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MODELLING METHODS OF MEDIAN NERVE FOR EARLY DIAGNOSIS OF CARPAL TUNNEL SYNDROME: A NARRATIVE REVIEW

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Abstract

Carpal Tunnel Syndrome (CTS) is a mononeuropathy, nerve entrapment and a condition in which the median nerve in the carpal tunnel of wrist is compressed as it passes under the transverse carpal ligaments through to the carpal tunnel. Consequently, individual will lead to feelings of pain, tingling, and numbness in the index, middle, thumb, and part of the ring fingers. Making models of the wrist and get the model simulated is a first step in diagnosing CTS. This study aims to review the narratives of different researches on certain biomechanical and electrophysiological models that can help determine at what extent the median nerve in the wrist through to the carpal tunnel is being squeezed. This study also aims to determine the effects and impact of muscles, tendons, and connective tissues work together in biomechanical modeling to find nerve compression and address issues in diagnosing CTS. This narrative review was conducted by searching keywords CTS on the Google Scholar database, modeling median nerve, and simulations. Research implies that creating models with the help of biomechanics and electrophysiology, and validating them with actual data on carpal tunnel syndrome, can help regulate the extent of pressure on the median nerve. Doctors can utilize the provided information to draw early decisions in curing Carpal Tunnel Syndrome. By employing electrophysiological and biomechanical models, one can revamp the understanding of CTS. Model results will help to identify the initial stages of CTS, create personalized treatment plans, and monitor how the disease develops. More research on these initial steps by building models with their validated results are required to strengthen diagnostic methods and scrutinize latest technologies for better CTS diagnosis.

INTRODUCTION

Carpal tunnel syndrome (CTS) is a frequent issue that happens when the median nerve in the wrist gets squeezed, resulting in numbness and tingling in the major parts of the fingers. The nerve doesn't function properly because of the increased pressure inside the carpal tunnel.[1] The most common type of nerve entrapment happens when the median nerve is compressed, causing a medical condition. [2] Around 10% of people will experience this at some time in their lives, but the chances increase to 84% for individuals who have diabetes. [3] Entrapment neuropathies are a group of conditions where nerves are compressed for a long time, causing

pain and difficulty in moving and feeling. Peripheral nerve entrapment disorders can result from trauma, inflammation, or birth defects. [4] Compression injuries, including entrapment neuropathies, are classified according to the state of the afflicted nerve trunk, both structurally and functionally. These injuries fall into three primary categories according to Seddon's classification: neurapraxia, axonotmesis, and neurotmesis. [5] Sunderland later expanded upon this classification, dividing them into five categories based on severity shown in Table no. 1. Neurapraxia encompasses the majority of entrapment neuropathies.[6] The most prevalent kind of entrapment neuropathy, neurapraxia, includes myelin degradation and slows down signal conduction. Axonal continuity and conduction are lost in axonotmesis, the second degree of severity. Two well-known theories regarding the fundamental reason for signal propagation loss are ischemia brought on by repeated compression and demyelination. [7] Endocrine diseases include hypothyroidism, pregnancy, menopause, obesity, and diabetes are among the common causes of carpal tunnel syndrome (CTS). Rheumatoid arthritis, Hand Arm Vibration Syndrome (HAVS), traumatic injuries such as fractures and dislocations of the distal radius and carpal bones, and repetitive wrist movements are some other causes that may be involved. Nevertheless, the majority of CTS cases are idiopathic, meaning that no particular cause can be identified. [8]

The fibro-osseous carpal tunnel is located between the flexor retinaculum and the carpal bones. The nine extrinsic flexor tendons of the thumb and fingers, as well as the median nerve, are located in this little area shown in Figure no. 1. The place where it is the narrowest is around 2.5 cm away from the entrance. The pressure inside the tunnel usually varies between 2 and 31 mmHg in people who do not have carpal tunnel syndrome (CTS). Still, this pressure can rise sharply in CTS patients, to as high as 32 to 110 mmHg, depending on where the wrist is positioned.[9] The subsynovial connective tissue (SSCT) surrounds the median nerve, nine flexor tendons, and the carpal tunnel. The tissue functions as a sliding interface, allowing these structures to move more easily among one another. [10]

For the purpose of diagnosing Carpal Tunnel Syndrome, several diagnostic techniques have been proposed throughout the years. These approaches include electrophysiological models and biomechanical models as well as nerve conduction tests, where Phalen's maneuver and Tinel's sign are important assessments. According to D'Arcy, C. A., & McGee et al. 2000 [11], a systematic study evaluated the effectiveness of using physical examination and medical history results to predict positive nerve conduction investigations.

Viera, A. J. et al. 2003 [12] stated that the Tinel's sign and Phalen's maneuver are the main initial clinical tests for carpal tunnel syndrome. When symptoms are induced in the median nerve distribution area by bending the wrist to 90 degrees for one minute, Phalen's procedure produces favourable results. When tapping on the carpal tunnel area, if it causes symptoms along the path of the median nerve, then Tinel's sign is considered positive.

Recently published articles have been focusing on using computational approaches in neuroprosthetics. These methods help researchers' study how nerve tissue interacts with electrodes and figure out the best stimulus parameters. Many studies have used a multiscale computational method to look at how nerves and electrodes connect, combining data from axon or neuron models with simulations using finite element models. Shiraz et al. [13] conducted a study on pudendal nerve stimulation using a different approach. Unlike the methods used in this study, they utilized a different stimulator and electrode. Additionally, they observed various tissues based on the position of the pudendal nerve in their model.

The objective of this review paper is to present modelling capabilities and opportunities for diagnosis and treatment of CTS using electrophysiological and biomechanical models in the early stages. Biomechanical models incorporate Finite Element Method (FEM) to predict the pressure inside the Carpal Tunnel in

CTS. On the other hand, electrophysiological models predict responses by giving electrical stimulus and measuring the action potential within the nerves or muscle cells. Through synthesis of cutting-edge research and methodologies, the review not only highlights improved diagnostic accuracy from these tools but also clarifies pathophysiology of CTS along with offering as aids to guide treatment strategies. These responses generated from the models will help doctors to diagnose CTS at the initial stages. The comprehensive evaluation addresses the benefits, drawbacks, and potential future advancements in using biomechanical and electrophysiological models for CTS.

