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RESEARCH ARTICLE

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DESIGN OF MEMS-BASED BIOSENSOR TO ESTIMATE THE BIOMECHANICAL PROPERTY OF COLORECTAL CANCER CELL

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Manuscript Info

Key words:-
Stiffness, Young's modulus, Cancer, Poisson's ratio, Hertz model

Abstract

Recently the evolving approach in medical applications, the biomechanical properties of single cells have been developed, as they are closely related to cell biological processes and eventually to human health conditions. The biomechanical properties can be used for early cancer diagnosis as biomarkers because cancer cells have moderately less Young's modulus. We measured the stiffness of individual benign (CCD-18), non-invasive malignant (HT-29), and highly-invasive malignant (SW480) colorectal cancer cells using the MEMS sensors. The elastic modulus of three colon cell lines could be extracted, where the cells were SW480~1.12 kPa, HT-29 cells were ~ 1.31 kPa and CCD-18 cells were ~2.34 kPa.

Introduction:-

This paper provides an overview of the rapidly expanding, evolving area of research that addresses cancer cell biomechanics [1]. Tumor cells change their physical properties during cancer development, including their deformation and adhesion, which may lead to their altered motility and invasive behavior [2]. These physical characteristics are critical to understanding how cells deform to invade blood or lymph vessels through narrow gaps thatarenecessary for metastasis. While the field of cancer research is growing to recognize the role in cancer metastasis of cell mechanical features, the implementation of these techniques lags far behind [3]. The screening of mechanical and morphometric cell properties provides valuable information to differentiate cell groups and stages [4].

Different approaches have been used to analyze the biophysical properties of single cells [5][6]. For the progression of cancer and disease, cell biomechanical characteristics are ideal potential label-free diagnostic markers. However, it is difficult to concentrate on the distinctive biomechanical properties of a single cell of concern while dealing with a large number of cells [7]. An upcoming interest in microfluidic-based approaches is therefore emerging, enabling highly accurate opportunities for single-cell screening. Based on the label-free analysis, we proposed a single cell screening method. The system is capable of trapping a single cell and stimulating it mechanically, as demonstrated

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with cell contraction. Effective real-time measurements and highly controllable mechanical stimulation allow the analysis of single cells at various levels of compression [19].

Working principle and Model Design:

Figure 1 provides an overview of the setup [8]. We propose a noninvasive bio-sensor to analyze the biomechanical properties of single cells [13-16]. To quantify the cell's mechanical properties, the prepared cell is made to trap in the constricted area. The deformation is induced by applying force on the PDMS layer placed over the constricted area. The cell deformation contour was extracted using simulation. In this study, the constriction chip possessed a cross-section of 25 µm X 25 µm X 15µm.

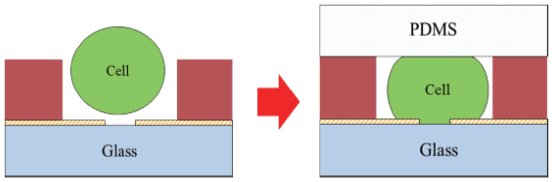

Figure 1:- The equivalent model for measuring the stiffness of the cell.

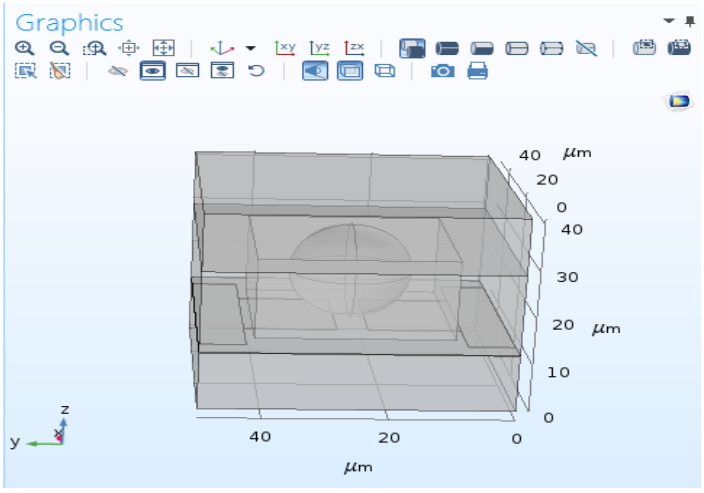

Figure 2:- Design of cell trap structure in FEM tool.

