Journal of Simulation and Analysis of Novel Technologies in Mechanical Engineering
13 (4) (2021) 0067~0079
HTTP://JSME.IAUKHSH.AC.IR

Research article

Investigation of cell biomechanics and the effect of biomechanical stimuli on cancer and their characteristics

Atefeh Ghorbani[1*], Sheyda Shahriari[2**], Amir Mohammad Gholami[3]

[1]*Biotechnology Department, Falavarjan Branch, Islamic Azad University, Isfahan, Iran*
[2]*Institute of Psychiatry, Psychiatry and Neuroscience, Kings College London, London, UK*
[3]*Department of Mechanical Engineering, Najafabad Branch, Islamic Azad University, Najafabad, Iran*

[*]atefeh.ghorbani79@gmail.com, [**]shahriari_sh@brunel.uk

(Manuscript Received --- 20 Jan. 2022; Revised --- 25 Mar. 2022; Accepted --- 11 Apr. 2022)

Abstract

Physical stimuli have a great impact on the survival, behavior, and function of all life. Recently, a theory has been proposed to understand cellular behavior in times of failure and disease, stating that cellular processes and damage can be affected by mechanical forces. Scientific evidence suggests that mechanical changes can affect many of the primary cellular mechanisms, as well as important aspects of cell behavior such as cell adhesion, movement, and signal transmission. In this study, we examine the history of the effects of mechanical stimulation from the beginning to the present, what is cell biomechanics, introduce features and methods to study cell characteristics such as micropipette suction and atomic force microscopy (AFM). In addition, to consider the effects of biomechanical stimulation it should be point out to cells using stimuli which can be useful including inducing differentiation into stem cells to produce bone cells that are applied by special devices that are briefly examined for the beneficial effects. It also has negative aspects for the cell, such as the occurrence of metastases in cancer cells. In this work, the effect of changes in the inclination, frequency and strain on the cancer cell was also investigated.

Keywords: Cell; Biomechanics; Cell biomechanics; Mechanical stimulation

1- Introduction

The effect of mechanical stimulation on cell function dates back to the 17th century; Galileo was the first to investigate the effect of mechanical loads on bone morphology [1-3]. Meyer et al. studied the orientation of the trabeculae in the cancellous bone. Culmann, in collaboration with Venir, proposed the theory of trajectory. Based on this theory, the orientation of the trabeculae is in line with the main stresses applied to the bone [4-6]. Wolff introduced a law called the Wolff Law, according to which the orientation of the trabeculae would also change if we changed the load on the bone; However, the first laboratory studies to investigate the effect of mechanical stimulation on cell function date back to 1939. Several researchers used different loads on these cells using cells obtained from chick tibia and evaluated the results.

After these experiments, a lot of research was done in this field, which led to the development of methods and a variety of devices to measure the effects of mechanical stimulation on performance [7-11]. Recently, a perspective on understanding cellular behavior in cases of failure and disease has been proposed, which states that cellular processes and damage can be affected by mechanical forces. Scientific evidence suggests that mechanical changes can affect many of the primary cellular mechanisms, as well as important aspects of cell behavior such as cell adhesion, movement, and signal transmission [12-15]. Taken together, these forces play an important role in the proliferation of biological tissue, its organization, and its response to stimuli. At the cellular level, mechanical forces are important in guiding how cells function, because it is actively felt by living cells. Cellular responses to mechanical stimuli often result in adaptive changes that alter shape and function [16-19]. It should be noted that any change in cell behavior due to biochemical processes that occur between the human body and invasive external factors or disease progression significantly alters the mechanical properties of the cell. Cancer may results from the malfunction of biological cells and many patient cells proliferate uncontrollably and disrupt tissue organization. Cancer alters the cytoskeleton and, by affecting the cell's mechanics, alters its ability to deform, causing the ability of healthy cells to move differently, causing these cells to move in the tissue and cause metastasis. Therefore, measuring mechanical properties can be considered as an indicator of its biological status and also help to diagnose the cause of the disease and distinguish between two diseases [12-16].

2- Cellular biomechanics

Mechanics is defined as the study of the relationships between forces acting on cells and their deformations. Functional characteristics of different cell types and the basic structure of living organisms as one of the most important factors for the very development of biology and biomechanics. The mechanical properties of cells include nonlinearity, anisotropy and stiffness. It also has various functional aspects including communication with separate components of the cytoskeleton and cell organs, cell response to external stimulation and effect on the extracellular matrix. To examine cellular characteristics, different methods such as magnetic tweezers, magnetic torsion cytometry, optical stretcher, laser deformation tracking, and cell inductors are used. One of the best and most efficient methods is atomic force microscopy [15-18].

