BioMEMS-EARLY DISEASE DETECTION

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BioMEMS 기반의 조기 질병 진단 기술에 관한 연구

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Abstract

Early detection of a disease is important to tackle treatment issues in a better manner. Several diagnostic techniques are in use, these days; for such purpose and tremendous research is going on to develop newer and newer methods. However, more work is required to be done to develop cheap and reliable early detection techniques. Micro-fluidic chips are also playing key role to deliver new devices for better health care. The present study focuses on a review of recent developments in the interrogation of different techniques and present state-of-the-art of microfluidic sensor for better, quick, easy, rapid, early, inexpensive and portable POCT (Point of Care testing device) device for a particular study, in this case, bone disease called osteoporosis. Some simulations of the microchip are also made to enable feasibility of the development of a blood-chip-based system. The proposed device will assist in early detection of diseases in an effective and successful manner.

1. Introduction

Osteoporosis (OP) is a disorder characterized by abnormal rarefaction of the bone occurring most frequently in postmenopausal women. It is called a 'silent epidemic' or a 'silent disease'. Thus, it is a bone disease, in which bone tissue is normally mineralized, but the amount of bone is decreased and the structural integrity of trabecular bone is impaired. Cortical bone becomes more porous and thinner. This makes the bone weaker and more likely to fracture. This deadly disease creeps silently inside the body. When the unaware patient when realizes he is already bed-ridden or the diagnosis and treatments become unaffordable. Hence there is an urgent need for the early detection of the dangerous disease. In this study, we have made an attempt to explore the methods to develop a Lab-on-chip-detection system for it (1).

Microfluidic lab-on-a-chip technology represents a revolution in laboratory experimentation, bringing the benefits of miniaturization, integration and automation to many research-based industries. Blood is a complex biofluid. In several pathological laboratories blood analysis has been used for several kinds of disease detection. There is an attempt to develop a Blood on chip POCT device for this purpose. The microfluidic device is suitable for large-scale screening of disease-related biomarkers. Protein biomarkers are useful as "molecular indicators" for a wide range of diseases including osteoporosis (2, 3).

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2. Microfluidics

The flow of a fluid through a microfluidic channel can be characterized by the Reynolds number, defined as

$$\mathrm{Re} = \frac{LV_{avg}\rho}{\mu}$$

where L is the most relevant length scale, μ is the viscosity, r is the fluid density, and V_{avg} is the average velocity of the flow. For many microchannels, L is equal to 4A/P where A is the cross sectional area of the channel and P is the wetted perimeter of the channel. Due to the small dimensions of microchannels, the Re is usually much less than 100, often less than 1.0. In this Reynolds number regime, flow is completely laminar and no turbulence occurs. The transition to turbulent flow generally occurs in the range of Reynolds number

2000. Laminar flow provides a means by which molecules can be transported in a relatively predictable manner through microchannels. (http://faculty.washington.edu/yagerp/microfluidicstutorial/tutorialhome.htm)

Benefits of Microchip for Disease detection

The main benefits of Microfluidic chip is the miniaturized size of the chip which can be easily used for developing the point of care testing device. The use of small volumes of biofluid is the added advantage. Lower energy consumptions and fabrication is easy, cheap, fast, reliable, parallel processing can be done. Built in detection system in the chip, multifunctionality and integration makes a new and novel device.

3. Review in Detection Techniques

3.1. Optical Technique

There are several optical methods used in this process:

a) Photomultiplier tubes with fluorescence detection

As part of the immunoassay process, antibodies specific for biomarkers of interest, such as gum or heart disease, are tagged with a fluorescent dye and then mixed with a patient's saliva or blood. Biomarkers present in the sample attach themselves to the fluorescent antibody. The mixture is injected into a microchip using a syringe. An applied electric field forces the sample to flow through a microchannel that is two to five centimeters long, tens of microns deep, and a few hundred microns wide. A photomultiplier tube then detects the fluorescence emission with extreme sensitivity. After quantifying the relative fluorescence of the two species bound and unbound antibodies researchers can determine the amount of biomarker present in the patient's sample. If the sample contains significant fluorescence emission from a bound antibody, indicating that biomarkers are present above a certain level, a conclude that the patient has or will eventually get the disease for which he or she is being tested (4).

b) Micro mass-spectroscopy

The lab-on-a-chip integrates a pump, valve, separation column, and detection interface onto a 3- by-1 inch glass microchip and delivers a performance to match benchtop instrumentation typically occupying a few square feet of lab space. These channels, which have dimensions in the micrometer domain, serve to generate an electroosmotic flow. This flow of liquid helps to separate the proteins which are then identified by state-of-the-art mass spectrometric detection instruments (1,2).

