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"CLINICAL AND EXPERIMENTAL STUDY OF PERIPHERAL NERVE REGENERATION"

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GENERAL PART

INTRODUCTION

Surgical repair of peripheral nerve injuries is not a new concept. Reports of successful peripheral nerve repair appeared in the literature as early as 1836. Additional reports of successful case management punctuated the 19th century. The first controlled study of experimental injury and subsequent repair was performed in dogs by Howell and Huber in 1893. This was followed by a similar study performed by Sherren in 1908.

Interest in advancement of knowledge in the area of peripheral nerve injury was fostered by World War I. Management of extremity wounds included recognition of the importance of restoration of nerve function as part of the process of reconstructive surgery. Numerous reports of peripheral nerve repair resulted from the experiences of this war. Very few of the techniques described were compatible with our present understanding of nerve biology and regeneration after injury.

Working independently, Babcock and Bunnell proposed standardized surgical techniques for peripheral repair. These principles encompassed management of injured nerve tissue, surgical techniques for repair of the injury, and postoperative management. Much of the information presented in these reports forms the basis for operative management today. It was recognized that not all nerve injuries were amenable to direct end-to-end repair. Many injuries resulted in loss of nerve tissue and thus the formation of nerve gaps. To restore function after injury, the possibility of nerve tissue grafting was explored. Nerve grafting was first reported by Philipeaux and Vulpian in 1870. The first human allograft was reported in 1878 by Albert. Sherren wrote of his experiences with nerve grafting in 1906. Huber described autologous nerve grafting in the dog with good results as early as 1920. Grafting gained popularity in 1932 with the work of Ballance and Duel. Bunnell and Boyes reported on the use of digital nerve autografts in 1937. No uniform success was reported by these authors. Alternate

experimental methods for lengthening nerve stumps centered around mobilization and transposition of existing nerve tissue. It was recognized that regardless of technique used, excessive tension at the suture line would increase the probability of clinical failure.It was observed at this time that further advancement in the management of peripheral nerve injuries could be a product only of greater understanding in basic biology of peripheral nerves. Research in this area intensified during the 1930s and was stimulated by the anticipation of an upcoming global conflict. Much research performed during this time provided a basis for our current understanding of nerve degeneration, regeneration, and healing of surgical repair.

The last several decades have evidenced refinement in basic principles of nerve injury and repair. Based on an improved understanding of basic nerve biology, advances have been made in surgical repair and management. Continuous research in the area of suture material and biologic implants has contributed to increased clinical success in the management of peripheral nerve injuries. Use of the operating microscope has contributed to the advancement in reconstructive techniques. Suturing of individual nerve bundles and alternate techniques for macroscopic nerve repair are an outgrowth of this technology.

An investigation into technology and basic biologic principles has accompanied the study of nerve grafting techniques.

Research in autografting, allografting, and heterografting techniques has helped to provide answers that add to our knowledge of the factors that Contribute to the success or failure of grafting techniques. Ongoing research will provide answers to questions concerning the relationship of immunologic response to allografting techniques.

Finally, the application of alternate reconstructive techniques is under study. Transposition of nerve trunks may help to restore activity to denervated musculoskeletal areas. Direct implantation of nerve stumps into muscle tissue resulted in return of motor function. Both of these topics are current areas of research in the quest for answers to
questions related to basic biology and clinical restoration of peripheral nerve function.

BIOLOGY OF NERVE REPAIR AND REGENERATION MORPHOLOGY

The basic subunit of any peripheral nerve is the axon. The axon is an extension of the nerve cell body. Histologically, the axon may be seen as several distinct components. The center of each axon is composed of axoplasm, which is the cytoplasmic extension of the nerve cell body. As will be described below, axoplasm comprises several physiologically distinct zones that aid in transport of nutrients and essential biochemical components from the nerve cell body to the terminal axon and neuromuscular terminals. The cell membrane surrounds the axoplasm and is referred to as the axolemma. Surrounding this axoplasmic unit is the Schwann cell. The Schwann cell may invest one or more axoplasmic units. A myelinated nerve has a Schwann cell and associated structures surrounding one axoplasmic unit (1 u - 15 u diameter).

The plasma membrane of the Schwann cell forms a lamellar spiral around the axoplasm. The myelin sheath is a double spiral of lipoprotein that is contiguous to the plasma membrane of the body of the Schwann cell. The formation of myelin sheath occurs during development of the Schwann cell and is a product of cytoplasmic extrusion from the lamellae. Each Schwann cell and its associated myelin encase a histologically distinct zone. This area is referred to as an internode zone. Gaps appear between two internodes and are referred to as nodes of Ranvier. Branching of axons always occurs at this junction.

Unmyelinated nerves are not as well organized histologically. Multiple small-diameter nerve fibers (0.2u-2.0u) are invested by invaginations or pseudopodia of a Schwann cell. Evidence for a feedback mechanism from the axon to regulate the production of myelin by the Schwann cells has been documented experimentally.

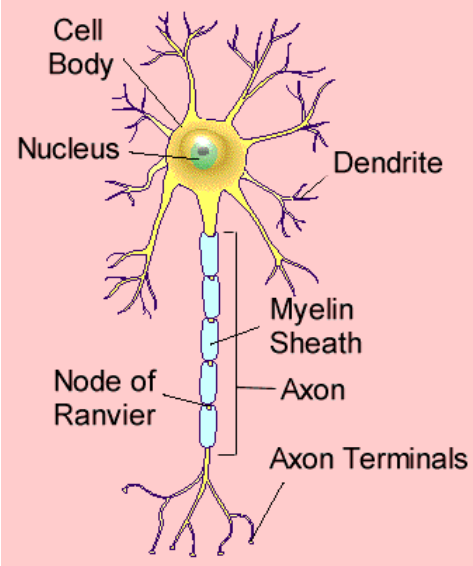


Fig. no. 1 – Neuronal structure

In regeneration after injury, the axon determines the degree and amount of myelin that the Schwann cell will produce.Enveloping the Schwann cell-axon unit is the basement membrane. This structure serves as a histologic demarcation between the neural and connective tissue elements of the peripheral nerve. Immediately adjacent to the basement membrane is the endoneurium. The endoneurium is composed of a fibrocytic stroma of a double layer of collagen, fibroblasts, and vascular components. It forms a tubular structure that surrounds the axon unit. In instances of injury, it does not degenerate as will axon components. Axons and associated endoneurium form aggregates that are referred to as nerve bundles, fascicles, or funiculi. A funiculus is enclosed by a collagenous envelope of larger diameter termed the perineurium.

The perineurium consists of 7 to 15 lamellae of fibrous connective tissue compressed into a tubular arrangement. The inner surface of the perineurium is lined with mesothelial cells. Within the funiculus, intrafunicular septae separate individual axon units. The function of these septae is not fully understood. The perineurium acts both as a diffusion barrier and as a lattice-work for vascular beds. Enclosing the bundles of funiculi is the outer covering of the nerve, the epineurium, which is a loose network of collagen, elastin, and fibrocytes. Much of the ability of the

peripheral nerve to undergo elastic deformation without rupture can be attributed to the tensile strength and elastic properties of the epineurium.

Funiculi are not arranged in simple uninterrupted strands along the course of a peripheral nerve. Frequent divisions and fusion with other funiculi form numerous plexuses along the course of the nerve tank. Redistribution is active along the entire length of the nerve but is particularly prominent in the proximal portion of the nerve trunk. Two types of funiculi are incorporated into every peripheral nerve. Simple funiculi are those that are composed of fibers that serve solely a particular muscle or cutaneous area. Compound funiculi are composed of axons from several sources in varying combinations and proportions. This feature allows for the integration of various funicular components that distribute to innervate specific anatomical regions. Several important considerations arise from this plexus formation. Unless complete transection of a nerve trunk occurs, partial function of the nerve may remain in cases of injury. Cross-sectional morphometric studies have indicated that funicular anatomy changes every 0.5 mm to 15 mm. If neural tissue is lost in the course of traumatic wounds, funicular continuity and alignment may not be possible at the time of surgical repair

The vascular supply to peripheral nerves is by small segmental nutrient arterioles that arborize into an extensive capillary network. The nutrient arterioles arise at irregular intervals and, as they course toward the peripheral nerve, are enclosed by a delicate connective tissue referred to as mesoneurium. Mesoneurium is analogous in function and certain anatomical features to the mesentery of the small intestine. All vessels entering the nerve do so at the mesoneurial border. After entry through the epineurium, vascular arborization and alignment parallel to the funiculi are noted. The second generation vessel aligns with the funiculus and courses parallel to the epineurial vessels. Tertiary arborization proceeds to supply individual axon units by means of an axon-capillary plexus. Multiple anastomoses between branches of perineurial and axon vessels ensure adequate collateral vascular supply in instances of segmental interruption. Peripheral nerve blood flow appears to be unaffected by autoregulation.

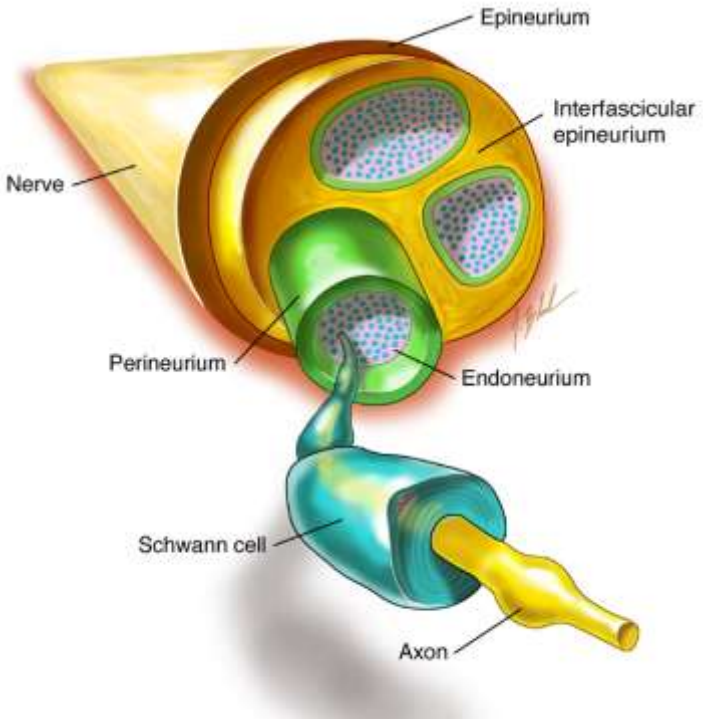


Fig. no. 2 – Nerve structure

The origin of the axon is the nerve cell body. The histologic components of the nerve cell body are the same as those of other cell types, including a centrally placed nucleus and surrounding substructures. The Golgi apparatus and mitochondria are histologically prominent within the cell. Other characteristic cell inclusions are classified as Nissl bodies or chromophil substance. Nissl bodies represent endoplasmic reticulum and associated polyribosomes. As will be discussed below, the role of these cellular components was misunderstood and improperly interpreted in much of the early work on the response of the cell body to injury.

Nerve cells may be classified as unipolar, bipolar, or multipolar. The configuration of the nerve cell can be associated with the function within the body. Sensory nerve cells of the dorsal root ganglion have a unipolar configuration in which one process exits from the nerve cell body and then divides into the dorsal root and afferent sensory branches, which The motor nerve is a sum of individual funiculi, which in turn are aggregates of axon subunits. Each axon is enclosed in a lamellar whorl of condensed lipoprotein classified as the Schwann cell. The intercellular zone is referred to as the node of Ranvier. Note the anatomy of regional vascularization

entering through the mesoneurium The neuromuscular junction is directly confluent with the sarcolemmal membrane. The postsynaptic invaginations (clefts) are the site of action for the biochemical transmitter acetylcholine.Bipolar nerve cells have one axon and one dendrite. They are located in retinal tissue. Motor cells of the ventral horn of the spinal cord are of the multipolar variety. One axon and multiple dendrites characterize this configuration. This cell type predominates in peripheral motor nerves.

There is a histologically distinct zone in which peripheral nerve tissue separates from the central nervous system. In this transitional area, the axons abruptly change envelope cell types from the central zone oligodendrocyte to the peripheral zone Schwann cell. The axons are enclosed by pia mater at this point, then subsequently pass through a dura mater tunnel and become enclosed in perineurium. This transition occurs in both dorsal and ventral roots. Microscopic evaluation of this pia mater-perineurial junction shows contiguous extension of the pia with the perineurium in a smooth layer transition. Efferent terminal motor units are of two types. Large diameter nerve fibers (alpha motor neurons) innervate the extrafusal muscle fibers. Alpha motor neurons subdivide at this juncture to supply innervation to multiple muscle fibers. These muscle fibers together with the terminal nerve branches are referred to as a motor unit. Gamma motor units supply intrafusal muscle fibers of the muscle spindle.

Their activity is influenced by basal muscle tone and control of sensory activity by the muscle spindle. Fine motor control is influenced by the number of motor unit components. The higher the ratio of motor units to muscle fibers, the finer control can be effected. This ratio is highest in extraocular muscles and lowest in skeletal musculature.

The neuromuscular junction is the transition zone from peripheral nerve to musculoskeletal systems. As the nerve approaches a neuromuscular junction, the sheath composed of myelin and the Schwann cell terminates. The cell membrane of the axon expands to form the terminal neural junction in association with the sarcolemmal membrane. A gap of 200 nm to 300 nm is noted on histologic evaluation and is referred to as the synaptic cleft. At the terminal border of the nerve, synaptic

vesicles filled with acetylcholine are opposed by invaginations of the sarcolemmal membrane classified as secondary synaptic clefts. From this area, release of acetylcholine and receptors for this chemical combine to transmit neural impulses to the musculoskeletal system.

Sensory receptors are the peripheral component of myelinated and unmyelinated afferent nerve fibers. These fibers, in turn, terminate in the dorsal spinal roots. The sensory receptors arise from skin, muscle spindles, joints, and other areas in which neural input is important for maintenance of homeostasis. They transduce various forms of energy into nerve impulses. These afferent impulses are integrated at the level of the spinal segment or at higher levels and evoke a response to compensate for the change in homeostasis. Of clinical importance in diagnosis of peripheral nerve disorders is the class of sensory receptors turned nociceptors. This class provides sensory input for recognition of noxious stimuli. In carnivores, a subcategory referred to as mechanonociceptors predominates. These receptors are influenced more strongly by mechanical damage than by thermal changes. When clinically evaluating peripheral nerve disease or injury, evaluation of nerve deficits by application of a noxious stimulus to nociceptors can aid in diagnosis of specific nerve injury.

The topography of cutaneous innervation is well documented for the hindlimb; however, some disagreement of zone boundaries for the forelimb still exists. This can be related to overlap of cutaneous nerve function in certain superficial regions. Cutaneous regions supplied by only one cutaneous nerve are referred to as autonomous zones. Some areas have a dual innervation from two or more peripheral nerve branches and are called intermediate zones. Knowledge of regional distribution is essential for correct diagnosis.

Mechanoreceptors predominate in joints and muscle spindle regions. Joint receptors detect acceleration in any direction of that joint and thereby provide input to compensate for gravitational influences. Muscle mechanoreceptors from the muscle spindle fibers and Golgi tendon organ at musculotendinous insertions represent sites of adherent input. These

receptors, along with alpha and gamma motor neurons and the spinal cord segment, form the arcade for segmental reflex evaluation.

NERVE PHYSIOLOGY

The axon consists of subunits that provide the vital functions of intracellular nutrition and transport of biochemical substances involved in the regeneration process following nerve injury. The proteins that make up this cytoskeleton are classified as microtubules, neurofilaments, and microfilaments. Microtubules are protein structures that possess an axial alignment with direction of the axion. Neurofilaments are of similar morphology; however, the internal diameter of the tube is narrower. Microfilaments have an actin component chemically related to contractile actin of skeletal muscle. Their orientation is both transverse and longitudinal with the long axis of the peripheral nerve.

These internal elements are important for the two types of substance transport within the nerve cell. By far the majority of proteosynthesis and nutritive substances are produced in the nerve cell body. Early experimental work in nerve injury and regeneration indicated that the average growth of the nerve was I mm to 3 mm per day. From this work, it was inferred that axoplasmic migration occurred in the direction from the nerve cell body to the periphery; this migration was classified as axoplasmic flow.This concept was accepted until certain observed phenomena could not be explained by the prevailing theory.

Following experimental constriction of peripheral nerves, swelling proximal to the constriction site occurred earlier than anticipated by calculated axoplasmic flow. Radioactive labeling of protein components using amino acids and tritium revealed migration as rapid as 410 mm per day in sciatic nerves. The rapidity of transport and organization provided the basis for recognition of a second type of motion, axonal transport. The function of axonal transport is movement of neurotransmitter substances and axolemmal replacement material from the nerve cell body to the periphery of the nerve. However, it has been deduced that axonal transport is not unidirectional. Retrograde as well as antegrade flow of materials can

occur in the microtubular network. This observation may aid in the explanation of retrograde migration from the periphery of central nervous system agents such as rabies, herpes viruses, and tetanus toxin. The normal function of retrograde transport is the return of cell membranes to the cell body for degradation or resynthesis and return of a portion of synaptic vesicles to the nerve cell body for recycling. The rate of retrograde transport is one half to two thirds that of antegrade conduction.

Axonal transport occurs by means of the cytoskeleton network described above. Although no definitive work has been done, it is postulated that motion imparted by one of several mechanisms provides the basis of propulsion down one microtubular or neurofilamentous track. Tracks probably have polarity so that only unidirectional flow can occur. The basis for propulsion is probably actin filaments arranged around the tubulofilamentous network that provide peristaltic waves or plasma flow changes to propel units up or down this network. Further work is needed to elucidate the exact transport mechanism and the relationship, if any, to maintenance or activity of the excitable neural membrane.

Nerve tissue has dynamic properties similar to any excitable membrane. A peripheral nerve may be thought of as an electrical conduit in which impulses are conducted from a central terminal (light switch) to an effector organ (light). The event that is produced by conduction of this impulse is referred to as an action potential. An action potential can be conducted only when the cell membrane is in an excitable state. This is achieved by development of concentration differences for sodium and potassium ions across the cell membranes. Maintenance of this differential by the sodiumpotassium pump within the cell membrane imparts an electrical differential across the cell membrane of - 85 mV. The value, referred to as a resting potential, remains in a stable state until a stimulus sufficient to create threshold occurs. When the threshold value is reached, activation of the cell membrane occurs.

Configurational changes in the membrane pore rearrange "gates" to allow for sodium ion influx. The membrane then depolarizes and transmits the length of the axon in either direction. This phenomenon is referred to as the "all-or-nothing" principle and states that once depolarization begins at

any point on the nerve, the entire membrane is obligated to depolarize. The rate of this propagation is referred to as nerve conduction velocity. Factors commonly involved in the speed of conduction include fiber diameter, degree of myelination, and membrane temperature. The effect of these factors on peripheral nerve conduction will be discussed below.

Repolarization always begins at the same point at which depolarization occurred. Efflux of potassium ions from cytoplasm to cell membrane surface allows for re-establishment of appropriate ionic barrier charge. Potassium ion is then exchanged for sodium ion by the sodium-potassium pump to reestablish baseline continuity of ion balance.

The velocity of depolarization depends upon the presence of organized myelin structure in the nerve fiber. Myelinated nerves have concentric layers of Schwann cell membranes interspersed by sphingomyelin. As noted above, histologic gaps occur at intervals between the Schwann cell units. These gaps are classified as nodes of Ranvier and constitute an important element in nerve impulse conduction. Schwann cell units with associated myelin are analogous to electrical insulation. Owing to its increased transmembrane potential, impulse conduction does not occur along the entire length of the nerve but only at the nodes of Ranvier. The cell membrane in this area is especially permeable to ion exchange and can aid in rapid impulse conduction. As an impulse travels along the surface of the cell membrane, its transmission occurs at the nodal junction and jumps from node to node in a manner classified as saltatory conduction. Because of the jumps in impulse transmission, velocity of conduction in a myelinated axon is greater than in its unmyelinated counterpart.

An additional benefit of saltatory conduction is the conservation of energy for the axon, accomplishing conduction with less of fewer ions than standard excitable tissue. This allows for more rapid repolarization with minimal energy expenditure. Unmyelinated nerves have no organized mechanism of saltatory conduction. Impulse propagation occurs in an organized sequential manner involving the entire membrane of the axon. Membrane depolarization is accompanied by an ion-exchange current across the cell membrane surface. This flow of ion exchange is described

as an eddy current. Speed of depolarization of the cell membrane by eddy currents is influenced by axon diameter. A larger cross-sectional diameter of an unmyelinated nerve allows for a larger current flow and faster local excitation and results in a higher conduction
velocity.

If an electrical impulse is applied to a nerve trunk and an oscilloscopic recording of this event is made, a characteristic wave form will be seen. This wave form is a summary of individual nerve fiber types and is termed a compound action potential. An analysis of this compound potential shows several distinct subunit waveforms. The earliest wave deflection reflects conduction of the largest-diameter myelinated nerve fibers. These fibers are classified as type A fibers and include three subcategories. Alpha waves represent the largest-diameter myelinated motor fibers and sensory fibers from muscle spindles. Beta waves represent sensory fibers from skin sensory receptors. Gamma waves are produced by gamma motor fibers arising from intrafusal muscle fibers of the muscle spindles.

As the impulse reaches the synaptic junctions, acetylcholine is liberated from storage vesicles, transverses the synaptic cleft, attaches to receptor sites on the secondary folds of the synaptic clefts, and initiates endplate potential formation.

This potential, in turn, initiates sarcolemmal depolarization and muscle contraction. After diffusion from the receptor site, acetylcholine is degraded by the enzyme acetylcholinesterase. The component substances are then metabolized or recycled to form new acetylcholine.

Sensory conduction is initiated by peripheral receptors and is conducted centrally to the dorsal spinal root. The impulse then initiates reflex arcs in the segmental gray matter and may be transmitted for further integration to the higher centers by internuncial neurons.

CLASSIFICATION OF NERVE INJURY

As interest in diagnosis and therapy of peripheral nerve injuries increased, a need arose to standardize the description of types of injury evaluated in clinical practice. The classification presented below is based on indirect diagnostic methods that include history, physical examination, including neurologic examination, and ancillary diagnostic techniques as represented by electrodiagnostics. The classification acts as a guideline for clinical assessment and prognostic evaluation related to medical or surgical management of the injury. The use of this classification can correlate, in addition, changes in neural tissue related to the injury process.

Table no. 1 – Classification of nerve injuries

	Severity	Description	Tinel Sign	Progress Distally	Recovery Pattern	Rate of Recovery	Surgery
First	Neurapraxia	Demyelination with restoration in weeks	—	Fast	Complete	Fast (days to 12 wk)	None
Second	Axonotmesis	Disruption of axon with regeneration and full recovery	+	+	Complete	Slow (3 cm/mo)	None
Third		Disruption of axon and endoneurium causing disorganized regeneration	+	+	Varies*	Slow (3 cm/mo)	Varies
Fourth		Disruption of axon, endoneurium, and perineurium, with intact epineurium and no regeneration	+	—	None	None	Yes
Fifth	Neurotmesis	Transection of the nerve	+	—	None	None	Yes
Sixth	Neuroma-in-continuity	Mixture of one or more of the above conditions	Varies by fascicle, depending on injury				

*Recovery is at least as good as nerve repair but varies from excellent to poor, depending on the degree of endoneurial scarring and the amount of sensory and motor axonal misdirection within the injured fascicle.

The mildest form of nerve injury is classified as neuropraxia. An acute insult to the peripheral nerve results in interruption of impulse transmission. Clinical evaluation will show sensory and motor deficits in the region that is innervated by the injured nerve. Partial function may be noted, with an imbalance between degree of sensory and motor deficits

noted on examination. Evidence of neurogenic atrophy of muscle fibers is usually not present. Histologic evaluation of tissue shows only minor morphologic alterations that are of a reversible nature. It has been proposed that microvascular alteration resulting in transient ischemia produces this class of injury. Recovery is accomplished with conservative therapy and occurs over a variable time period but is usually complete within 21 days of injury. This time is faster than that expected by regeneration following wallerian degeneration, as will be noted below.

If there is physical disruption of one or more axons without injury to stromal tissue, the injury is described as axonotmesis This type of injury is generally noted in conjunction with closed long-bone fractures in humans. In this type of injury, the axoplasm and cell membranes are damaged; however, the Schwann cell and connective tissue elements remain intact. Clinical evaluation will reveal deficits related to the zones innervated by the damaged axons. Loss of sensory and motor function will be dependent upon the number and type of injured axons. After the 90th hour post injury, no conduction of electrical potentials past the site of injury will be seen. Neurogenic atrophy of skeletal muscle will be evident in the injured autonomous branch.

Neurotmesis refers to complete severance of the peripheral nerve trunk. Sensory and motor innervation to all autonomous branches of the injured nerve is lost . Clinical and diagnostic evaluation will show complete loss of clinical function of the nerve. Histologically, degeneration of all axons occurs distal to the site of injury. Axons will also manifest degenerative changes for one to two nodes of Ranvier proximal to the site of injury. Except in rare cases, spontaneous recovery from lesions of this class does not occur.As can be noted from the classifications of injuries described above, certain types of injuries border on more than one category. In an attempt to improve and further define types of peripheral nerve injury, an alternate classification by degree of injury was later proposed. The advantage to this classification is that description of injury to individual components of the nerve trunk can be accounted for more accurately. A first-degree injury correlates with neuropraxia. A second-degree injury is one in which only the axon is disrupted. A third-degree

injury involves the axon and associated endoneurial tube while the nerve funiculus remains intact. A fourth-degree injury disrupts axons, endoneurium, and funiculi while the epineurial sheath remains intact. A fifth-degree injury is evidenced by complete severance of the nerve trunk.

Although not all aspects of the classification systems can be appreciated on a clinical basis, certain parallels between clinical presentation of injury and severity of peripheral nerve damage may be drawn. In cases of blunt compression injury to soft tissue, it is likely that neuropraxia results from temporary peripheral nerve compression. This can produce temporary ischemia and loss of neural conduction. A mild form of injury of this class would be loss of sensation after steady pressure has been placed on a nerve trunk for a short period of time. Axonotmesis, or secondand third-degree peripheral nerve injuries, may be the sequel of closed long-bone fracture and traction injury to peripheral nerves from altered orthopaedic biomechanics. Neurotmesis, or fourth- and fifth-degree injury, may be associated with open long-bone fractures, penetrating wounds, and altered biomechanics resulting from trauma.

RESPONSE TO INJURY

Injury to a peripheral nerve triggers an initiation of a response that incorporates a sequence of biochemical and morphologic alterations. Each component of the injured nerve reacts in an individual manner to the injury process. The effects of injury may be categorized into those that involve:

(1) the spinal cord, particularly the ventral cell body;

(2) the proximal nerve stump;

(3) the distal nerve stump and its associated end-organs.

Ventral Cell Body

After injury, sequential histologic evaluation of the ventral cell body shows marked changes in response to injury. The size of the nerve cell body enlarges for 10 to 20 days after injury. This "hypertrophy" is visible for the course of the regenerative process, and "atrophy" back to normal size occurs once healing is complete. It was once accepted that this change in cell body size, along with changes in staining characteristics described below, represented nuclear degeneration of the injured nerve cell. Recent observations with electron microscopy, along with an improved understanding of nerve repair biology, now suggest that the alterations noted represent early induction of metabolic processes required for nerve regeneration.

The degree of cellular change is dependent upon the level of the lesion in relation to the cell body. If the level of the injury is close to the nerve cell body, proportionally more axoplasm is lost, and greater biosynthesis must occur for regeneration to result. A proximal injury may exceed the biosynthetic capability of the cell, thereby causing failure of regeneration. Distal nerve lesions do not activate the cell body to a high degree of biosynthesis. The nerve cell, therefore, is capable of limited regenerative potential without initiating severe changes in cellular metabolism.