Table no.1 Entrapment Neuropathies [6]

Nerve	Site of entrapment
Suprascapular The lower portion of the brachial plexus or the medial cord.	Spinoglenoid notch Cervical rib or band at thoracic outlet (neurogenic thoracic outlet syndrome)
Median Wrist Elbow	 Carpal tunnel Between heads of pronator teres (pronator teres syndrome)
Ulnar Wrist Elbow	 Guyon's canal (ulnar tunnel) Bicipital groove, cubital tunnel
Posterior interosseous	Radial tunnel- at point of entrance into supinator muscle (arcade of Frohse)
Lateral femoral cutaneous (meralgia paraesthetica)	Inguinal ligament
Posterior tibial	Obturator canal Tarsal tunnel, medial malleolus-flexor retinaculum
Interdigital plantar (Morton's metatarsalgia)	 Plantar fascia (heads of 3rd and 4th metatarsals)

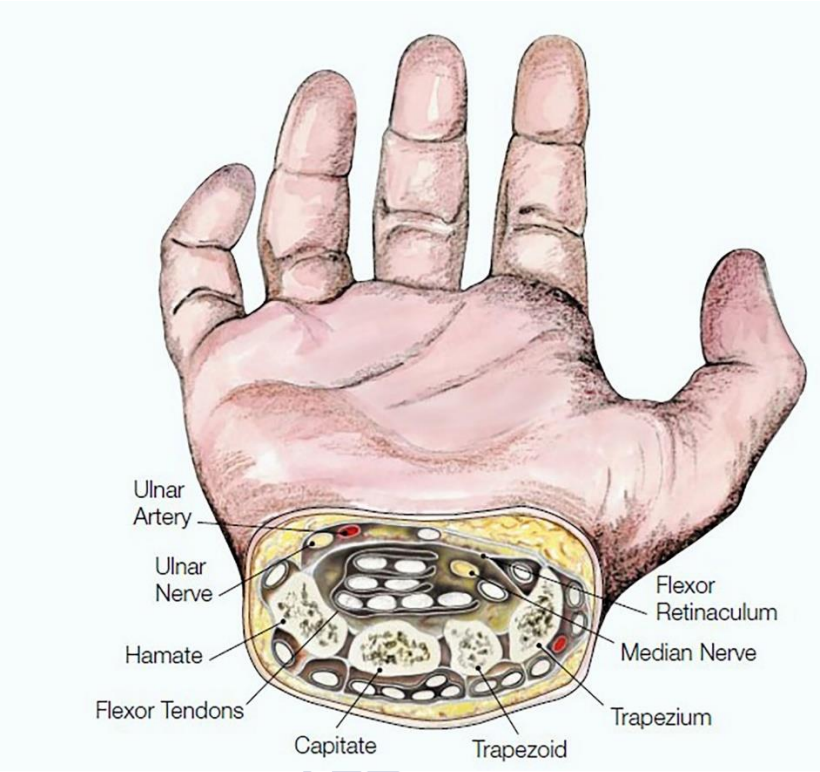

Figure no.1 Localization of median nerve [14]

Biomechanical Modelling

Guo et. al [15] conducted a study to examine how mechanical forces influence the shape of the carpal tunnel, specifically looking at the role of the transverse carpal ligament. By utilizing computer modeling, Guo was able to construct a highly detailed representation of the wrist. This model was created by integrating anatomical data with CT scan images, resulting in a thorough depiction of the carpal bones. Advanced software was then used to generate a surface mesh model, which was transformed into a solid mesh for comprehensive analysis. Cartilage layers were incorporated as contact elements within the model, as illustrated in Figure 2. Additionally, a 3D model of the transverse carpal ligament (TCL) was created using CT scans and anatomical software, connecting to specific parts of the carpal bones through tetrahedral components. The ligaments were simulated with non-linear, tension-only spring components that linked the appropriate attachment nodes on the bones. To the bone, cartilage and TCL elastic modulus (10 kPa), Poisson's ratio (0.3) were assigned for each material properties [50], respectively. The stiffness of the intercarpal ligament was determined using data from existing studies. Three nodes were placed on each carpal bone to restrict movement in various directions. MSC.Marc software was employed to simulate the changes in the ligament and carpal tunnel area under stretching conditions. The simulation results closely aligned with actual experimental findings. The researchers also conducted sensitivity analyses to examine how varying the TCL's flexibility and compression ratio affected its shape changes. This advanced model provides important information on wrist mechanics and potential implications for conditions such as carpal tunnel syndrome.

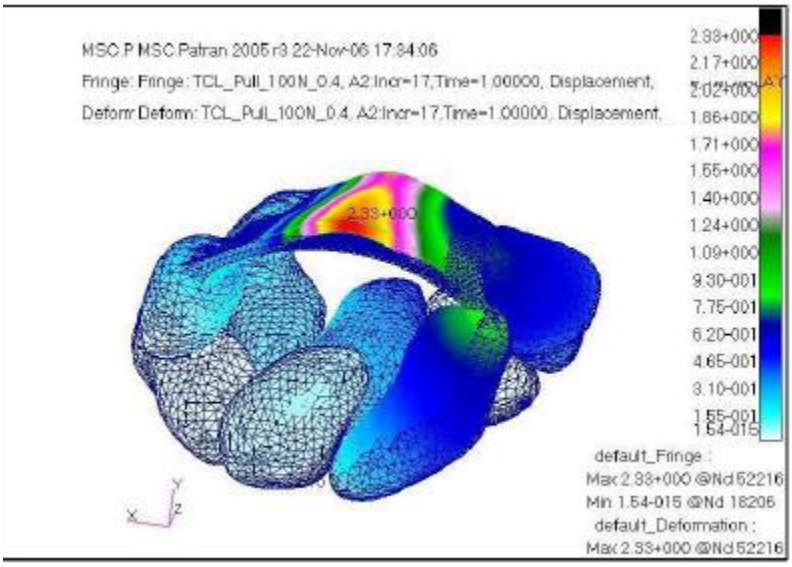

Figure no.2 Fringe image of the displacement of the transverse carpal ligament under 100N palmarly directed stretch force [15]

