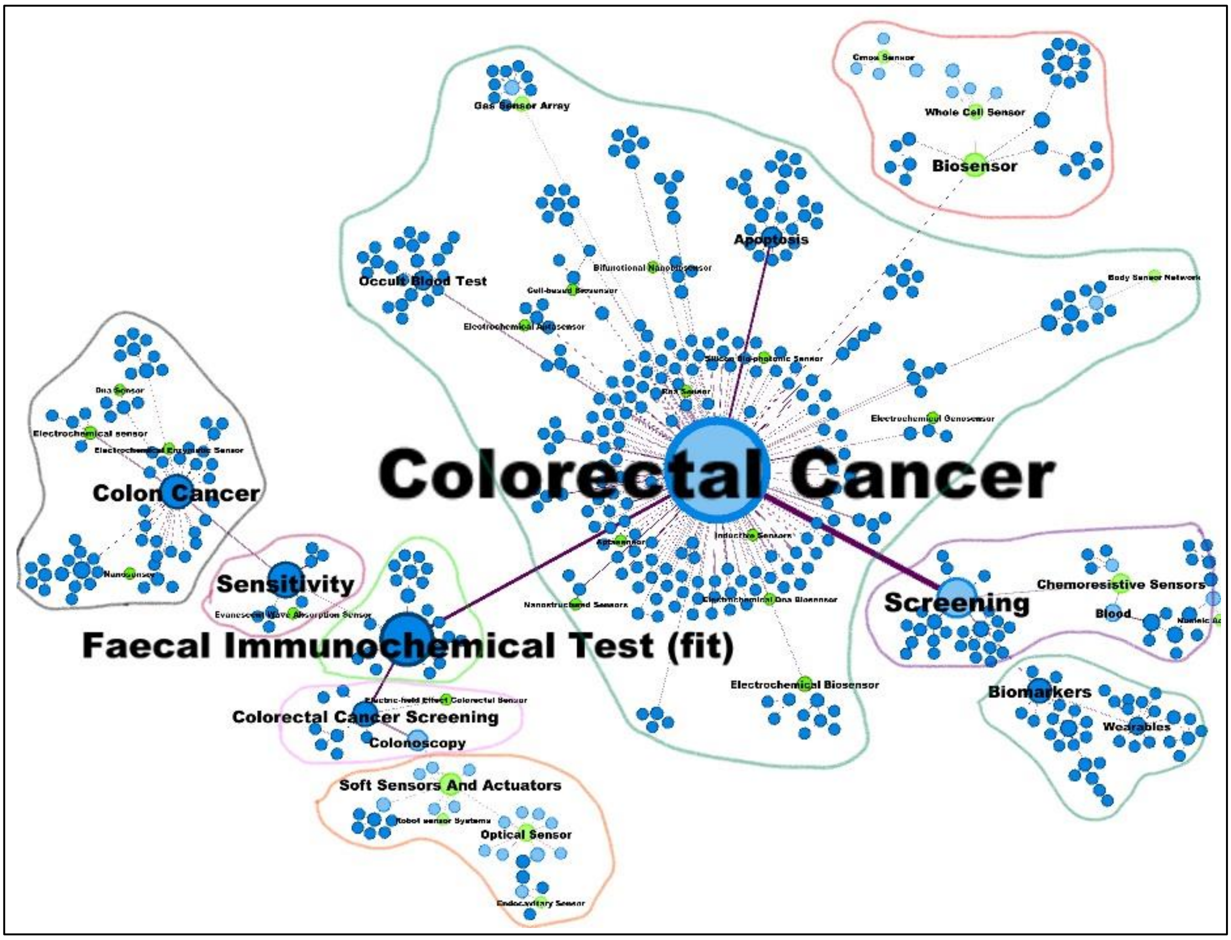

Figure 5. Co-word analysis map of colorectal cancer

Group 4 with the head of Sensitivity is related to important keywords of Antibody, Prostatic Carcinoma, DNA, Acoustic Wave Sensor, and Cancer Metastasis. Biosensor, Optical Sensor, Acoustic Wave Sensor, Bio-mems Force Sensor are element of this path group.

