*engineering proceedings*

MDPI

*Proceeding Paper*

# An Innovative Analysis of Time Series-Based Detection Models for Improved Cancer Detection in Modern Healthcare Environments †

**Uma Shankari Srinivasan [1,*], Venkat Pavithra [1], Kaliappan Sutha [1], Sridevi Ramachandiran [2] and Nallathambi Indumathi [1]**

[1] Department of MCA, College of Science and Humanities, SRM Institute of Science and Technology, Ramapuram Campus, Chennai 600089, India; vpavithra.1989@gmail.com (V.P.); ksutha1986@gmail.com (K.S.); induarivu27@gmail.com (N.I.)
[2] Department of Computer Science and Engineering, K. Ramakrishnan College of Engineering, Samayapuram, Trichy 621112, India; sridevivelon@gmail.com
* Correspondence: uma715129@gmail.com
† Presented at the International Conference on Recent Advances on Science and Engineering, Dubai, United Arab Emirates, 4–5 October 2023.

**Abstract:** Early detection of cancer is important for successful treatment and improved survival of many cancer types. Technological advances have enabled researchers to develop more precise and reliable methods of cancer detection that go beyond traditional methods, such as biopsy and imaging. Through methods such as blood tests, MRI scans, and gene expression profiling, it is now possible to quickly and accurately diagnose many types of cancer. Early detection of cancer can lead to improved outcomes for patients and can even help save lives. Time series analysis is a data mining technique used to identify and analyze the temporal patterns in datasets. The proposed model reached 91.30% accuracy, 90.11% precision, 92.46% recall, and a 90.12% F1-score. This enhanced version of time series analysis incorporates multiple layers of data sources and uses advanced machine learning algorithms to identify patterns that could signal the presence of a tumor. Innovations in time series analysis for cancer detection can have a significant impact on modern healthcare. Time series analysis is a mathematical method used to analyze trends in data over multiple periods. It can be used to identify patterns that may indicate early signs of cancer.

**Keywords:** time series analysis; data mining; cancer detection; tumor; machine learning



**Citation:** Srinivasan, U.S.; Pavithra, V.; Sutha, K.; Ramachandiran, S.; Indumathi, N. An Innovative Analysis of Time Series-Based Detection Models for Improved Cancer Detection in Modern Healthcare Environments. *Eng. Proc.* **2023**, *59*, 114. https://doi.org/10.3390/engproc2023059114

Academic Editors: Nithesh Naik, Rajiv Selvam, Pavan Hiremath, Suhas Kowshik CS and Ritesh Ramakrishna Bhat

Published: 25 December 2023



## 1. Introduction

Cancer is one of the world's most prevalent and deadly diseases, and detection is essential for successful treatment [1]. Insights into structural, molecular, and clinical characteristics play an important role in improving early detection and treatment [2]. In addition, DL, a form of ML, can be deployed to identify complex patterns within medical images [3]. It can then be used to improve the accuracy of predictions made about the presence of cancer [4]. Using sequencing techniques, scientists can identify and sequence the genes within cancer cells [5]. These studies aim to analyze the genetic makeup of large populations to search for genetic variations associated with wither [6]. Another valuable technology is that of high-throughput single-cell genomic analysis [7]. The development of these computational technologies has drastically improved the accuracy of cancer detection, and has even allowed for the targeted treatment of certain conditions [8]. Cancer detection has become a priority in modern healthcare, with good reason. Every year, millions worldwide are diagnosed with cancer, and many lose their battle. It is why we must detect and diagnose cancer as early as possible [9]. Early-stage treatment is often much less expensive than treatment for advanced cancer [10]. Early cancer detection gives cancer

patients more treatment options, which are usually much broader and more advanced. Radiation, chemotherapy, surgery, and even immunotherapy are all potential options, for which a patient may not be eligible if their cancer is already in the advanced stages [11]. The key to beating cancer is to catch and diagnose it as early as possible. It involves regular visits to the doctor, undergoing appropriate screenings, and striving to lead a healthy lifestyle. This approach aims to leverage specific genetic characteristics of individuals to provide personalized treatment plans [12]. Doctors can tailor more effective treatments by studying the unique DNA makeup of a patient's tumor. AI algorithms can sift through large amounts of medical data in order to identify patterns, as well as generate predictions about the development of cancer [13]. The key contributions of the research include the following:

- Automated detection of early-onset cancer is possible by observing current and past cancer patterns, obtaining maximum accuracy in classifying tumor subtypes through time series analysis.
- Improved understanding of the complex progression patterns of tumors by combining clinical and molecular data, predicting diagnosis and survival rates based on temporal changes in tumor sizes.
- Improved accuracy of imaging modalities for diagnosis by including temporal information and intelligently identifying new patterns in tumor characteristics that could indicate prognosis or treatment outcomes.

The rest of the paper is organized as follows: Section 2 describes associated works and explains the proposed model, Section 3 describes the outcomes and discussions, and Section 4 indicates the notion and destiny scope of the proposed studies.

## 2. Materials and Methods

King, A., et al. [14] mentioned that early cancer detection is critical in improving patient consequences and decreasing mortality. MR imaging is an effective tool for early cancer detection, allowing for correct evaluations of tumor length, form, and unfold, in addition to the presence and volume of lymph node involvement. Crosby et al. [15] mentioned that early detection of cancer involves figuring out cancers in their earliest levels before they have a chance to unfold throughout the body. Van Der Pol et al. [16] mentioned that the early detection of maximum cancers via decoding the epigenetic and environmental fingerprints of mobile-unfastened DNA is a superior technique. Scientists use this method to detect cancers in their earliest stages by studying DNA fragments released with the resource of cells into the bloodstream. Roy et al. [17] discussed the ongoing study and evaluation of DNA methylation classifiers' diagnostic energy for early cancer detection. Cutting-edge research looks at the capacity of these DNA methylation classifiers to become aware of early levels of diverse cancers. Chen et al. [18] stated that the non-invasive early detection of cancers four years before conventional prognosis, using a blood test, is a breakthrough in the fight in opposition to cancer. This test is primarily based on detecting ctDNA, genetic cloth released into the blood by tumor cells. Islam et al. [19] has mentioned the eye mechanism is used to capture patterns among incremental layers. Jeyaraj et al. [20] mentioned that the laptop-assisted clinical photograph for the early analysis of oral cancer is conducted through the usage of deep studying rules trained on medical photograph-graph statistics for the automatic classification of medical images associated with oral cancer.

Yao et al. [21] described a technique utilizing an attention-based time-incremental CNN to detect multi-magnificence arrhythmias from 12-lead various-duration ECG. Ginsburg et al. [22] discussed the importance of early detection of breast cancer, the main reason of death among women, including crucial tests such as mammography and clinical breast exams. Liu et al. [23] has mentioned that low-fee thermophoretic profiling is a technique for detecting and classifying cancers by analyzing Extracellular-Vesicle (EV) surface proteins. This approach utilizes thermophoresis, a phenomenon in which particles at a specific temperature move in response to heat distinction. Particles circulate closer to hotter or

cooler temperatures, relying on the heat difference. Cai et al. [24] discussed genome-wide mapping of 5-hmC in cfDNA as a non-invasive approach for the early detection of HCC.

### *2.1. Proposed Model*

The Enhanced Time Series Analysis for Cancer Detection (ETSC) is a method that uses an ensemble of statistical, temporal, and machine learning methods to identify and classify cancer progression and chromosome aberration patterns across multiple cancer types, as shown in Figure 1.

