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MATHEMATICAL MODELING OF SPINAL CORD INJURY

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Abstract

This study revealed that body forces are the forms of stress present in the nerve cells or soft tissue cells that can lead to damage or injury when external forces act upon the spinal cord. The study showcased that spinal cord injuries have viscous and elastic characteristics in the body of the living organisms when the adjoining cells are damaged. The spinal cord injury was created by contusion at C3 level. The model solution depicts that location or displacement of the injury on the spinal cord determines the measure of the severity of the injury which may show tetraplegia or paraplegia on the affected area. The analytic solution explicates that the wall surrounding the injured spinal cord (matrix density) gives an exponential rise in the time taken for the injured wall to increase. The study elucidates that the body forces (stress) increase the location or displacement of the injured area in a linear shape. These results were ascertained by using MATLab to plot the graphs with the given parameter values in the discussion of results. Finally, the solution of this study illustrates that there are dead nerve cells in the injured part of the spinal cord due to stress.

Keywords: Spinal Cord Injury, Complete and Incomplete Injury, tetraplegia, Paraplegia.

Introduction

The central nervous system consists of the brain and spinal cord. The spinal cord is made of soft tissues surrounded by the vertebral bones which extend downward from the base of the brain to its coccygeal end. The spinal cord is a bundle of nerves that carries messages between the brain and the rest of the body. It is made up of nerve cells and a group of nerves called tracts. The lower end of the spinal cord stops a little above the waist region called the conus medullaris and below the waist is a group of nerve roots called the cauda equina. The spinal cord is very sensitive to injury (National Rehabilitation Information Center [NARIC], 2019; National Spinal Cord Injury Association [NASCIA], 2019). Unlike other parts of the body, the spinal cord cannot repair itself if it is damaged. A spinal cord injury occurs when there is damage to the spinal cord either from trauma, loss of its normal blood supply or compression from a tumour, infection, or inflammation, (National Institute on Disability and Rehabilitation Research [NIDRR], 2018). The most common cause of spinal cord injury is trauma.

Acute spinal cord injury is due to a traumatic injury that either result in a bruise (also called a contusion), a partial tear, or a complete tear (called a transection) in the spinal cord. Spinal cord injury is a common cause of permanent disability and death in children and adults. Virtually half of the injuries are caused by motor vehicle accidents, birth injuries, trampoline accidents, alcohol usage, diseases, cancer, arthritis, osteoporosis, and inflammation of the spinal cord can also cause spinal cord injuries, Norton (2019). Other types of trauma include fall from heights, violence (stabbing or gunshot wounds to the spine), and sporting injuries (diving, football, rugby, equestrian, etc). Spinal stenosis which occurs as a result of narrowing of the spinal canal can lead to spinal cord injury. All tissues in the body including the spinal cord require a good blood supply to deliver oxygen and other nutrients. Failure of the blood supply to the spinal cord can cause spinal cord injury and this can be caused by an aneurysm (ballooning of a blood vessel), compression of a blood vessel, or a prolonged drop in blood pressure (Spinal Cord Society [SCS], 2019).

Tracts in the spinal cord carry messages between the brain and other parts of the body. Motor tracts carry signals from the brain to control muscle movement. Sensory tracts carry signals from the body parts to the brain relating to heat,

Nkuturum, C., & David, L.K..(2022). Mathematical modeling of spinal cord injury. *FNAS Journal of Scientific Innovations*, 3(2), 43-52

cold, pressure, pain, and the position of the limbs. Spinal cord injury is damage to any part of the spinal cord or nerves at the end of the spinal canal called cauda equina which causes permanent changes in strength, sensation, and other body functions below the site of the damage or injury. The effects of spinal cord injury show up mentally, emotionally, and socially on the individual. Many scientists are optimistic that advances in research will someday repair spinal cord injuries possible. In the short term, treatments and rehabilitation allow many people with spinal cord injuries to lead productive and independent lives (Blokhina & Fagerstedt, 2006). The ability to control ones' limbs after a spinal cord injury depends on two factors: the place of the injury along the spinal cord and the severity of injury to the spinal cord. The lowest normal part of the spinal cord is referred to as the neurological level of injury. Complete spinal cord injury occurs when all the feeling (sensory) and ability to control movement (motor function) are lost below the spinal cord injury; while incomplete injury occurs when there is some motor or sensory function below the affected area (Black, et al., 1986). There are different degrees of incomplete injury.