Group 5 is based on Colon Cancer having connections to top five keywords of Zinc, Chromogranin A, Fluorescent Sensor, making Diagnosis, and Peptide related to four sensors of Trans-rectal Pressure Sensor Array, Chemosensor, and Fluorescent Sensor.

Group 6 has Colorectal Cancer Screening in the most important position for creating the path among different sensors and keywords and for bridging Nanosensor, Flutamide Sensor, Bicalutamide Sensor and most frequent keywords of Flutamide, Nanocomposite, Voltammetry, Anticancer Drug, and Electrophilicity.

Group 7, based on Biomarkers, includes five keywords of Endoscopy, Au Nps, Signal Enhancement, Erlotinib, and Tollen's Reagent, and two sensors (Histidine sensor and Fiber Optic Biosensor).

Group 8, related to Biosensor, has DNA Mutation, Chemical Sensor, Urine Headspace, Colorimetric Sensor, and Tuberculosis keywords. Chemical Sensor, Colorimetric Sensor, Cancer Sensor, Array-based Sensor, Temperature Sensors, Impedance-based Sensor, Attachable Gas Sensors, Hg(ii) Sensor, Eis Aptamer Sensor, and MicroRNA Sensor are the most important sensing technologies in this group.

Group 9, led by Soft Sensors and Actuators, is related to five topics: Gold Nanoparticle, Immunosensor, Detection, Porcine Liver Esterase, and Fluorescent Probe. Twenty-seven sensors are interconnected to this path. Immunosensor, Near-infrared Biosensor, Resonance Sensor, Fna-based Electrochemical Sensor, Impedimetric Sensor, and Aptasensor are main sensors involved in the creation of linkage path among nodes in this group.

3.5. Frequent sensor technologies in cancer studies

According to Table 2, Biosensor is the only type of sensor that plays an essential role in all types of cancer research: breast cancer, lung cancer, prostate cancer, and colorectal cancer. After that, the electrochemical sensor is in all types of cancer, except lung cancer research. Surprisingly, electrochemical biosensor is used in breast cancer, lung cancer, and prostate cancer research but not in colorectal cancer. Optical Sensor can also be considered one of the sensor technology that is significantly used in studies of three types of cancer: breast cancer, prostate cancer, and colorectal cancer. This study shows that this type of sensor is applied in more diversified approaches. Moreover, the oxygen sensor, as a type of gas sensor, is mostly applied in lung cancer and breast cancer studies because of the usage for breath analysis in the treatment process. CMOS Sensor is another technology investigated in two types of cancer studies, including lung cancer and colorectal cancer.

Table 2. The most frequent sensors in cancer studies

Sensor technologies	Breast Cancer	Lung Cancer	Prostate Cancer	Colorectal Cancer
Biosensor	*	*	*	*
Electrochemical Sensor	*		*	*
Electrochemical Biosensor	*	*	*	
Oxygen sensor	*	*		
Tactile Sensor	*			
Immuno Sensor	*			
Fiber Optic Sensor	*			
Cancer Sensor	*			
Optical Sensor	*		*	*
Pressure Sensors	*			
Dna Sensor	*			
Impedimetric Sensor	*			
Terahertz Sensor	*			
Genosensor	*			
Biomimetic Sensor	*			
Electrochemical Cytosensor	*			
Gas sensor		*		
Chemical Sensor		*		
Fluorescence Sensor		*		
Cell Sensor		*		
Metal Oxide Semiconductor Sensor		*		
Breath Sensor		*		
Electrochemical Immunosensor		*		
Capacitive Biosensor		*		
Exhaled Breath Sensor		*		
Acetone Sensor		*		
Volatile Organic Compound Sensors		*		
Cmos Sensor		*		*
Electrochemical Genosensor		*		
Colorimetric Sensor		*		
Immunosensor			*	
Near-infrared Biosensor			*	
Resonance Sensor			*	
Chemosensor			*	
Glucose Sensor			*	
Impedimetric Sensor			*	
Soft Sensors and Actuators				*
Whole Cell Sensor				*

4. Concluding Remarks

The evolution of sensor technology over the last few decades has been unparalleled by the intensive activity of research in public and private laboratories [1, 4, 51-54]. Sensor research and technology are co-evolving with growing interactions in different research fields directed to fulfil human goals and needs and solve problems in society. Cancer is still one of the leading diseases and causes of death in the world. More than 250 types of cancer are currently known. The types of cancer under study here are a major cause of cancer-related deaths globally due to the difficulty of diagnosis in early stages that generates late treatments and a low probability of survival. In fact, in the health domain, a major challenge is the detection of diseases using rapid and cost-effective technology. Many cancer detection methods show poor sensitivity and selectivity, are time-consuming, and have a high cost for healthcare [16]. In short, early diagnosis is an important phase of the process of cancer treatment. For this reason, the role of sensor technology and research in these topics plays basic aspects for improving clinical diagnosis and early treatment for patients and, as a consequence, for reducing the mortality worldwide.

