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Bridging the Gap: Nanosensors' Role in Tracking Biomarkers for Health Monitoring

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ABSTRACT

Nanosensors, a miniscule sensing device, are used for many things that can be helpful to human life. For one, they can help detect the presence of biomarkers, and are used to correctly identify the presence of a disease, infection, or environmental exposure to contagions. This has been proven helpful as they can detect these diseases or infections at very low concentrations. They can also be extremely specific and eliminate false positives, and can be very cost efficient. However, there seems to be a research gap as biomarkers can actually change a lot over time in certain diseases like cancer. Because of these changes, the results of certain biomarker tests may not be as accurate and efficient in terms of treatments. Many consequences of this include delayed or wrong treatments, psychological stress, and can even result in a lot of medical debt. This can provide negative after effects, especially if one lives in a country with poor healthcare. The problem here is that biomarker tests may not be accurate in terms of detecting biomarkers in the body, due to the ability of biomarkers to change drastically. To further investigate the different types of nanosensors, the methodology will include six experimental groups selected from multiple countries, correlating with six diseases, and one control group. Every three months over the course of two years, the experimental groups will receive the nanosensors that will detect their biomarkers change over time, and the control group will be receiving regular biomarker tests. The results will be used to develop more effective personalized treatment.

Introduction

Over the last decade, biomarker tests have been very promising and useful in the field of pharmacy and biomedicine internationally as they have been able to detect biomarkers, which are indicators of diseases, biological processes, and pathological processes. Their measurements are extremely precise, they have a rapid warning signal, are reliable, the assessment is objective, and there is less bias than questionnaires, just to name a few of the benefits (Bodaghi et al., 2023). This in turn has allowed for patients to have improved outcomes by allowing for earlier diagnoses and personalized treatment strategies.

However, there are some disadvantages such as cost, ethical responsibility and laboratory errors. The development of nanosensors can help eliminate these problems by being less expensive and more accurate in detecting biomarkers. However, the biomarkers can change over time depending on the disease, which can have severe consequences, particularly in countries without affordable healthcare. Currently, ten countries do not have affordable healthcare and they are South Africa, Iran, Egypt, Nigeria, Pakistan, Afghanistan, Yemen, Syria, China, and the United States of America (Shvili, 2020). Incorrect biomarkers tests, especially in the countries mentioned, will result in high medical bills due to more purchases of medicines and treatments, financial debt, psychological stress and delay of any potential lifesaving medical treatments.

The United States has a very huge reputation for having the most expensive healthcare at $12,555 per capita costs as per 2022 (Health Care Costs By Country 2024, 2024). The research gap can have many negative impacts on the citizens of America. In a survey conducted by The Commonwealth Fund (2023), forty-three percent of workingage adults with employer coverage, fifty-seven percent with marketplace or individual-market plans, forty-five percent with Medicaid, and fifty-one percent with Medicare stated that it was very difficult to afford their healthcare. Fifty-one percent of the adults in total (nineteen to sixty-four years old) said it was difficult. Fifty-four percent of those with employer coverage had no choice but to forgo treatments due to extremely high and unaffordable costs, negatively impacting either their health or a loved one's health. Insurance coverage, a tool supposed to provide aid in terms of health care costs, has landed people in medical debt. Thirty percent of adults with employer coverage, thirty-three percent of those in marketplace or individual-market plans, twenty-one percent with Medicaid, and thirty-three percent with Medicare have not been able to avoid medical debt, though they had insurance.These statistics could increase in the United States if the research gap is not solved. However, if the research gap is addressed, it could lead to more efficient healthcare options, thus drastically reducing healthcare costs and making it more accessible to individuals.

Georgia, also known as the Peach state, has been ranked as the worst state in terms of healthcare, as found in study conducted by Forbes magazine (2023). In fact, it has the highest score out of all fifty states: a not so perfect score of 100/100. If the score is lower, then it means that healthcare is decent. 15.5% of Georgians chose not to see a doctor due to cost, as reported by Forbes (2023). After 2020, the death rate in Georgia increased, with about 997.6 deaths per 100,000 residents (USAFacts, 2023). 12.63 % of Georgia residents do not have medical insurance. In 2020, $10,233 was spent on healthcare by Georgia residents, and that cost could increase quickly if the research gap is not addressed. Georgia also has the third-highest share in terms of an uninsured population, and about 3.3 million people live in an area with primary care shortage (Gratas, 2023). This can increase mental health issues, such as depressive and anxiety disorders, amongst residents. 8.47% of Georgia residents eighteen or older have had at least one depressive episode, and 4.7 % of adults have had serious thoughts of suicide as found by the Substance Abuse and Mental Health Services Administration (2023).

