A novel, non-invasive and inexpensive test to detect 7 of the most common types of cancers.

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Abstract : Cancer is a growing problem around the world. A major cause of mortality among cancer patients is late-stage diagnosis, prompted by difficult testing strategies and inability of patients to recognize that they need to visit a doctor. This paper proposes a non-invasive and inexpensive test kit that can be used to screen patients for 7 of the most common types of cancer through qualitative and quantitative analyses of polyamine levels in cancer patients using data from peer-reviewed sources. This tool can help in cancer detection without the use of expensive machinery. As is common with competitive LFIAs, it would be necessary to use a digital reading scale (compiled using data from actual tests taken by cancer patients) to accurately determine if the test taker actually has cancer.

Introduction

Cancer refers to a group of conditions wherein there occurs uncontrolled growth of abnormal cells in the human body. Cancer cells tend to invade and destroy normal body tissue. According to the WHO, cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020. [1]

A leading cause of death among cancer patients is a late diagnosis. Cancer is often diagnosed late due to the existing approach to screening and diagnosis. Diagnosing cancer early can go a long way because survival rates tend to go down with passing time. In a retrospective case-only study on 8,860 adolescent and young adult breast cancer cases diagnosed from 1997 to 2006 using data from the California Cancer Registry database, The 5-year survival rate in women who were treated by surgery and had a treatment delay of more than 6 weeks was estimated to be 80% compared with a 90% survival rate in those with a treatment delay of <2 weeks [2]. The following graph shows the 5-year Relative Survival rates for colorectal cancer patients at different stages of progression using data from the SEER programme.[14]A sharp decrease in survival rate can be seen as we
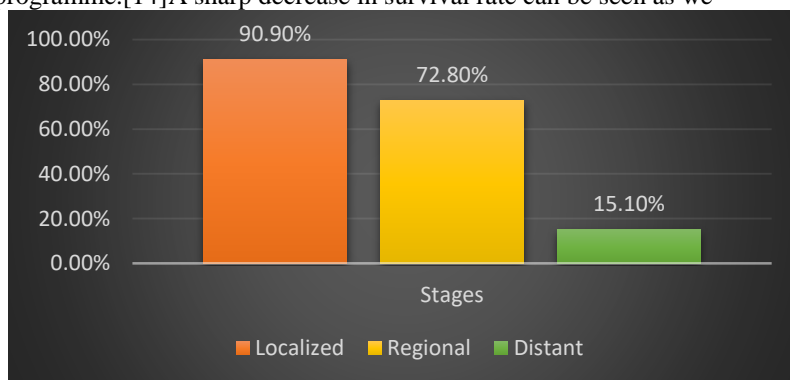
So, how can we diagnose cancer early? We can do this by screening as many people as possible for cancer. To do this economically and on a large scale, we require a screening tool which does not call for additional infrastructure.

Polyamines are small organic compounds found in nature that play important biological roles in both eukaryotic and prokaryotic cells. They play an important role in cell proliferation. High polyamine levels increase the malignant potential of cancer cells while decreasing anti-tumour immunity. Additionally, Immune cells that are exposed to high polyamine levels lose their anti-tumour immune functions. Polyamine levels may also correlate with cancer development in cancer patients. [3,15] Thus, Polyamines and their metabolites in urine can be used as biomarkers of tumour occurrence and progression in a variety of cancers, including breast cancer, lung cancer, colorectal cancer, ovarian cancer, prostate cancer, and pancreatic cancer.[4] Salivary polyamines are also potential cancer biomarkers.[10]

Taking advantage of increased polyamine levels in the saliva and urine of cancer patients, a screening tool can be proposed.

Data Analysis

Data collected from various peer-reviewed sources has been tabulated below. The following table shows the elevation levels in urine for four types of cancer.