This study shows an exploratory analysis of the role of sensor technology in cancer research to see possible new directions for improving diagnosis and therapeutic treatments. The results of this analysis are:

- Biosensor is the only type of sensor that plays an essential role in research for all types of four cancer under study.
- Electrochemical sensor is in all types of cancer research, except lung cancer.
- Electrochemical biosensor is used in breast cancer, lung cancer, and prostate cancer research but not in colorectal cancer research.
- Optical Sensor is a technology investigated and applied in three types of cancer: breast cancer, prostate cancer, and colorectal cancer.
- Oxygen sensor has a role in lung cancer and breast cancer studies due to the usage for breath analysis in the treatment process.
- Finally, CMOS Sensor is another technology investigated and used in two types of cancer studies (lung cancer and colorectal cancer).

Overall, then, results suggest new directions of sensors for cancer research, such as optical biosensors that are rapid, real-time, and portable. They have a low detection limit and high sensitivity, and have great potential for diagnosing various types of cancer. In fact, optical biosensors can detect cancer in a few million malignant cells, in comparison to conventional diagnosis techniques that use 1 billion cells in tumor tissue with a diameter of 7–10 nm (traditional methods that are also costly, inconvenient, complex, time-consuming, and require technical specialists [6]). Moreover, cancer biomarkers using luminescence and electrochemical metal-organic framework sensors are opening the way for personalized patient treatments and the development of new cancer-detecting devices [16]. The challenge of sensor technology in cancer research is the development of simple, reliable, and sensitive point-of-care testing biosensors for cancerous exosome detection to early cancer diagnosis and prognosis. The biosensor is a main technology for cancer research that could also avoid the influence of the external environment, including surrounding light and temperature [55].

These conclusions are, of course, tentative. Although this study has provided some interesting, albeit preliminary results, it has several limitations. First, a limitation of this study is that sources understudy may only capture certain aspects of the ongoing dynamics of sensor research and technology in cancer studies. Second, there are multiple confounding factors that have an important role in the interaction between sensor technology and cancer research for diagnosis to be further investigated, such as high R&D investments, collaboration intensity, intellectual property rights, etc. [40, 41, 56, 57]. Third, the computational and statistical analyses in this study focus on data in a specific period and should be extended to other periods. Forth, sensor research associated with cancer studies changes their borders during the evolution of science and technology, such that the identification of stable technological trajectories and new patterns in the evolution of sensors in cancer research are a non-trivial exercise [58, 59].

To conclude, future research should consider new data and apply new approaches to reinforce proposed results [60-68]. Despite these limitations, the results presented here clearly illustrate the evolutionary paths of the main sensor technologies that can be powerful tools in the future diagnosis and treatment of cancer. However, future studies need a detailed examination of other factors for detecting new technological trajectories and supporting appropriate strategies of research and innovation policy and management of technology to foster the technology transfer of sensor technology in cancer research for improving diagnosis and therapies directed to reduce, as far as possible, world-wide mortality of cancer in society.

5. Declarations

5.1. Author Contributions

Conceptualization, M.C., M.M. and S.R.; methodology, S.R.; software, S.R.; validation, M.C., and S.R.; formal analysis, M.M. and S.R.; investigation, M.C., M.M. and S.R.; resources, M.C., M.M. and S.R.; data curation, M.M. and S.R.; writing—original draft preparation, M.C., M.M. and S.R.; writing—review and editing, M.C.; visualization, M.C., S.R., and M.M.; supervision, M.C.; project administration, M.C. All authors have read and agreed to the published version of the manuscript.

5.2. Data Availability Statement

- The data presented in this study are openly available in:
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- Data is contained within the article (Appendix I).