Walia et al. [16] proposed a study which aimed to investigate the therapeutic potential of adjusting the carpal arch width to ease and soothe the compression of the median nerve in the carpal tunnel. In order to do this, researchers created a carpal tunnel finite element model. Using cross-sectional MRI images collected at the level of the hamate hook under unloaded conditions (0 mmHg), a reference geometric configuration of the transverse carpal ligament and carpal bones (containing the trapezium, trapezoid, capitate, and hamate) was constructed. The polygon selection tool was used to manually segment the bones and ligament shown in figure no. 3. By considering the combined reaction of cartilage and intercarpal ligaments, the model integrated the mechanical properties of bones. Rather than cartilage and ligaments being physically represented, the interstitial gaps were filled with substitute tissue that reflected their mechanical characteristics. Shown in figure no. 4. Carpal bones were modelled as co-rotational linear materials with determined Poisson's ratio and Young's modulus. Inverse finite element analysis was used to identify the characteristics of the surrogate tissue. A co-rotational method was used in the non-linear finite element analysis to account for large rotations. The trapezium was stabilized, and a connection between the bones and surrogate tissue was made using tie restrictions. By using loading boundary conditions that corresponded to different pressures inside the carpal tunnel, the mechanical behaviour of the transverse carpal ligament was integrated. Researchers discovered that when pressure is applied in the radial-volar quadrant at an angle of 138°, the total cross-sectional area of the carpal tunnel reaches its highest value. To find out the unique properties of the material (E and v) for the substitute tissue, we used a reverse finite element analysis on the model. We adjusted the loading and boundary conditions by making small, gradual changes in pressure in the carpal tunnel space to describe the forces and movements. The surrogate tissue's material characteristics were repeatedly changed to match experimental data collected at pressure levels between 50 and 200 mmHg with model predictions of bone motion. Using Rhinoceros software, the shape of template bones at various pressure levels was matched to calculate the experimental bone motion. By modifying surrogate tissue characteristics to reduce the discrepancies between model-predicted and experimentally observed bone marker

coordinates, an optimization process optimized the objective function. (Equation no.1)

$$f = \sum_{p=1}^{4} \sum_{n=1}^{6} \left[(X_{p,n}^{e} - X_{p,n}^{m})^2 + (Y_{p,n}^{e} - Y_{p,n}^{m})^2 \right] \quad \text{(Equation no. 1)[16]}$$

Where,

X^e and Y^e are the x and y coordinates of the bony landmarks
X^m and Y^m are the model-predicted x and y coordinates of the same bony landmarks
p and n are the pressure levels
Limitations of this study are that the cartilage and ligaments in the study's finite element model were represented by surrogate tissue, which simplified computation but could have compromised anatomical correctness. Furthermore, the model's capacity to represent intricate three-dimensional biomechanics is restricted by the use of a two-dimensional model that is exclusively concentrated on the distal level of the carpal tunnel.

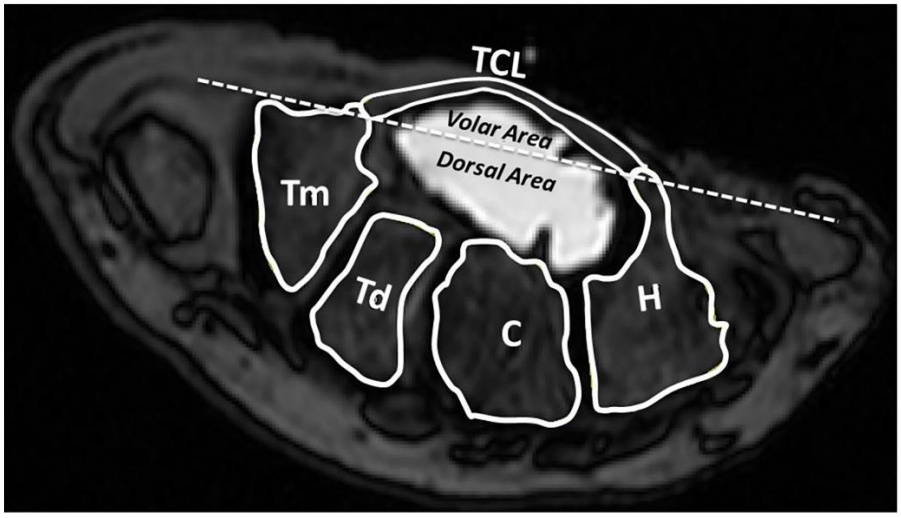

Figure no.3 Magnetic resonance imaging segmentation of the four distal carpal bones and the transverse carpal ligament (TCL). Tm = Trapezium, Td = Trapezoid, C= Capitate, H = Hamate, and TCL = transverse carpal ligament. [16]

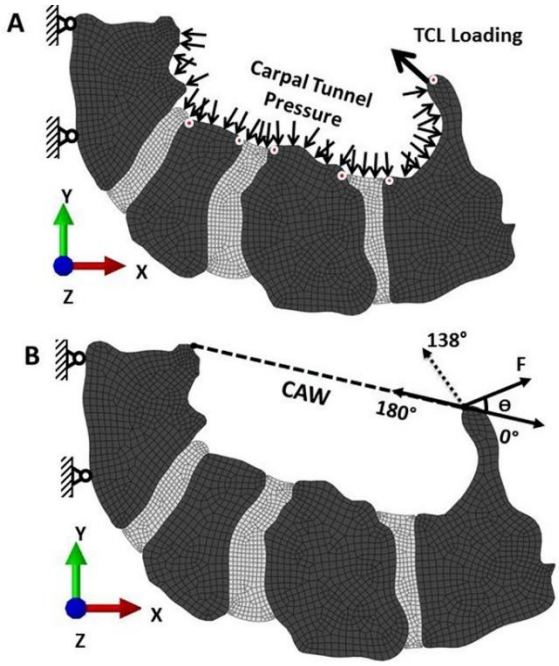

Figure no.4 The planar finite element model of the distal carpal tunnel for inverse finite element analysis (A) and simulation (B). [16]