The Atomic Force Microscope (AFM) examines the sample surface with a sharp needle 2 microns long and often with a tip diameter of less than 10 nm. The needle is located at the free end of the cantilever, about 100 to 450 microns long as shown in Figure 1. The forces between the sample surface and the needle cause the cantilever to bend or deflect, and a detector measures the amount of cantilever deflection while the needle scrubs the sample surface; Measures in systems where the sample performs scanning motion as shown in Fig. 2.

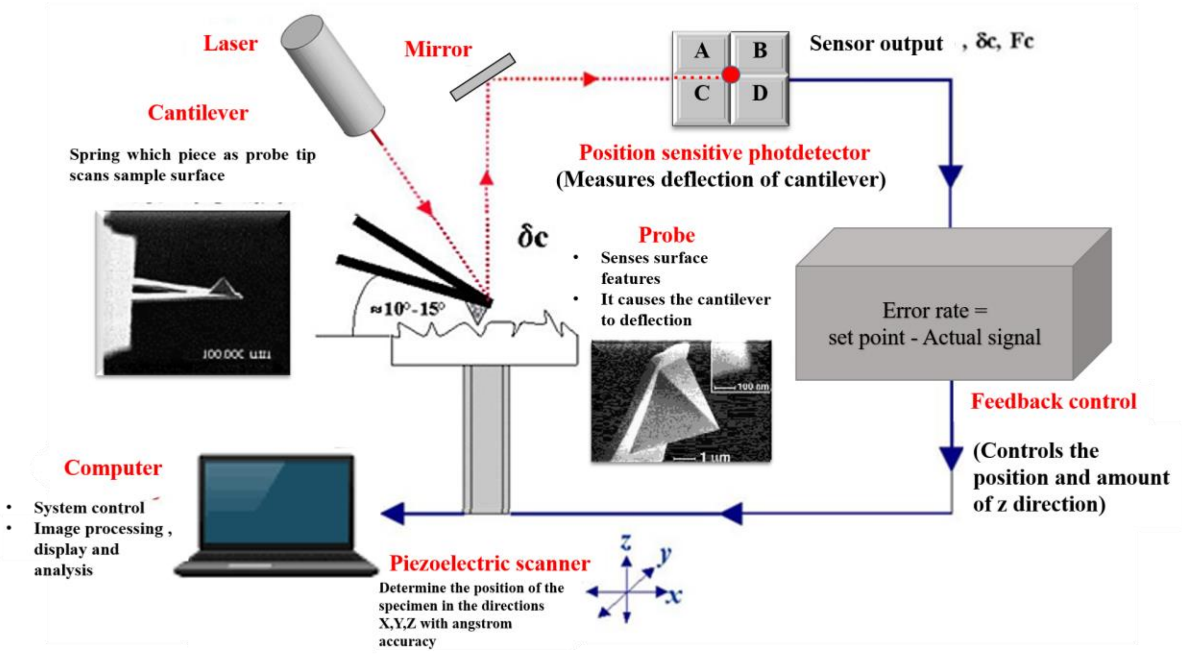

Fig. 1 Atomic force microscope (AFM) system

.

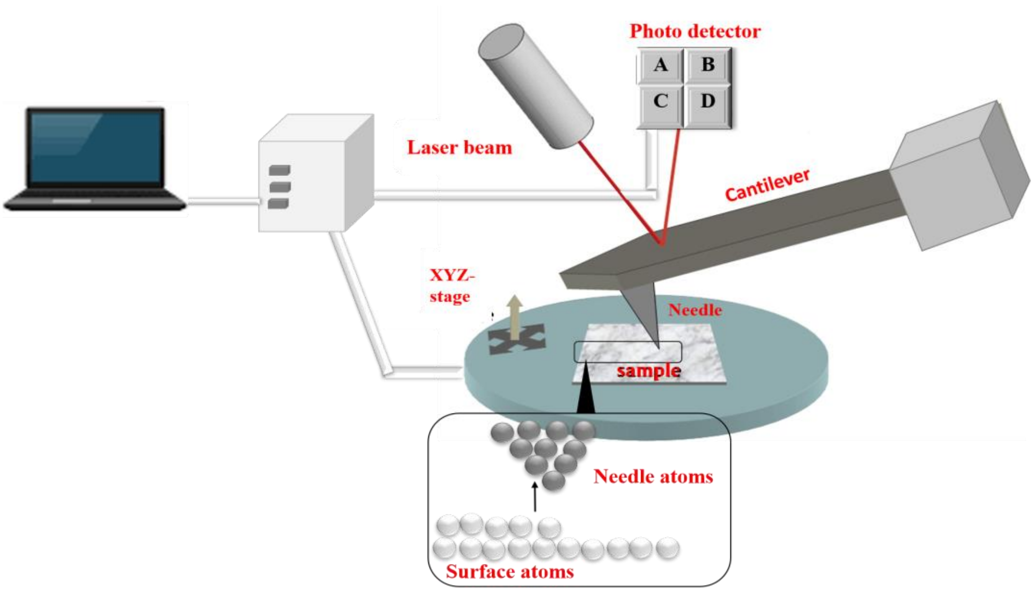

Fig. 2 Laser beam is reflected back to the cantilever towards a position-sensitive