5.3. Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

5.4. Institutional Review Board Statement

This study did not require ethical approval, not involving humans or animals.

5.5. Informed Consent Statement

The study did not involve humans.

5.6. Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix I

Table 1A. Groups, Core keywords and related sensors in the breast cancer network

Group	Core Keyword	Top 5 keywords	Related sensors
1	Breast Cancer	Autophagy Immunoassay Electrochemical Biosensor Tumorigenesis Microrna	1. Electrochemical Biosensor 2. Electrochemical Sensor 3. Oxygen sensor 4. Immuno Sensor 5. Array-based Sensor 6. Terahertz Sensor 7. Dna Sensor 8. Fiber Optic Sensor 9. Impedimetric Sensor 10. Fluorescence Sensor 11. Dna Biosensor 12. Single-use Sensors 13. Impedance Sensor 14. Photoelectrochemical Biosensor 15. Electrochemical Cytosensor 16. Optical Biosensor 17. Antifouling Biosensor 18. Electrochemical Dna Sensor 19. Electrochemical Dna Biosensor 20. Cytosensor 21. Surface Plasmon Resonance Biosensor 22. Micro Sensor 23. Dna Damage Sensor 24. Nuclease Optical Sensor 25. Microfluidic Immunosensor 26. Gan Hemt Based Biosensor 27. Aptasensor 28. Chemical Sensor 29. Radio Sensor Technology (rst) 30. Miniature Sensor 31. Electrochemical Genosensor 32. Cell-based Biosensor 33. Metabolic Sensor 34. Multimodal Sensors 35. Multi-modal sensor Data 36. Acoustic Biosensors 37. Silicon-sensor Chips 38. Electrochemical Aptasensor 39. Estrogen Biosensor 40. Stress Sensor 41. Spr-based Pcf Sensor 42. Oil Adulteration sensor 43. New Ion-channel Sensor Model 44. Environmental Sensor 45. Fluorescent Biosensor 46. Body Sensor Network 47. Breath Sensor 48. Optical 3-d Sensor 49. Mems Sensor 50. Nanobiosensor 51. Quartz Crystal Microbalance Sensor 52. Aunps Sensor 53. Nanomechanosensor 54. Ratiometric Aptasensor 55. Recyclable Sensor 56. Redox Sensor 57. Thermal Sensors 58. Bionic Sensor 59. Mems Mass Sensor 60. Genomagnetic Sensor 61. on-off Type Aptasensor 62. Piezoresistive Force Sensor 63. Sandwich-type Immunosensor 64. Dsrna sensor 65. Cmos Capacitance Sensor 66. Plasmonic Biosensors 67. Cell Sensor 68. E-DNA Sensor 69. Metal Nanoparticles-graphene Hybrid Biosensors 70. Multiplex Dna Sensor 71. Genetically-encoded Sensor 72. Apoptosis Sensor