The equivalent model for measuring the mechanical properties of the cell is shown in (Figure 1). The design of the trap structure (Figure 2) for measuring the mechanical property of the cell is modeled using the (COMSOL 5.3) FEM tool. This region is set to the region of interest (ROI) for extracting cell deformation [17-20]. In our work, a linearized Hertz model equation has been considered for the spherical indenters to calculate Young's modulus of the cell.

$$F^{2/3} = \left(\frac{4}{3}\frac{E}{(1-\mu^2)}\sqrt{R}\right)^{2/3}\delta \qquad (1)$$

Where F is the applied loading force, E is Young's modulus of the cell, δ is the indentation depth, µ is the Poisson's ratio, and R is the contact radius. Cells are generally considered to be incompressible materials, so we used a Poisson's ratio value of 0.5.

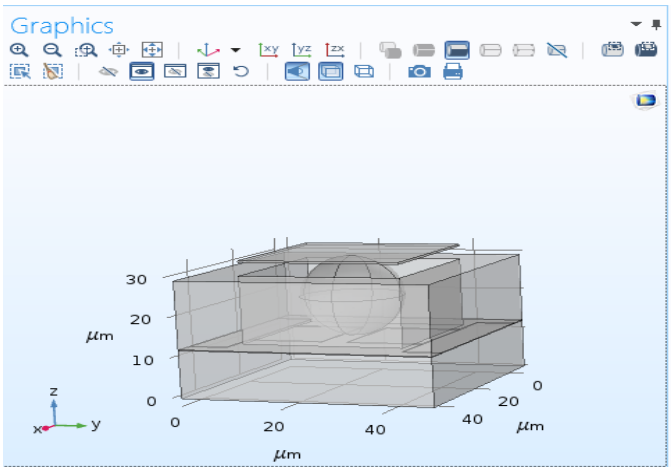

Figure 3:- The model implemented in the FEM tool.

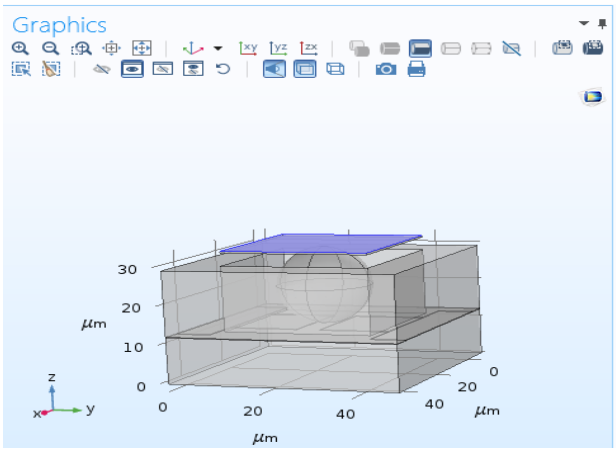

Figure 4:- Force applied on PDMS layer.

As shown in (Figure 4), cell deformation is proportional to the force applied to the top of the PDMS layer [8]. In this report, the deformation degree and elastic modulus of three types of colorectal cancer cell lines(HT-29, CCD-18, and SW480) were quantified with applied force [9-12]. Here, CCD-18, HT-29 SW480 are colon cancer cell lines with low, moderate, and high metastatic potential, respectively. Cancer cells with higher metastatic potential should possess lower stiffness than cancer cells with lower metastatic potential.In Figure 3 the circuit model implemented using the FEM tool is shown. Figure 4 model represents how force is applied tothe PDMS layer that deformsthe cell.