Based on the statements and statistics above, the change of biomarkers must be addressed. Nanosensors have been used in healthcare, mainly for drug delivery purposes, which has been proven to be successful (Wu et al., 2020). Given this information, nanosensors can potentially be developed to detect changing biomarkers. Wrong treatments could occur, which can lead to the increasing of one's medical debt and mental health issues, if this research is not carried out thoroughly. It can affect everyone negatively, especially those living in the ten countries that do not have affordable healthcare. By tracking the changes in biomarkers, collecting genetic information, and developing nanosensors this way, the lives of these many people can be greatly improved and reduce a lot of medical debts as integrating nanosensor technology can allow for the development of medicine and treatments.

Methodology

It is proposed that the following methodology to solve the research gap created by the biomarkers changes is used. The main criteria for selecting the biomarkers, the design of the nanosensors, and the experimental groups are that biomarkers should change over time, the nanosensors should be able to detect each specific biomarker accurately, and the selected biomarkers belong to the following categories: cancerous, hereditary, infectious, inflammatory, hormonal and neurological. The categories are chosen because they contain biomarkers that change. Biomarkers from breast cancer, diabetes, Alzheimer's Disease, prostate cancer (hormonal), lupus, and pneumonia are being used as they are from those categories. By having a diverse representation of biomarkers, a diverse set of nanosensors is being developed to satisfy different types of biomarkers and allow for more efficient treatments. Then, nanosensors are being developed for detection of each of these biomarkers. Various transmitters are being combined to form the bio-sensing aspect of it (Chelliah et. al, 2021). These are integrated into single-use polymer- based chips for medical analysis and diagnostics. These chips, also known as lab-on-a-chip, are extremely small devices that can conduct DNA analysis, human diagnostics, and chemical synthesis as well as multiple- sample biological and biochemical analyses on a single platform (Casquillas & Houssin, 2023). The components of the biosensors allow for susceptibility and accuracy in polymer technology by allowing for the chemistry of peptides to resemble that of different electron transducing units (Chelliah et. al, 2021). The design is very simple, given the advanced technology, but holds a lot of promises in terms of biological analysis and medical treatments. Each of the nanosensors being produced contain features that adapt to changes in their respective biomarkers, depending on which disease they target. This design can work on the diverse characteristics of biomarkers, make healthcare more accessible to the general public, and allow for effective treatments, especially in environments where healthcare is not affordable and poverty rates are high.

After the development of nanosensors, there are six experimental groups consisting of individuals from South Africa, Iran, Egypt, Nigeria, Pakistan, Afghanistan, Yemen, Syria, China, and the United States of America, since those countries have the most expensive healthcare (Shvili, 2020). Out of the American participants, half of them are from Georgia since the state has the ranking of number one in the most expensive healthcare. Each group is currently receiving the specific nanosensor depending on what disease they have. For example, if individuals in group one have diabetes, they will receive the nanosensor that detects the biomarker for diabetes. The experimental groups receive the nanosensor every three months for two years for a total of eight times to see if it has detected the diseases correctly despite the changes. There is also a control group, consisting of different individuals from the same ten countries once again. The control groups are receiving regular biomarker tests every three months for two years for a total of 8 times to see if the detection of the diseases were accurate. By having these groups, effective comparisons and conclusions can be made. The study is longitudinal and will last for two years. There is also aid given out to the participants for their healthcare as well as consent. Any participant is allowed to drop out of the study if they feel any psychological or physical stress or extreme discomfort in any way. Data collection occurs by tracking changes in biomarker patterns for both experimental and control groups. Lastly, the financial aspect of this is being considered. The current healthcare systems from all over the world, especially from the ten countries with poor healthcare systems, are looked at closely. The participants are required to talk about the healthcare systems in their country or state, and how it has deeply impacted them.