Moreover, paralysis from a spinal cord injury may be referred to as tetraplegia. Also known as quadriplegia; this means that the arms, hands, trunk, legs, and pelvic organs are all affected by the spinal cord injury while paraplegia is paralysis that affects all or part of the trunk, legs, and pelvic organs as well which may be confirmed through series of tests performed by the health care provider to determine the neurological level and completeness of the injury, (Choung & Fung, 1986). Spinal cord injuries of any kind may result in one or more of the following signs and symptoms: loss of movement, loss or altered sensation, including the ability to feel heat, cold, and touch, loss of bowel or bladder control, exaggerated reflex activities or spasms, changes in sexual function, sexual sensitivity and fertility, pain or an intense stinging sensation caused by damage to the fiber nerves in the spinal cord and difficulty in breathing, coughing or clearing secretions from the lungs (Humphery, 2002). Other signs and symptoms of spinal cord injury after an accident are as follows: extreme back pain or pressure in the neck, head or back, weakness, incoordination or paralysis in any part of the body, numbness, tingling or loss of sensation in the hands, fingers, feet or toes, loss of bladder or bowel control, difficulty with balance and walking and an oddly positioned or twisted neck or back, (Kushner et al., 1986; Rasmussen, 2006).

Spinal cord injuries may result from damage to the vertebrae, ligaments or disks of the spinal column or to the spinal cord itself which could be classified as trauma. A traumatic spinal cord injury may stem from a sudden traumatic blow to the spine that fractures, dislocates, crushes or compresses one or more of the vertebrae. It may also result from a gunshot or knife wound that penetrates and cuts the spinal cord. Additional damage usually occurs over days or weeks because of bleeding, swelling, inflammation and fluid accumulation in and around the spinal cord. A non-traumatic spinal cord injury may be caused by arthritis, cancer, inflammation, infections or disk degeneration of the spine. Whether the cause is traumatic or non-traumatic the damage affects the nerve fibers passing through the injured area and may impair part or all of the surrounding muscles and nerves below the injury site. A chest (thoracic) or lower back (lumbar) injury can affect the torso, legs, bowel and bladder control, and sexual function. A neck (cervical) injury affects the same areas in addition to affecting movements of the limbs and possibly the ability to breathe, (Roy, 1880; Rodriguez, et al., 1994).

On the other hand, scientists have researched spinal cord injury except for the use of the damage mechanics method to ascertain solutions to a mathematical model of spinal cord injury. Thus, the first applications of continuum mechanics to the study of growth in deformable cells; a model of homogeneous stress-dependent growth for linearly elastic cells or soft tissues developed by Lemaitre (1934). Currently, the occurrence of continuities and discontinuities of materials, injury, deformation, alteration and escalation in soft elastic tissue cells were of key interest to several researchers like (Murray, 1989; Nkuturum, 2021). Others such as (Nkuturum, 2018; Nkuturum & Onwubuya, 2019) worked on continuum biomechanics of soft biological tissues, cell damage, injury, oxidative stress, and cancer. The study reviewed a few of the many achievements in the biomechanics of soft tissues and the tools used to identify some problems that value improved attention of those in applied mathematics, mechanics, and mechanobiology. The results of the researchers mentioned above are related to this current study because it was carried out on oxidative stress, injury, cell damage, disease, and cancer (Oyesanya & Nkuturum 2019). In the results, it was evident that dead cells reduce oxygen to produce energy and this is a fundamental activity to aerobic life. This means that the production of energy leads to the generation of reactive oxygen species which causes oxidative stress and oxidative stress causes broad damage to cellular components which can lead to a good number of injuries and diseases including cancer. Based on the above-elucidated literature, the researchers discovered that the spinal cord wound or injury that causes tetraplegia and paraplegia in the nerve cells of living organisms using the damage mechanics method has not been