Results and Discussion:-

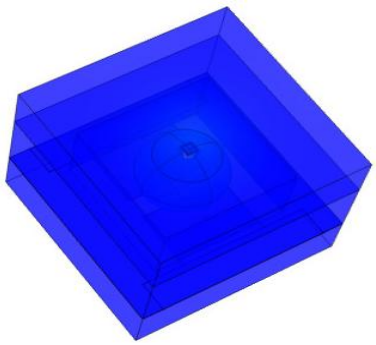

Figure 5:- Simulation result of a deformed cell due to the applied force.

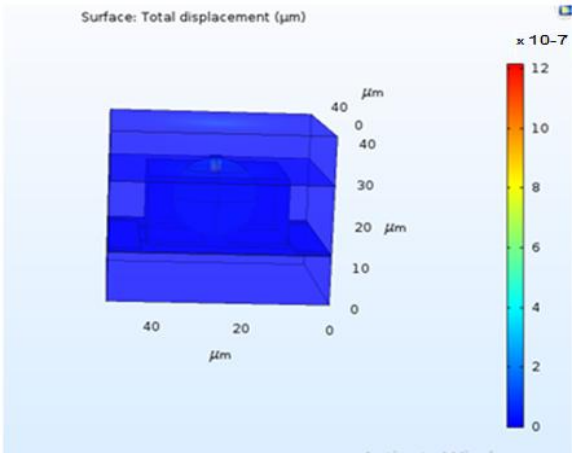

Figure 6:- Simulation result of deformation of Normal cell when the applied force is 1kPa.

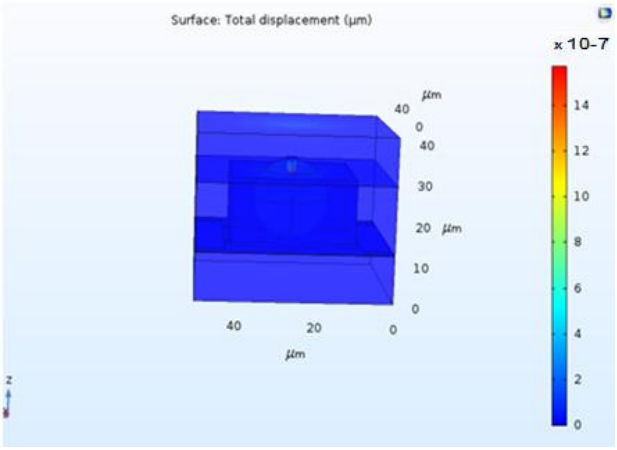

Figure 7:- Simulation result of deformation of cancer cell when the applied force is 2kPa.

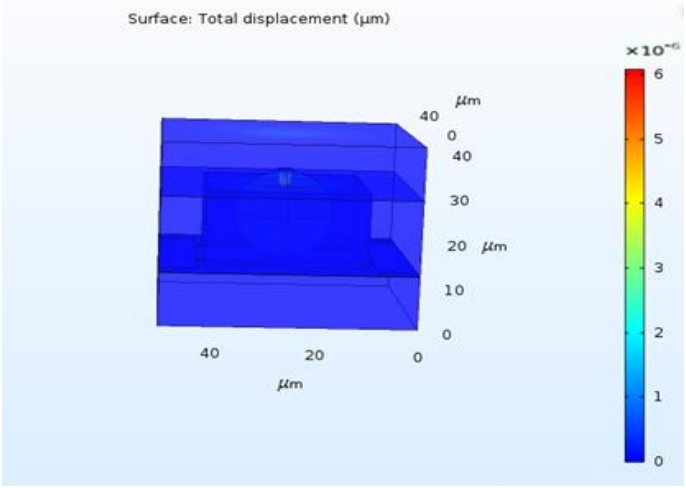

Figure 8:- Simulation result of deformation of Normal cell when the applied force is 5kPa.