Type of cancer	Urinary N1- acetyl spermine	Urinary N1- Acetyl spermidine
Lung	4.44 ± 4.12 ng/mg creatinine [5]	300.1 ± 38.32 ng/mg creatinine [5]
Liver	1.82 ± 1.74 ng/mg creatinine [5]	11.6 ± 128.3ng/mg creatinine [5]
Ovarian	NA-0.32 µmol/g creatinine [6]	2.52-18.50 µmol/g creatinine [6]

Control	3074.2 nmol/L or NA-0.01 µmol/g creatinine [6]	3034.6 nmol/L or 1.78-8.92 µmol/g creatinine [6]

Urinary N1-Acetylspermine and N1-acetylspermidine have been found to be potential indicators of colorectal cancer in a study conducted by Udo, Katsumata et al.; they found these levels to be higher in patients with polyps and colorectal cancer as compared to those in healthy controls.[9]

Salivary Spermine has been found to be elevated in patients with pancreatic cancer. The following graph by Asai, Itoi et al compares the salivary concentration of Spermine in pancreatic cancer patients in different stages and healthy controls.[8]
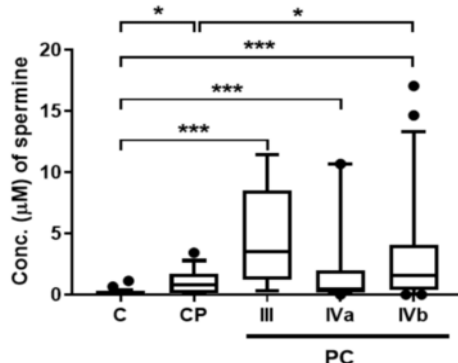
In a study conducted by Jinno et al., a metabolite analysis of samples obtained from 60 breast cancer patients and 20 healthy controls by capillary electrophoresis time-of-flight mass spectrometry assigned an AUC value of **0.716 to spermine as a biomarker.**[10]

In a study conducted by Ishikawa et al., both spermine and spermidine were found to have higher concentrations in the saliva of patients with oral cancer. Their research also indicates that using 2 biomarkers would lead to a more accurate result.[12]

Design

After performing an analysis of polyamine levels in the urine and saliva of cancer patients with different types of cancers, I propose an LFIA-based test kit with 2 test strips: one each for urine and saliva. This method would be inexpensive and non-invasive. This test kit consists of 2 test strips that collect saliva and urine samples. The first is the *saliva test strip* -- If the saliva strip tests positive, the patient might have oral, pancreatic or breast cancer. Using a competitive lateral flow immunoassay, two polyamines-spermidine and spermine; the quantities of which are elevated in cancer patients of these three types are detected. The second strip will be the *urine test strip* -- If the urine strip tests positive, then the patient might have lung, liver, ovarian, or colorectal cancer. The urine strip will also be a competitive lateral flow immunoassay which would test for N1-Acetylspermidine and N1-Acetylspermine. Thus, by using this test kit, we can screen patients for 7 types of the most common and fatal cancers:

- Oral
- Lung
- Breast
- Pancreatic
- Ovarian
- Liver
- Colorectal.

Working of test strips

1. Urine/saliva is applied to the sample pad.
2. The sample goes through the reactive zone where the target polyamines; spermidine and spermine attach to the monoclonal antibodies marked with colloidal gold particles.
3. The sample would go through 2 test zones, one for each polyamine.
4. At the control zone the antibodies will attach to the free antibodies and conjugated antibodies from the reaction zone produce colour. This will indicate that the test is not faulty.
5. The rest of the sample goes to the absorbent pad.
6. The urine strips will have antibodies of N1-Acetylspermidine and N1-Acetylspermine.
7. The saliva strips will have antibodies of spermidine and spermine.

Image taken from Abingdon Health's Website [13]

Discussion

Since this is a non-invasive test, the exact location of the tumour cannot be determined. However, the test can make large-scale testing for cancer easier. This test kit can be used regular health check-ups. The test would only be used for screening and not diagnosing as the levels of the biomarkers are too broad to give a reliable diagnosis. The test kit might show inaccurate results in patients with Alzheimer's and Parkinson's disease. The levels of spermidine and spermine were found to be high in patients suffering from these diseases. [11] It can also be falsely positive in patients with certain types of benign tumours. Since polyamine metabolism is central to cancer cell proliferation, there is also scope for expansion of types of cancer that can be detected by the test kit.

Citations

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