After the data collection, statistical analysis is currently being done. The measures of central tendencies have been found and a T-test has been conducted. A T-test is a statistical test that measures the difference between the means of two or more groups and how they are related or different (Hayes, 2022). Regression analysis is currently utilized, as it can help describe the extent of which certain factors, such as the biomarkers being evaluated and the progression of the disease, impact the results of nanosensor tests. Graphs, such as histograms, and pictures are being made to visually represent the distribution and relationships that the data shows. This is providing a clear picture and pattern of the biomarker measurements that have been obtained as well as their effectiveness. Additionally, there are scatter plots being developed to show the differences between the different nanosensors and regular biomarker tests. Error bars may also be used to effectively highlight the differences in data. All in all, the overall use of statistics combined with graphical representations ensures the accuracy of the data as well as allow for a thorough explanation and interpretation of the data. By doing this, the statistical methods will provide an insight into the advancement of healthcare technologies.

Biomarkers Through Time, The Inaccuracy of Biomarker Tests, And The Usage of Nanosensors

There are many incidences of changing biomarkers in human beings, inaccuracies of biomarker tests, and how nanosensors are currently being applied to the human body. The first example is the discovery of changing biomarkers due to the change of age. The sample was a population-based sample involving people of Taiwanese descent aged 54 and older in 2000 (Glei et al., 2012). The changes in biomarkers were predicted over a six year period in a given biomarker for both men and women. As for the results, the sample mean of the biomarkers decreased significantly between the six-year period for both men and women while the sample mean for other biomarkers increased. Another study evaluated how biomarkers in cigarette smokers changed as they transitioned from traditional cigarettes to electronic devices, such as vapes for example. The study found that reduced exposure to various biomarkers occurred as a result of switching delivery systems or quitting overall, while dual users had selective reductions due to the change in cigarettes (Anec et al., 2022). A third study evaluated changes in the biomarker status in patients with a type of cancer called metastatic breast cancer. 152 patients were included in this study, which revealed the varied metastatic sites found, uses of neoadjuvant therapy, and a predominant subtype being an invasive carcinoma. Not much was found in this study. A fourth study has found that 30 years before the onset of Alzheimer's disease, changes in biomarkers occur (Thomas, 2023). This was detected due to the changes present in the secreted and excreted proteins in the cerebrospinal fluid. A fifth study showed that DNA methylation, a certain type of biomarker, changes in the body when a person has cancer, which can possibly be leveraged for early detection (Leygo et al., 2017). A sixth study has even criticized the assumption that biomarkers are accurate when it comes to developing treatments, possibly due to the fact that certain measures, like sensitivity for example, cannot be estimated without assumptions being made (Janes et al., 2015). A seventh study has found that blood biomarkers change over time in biracial participants with Alzheimer's, which corresponds to cognitive decline (Rajan et al., 2023). An eighth study showed that biomarkers such as HbA1C, fasting glucose, and insulin change over time when measured in many labs, which cause biomarker tests to be inaccurate (Comite et al., 2019). A ninth study shows that tumor biomarker levels change as a result of neoadjuvant chemotherapy (Jin et al., 2015). A tenth study shows that evaluating the accuracy of biomarkers is incredibly difficult, which is shown when two biomarkers provide different results in the trial (Borrebaek, 2017). An eleventh study showed that biomarker tests for Estrogen Receptor in Breast Carcinoma have had a high rate of inaccuracy, almost as high as 20 % (Tolles et al., 2011). A twelfth study has shown that cancer biomarkers are not reliable for detection as they are too sensitive and specific with detection (Mishra et al., 2010). A thirteenth study shows that Blood-based Alzheimer's Disease biomarkers have to overcome invasiveness and accessibility for early detection and prevention strategies (Hampel et al., 2018). A fourteenth study showed that new cancer biomarkers had challenges in the detection of cancer, which could disable personalized treatments (Bensalah et al., 2007). A fifteenth study shows that identifying proper biomarkers for epilepsy will lead to accurate prediction of epilepsy (Engel et al., 2013). A sixteenth study utilized nanosensors for early cancer detection by allowing the usage of nanosensors to extract and detect tumor specific biomarkers, circulating tumor cells, and extracellular vesicles which came from the tumors (Salvati et al., 2015). A seventeenth study showed that nanobiosensors, which were DNA based, could be used to detect cancerous, infectious, and genetic diseases. They could also be used to detect immunodeficiency and other neurological diseases, thus decreasing healthcare costs (Abu-Salah et al., 2015). An eighteenth study showed how effective biosensors made of carbon could be used to detect non-invasive cancer for clinical diagnosis (Pasinszki et al., 2017). Lastly, a nineteenth study showed how nanoarchitectures could sense biomarkers in the urine, blood, and saliva, where molecules are low in abundance (Masud et al., 2019).