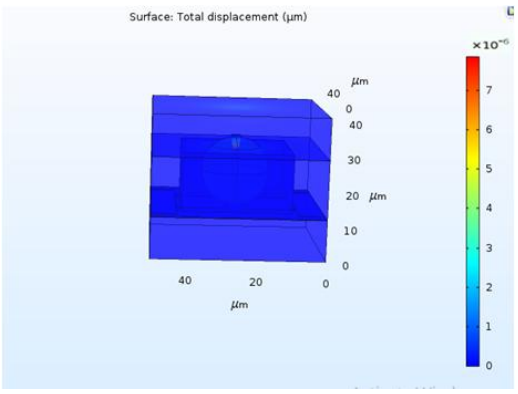

Figure 9:- Simulation result of deformation of cancer cell when the applied force is 5kPa.

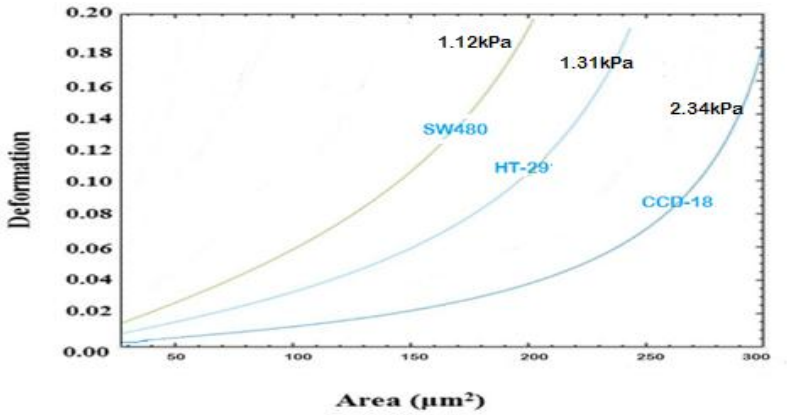

Figure 10:- The deformation of a cancer cell with applied pressure.

Table 1:- Displacement of the PDMS layer with applied pressure.

Pressure Applied	Displacement (m) (Normal Cell)	Displacement(m) (Cancer Cell)
1KPa	$1.2x10^{-6}$	$1.4x10^{-6}$
2KPa	$2x10^{-6}$	$3x10^{-6}$
5KPa	$6x10^{-6}$	$7x10^{-6}$
8KPa	$9x10^{-6}$	$12x10^{-6}$
10KPa	$12x10^{-6}$	$14x10^{-6}$
15KPa	$18x10^{-6}$	$20x10^{-6}$

The material properties for benign cells and cancerous cells are embedding in simulation. After the simulation, the deformation of cells with applied pressure per area is shown in(Figure 5). The result in (Figure 6) is the deformation of a normal cell when the applied pressure is 1kPa. We observed that the deformation normal cell is 1.2µm from the result. The result in (Figure 7) is the deformation of a malignant cell when the applied pressure is 1kPa. We observed that the deformation normal cell is 1.4µm from the result. The result in (Figure 8) is the deformation of a benign cell when the applied pressure is 5kPa. We observed that the deformation normal cell is 6µm from the result. The result in (Figure 9) is the deformation of a malignant cell when the applied pressure is 5kPa. We observed that the deformation malignant cell is 7µm from the result. According to the simulated results as shown in (Figure 10) the deformation of iso-elasticity lines, the elastic modulus of three colon cell lines could be extracted, where the SW480 cells were ~1.12 kPa, HT-29 cells were ~ 1.31 kPa, and CCD-18 cells were ~ 2.34 kPa.

Conclusion:-

The measured results showed the three types of colon cells possessed significant differences in their stiffness and area. SW480 cells were softer than CCD-18 and HT-29.It is understood that the mechanical properties of colon cancer cells can be used as potential biomarkers for early identification of colon cancer and predict the stages of cancer lines.

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Conflict of Interests:

The authors declare that there are no conflicts of interest exist among them regarding the publication of this paper.

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