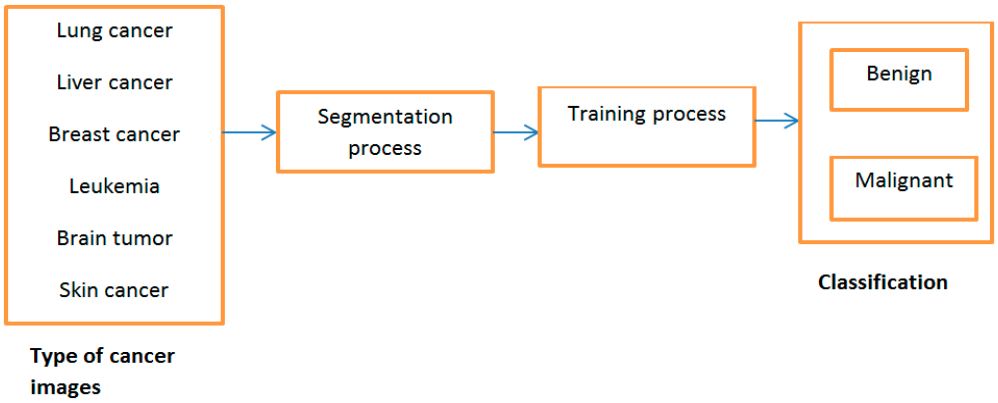


**Figure 1.** Cancer detection methodology.

Machine learning is an important component in the enhanced time series analysis for cancer detection.

### *2.2. Dataset Description*

The details of the dataset are provided at https://www.kaggle.com/code/adithyajere/cancer-dataset (accessed on 10 May 2023). Table 1 contains details about the dataset.

**Table 1.** Dataset description.

| Dataset | Description |
|---|---|
| Lung Tumor | No.of Samples: 6125<br>Training Samples: 75% (4778 Samples)<br>Testing Samples: 25% (1347 Samples) |
| Liver Tumor | |
| Breast Tumor | |
| Leukemia Tumor | |
| Brain Tumor | |
| Skin Tumor | |

It can be used to develop an enhanced time series analysis model to improve the accuracy of detection and reduce false positives and negatives. This can ultimately improve the accuracy of cancer detection and treatment. Improved bioavailability in the context of cancer detection is significant because it allows physicians to more accurately detect and diagnose cancer. This accuracy is critical for determining the most effective treatment options for patients. By using a time series-based model, improved bioavailability can be achieved by taking into account changes in laboratory data, such as hormone levels, blood counts, and imaging scans, over time. Such models allow physicians to more accurately detect microscopic changes in tumor features, providing a more precise diagnosis and treatment for cancers. Improved bioavailability also helps to resolve the number of FPs and FNs, ensuring the accurate detection of cancer in a timely fashion, improving patient outcomes.

### 2.3. Pre-Processing

Pre-processing is the process of preparing a time series dataset for further analysis. It involves the detection of seasonal patterns, noise removal, outlier removal, increased accuracy, data smoothing, and feature vector creation for modeling. By performing pre-processing, data scientists can gain valuable insights from the time series and improve the accuracy of cancer detection models. The time series-based detection model can be applied to a variety of cancers, including breast, prostate, pancreatic, ovarian, cervical, colorectal, and lung cancer. The model is designed to detect changes indicative of cancer progression, such as increases or decreases in tumor size, metabolic activity, tissue stiffness, or tissue composition. The model can be used to detect changes in cancer at its earliest stages, providing an opportunity to intervene in the progression of the disease before it becomes more severe. In addition, the model can be used to monitor cancer progression in response to treatments, enabling physicians to adjust treatments as needed. This approach has potential applications across different cancer types, helping physicians identify and monitor cancer progression in individual patients.

### 2.4. Feature Extraction

This step extracts important features from the data, which can be used to differentiate between normal and abnormal cell activities. These features are then used to identify any anomalies that might suggest the presence of cancer. The extracted features can also be used to quantify the accuracy of the predictive model and build a better predictive model with improved accuracy.

### 2.5. Segmentation

The segmentation process in enhanced time series analysis for cancer detection serves the purpose of organizing large datasets into bite sizes for faster processing. Segmentation divides datasets into smaller chunks, aiding in better understanding and analysis. Each segment is specifically designed to extract meaningful information from the data, which can be used to detect cancer.