To simulate how tendon movement affects compression of the median nerve in Carpal Tunnel Syndrome (CTS), Peshin et al. [17] used Finite Element Analysis shown in figure no. 5. Patient-specific phalanges and soft tissues of the carpal tunnel were modelled using publicly available MRI data. The transverse carpal ligament, flexor tendons, median nerve, and SSCT are examples of the soft tissues in the carpal tunnel that display hyper-elastic behavior that may be represented using first-order Ogden material characteristics. Strain energy is defined by:

$$W(\lambda_1\lambda_2\lambda_3) = \frac{2\mu}{\alpha^2}(\lambda_1^\alpha + \lambda_2^\alpha + \lambda_3^\alpha - 3) \quad \text{..... (Equation 2)[17]}$$

Where,
W= strain energy
λ_i= principal stretches
μ= material behavior in the low strain region
α= material behavior in the high strain region

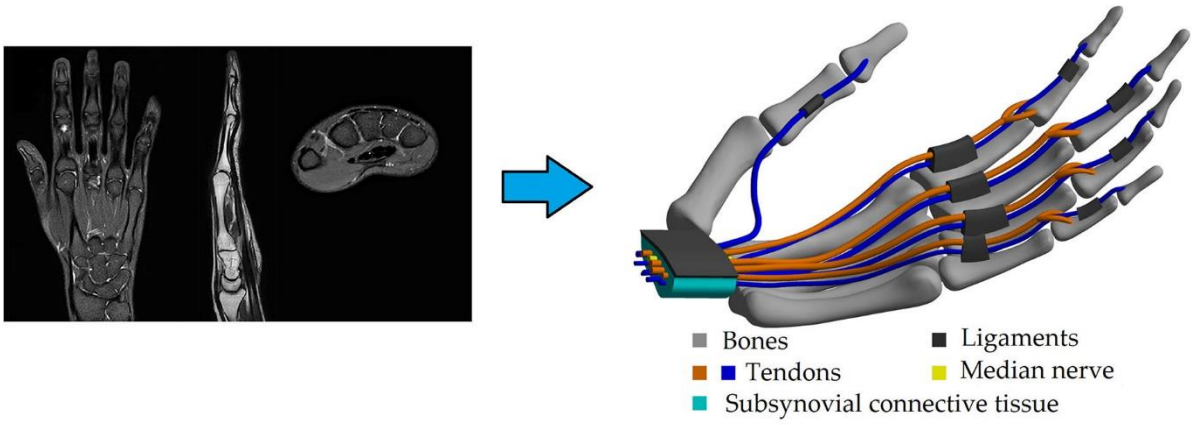

Figure no.5 (a) Image of human hand based on MRI (b) Geometrical model of human hand [17]

The simulation consisted of four cases with their boundary conditions shown in figure no.6. Case 1 dealt with isolated finger flexion with a fixed wrist; Case 2 looked at wrist extension with free fingers; Case 3 looked at finger flexion followed by wrist extension; and Case 4 looked at wrist flexion with fixed fingers. Joint rotations and tendon displacements have to be adjusted specifically for each patient. The results demonstrated varying degrees of compression of the median nerve, providing information about how various hand gestures affect the development of CTS. The results of wrist movement scenarios showed that the median nerve was compressed to different degrees, ranging from 129 Pa to 227 Pa. Remarkably, wrist flexion caused compression to occur more quickly than either finger or extension flexion by itself. Furthermore, it was shown that if wrist extension came first, there was less compression experienced during finger flexion. Major limitations of this work include that the movement of the carpal bones during wrist flexion and extension, which can change the geometry of the carpal canal and have an influence on the movement of the tendon and median nerve, was not taken into consideration in the study. Including this interaction will greatly increase computing time and complicate computations, even though other research has acknowledged its importance. Moreover, tendons were enveloped by connective tissue, with the majority of their surface area remaining unoccupied. Even though some tendon movement perpendicular to the phalanges was shown, demonstrating proper boundary conditions, this incomplete depiction of tendon-tissue interaction raises questions about possible limitations in precisely modelling real-world dynamics.

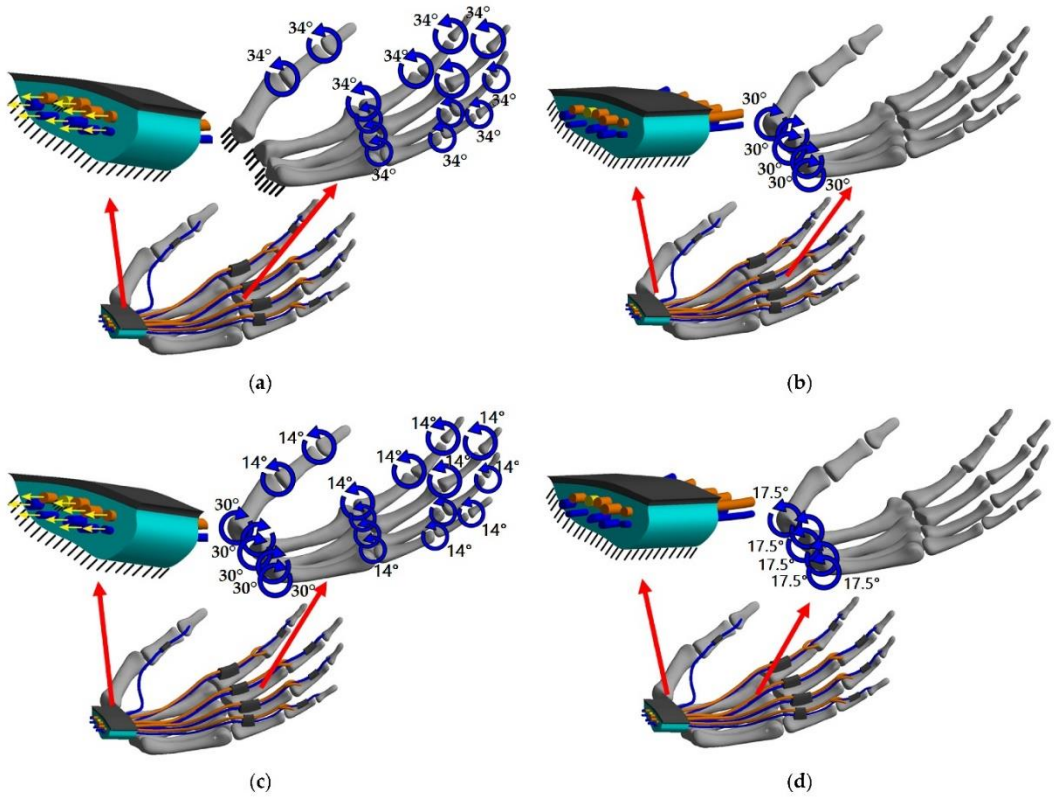

Figure no.6 Boundary conditions for four cases (a) flexion (fingers) (b) extension (wrist) (c) extension (wrist) and subsequent flexion (fingers) (d) flexion (wrist) [17]