Proximal Nerve Stump

If the nerve trunk has been severed, retraction of the stumps occurs owing to elastic tissue contained within the epineurial sheath. Hemorrhage and clot projection are evident immediately at the severed ends. Intraneural swelling due to tissue edema and exudation of acid mucopolysaccharides may be noted within one hour after injury. Acid mucopolysaccharides have an affinity for water and an indirect affinity for plasma, blood, and serum. The swelling and tissue constituents form a clot that is evident for 7 to 10 days.

The extent of degeneration in the proximal stump is related to the etiology of injury. Sharp lacerations or surgical wounds produce minimal proximal stump degeneration. Traction or jagged laceration injuries result in extensive degeneration. In either case, within 24 to 72 hours, neurofibrillar degeneration in a clean wound occurs for a minimum of two to three nodes of Ranvier proximal to the point of injury. Loss of axoplasmic components quickly follows during this time. The myelin sheath begins to lose its defined layered appearance and blends into a homogenous granular tissue that appears as a series of rings surrounding degenerating axoplasm. These contorted lamellar rings, which form hollow luminal structures, are classified as digestion chambers. Macrophage invasion begins to digest and remove degenerated myelin from the damaged nerve tissue. Schwann cells respond vigorously at this time and proliferate to form dense cords along the axis of the now digested axoplasm. These cords possess phagocytic properties and ingest clumps of degenerating axon, myelin fragments, and other cellular debris. Mesenchymal cells proliferate in response to the inflammatory process and initiate collagen deposition at the end of the proximal stump. This, in conjunction with fibrin remnants from the initial hemorrhage, may lead to formation of a neuroma.

Approximately 2 to 20 days after injury, axoplasmic regeneration may begin. This event is associated with the increased biosynthetic capabilities of the nerve cell body. Synthesis of new axoplasm is transported by migration along the remaining viable axon to the site of injury. The flow rate for this process is approximately 1 mm to 3 mm per day and advances by the intracellular fibrillar network described above. At

the site of injury, cellular proliferation of Schwann cells has already commenced. The Schwann cell outgrowth attempts to connect the proximal stump with the Schwann cell elements of the distal nerve stump. The Schwann cell attempts to grow concurrently with the axoplasm, thus providing a framework for axonal growth. If surgical realignment or nerve stump approximation does not occur, the migration axoplasm may form a neuroma, a meshwork of organized clot elements, mainly fibrin strands, that provides an errant scaffolding framework for axonal migration.

As the Schwann cells migrate distally, their pathway is deviated to align with the random fibrin clot at the nerve stump. The regenerating axons follow the Schwann tubules and continue the random growth pattern. Axoplasm migration in this disorganized tissue produces multifilamentous branching that attempts to seek the distal nerve stump.

Extraneural connective tissue may also produce ingrowth to the site of injury and can additionally distort and block the path of axon migration. In contrast, surgical repair of peripheral nerve injury permits smooth, unbranched axoplasmic migration into the distal stump. It is hypothesized that axoplasmic branching attempts to compensate for the neuroma roadblock to ensure axonal migration into the distal stump.

The Distal Nerve Stump

The entire distal stump undergoes a process of degeneration first described by Waller and referred to as wallerian degeneration. Within 24 to 48 hours after injury, axon thickening is evident histologically. An increase in acid phosphatase and nicotinamide adenine dinucleotide (NAD) diaphorase in surrounding myelin reflects increased metabolic activity. Evidence of axoplasmic fragmentation and clumping is noted at this time. Four to five days after injury, all axoplasm is absent, and myelin degeneration and clumping occur by a process similar to that described for proximal stump degeneration. Tissue macrophage invasion is noted during this period. The origin of the macrophage activity is thought to be connective tissue histiocytes and converted monocytes from the peripheral blood. This activity may last from 7 to 32 days after injury. After

macrophage and Schwann cell activity diminishes, only Schwann cells and connective tissue remain. These diminish with time, and total atrophy of the distal stump may occur 18 months after injury owing to the increased intertubular deposition of collagen, which reduces the diameter of the lumen of individual neural elements.

The proximal end of the distal stump deserves special note. The axons in this region tend to enlarge and isolate from the other portions of the degenerating nerve stump. This unit may survive for as long as 2 weeks prior to degeneration. As connective tissue elements proliferate in the early degenerative phase, endoneural fibroblasts intertwine in this isolated segment. This swelling is referred to as a glioma, schwannoma, or distal neuroma. Its gross appearance is not as marked as the previously described neuroma because it is composed solely of connective tissue elements originating from perineurium, endoneurium, and pleomorphic Schwann cells. With the passage of time, shrinkage of the glioma will occur in conjunction with distal stump atrophy.

Regeneration of axons in the distal stump occurs at a rate of 1 mm to 3 mm per day. This rate is variable depending upon the zone in which regeneration is occurring. Near the site of injury and at the motor endplate region, growth is slower owing to external factors. More rapid regeneration occurs in the body of the distal nerve stump. Extension of Schwann cell and connective tissue elements provides a pathway for migration of axoplasm filaments into the tubules of the distal stump. As regrowth of axoplasm into the distal stump proceeds, myelination of the Schwann cell envelope occurs in regions recently recannulated by axoplasmic elements. Marked enzymatic activity is present to aid in the myelination process. The presence of myelin sheaths is evident 6 to 7 days after regeneration has occurred in any zone Nodes of Ranvier appear after day 14 in the regenerative process. Apposition of myelin occurs for as long as one year following the repair process.

It is important to recognize that even under the best of circumstances, aberrant recannulation of the distal stump may occur. Transposition of sensory and motor components in a mixed-function nerve is a common sequel to injury. As the motor end-plate region is reached by

the advancing axoplasm, rapid division of the axoplasm occurs until a myoneural junction is formed.

FACTORS INVOLVED IN NERVE HEALING

Numerous reports in the literature attempt to assess various factors that contribute to successful nerve healing. Factors may be described as intrinsic, or those beyond control of the surgeon, and extrinsic, those in which clinical management may influence return of function.

Intrinsic factors include species, age, state of tissue nutrition, time since injury, type of injury, nerve or nerves involved,and level at which injury occurred. This information can be gathered from history and physical examination and may aid in prognostic evaluation. As has been discussed earlier, the time since injury, level of injury, and type of injury relate to factors concerned with nerve biology. Young patients heal more rapidly and to a more complete recovery, probably related to increased biosynthetic capabilities already present and to a greater capacity for adaptation. Tissue nutrition is important to meet anabolic requirements related to the regenerative process.

Extrinsic factors relate to surgical and postoperative management of nerve lesions. Attention to surgical technique and appropriate selection of instrumentation and suture material can contribute to return of function.

DIAGNOSIS AND RECOGNITION OF NERVE INJURIES

A careful history regarding nerve injury provides important information aiding in treatment and in predicting outcome. Patient age and mechanism of injury are well-known to affect outcome after nerve repair. As part of the medical history, a careful assessment of comorbid conditions that detrimentally affect the peripheral nervous system is important.

Table no. 2: Selected Muscle Evaluation for Diagnosis of Motor Nerve Injury

I.	Median nerve: intrinsic
	A. Thumb-palmar abduction (abductor pollicis brevis)
II.	Median nerve: extrinsic
	A. All flexor digitorum sublimi
	B. Flexor profundus digitorum to index
	C. Flexor pollicis longus
	D. Flexor carpi radialis
III.	Ulnar nerve: intrinsic
	A. First dorsal interosseous muscle
	B. Muscles of the hypothenar eminence
IV.	Ulnar nerve: extrinsic
	A. Flexor digitorum profundus, small finger
	B. Flexor carpi ulnaris
V.	Radial nerve: extrinsic
	A. Wrist extension (extensor carpi radialis brevis and longus, extensor carpi ulnaris)
	B. Extension of fingers at metacarpophalangeal joint (extensor digitorum communis, extensor indicis proprius, extensor digiti minimi)

A careful motor examination should indicate whether a specific muscle is functioning and, if so, how well. Specific muscles are useful in identifying selected peripheral nerve injuries. Since cross innervation and joint motion aided by several muscles are a source of potential confusion, a

working knowledge of the specific muscles that correlate to specific peripheral nerve function is essential.

Sensory evaluation in the clinical setting requires patient cooperation and interpretation of various stimuli. There are only three objective tests of sensation: the triketohydrindene hydrate (Ninhydrin) sweat test, the O'Riain skin wrinkle test, and electrophysiologic testing. None of these is particularly practical in the initial patient evaluation; therefore, tests that require patient interpretation are most commonly used.

The most commonly used clinical tools are two-point discrimination (2-PD) (both moving and static), Semmes-Weinstein monofilaments, and vibrometer testing. Initial evaluation of the nerve-injured patient should at least include assessment of static 2-PD in the digits and touch sensation in the cutaneous distribution of potentially injured nerves. Crossover in sensory territories is normal, and only selected areas will provide accurate information concerning specific nerve injury

Table no. 3: Sensory Evaluation for Specific Peripheral Nerve Injury

I.	Median nerve -- Pulp of thumb and index finger
II.	Palmar cutaneous branch of median nerve -- Proximal palm over thenar eminence
III.	Ulnar nerve -- Pulp of small finger
IV.	Dorsal cutaneous branch of ulnar nerve -- Dorsal ulnar surface of hand
V.	Radial nerve -- Dorsal radial hand over first web space
VI.	Digital nerve -- Area of the distal phalangeal joint flexion crease

The available methods of sensory evaluation provide different and specific information regarding reinnervation.

Electrophysiologic Testing

Electrodiagnostic testing is a useful adjunct to evaluation in patients with nerve injury. It is rarely needed for initial diagnosis but may be helpful

in evaluation after repair and especially in assessing nerve lesions in continuity. Electrodiagnostic testing includes somatosensory-evoked potentials, intraoperative nerve-to-nerve stimulation, nerve conduction studies, and electromyography.

Nerve conduction studies provide a measure of the speed with which a nerve carries information over a known distance. The time from which the stimulus is initiated until it is recorded is called the latency period. Since time and distance are known, conduction velocity can be calculated. Normal values have been established for both latency and nerve conduction velocity (NCV) for specific nerves and specific locations. In evaluating nerve injury, as opposed to compression neuropathy, determining the presence or absence of response is frequently more important than learning the latency or NCV.

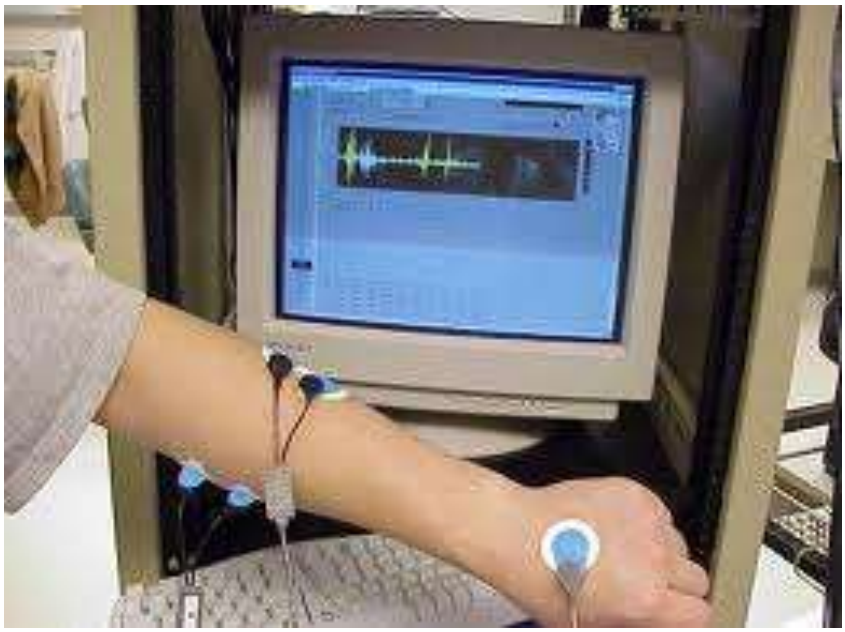


Fig. no. 3 - Electromyography

Electromyography is distinctly different from nerve conduction studies and provides different information. A needle electrode is placed into a specific muscle, and electrical activity is recorded both at rest and with attempts at muscle contraction. Normal muscle will show a short burst of insertional activity related to the local trauma of needle insertion. This burst of activity is brief, and normal muscle at rest will rapidly become electrically silent.

Abnormal insertional activity is seen in denervated muscle or in muscle that is being reinnervated. Spontaneous depolarization in denervated muscle produces fibrillation potentials and positive sharp waves. These are descriptive terms identifying recognizable patterns of electrical activity, as recorded on an oscilloscope.

Electrical activity can also be recorded during active muscle contraction. Contraction of fibers produces an M wave, indicating electrical potential change in the muscle. As the force of contraction continues, multiple M waves are progressively created; these result in a recognizable sequence called a recruitment pattern. Changes in M-wave amplitude or recruitment pattern are present with neuropathy and can be helpful in identifying denervated muscle or in following recovery.

TREATMENT OF PERIPHERAL NERVE INJURIES

The majority of peripheral nerve injuries are best treated by a thoughtful surgical reconstruction. However, nonoperative treatment is indicated in several circumstances. The first of these is injury to a sensory nerve innervating a noncritical area. In the digits, this would include the ulnar border of the ring finger and possibly the middle finger. After discussion with the patient concerning symptoms, functional needs, and realistic outcomes, other digital sensory areas may occasionally be considered noncritical.

Other injuries, such as those to the cutaneous nerves of the forearm, may be treated nonoperatively if agreed on during careful discussion of options with the patient. It is important to emphasize patient involvement in the consideration of nonoperative treatment of peripheral nerve injury. Decreased sensation in an area that might seem trivial to one patient may be critical to another. In some situations (eg, after injury of the radial sensory nerve), nerve repair may be indicated primarily to reduce neuroma symptoms; in these cases, sensory return is a secondary goal.

Realistic expectations for recovery should be considered when discussing operative versus nonoperative treatment. Patient age, level of injury, mechanism of injury, and associated medical conditions all influence outcome and, in certain cases, may make repair or grafting unreasonable.

Operative Treatment

In discussing the timing of nerve repair, treatment is commonly described as primary or secondary. Primary nerve repair includes repairs carried out within 1 week of injury. Any repair carried out later is termed secondary. The classification is, arguably, somewhat arbitrary, but a precise definition is extremely useful in discussion of results. Experimental evidence has shown very clearly that axons regenerate more quickly in the setting of secondary repair. In spite of the experimental evidence, no clinical advantage has been shown with secondary repair. Primary suture under appropriate conditions has proven superior in animal models and in

clinical series. Primary repair is preferable, but situations may arise in which delayed suture is desirable.

Conceptually, nerve repair should result in the appropriately aligned coaptation of healthy fascicles in a well-vascularized tissue bed under minimal tension. If any of these goals cannot be achieved in the primary setting, secondary repair is more appropriate. For crush injury, the extent of neural injury cannot initially be accurately determined. Repair under these circumstances risks joining injured fascicles and thereby severely compromising the success of the repair. The condition of the patient in relation to either injury or associated medical conditions may preclude primary repair. Appropriate surgical equipment and adequately trained staff must be available. Every attempt should be made to ensure that the first nerve repair is carried out under the best possible conditions.

Nerve Repair

Epineural repair requires adequate exposure. Anesthesia should be selected to provide adequate time for careful exposure, assessment, mobilization, and repair. Use of a pneumatic tourniquet provides a bloodless field for dissection. Magnification with loupes or, more commonly, the operating microscope improves the technical quality of the repair and favorably affects outcome. The nerve ends for repair are gently mobilized and cleared of soft tissue, which may obscure visualization of the epineurium at the repair site. Hemostasis is obtained with bipolar cautery. Careful note is made of external nerve markings, which may aid in appropriate orientation of the repair. In addition, inspection of the internal neural topography improves correct fascicular alignment. The nerve ends are then sharply transected perpendicular to the long axis. After transection, the nerve is carefully inspected with magnification to ensure that healthy-appearing, uninjured fascicles are exposed for the repair. Several sequential transections at short intervals (1 to 2 mm) may be necessary before the nerve endings are appropriate for repair. This step in the repair cannot be overemphasized. Failure to adequately resect injured tissue severely compromises the outcome of the repair. If this step results

in a nerve gap so large that grafting becomes necessary, the surgeon should not hesitate to proceed with grafting instead of direct repair. Nerve grafting of uninjured nerve tissue over a short distance will provide results far superior to direct repair of injured neural tissue.

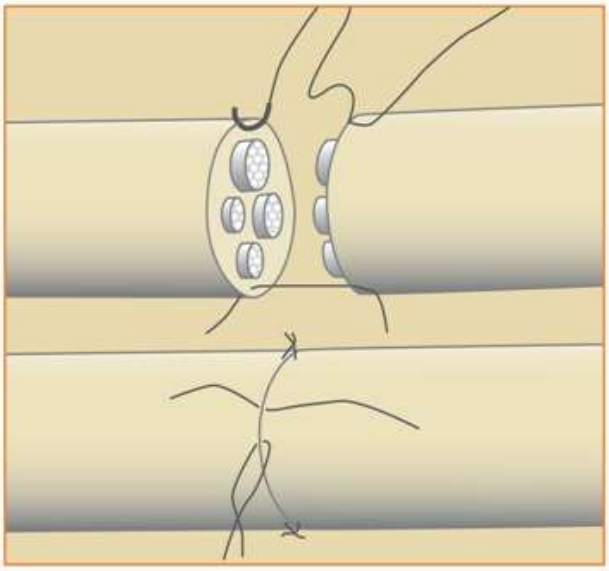


Fig. no. 4 – Epineural suture

The repair is begun by placing two epineural sutures 180° to each other. Careful alignment is the critical factor in this first step. Observation of the repair during the first few minutes provides an interesting illustration of the speed with which the epineurium can be sealed simply from surface tension of local fluids. Therefore, additional sutures are placed sparingly.

To accomplish ***group fascicular repair***, the initial exposure and mobilization of the nerve are the same as those described above for epineural repair. With the aid of an operating microscope, the nerve ends are inspected to identify fascicular groups amenable to individual repair. Matching fascicles are identified proximally and distally. The internal epineurium is then divided between fascicular groups. After mobilization is complete, the repair process is initiated to facilitate the repair -- in general, the least accessible fascicles, which are often farthest from the surgeon, are repaired first. Repair of the external epineurium may be helpful in alleviating tension during the repair. The internal epineurium is sutured with

the fewest sutures necessary (commonly two) to oppose the fascicular group.

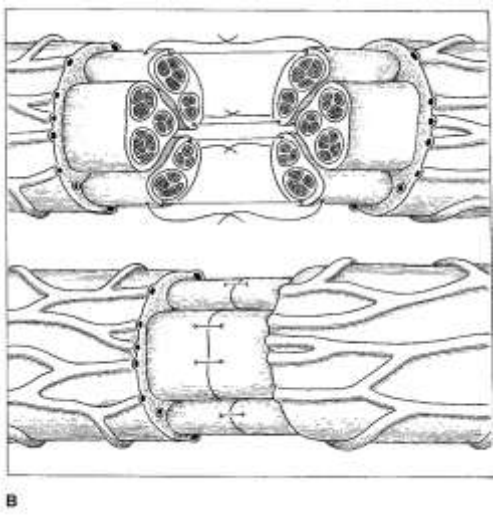


Fig. no. 5 - Group fascicular repair

Individual fascicular repair requires isolation of individual fascicles. The fascicle is the smallest unit of nerve tissue that can be manipulated surgically. Interfascicular connections occur, and care must be taken to avoid injury during the dissection. The repair follows a pattern similar to that of group fascicular repair.

Sutureless Nerve Repair

Coaptation of nerve tissue without suture is appealing and would potentially eliminate the trauma associated with traditional suturing technique. The method has the potential to :

- be more efficient,
- eliminate variables of tension due to suture placement and technique,
- improve alignment of fascicles.

Fascicle-Matching Techniques

The more precisely axons are directed toward their appropriate end organ, the better the chance for successful nerve

regeneration. ***Intraoperative nerve stimulation*** in the awake patient is a readily available tool that can aid in this goal. Hakstian provided an early description of intraoperative nerve stimulation in 1968. The technique has been modified and improved over the years. Patient response to stimulation of selected fascicles in the proximal nerve stump can differentiate motor and sensory groups. However, caution should be exercised. Awake stimulation requires a high degree of patient cooperation and is not tolerated by all patients. A thorough preoperative discussion, which outlines the proposed procedure and describes what the patient will experience, is crucial to the success of the procedure.

Histologic staining methods are available to identify motor and sensory fascicles in the divided nerve. Acetylcholinesterase is found in myelinated motor axons and in some unmyelinated axons, but not in myelinated sensory axons. Carbonic anhydrase is found in myelinated sensory axons. The detection of these enzymes with available staining techniques makes fascicle identification possible. Identification in the proximal nerve is possible indefinitely. Accurate staining in the distal stump is possible for about 9 days after nerve division. The time required for intraoperative staining (about 1 hour) and the lack of clear evidence that the technique improves outcome have limited the use of this technique.

Results of Nerve Repair

An accurate and reproducible evaluation of results after treatment is difficult. Multiple variables in injury, patient comorbidity, treatment, postoperative evaluation, and the reporting of results contribute to this difficulty. The most accurate information would be gained from a prospective standardized assessment. Even more difficult would be limiting each group to a certain age, injury type, specific nerve, level of injury, type of repair, postoperative protocol, and assessment. In spite of these difficulties, there is a great deal of useful information available regarding nerve repair and results.

The objective evaluation of motor and sensory recovery is essential to accurate assessment. The Medical Research Council provided a basis

for the assessment of motor and sensory function after nerve injury using the relatively simple and reproducible system

The recovery of sensory perception is evaluated by static 2-PD, moving 2-PD, and pinprick. Static 2-PD is perceived primarily through the Merkel cell, which is slowly adapting and thus well-suited to continuous pressure. The Meissner corpuscle, a rapidly adapting receptor, fires at the beginning of a stimulus and then dissipates, making it more suitable for relaying information from moving 2-PD. Free nerve endings transmit painful stimuli, such as those from a pinprick. Dellon and Clayton[55] reported that moving 2-PD best correlates with a patient's ability to identify objects, and static 2-PD correlates with the time to identify objects. Both tests are needed to accurately assess functional sensation. Threshold density may be measured with 2-PD, and innervation density may be measured with monofilament testing.

Nerve Grafting

Reconstruction after peripheral nerve injury may require management of segmental defects or "gaps" in the injured nerve. Local measures to overcome the problem include nerve mobilization, local joint positioning, nerve transposition, and bone shortening. Risks and benefits of each strategy must be carefully considered. Paramount to the decision-making process is the understanding that nerve repair under excess tension does poorly. Nerve grafting is a readily available solution to the problem of excessive tension at the repair site. With the dependable outcomes after nerve grafting, extremes of joint positioning to accomplish end-to-end repair are not indicated.

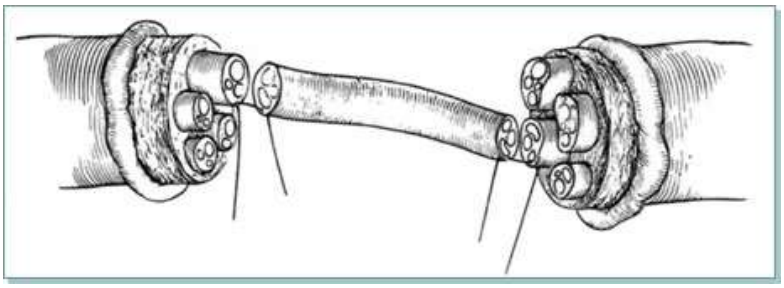


Fig. no 6 – Nerve grafting

Under ideal circumstances, the nerve graft will behave as the distal nerve stump would. Therefore, the graft must also undergo wallerian degeneration to provide a conduit for axon regeneration. Schwann cell survival in the graft is critical to this process. For the Schwann cells to survive, the graft must be appropriately revascularized. This process occurs both from the proximal and distal nerve stumps and from the surrounding tissue bed. In animal models, graft revascularization reaches supranormal levels in 4 to 5 days.

Initial revascularization occurs through the proximal and distal stumps and then the surrounding tissue. Ingrowth from local tissue creates extensive adhesions, which limit graft excursion. The first few days after grafting, cellular viability is dependent solely on diffusion from the tissue bed. As graft size increases, central cellular necrosis occurs, because the volume of nerve tissue increases beyond the limits of perfusion or revascularization. This limitation contributes to poor outcome with trunk grafting. Trunk grafts are now used uncommonly, unless harvested as vascularized nerve grafts.

Nerve Grafting Techniques

In ***group fascicular grafting****,* every attempt is made to accurately deliver regenerating axons through the graft material to a matching fascicular group in the distal stump. The distal nerve tissue may be marked and sent for histochemical staining, depending on clinical needs and laboratory capabilities. After graft harvest and careful hemostasis, grafts are sutured to individual fascicular groups with the minimally needed number of sutures. Emphasis again is placed on appropriate fascicular matching without tension.

Individual fascicular grafting is uncommon. A distal digital nerve defect is a specific, useful indication for individual fascicular grafting Other indications may arise when clinically critical single fascicles (eg, the thenar motor branch) can be identified.

Graft Material

Autogenous nerve graft is the most commonly used material for bridging nerve gaps. Ideally, the donor nerve provides a suitable environment for regeneration and results in acceptable donor morbidity. The sural nerve meets many requirements for nerve tissue quality and donor site morbidity and has become the standard autogenous graft for bridging large upper-extremity nerve gaps. Through a longitudinal incision or sequential small transverse incisions, up to 40 cm of nerve can be harvested from each leg.

The resulting sensory loss over the lateral aspect of the foot is not inconsequential; careful preoperative counseling is necessary to avoid postoperative disappointments. Blocking the nerve preoperatively with local anesthetic is very helpful in illustrating the resultant defect to the patient. In addition to the expected sensory loss, neuroma symptoms can produce morbidity.

In the forearm, cutaneous nerve branches are available as graft material. Preoperative counseling and local anesthetic blocks to reproduce the donor defect are particularly useful here. The medial antebrachial cutaneous nerve (MACN) may be harvested and provides up to 10 cm of graft. The resultant sensory deficit lies along the medial aspect of the mid-forearm.

The lateral antebrachial cutaneous nerve provides significantly more graft material than the MACN does -- up to 20 cm. However, the resultant sensory loss along the lateral aspect of the forearm can extend onto the thenar area, making it undesirable for median nerve defects in general and thumb digital nerve injuries in particular.

The posterior interosseous nerve may be harvested at the wrist level and yields approximately 3.5 cm of graft material. The graft may be particularly useful in digital nerve defects, and there is no donor morbidity from sensory loss.

The use of ***vascularized nerve grafts*** provides several potential advantages. The initial period of ischemia (2 to 3 days) after nonvascularized grafting is avoided, the necessity for revascularization via the recipient bed (which may be severely scarred and poorly vascularized)

is eliminated, and larger sizes of nerve tissue (in cross section) may be used as graft without the problems of central necrosis.

Table no. 4 - Vascularized Nerve Grafts: Donor Nerves and Associated Vessels

Nerve	Vascular Supply
Superficial radial	Radial artery
Ulnar	Superior ulnar collateral artery
Sural	Superficial sural artery
Anterior tibial	Anterior tibial artery
Superficial peroneal	Superficial peroneal artery
Saphenous	Saphenous artery

There is experimental evidence that vascularized nerve grafting can produce superior outcomes, though conclusive evidence is still lacking. Clinical series reported superior results with vascularized nerve grafts, though none had control groups and follow-up was frequently limited. As more clinical follow-up becomes available, the indications for this technique may expand. The most compelling present indication is grafting in a severely scarred tissue bed. Situations where transfer of large nerve trunks is desirable and feasible (eg, brachial plexus reconstruction using the ulnar nerve) may benefit from this technique, as well.

Ease of harvest and frequently perfect size match make *autologous vein* a predictable material for use in bridging nerve defects. Of course, the advantage of negligible donor morbidity must be offset by acceptable clinical results. A consideration of nerve regeneration biology suggests the ideal peripheral nerve for this technique would be small in caliber, motor or sensory only, and have a limited end-organ target area. The technique is reported in clinical studies for digital nerve repair. Superiority over conventional nerve grafting has not been established. However, as our understanding of nerve regeneration through hollow tubes improves in general, indications may expand.