### 2.6. Classification

Classification combines several existing tools and techniques to achieve a high degree of accuracy. The process involves applying selected features to develop a predictive model that is able to accurately distinguish cancer from non-cancer samples. The performance of the model can be validated by comparing results to experimental data from SCC 29 colon cancer cell lines. This can be done by evaluating the model's accuracy in predicting cellular proliferation and drug response/resistance. Additionally, one can measure how closely the model's predicted gene-expression profiles match those observed in SCC 29 colon cancer cell lines. Furthermore, the model's sensitivity and specificity can be analyzed in different scenarios and compared to available data. Finally, one can also assess the model's generalizability by examining its performance when applied to similar yet distinct cancer cell lines. The multi-dimensional clustering algorithm will use a combination of unsupervised machine learning techniques to detect patterns and group similar data points in the time series. This will help the identification of clusters of data points that correspond to specific types of cancer. The statistical analysis will use predictive models to analyze the data and build a model. The ML algorithms employed will use supervised learning algorithms to learn from labeled data and identify patterns in the data.

### 2.7. Proposed Algorithm

Time series algorithms for cancer detection can be used to detect changes in biomarkers over time, such as an increase in the levels of certain proteins, chemicals, or markers in a patient's blood or tissue, that could indicate the presence of cancer. AI can be used to analyze time series data in cancer detection, with several machine learning algorithms and data mining methods. RF, a supervised learning algorithm, can be used to extract detailed

structural information from time series datasets. In comparison, LSTM, memory-based neural network architecture, can be used to detect long-term dependencies and periodic patterns in the given data. Combining these two architectures can help model the data more accurately and accurately predict its future behavior. Considering the number users ($u$) wearing the smart sensor in a particular time interval (t), the multivariate time series of user '$u$' is denoted as Au, and in the $i$-th dimension, as ${A_u}^i$. It is written as follows:

$$A_u = \left\{ A_u^1, A_u^2, A_u^3, \ldots\ldots, A_u^X \right\} \tag{1}$$

$$A_u^i = \left\{ A_{u,1}^i, A_{u,2}^i, A_{u,3}^i, \ldots\ldots, A_{u,T}^i \right\}; i = 1, 2, 3, \ldots, T; \tag{2}$$

where $X$ denotes the total number of dimensions, and $T$ denotes the length of the time series. The convolution operation is performed as follows:

$$A(t) = f\left( \sum_{a=1}^{i} \sum_{b=1}^{t} e_{a+x(d-1),b^{\alpha}a,b} + y \right) \tag{3}$$

Let's identify the pooling operation time ($t$), which can be formulated as follows:

$$p(t) = g(A((t-1) * i + 1), (t-1) * i + 2), \ldots\ldots, A(ti)) \tag{4}$$

where $A(*)$ indicates the convolution output, $i$ indicates the size of kernel ($k$), and $g$ indicates the strategy followed for the pooling operation. In terms of accuracy, combining Random Forest and Long Short-Term Memory algorithms has been found to improve the performance of cancer detection models. This comes from the ability of RF to capture the complex nonlinearity of the data and the memory units in LSTM to store the temporal patterns of the time series data. Additionally, combining these two algorithms gives the model more robustness and the ability to make more informed predictions.

## 3. Results and Discussion

The proposed Time Series-Based Detection Model (TSBDM) has been compared with existing models such as Computer-assisted Medical Image Classification (CMIC), Multi-class arrhythmia detection (MCAD), DHO-Based Pretrained CNN Model (DPCM), and deep DNA Machine Learning Model (DDMLM). Matlab r2022a was the tool used to simulate the results.

### *3.1. Computation of Accuracy*

Accuracy for a time series algorithm in cancer detection is the ability of the algorithm to correctly identify instances of cancer based on data collected over a period of time. The accuracy is computed with the help of the following Equation (5).

$$A = \left( \frac{TP + TN}{TP + TN + FP + FN} \right) \tag{5}$$

Figure 2 shows the comparison of accuracy. In a computation cycle, the existing CMIC reached 67.98%, MCAD reached 56.78%, DPCM obtained 82.74%, and DDMLM reached a 60.91% accuracy rate. The proposed model achieved a 91.30% accuracy rate.