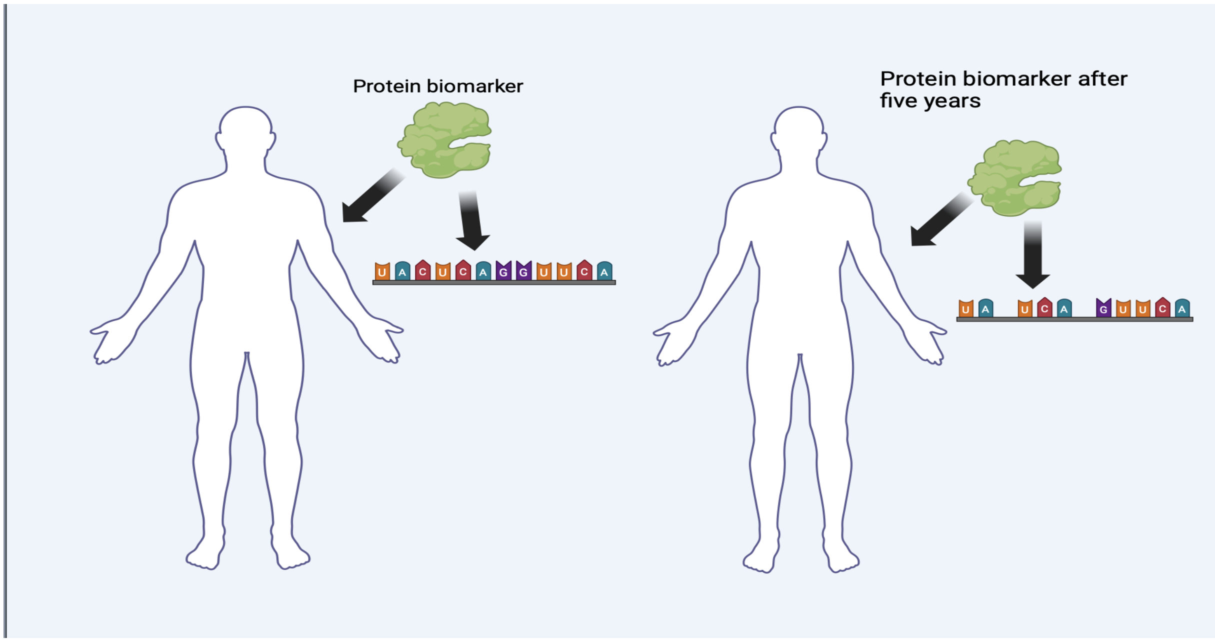

Figure 1. An Example of Changing Biomarkers
Source: Manasa, 2024 (Created on Biorender.com)
Description: Figure one shows an example of how biomarkers, which are indicators of certain diseases and conditions, change drastically. The biomarker in this picture is a protein biomarker, though this concept does apply to all types of biomarkers. Initially, the regular protein biomarker on the left has the correct genetic sequence. If a biomarker test was administered then, it might be able to identify it correctly. However, the genome of the biomarker on the right has missing nucleotides such as cytosine and guanine, which is an example of deletion, a type of genetic mutation that in this example, has occurred in a period of five years. If a biomarker test was administered after the changes, then it would most likely not detect the biomarker correctly. The periods of time that biomarkers change can vary from a few weeks to a few years. This is just one way of how biomarkers change and can be related to epigenetic changes, which are changes in the genetic sequences caused by external factors, such as the environment you live in, or your behaviors, changes in concentration, changes in metabolic pathways, and many more. A majority of biomarker tests will not be able to correctly identify the biomarkers like the one in the diagram, due to them changing, which is why nanosensors are very much needed.

Results, Discussion, and Implications

The proposed methodology will provide very promising results in terms of how effective the nanosensors were.We suggest that every type of nanosensor should be able to effectively detect the biomarkers every three months over the course of two years, making treatment for these individuals much easier. Developing a diverse set of nanosensors is currently proving to be an adaptable and efficient detection system when it comes to identifying changing biomarkers.We expect that as compared to the nanosensors, the traditional biomarker tests that the control group receives will not be able to detect the nanosensors correctly a few times over the five month period. Adding a diverse group of people will aid in the gathering of the results. Not only will the nanosensors be effective, but having so many diverse groups of participants will make it easier for real-world application as well as adaptability. The different environments, healthcare systems and accessibilities, and economic conditions were taken into consideration, will allow for a deeper understanding of how the nanosensor technology developed, helping so many people who are from countries like the ten mentioned in the paper. The diversity of the groups will also allow for the research study to be very valid. The statistical analysis tools like the T-test are being used to have proven that the different nanosensors developed have been able to spot biomarkers though they have changed by showing the differences between the experimental and control groups. The histograms are being created to show the distribution patterns of the biomarker measurements for the groups, and it shows that the experimental groups were able to have their biomarkers detected correctly more frequently, compared to the control groups. The developed nanosensors will outperform the regular biomarker tests. All in all, the methodology that was proposed, the diverse experimental and control groups, and the statistical tools can help us determine how successful the nanosensors are in detecting changing biomarkers.