The use of ***allograft nerve*** material is particularly appealing because of its available quantity and lack of donor site morbidity. However, the risks

of immunosuppression required to maintain Schwann cell viability limit clinical implementation of this method. In animal models, if continuous immunosuppression is used and the Schwann cell population in the graft survives, then regeneration equivalent to autograft can be expected. Future improvements in immunosuppression may expand the use of allografts, but at present, they are not indicated in clinical practice.

Bridging nerve gaps with a hollow tube has been considered for over a century, utilizing a vast array of materials. As our understanding of nerve regeneration biology has improved, the conduits for regeneration have been refined considerably. The ideal conduit would allow inflow of supportive local nutrient factors but prevent escape of substances supportive of regeneration inside the tube. Ultimately, conduits filled with neurotrophic substances that are resorbable over appropriate periods may be available.

Lundborg et al reported a prospective clinical series evaluating median and ulnar nerve lesions in the forearm treated by conventional nerve suture or tubulation. Similar outcomes were found in the two groups. Further clinical trials are needed before the technique can be advocated for routine use.

Nerve Lesions in Continuity

Nerve lesions in continuity are also called a "neuroma in continuity." This clinical situation presents unique challenges to the surgeon managing peripheral nerve injury. The goal of management is the reconstruction of nonfunctioning neural elements without compromise of existing function. Regeneration failure can occur in a wide variety of clinical situations, including that following nerve repair. However, most commonly, crush injury, stretch injury (as may be seen with certain fractures), or gunshot wounds leave the nerve in continuity, but injured to some degree. The progress of nerve recovery can be followed clinically by assessment of functional -- both sensory and motor -- recovery. In addition, an advancing Tinel's sign is followed. After regeneration commences, the advancing axons progress approximately 1 mm/day. This information, coupled with a

thorough understanding of the local peripheral nerve anatomy, allows the clinician to predict recovery. Partial recovery, anomalous innervation, or regeneration across long segments of nerve without branching (such as in the forearm) can challenge even the most careful observer.

When clinical progress is not proceeding as expected, electrodiagnostic studies can be useful in identifying regeneration before it is evident by examination. Electromyography provides specific information about muscle degeneration. Information gained may obviate the need for surgical treatment of the lesion and may avoid the situation in which exploration is delayed so long that end-organ degeneration occurs. If partial recovery is occurring, further management decisions are based on the critical nature of missing functions. When motor recovery has occurred but sensory return is lacking, exploration and intraoperative recordings can be done with a peripheral nerve stimulator, available in most operating rooms. Mackinnon has described the intraoperative management sequence in detail. In brief, functioning motor fascicles are identified and excluded, allowing section and reconstruction of the injured sensory fascicles.

When sensory recovery is present but motor function is deficient, nerve-to-nerve recording is required. Specialized equipment for this process is not commonly available. In this situation, tendon transfers or referral to centers familiar with the technique may be appropriate. Happel and Kline describe the intraoperative technique in detail.

Intraoperative testing, in general, identifies functioning fascicles before end-organ innervation. This information correlates well with eventual function and can therefore dependably identify fascicles that may be reconstructed.

Aftercare and Rehabilitation

Postoperative management after nerve repair or reconstruction is directed toward wound healing, maintaining joint mobility, and reestablishing longitudinal excursion of the nerve. Repairs are immobilized for approximately 3 weeks. Adjacent joints are splinted in a safe position.

Extremes of positioning are not indicated to allow repair without grafting, as discussed in the introductory section on nerve grafting. After digital nerve repair, a careful intraoperative assessment of tension on the repair site, where the metacarpophalangeal (MP) joints are held in flexion and the interphalangeal joints in extension, provides critical information concerning early postoperative motion after tendon repair. Splinting for specific nerve injuries should prevent contracture during the months required for regeneration. After ulnar nerve repair, blocking the MP joints in 30° of flexion allows active interphalangeal motion but prevents hyperextension deformity at the MP joints. Abduction splinting prevents contractures of the first web space when thumb abduction is lost.

Sensory Reeducation

After nerve regeneration, a new and confusing set of signals is relayed from the hand to the brain. Innervation density is significantly reduced. Imperfect topographic specificity results in axon regeneration to new locations. For example, after median nerve repair, axons once destined for the middle finger may now innervate the palm. In addition, end-organ innervation is significantly altered. The resultant signal to the brain from sensory stimulation may be nearly unrecognizable. Sensory reeducation is designed to help the patient recognize new input in a useful manner. The ability to change cortical maps of sensory input and alter them to allow accurate identification of new sensory input is called cortical plasticity. Children are particularly adept at this process, which probably contributes greatly to their improved outcome after peripheral nerve injury.

Sensory reeducation is carried out in three stages: desensitization, early-phase discrimination and localization, and late-phase discrimination and tactile gnosis. Initial efforts are directed toward helping the patient understand the potential risks present with a lack of protective sensation. As early recovery occurs, desensitization is accomplished by a program of graded stimuli, which gradually decreases unpleasant stimuli and builds tolerance for increasing levels of stimulus.

When a 30-cps tuning fork can be perceived in the palm, early-phase discrimination and localization begins. During this stage, the patient is taught to distinguish between static and moving touch. In addition, false localization of stimuli is addressed. Sensory stimuli are presented with and without visual clues. Once moving and constant touch can be dependably identified, late-phase training begins.

The goal of late-phase training is the reestablishment of tactile gnosis. Tactile gnosis describes the hand's unique ability to "see" an object and to provide extraordinary detail concerning its shape, texture, and temperature.[88]Objects that differ greatly in size, shape, and texture are presented sequentially to the patient. As perception improves, increasingly complex objects are used.

UPPER LIMB INNERVATION

Median nerve

The median nerve originates in the brachial plexus as branches from the lateral and medial cords come together. These cords bring fibers from all roots of the brachial plexus, from C5 to T1. The median nerve runs through the anteromedial compartment, through the cubital fossa just medial to the brachial artery, and enters the forearm between the heads of the pronator teres.

The median nerve supplies most of the flexor muscles in the forearm and a few muscles in the hand. Once in the forearm, the median nerve splits into a superficial and deep branch. The superficial branch supplies the pronator teres, flexor carpi radialis, and palmaris longus before the distal portion supplies the flexor digitorum superficialis.

The deep trunk runs medially down the forearm deep to the muscles and supplies motor innervation to the flexor pollicis longus, pronator quadratus, and the portions of flexor digitorum profundus (FDP) that flex the index and long fingers and sends articulate branches to the radial carpal joint via the anterior interosseous. At the wrist, the deep median branch sits between the palmaris longus and flexor pollicis longus, travels through the carpal tunnel with the flexor tendons, and splits into 6 branches once clear of the flexor retinaculum. The recurrent branch of the median nerve innervates the palmaris brevis and the muscles of the thenar eminence, namely the abductor pollicis brevis, opponens pollicis, the first and second lumbricals, and the superficial head of the flexor pollicis brevis. The remaining branches are sensory and include 3 common digital nerves to the second, third, and fourth digits and 2 proper digital nerves to the thumb.

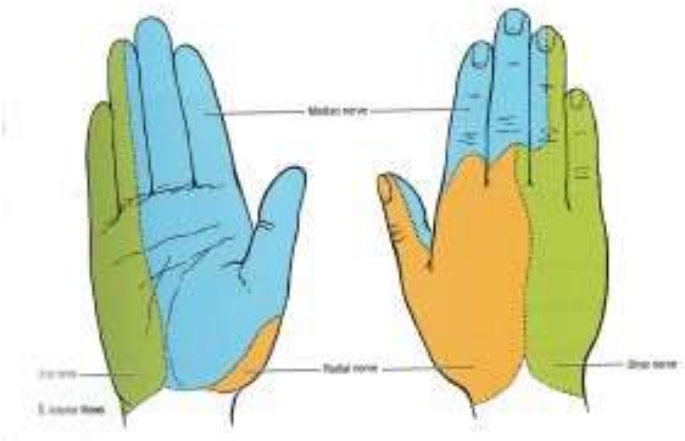


Fig. no. 7 – Sensorial innervation of the hand

These digital nerves run along the lateral (radial) and medial (ulnar) sides of the fingers with the digital arteries. The median nerve has 2 other sensory branches not yet mentioned that supply the elbow and a palmar cutaneous branch that passes over the top of the flexor retinaculum to innervate the palm.

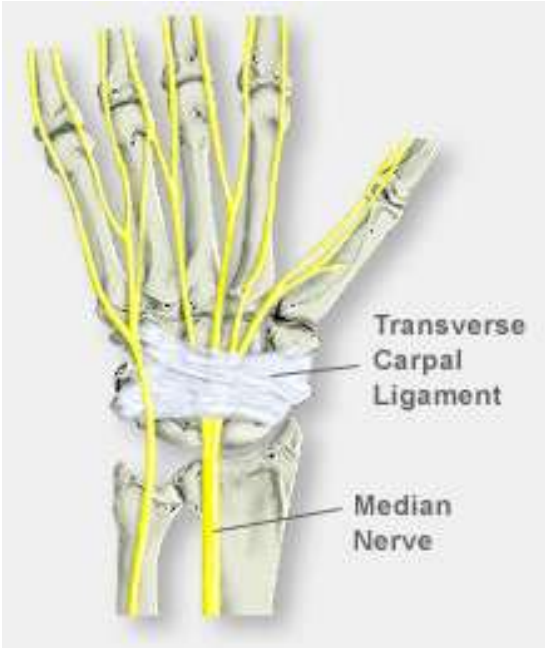


Fig. no. 8 – Median nerve branches

Motor targets of the median nerve are as follows:

- Pronator teres
- Flexor carpi radialis

- Palmaris longus
- Flexor digitorum superficialis
- Flexor digitorum profundus
- Flexor pollicis longus
- Pronator quadratus
- Palmaris brevis
- Abductor pollicis brevis
- Flexor pollicis brevis - Superficial head
- Opponens pollicis
- First and second lumbricals

Some notable variations in the pattern of innervation exist in the median distribution. In the forearm, the median nerve supplies approximately one half of the FDP muscle, sharing it with the ulnar nerve. However, in 50% of patients, the median and ulnar nerves overlap and the median nerve encroaches on the ulnar innervation to the FDP. However, in the hand, the ulnar nerve tends to extend across the palm and innervate a larger portion of the thenar eminence.

Another clinically important variation is the presence of Martin-Gruber anastomoses in the forearm and Riche-Cannieu anastomoses in the palm. Martin-Gruber anastomoses are believed to be present in approximately 17% of patients, while Riche-Cannieu anastomoses may be present in as many as 70%. Because these anastomoses allow unique patterns of innervation, they can mask lesions by changing the symptoms present.

Ulnar nerve

The ulnar nerve arises from the medial cord and contains fibers from the C7, C8, and T1 roots. It passes through the arm, behind the medial epicondyle, and into the flexor compartment. In the forearm, the ulnar nerve gives off motor branches to the flexor carpi ulnaris and the medial (ulnar) portion of FDP that supplies the ring and little fingers. Usually, the ulnar nerve gives a small branch to the ulnar artery, known as the nerve of Henle, which is present in approximately 60% of people. The remaining

40% of people have a palmar cutaneous branch.[63] At the level of the wrist, the ulnar nerve passes through the Guyon canal, right next to the hook of the hamate.

In the hand, the ulnar nerve divides into a deep motor and a superficial sensory branch. The deep motor branch supplies all of the intrinsic muscles of the hand: the muscles of the hypothenar eminence, the interossei, the third and fourth lumbricals, adductor pollicis, and the deep head of the flexor pollicis brevis. The superficial sensory nerve supplies sensation to the little finger and the ulnar side of the ring finger. The ulnar nerve also supplies sensation to part of the dorsum of the hand via the dorsal sensory branch that wraps around to the dorsum near the level of the dorsal carpal ligament. This provides sensation in the same distribution as on the volar surface.

Fig. no. 9 – Ulnar nerve

Motor targets of the ulnar nerve are as follows:

- Flexor carpi ulnaris
- Flexor digitorum profundus
- Hypothenar muscles

- All interossei
- Third and fourth lumbricals
- Adductor pollicis
- Flexor pollicis brevis - Deep head

Radial nerve

The radial nerve is a branch off the posterior cord and contains fibers from roots C7-T1. This nerve wraps around the humerus in the spiral groove as it passes through the upper arm, supplying motor innervation to all 3 heads of the triceps muscle, the anconeus, the brachioradialis, and a small part of the brachialis muscle before entering the cubital fossa lateral to the biceps tendon. In the forearm, the nerve supplies motor innervation to the extensor carpi radialis longus, extensor carpi radialis brevis, and the supinator before splitting into deep and superficial branches.

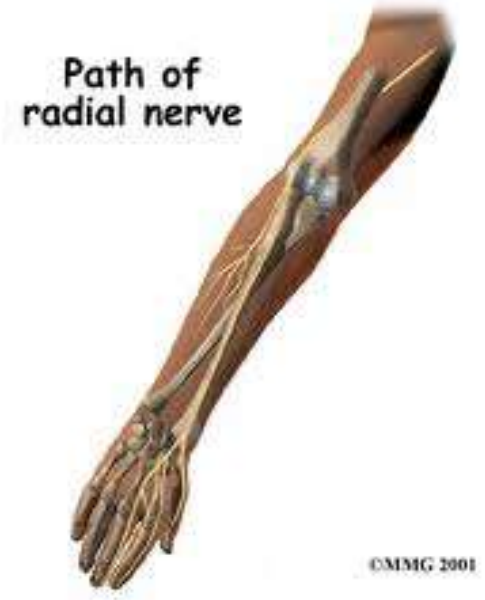


Fig. no. 10 – Radial nerve

The deep branch provides motor innervation to the muscles of finger and thumb extension before becoming the posterior interosseous nerve and supplying sensation to the dorsal aspect of the carpal joints. The superficial sensory branch passes through the anatomic snuffbox on its

way to supply sensation to the dorsum of the hand, thumb, and first 2.5 fingers. The radial nerve also provides sensation to a portion of the forearm via the posterior cutaneous nerve and to the elbow.

Motor targets of the radial nerve are as follows:

- Triceps (long, medial, lateral)
- Anconeus
- Brachioradialis
- Extensor carpi radialis longus
- Extensor carpi radialis brevis
- Supinator
- Extensor digitorum communis
- Extensor indicis proprius
- Extensor digiti minimi quinti
- Extensor carpi ulnaris
- Abductor pollicis longus
- Extensor pollicis longus
- Extensor pollicis brevis

PERSONAL CONTRIBUTIONS

MATHERIAL AND METHODS

Alternative methods for nerve repair

Study of nerve regeneration using a silicone tube

Aim of this study is to determine alternative methods for nerve repair to avoid nerve graft.

We randomized 6 Wistar rats, aprox 450g each, in 2 groups:

- Control group
- Silicone tube group

- For control group we used epineural neuroraphy
- For Silicone tube group I used a silicone tube with 2mm internal diameter and wall thickness of 0,18mm

Surgical protocol

- We used inhalation anaesthesia with Halotane and O2.
- For surgical intervention I used a surgical microscope with magnification between 10-40x in aseptic conditions.
- We did an oblique incision in the dorsal part of rat thigh.
- We dissected the muscles and I exposed sciatic nerve.
- For silicone tube group I used an 1 cm silicone tube and I let between nerve stump 5mm
- For control group I used epineural neuroraphy
- Sutureing was done with 9/0 Polipropylene suture

New experiment for nerve regeneration

We will use a new experiment to determine nerve regeneration comparing with suture only control.

Two different experimental groups will be tested;

- Suture only
- Suture + seeding with chopped nerve

Protocol

Adult rats (7 animals per group) will be anaesthetised and the left sciatic nerve exposed.

The sciatic nerve was transected 1 mm segment of nerve will be excised and the nerve sutured with a perineural technique with 9/0 sutures.

In the study group, the segment of nerve will be chopped and seeded around the nerve suture, while nothing will be done in the control group.

Two different time-points will be examined, allowing study of the extent of early stages of nerve regeneration (14 days) and muscle reinnervation (180 days).

In both studies we used EMG machine for assessing the results:

Protocol for EMG assesing

- We will use an EMG machine
- We will reexpose the sciatic nerve of the rats
- We will stimulate sciatic nerve proximal and distal with 2 electrodes
- We will put the electrode for recording in the muscles of the calf
- We will put the referent electrode to the calcanean tendon
- We will put the closeing electrode subcutaneous between stimulation and recording electrodes
- We will use a pulse 0,2ms, 20mA,10Hz and 6 continous stimulation
- We will record NCV and I will compare the 2 groups
- We will compare NCV for the 2 groups with NCV from healthy thigh of the rats

Topography of peripheral nerves (median nerve, ulnar nerve, radial nerve, sciatic nerve) – anatomic study on cadavers

This anatomical study followed fascicular dissection of main nerves involved in reconstructive surgery of peripheral nerves of the upper

extremity (median, ulnar radial). Nervous branches are dissected from distal to proximal and followed till were is possible.

We dissected upper extremity of 3 fresh cadaver and individualised nervous traiect of main nerves.

Material used were standard surgical instruments. We took pictures with digital camera.

Clinical experience in peripheral nerve repair (FLOREASCA PLASTIC SURGERY DEPARTMENT BUCHAREST, CONSTANTA PLASTIC SURGERY DEPARTMENT) – retrospective and prospective study

This study is a retrospective and prospective study concerning the affections of peripheral nerves in plastic surgery department of Constanta emergency hospital and “Floreasca” emergency hospital Bucharest.

We studied 2 groups of pacients.

- First group – 478 patients treated in plastic surgery department of Constanta emergency hospital between 2006-2010
- Second group – 1742 patients treated in plastic surgery department of “Floreasca” emergency hospital Bucharest between 2006-2010.

We studied the following parameters:

- Distribution over years
- Sex ratio
- Distribution over age
- Smoking
- Alcohol consumption
- Upper extremity involved]
- Affected nerve
- Accident location
- Type of anaesthesia

- Time of repair
- Surgical procedure
- Hospitalization period

For the retrospective study we used patient file and for the prospective we used anamnestic data. All data were recorded in a standard worksheet and introduced in a database built in Microsoft Access 2010 software.

All data were transposed in table and graphs using Microsoft Excel 2010 software.

TOPOGRAPHY OF PERIPHERAL NERVES (MEDIAN NERVE, ULNAR NERVE, RADIAL NERVE) – ANATOMIC STUDY ON CADAVERS

Initially, when Sunderland looked at the fascicular patterns of peripheral nerves in 1947, he described a pattern of twisting and crossing fascicles that branched so often that nerve grafting and intraneural dissection were assumed to be impossible. Fortunately, the pattern described by Sunderland is only true for the proximal part of the nerve. As described by Jabaley in 1980, the fascicular pattern in the distal forearm is much straighter, with less crossing over. Apparently, the crossing over in the proximal portion sorts the nerve fibers into bundles by function. This means that by the time the distal forearm is reached, the fascicles contain nearly pure motor or sensory axons.

While the arrangement varies by individual and by nerve, generally, the sensory fascicles are considered to sit more superficially and the motor fibers more dorsal.

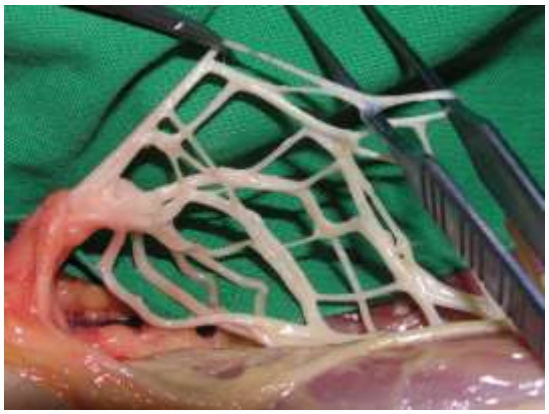


Fig. no. 11 – 12: Fascicular pattern of sciatic nerve

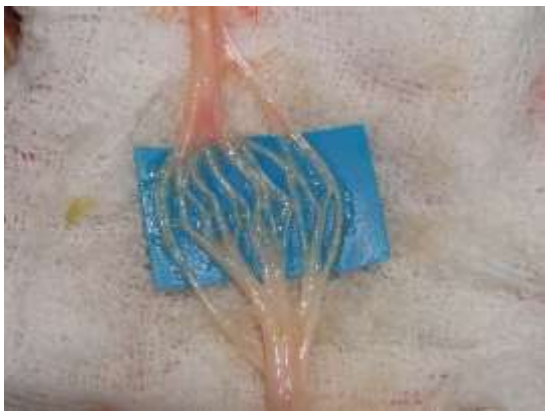
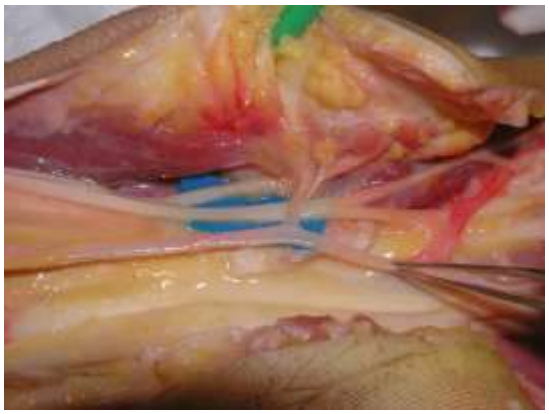


Fig. no. 13: Fascicular pattern of ulnar nerve



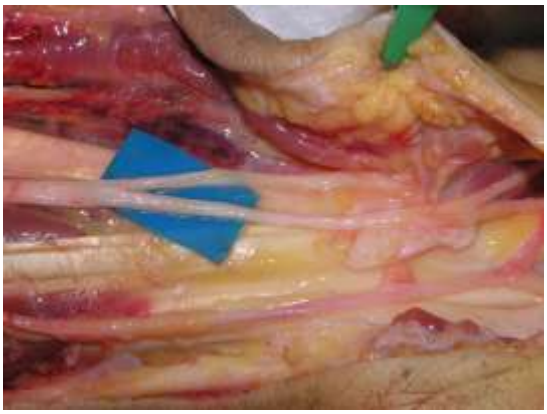


Fig. no. 14 – 15 – Branches of ulnar nerve

The ulnar nerve arises from the medial cord of the brachial plexus. The ulnar nerve travels posterior to the brachial artery and remains within the flexor compartment of the upper extremity until it reaches the medial epicondyle. The nerve travels behind the medial epicondyle back into the flexor compartment underneath the flexor musculature. Above the elbow, the ulnar nerve lies on the long head and then the medial head of the triceps muscle, directly posterior to the medial intermuscular septum between the brachialis and the triceps muscles.

The fascial bands over the median nerve constitute the Struthers arcade. The nerve passes within the cubital tunnel posterior to the medial epicondyle. It is directly underneath a tight fascial roof known as the Osborne band, which is contiguous with the leading fascial heads of the flexor carpi ulnaris (FCU) muscle. Just above the elbow branches, the

nerve branches to the superficial head of the FCU. The nerve lies directly over the top of the FDS muscle and beside the FDP muscle at the elbow.
As the ulnar nerve travels down the forearm, it is wedged between the FDS and the FDP muscle bellies to exit in the distal forearm just ulnar to the ulnar artery and the FDP tendons. The FCU tendon protects the nerve on its ulnar aspect. The ulnar nerve travels within the Guyon canal at the wrist to supply the hypothenar muscles, including the opponens digiti quinti and the abductor digiti quinti. It also supplies the 2 ulnar lumbrical muscles and the interossei to the hand and the deep branch to the flexor pollicis brevis muscle. The ulnar nerve supplies sensation to the 1-5 digits of the ulnar aspect. The dorsal cutaneous branch of the ulnar nerve supplies sensation to the dorsal ulnar half of the hand and fingers. This nerve arises from the main ulnar nerve approximately 6 cm proximal to the wrist.

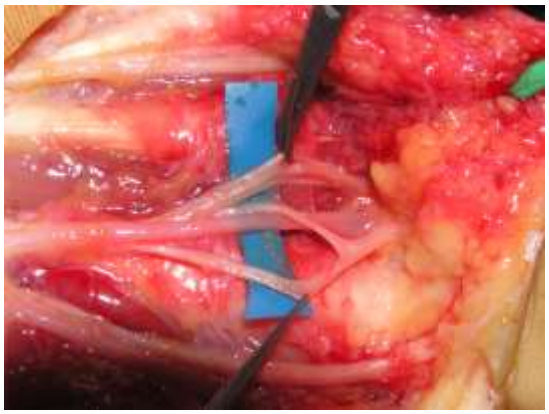


Fig. no. 16 – Fascicular pattern of digital nerve

In the hand, the common digital nerves are derived from the median and ulnar nerves and divide in the distal palm into paired volar (or palmar) branches. These run with the digital vessels on either side of the flexor tendon sheath of each finger and supply the lateral and palmar aspect of each finger together with the tip and nail bed area. The smaller dorsal digital nerves, derived from the radial and ulnar nerves, run on the dorsolateral aspect of each finger and supply sensation to the back of the finger.

In the palm of the hand the median nerve is covered by the skin and the palmar aponeurosis, and rests on the tendons of the Flexor muscles. Immediately after emerging from under the transverse carpal ligament the median nerve becomes enlarged and flattened and splits into a smaller, lateral, and a larger, medial portion.

The lateral portion supplies a short, stout branch to certain of the muscles of the ball of the thumb, viz., the Abductor brevis, the Opponens, and the superficial head of the Flexor brevis, and then divides into three proper palmar digital nerves of median nerve (proper volar digital nerves):

- two of these supply the sides of the thumb,
- while the third gives a twig to the first Lumbricalis and is distributed to the radial side of the index finger.

Each **proper digital nerve**, opposite the base of the first phalanx, gives off a dorsal branch which joins the dorsal digital nerve from the superficial branch of the radial nerve, and supplies the integument on the dorsal aspect of the last phalanx.

At the end of the digit, the proper digital nerve divides into two branches,

- one of which supplies the pulp of the finger,
- the other ramifies around and beneath the nail.