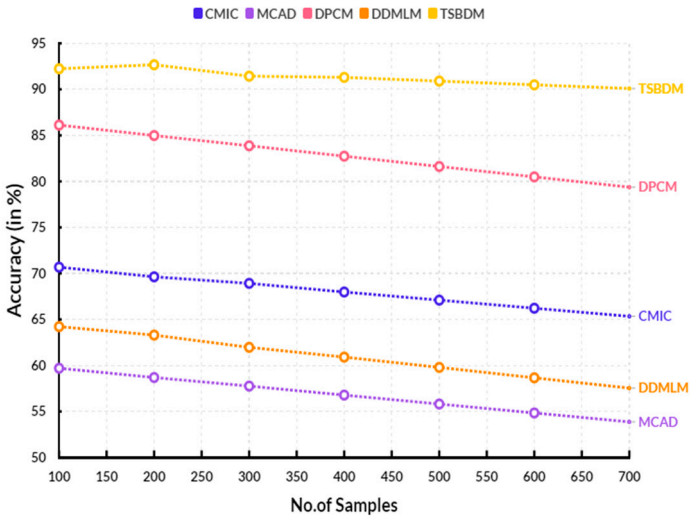


**Figure 2.** Accuracy.

### *3.2. Precision*

Precision for a time series algorithm in cancer detection is computed by dividing the total number of true positive detections (i.e., correctly identified cancer cases) by the total number of all detections made (true positives plus false positives). Precision is computed with the help of the following Equation (6).

$$P = \left( \frac{TP}{TP + FP} \right) \tag{6}$$

Figure 3 shows the comparison of precision. In a computation cycle, the existing CMIC reached 64.76%, MCAD reached 53.84%, DPCM obtained 80.05%, and DDMLM reached a 57.84% precision rate. The proposed model achieved a 90.11% precision rate.

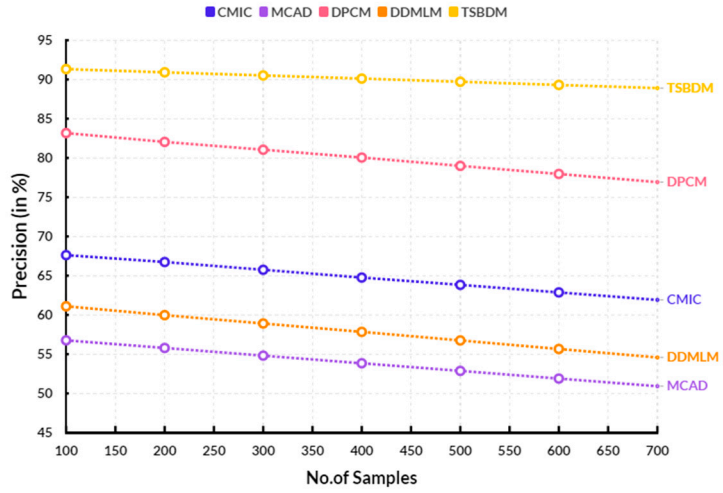


**Figure 3.** Precision.

### *3.3. Recall*

Recall is the degree of true fine predictions out of all actual proper positives. It helps you understand how well an algorithm is classifying cancer instances that are effectively recognized. Recall is computed with the assistance of the following Equation (7).

$$R = \left( \frac{TP}{TP + FN} \right) \tag{7}$$

Figure 4 shows the comparison of recall. In a computation cycle, the existing CMIC reached 71.15%, MCAD reached 58.71%, DPCM obtained 86.61%, and DDMLM reached a 63.61% recall rate. The proposed model achieved a 92.46% recall rate.