3- Cantilever position detection

The laser beam is reflected back to the cantilever towards a position-sensitive optical detector (PSPD). The ratio of the distance between the cantilever and the detector to the length of the cantilever acts as a mechanical amplifier. As a result, the system can measure the vertical motion of less than one angstrom of the cantilever tip.

3-1- Micropipette suction

In this method, a pipette (a thin glass tube is used to transfer small and precise amounts of liquid) and is fixed on the surface of a cell and enters the pipette by creating a negative pressure and sucks part of the cell into the pipette. In other words, the pipette head is very small compared to the size of the cell; by applying negative pressure to the cell membrane, a small part of the cell enters the pipette head. This method is a fixed technique for measuring the stiffness of mammalian cell membranes, in which the scale of inverse measurement of cell stiffness is considered to be the height of the sucked part. The pressure application technique can also be used to determine the cell response time. In this technique, the rest time is a scale for measuring the viscoelastic properties of the cell.

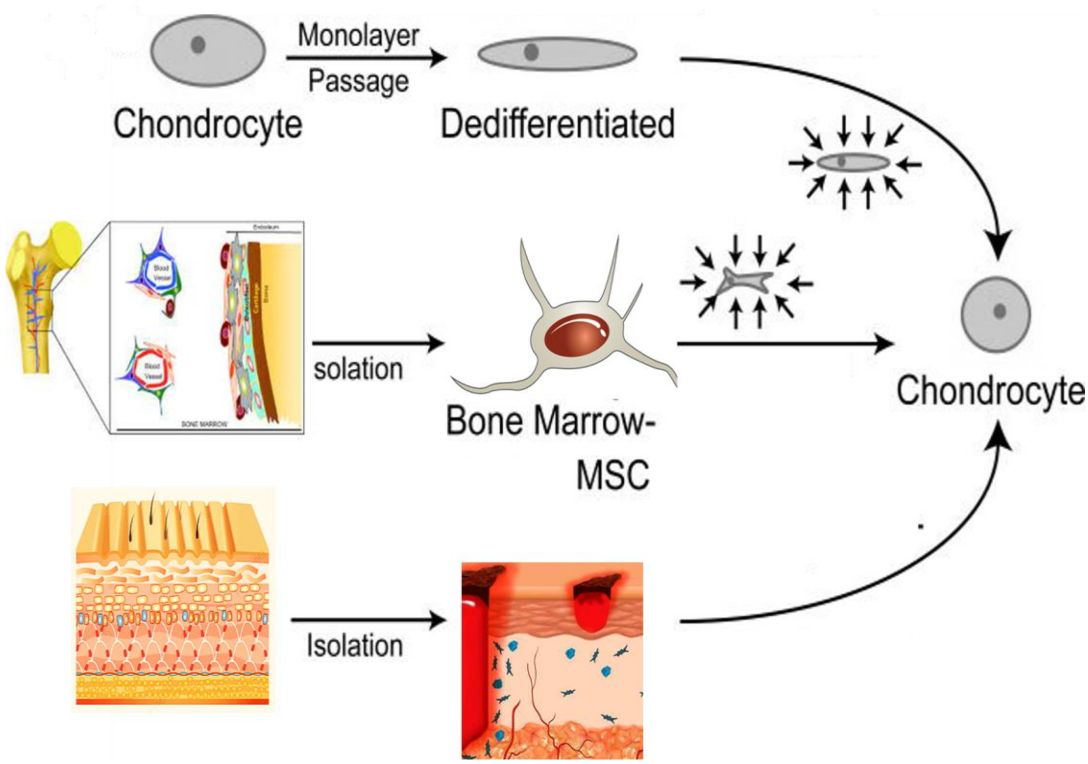

Fig. 3 Cancer cells can easily change their shape and structure

The evaluation of biomechanics cells shows that round, spherical and more rigid than cancer cells. They are usually reluctant to detach from the source of their formation and presence, and as long as they are not affected by an invasive factor or a chain of adverse reactions at the location of these cells, they are likely to change spontaneously in shape and structure as shown in Fig. 3.