The proper digital nerves, as they run along the fingers, are placed superficial to the corresponding arteries

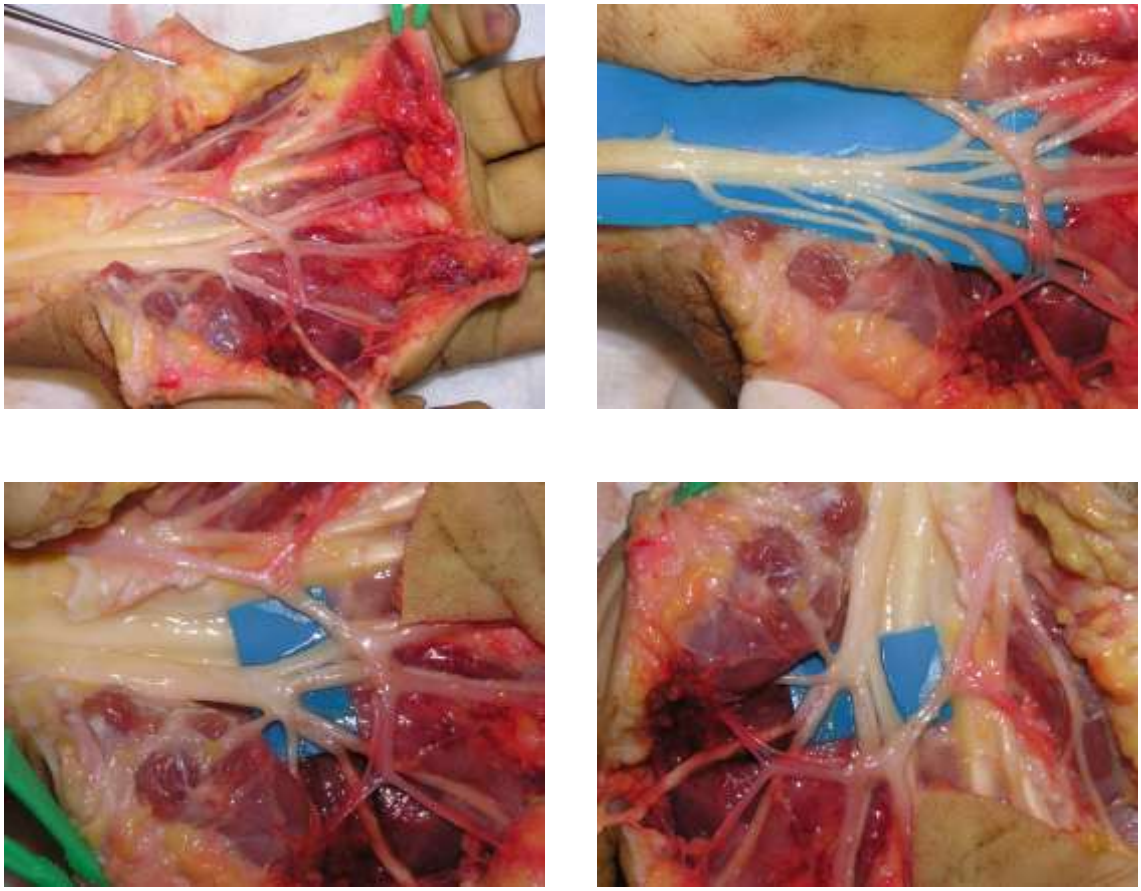


Fig. no. 17 – 20: Terminal branches of median nerve

The nerve is superficial to the brachialis muscle and usually lies in a groove with the brachial artery, between the brachialis and biceps muscle. It travels across the antecubital fossa, underneath the bicipital aponeurosis, and between the biceps tendon and the pronator teres. At this level, the median nerve is on the distal aspect of the brachialis muscle. The nerve then travels underneath the 2 heads of the flexor digitorum sublimis (FDS) muscle to lie between this muscle and the flexor digitorum profundus (FDP) muscle. The median nerve emerges between these 2 muscles in the distal forearm to then travel ulnar to the flexor carpi radialis and radial to the sublimis tendons, usually directly underneath the palmaris longus tendon, and enters the carpal tunnel in a more superficial plane to the flexor tendons.

The motor branch emerges at variable sites but most frequently at the distal aspect of the carpal ligament to service the thenar musculature. Just beyond the end of the carpal ligament, the median nerve trifurcates to

become the common digital sensory nerves to the fingers. The palmar cutaneous branch of the median nerve is a sensory branch that comes from the main body of the nerve approximately 6 inches above the rest of the nerves and services an elliptical area at the base of the thenar eminence. This superficial nerve does not lie within the carpal tunnel.

Just distal to the antecubital fossa, the median nerve branches into the anterior interosseous nerve, which travels on the interosseous membrane and innervates the flexor pollicis longus (FPL), the FDP to the radial 2 digits, and the pronator quadratus at its termination. The nerve innervates the pronator teres, flexor capri radialis, the FDS, and the 2 radial FDP tendons. It also supplies the FPL and the pronator quadratus.
Within the hand, the motor branch of the median nerve supplies the opponens pollicis, the flexor pollicis brevis, and the abductor pollicis brevis musculature. It also supplies the 2 radial lumbrical muscles in the hand. The median nerve supplies sensation to the 3.5 digits on the radial aspect.

In the distal half of the arm, the branches of the median nerve consistently collect into three fascicular groups, which are located at the anterior, middle, and posterior parts of the median nerve trunk. The anterior fascicular group is composed of the branches to the pronator teres and the flexor carpi radialis, the posterior fascicular group is composed mainly of the anterior interosseous nerve and the branches to the palmaris longus, and the middle fascicular group is made up mostly of the branches to the hand and the flexor digitorum superficialis.

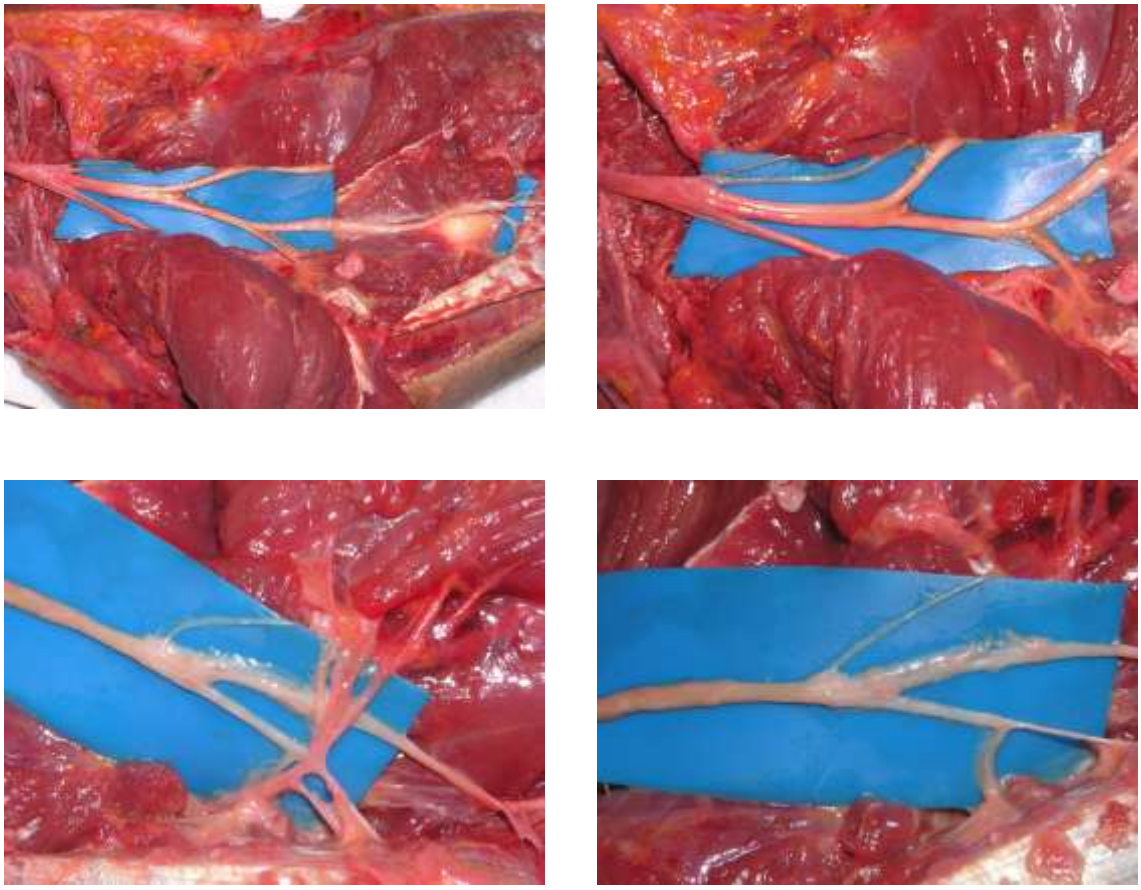


Fig. no. 21 – 24: Branches of radial nerve

The radial nerve emerges from the posterior aspect of the humerus in the spiral groove between the brachialis and brachioradialis muscles above the elbow. It leaves the extensor compartment to travel in front of the elbow underneath the brachioradialis muscle, sending branches of innervation to it just above the elbow. The radial nerve divides at the level of the radial capitellar joint into the deep motor branch of the radial nerve (ultimately becoming the posterior interosseous nerve) and the superficial radial nerve. At this point, it branches to the extensor carpi radialis brevis.

The superficial radial nerve continues to travel underneath the brachioradialis muscle to ultimately emerge between that muscle and the extensor carpi radialis longus tendon. The superficial radial nerve supplies sensation to the radial half of the dorsum of the hand. The deep motor branch of the radial nerve travels within the fat pad and runs below the supinator muscle to emerge the supinator and become the posterior interosseous nerve in the distal dorsal aspect of the forearm. The posterior

interosseous nerve travels at the level of the interosseous membrane to ultimately provide sensation to the posterior aspect of the wrist. This nerve innervates the extensor indicis proprius, extensor digiti quinti, extensor carpi ulnaris, abductor pollicis longus, extensor pollicis brevis, and extensor digitorum communis muscles.

ALTERNATIVE METHODS FOR NERVE REPAIR

In recent past there have been significant developments in the management of peripheral nerve injuries. The advent of microsurgical techniques with use of magnification, micro-sutures and micro instruments has considerably improved the results in nerve repairs. Many advances have been made in the area of neurobiology of nerve injury and regeneration, and increasing attempts are being made in the use of nerve allografts and nerve conduits for bridging the gaps.

NERVE AUTOGRAFTS AND ALLOGRAFTS

Nerve autografts are considered the gold standard technique for the peripheral nerve lesions. The nerve grafting technique was first reported between the years 1870 and 1900, but it was Millessi who worked extensively on the nerve grafting techniques. He made it clear that nerve grafting without tension was superior to epineural suture under tension. Tension across a direct suture repair decreases blood flow and excessive tension will cause the repair to break down. The sural nerve is by far the most commonly used donor nerve, others being the cutaneous nerves of arm and forearm, dorsal sensory branch of radial nerve and distal portion of anterior interosseous nerve.

One current practice that accounts for the success of nerve grafts is the use of small, thin grafts which get vascularized faster than the large and thick grafts. For bridging the long gaps (greater than 20 cm) with associated soft tissue loss over the repaired area, current recommendation is to use free vascularized nerve grafts 2,3 In global brachial plexus palsy with C8 . and T1 root avulsions, pedicled vascularized ulnar nerve has been used for a contralateral C7 root transfer to the median nerve.

The use of allografts has been experimented in nonhuman primates and later practiced by Mackinnon et al in the humans and the groups involved in hand Transplantation Nerve allografts act as a temporary scaffold across which host axons regenerate. Ultimately, the allograft tissue is completely replaced with host material. Once regeneration has occurred through the graft,immunosuppression may be discontinued. A new immunosuppressant FK 506, also known as tacrolimus, has greater potential and fewer side effects than other immunosuppressants. It has been established that FK 506 has neuroregenerative and neuroprotective effects regardless of its immunosuppressive activity.

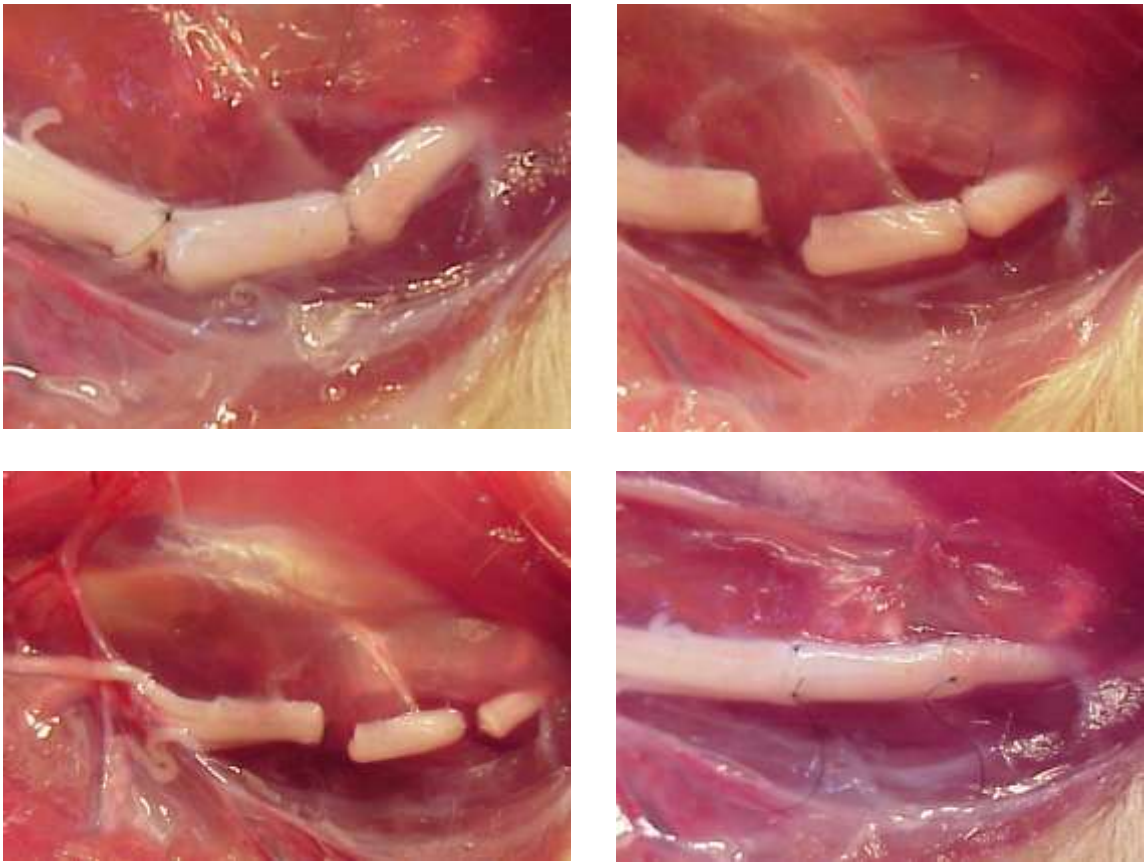


Fig. no.25 - 28 – Rat sciatic nerve autograft

USE OF FIBRIN GLUE IN NERVE REPAIR

Synthetic nerve suture may induce considerable fibrotic and inflammatory reactions at the coaptation site which could seriously hamper regeneration of nerve fibres.

Young and Medawar devised a method by which the nerve stumps were held together with concentrated coagulated blood plasma. In 1988 Narakas revived the use of fibrin in nerve repair. Since then, its use has steadily gained popularity amongst the peripheral nerve surgeons.

A recent study has compared the use of fibrin glue and microsutures in the repair of rat median nerve and found that nerve repairs performed with fibrin sealants produced less inflammatory response and fibrosis, better axonal regeneration, and better fiber alignment than the nerve repairs performed with microsuture alone. In addition, the fibrin sealant techniques were quicker and easier to use. Bozorg at al have reported promising results with fibrin glue in he repair of facial nerve in human beings.

END TO SIDE NEURORRHAPHY

In last two decades, there has been a volume of research evaluating end-to-end versus end-to-side repairs but it is generally accepted that end-to-side will provide only limited sensory recovery.

The technique seems most successful when the epineurium is opened and there has been a small amount of damage to the enclosed fascicles during the placement of a distal nerve stump to the whole nerve. An end-to-side repair will allow motor reinnervation through collateral sprouting only when there has been a direct nerve injury at the repair site, such as a partial neurectomy

NERVE GUIDANCE CONDUIT

Nerve guidance conduit (also referred to as an artificial nerve conduit or artificial nerve graft, as opposed to an autograft) is an artificial means of guiding axonal regrowth to facilitate nerve regeneration and is one of several clinical treatments for nerve injuries. When direct suturing of the two stumps of a severed nerve cannot be accomplished without tension, the standard clinical treatment for peripheral nerve injuries is autologous nerve grafting. Due to the limited availability of donor tissue and functional recovery in autologous nerve grafting, neural tissue

engineering research has focused on the development of bioartificial nerve guidance conduits as an alternative treatment, especially for large defects. Similar techniques are also being explored for nerve repair in the spinal cord but nerve regeneration in the central nervous system poses a greater challenge because its axons do not regenerate appreciably in their native environment.

Despite some limited improvements in surgical technique, for more than 5 decades we have continued to use autologous nerve grafts to reconstruct nerve lesions, consequently creating donor site morbidities leading to non sensitive areas or even ulcers or pressure sores. This project will aim to show how seeding cells around a nerve suture could be of therapeutic use for the treatment of nerve injury, a nerve cells may serve as a stimulus to nerve regeneration.

Scientifically, the project will serve as the bases for the future use of ADSC, differentiated to a Schwann cell phenotype for the treatment of nerve lesions. Since nerve lesions are common within the population we expect this research to have widespread health and socioeconomic consequences. Division of a peripheral nerve results in impaired sensation, reduced motor function and sometimes pain. Such injuries have a profound and permanent impact of the patient's life as they do not regain normal function. There are also serious economic implications for both the individual patient and society as a whole as a result of the intensive period of rehabilitation required and a mean time off work ranging from 21.4 to 31.3 weeks, with just 59 – 69% of patients back in full time work 1 year after injury. The total expense per patient is estimated to be EUR 51,238 for median and ulnar nerve injuries.

The results of this project will define a new clinical possibility, using cells, to easily repair nerves without implanting non human derived substances, allowing surgeons to address nerve gap lesions in a fast and easy way. The recommendations derived from this study will result in improved outcome of nerve lesions without the drawback of a de-sensitised area either at the donor site or at the reconstructed area. The project also aims to prove the positive effect of modified neural repair on reinnervation and consequently muscle tone and activity. The results could have

beneficial effects on muscle restitution after trauma with or even without nerve damage. In summary, these experiments will examine the extent of nerve regeneration in combination with analysis of muscle morphology and biochemistry to evaluate fully the effectiveness of using nerve cells around the neural suture for nerve repair. This could allow new ways of treating nerve lesions providing a better outcome and minimal morbidity.




Fig. no. 29 – 32: Microsurgery lab of Floreasca Emergency Hospital

NERVE REPAIR USING SILICONE TUBE

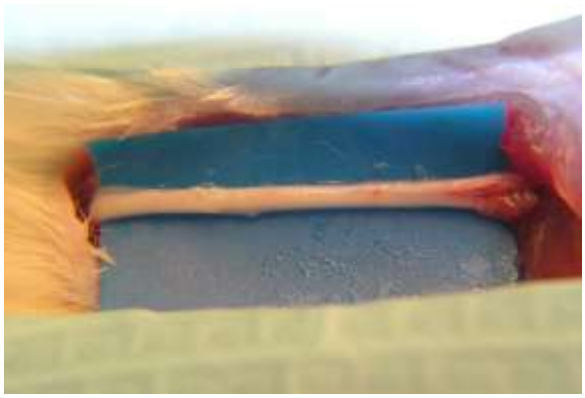
Aim of this study is to determine alternative methods for nerve repair to avoid nerve graft.

- We randomized 6 Wistar rats, aprox 450g each, in 2 groups:
- Control group
- Silicone tube group
- For control group we used epineural neuroraphy

- For Silicone tube group we used a silicone tube with 2mm internal diameter and wall thickness of 0,18mm

SURGICAL PROTOCOL

- We used inhalation anaesthesia with Halotane and O2.
- For surgical intervention we used a surgical microscope with magnification between 10-40x in aseptic conditions.
- We did an oblique incision in the dorsal part of rat thigh.
- We dissected the muscles and exposed sciatic nerve.
- For silicone tube group we used an 1 cm silicone tube and we let between nerve stumps 5mm.
- For control group we used epineural neuroraphy.
- Sutureing was done with 9/0 Polipropylene suture.



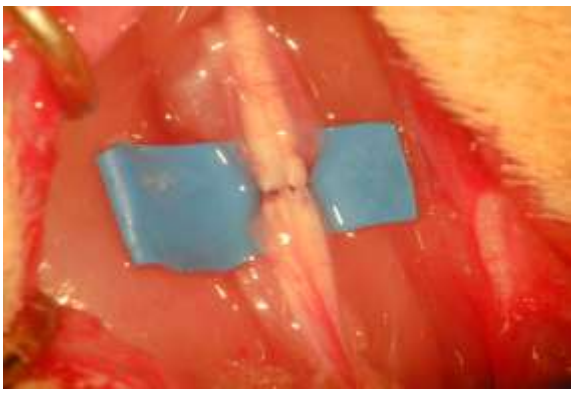


Fig. no. 33 – 34: Epineural suturing – Control group

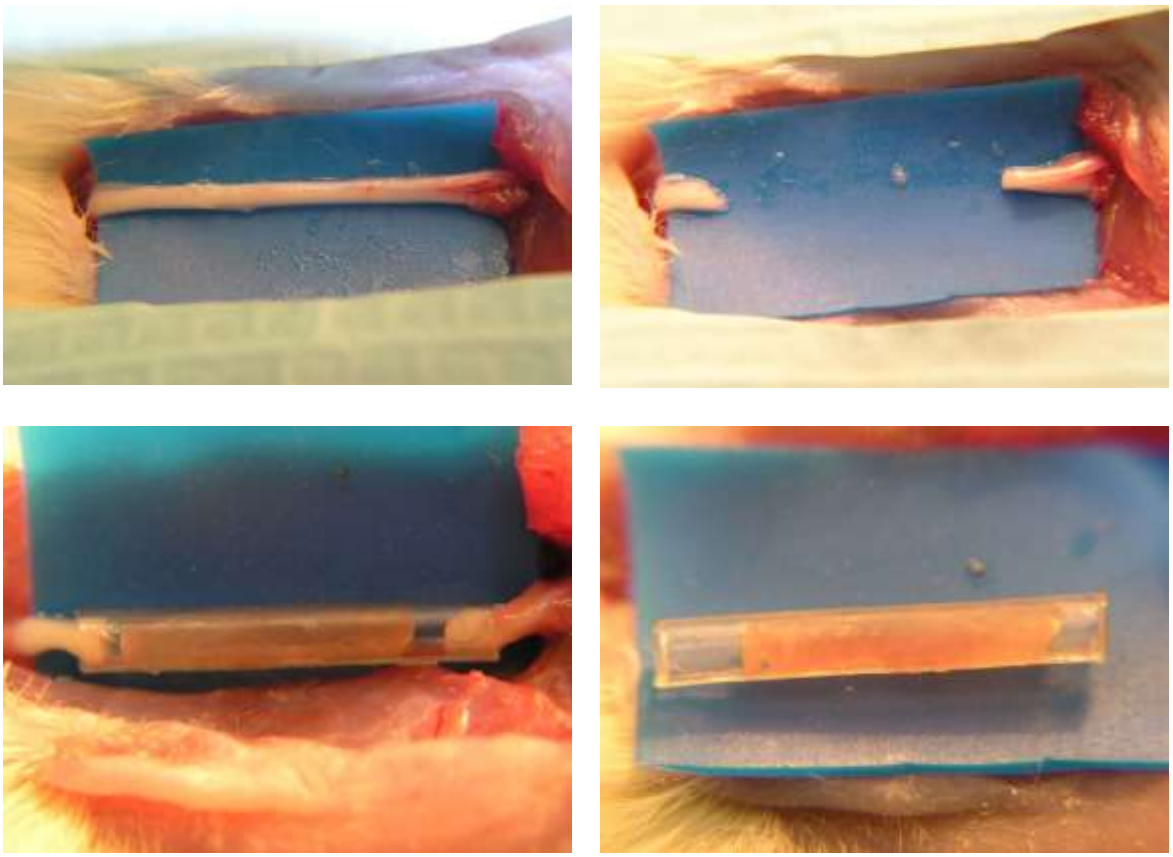


Fig. no.35-39: Silicone tube group

We asses the rats at 6 and 9 months postoperatively

- 2 rats died from control group
- 1 rat died from silicone tube group

PROTOCOL FOR EMG ASSESING

- We used an EMG machine
- We stimulated sciatic nerve proximal and distal with 2 electrodes
- We put the electrode for recording in the muscles of the calf
- We put the referent electrode to the calcanean tendon
- We put the closing electrode subcutaneous between stimulation and recording electrodes
- We used a pulse 0,2ms, 20mA,10Hz and 6 continous stimulation
- We recorded NCV

- We compared NCV for the 2 groups with NCV from healthy thigh of the rats

NCV RECOVERY RATE

- For unoperated limb NCV was between 65,40 – 93,20 m/s
- For control group at 6 months p.o NCV was 72 m/s
- For control group at 9 months p.o NCV was 49.68 m/s
- For silicone tube group at 6months p.o NCV was between 35.97-50.32 m/s
- For silicone tube group at 9 months p.o NCV was between 37.93-55.26 m/s

Table no.5

Group	Unoperated limb	6 months	9 months
Control	72,40 m/s	43.20 m/s	49.68 m/s
Silicone tube-rat #1	65.40 m/s	35.97 m/s	37.93 m/s
Silicone tube-rat #2	93.20 m/s	50.32 m/s	55.26 m/s

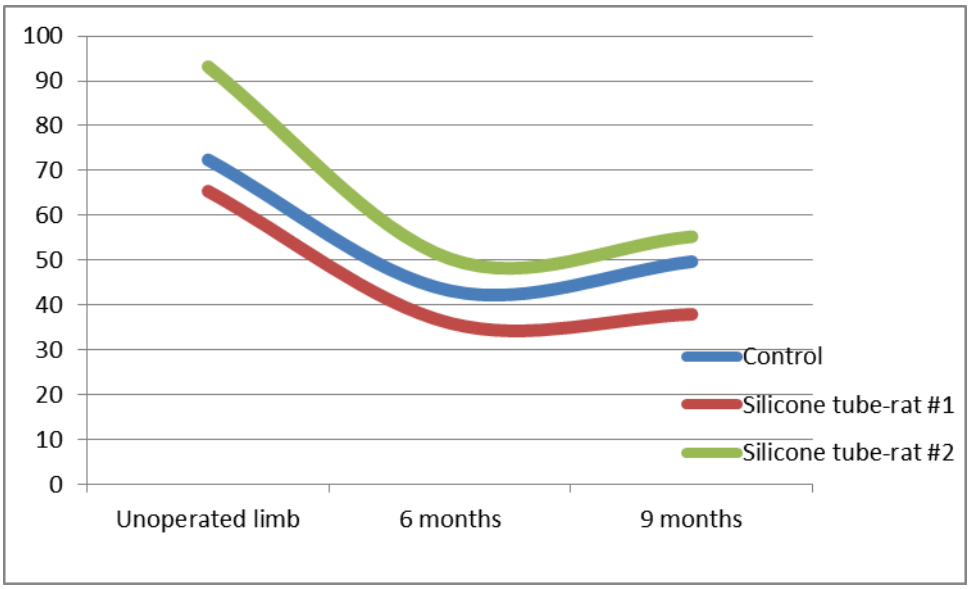


Chart no. 1 – Ncv recovery rate

Table no. 6

Group	UNOPERATED LIMB	6 MONTHS	9 MONTHS
Control	72,40 m/s	59.66	68.61
Silicone tube-rat #1	65.40 m/s	55	58.46
Silicone tube-rat #2	93.20 m/s	54	59.3

- Both groups have a difference between unoperated limb and operated limb at 9 months.
- Are not significant differences for nerve recovery between silicone tube group (54.5%recovery at 6 month, 58.85%at 9 months) and control group (59.66% at 6 month, 68.61% at 9 months)
- We conclude that silicone tube technique is a good technique as an alternative for nerve graft.

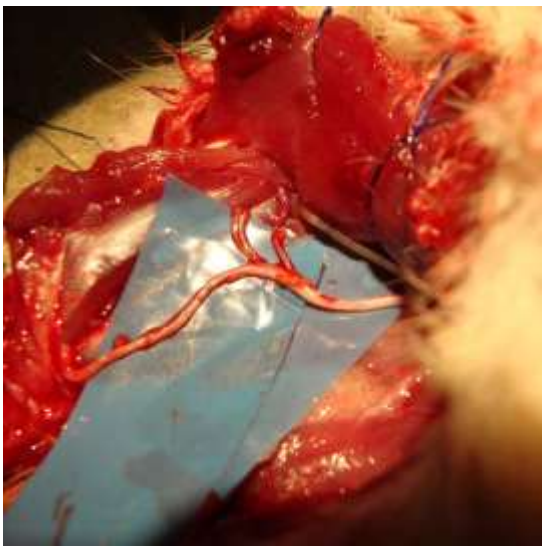
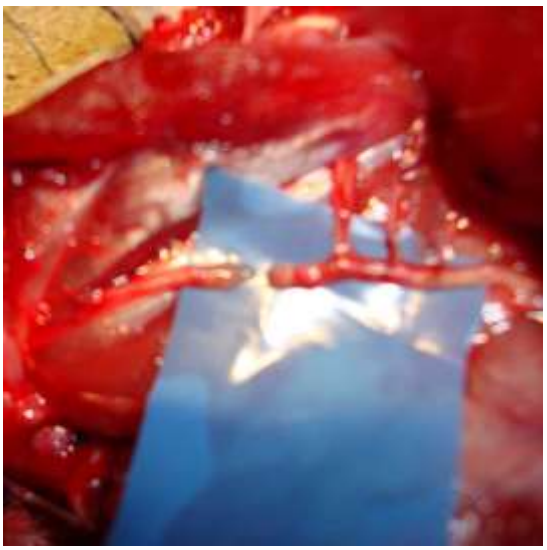
NERVE REPAIR USING CHOPPED NERVE AROUND THE SUTURE

Two different experimental groups will be tested:

- Suture only
- Suture + seeding with chopped nerve

- Adult rats (7 animals per group) are anaesthetised useing Ketamin and Dormicum injection.
- The sciatic nerve is transected
- 3 mm segment of nerve is excised and the nerve sutured with a perineural technique with 9/0 sutures.