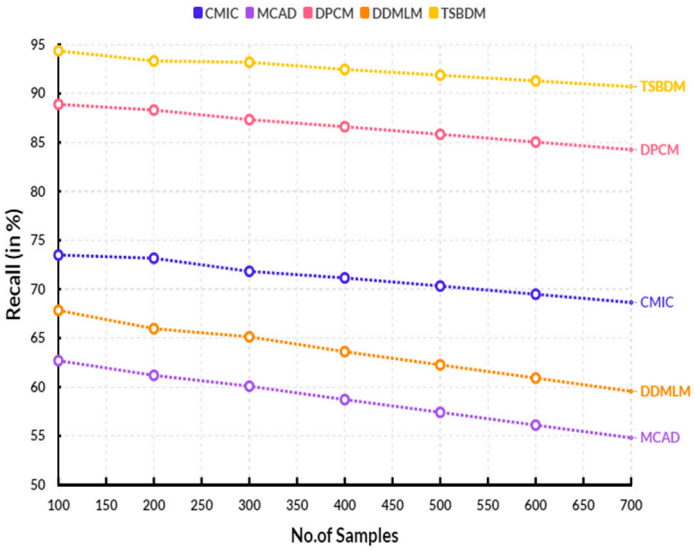


**Figure 4.** Recall.

### *3.4. F1-Score*

F1-score is an overall performance metric that is used to assess the accuracy of time series algorithms for cancer detection. It measures the stability between precision and recall, and is calculated by the following Equation (8).

$$F1 - Score = \left( \frac{2TP}{2TP + FP + FN} \right) \quad (8)$$

Figure 5 shows the comparison of F1-scores. In a computation cycle, the existing CMIC reached 67.81%, MCAD reached 53.49%, DPCM obtained 83.47%, and DDMLM reached a 58.21% F1-score. The proposed model achieved a 90.12% F1-score. Overall, the proposed TSBDM reached 91.30% accuracy, 90.11% precision, 92.46% recall, and a 90.12% F1-score.

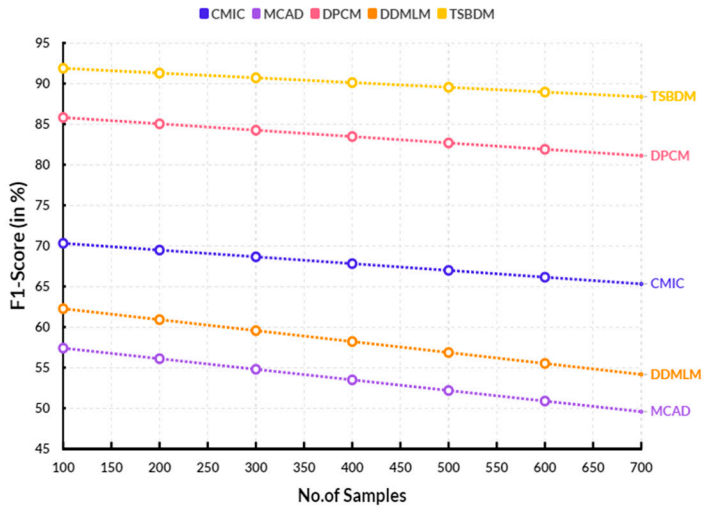


**Figure 5.** F1-Score.

- Limited application: Time series-based detection models are limited in their ability to detect cancers effectively in all parts of the body, as their detection methodology is largely reliant on the type of physiological signal being monitored.
- Sensitivity: Time series-based detection models are limited in their sensitivity, as most of the current models only detect changes that occur over long time periods. This means that early-stage cancers may be missed.
- Invasive: Time series-based detection models rely on invasive techniques for some of their measurements, which can be uncomfortable and even painful for some patients.

## 4. Conclusions

Time series algorithms have great potential in cancer detection. They have been successfully used in predicting individual patterns and detecting changes in tumor growth, as well as aiding in diagnosis, prognosis, and treatment decisions. Time series algorithms can be adapted to different types of cancers, providing an automated approach to medical analysis. The proposed model reached 91.30% accuracy, 90.11% precision, 92.46% recall, and a 90.12% F1-score. However, further research on these algorithms is needed to improve accuracy. Additionally, formal validation studies must be conducted to ensure these algorithms are safe and effective for clinical use. The future scope for time series algorithms in cancer detection is very promising. By utilizing the temporal patterns of medical data, time series algorithms can detect anomalies and changes in a patient's health that may be indicative of cancer or other conditions.