Yu, Lu, et al. [18] examined the repercussion of transverse carpal ligament (TCL) transection site on the biomechanical characteristics and properties of the carpal arch structure. The idea was to promote carpal arch compliance (CAC) location-specifically by executing carpal tunnel release. In this work, a pseudo-3D model of the volar carpal arch structure was created using SolidWorks computer-aided design and examined using ABAQUS CAE for the Finite Element (FE) analysis shown in figure no.7. Anatomical features included in the model were the transverse carpal ligament (TCL), skin, fat, thenar muscles, and hamate and trapezium bones. Using ultrasound scans of a cadaveric hand, tissue segmentation was done by hand. The literature and experimental data were used to assign material characteristics. The response of the model was evaluated by varying the intra-tunnel pressure using the

To determine the optimal mesh parameters, mesh convergence experiments were conducted in the FE simulation. This study investigated the effects of different transection locations in TCL on Carpal Arch Compliance (CAC). In the first set of experiments, transections were performed at the central position (C), 4 mm radially (CR) and ulnarly (CU) from C, and 8 mm radially (R) and ulnarly (U) from C. The second set involved transecting the ulnar region of the TCL at 1 mm intervals from the center site (U1–U8). Mesh convergence analysis was employed to ensure accurate results. Carpal arch areas were measured under various intra-tunnel pressures, and CAC was determined using linear regression analysis based on the slope of the linear regression equation.

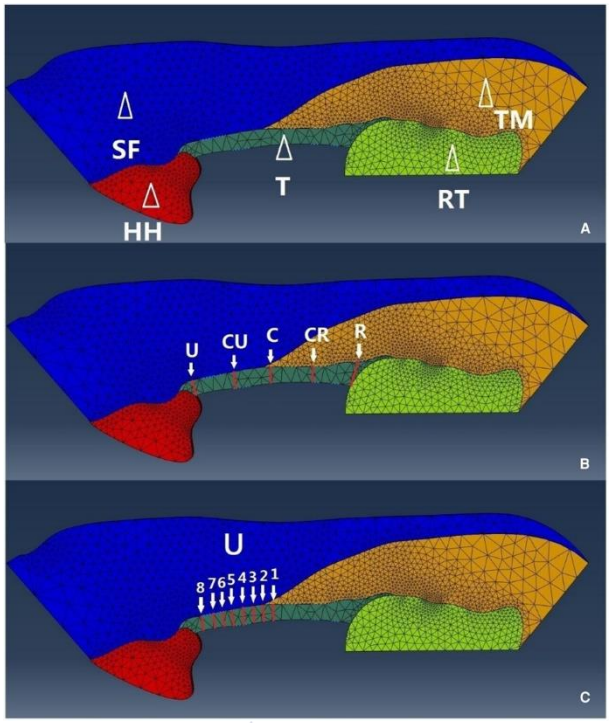

Figure no.7 (a) Based on an ultrasound scan, the FE model of the volar carpal tunnel (b) Transection position on the TCL denoted as U, ulnar; CU, central-ulnar; C, central; CR, central-radial and R, radial (c) On the ulnar half of the TCL, the transection location is designated from 1 to 8.[18]

According to the study, the site of the transection on the ulnar half of the transverse carpal ligament (TCL), which is frequently done during carpal tunnel release procedures, would not have a major effect on the improvement in carpal arch compliance (CAA). The study discovered that CAA stayed comparatively constant at many points (U1–U5) on the ulnar side of the TCL, in contrast to the conventional method, which focused on the ring finger's radial boundary. For this reason, optimizing carpal tunnel space during the treatment may not need surgeons to pinpoint the exact placement of the transection inside this area. Limitations of this work include that the research may have underestimated pressure changes during surgery because it failed to take into consideration the interacting effects of intra-tunnel pressure and TCL transection. Furthermore, A complete 3D model is required for more accurate evaluations, as the pseudo-3D FE model's emphasis on the distal level of the carpal tunnel limits its capacity to accurately represent volumetric changes following carpal tunnel release. One drawback is that the model only considered the intra-tunnel pressure as constant, without considering how it interacts with TCL transection. Moreover, the pseudo-3D model primarily concentrates on the far end of the carpal tunnel, so it does not display any volume changes following CTR.

Oflaz, H. and Gunal, I. et. al designed a model in which a 3D model of a wrist was made by reconstructing CT images from a 25-year-old man's wrist. The images, considered normal by a radiologist, were taken with the wrist and forearm positioned neutrally. The DICOM images were used in Mimics 17.0 to create 3D models, which were then turned into solid parts for analysis in ANSYS 16.1. The researchers made the radius and ulna stay still like stiff objects, giving them properties of hard and spongy bone.[19] They represented ligaments as springs that can bend. They tested the wrist bones with different wrist movements and compared the results with other

studies. They then measured the highest amount of pressure on the bones in different wrist positions. The research discovered that the radius carried 79% of the wrist load, while the ulna carried 21%. In the radiocarpal joint, the load distribution was 62% scaphoradial, 17% lunoradial, and 21% lunoulnar. In the midcarpal joint, the triquetrolunohamate interface bore the highest load at 44%. Depending on the wrist position, the trapezium bore the highest loads in neutral and ulnar deviation, while the scaphoid bore the highest loads in radial deviation and extension. Certain wrist bones experience pressure when they move, like the lunate and triquetrum bearing weight towards the center when bending and straightening, while other bones bear weight towards the sides in different positions.[20]