- In the study group, the segment of nerve is chopped and seeded around the nerve suture, while nothing will be done in the control group
- Two different time-points will be examined, 6 months and 9 month

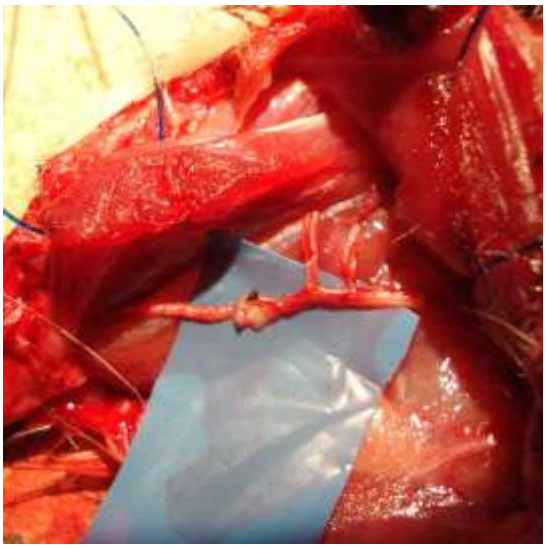


Fig. no. 40 – 44: Nerve repair using chopped nerve around the suture

We asses the rats at 6 and 9 months postoperatively

- 2 rats died from control group
- 3 rats died from suture+chopped nerve group

- We used an EMG machine
- We stimulated sciatic nerve proximal and distal with 2 electrodes
- We put the electrode for recording in the muscles of the calf

- We put the referent electrode to the calcanean tendon
- We put the closing electrode subcutaneous between stimulation and recording electrodes
- We used a pulse 0,2ms, 20mA,10Hz and 6 continous stimulation
- We recorded NCV
- We compared NCV for the 2 groups with NCV from healthy thigh of the rats

Table no. 7

	UNOPERATED LIMB (m/s)	6 MONTHS (m/s)	9 MONTHS (m/s)
RAT #1	72,50	44.22(61%)	48.75(67%)
RAT #2	78.40	49.39(63%)	54.09(69%)
RAT #3	69.10	41.46(60%)	45.60(66%)
RAT #4	84.60	52.90(62.54%)	56.96(67.34%)
RAT #5	87.30	55.95(64.10%)	60.58(69.40%)

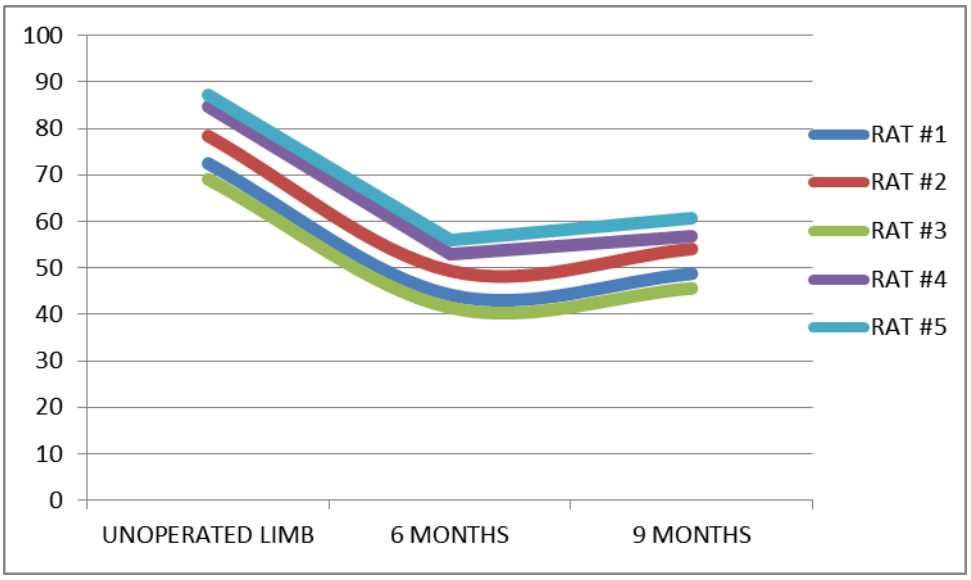


Chart no. 2 – NCV in control group

Table no. 8

	UNOPERATED LIMB (m/s)	6 MONTHS (m/s)	9 MONTHS (m/s)
RAT #1	69,50	2.9	3.3
RAT #2	62.40	3.6	3.9
RAT #3	89.10	2.4	2.7
RAT #4	76.30	4.1	4.9

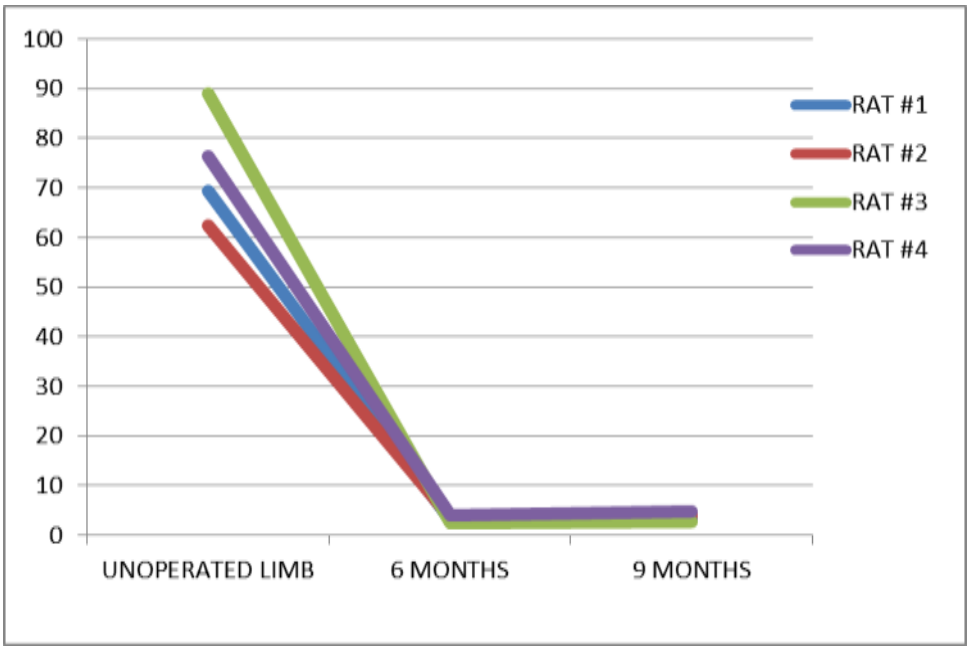


Chart no. 3: NCV in chopped nerve around the suture group

- For unoperated limb NCV was between 62,40 – 89,10 m/s with a medium value of 76,5m/s
- For control group at 6 months p.o NCV was between 41.46-55.9 m/s with a medium value of 48.78 m/s
- For control group at 9 months p.o NCV was between 48.75-60.58 m/s with a medium value of 53.19 m/s

- For suture+chopped nerve group at 6 months p.o NCV was between 2.4-4.1 m/s with a medium value of 3.25 m/s
- For suture+chopped nerve group at 9 months p.o NCV was between 2.7-4.9 m/s with a medium value of 3.7 m/s
- We conclude that seeding chopped nerve in the suture is not a viable alternative for nerve graft, so we don't continue this study in the future

CLINICAL EXPERIENCE IN PERIPHERAL NERVE REPAIR (FLOREASCA PLASTIC SURGERY DEPARTMENT BUCHAREST, CONSTANTA PLASTIC SURGERY DEPARTMENT) – RETROSPECTIVE AND PROSPECTIVE STUDY

Total number of patients

Table no. 9

City	No of patients
Constanta	478
Bucharest	1742

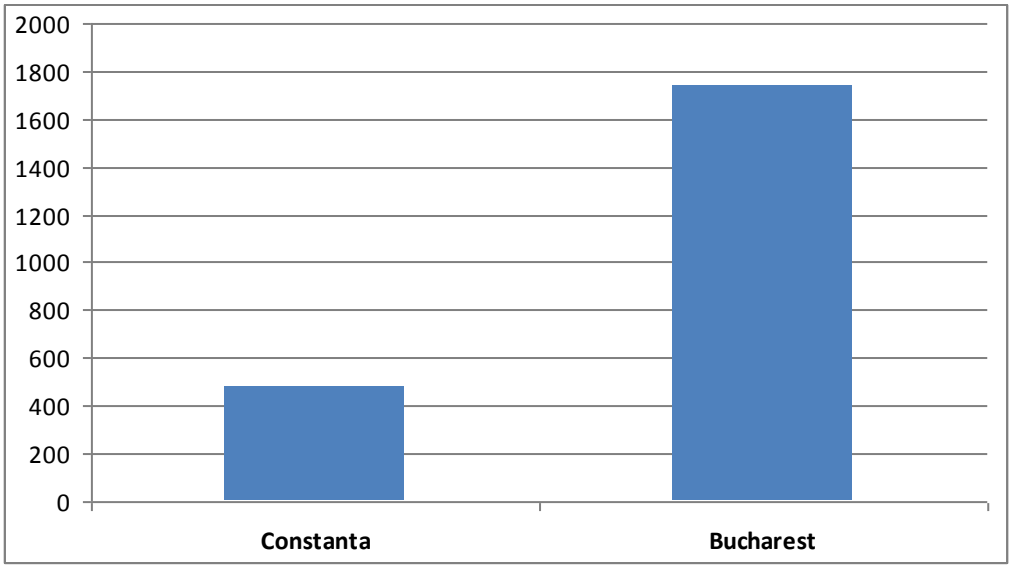


Chart no. 4

Distribution over years

Table no.10

	Constanta	Bucharest	%Constanta	%Bucharest
2006	90	281	18.83	16.13
2007	110	439	23.01	25.20
2008	121	382	25.31	21.93
2009	89	354	18.62	20.32
2010	68	286	14.23	16.42
Total	478	1742	100	100

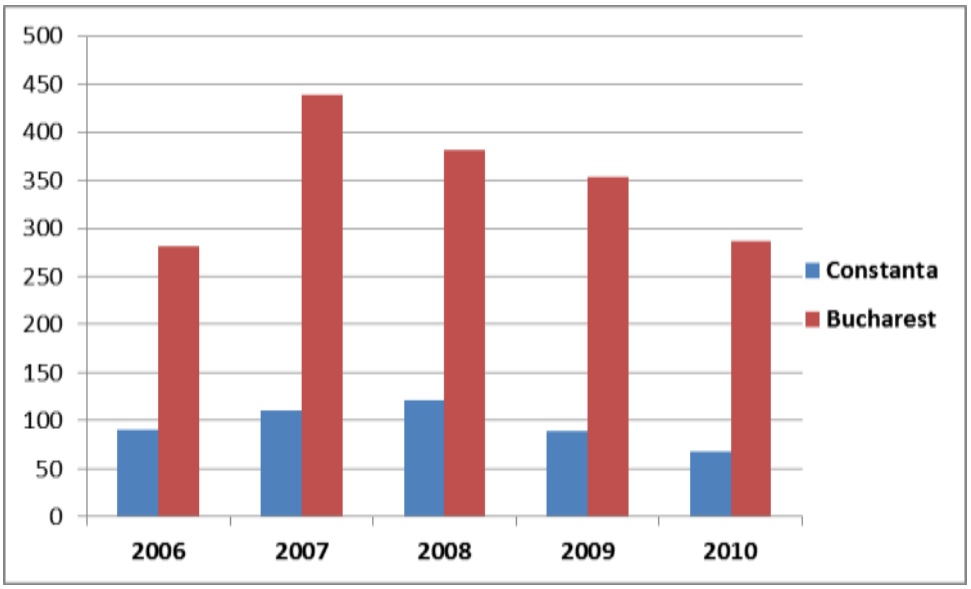


Chart no.5

As we see in the previous table and graph in both locations the peak of frequency is in the year 2007 and 2008.

Sex ratio

Table no. 11

	Constanta	Bucharest	%Constanta	%Bucharest
Male	362	1352	75.73	77.61
Female	116	390	24.27	22.39

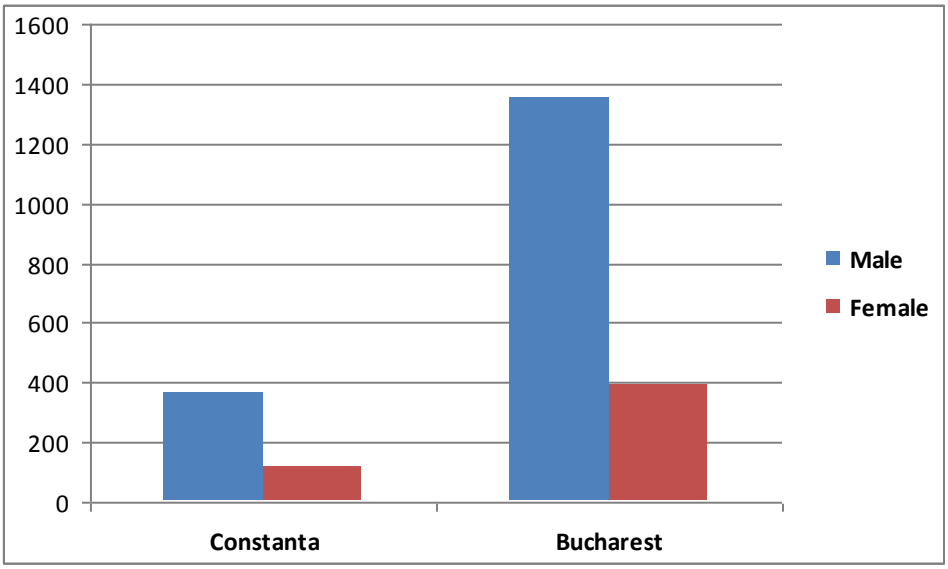


Chart no. 6

The table and graphs reveal that men present more hand traumatic lesions than women because of their professional and domestic activities that predispose them to accidents.

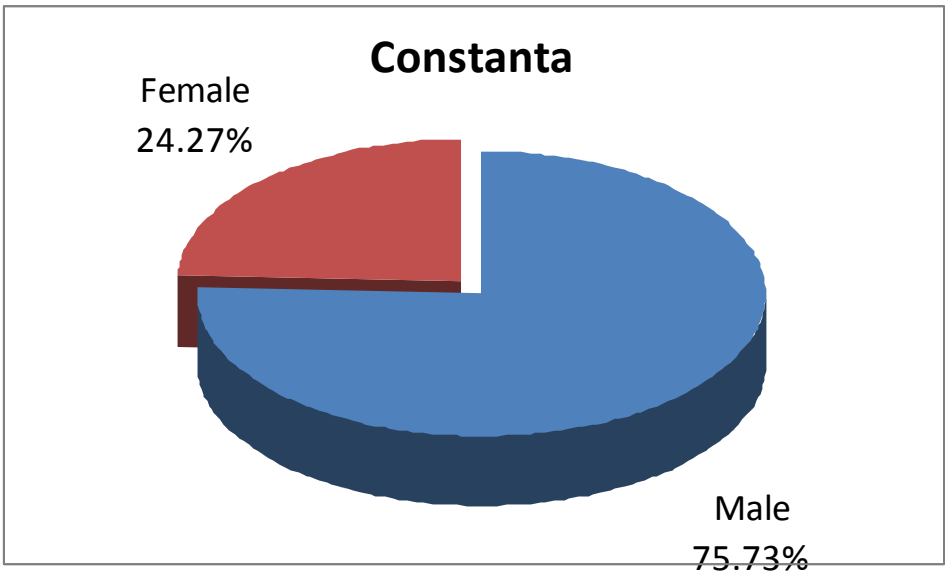


Chart no. 7

A total number of 478 consecutive patients with nerve injury attended the Plastic Surgery Clinic of Constanta Emergency Hospital of which 362 were men and 116 were female. The distribution of hand injury according to the sex group is seen in table and graph

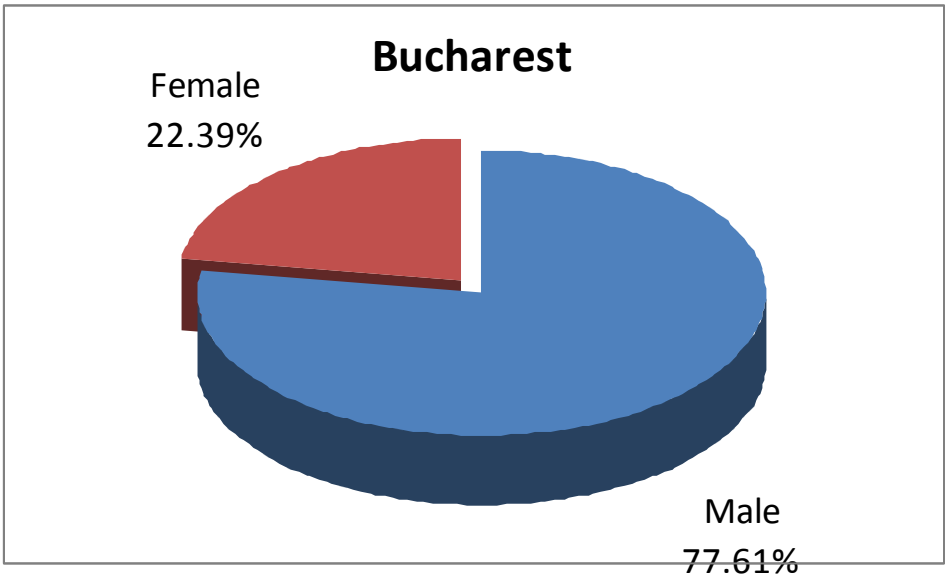


Chart no. 8

A total number of 1742 consecutive patients with nerve injury attended the plastic surgery clinic of "Floreasca"Emergency Hospital Bucharest of

which 1352 were men and 390 were female. The distribution of hand injury according to the sex group is seen in previous table and graph.

Distribution over age

Age of the patient is the single most critical factor in sensory recovery after nerve repair, but results are adversely affected by associated injuries to muscle, arteries, tendons, and bone;

Young patients can recover close-to-normal nerve function. In contrast, a patient over 60 years old with a cut nerve in the hand would expect to recover only protective sensation; that is, the ability to distinguish hot/cold or sharp/dull.

Results of nerve repair begin to decline after second decade (75% good results in children vs 50% good results in adults).

Results of nerve repair may be poor after the sixth decade;

Table no. 12

Decade	Constanta	Bucharest	%Constanta	%Bucharest
0 - 10	9	19	1.88	1.09
11 - 20	27	94	5.65	5.40
21 - 30	63	320	13.18	18.37
31 - 40	118	428	24.69	24.57
41 - 50	127	468	26.57	26.87
51 - 60	94	278	19.67	15.96
>60	40	135	8.37	7.75

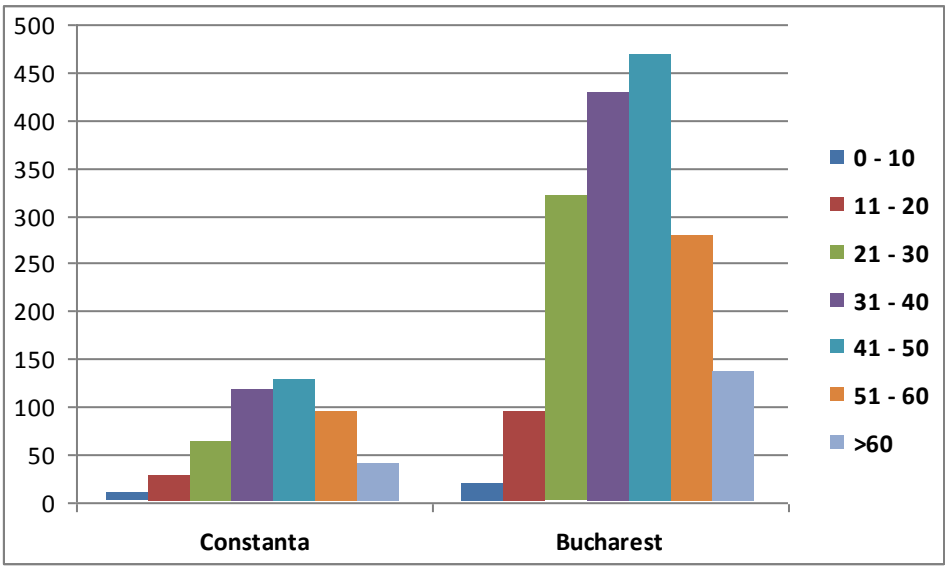


Chart no. 9

The table and graphs lead to the conclusion that the most exposed subjects are patients between 30 and 50 year because their involvement in the proces of work. This is very important because this type of accidents can affect the work capacity needing a long period of rehabilitation and sometimes can cause the total loss of this work capacity and profesional reintegration.

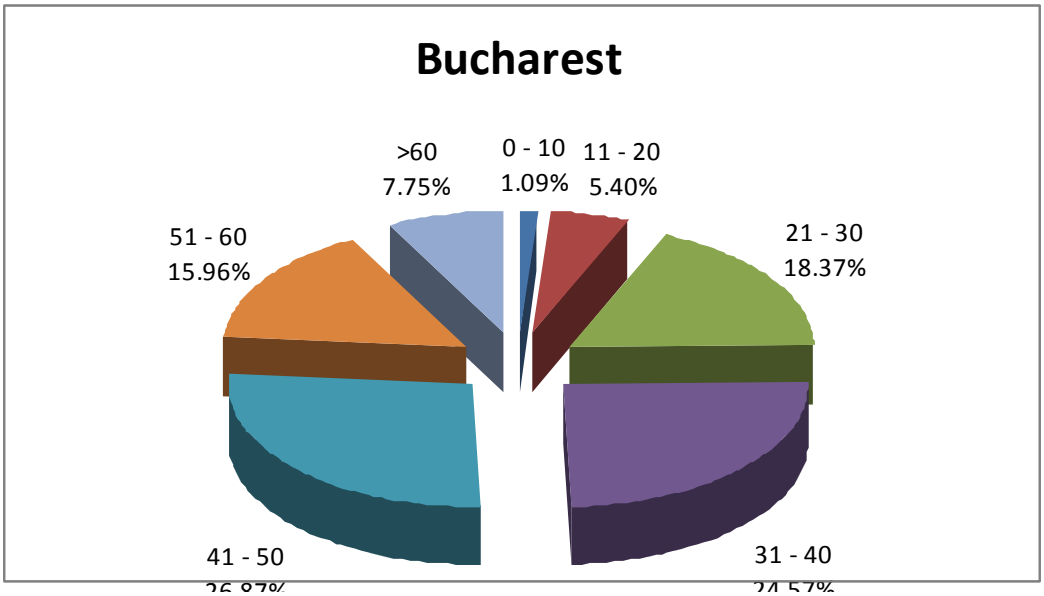


Chart no.10

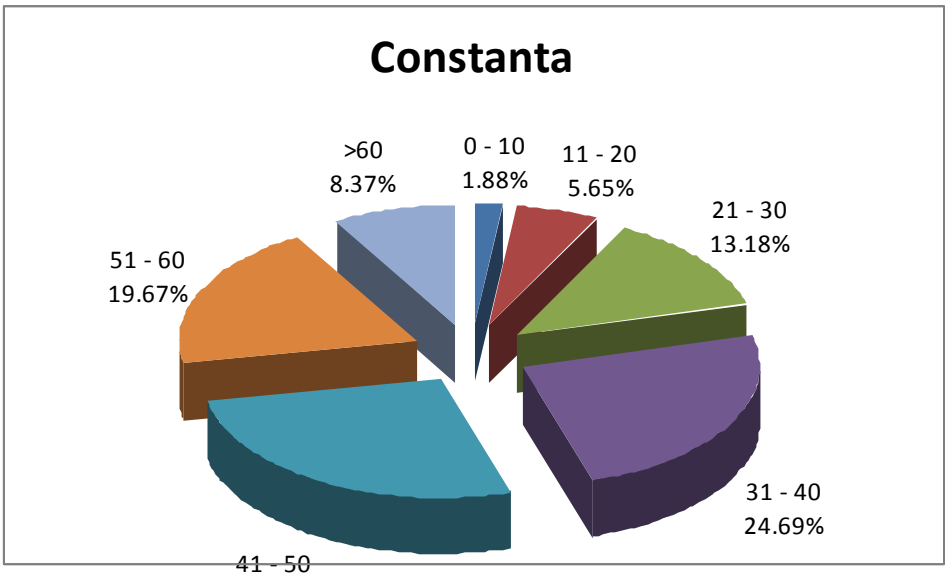


Chart no. 11

Smoking

Peripheral nerves have a high metabolic demand and require a continuous energy supply to support impulse transmission and axonal transport. They are perfused through a rich network of extrinsic and intrinsic blood vessels. In the event of interruption of this blood flow, high energy phosphates are rapidly depleted and conduction failure ensues. Nicotine has been shown to worsen the severity of ischemia/reperfusion injury in experimental models.

This suggests that cigarette smoking may worsen the damage caused to peripheral nerves by ischemia and reperfusion. If true, this holds important implications for cigarette smokers who sustain extremity injuries or who suffer from nerve damage syndromes. Smoking cessation may prove to be a useful adjunct in the treatment of patients with nerve injuries

Further, pharmacologic manipulation of the effects of nicotine upon peripheral nerves could prove to be a useful adjunct to the established treatment modalities for neuropathic conditions.

Table no. 13

	Constanta	Bucharest	%Constanta	%Bucharest
Smokers	354	1240	74.06	71.18
Non-smokers	124	502	25.94	28.82

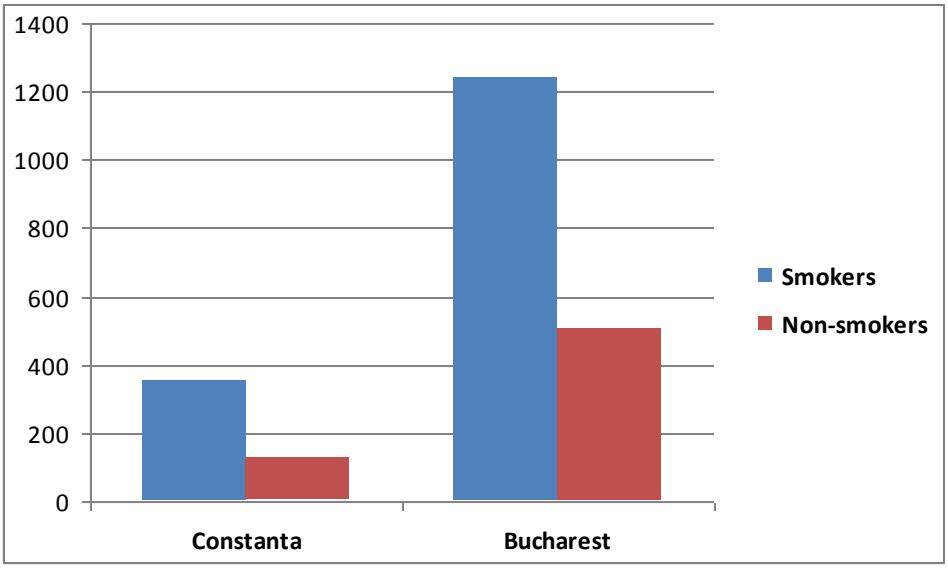


Chart no. 12

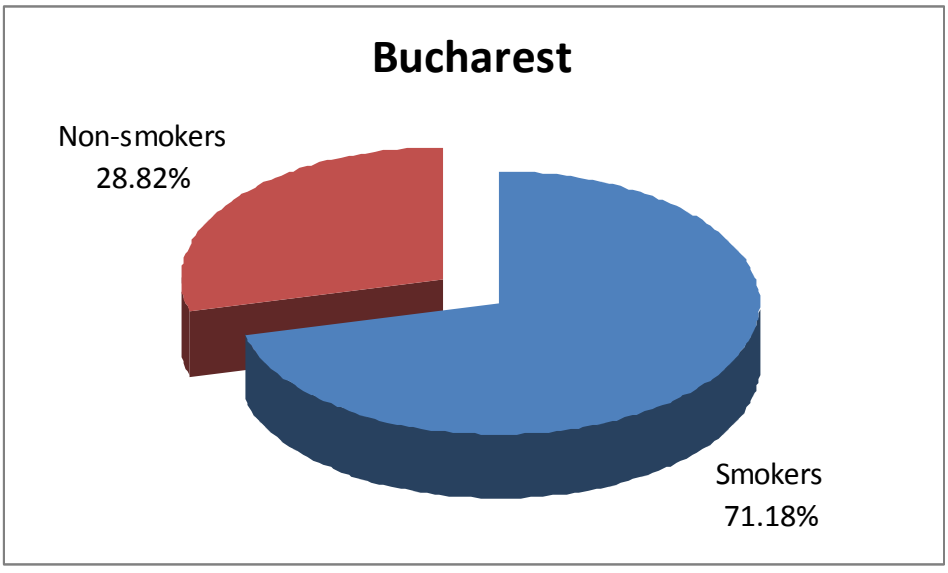


Chart no. 13

Number of smokers in Floreasca" Emergency Hospital Bucharest was 1240 (71.18%) and in Constanta Emergency Hospital 354 (74,06%). This patients have a poor prognostic campareing with non-smokers patients.