We expect that the anticipated results demonstrate a huge success when it comes to detecting changes in biomarkers. The detections of all of these biomarkers at regular time intervals, about every five months, will most likely show that there is a significant advancement in the field of nanoscience. More efficient and diverse treatments will be developed for individuals suffering from different types of diseases involving biomarkers, which gives healthcare providers and patients a sense of security in terms of mental and physical health. More personalized treatments will be developed to suit a patient's needs in terms of their personalized biomarker. Along with these treatments, healthcare costs will be reduced in so many ways, which can allow for people to not go into medical debt. All in all, the findings of this research study will help us understand the development of nanosensors and develop healthcare strategies and treatments designed to suit a patient's needs.

Number of Times the Biomarker Tests or Nanosensors were Given	Did the Types of Nanosensors Detect the Biomarkers correctly?	Did the Biomarker Tests Detect the Biomarkers Correctly?
1st Time	Yes	No
2nd Time	Yes	No
3rd Time	Yes	No
4th Time	Yes	No
5th Time	Yes	No
6th Time	Yes	Yes
7th Time	Yes	Yes
8th Time	Yes	No

Figure 2. Expected Data Set From Methodology
Source: Manasa, 2024
Description: Table 1 shows a hypothetical data set of the insights on the expectations in the data set after running the proposed methodology. The expected results would be for the nanosensors to detect the changing biomarkers every single time due to its advanced development. As for the biomarker tests, it is expected that they detect the changing biomarkers correctly in less than twenty-five percent of the time. To quickly summarize, the disparity in results of the expected biomarker tests and nanosensors will highlight the need for the development of nanosensors to enhance treatments and improve healthcare options and costs. The anticipated results clearly demonstrate a potential in integrating nanosensors technology with biomarker identification to accurately detect biomarkers.

Conclusion

Nanosensors must be developed in a specific way that makes the detection of changing biomarkers more accurate and easy. This can be done by integrating nanosensor technology. There have been many incidences where biomarkers have changed over time, and as a result, regular biomarker tests have provided insufficient and inaccurate results. To solve this problem, changing biomarkers for certain diseases are being identified, allowing for the development of multiple nanosensors. The suggested methodology contains six experimental groups, correlating with six diseases . The individuals will also be selected from multiple countries. The control group is the group that will receive regular biomarker tests. Every three months over the course of two years, the experimental groups will receive the nanosensors detecting their biomarkers. The results will be analyzed, showing that the nanosensors are more effective and accurate in detecting the changes in biomarkers than the regular biomarker tests. Using these results, the development of personalized and effective treatments will occur. A further improvement can be caused by reducing the limitations through collecting every individuals' health history, reducing the Digital Divide, and diving deeper into how nanosensors can be developed to improve sustainability.

Limitations

While the methodology that has been developed fits to the nature of the current study, there are some limitations. Firstly, there may be confounding variables, such as genetics for example, that can affect the results of the methodology. Confounding variables are any types of variables that are not being thoroughly studied, but they affect a study's results. Therefore, when statistical analysis is being performed, data interpretation may not be as accurate as needed. Second, there may possibly be significant costs in the development of nanosensors, which can be very limiting when it comes to making them a type of treatment option for affected individuals. Thirdly, it is very uncertain how long and sustainable these nanosensors could be. Third, a huge limitation could be the participants. Consequently, due to the digital divide, which is the differing access to technology in certain areas of the world, it is uncertain as to how individuals from many countries can receive the nanosensors. To reduce these limitations, it must be ensured that the digital divide is reduced by increasing access to technology around the world. This can allow individuals to use online resources to learn about nanosensors and what they can do regarding their health. The participants must also be required to give their health history so that confounding variables are known and statistical analysis can be performed more correctly. Lastly, the sustainability of nanosensors must be studied deeply so that they can be developed appropriately and last longer.

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