⁴⁴ *Cite this article as:*

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modeled, analyzed, and proffer solutions to such formulated model equations. Other factors are that the spinal cord injuries have viscous and elastic features; the location of the injury determines whether it is tetraplegia and paraplegia on the affected area. It also suffices to expose that the wall surrounding the injured spinal cord nerve cells has density and it increases with time due to reduction of oxygen. It is this negated part left unstudied and the global experience of spinal cord injury that led the researchers to carry out this study titled mathematical modeling of spinal cord injury.

Materials and Methods

Contusion of Spinal Cord to Create Injury

Cervical contusion injury (SCI), was carried out indicating where it has been shown that a moderate wound or injury spares a small number of corticospinal tract (CST) axons bilaterally. With the loss of most CST axons due to the bilateral contusion injury in a rat model (figure 6). The protocol of Anderson, Sharp, and Steward (2009) and Martin (2016) was adopted to create injury by contusion.

The Mathematical Model

Since the nerve cells have the features of soft tissues, the model of spinal cord injury is developed by exploring the method of damage mechanics in the area of viscoelastic and thermoelastic constitutive relationship in its mathematical perspective of modeling. However, the factors to be modeled are stress relation, strain coupled with constitutive equation and law of elasticity coupled with damage or injury, viscoelastic tensor equation, mechanotaxis equation with cell division (mitosis, m), and conservation equation for the surrounding wall of the injured area (matrix material). From all hints, the model equation showed three dimensions in the direction of Force Balance Equation in terms of displacement or location of the injury, u, Cell Conservation Equation in terms of nerve cells density, N_c, and the Matrix Conservation Equation in terms of the surrounding wall of the injured area i.e matrix density, Wp respectively. Since a linear viscoelastic material gives the stress-strain constitutive relation for soft tissues, then the equation for a linear viscoelastic material was adopted and deemed necessary to govern the spinal cord injury model as given below:

$$\mu_{1}\frac{\partial^{2}\varepsilon}{\partial x_{i}\partial t} + \mu_{2}I\frac{\partial^{2}\theta}{\partial x_{i}\partial t} + \frac{\partial\varepsilon}{\partial x_{i}} + \nu'I\frac{\partial\theta}{\partial x_{i}} + \frac{\left(\frac{\partial W_{\rho}}{\partial x_{i}}\right)\tau I\left(\frac{\partial n}{\partial x_{i}}\right)}{\left(1+\lambda n^{2}\right)} + \frac{\tau\left(\frac{\partial n}{\partial x_{i}}\right)\gamma I\left(\frac{\partial W_{\rho}}{\partial x_{i}}\right)}{\left(1+\lambda n^{2}\right)} = s\rho u$$
(1)

$$\frac{\partial N_c}{\partial t} = d_1 \left(\frac{\partial^2 n}{\partial x^2} \right) - d_2 \left(\frac{\partial^4 n}{\partial x^4} \right) - a_1 \left(\frac{\partial n}{\partial x} + \frac{\partial^2 W_{\rho}}{\partial x^2} \right) + a_2 \left(\frac{\partial n}{\partial x} + \frac{\partial^4 W_{\rho}}{\partial x^4} \right) - \nabla \bullet (nu_t) + rn(N - n)$$
(2)

$$\frac{\partial W_{\rho}}{\partial t} + u_t \left(\nabla \bullet W_{\rho} \right) + W_{\rho} \bullet \left(\nabla u_t \right) = 1 - v\theta \tag{3}$$