3-2- Atomic Force Microscope (AFM)

AFM is a method that is widely used to determine cell components and characteristics. The AFM microscope used as an imaging tool and led to a new approach in biological research, although this microscope is different from the electron light microscope. In this technique, the specimens are inserted with a needle at the end of a pedestal The corresponding tine is followed by a laser, probed. In addition, the measurement of the force applied between the tip of the probe and the specimen, i.e. the force-displacement curve, is important to determine the physical properties of the specimen. As a result, because the needle moves on the sample surface, the AFM force curve can be used to evaluate the hardness and adhesion properties of the cell membrane. It is worth mentioning that its most important advantage is the possibility of using it in aqueous and liquid environments. Other prominent applications include non-invasive imaging and measurement of cellular mechanical properties in tissues. Wu et al. used it to measure heart cells. Researchers also used the technique to identify the mechanisms of force transmission in tendons to investigate the mechanical behavior of surfaces in a fiber tensile test. Stewart et al. were able to obtain mechanical stress strength and volume of pressurized animal cells with the support of a cantilever at constant altitude in AFM and a light microscope. They also managed to provide a way to ensure the stability of measurement parameters such as volume and tracking of intracellular activity and interpretation of physical parameters [19-28].

4- Mechanical stimulation of cells

To provide the general characteristics of the cell, the mechanical properties of the nucleus, which is the main component of the cell, are important. The forces are transmitted from the surface of the cell and change the overall characteristics of the cell [29-33]. Different mechanisms have been proposed to convert mechanical stimulation into physiologically understandable stimulation of the cell. In general, the process of converting mechanical excitation can be divided into three parts. First, the stimulation is received by the cell surface mechanical receptors and transmitted to the cell. In the next step, this stimulus is transmitted into the cell and to the target receptor. Cells are likely to use their chemical or skeletal pathways to transmit stimuli. Finally, by activating the target section, the desired activity is performed. Mechanical receptors in the space between inside and outside the cell include integrins, stretch-sensitive ion channels, and cell surface proteins. Stimulation is also transmitted in two ways, one via the skeleton and the other biochemically. It is noteworthy that the transmission of a mechanical stimulus in the form of a mechanical wave propagation is much faster than the transfer of a stimulus in the form of a chemical wave. According to research, the transfer of excitation through mechanical diffusion takes about 1 to 5 milliseconds, while its chemical transfer through penetration or displacement takes about 5 to 10 seconds. As a result, the only path of mechanical excitation to the nucleus is not the chemical path, and the transmission through mechanical wave propagation and its conversion to chemical excitation at the core surface can also be mentioned. However, with many researches that have been done in the field of studying the paths of receiving, transmitting and converting mechanical stimuli, the exact mechanism of this process is still unknown [33-35]. Mechanical stimuli applied to the body can cause changes in cell function that can be positive (e. g, improvement in bone mechanical properties) or negative (such as damage to a vessel wall or ECM cancer due to a change in the nature of the cancer) [6-12]. One of the most common methods for mechanical stimulation of cells is called bed tension. Also, micropapillary bed can be used to measure the forces produced by cells. As mentioned earlier, cancer is caused by malfunctioning biological cells. In cancer, cells begin to multiply uncontrollably, disrupting tissue structure. The cytoskeleton is the cell's internal scaffold, which consists of a complex network of biopolymer molecules that determine the shape and characteristics of the cell's mechanical deformation and, along with proteins, play an important role in cellular processes such as migration, cell division, and mechanical conduction. The ECM, is the latent protein in the intercellular space that binds cells together to form tissue. Cancer changes the structure of the cytoskeleton and ECM [24-28]. This structure of the protein-woven deformation also affects the cancer cell's ability to contract and expand by affecting the deformation mechanism. Therefore, the rate at which cancer cells move can be very different from that of normal cells, causing the metastasis to occur; That cells migrate throughout the tissue to various organs of the human body and cause tumor metamorphosis [36-38]. In contrast, the presence of cytoskeletal defects is effective in many diseases, such as cancerous tumors, guiding the cytoskeleton to modify its structure and mechanical and biomechanical functions can provide a way to treat cancer. According to the latest statistics from the World Cancer Registry, the International Agency for Research on Cancer predicts that in the next two decades the number of new people with cancer may increase by 47%. Contrary to advances in treatment as well as the findings of cancer studies, different types of cancers have not yet responded to treatment and can be treated for a variety of reasons, such as environmental factors or lifestyle. Biochemical processes between the human body and invasive external factors or disease progression cause various changes that cause changes in cell function, which in turn changes the mechanical properties of the cell, so the biological status index can be measured. It should be considered mechanical properties and also helped to diagnose the cause of the disease and to differentiate between the two diseases [36-38].