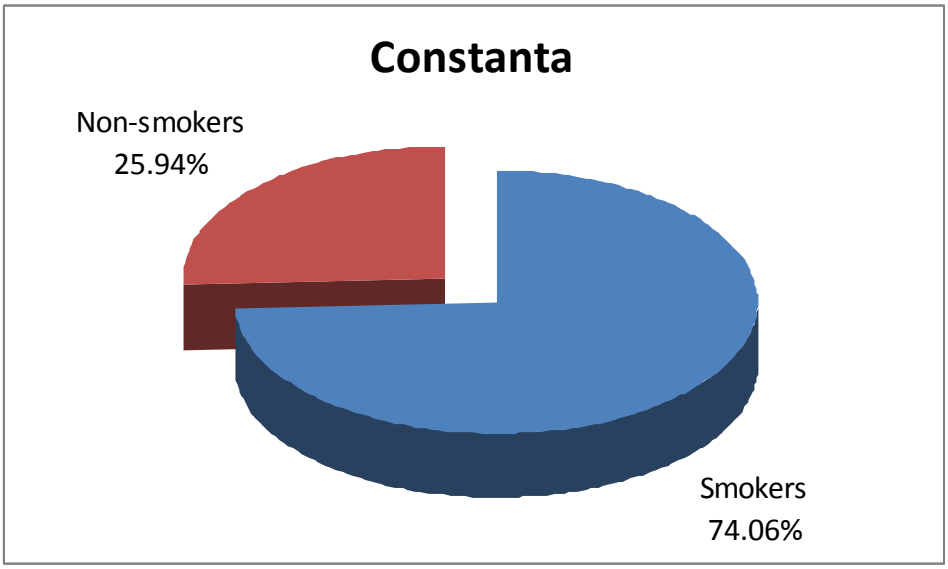


Chart no. 14

Alcohol consumption

Experimental studies show that chronic alcoholism has a negative influence on peripheral nerve regeneration associated with a significant decrease in axon number and increased axonal degeneration.

Table no. 14

	Constanta	Bucharest	%Constanta	%Bucharest
Drinkers	220	1014	46.03	58.21
Non-drinkers	258	728	53.97	41.79

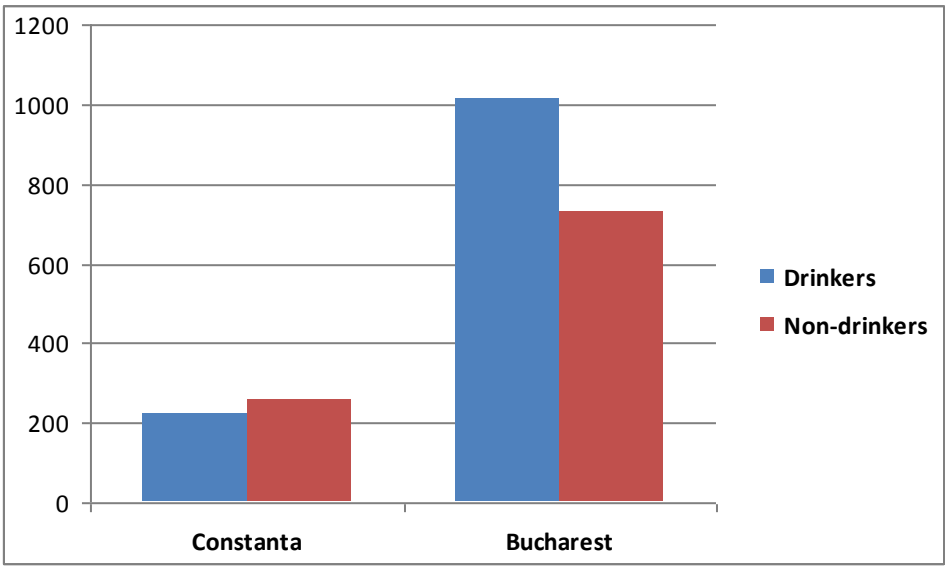


Fig. no. 15

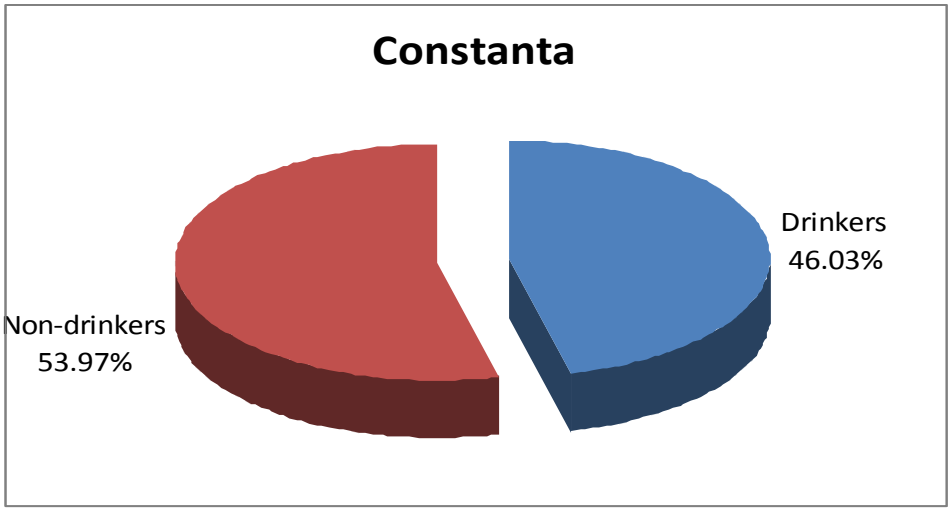


Fig. no. 16

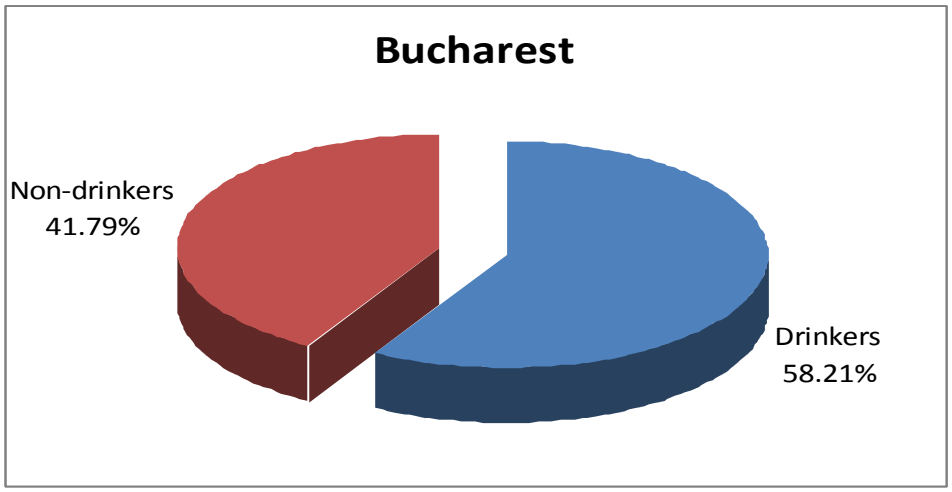


Fig. no. 17

Affected upper limb

Table no.15

	Constanta	Bucharest	%Constanta	%Bucharest
Left	311	1114	65.06	63.95
Right	167	628	34.94	36.05

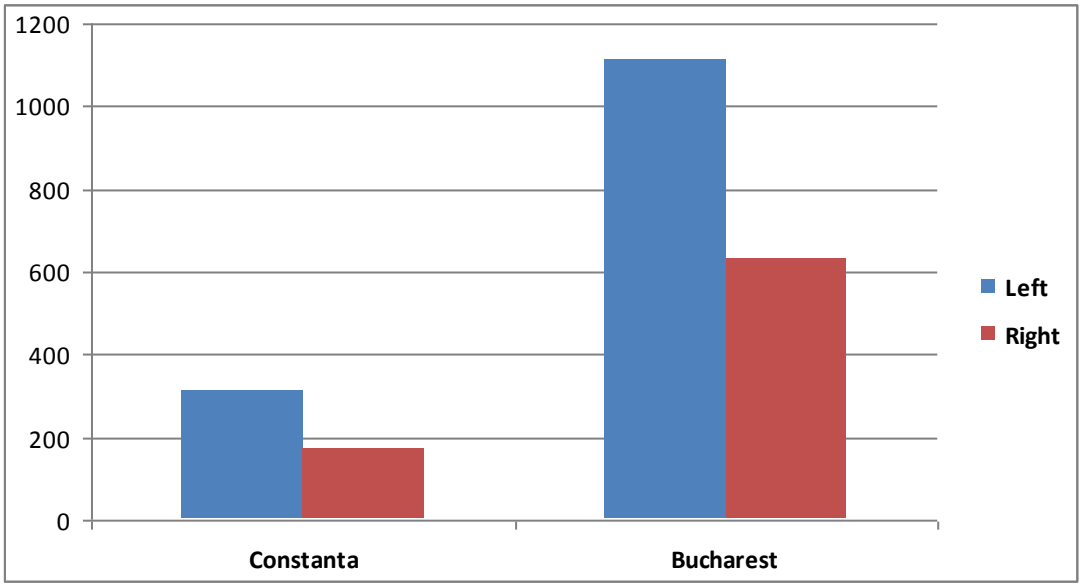


Chart no. 18

The right hand was injured in 167 patients (34.9%)in Constanta Emergency Hospital and 628 patients in “Floreasca” Emergency Hospital Bucharest (36%), the left hand injured in 311 patients (65.06%), in Constanta Emergency Hospital and 1114 patients in “Floreasca” Emergency Hospital Bucharest (63.95%) and this reflects the finding of other reports. Graphs showed the sides involved in hand injuries. In 99% of patients right hand was dominant hand.

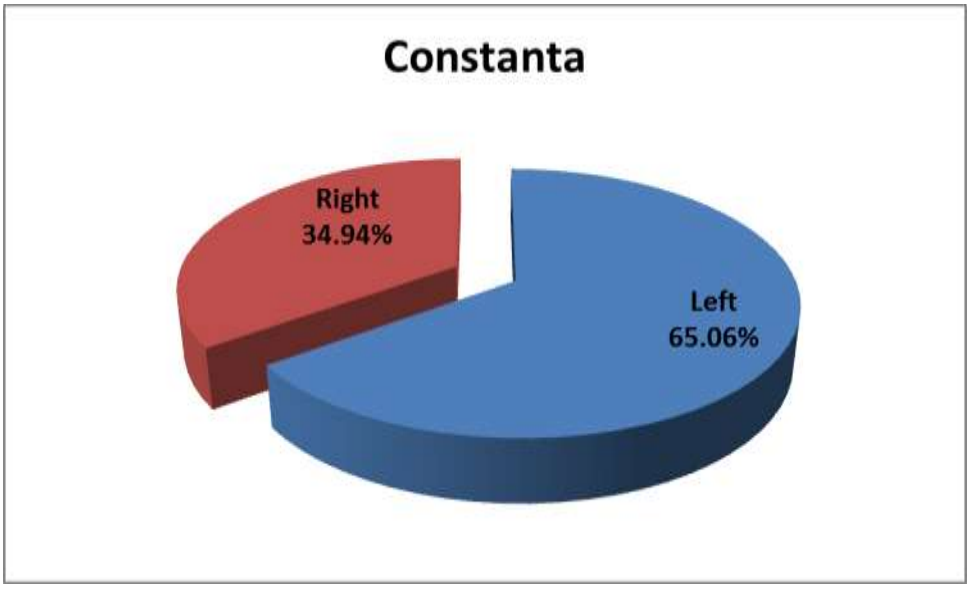


Chart no. 19

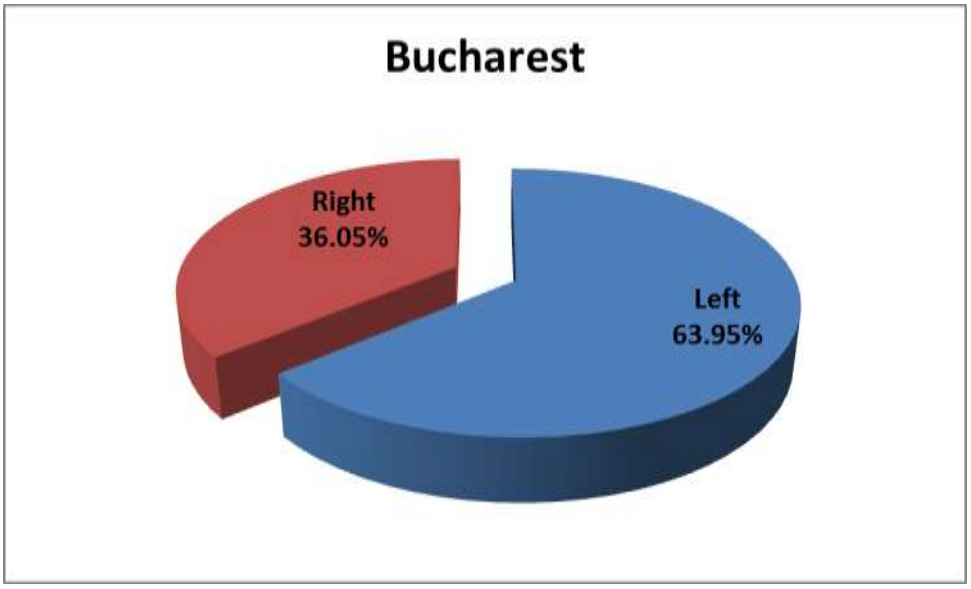


Chart no. 20

Affected nerve

Table no.16

	Constanta	Bucharest	%Constanta	%BucharestR
Median	162	530	33.89	30.42
Ulnar	148	490	30.96	28.13
Radial	17	51	3.56	2.93
Digital	151	671	31.59	38.52

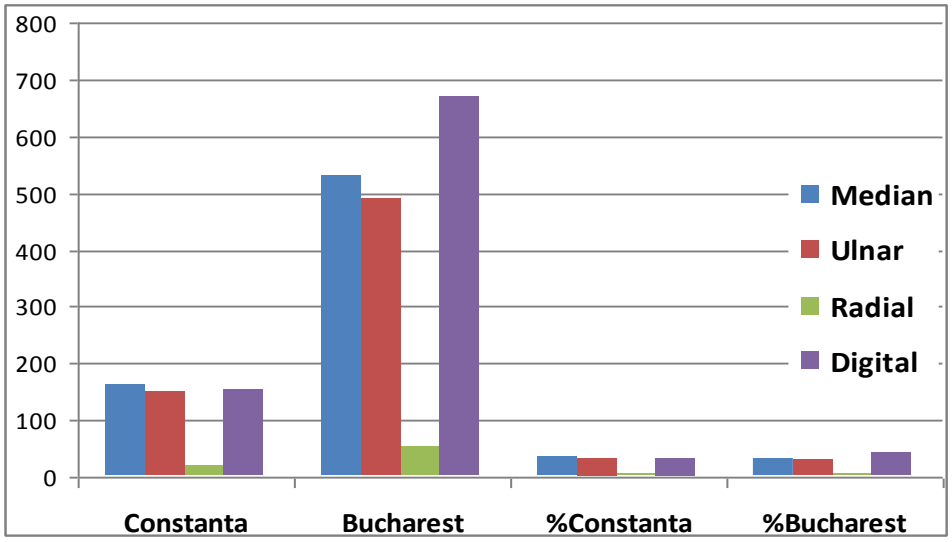


Chart no. 21

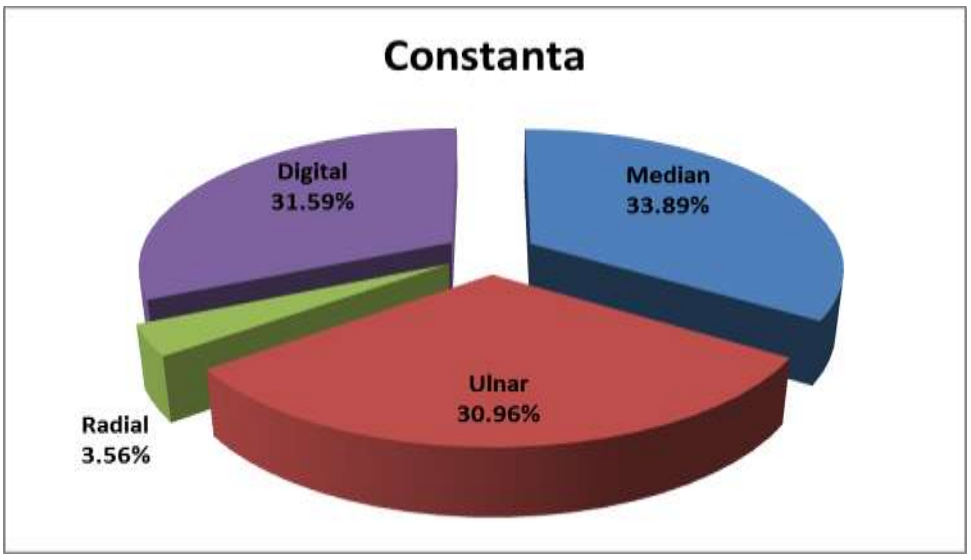


Chart no. 22

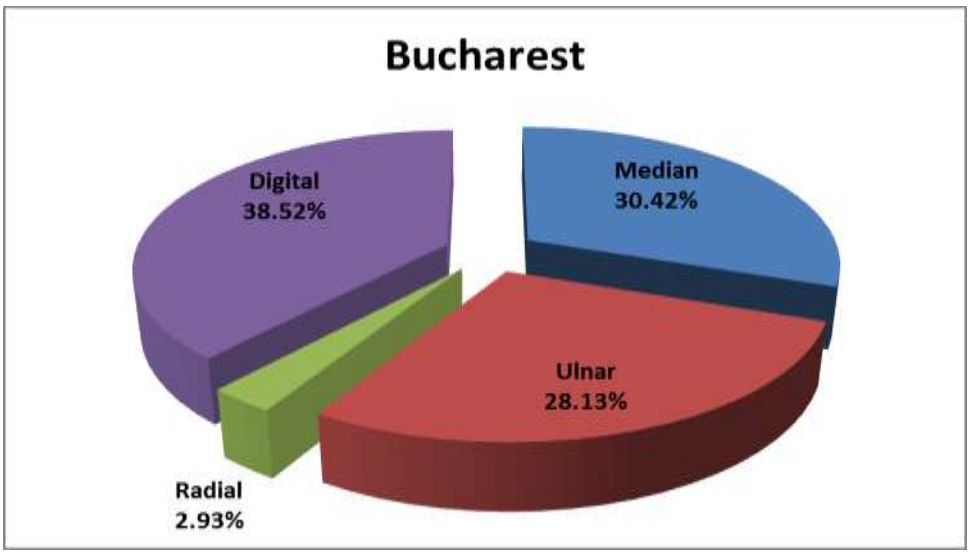


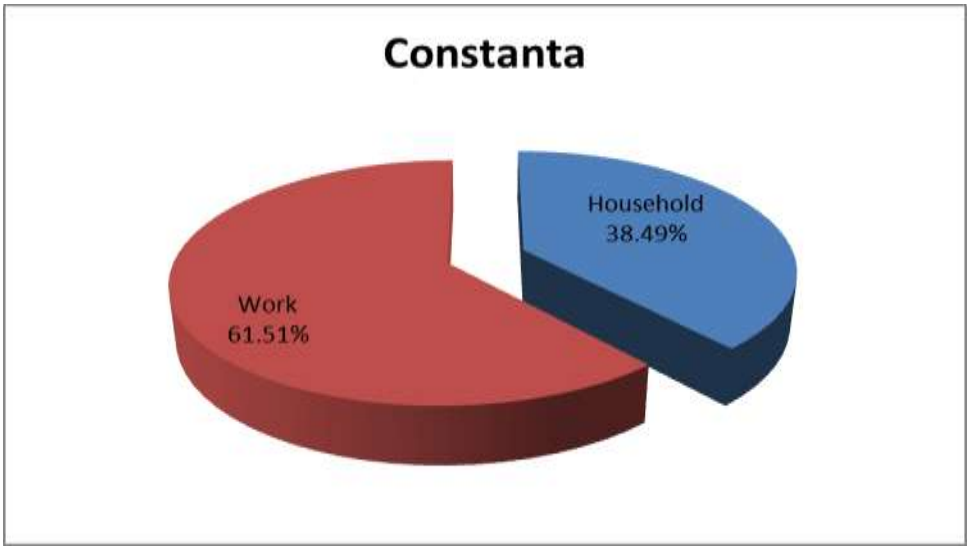
Chart no. 23

Like we saw in previous table and graphs the most affected nerves were digital nerves (151 in Constanta Emergency Hospital and 671“Floreasca” Emergency Hospital Bucharest) followed by median and ulnar nerve in the forearm.

Accident location

Table no. 17

	Constanta	Bucharest	%Constanta	%Bucharest
Household	184	571	38.49	32.78
Work	294	1171	61.51	67.22



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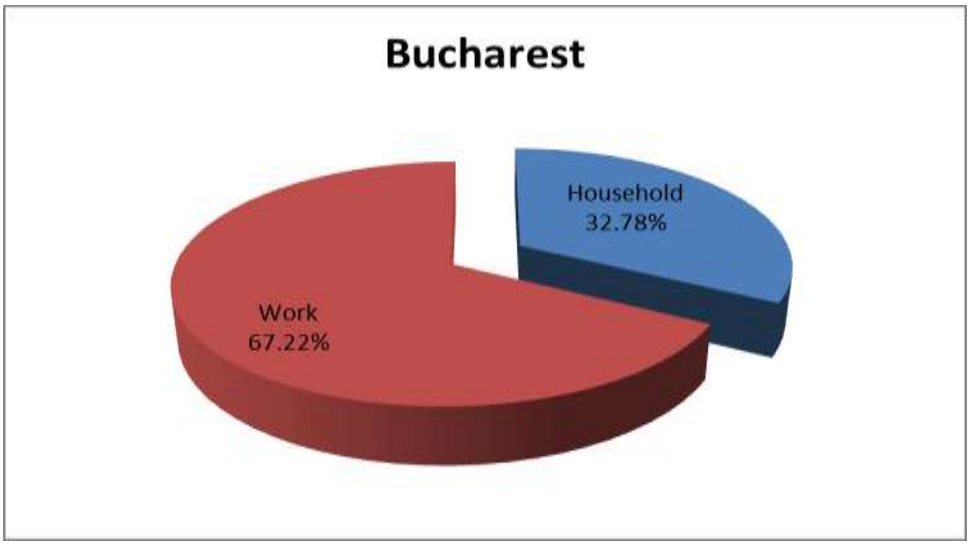

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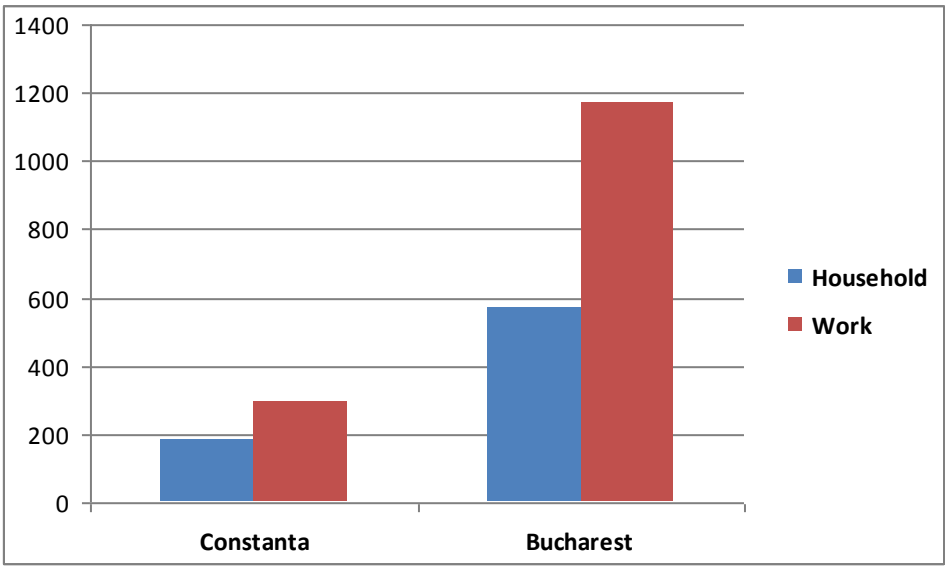
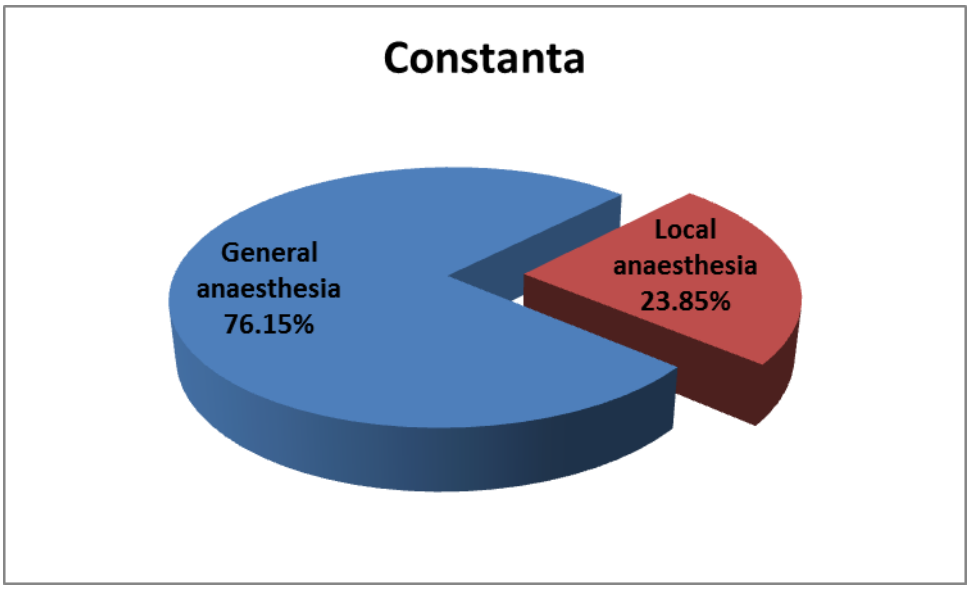