In 2023, Peng and his team used finite element analysis to inspect about the correlation of shear wave speed in transverse carpal ligament (TCL) and carpal tunnel pressure. They developed a 3D model of the carpal tunnel with the TCL and structures around them resembling a real carpal tunnel in the human hand. In shear wave elastography simulations, they determined the shear wave speed at multiple pressure levels in the tunnel. they measured the shear wave speed at various pressure levels within the tunnel. This points to the fact that this technique could perhaps help in the observation of pressure levels without using invasive procedures. However, the finite element model does have its drawbacks due to the fundamental assumptions taken which does not take the actual varying conditions of the material properties and boundary conditions of the carpal tunnel taken in practical life situations into account. Therefore, further research with more detailed models and empirical validation is recommended.[21]

Table no.2 Review Matrix of Biomechanical models of human hand affected by CTS

Paper No.	Year	Author	Title of Article	Research Problem	Proposed Technique/Method used	Drawback of technique
[15]	2007	X. Guo, Y. Fan, and Z.-M. Li	Three-Dimensional Finite Element Analysis on the Morphological Change of the Transverse Carpal Ligament.	To create a three-dimensional carpal tunnel finite element model to investigate how the transverse carpal ligament's (TCL) mechanical characteristics impact the morphological alterations of the ligament under mechanical stresses.	Three-dimensional finite element analysis (FEA).	Model complexity and accuracy, linear material assumption and validation
[15]	2017	Walia, Piyush, Ahmet Erdemir, and Zong-Ming Li.	Subject-Specific Finite Element Analysis of the Carpal Tunnel Cross-Sectional to Examine Tunnel Area Changes in Response to Carpal Arch Loading	Investigating the biomechanical response of the carpal tunnel to directional variations of force applied at the hook of hamate	MRI-based geometric reconstruction, experimental data collection, inverse finite element analysis for material property	Simplified tissue representation compromises anatomical accuracy. wo-dimensional model restricts representation of full

					determination, and finite element modeling for simulation purposes.	biomechanical complexity.
[17]	2023	Peshin, Saveliy, Yulia Karakulova, and Alex G. Kuchumov.	Finite Element Modeling of the Fingers and Wrist Flexion/Extension Effect on Median Nerve Compression	Simulating the impact of tendons movement caused by fingers flexion on Carpal Tunnel Syndrome (CTS)	Biomechanical modelling, Finite Element Analysis	The absence of consideration for wrist muscles and finger extensor tendons, which resist flexion, may have underestimated pressure in the carpal tunnel.
[18]	2023	Yu, L., Jia, J., Lakshminarayanan, K., Li, Y., Gan, Y. and Yao, Y.	A finite element analysis of the carpal arch with various locations of carpal tunnel release	To figure out how cutting the transverse carpal ligament at various sites impacts the flexibility of the carpal arch during carpal tunnel release surgeries.	pseudo-3D model of the volar carpal arch using SolidWorks and conducting Finite Element (FE) analysis with ABAQUS CAE	Ignoring changes in volume within the carpal tunnel after transection the transverse carpal ligament and assuming the pressure inside the tunnel remains constant.
[20]	2018	Oflaz, H., & Gunal, I	Maximum loading of carpal bones during movements: a finite element study	Stress points on maximum loading points of carpal bones.	A finite element wrist model, Biomechanical modelling	Model used in this study is with healthy individual. This can be overcome by some pathological conditions.
[21]	2023	Peng, L., Wu, Y., Lakshminarayanan, K., Zhang, A., Gan, Y., Li, Y., & Yao, Y.	The relationship between shear wave velocity in transverse carpal ligament and carpal tunnel pressure: A finite element analysis	Elevated Carpal Tunnel Pressure measurement which cannot be achieved non-invasively, can be done by finding shear wave velocity and in transverse carpal ligaments (TCL) and carpal tunnel	Subject-specific carpal tunnel finite element model reconstrued by MRI imaging	Ignoring the viscoelasticity in the instantaneous response of TCL deformation under impulsive force.

				pressure		
[22]	2022	Anderson, D. A., Oliver, M. L., & Gordon, K. D.	Carpal tunnel volume distribution and morphology changes with flexion-extension and radial-ulnar deviation wrist postures	The potential imperfection of carpal tunnel volume (CTV) as a measure to abduct the effects of subtle non-neutral wrist postures on carpal tunnel syndrome.	Morphological, volume and statistical analysis to evaluate distribution of carpal tunnel volume with changing wrist posture.	Dividing of tunnel length evenly in quartiles however in reality, tunnel length does not divide in evenly pattern

Electrophysiological Modelling

Cheever et al. (1995) developed a mathematical model that describes the pathophysiology of Carpal Tunnel Syndrome (CTS), a cumulative trauma condition. Cheever and colleagues proposed a mathematical model equation that gives the radius of the median nerve changes throughout the disease progression. Following is the Equation (3) which is used to estimate the carpal tunnel pressure non-invasively. [23]

$$r_n = r_{n_o} e^{c\left(2-4\pi K^* \sum_{t=1}^{9} \frac{r_o\left[e^{\beta_t T_w E_w} - e^{\alpha_t T_r \theta_t}\right]}{r_o\left[1+e^{\beta_t T_w E_w} - e^{\alpha_t T_r \theta_t}\right]}\right)} \quad (3)$$

Where, r_n= the radius of the median nerve, c= the coefficient that manages how much the size decreases when the pressure increases, β_t= growth coefficient, E_w= the work level is connected to the energy produced by the wrist system in each unit of time, T_w= work time with repetitive work, α_t= recuperative coefficient, T_r= rest time, and θ_t= carpal tunnel homeostatic coefficient. This study was observed with the limitation that the carpal tunnel's inelastic closed compartment model was dissatisfied, consequently an elastic compartment model is offered. However, this model presents a novel viewpoint but validation of their empirical data and clinical studies with its accuracy and suitability were mislaid. [23]