			73. Lectin Sensor 74. Glucose Biosensor 75. Molecular Sensors 76. Electrochemical Sandwich Immunosensor 77. sensor Activity 78. Label-free Electrochemical Sensor 79. Self-powered Sensor 80. Bio-mems Force Sensor 81. Sandwich-type Biosensor 82. Fiber Optic Biosensor 83. Fluorescent Sensor 84. Aptamersensor 85. Gold Nanostructured Sensor 86. Luminescent Sensor 87. Electronic Sensor 88. Laser Distance Sensor 89. Active Radio Sensor 90. Stimulus Response sensor 91. Lspr sensor Multiplexed Detection 92. Plow-through Biosensor 93. Fluorescence Turn-on Sensor 94. Rhodamine-coumarin Based Chemo sensor 95. Biochemosensor 96. Sh-saw Biosensor 97. Electrochemiluminescence Immunosensor 98. Live Cell Non-invasive Apoptosis Detection Sensor (niads) 99. Breast Cancer Sensor 100. Kinase Biosensor
2	Biosensor	Her2 Cancer antigen Nanoparticle Tactile Sensor Signal Amplification	1. Biosensor 2. Optical Sensor 3. Colorimetric Sensor 4. Colorimetric Nanosensor 5. Ph. Sensor 6. Refractive Index Sensor 7. Nanosensor 8. Label-free Optical Sensor 9. Label-free Aptasensor 10. Electrogenerated Chemiluminescence Aptasensor 11. Fluid-type Tactile Sensor 12. Vision-based Sensor 13. Spr Sensor 14. Label-free Electrochemical Immunosensor 15. Silicon Nanobiosensor 16. Protease Sensor 17. Environmental Sensor 18. Biochemosensor 19. Tactile Sensor 20. Pressure Sensors 21. Genosensor 22. Cancer Sensor 23. Biomimetic Sensor 24. Mirna sensor 25. Electrochemical Immunosensor 26. Occipital Structure Sensor 27. Multiplexed Immunosensor 28. Acoustic Sensor 29. Ratiometric Electrochemical Biosensor 30. Lspr Biosensor 31. Atomic Force Microscopy Sensor
3	Reactive Oxygen Species	Apoptosis Mcf-7 Cancer Cells Circulating Tumor Cell Dna Hydrogel Biosensor Carbon Dot	1. Raman Biosensor 2. Dna Hydrogel Biosensor 3. Light Addressable Potentiometric Sensor (laps) 4. Capacitive Sensor 5. Label-free Biosensor 6. Nanowire Biosensor 7. Motion Sensor 8. Targeted Drug Delivery sensor 9. Ratiometric Fluorescent Sensor 10. Hall Sensor 11. Cell-based Sensor 12. Metal Ion Sensors 13. Conductivity Sensor 14. Turn Off Fluorescence Sensor 15. Hydrogel Sensor 16. Magnetoelastic Sensor 17. Cmos Image Sensor 18. Pb2+ Ions sensor

Table 2A. Groups, Core keywords and related sensors in the lung cancer network

Group	Core Keyword	Top 5 keywords	Related sensors
1	Lung Cancer	Electronic Nose (e-nose) Pattern Recognition Mutation Nrf2 (Nuclear factor-erythroid factor 2-related factor 2) Calix[4]arene	1. Oxygen sensor 2. Electrochemical Biosensor 3. Cell Sensor 4. Metal Oxide Semiconductor Sensor 5. Chemiresisitve Sensor 6. Breath Sensor 7. Electrochemical Immunosensor 8. Capacitive Biosensor 9. Photoelectrochemical Immunosensor 10. Vapor sensor 11. Ammonia Gas Sensor 12. Voc Gas Sensor 13. Electrochemical Sensor 14. Mems Magnetic Sensor 15. Immunosensor 16. Sensor-based Gas Analyzer 17. Nonconjugated Polymer Gas Sensor 18. Color Sensor 19. Computed Tomography-guided Sensor Implantation 20. Metal Oxide Mox Sensor 21. Dna Damage Sensor Protein 22. Sensor Phenomena And Characterization 23. Label-free Electrochemical Immunosensor 24. Mox Sensors 25. Low sensor Chamber Volume 26. Metal Oxide Sensors 27. Artificial Olfactory Sensor 28. Optical Fiber Sensors 29. Optical Sensor 30. Electronic Smell Sensor 31. Colorimetric Cross-responsive Sensor 32. Sensor-type Prototype System 33. Mos Sensors 34. Sensor Selection 35. Fluorescence Turn-on Chemosensor 36. Coumarin Based Sequential Chemosensor 37. Nanostructured sensor Materials 38. Love-wave Sensor 39. Calorimetric Sensor 40. Gas-sensor Property 41. Electrokinetic Sensor 42. Chemosensors 43. Surface Stress Sensor 44. Nanomechanical Sensor 45. Label-free Immunosensor 46. Chemical Gas Sensor 47. Mach Zehnder Interferometer Sensor 48. Picric Acid Sensor 49. Diverse Sensor Array 50. Virtual Sensors Array 51. Aptasensor 52. Label-free Nanoimmunosensor 53. Microarray Sers Sensors 54. Capacitive Sensor 55. Nh3 Gas Sensor 56. Smartphone-integrated Sensor 57. sensor For Health 58. Silicon Biophotonic Sensor 59. Nanobiosensor 60. Single Molecule sensor 61. Fluoride Ions sensor 62. Breath Ethanol Sensors 63. Silicon Nanobiosensor 64. Poly-silicon Wire Sensor 65. Cytosensor 66. Adsorption-based Sensor 67. Graphene Biosensor 68. Alkane Sensor