**Author Contributions:** Conceptualization, U.S.S. and V.P.; methodology, K.S.; software, S.R.; validation, S.R., K.S. and N.I.; formal analysis, N.I.; investigation, K.S.; resources, N.I.; data curation, N.I.; writing—original draft preparation, V.P.; writing—review and editing, U.S.S.; visualization, S.R.; supervision, V.P.; project administration, V.P. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Data are contained within the article.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## References

1. Li, C.; Liu, Y.; Xue, D.; Chan, C.W. Effects of nurse-led interventions on early detection of cancer: A systematic review and meta-analysis. *Int. J. Nurs. Stud.* **2020**, *110*, 103684. [CrossRef] [PubMed]
2. Upadhyaya, A.M.; Srivastava, M.C.; Sharan, P. Integrated MOEMS based cantilever sensor for early detection of cancer. *Optik* **2021**, *227*, 165321. [CrossRef]
3. Froelich, M.F.; Capoluongo, E.; Kovacs, Z.; Patton, S.J.; Lianidou, E.S.; Haselmann, V. The value proposition of integrative diagnostics for (early) detection of cancer. On behalf of the EFLM interdisciplinary Task and Finish Group "CNAPS/CTC for early detection of cancer". *Clin. Chem. Lab. Med. (CCLM)* **2022**, *60*, 821–829. [CrossRef] [PubMed]
4. Ullah, M.; Akbar, A.; Yannarelli, G. Applications of artificial intelligence in, early detection of cancer, clinical diagnosis and personalized medicine. *Artif. Intell. Cancer* **2020**, *1*, 39–44. [CrossRef]
5. O'Connell, T.M.; Golzarri-Arroyo, L.; Pin, F.; Barreto, R.; Dickinson, S.L.; Couch, M.E.; Bonetto, A. Metabolic biomarkers for the early detection of cancer cachexia. *Front. Cell Dev. Biol.* **2021**, *9*, 720096. [CrossRef] [PubMed]
6. Hamadani, J.D.; Hasan, M.I.; Baldi, A.J.; Hossain, S.J.; Shiraji, S.; Bhuiyan, M.S.A.; Pasricha, S.R. Immediate impact of stay-at-home orders to control COVID-19 transmission on socioeconomic conditions, food insecurity, mental health, and intimate partner violence in Bangladeshi women and their families: An interrupted time series. *Lancet Glob. Health* **2020**, *8*, e1380–e1389. [CrossRef] [PubMed]
7. Marcuello, M.; Vymetalkova, V.; Neves, R.P.; Duran-Sanchon, S.; Vedeld, H.M.; Tham, E.; Gironella, M. Circulating biomarkers for early detection and clinical management of colorectal cancer. *Mol. Asp. Med.* **2019**, *69*, 107–122. [CrossRef] [PubMed]
8. Ireland, A.S.; Micinski, A.M.; Kastner, D.W.; Guo, B.; Wait, S.J.; Spainhower, K.B.; Oliver, T.G. MYC drives temporal evolution of small cell lung cancer subtypes by reprogramming neuroendocrine fate. *Cancer Cell* **2020**, *38*, 60–78. [CrossRef]