Tekieh, Tahereh, et al. (2016) examined the electrophysiological consequences of deformation by simulating the propagation of action potentials in a compressed neuron. They investigated the effects of different axon structural deformation levels on propagation speed, refractory time, and action potential breadth using a modified cable equation. To include the impact of various ionic compartments, researchers incorporated the effects within the HH model. The model includes the following Equation (4) and (5). [24]

$$\left(C_m \frac{\partial V_m(z,t)}{\partial t} + I_{ion}\right)\frac{ds}{dz} = \frac{r}{2(R_e+R_i)}\frac{\partial^2 V_m(z,t)}{\partial z^2} + \frac{1}{(R_e+R_i)}\frac{dr}{dz}\frac{\partial V_m}{\partial z} \quad (4)$$

Where, C_m=membrane's capacitance,

These simulations, however, may fall short of accurately representing the intricate biomechanical and physiological dynamics that exist in vivo since they rely on assumptions and simplifications. To validate their conclusions against experimental data, more validation is required to ensure their correctness. [24]

Colmenares, Sergio, et al. [25] used a mathematical model and related interface to simulate and measure carpal tunnel syndrome through the median nerve electroneurography. Numerous studies have replicated the typical actions of muscles and nerves, but none have measured the negative reactions. By creating a mathematical model to mimic the anatomical reaction to CTS, Sergio and colleagues sought to

close this gap. The process entails building an interface using a mathematical model that was constructed using five equations. This interface simulated the pathophysiology in conjunction with two 3D models. The values stated in the literature were the model's design goal.

Snarrenberg et al. [26] proposed that surgery is one option for treatment of CTS, although the main goal is to relieve symptoms. It is difficult to make a diagnosis based only on symptoms, thus more accurate indicators are required. In the absence of other information for a prediction model, their work suggests the possibility of employing conduction delay measures as a clinical tool for detecting nerve compression in carpal tunnel syndrome. This is because higher conduction delay is correlated with clinically observable nerve compression. Although there is potential here, this method's efficacy depends on the existence of a link between conduction delay and clinically detectable nerve compression, which may not always be the case. The study also notes that more information and validation are required in order to create a completely predictive model. [26] The aim of this study was to gain insight into slower nerve conduction in carpal tunnel syndrome it targeted the delay that occurs when an action potential is conducted. They built a simulation of an active node and myelinated segment on a hypothetical nerve axon. The voltages at each of the nodes were calculated using Equations 5, 6 and 7 (Hodgkin-Huxley cable equations 5, 6 and 7) upon which we applied a zero-density weighting scheme during computation as recommended in literature. Using this equation, the model introduced scalp compression from MR images and previous simulations with various levels of pressure. That approach could allow doctors match nerve compression seen in people with delays of nerves signals, possibly improving the detection and treatment of Carpal Tunnel Syndrome (CTS).

$$C_m \frac{dV_1}{dt} = I_\circ - g_{Cl}(V_1 - E_{Cl}) - g_k n^4 (V_1 - E_k) - g_{Na} m^3 h (V_1 - E_{Na}) - g_i (V_1 - V_2) \quad (5)$$

$$C_m \frac{dV_n}{dt} = -g_{Cl}(V_n - E_{Cl}) - g_k n^4 (V_n - E_k) - g_{Na} m^3 h (V_n - E_{Na}) - g_i (V_n - V_{n+1}) \quad (6)$$

$$C_m \frac{dV_{end}}{dt} = -g_{Cl}(V_{end} - E_{Cl}) - g_k n^4 (V_{end} - E_k) - g_{Na} m^3 h (V_{end} - E_{Na}) - g_i (V_{end-1} - V_{end}) \quad (7)$$

To measure conduction delay, researchers found the highest point of the action potential at nodes 1 and 100, and then we subtracted the times they occurred. The researchers initiated their study by setting a baseline without any pressure and then calculated the rise in conduction delay associated with each pressure type. During the experiment, they measured conduction delay values at various sensory and motor points in the palm, wrist, and elbow. Because of the elongated greater distance from the designated location of wrist compression, the stimulus in the palm is apportioned as a reference. Comparison of the percentage increase in conduction delay is made thereafter between individuals with mild Carpal Tunnel Syndrome (CTS) and those without the condition. [27]

According to Sundar et. al, [28] Sundar and colleagues conducted a study, on diagnosing Carpal Tunnel Syndrome (CTS) that centered on nerve fibers. They utilized surface electrodes to target these fibers selectively. By employing models and simulations in MATLAB they determined the required stimulation intensities, for nerve fibers of varying sizes. The research revealed that smaller fibers could be activated with stimulation levels whereas higher current levels impeded the fibers. These findings indicate that doctors can assess CTS severity by analyzing the size and velocity of nerve signals in both healthy individuals and those affected by CTS. [29] This method allows for gauging the severity of CTS and identifying the affected nerves. Research shows that an increment of a stimulus strength gives a discharge in the larger nerve fibers first before giving in the smaller ones. It was shown by research that as the stimulus current increases, more nerve fibers start out

activated first are large ones, then small. As stimulation intensity increases, the bigger fibers are blocked sooner than small ones and smaller fibres continues to be take off. The study also shows that fibers as small as 9 μm in diameter with conduction velocities of 35 m/s can be selectively activated. It also investigates the impact of nerve-fiber thickness on the block-signaling threshold. It improves the assessment of CTS severity by comparing nerve signal strength and timing in people with (or without) Carpal Tunnel Syndrome (CTS). Less involvement of the larger nerve fibers would be indicative of milder CTS, while damage to smaller fibers implies more severe cases. [30]

Table no.3 Review Matrix of Electrophysiological models of human hand affected by CTS