The model equations are (1-3) above with three dependent variables such as the density terms $N_c(x,t)$, $W_\rho(x,t)$ and displacement terms, u(x,t) is visible in real life spinal cord injury. The parameters involved are $d_1, d_2, a_1, a_2, \mu_1, \mu_2, r, N, \tau, \lambda, \gamma, s$ and v, where matrix flux is taken to be during convection and $S(n, \rho, u) = 1 - v\theta$ is taken to be the rate of secretion or spread of injured nerve cells in the surrounding wall (matrix). Using the product rules for vector calculus to expand equations (1-3) then, it can be solved by using the method of travelling wave solution and all the dimensionless parameters are positive. Where $a_1, a_2, d_1, d_2, r, \tau, \lambda, N$ are associated with the cell properties and $\mu_1, \mu_2, v, \dot{\gamma}, s$ are related to the matrix properties. The assumption of the initial boundary condition is $u = 1, N_C = 1, W_\rho = 1$ and that position (x) changes with time (t) and is a constant. Since the position damaged in the spinal cord or tract in the body starts at a point which can be any positive real number (constant) such as 1, 2, 3, Putting $\frac{\partial u}{\partial t} = 1$ since equation (3) showcased how dense the

damaged nerve cells are packed in the surrounding wall of the matrix. Equation (3) is a nonhomogeneous partial differential equation and can be solved using travelling wave method of solution. This method of solution is appropriate because dead or damaged cells move and also has a viscous property. From equation (3), there is no convective motion. Thus, $\nabla \bullet (W_{\rho}u_t) = 0$; [5, 6, 10] therefore equation (3) becomes:

$$W_{\rho t} = 1 - \theta v \tag{4}$$

Integrating w.r.t. x, t yields

Nkuturum, C., & David, L.K..(2022). Mathematical modeling of spinal cord injury. FNAS Journal of Scientific Innovations, 3(2), 43-52

$$W_{\rho}(x,t) = t - 3vx_{i}t + \frac{3}{2}vkt^{2}.$$
(5)

Similarly, to solve for $N_c(x,t)$ upon integration using equation (2) gives

$$N_{c}(x,t) = 3D_{1}t\left(x_{i} - \frac{kt}{2}\right) - 3D_{2}t\left(x_{i} - \frac{kt}{2}\right) - 3a_{1}v\left(\frac{x_{i}^{2}t^{2}}{2} - \frac{3x_{i}kt^{3}}{2 \cdot 3} + \frac{k^{2}t^{4}}{2 \cdot 4}\right) - 3a_{2}v\left(\frac{x_{i}^{2}t^{2}}{2} - \frac{3x_{i}kt^{3}}{2 \cdot 3} + \frac{k^{2}t^{4}}{2 \cdot 4}\right) - 3k_{2}v\left(\frac{x_{i}^{2}t^{2}}{2} - \frac{3x_{i}kt^{3}}{2 \cdot 3} + \frac{k^{2}t^{4}}{2 \cdot 4}\right) - 3k_{2}v\left(\frac{x_{i}^{2}t^{2}}{2} - \frac{3x_{i}kt^{3}}{2 \cdot 3} + \frac{k^{2}t^{4}}{2 \cdot 4}\right)$$

$$(6)$$

Finally, to solve for u(x,t) by integrating w.r.t x,t using equation (1) yields

$$u(x,t) = \frac{-3k\left(\chi_{i}^{2} - 2x_{i}kt + k^{2}t^{2}\right)\left(\mu_{1} + \mu_{2}I\right) + 3(x_{i} - kt)\left(1 + vI\right) - \frac{27\tau vtI\left(x_{i} - \frac{3x_{i}kt}{2} + \frac{k^{2}t^{2}}{2}\right)}{1 + \lambda\left(\chi_{i}^{2} - 2x_{i}kt + k^{2}t^{2}\right)}\left(1 + \gamma\right)}{s\left(t - 3vtx_{i} - \frac{3vkt^{2}}{2}\right)}$$
(7)

Hence, the analytic solutions to the three equations of the spinal cord injury model are given in equations (5, 6, 7) and this implies that the surrounding wall density $W_{\rho}(x,t)$, Nerve cell density $N_{c}(x,t)$ and Cell location or Displacement u(x,t) are functions of the position, x and time, t respectively. From all indications, the result of the model equations presented a steady-state solution showing that the injured nerve cells in the spinal cord are increasing by defiling all medications and grows exponentially with time. **Table 1: Description of variables and parameters in the model**