Chart no. 26

Type of anaesthesia

Table no.18

	Constanta	Bucharest	%Constanta	%Bucharest
General anaesthesia	364	1564	76.15	89.78
Local anaesthesia	114	178	23.85	10.22



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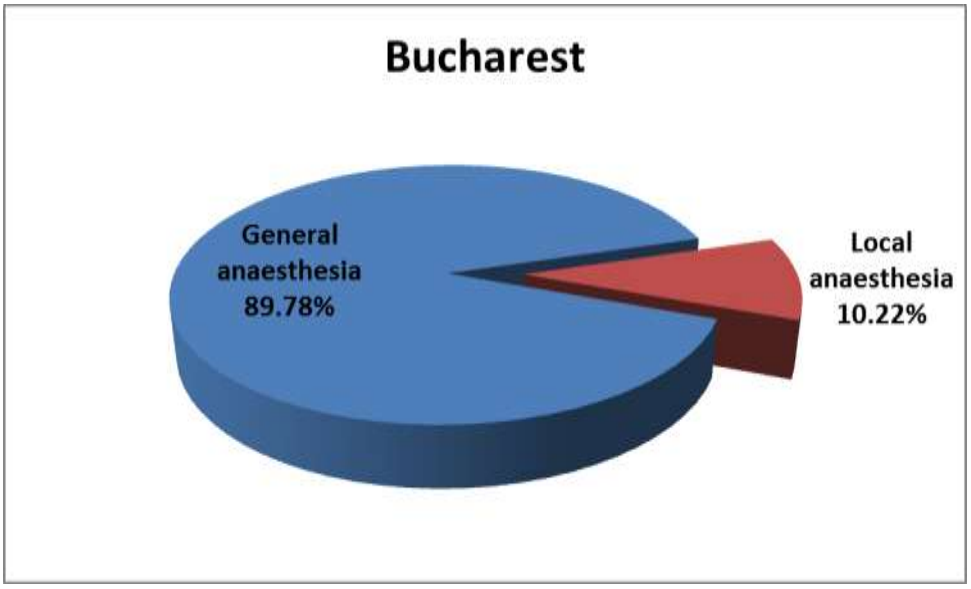

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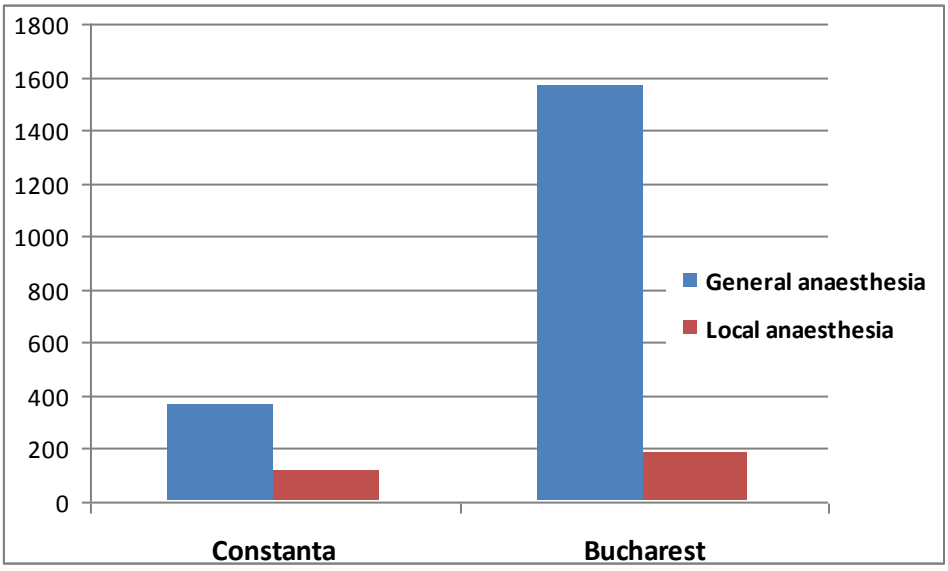


Chart no. 29

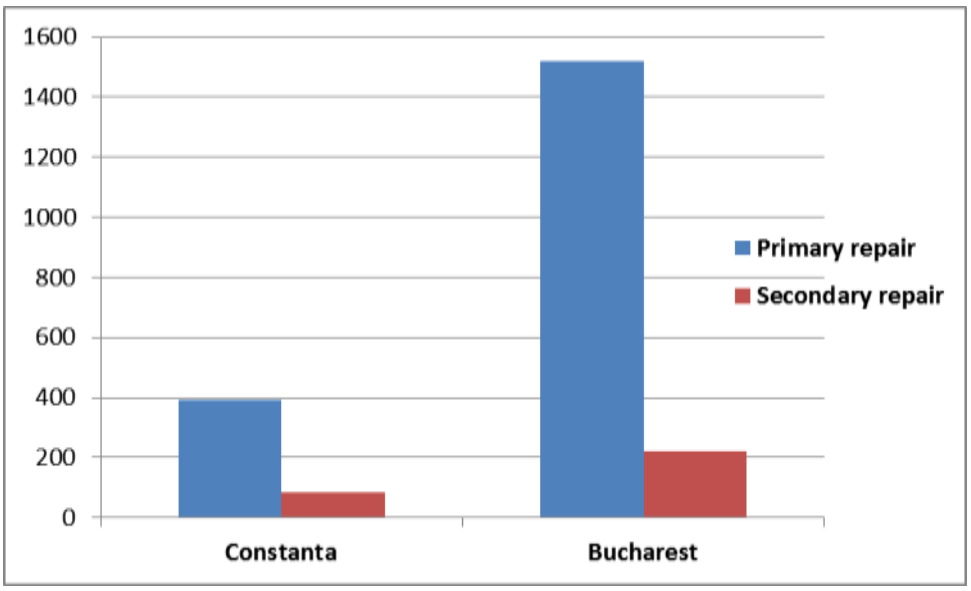
When performing procedures on the hands and upper extremities, many options are available for anesthesia. General anesthesia techniques can be applied for hand and upper extremity procedures the same as for procedures on the rest of the body. However,regional anesthetics have a unique application for procedures of the hand, including axillary,, wrist, and digital blocks. When used in the proper setting and patient population, regional anesthesia can be applied safely for procedures involving the upper extremities and the hands. In general, small needles and lower

volumes of local anesthetic should be used in regional anesthesia to minimize the risk of neurovascular complications. Moreover, epinephrine can be used to augment local anesthetics to provide a longer duration of action, lower risk of adverse systemic effects, and less bleeding at the surgical site.

Time of repair

Table no.19

	Constanta	Bucharest	%Constanta	%Bucharest
Primary repair	392	1521	82.01	87.31
Secondary repair	86	221	17.99	12.69



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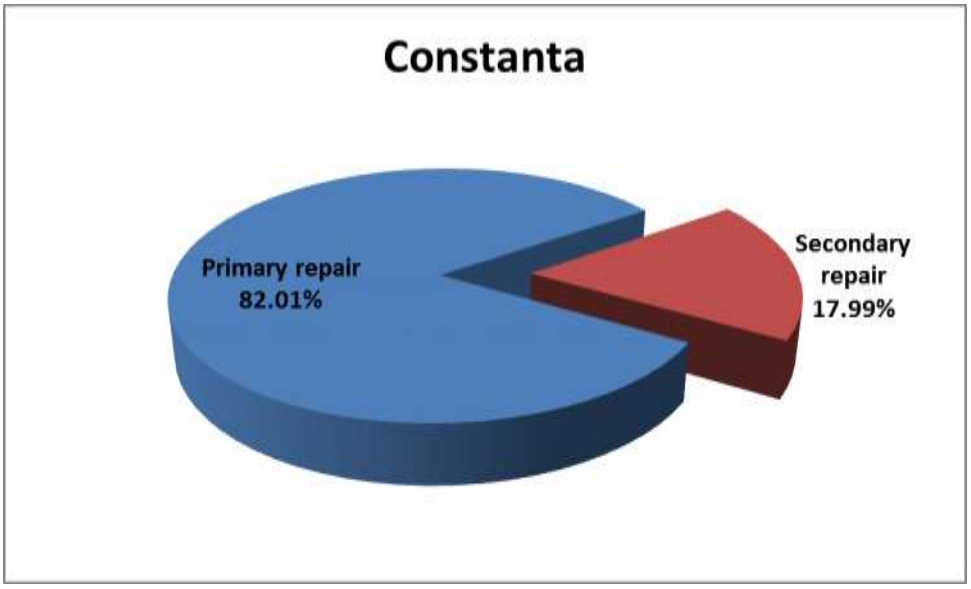

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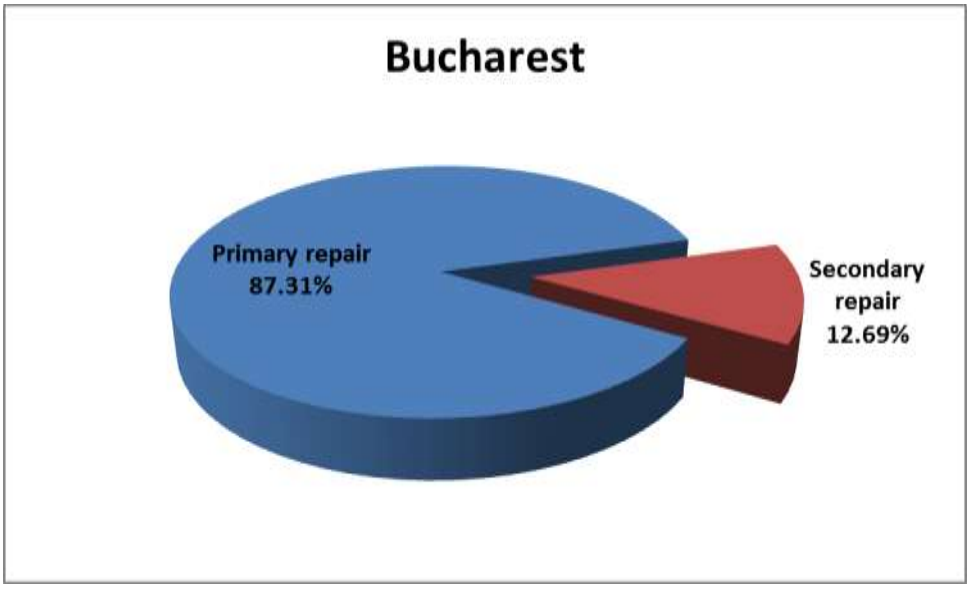
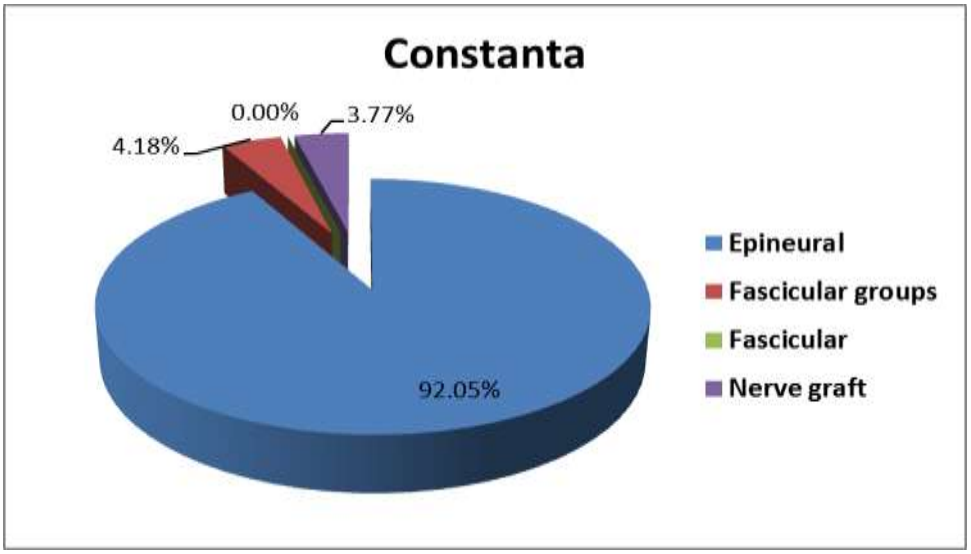


Chart no. 32

Surgical procedure

Table no. 20

	Constanta	Bucharest	%Constanta	%Bucharest
Epineural	440	972	92.05	55.80
Fascicular groups	20	420	4.18	24.11
Fascicular	0	220	0.00	12.63
Nerve graft	18	130	3.77	7.46



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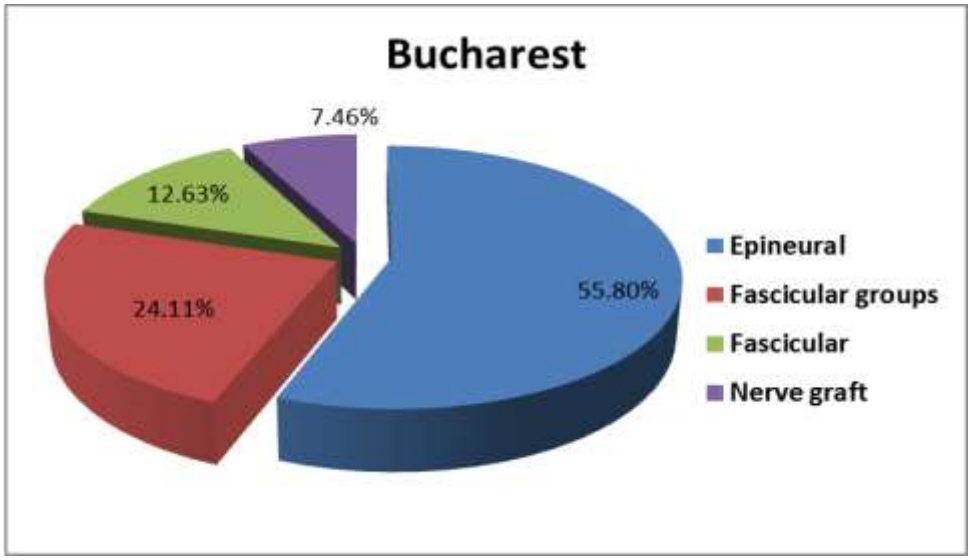

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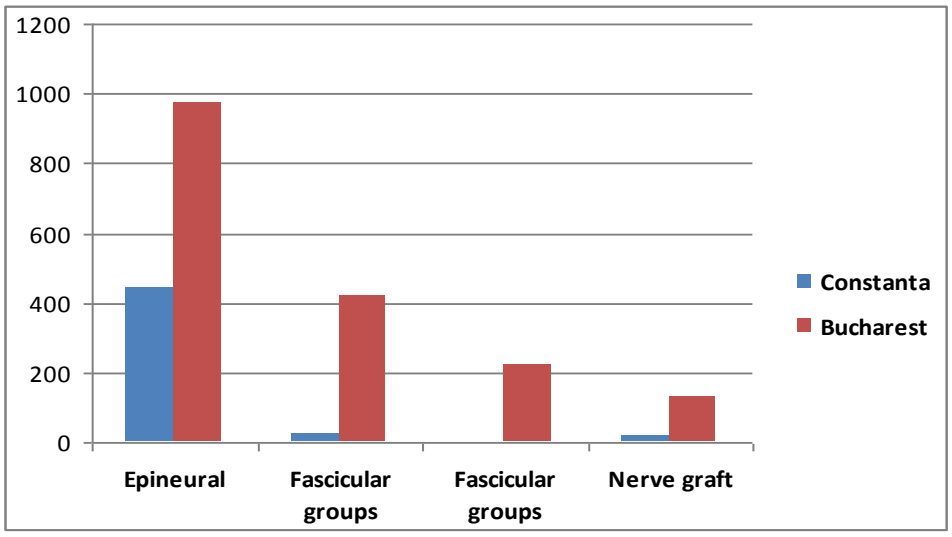

Chart no. 35

Nowadays there is no surgical repair technique that can ensure recovery of tactile discrimination in the hand of an adult patient following nerve repair while very young individuals usually regain a complete recovery of functional sensibility. Post-traumatic nerve regeneration is a complex biological process where the outcome depends on multiple biological and environmental factors such as survival of nerve cells, axonal regeneration rate, extent of axonal misdirection, type of injury, type of nerve, level of the lesion, age of the patient and compliance to training. A major problem is the cortical functional reorganization of hand representation which occurs as a result of axonal misdirection. Although protective sensibility usually occurs following nerve repair, tactile discriminative functions seldom recover--a direct result of cortical remapping. Sensory re-education programmes are routinely applied to facilitate understanding of the new sensory patterns provided by the hand.

In severe injuries of different causes there may be a defect between the severed nerve ends after resection of necrotic tissue of the nerve trunk. As a support for the axons such a defect has to be bridged by a nervegraft . A number of different donor nerves,preferably sensory branches, are available. The most common donor nerve is the sural nerve. At harvest it is possible to get a long (from the lateral malleolus up to just below the knee) graft with few branches . Other donor nerves are the medial antebrachial cutaneous nerve in the forearm and the terminal branch of the posterior interosseous nerve. The latter two are particularly suitable for digital nerves. For digital nerves the use of autologous nerve grafts has been questioned due to potential sequelae after harvesting. Nerve tubes or other alternatives may be selected in such situations.

Choice of nerve repair

- **Epineural**
  - Sutures through the epineural sheath
  - Used in pure motor or pure sensory nerves, digital, radial and median nerves, sharply or evenly severed nerves

- **Group fascicular**
  - Connection of matching groups or bundles of fascicles by placement of sutures in epi-fascicular epineurium
  - Used in larger nerves and partially severed or unevenly transected or avulsed nerves
- **Fascicular**
  - Connection of isolated fasciculi, by placement of sutures in the perineurium
  - Used in neuroma, in continuity, in small nerves, partially severed nerve when only a few fascicles are severed
- **Graft**
  - Nerve grafting is indicated, if gap is 3 - 7 cm or if repair is impossible without tension
  - Nerves which can be used as grafts are the lateral cutaneous nerve of the thigh, the saphenous nerve, the sural nerve, and the medial cutaneous nerve of the forearm
  - If ulnar and median nerves are irreparable, a segment of the ulnar nerve can be used to bridge the median nerve
  - If the graft nerve diameter is small, several strips may be needed (cable graft) and grafts should be 15% longer to avoid tension

Hospitalization period

Table no. 21

	Constanta	Bucharest	%Constanta	%Bucharest
1 - 5 days	287	1342	60.04	77.04
6 - 14 days	178	298	37.24	17.11
>14 days	13	92	2.72	5.28

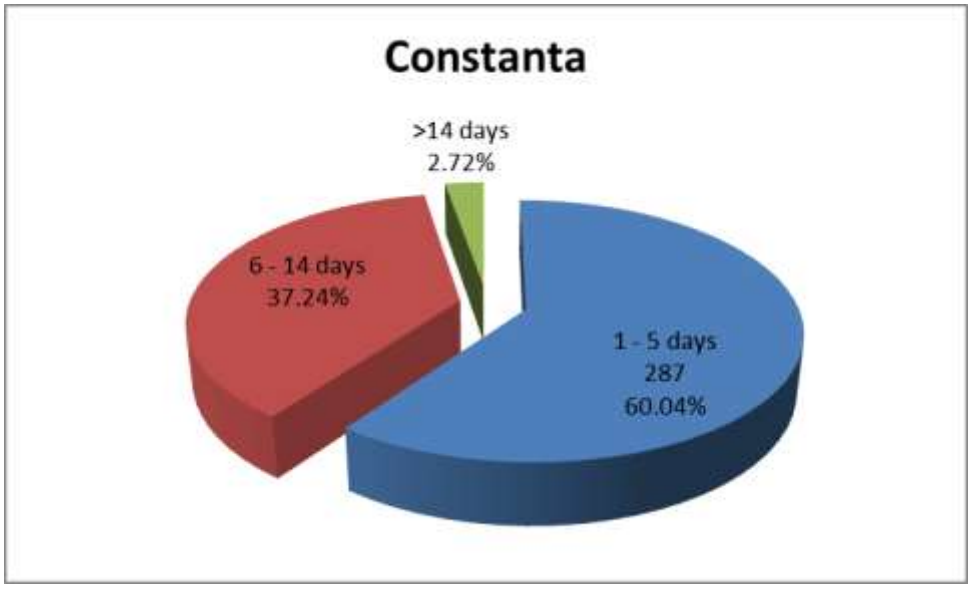

Chart no.36

The hospitalisation period was in Constanta Emergency Hospital in 60.04% of cases between 1 and 5 days with an average period of 3 days.

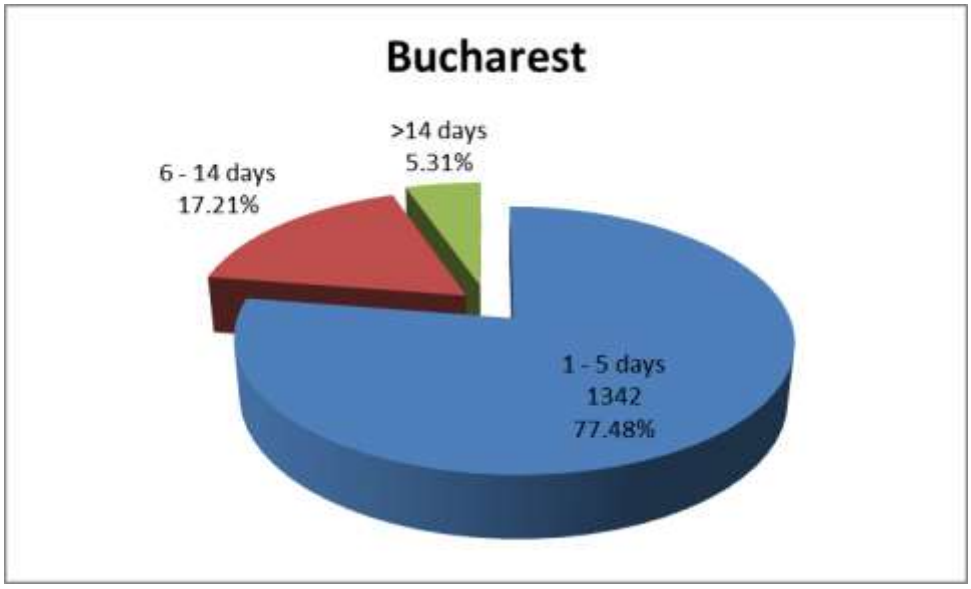

Chart no. 37

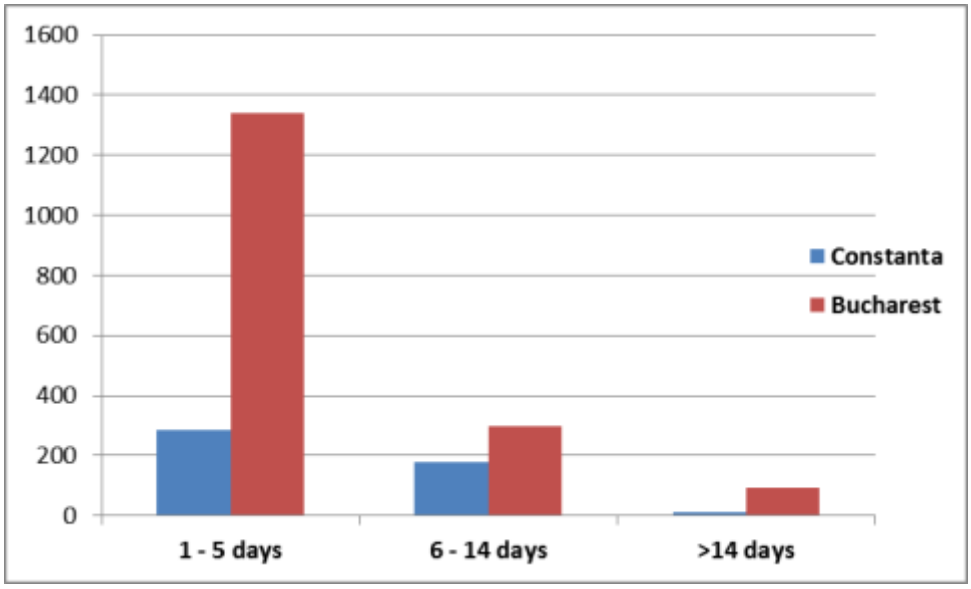

Chart no. 38

ASSESSMENT CRITERIA

The evaluation of motor and sensitive function was done following the international criteria:

MOTOR FUNCTION

RADIAL NERVE:

M0 – complete palsy
M1 – visible contraction
M2 – poor forearm muscles contraction against gravitation
M3 - contraction against gravitation gravitation
M4 - contraction against resistance
M5 – normal contraction

MEDIAN NERVE

M0 – complete palsy

M1 – poor forearm muscles contraction

M1* - forearm muscles contraction against gravitation but thenarian muscles palsy

M2 - forearm muscles contraction against gravitation and poor thenarian muscles contraction

M3 – forearm and thenarian muscles contraction against resistance

M4 – all muscles contraction against hard resistance

M5 - normal contraction

ULNAR NERVE

M0 – complete palsy

M1 – poor forearm muscles contraction

M1* - forearm muscles contraction against gravitation but hand intrinsic muscles palsy

M2 - forearm muscles contraction against gravitation and poor hipothenarian muscles contraction, interossei muscles palsy

M3 – forearm, thenarian muscles, and interossei muscles for comisural space I contraction against resistance

M4 – all muscle contraction against resistance

M5 - normal contraction

SENSITIVE ASSESSMENT

S0 – loss of sensitivity in entire sensitive area

S1 – deep pain feelling

S2 – poor superficial pain feelling and restore of sensitivity in some areas

S2* - pain feelling and restore of sensitivity but presence of overreactions

S3 - - pain feelling and restore of sensitivity without overreactions

S3* - pain feelling and restore of sensitivity without overreactions and some areas of 2 points discriminations