			69. Luminescent Sensor
2	Volatile Organic Compounds (voc)	Breath Diagnosis Gold Nanoparticle Nanoparticles Exhaled Breath	1. Exhaled Breath Sensor 2. Dna Sensor 3. Volatile Organic Compound Sensors 4. Cmos Sensor 5. Electrochemical Genosensor 6. Metal Oxide Semiconductor Gas Sensor 7. Intracellular Sensor 8. Amperometric Immunosensor 9. Odor Sensors 10. Chemical Piezosensor 11. Chip Integrated Biosensor 12. Nanophotonic Biosensor 13. Stochastic Sensor 14. Lectin Sensor 15. Hydrogen Gas Sensor 16. Impedance Biosensor 17. Alcohol Nanosensor 18. Paper-based Sensors 19. Chemoresistive Sensors 20. Multianalyte Biosensor 21. Co2 Biosensor 22. Characterization Of The Sensor 23. Trace Gas sensor
3	Breath analysis	Real Time Diabetes Non-invasive Formaldehyde Sno2	1. Piezoresistive Membrane Sensors 2. H2s Sensor 3. Formaldehyde Gas Sensor 4. Quantum Resistive Vapor Sensor 5. Quantum Resistive Sensor 6. Acetone Sensor 7. Genetically Encoded Nanosensor 8. Gas Biosensor
4	Gas Sensor	Humidity sensor Health Monitoring Reduced Graphene Oxide Acetone Tin Oxide	9. Gas sensor 10. Lung Cancer Sensor 11. Multiparameter Virtual Sensor Array 12. Humidity sensor 13. sensor Mechanism 14. Flexible Sensor
5	Biosensor	Wireless Sensor Networks Radon Smart Home Electrochemical Inhibitors	15. Biosensor 16. Fluorescence Biosensor 17. Wireless Sensor Networks 18. Photoelectric Aerosol Sensor 19. Direct Progeny Sensor 20. Pid Sensor 21. Chemo-resistive Gas Sensor 22. Hydrocarbon Gas Sensor
6	Exosome	Cancer Diagnosis Lung-cancer Biomarker Immunoassay Multi-wall Carbon Nanotubes	23. Optical Biosensor 24. Saw Gas Sensor 25. Optical Chemical Sensor, Vocs Identification 26. Saw Immunosensor 27. Impedimetric Sensor
7	Surface Plasmon Resonance (spr)	Endoscopy Au Nps Signal Enhancement Erlotinib Tollen's Reagent	28. Histidine sensor 29. Fiber Optic Biosensor
8	Graphene	Dna Mutation Chemical Sensor Urine Headspace Colorimetric Sensor Tuberculosis	30. Chemical Sensor 31. Colorimetric Sensor 32. Cancer Sensor 33. Array-based Sensor 34. Temperature Sensors 35. Impedance-based Sensor 36. Attachable Gas Sensors 37. Hg(ii) Sensor 38. Eis Aptamer Sensor

			39. Microrna Sensor

Table 3A. Groups, Core keywords and related sensors in the Prostate cancer network