N	Number of dead cells in the injured area

$\sigma(x,t)$	Stress tensor
x	Position
t	Time
f	Body force
$W_{\rho}(x,t)$	Surrounding wall of the injured area (Density of the ECM)
$N_c(x,t)$	Nerve Cell density
$N_{c,t}$	Partial differentiation of nerve cell density w.r.t, t
∇	Laplacian operator
n(x,t)	Number of cells per unit volume
u(x,t)	Displacement vector of the matrix or location of the spinal cord injury
d_1 , d_2	Diffusion parameters
μ_1 , μ_2	Shear and bulk viscosities of the ECM

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a ₁ , a ₂	Long-range effect for mechanotaxis flux
τ	Cell traction force
θ	Dilation
ε_t	Partial differentiation of strain tensor w.r.t. t
θ_t	Partial differentiation of dalition w.r.t. t
u_t	Partial differentiation of displacement w.r.t. t (velocity of deformation of the matrix)
n_t	Partial differentiation of cell density w.r.t. t
$W_{\rho,t}$	Partial differentiation of density of the ECM w.r.t. t
γ	Measure of the severity of the injury
r	Initial rate of nerve cell death
Ι	Unit tensor
S	Elastic parameter for the substrate attachments
λ	Parameter that controls the activator of dead nerve cell growth (complete injury)
V	Poisson ratio

Discussion of findings



Figure 1 is showing the graph of Stress in the ECM against Time with arbitrary parameter values: $\tau = 0.7$, $\rho = 1.2 \times 10^{-2}$, $\lambda = 30$, I = 0.3, $x_1 = 2.1$, $x_2 = 2.4$, $x_3 = 3.0$, k = 0.5, t = 0:5:100

Figure 1 depicts the graph of stress against the time taken (in days) in the surrounding wall of the injured area of the spinal cord which increases the volume of ECM linearly as it harbours damaged nerve cells. This study revealed that body forces are the forms of stress existing in soft tissue cells that leads to damage or wound or injury when external forces act upon the spinal cord. This figure explains that the intensity of stress action on the nerve cells is on the high side and it is linearly directly to the time in days it takes to broaden the spinal cord of the organism.



Figure 2 is showing the graph of Displacement against the magnitude of Contusion on the spinal cord at C3 with arbitrary parameter values: $\mu_1 = 1$, $\mu_2 = 0.4$, $x_1 = 2.1$, k = 0.5, $\tau = 0.7$, I = 1, $\gamma = 0.5$: 100, $\lambda = 0.5$, $s = 10^6$, v = 0.2, r = 0.8, N = 1, t = 2

Figure 2 showcases the displacement or location of the injury against coalescence time in days (a measure of severity) of the spinal cord injury in the spinal tract of the organism. The model solution depicts that location or displacement of the injury on the spinal cord determines the severity of the injury which also showed tetraplegia or paraplegia on the affected area. The figure shows that the level of damage on the spinal cord could be either a complete or incomplete wound. A complete injury means that there is no movement or feeling below the level of the injury. An incomplete injury means that there is still some degree of feeling or movement below the level of the injury. The graph explains that the position, size, and direction of the injured nerve cells is linearly directly to the time in days it takes to spread and coalescence in the spinal tract. For instance, a wound on the cervical spine in the neck can also originate loss of muscle function or strength in all four extremities. This is referred to as quadriplegia (tetraplegia). An injury of this type often requires mechanical breathing assistance which has to do with a ventilator as the chest muscles may also be weakened. Paraplegia is a spinal cord injury to a lower part of the spinal cord that leads to paralysis, loss of function in the legs and lower body. There is no displacement and coalescence at point (0,0) because the injury is still in its fresh state.