5- Mechanical stimulation on cancer cells

In this section, we discuss the results of one of the studies performed on the ability of cancer cells to malform under pressure between two glass plates, or in other words, microplates in different conditions [6-10]. In this experiment, the cell was modeled with two separate parts (showing the cytoplasm and showing the cell membrane) and Maxwell's viscoelastic model was considered; it is possible to consider different mechanical models for epithelial cells, but according to research, Maxwell viscoelastic models provide closer proximity to laboratory results, and also because in cell mechanics, cytoskeletal components have the greatest impact. They also have viscoelastic properties. It can be said that the most suitable material model for the cell is the viscoelastic model. It is worth mentioning that in the study, the inner part or cytoplasm of Maxwell viscoelastic model was homogeneous, isotropic and incompressible and its membrane was considered homogeneous and isotropic.

5-1-Membrane thickness changes

According to research in a process of cancer by Sphingosylphorylcholine (SPC) protein, changes in membrane thickness due to the presence of actin in it and the effect of SPC on actin organization are well known. Increasing the thickness of the membrane leads to a decrease in the reaction force of the cell. In other words, there is an inverse relationship between force and thickness.

5-2-Effect of frequency thickness changes

Frequency is another factor that can affect the mechanical properties of the cell, which increases with increasing frequency, force and reaction of the cell.

5-3- Effect of strain changes on malignant

Because only cancer cells can metastasize, it can only be evaluated in this group of cells. In this case, the strain force increases, the reaction force may increase.

5-4- Effect of elastic changes

The effects of elastic changes are also directly related to the reaction force, and with increasing membrane elasticity, the reaction force increases [8-12].

5-5- Effect of biomechanical stimuli on bone cells

As mentioned, mechanical stimulation can also have positive effects, for example, their effect on stem cells and their transformation into bone cells, which may explain in more detail below Stem cells are cells that are not yet specialized and can differentiate into other cell lines. These cells are divided into different categories, including the ability to differentiate based on the degree of differentiation, which is one of the most important of these categories. This category can also be divided into the following categories: all power, high power and multi power [7-12]. Bioreactor refers to any system or artificial device built or engineered that is used in the subject as a differentiator. There are 5 types of commercial bioreactors for different tissues, including: Flask Spinner SFs, Perfusion bioreactors, Wall-mounted bioreactors (RWV: Vessel Wall Rotating), Z-reactorP, and reactors. Biot rotating biaxial (BXR) [1]. In addition to fluid flow to create shear stresses, these bioreactors improve the growth and proliferation of cells within the scaffold by using appropriate mass transfer. Many researchers have studied the efficiency and effectiveness of bioreactors to induce differentiation, However Sim et al. worked on the effect of compressive stress on the fate of human pneumatic stem cells. They extracted human mesenchymal stem cells (MSCs) from bone marrow cells (BMC) and cultured them on a bed that had the flexibility and for 5 weeks at a pressure of 5 KPa and a frequency of 1 Hz, twice daily and each loads last for 10 minutes. In order to be able to compare the results, they placed the control cells in the previous chip, except that this group of cells was not mechanically stimulated. In these experiments, in order to be able to investigate only the effect of mechanical stimulation on the cell, bone growth medium without growth factors was used [42-50]. In addition to their initial goal mentioned earlier, Sim et al. Also investigated the effect of different loading amplitudes on cell fate, and the results of their experiments showed that the rate of cell proliferation in a group was 1.5 times higher than that of control cells. However, the rate of reproduction decreases compared to when bioreactors are used. One of the reasons that can be mentioned is the reduction of food and gas transfer. Experiments also show that this mechanism and the use of microchips induce the early stages of bone tissue production [8]. The cells were subjected to mechanical stimulation for 15 minutes, 60 minutes and 2 hours. Each was repeated 3 times and the loading results were examined each time. The general conclusion that can be drawn from this study is that by increasing the time of each loading period, it can cause damage to the cells but increase the expression of markers. In addition, the results showed that repetition of processes reduces cell damage, which is due to the adaptation of cells to mechanical stimulation, but reduces the rate of expression of markers [9]. Using stem cells is not without problems It is also associated with problems, including the fact that in the laboratory, mesenchymal stem cells lose their differentiation and proliferation, which must be prevented by various chemical and physical methods [2-10]. In general, and with respect to studies and advances in stem cell differentiation, It can be said that chemical stimuli are not just the crucial stimuli of the cell and physical stimuli such as electrical, mechanical stimuli, even surface geometry affect the fate of the cell. It is also noteworthy that the application of a mechanical parameter alone does not determine the behavior of cells; In addition, biaxial traction, uniaxial traction and compressive stress can help to differentiate stem cells towards bone cells [10-18]. The cells of the body, including MSCs are exposed to various mechanical forces. The type and magnitude of these forces vary in different physiological and pathological conditions and produce a wide variety of responses in cells that have the ability to alter cell function. The study of the response of stem cells to mechanical forces is of great importance in understanding the function of cells and tissues in healthy and diseased conditions. The ability to differentiate MSCs from other cells has made them a very important cellular resource in tissue engineering. In this study, using AFM we consider the effect of mechanical loads on the stem cells which includes examining the behavior of the cell, affected by the behavior of its internal components, through stress distribution and large deformations. Recently, models of hyper elastic materials for the brain have been used to express the nonlinear mechanical behavior of brain tissue under great deformation. Rashid et al. [39] consider the effect of strain rate on mechanical behavior of brain tissue, high strain rate tensile tests on brain tissue samples. They presented a one-term model for the hyper elastic nonlinear behavior of brain tissue and presented the parameters of a 6-behavior model by inverse finite element method, which is obtained by matching finite element results with laboratory results. Feng et al. [40] performed a dynamic shear test on the white part of the brain to determine the behavioral model of brain tissue under various model determine the parameters required in the hyper elastic structural model that reflects the non-isotropic mechanical behavior of the white matter. Laksari et al. [41] performed stress-limiting stress tests.