3.2. Electrochemical detection

The electrochemical blood diagnostics chip employing screen-printed carbon electrodes on a polymer film allowed to achieve a cheap, multi-item and simultaneous measurement. Cyclic voltammetry and chronoamperometry were conducted to characterize the immunosensor. Compared with the traditional immunosensor using bulky gold electrode or screen-printed electrode and the procedure directly binding protein A to electrode for immobilization of antibodies, it had attractive advantages, such as miniaturization, compatibility with CMOS technology, fast response, broad linear range and low detection limit. In addition, this immunosensor was easy to be designed into micro array and to realize the simultaneously multi-parameter detection.

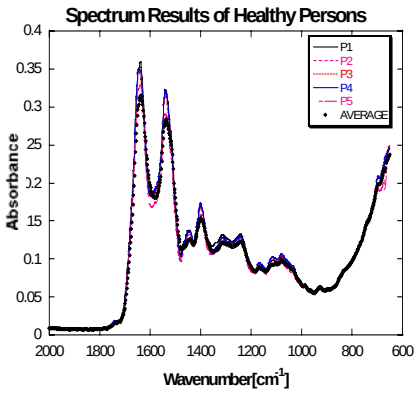
3.3. Other detection Techniques

The BCA (bi-bar code assay) is uniquely capable of multiplexed detection of targets (through the use of barcode labeling), have improved the chip design and optimized the operation to accommodate simultaneous identification of six different targets. Meanwhile, increased sensitivity and time reduction has been achieved by modifying designs and functionalization.

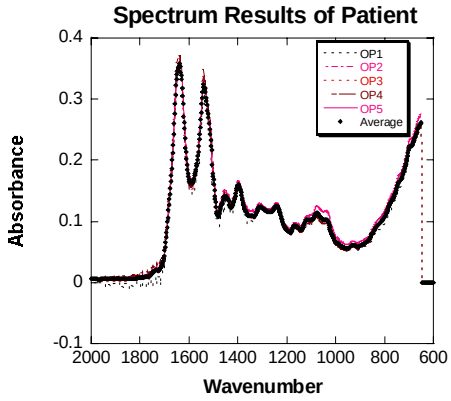
4. New Detection Techniques

Serum spectra were recorded between 4 000 and 600 cm–1 using a FTIR spectrometer (Nicolet 380, Nicolet Instrument, Thermo-electron cooperation) equipped with a KBr beamsplitter and a DTGS detector. Thirty two scans were averaged per spectrum at a resolution of 4 cm^{-1}. After this test, validated spectra were normalized to one absorbance unit using the amide I spectral band located at about 1640 cm^{-1}. All observations were taken five times in successive way. The Wavenumber precision better than $0.1cm^{-1}$. The software used for the analysis was OMNIC version 7. The baseline correction and spectra normalization was done by OMNIC software and also by obtaining the background spectra

The second study was made in for the UV-visible spectroscopy which was investigated. The results will be added later (See figure 1)



(a)



(b)

Fig 1: Spectrum Results: (a) P1-P5 Healthy and (b) OP1-OP5 Patient serum samples

5. Results

There are major variations where the absorbance is mainly due to CH2 and CH3 stretching vibrations from the lipids and proteins. The spectra are dominated by the absorbance bands at 1643 and 1544 cm_1, i.e. the amide I and II bands, respectively. The amide I band arises from C-O hydrogen bonded stretching vibrations, and the amide II from C–N stretching and CNH bending vibrations. Amide III band at 1270 cm^{-1} is contributed by proteins arising from coupling of C–N stretching and N–H bending.

In this study the new optical study was explored. FTIR spectroscopy was investigated and blood serum analysis was made. FTIR has been used to identifying the unique structure of the biomolecules. It helps in identifying the blood contects in the healthy patient's blood serum sample and it was compared with the osteoporotic blood serum samples. The FTIR spectra acquisitions of the normal and abnormal samples showed the new peaks which have been due to the biomarker levels in the blood for patient. The results are considered to be the preliminary results but several spectral differences could be useful as biomarkers for discrimination between the two types of samples.

6. Conclusions

The main emphasis is on the development of a biochip which may provide a new, early, cheap, portable point of care detection device. Several techniques have been studied and special technique has been identified.

An experimental study of the optical techniques was studied and promising results were obtained by comparing the serum of the normal and abnormal blood samples. New electrochemical techniques are also being explored in the present state.

There is a need for further research in this direction. The more details can be read in our paper which will be submitted in the journal, when it is finalized.

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