Figure 3 is showing the graph of Stress against displacement of injured nerves with arbitrary parameter values: $\mu_1 = 1$, $\mu_2 = 0.4$, $x_1 = 2.1$, k = 0.5, $\tau = 0.7$, I = 1, $u = 0:5:100 \ \lambda = 0.5$, $s = 10^6$, v = 0.2, r = 0.8, N = 1, $t = 2 \sec s$, $\gamma = 0.7$

Above is the graph showing the action of stress in the displacement of the injured nerve cells in the spinal cord of the organisms. The study elucidates that the body forces (stress) increase the location or displacement of the injured area in a linear shape. This figure explains that the intensity of the external and internal forces acting on the injured nerve cells location at zero is minimal because there is no injury for it to act upon; but when the stress action is on the high side and become linear in growth as the displacement increases from position one (x_1, x_2, x_3) to infinity with time it takes the injured cells to spread in the matrix.





Figure 4 shows the matrix density against time in days with arbitrary values of x_1 . This graph explicates that the wall surrounding the injured spinal cord (matrix density) gives an exponential rise in the time taken for the injured wall to increase. The graph portrays that the matrix is quadratic in t. In terms of the time, it shows that the lower the time the lower the matrix density and as the time increases the damaged nerve cells in matrix density also increases.

 49 Cite this article as: Nkuturum, C., & David, L.K..(2022). Mathematical modeling of spinal cord injury. FNAS Journal of Scientific Innovations, 3(2), 43-52



Figure 5 is showing the graph of Injured Nerve Cell Density against Time with arbitrary parameter values: $d_1 = 1$, $d_2 = 0.6$, $x_1 = 1$, k = 0.5, r = 0.8, N = 1, t = 0:5:100

Figure 5 is the graph of nerve cell density against time which is showing the change in the injured nerve cell density with time. The figure is showcasing that the cell density at different values of position (x_i) increases linearly as the time increases. The figure is also depicting the effects of stress, temperature and traction force with the time taken in days in the matrix of the organism is revealing that the volume of dead nerve cells have increased as the matrix harbours more injured nerve cells.

Testing of potential therapies for spinal cord injury has been drastically affected the unavailability of a standardized, reproducible animal model with the predictable outcome at a given force of injury (dose-response). Kushner et al (1986) constructed a mathematical model of spinal cord injury to predict motor performance in rats for 8 weeks after the damage. Their study used experimental data generated from the investigation of static-load technique by inducing cord injury and the analysis was carried out using multiple linear regression. Their model was used to establish expected motor deficits and to derive dose-response curves. In this study, we used the damaged mechanics model and MATLab for the stimulation. The results show that the wall surrounding the injured spinal cord (matrix density) gives an exponential rise in the time taken for the injured wall to increase. The study elucidates that the body forces (stress) increase the location or displacement of the injured area in a linear shape (Figure 6).



Figure 6 is showing: (A) Normal spinal cord section at C3 and (B) Contusion of spinal cord at C3

With the loss of most CST axons due to the bilateral contusion injury in a rat model (green; loss of most of the dorsal CST bilaterally), there are only sparse projections from axons located in the lateral and ventral columns (Figure 6B).

Finally, the solution of this study illustrates that there are dead nerve cells in the injured part of the spinal cord due to stress. This figure is revealing that when the dead nerve cells are packed up thereby blocking some parts of the sensitive system of the body can lead to complications which include urinary tract infections or urinary incontinence that is the inability to control the flow of urine, bowel incontinence which is the inability to control bowel movements, pressure sores, pneumonia that is infections in the lungs, blood clots, muscle spasms, skin sensation, chronic pain, sexual health, wellness and fitness, respiratory system and depression.

Conclusion

Conclusively, this study reveals that the extent of the damage to the spinal cord determines whether the injury is complete or incomplete injuries. That a complete injury means that there is no movement or feeling below the level of the injury while an incomplete injury means that there is still some degree of feeling or movement below the level of the injury.

Recommendation

The study recommends that spinal cord injuries should be given serious attention to avoid loss of movement, loss or altered sensation, changes in sexual function, sexual and difficulty in breathing. Areas of further research can be carried out by considering the same spinal cord model with medications and healing.

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