6- Conclusion

Biochemical processes between the human body and invasive external factors or disease progression cause various changes that cause changes in cell function, which in turn causes changes in the mechanical properties of the cell, so the biological status index can be measured. It considered mechanical properties and also helped to diagnose the cause of the disease and to differentiate between the two diseases. According to the study of mechanical stimuli in the body can cause changes in cell and tissue function, which can be negative or positive. The occurrence of a positive change depends on the optimal choice of parameters such as amplitude, frequency waveform and loading time. However, if any of these parameters are not within their proper range, they may not be able to induce the desired effect on the cell and can even cause cell damage or death. Therefore, optimization of mechanical parameters is very important. However, in addition to applying parameters to cells for a specific purpose, cells can be exposed to other biomechanical stimuli and alter cell behavior.

References

[1] Majid, H., Atefeh, S., Nabiollah, A., Nooshin, H., Mahnaz, E., & Mohammad Ali, S. (2013). Effect of mechanical stimulations on the fate of stem cells-a review

[2] Suresh, S. (2007). Biomechanics and biophysics of cancer cells. *Acta Materialia*, *55*(12), 3989-4014.

[3] Jacobs CR, Huang H, Kwon RY. Introduction to Cell Mechanics and Mechanobiology. Garland Science. 2013.

[4] Evans EA, Skalak R. Mechanics and thermodynamics of biomembranes. Boca Raton, Florida. 1980..

[5] Wu X, Sun Z, Meininger GA, Muthuchamy M. Application of atomic force microscopy measurements on

[6] Ross TD, Coon BG, Yun S, Baeyens N, Tanaka K, Ouyang M, Schwartz MA. Integrins in mechanotransduction. Curr Opin Cell Biol 2013; 25(5): 613-8.

[7] Goldstein LSB, Schneider M. Stem cells for dummies. Hoboken, NJ: Wiley Publishing, Inc, 2010; p: 19-25, 99-119.

[8] Sim WY, Park SW, Park SH, Min BH, Park SR, Yang SS. A pneumatic micro cell chip for the differentiation of human mesenchymal stem cells under mechanical stimulation. Lab Chip 2007; 7(12): 1775-82.

[9] Kasper C, Griensven M, Portner R, Al-Rubeai M. Bioreator systems for tissue engineering. Berlin: Springer, 2009; p: 95-125.

[10] Kim JH,Cho CS, Choung YH, Lim KT, Son HM, Seonwoo H, Baik SJ, Jeon SH, Park JY, Choung PH, Chung JH. Mechanical stimulation of mesenchymal stem cells for tissue engineering. TERM 2009; 6(1): 199-206

[11] Navidbakhsh, M., & Jaafarnejad, M. (2010). Modeling the Effects of Biomechanical Factors on the Deformability of Metastatic Cancer Cells. *Iranian Journal of Biomedical Engineering*, *3*, 399-306

[12] Shamsehkohan, P., & Sadeghi, H. (2017). Overview of the mechanical function of tissue cells affecting human movement. *Scientific Journal of Rehabilitation Medicine*, *5*(4), 271-281.

[13] Saeedi, M. R., Morovvati, M. R., & Mollaei-Dariani, B. (2020). Experimental and numerical investigation of impact resistance of aluminum–copper cladded sheets using an energy-based damage model. Journal of the Brazilian Society of Mechanical Sciences and Engineering, 42(6), 1-24.

[14] Kardan-Halvaei, M., Morovvati, M. R., & Mollaei-Dariani, B. (2020). Crystal plasticity finite element simulation and experimental investigation of the micro-upsetting process of OFHC copper. Journal of Micromechanics and Microengineering, 30(7), 075005.