9. Yang, G.; Xiao, Z.; Tang, C.; Deng, Y.; Huang, H.; He, Z. Recent advances in biosensor for detection of lung cancer biomarkers. *Biosens. Bioelectron.* **2019**, *141*, 111416. [CrossRef]
10. Zhang, Y.; Li, M.; Gao, X.; Chen, Y.; Liu, T. Nanotechnology in cancer diagnosis: Progress, challenges and opportunities. *J. Hematol. Oncol.* **2019**, *12*, 137. [CrossRef]
11. Pashayan, N.; Antoniou, A.C.; Ivanus, U.; Esserman, L.J.; Easton, D.F.; French, D.; Widschwendter, M. Personalized early detection and prevention of breast cancer: ENVISION consensus statement. *Nat. Rev. Clin. Oncol.* **2020**, *17*, 687–705. [CrossRef] [PubMed]
12. Venugopalan, J.; Tong, L.; Hassanzadeh, H.R.; Wang, M.D. Multimodal deep learning models for early detection of Alzheimer's disease stage. *Sci. Rep.* **2021**, *11*, 3254. [CrossRef] [PubMed]
13. Klein, E.A.; Richards, D.; Cohn, A.; Tummala, M.; Lapham, R.; Cosgrove, D.; Liu, M.C. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. *Ann. Oncol.* **2021**, *32*, 1167–1177. [CrossRef] [PubMed]
14. King, A.; Woo, J.K.S.; Ai, Q.Y.; Mo, F.K.F.; So, T.Y.; Lam, W.K.J.; Chan, K.C.A. Early detection of cancer: Evaluation of MR imaging grading systems in patients with suspected nasopharyngeal carcinoma. *Am. J. Neuroradiol.* **2020**, *41*, 515–521. [CrossRef] [PubMed]
15. Crosby, D.; Bhatia, S.; Brindle, K.M.; Coussens, L.M.; Dive, C.; Emberton, M.; Balasubramanian, S. Early detection of cancer. *Science* **2022**, *375*, eaay9040. [CrossRef] [PubMed]
16. Van Der Pol, Y.; Mouliere, F. Toward the early detection of cancer by decoding the epigenetic and environmental fingerprints of cell-free DNA. *Cancer Cell* **2019**, *36*, 350–368. [CrossRef] [PubMed]
17. Roy, D.; Tiirikainen, M. Diagnostic power of DNA methylation classifiers for early detection of cancer. *Trends Cancer* **2020**, *6*, 78–81. [CrossRef] [PubMed]
18. Chen, X.; Gole, J.; Gore, A.; He, Q.; Lu, M.; Min, J.; Jin, L. Non-invasive early detection of cancer four years before conventional diagnosis using a blood test. *Nat. Commun.* **2020**, *11*, 3475. [CrossRef]
19. Islam, N.; Shkolnikov, V.M.; Acosta, R.J.; Klimkin, I.; Kawachi, I.; Irizarry, R.A.; Lacey, B. Excess deaths associated with covid-19 pandemic in 2020: Age and sex disaggregated time series analysis in 29 high income countries. *BMJ* **2021**, *373*, n1137. [CrossRef]
20. Jeyaraj, P.R.; Samuel Nadar, E.R. Computer-assisted medical image classification for early diagnosis of oral cancer employing deep learning algorithm. *J. Cancer Res. Clin. Oncol.* **2019**, *145*, 829–837. [CrossRef]
21. Yao, Q.; Wang, R.; Fan, X.; Liu, J.; Li, Y. Multi-class arrhythmia detection from 12-lead varied-length ECG using attention-based time-incremental convolutional neural network. *Inf. Fusion* **2020**, *53*, 174–182. [CrossRef]
22. Ginsburg, O.; Yip, C.H.; Brooks, A.; Cabanes, A.; Caleffi, M.; Dunstan Yataco, J.A.; Anderson, B.O. Breast cancer early detection: A phased approach to implementation. *Cancer* **2020**, *126*, 2379–2393. [CrossRef]
23. Liu, C.; Zhao, J.; Tian, F.; Cai, L.; Zhang, W.; Feng, Q.; Tan, W. Low-cost thermophoretic profiling of extracellular-vesicle surface proteins for the early detection and classification of cancers. *Nat. Biomed. Eng.* **2019**, *3*, 183–193. [CrossRef]
24. Cai, J.; Chen, L.; Zhang, Z.; Zhang, X.; Lu, X.; Liu, W.; Fan, J. Genome-wide mapping of 5-hydroxymethylcytosines in circulating cell-free DNA as a non-invasive approach for early detection of hepatocellular carcinoma. *Gut* **2019**, *68*, 2195–2205. [CrossRef]