Group	Core Keyword	Top 5 keywords	Related sensors
1	Prostate cancer	Gold Nanoparticle Immunosensor Detection Porcine Liver Esterase Fluorescent Probe	1. Immunosensor 2. Near-infrared Biosensor 3. Resonance Sensor 4. Fna-based Electrochemical Sensor 5. Impedimetric Sensor 6. Aptasensor 7. Piezoelectric Sensor 8. Boronate Sensor 9. Zinc sensor 10. Nanopore-based Sensor 11. Nanowire Biosensor 12. Microsensors 13. Voltammetric Sensor 14. Hall Sensor 15. Electrochemical Aptasensor 16. Tactile Sensor 17. Array-based Sensor 18. Non-enzymatic Sensor 19. Electrochemical Aptamer Sensors 20. Ratiometric Aptasensor 21. Light Addressable Potentiometric Sensor (laps) 22. Camera Sensor 23. Fluorescence Gas-sensory Arrays
2	Activated Protein Kinase (Ampk)	Apoptosis Lkb1 Lung Cancer Mtorc1 Castrate-resistant	1. Label-free Nanoimmunosensor
3	Prostate Specific Antigen (psa)	Aptamer Prostate Cancer Diagnosis Cancer Biomarker Silicon Nanowire	1. Glucose Sensor 2. Ph Sensor 3. Colorimetric Sensor 4. Quantum Resistive Sensor 5. Label-free Biosensors 6. Love Wave Sensor 7. Biomarker sensor 8. Photonic Sensor 9. Biomarker Pressure Sensor 10. Carbon Nanotube Sensors 11. Ion Selective Sensors 12. Rna Biosensor 13. Affinity Sensor 14. Electrical Conductivity Sensor 15. Conductivity Sensor 16. Memristive Biosensors 17. Ring Resonator Biosensor 18. Nanobiosensor 19. Metal Nanoparticles-graphene Hybrid Biosensors 20. Impedimetric Immunosensor 21. Single-molecule Sensor 22. Sandwich-type Electrochemical Immunosensor
4	Biosensor	Antibody Prostatic Carcinoma Dna Acoustic Wave Sensor Cancer Metastasis	1. Biosensor 2. Optical Sensor 3. Acoustic Wave Sensor 4. Bio-mems Force Sensor
5	Prostate	Zinc Chromogranin A Fluorescent Sensor Imaging Diagnosis Peptide	1. Trans-rectal Sensor 2. Pressure Sensor Array 3. Chemosensor 4. Fluorescent Sensor
6	Electrochemical Sensor	Flutamide Nanocomposite Voltammetry Anticancer Drug Electrophilicity	1. Electrochemical Sensor 2. Nanosensor 3. Flutamide Sensor 4. Bicalutamide Sensor
7	Sarcosine	Urine Electrochemical Biosensor Oligonucleotides Label Free Detection	1. Sarcosine Biosensor 2. Potentiometric Sensor 3. Electrochemical Biosensor 4. Urine Sensors 5. Graphene-based Electrical Sensor 6. Disposable Sensor Chips 7. Colorimetric Biosensor
8	Apoptosis	Chemotherapy Dna Damage	1. Carbon Nanotube Biosensor 2. Wireless Pressure Sensor

	Dna Repair Rad9 Tumor Suppressor	3. Implantable Pressure Sensor

Table 4A. Groups, Core keywords and related sensors in the colorectal cancer network

Group	Core Keyword	Top 5 keywords	Related sensors
1	Colorectal Cancer	Apoptosis Occult Blood Test Precision Medicine Social Health Electrochemical Biosensor	1. Electrochemical Biosensor 2. Gas Sensor Array 3. Nanostructured Sensors 4. Bifunctional Nanobiosensor 5. Inductive Sensors 6. Body Sensor Network 7. Electrochemical Genosensor 8. Electrochemical Dna Biosensor 9. Silicon Bio-photonic Sensor 10. Aptasensor 11. Cell-based Biosensor 12. Electrochemical Aptasensor 13. Rna Sensor
2	Faecal Immunochemical Test (fit)	Inflammatory Bowel Disease Reg3 Quality Assurance Advance Notification Letter	-
3	Screening	Chemoresistive Sensors Blood Tumor Marker Tissue Microarray Faecal Occult Blood Test	1. Chemoresistive Sensors 2. Nucleic Acid-sensor
4	Sensitivity	Stability Specificity	1. Evanescent Wave Absorption Sensor
5	Colon Cancer	Transmission Electron Microscopy (tem) Oxidative Stress Kras Drug Screening	1. Electrochemical Sensor 2. Electrochemical Enzymatic Sensor 3. Dna Sensor 4. Nanosensor
6	Colorectal Cancer Screening	Colonoscopy Quantitative Fecal Immunochemical Test For Hemoglobin Sample Stability	1. Electric-field Effect Colorectal Sensor
7	Biomarkers	Wearables Sex Circadian Rhythms Nanotechnology Hemolysis Assay	-
8	Biosensor	Cancer Markers Surface Plasmon Resonance Whole Cell Sensor Circular Dichroism Spectroscopy	1. Biosensor 2. Whole Cell Sensor 3. Cmos Sensor
9	Soft Sensors And Actuators	Optical Sensor Bowel Viability Colon Cloud Serve Pulse Oximetry	1. Optical Sensor 2. Robot sensor Systems 3. Endocavitary Sensor