[15] Fazlollahi, M., Morovvati, M. R., & Mollaei Dariani, B. (2019). Theoretical, numerical and experimental investigation of hydro-mechanical deep drawing of steel/polymer/steel sandwich sheets. Proceedings of the Institution of Mechanical Engineers, Part B: Journal of Engineering Manufacture, 233(5), 1529-1546.

[16] Saeedi, M. R., Morovvati, M. R., & Alizadeh-Vaghasloo, Y. (2018). Experimental and numerical study of mode-I and mixed-mode fracture of ductile U-notched functionally graded materials. International Journal of Mechanical Sciences, 144, 324-340.

[17] Morovvati, M. R., & Mollaei-Dariani, B. (2018). The formability investigation of CNT-reinforced aluminum nano-composite sheets manufactured by accumulative roll bonding. The International Journal of Advanced Manufacturing Technology, 95(9), 3523-3533.

[18] Morovvati, M. R., & Dariani, B. M. (2017). The effect of annealing on the formability of aluminum 1200 after accumulative roll bonding. Journal of Manufacturing Processes, 30, 241-254.

[19] Morovvati, M. R., Lalehpour, A., & Esmaeilzare, A. (2016). Effect of nano/micro B4C and SiC particles on fracture properties of aluminum 7075 particulate composites under chevron-notch plane strain fracture toughness test. Materials Research Express, 3(12), 125026.

[20] Fatemi, A., Morovvati, M. R., & Biglari, F. R. (2013). The effect of tube material, microstructure, and heat treatment on process responses of tube hydroforming without axial force. The International Journal of Advanced Manufacturing Technology, 68(1), 263-276.

[21] Pourmoghadam, M. N., Esfahani, R. S., Morovvati, M. R., & Rizi, B. N. (2013). Bifurcation analysis of plastic wrinkling formation for anisotropic laminated sheets (AA2024–Polyamide–AA2024). Computational materials science, 77, 35-43.

[22] Morovvati, M. R., Fatemi, A., & Sadighi, M. (2011). Experimental and finite element investigation on wrinkling of circular single layer and two-layer sheet metals in deep drawing process. The International Journal of Advanced Manufacturing Technology, 54(1), 113-121.

[23] Morovvati, M. R., Mollaei-Dariani, B., & Haddadzadeh, M. (2010). Initial blank optimization in multilayer deep drawing process using GONNS. Journal of manufacturing science and engineering, 132(6).

[24] Fatemi, A., Biglari, F., & Morovvati, M. R. (2010). Influences of inner pressure and tube thickness on process responses of

hydroforming copper tubes without axial force. Proceedings of the Institution of Mechanical Engineers, Part B: Journal of Engineering Manufacture, 224(12), 1866-1878.

[25] Khandan, A., Abdellahi, M., Ozada, N., & Ghayour, H. (2016). Study of the bioactivity, wettability and hardness behaviour of the bovine hydroxyapatite-diopside bio-nanocomposite coating. Journal of the Taiwan Institute of Chemical Engineers, 60, 538-546.

[26] Karamian, E., Motamedi, M. R. K., Khandan, A., Soltani, P., & Maghsoudi, S. (2014). An in vitro evaluation of novel NHA/zircon plasma coating on 316L stainless steel dental implant. Progress in Natural Science: Materials International, 24(2), 150-156.

[27] Karamian, E., Abdellahi, M., Khandan, A., & Abdellah, S. (2016). Introducing the fluorine doped natural hydroxyapatite-titania nanobiocomposite ceramic. Journal of Alloys and Compounds, 679, 375-383.

[28] Ghayour, H., Abdellahi, M., Ozada, N., Jabbrzare, S., & Khandan, A. (2017). Hyperthermia application of zinc doped nickel ferrite nanoparticles. Journal of Physics and Chemistry of Solids, 111, 464-472.

[29] Kazemi, A., Abdellahi, M., Khajeh-Sharafabadi, A., Khandan, A., & Ozada, N. (2017). Study of in vitro bioactivity and mechanical properties of diopside nano-bioceramic synthesized by a facile method using eggshell as raw material. Materials Science and Engineering: C, 71, 604-610.

[30] Khandan, A., & Ozada, N. (2017). Bredigite-Magnetite (Ca7MgSi4O16-Fe3O4) nanoparticles: A study on their magnetic properties. Journal of Alloys and Compounds, 726, 729-736.

[31] Khandan, A., Jazayeri, H., Fahmy, M. D., & Razavi, M. (2017). Hydrogels: Types, structure, properties, and applications. Biomat Tiss Eng, 4(27), 143-69.

[32] Khandan, A., & Ozada, N. (2017). A novel and economical route for synthesizing akermanite (Ca2MgSi2O7) nano-bioceramic. Materials Science and Engineering: C, 71, 1072-1078.