S4 – complete recovery

RESULTS ASSESSMENT

MEDIAN NERVE

Good : S4 or S3* M3

Poor : S3 M2

Bad : S1 or S2 M1 or M0

CONSTANTA

Table no. 22 - Constanta

RESULTS	NO. OF CASES	PERCENTAGE %
GOOD	96	59.26
POOR	53	32.72
BAD	13	8.02

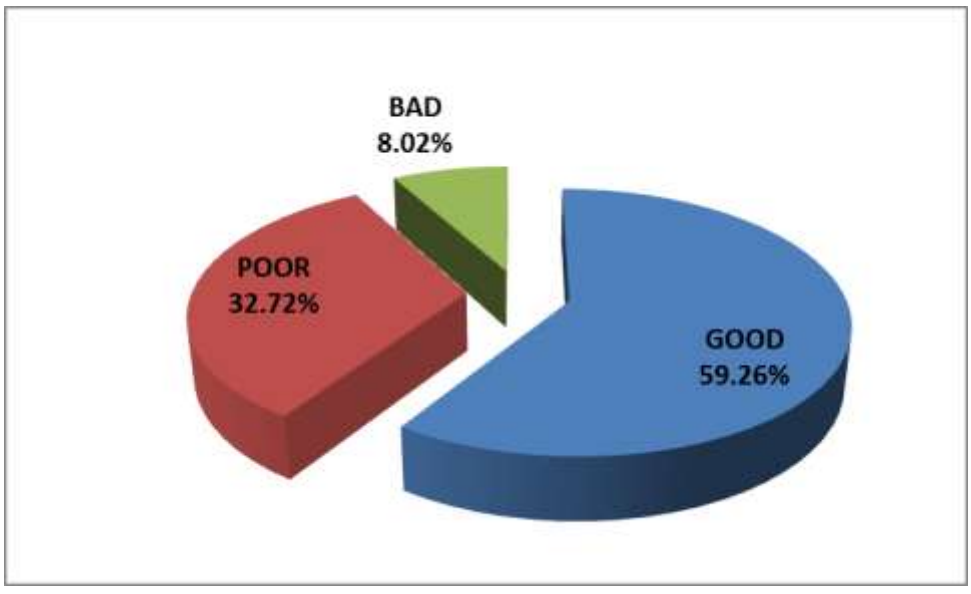

Chart no. 39

BUCHAREST

Table no. 23 - Bucharest

RESULTS	NO. OF CASES	PERCENTAGE %
GOOD	396	74.72
POOR	96	18.11
BAD	38	7.17

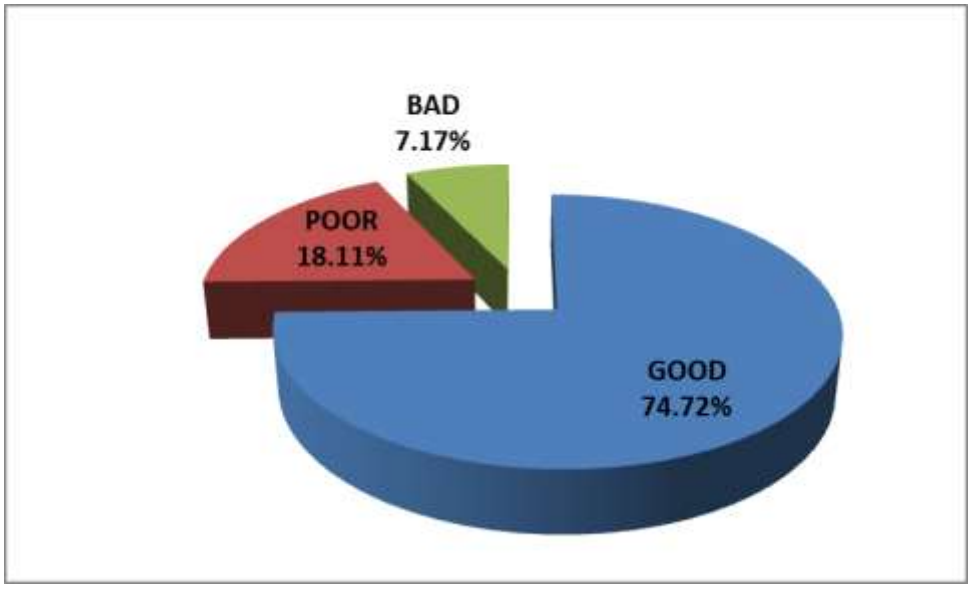

Chart no. 40

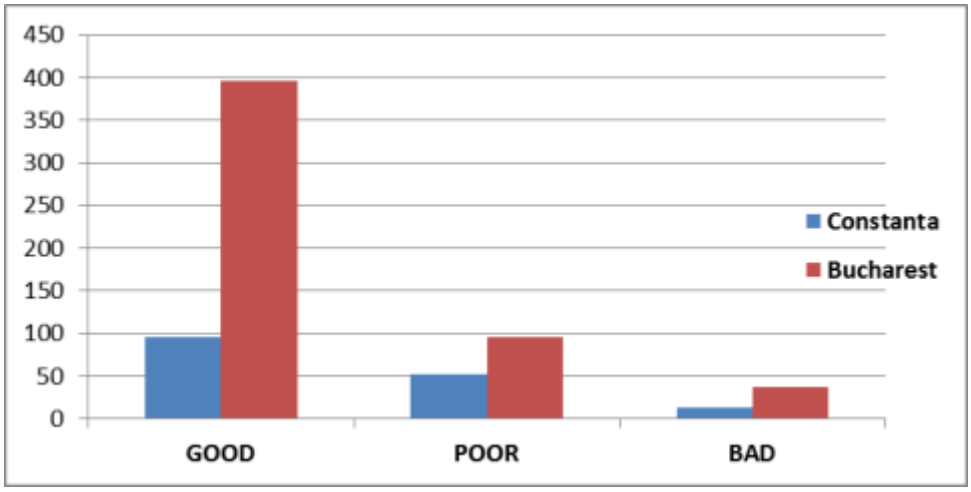

Chart no. 41

ULNAR NERVE

Good : S3 M4

Poor : S2 M3

Bad : S1 or S0, M1 or M2

CONSTANTA

Table no. 24

RESULTS	NO. OF CASES	PERCENTAGE %
GOOD	89	64.19
POOR	42	24.32
BAD	17	11.49

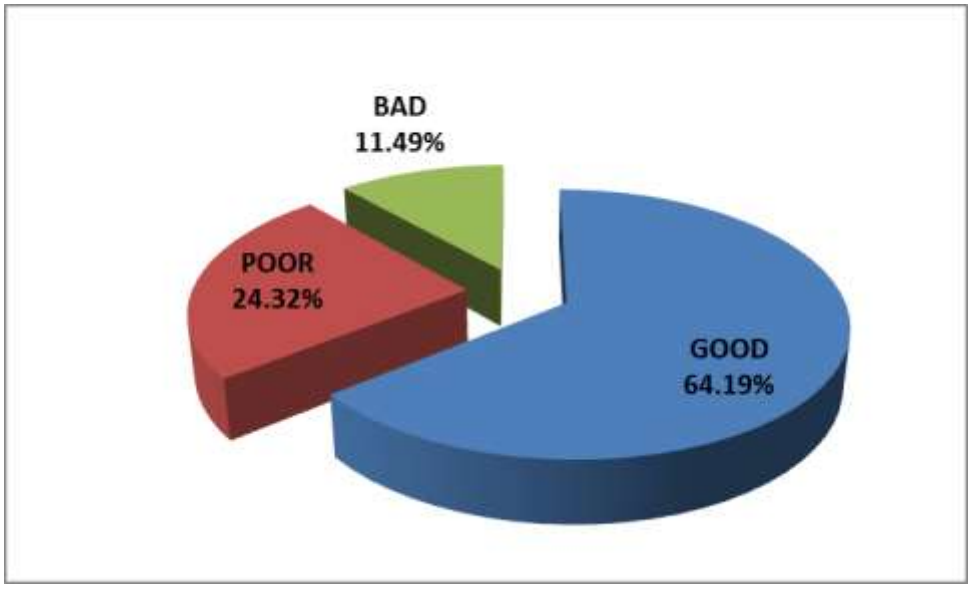

Chart no. 42

BUCHAREST

Table no. 25

RESULTS	NO. OF CASES	PERCENTAGE %
GOOD	361	73.67
POOR	84	17.14
BAD	45	9.18

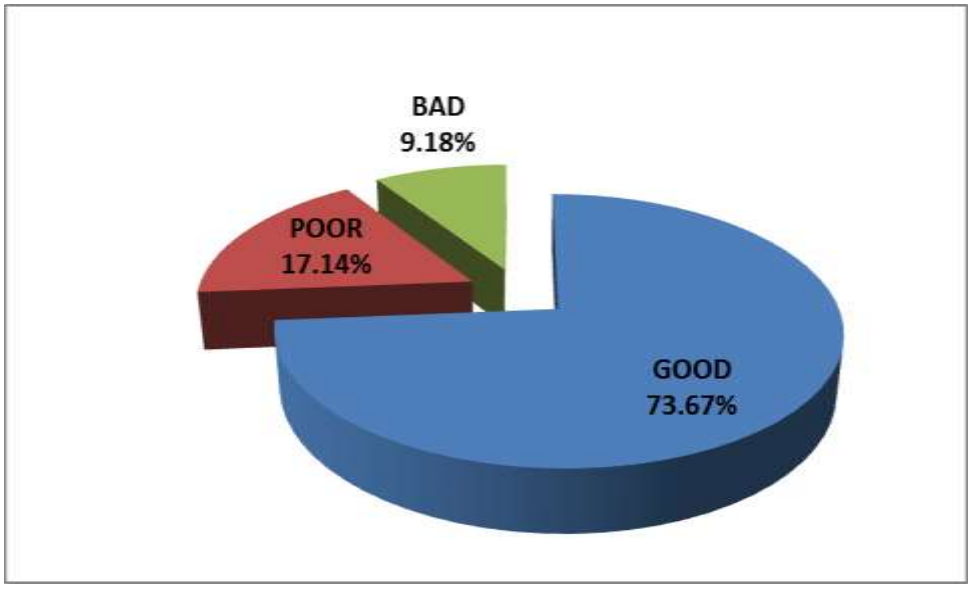

Chart no. 43

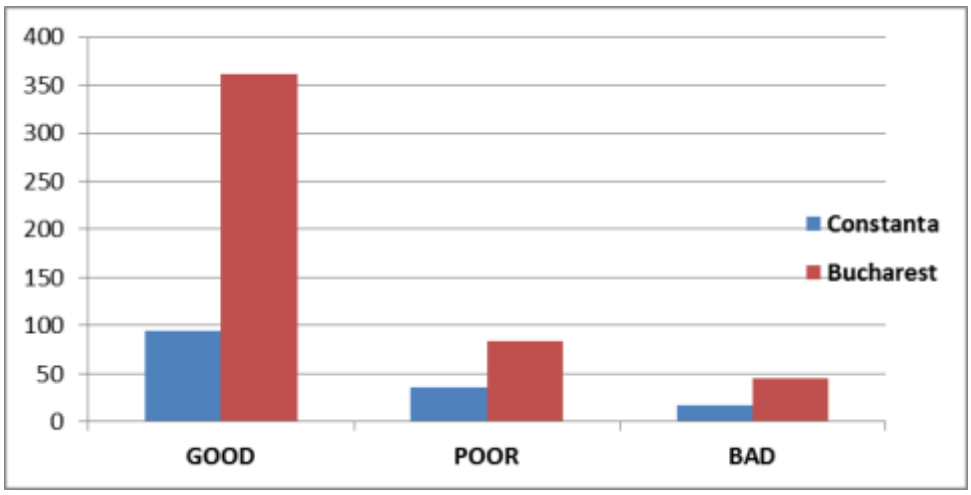

Chart no. 44

RADIAL NERVE

Good : M4

Poor : M3

Bad : M2 or M1

CONSTANTA

Table no. 26

RESULTS	NO. OF CASES	PERCENTAGE %
GOOD	10	58.82
POOR	5	29.41
BAD	2	11.76

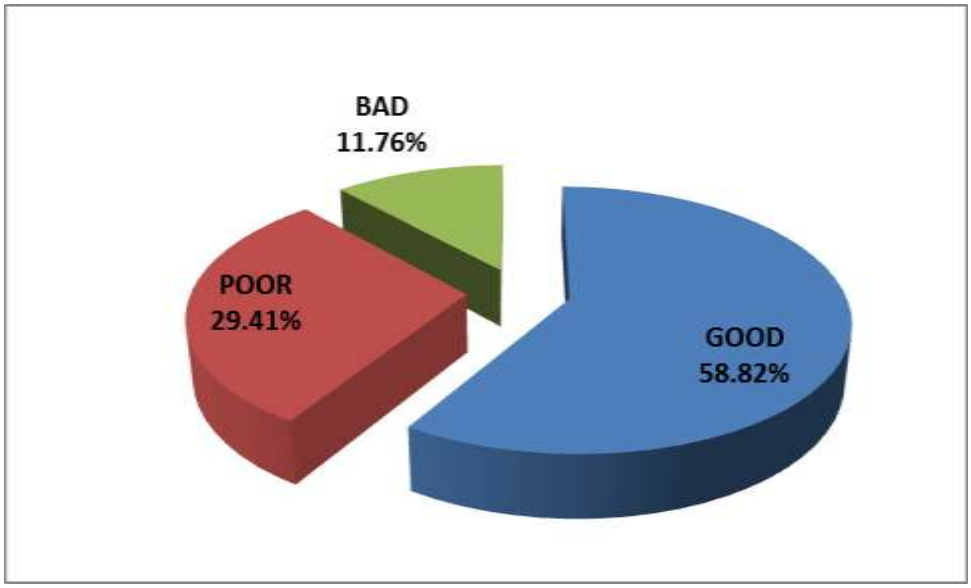

Chart no.45

BUCHAREST

Table no. 27

RESULTS	NO. OF CASES	PERCENTAGE %
GOOD	37	72.55
POOR	10	19.61
BAD	4	7.84

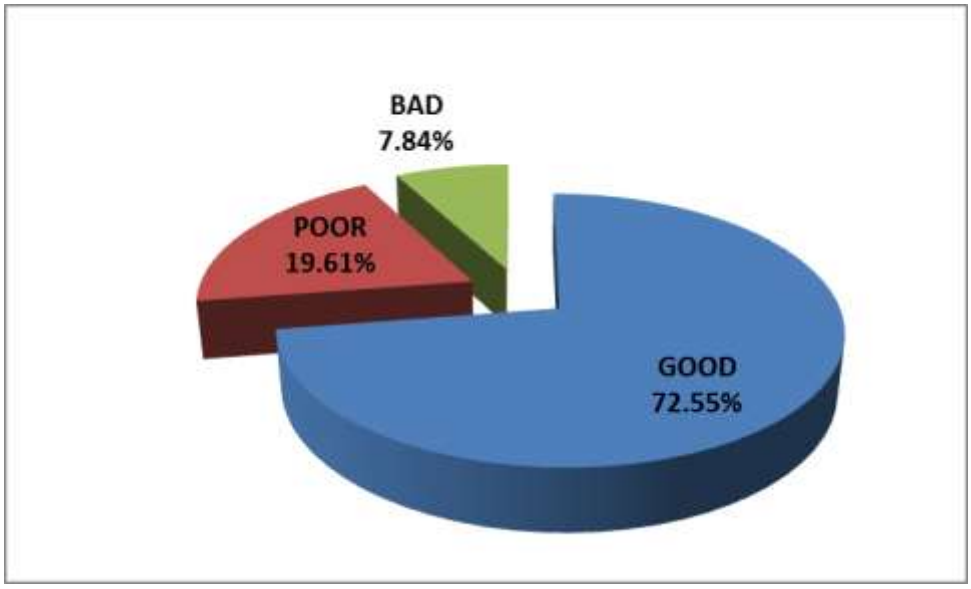

Chart no. 46

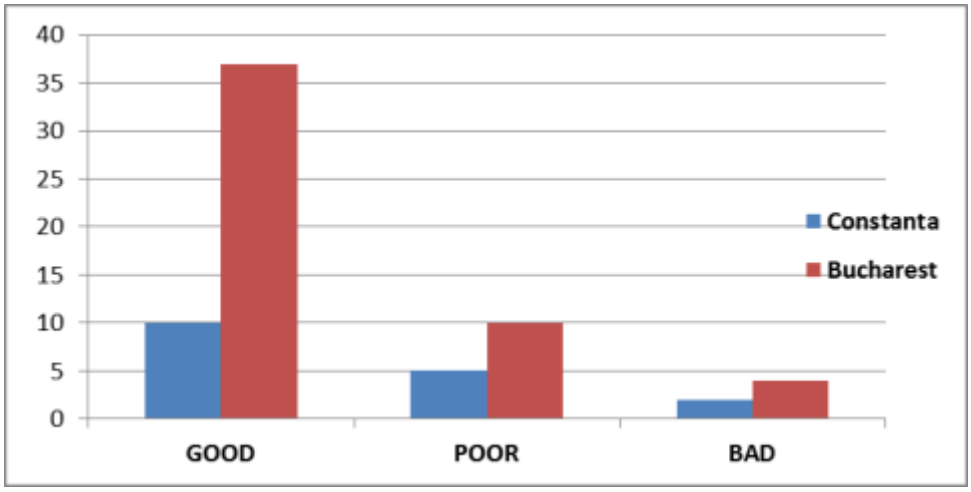

Chart no. 47

DIGITAL NERVES

Good : S4 or S3*

Poor : S3

Bad : S1 or S2

CONSTANTA

Table no.28

RESULTS	NO. OF CASES	PERCENTAGE %
GOOD	132	87.42
POOR	15	9.93
BAD	4	2.65

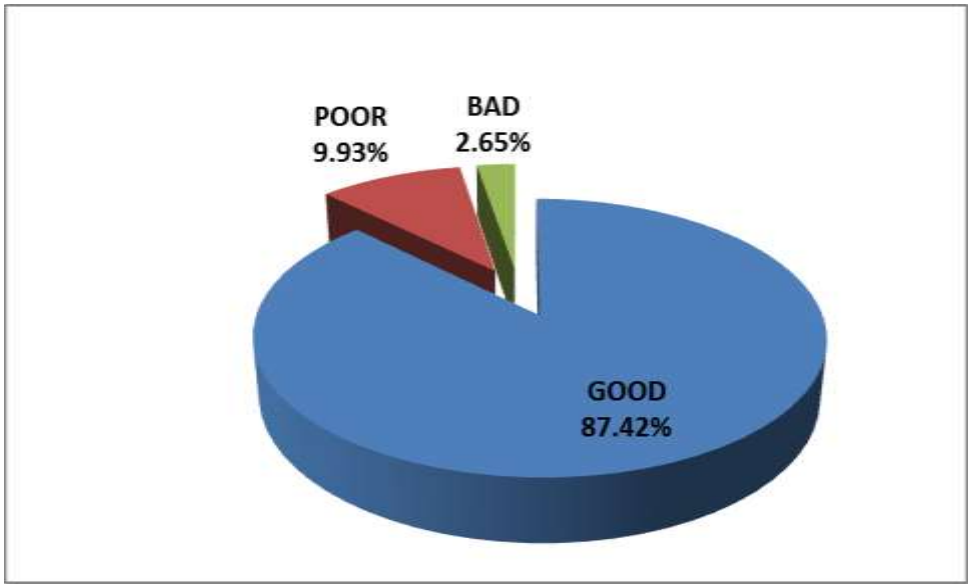

Chart no. 48

BUCHAREST

Table no. 29

RESULTS	NO. OF CASES	PERCENTAGE %
GOOD	592	88.23
POOR	68	10.13
BAD	11	1.64

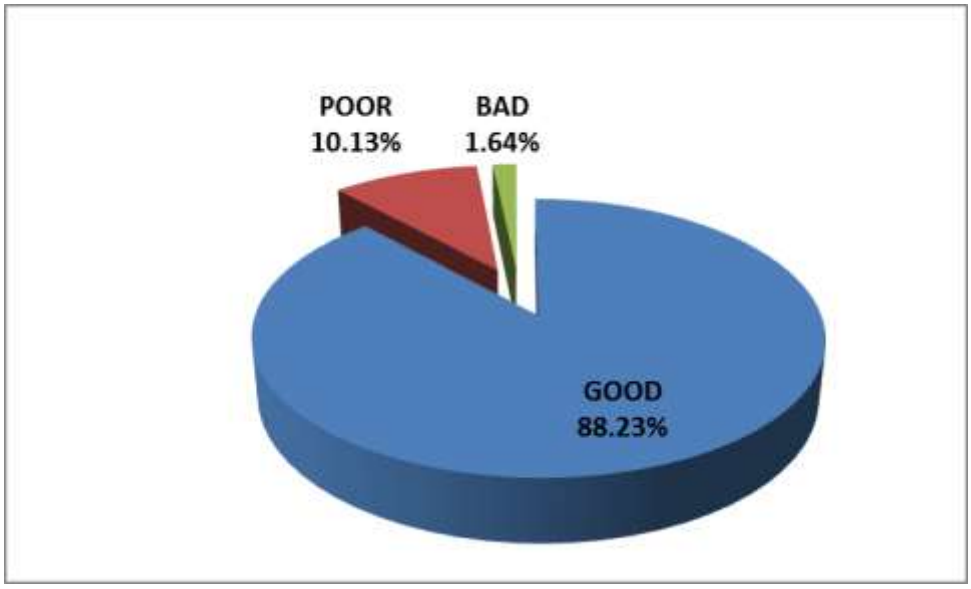

Chart no. 49

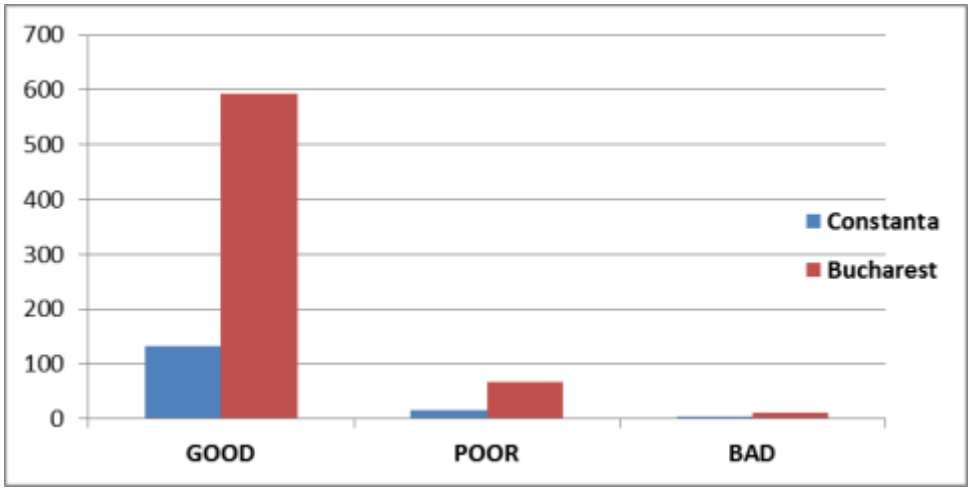

Chart no. 50

In lesions of the median or ulnar nerves, DASH-score and strength measured with the vigorimeter correlated significantly . The higher the DASH-score, the lower the corresponding grip strength and return of sensibility . Seventy-four percent of patients were satisfied with the regenerative results.

The Tinel's sign was positive in 50% of the patients. Its prevalence at the time of examination correlated significantly with an inferior return of sensitivity.

The median period of disability after nerve reconstruction was 33 days (7-150 days) for lesions to the digital nerves and 90 days (28-1,050 days) for those to the ulnar and median nerves. Longer periods were associated with severe concomitant injuries.

Seventeen percent of the patients suffered from concomitant diseases such as diabetes mellitus, coronary heart diseases, or polyneuropathia. We did not detect significant correlation with the return of sensibility.

DISCUSSIONS

Currently even under perfect conditions, nerve regeneration can never achieve complete histological and clinical recovery. Thus, recovery is often disappointing. However, the period of functional improvement following nerve repair can last for at least 3 to even 5 years. Care should be taken that nerve reconstruction is being performed by micro- and hand surgically experienced physicians to guarantee proper surgical treatment. Consistent sensory training by the physiotherapist plays a major role in the postoperative care. But, because of the limited evidence available and the variation between the interventions studied, no specific sensory reeducation intervention can be recommended yet . The strategy is to activate the cortical area representing the damaged nerve to maintain the cortical representation of the affected body part that is increasing with prolonged denervation

The patient's age is one of the major predictors for recovery. Results deteriorate with advancing age as was demonstrated in this study. The best results are seen in children. Furthermore, nerve regeneration seems to deteriorate after the fifth- to sixth-life decade. No evidence was found that gender influences recovery .

Delay of nerve reconstruction after transection also has detrimental effects on functional outcome .In some injuries, for example, with strong contamination, secondary reconstruction is required. But if possible, nerve continuity should be re-established primarily. With a delay of 6 months between injury and reconstruction, the chance of satisfactory recovery declines slowly.

There is general consent that tension on the nerve coaptation is substantially detrimental for nerve regeneration. If tensionless coaptation cannot be achieved, the nerve gap requires reconstruction, usually performed with a nerve graft. Tubulization seems to provide comparable

results given a gap length of less than 3 cm. But even if longer distances can be bridged by autologous nerve grafting, recovery deteriorates with nerve grafts measuring more than 3-5 cm in length .

Nerve regeneration also seems to deteriorate with increasing distance to the innervated organ, which was confirmed in this study. The reasons for this phenomenon are manifold and not completely understood. Axons have to reorganize and search for their distal counterparts after complete transection (neurotmesis). The more proximal the nerve injury, the lower the chances for the axons to re-innervate adequate terminal receptors and organs because possible misdirections increase.

In proximal nerve lesions, atrophy of muscle and sensory receptors may have occurred because of too long a time lapse before re-innervation can take place .

In experimental settings, different neurotrophic (growth support) and neurotropic (directional guiding) substances showed abilities to improve peripheral nerve regeneration when administered systemically or locally, but for now all these approaches only render rather minor improvements .

Even though there are a multitude of extensive and precise modalities for documentation of outcome after nerve repair , for the daily clinical practice, tools for examination of nerve regeneration have to be fast and easy to handle, while being highly reproducible and objective. Retained values should be easily understandable and should allow good comparability for follow-up. 2PD measurement has been the gold standard for years. It does not need special equipment; a paper clip may be enough. While m2PD aims at the fast adapting mechanoreceptors, the Pacinian and Meissner's corpuscles , s2PD indicates the function of the slowly adapting receptors, the Merkel's discs . Both values show high correlation, with the values of the m2PD being usually slightly below those of the s2PD. For standard clinical examination, the measurement of s2PD seems to be sufficient.

Some studies argue that monofilament testing provides advantages in terms of validity, but in general, results show high correlation with 2PD-measurement. In our experience, s2PD is faster and easier to handle.

Techniques to measure changes in skin structure and function are rather intricate and generally found no place in the daily clinical practice.

Measurement of grip strength, for example, with the Jamar dynamometer or vigorimeter is a valuable tool to estimate the return of motor function that can be easily assessed with every consultation . All values should always be compared with the results of the uninjured contralateral side.

Summing up, for the daily clinical practice, s2PD, location of the Tinel's sign, and grip strength measurement seem to be fast and reproducible tools to follow up nerve regeneration at the upper extremity. Protection sensibility should be checked if no s2PD can be detected. Patients should further be asked for the prevalence of disturbing hyperesthesia or cold intolerance. However, further examinations may be required for study purposes or detailed medical reports.

CONCLUSIONS

1. In recent past there have been significant developments in the management of peripheral nerve injuries. The advent of microsurgical techniques with use of magnification, micro-sutures and micro instruments has considerably improved the results in nerve repairs. Many advances have been made in the area of neurobiology of nerve injury and regeneration, and increasing attempts are being made in the use of nerve allografts and nerve conduits for bridging the gaps.

2. We conclude that silicone tube technique is a good technique as an alternative for nerve graft

3. Are not significant differences for nerve recovery between silicone tube group (54.5%recovery at 6 month, 58.85%at 9 months) and control group (59.66% at 6 month, 68.61% at 9 months)

4. We conclude that seeding chopped nerve in the suture is not a viable alternative for nerve graft, so we don't continue this study in the future

5. The body of knowledge regarding nerve grafts is extensive, long-term motor and sensory recovery is not always achieved. Continued research and experimentation by plastic surgeons can determine the maximum time for immobilization, time from injury to graft, and amount of suture tension, as well as the relative importance of these and other factors in determining outcomes.

6. Repair of a short gap in the nerve by stretch repair with an end-to-end anastomosis, even with some degree of tension, is followed by better recovery than by grafting. However, where a graft is necessary, a similar level of recovery will result from use of a sural nerve graft.

7. In this moment microsurgical repair of peripheral nerves remain the “golden standard” for plastic surgery departments.

8. In most of the cases epineural sutureing is enough for a good peripheral nerve recovery but fascicular groups repair is a good alternative when is possible. Fascicular repair is limited to selected cases.

9. Treatment of peripheral nerves injuries is not only a mechanic problem and surgery cannot solve it . Surgeon can aproximate and suture nerve fascicles but axon recovery canot be managed surgical – this is a complex process regulate biological to molecular level.

10. Peripheral nerve injuries requiring surgical intervention will have better results the earlier the nerve is repaired after injury. Therefore, repairs with or without grafting done immediately after the injury have better results, with progressively worsening results if done 3, 6, 9, or 12 months or longer after the injury.

11. Young patients can recover close-to-normal nerve function. In contrast, a patient over 60 years old with a cut nerve in the hand would expect to recover only protective sensation; that is, the ability to distinguish hot/cold or sharp/dull.

12. Smoking may worsen the damage caused to peripheral nerves by ischemia and reperfusion. This holds important implications for cigarette smokers who sustain extremity injuries or who suffer from

nerve damage syndromes. Smoking cessation may prove to be a useful adjunct in the treatment of patients with nerve injuries.

13. Men present more hand traumatic lesions than women because of their professional and domestic activities that predispose them to accidents

14. Results of microsurgical nerve repair depends of many important factors: age, level of injury, associated comorbidities, quality of sirgical technique, patient level of understanding, moment of repair, postoperative care, rehabilitation program.

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