Paper No.	Year	Author	Title of Article	Research Problem	Proposed Technique/Method used	Drawback of technique
[23]	1995	Daniel H. Cheever	A mathematical model of the pathophysiology Of carpal tunnel syndrome	A mathematical model accurately shows how carpal tunnel syndrome affects the body.	The approach dependent on a mathmetical model that dipicts how tissue moves, nerves get squeezed, and fluid flow in carpal tunnel.	The inflexible closed compartment design of the carpal tunnel did not work well.
[23], [24]	2016	Tekieh	Are Deformed Neurons Electrophysiologically Altered? A Simulation Study	Determine whether mechanical deformation of neurons leads to changes in their electrophysiological properties through simulation studies.	Use of simulation studies to create models of neurons experiencing mechanical deformation and study their electrical properties.	Simulations lack in vivo accuracy.
[25]	2018	Colmenares, Sergio	Carpal Tunnel Syndrome Electroneurography, modeling and simulation	To explore how electroneurography, modeling, and simulation can help us learn more about the causes and diagnosis of Carpal Tunnel Syndrome.	Using electroneurography along with modeling and simulation techniques to study and understand the CTS phenomena.	Modeling neurophysiological processes' complex assumptions
[26]	2018	Snarrenberg	Modeling Nerve Compression in Carpal Tunnel Syndrome	To mimic nerve compression in carpal tunnel syndrome to better understand its effects on the body and explore treatment options.	Using computer modeling techniques to imitate and study nerve compression in carpal tunnel syndrome by combining clinical information and physiological factors.	Model simplification for accuracy
[28]	2006	Swarna Sundar, José A.	Selective Activation of Small Nerve	To explore how a method called anodal blocking,	Using McNeal's model and MATLAB simulations to find out	There is a chance that the depth of the median nerve varies

		González-Cueto	Fibers for Assessing Carpal Tunnel Syndrome	using tripolar surface electrodes, can activate specific areas.	the levels of stimulation and blocking for various sizes of nerve fibers using a tripolar surface electrode setup, then comparing CNAP parameters to identify the severity of CTS	among people, which can impact blocking thresholds. Using simulations instead of testing on living organisms is also a common practice. Furthermore, getting accurate CNAP values involves collecting data from healthy individuals, which may vary depending on their age and gender.

Challenges and Future Directions

The human hand is composed of numerous small bones, joints, tendons, muscles, and nerves, necessitating clear images and detailed anatomical information for accurate modeling. In mimicking the movements and actions of the hand during activities, replicating these complex interactions is daunting. Imaging a cadaveric hand with high resolution MRI and 3D ultrasound is necessary to obtain finer detail of anatomical movements and nerve branching. Live imaging of the hand allows better-calibrated simulations of how the hand is moving, and biomechanical models of how the nerve connections act. Each person's 'individuality' contributes to pathology and, with a consideration of the unique hand anatomy and physiology, it is difficult to develop and reliably affirmed diagnostic models for disease states, such as CTS. The placement of nerves within the confines of connective tissue is unique to each patient, and as a result, traditional diagnostic methods could lead to under- and over-diagnosis. This variation in nerve location, as well as in surrounding tissue characteristics and responses to stimuli, highlights the need for personalized approaches in order to improve the accuracy of diagnosis and aid in determining the most effective treatment options. For example, the development of models that reflect this unique anatomy and physiology both from an electrical and mechanical perspective will aid in establishing a definitive diagnosis and allow for individualized treatments of these complex conditions. The challenge in these models is that they will need to accurately simulate nerve electrical activity and tissue mechanisms that respond to stimuli under a wide set of conditions. We know that simulating an actual hand and its condensed nerve wrappings presents difficulties in verifying results from the models; we require validation by performing tests on patients. Although we will not need to do an invasive testing protocol on every patient to test the location and response activity of nerves in one part of the hand based on our model, it will be necessary to go back to the clinic to rigorously confirm the accuracy of the model when it is applied to real patients and determine the condition. Close collaboration between modelers and doctors is crucial to ensure that the models are realistic and practical in medical settings. This collaboration will help develop tools that improve the diagnosis and treatment planning for conditions like Carpal Tunnel Syndrome and other related disorders.

Conclusion

In conclusion, this review has combined information from many studies on different methods to model the median nerve for carpal tunnel syndrome. The main ideas that came up are various ways to diagnose CTS using different modeling methods. Carpal Tunnel Syndrome can

be diagnosed non-invasively by developing the models as nerve conduction studies, electrophysiological models and biomechanical models. Amongst biomechanical models, researchers put their best effort to diagnose CTS with certain techniques and methodologies. Peshin et. al showed how moving tendons in the fingers affects Carpal Tunnel Syndrome (CTS) through simulation, outperforms the other researches based on finite element modeling and analysis in several ways. This study improves upon past research in analyzing fingers and wrists using finite element analysis (FEM) by creating detailed models based on MRI data from individual patients. These models make the simulations more accurate. Unlike other studies, this research uses hyper elastic materials to represent soft tissues, making the mechanical behavior more realistic. The study concentrates on how the median nerve is compressed during different movements of the wrist and fingers, a detail that hasn't been looked at closely in previous studies. With respect to electrophysiological modelling, Snarrenberg et. al imitated nerve compression in carpal tunnel syndrome to learn more about its impact on the body and ways to treat it. Snarrenberg's research surpasses the findings of Cheever et al. and Takieh et al. by concentrating specifically on Carpal Tunnel Syndrome (CTS) and examining the distinct mechanical factors involved in nerve compression for this condition. By using advanced computer models, Snarrenberg accurately imitates nerve compression, giving important information about how CTS develops. This study is very helpful for doctors and patients, focusing on useful mechanical details. Although Al Takieh and Cheever also give valuable information in their studies, Snarrenberg's research stands out for its thorough examination of CTS. By combining biomechanical and electrophysiological methods, the study provides a comprehensive understanding of the condition. Snarrenberg's work on CTS reinforce the interpretations of the median nerve compression and features the possible prerequisites of the customized plans for treatment in medical practice. Regardless of compelling contributions of researchers, considerable number of limitations are required to be recognized. Some of the important limitations include intricacy and precision of the models, presumptions related to material properties, validation of models to real world problems, accuracy related to simulating results, presumptions related to neurophysiological processes, and the simplification of models. Moreover, in the future, researchers need to concentrate on using better imaging methods, making models tailored to each patient, using models at different levels, improving computer techniques, and testing models in real medical trials. By doing this, we can fill the gaps in our knowledge and improve how we understand median nerve modeling for carpal tunnel syndrome. Overall, making progress in this field can result in better outcomes for patients, highlighting the significance of ongoing research. The progress made in this area can highlight the importance of research efforts in the end.

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