[33] Heydary, H. A., Karamian, E., Poorazizi, E., Khandan, A., & Heydaripour, J. (2015). A novel nano-fiber of Iranian gum tragacanth-polyvinyl alcohol/nanoclay composite for wound healing applications. Procedia Materials Science, 11, 176-182.

[34] Khandan, A., Karamian, E., & Bonakdarchian, M. (2014). Mechanochemical synthesis evaluation of nanocrystalline bone-derived bioceramic powder using for bone tissue engineering. Dental Hypotheses, 5(4), 155.

[35] Karamian, E., Khandan, A., Kalantar Motamedi, M. R., & Mirmohammadi, H. (2014). Surface characteristics and bioactivity of a novel natural HA/zircon nanocomposite coated on dental implants. BioMed research international, 2014.

[36] Jabbarzare, S., Abdellahi, M., Ghayour, H., Arpanahi, A., & Khandan, A. (2017). A study on the synthesis and magnetic properties of the cerium ferrite ceramic. Journal of Alloys and Compounds, 694, 800-807.

[37] Razavi, M., & Khandan, A. (2017). Safety, regulatory issues, long-term biotoxicity, and the processing

environment. In Nanobiomaterials Science, Development and Evaluation (pp. 261-279). Woodhead Publishing.

[38] Karamian, E. B., Motamedi, M. R., Mirmohammadi, K., Soltani, P. A., & Khandan, A. M. (2014). Correlation between crystallographic parameters and biodegradation rate of natural hydroxyapatite in physiological solutions. Indian J Sci Res, 4(3), 092-9.

[39] Rashid, B., Destrade, M., and Gilchrist, M.D., "Inhomogeneous Deformation of Brain Tissue during Tension Tests", Computational Materials Science, Vol. 64, pp. 295-300, (2012).

[40] Feng, Y., Okamoto, R.J., Namani, R., Genin, G.M., and Bayly, P.V., "Measurements of Mechanical Anisotropy in Brain Tissue and Implications for Transversely Isotropic Material Models of White Matter", Journal of the Mechanical Behavior of Biomedical Materials, Vol. 23, pp. 117-132, (2013).

[41] Laksari, K., Shafieian, M., and Darvish, K., "Constitutive Model for Brain Tissue under Finite Compression", Journal of Biomechanics, Vol. 45, No. 4, pp. 642-646, (2012).

[42] Heydari, E., Mokhtarian, A., Pirmoradian, M., Hashemian, M., & Seifzadeh, A. (2020). Sound transmission loss of a porous heterogeneous cylindrical nanoshell employing nonlocal strain gradient and first-order shear deformation assumptions. Mechanics Based Design of Structures and Machines, 1-22.

[43] Torkan, E., & Pirmoradian, M. (2019). Efficient higher-order shear deformation theories for instability analysis of plates carrying a mass moving on an elliptical path. Journal of Solid Mechanics, 11(4), 790-808.

[44] Torkan, E., Pirmoradian, M., & Hashemian, M. (2019). Dynamic instability analysis of moderately thick rectangular plates influenced by an orbiting mass based on the first-order shear deformation theory. Modares Mechanical Engineering, 19(9), 2203-2213.

[45] Torkan, E., Pirmoradian, M., & Hashemian, M. (2017). Occurrence of parametric resonance in vibrations of rectangular plates resting on elastic foundation under passage of continuous series of moving masses. Modares Mechanical Engineering, 17(9), 225-236.

[46] Pirmoradian, M., Torkan, E., Zali, H., Hashemian, M., & Toghraie, D. (2020). Statistical and parametric instability analysis for delivery of nanoparticles through embedded DWCNT. Physica A: Statistical Mechanics and Its Applications, 554, 123911.

[47] Pirmoradian, M., Torkan, E., & Toghraie, D. (2020). Study on size-dependent vibration and stability of DWCNTs subjected to moving nanoparticles and embedded on two-parameter foundations. Mechanics of Materials, 142, 103279.

[48] Pirmoradian, M., & Karimpour, H. (2017). Parametric resonance and jump analysis of a beam subjected to periodic mass transition. Nonlinear Dynamics, 89(3), 2141-2154.

[49] Heydari, S., Attaeyan, A., Bitaraf, P., Gholami, A., Kamyab Moghadas, B. (2021). Investigation of modern ceramics in bioelectrical engineering with proper thermal and mechanical properties. Journal of Simulation and Analysis of Novel Technologies in Mechanical Engineering, 13(3), 43-52.

[50] Heydari, S., Sadat Mirinejad, M., Malekipour Esfahani, M., Karimian, F., Attaeyan, A., Latifi, M. (2021). A brief review on titanium alloy for dental, biotechnology and biomedical applications. Journal of Simulation and Analysis of Novel Technologies in Mechanical Engineering, 13(2), 47-58.