Review

Ultrasound-Guided Nerve Hydrodissection for Pain Management: An Updated Review of Anatomy and Techniques

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Abstract: Nerve hydrodissection (HD), a technique used when treating nerve entrapments, involves using an anesthetic or solution such as saline or 5% dextrose solution to separate the nerve from the surrounding tissue, fascia, or adjacent structures. This technique aims to treat neuropathic pain, or pain caused by the nerve. Ultrasound-guided HD of peripheral nerves has gained significant attention in the medical profession and pain management fields in recent years. This is due to a number of high impact publications of randomized control trials demonstrating the efficacy and safety of this technique for the treatment of carpal tunnel syndrome. Even the 20th edition of Harrison's Principles of Internal Medicine textbook lists injection of 5% dextrose as an alternative local treatment that does not have the side effects of corticosteroids. The aim of this review is to provide a summary of the current literature on ultrasound-guided HD. The following major topics will be discussed: 1) the different procedural approaches, 2) its usage in different clinical situations, 3) its clinical pearls, 4) the solution used, and 5) the postulated mechanisms of action.

Keywords: nerve hydrodissection; pain management; ultrasonography; neuropathic pain

1. Introduction

The technique of ultrasound-guided HD of peripheral nerves has recently drawn the attention of the medical profession, especially in the pain and musculoskeletal medicine fields. This follows evidence from randomized control trials published in high impact journals that this technique can safely and effectively treat carpal tunnel syndrome [1-4]. Notably, the 20th edition of Harrison's Principles of Internal Medicine textbook now lists injection of 5% dextrose as an alternative local treatment that does not have the side effects of corticosteroid. The most extensively studied clinical condition treated by ultrasound-guided HD of peripheral nerves is carpal tunnel syndrome[1-8]. Other clinical studies have also used this technique to treat neuropathic pain related to deep nervous structures or neuro-axial spine [9]. There are currently no reviews available which summarize the key literature on this technique and its use in clinical practice.   The aim of this review is to provide that summary, in order to assist physicians in better utilizing this ultrasound-guided HD for the treatment neuropathic or nerve related pain.

Nerve hydrodissection (HD) is a technique which uses high-resolution ultrasound-guided fluid injection to separate nerves from a surrounding or adjacent structure, usually the fascia, which is believed to constrict or irritate the nerve either during movement or at rest [10, 11]. The vulnerability of mixed sensory/motor nerves for circumferential compression was demonstrated by Bennett [12], who developed the most commonly used animal model of neuropathic pain by placing self-dissolving ligatures about the sciatic nerve of rats. A key aspect of his approach was the exclusive use of light constriction to prevent the restriction of epineural blood flow; moreover, the ligatures could be moved up and down the nerve to ensure minimal indentation[13]. This light constriction led to prominent and rapid reactive morphological changes, and development of allodynia and hyperesthesia, and therefore, provided a reliable animal model. Additionally, this model provided a rationale to suspect that in humans, the peripheral nerves may be more vulnerable to light compression and entrapment effects at multiple locations than that previously reported.

Nerve HD techniques can be used to treat neuropathic pain, or pain caused by nerve entrapment/ injuries in the following conditions. These are listed alongside their proposed, but as yet, unconfirmed mechanisms.

1. Sports injuries: sudden nerve elongation during sprain or strain injuries, which exceeds the stretch limit of the semi-elastic nerve components of a nerve or forced nerve movement through areas of fascial constrictions or through the bony prominences; e.g., forced movement of the common peroneal nerve about the fibular head during an inversion sprain injury.

2. Osteophytosis/tendinosis/other degenerative changes with osteophytic changes which alters the course of a nerve or causes friction or nerve irritation within the areas of chronic tendinosis, ligamentosis or osteophytosis which subsequently sensitizes the innervating peripheral nerves, or alters the free movement of the related nerves because of reduced flexibility when innervating through areas of degenerated tissues.

3. Post-fracture or post-surgical pain: uncontrolled pain leading to central and/or peripheral sensitization; stretching of nerves to facilitate surgical access or to avoid inadvertent nerve lysis, contusions at the time of injury with secondary nerve swelling resulting in abnormal friction/compression during nerve movement, altered gait patterns because of limited ability to bear weight or antalgia, and formation of scars or fibrosis about a surgical/fracture site.

4. Idiopathic acute or chronic neuropathic pain without an apparent cause.

Neuropathic pain is defined as pain caused by a lesion or disease of the somatosensory system. [14, 15], It usually has the following characteristics:
   a. Deep-seated pain with poor localization of the source of pain.
   b. The degree of pain is usually not proportional to the degree of tissue/nerve damage.
   c. The pain can be sore, numb, or with electric shock; presence of hyperalgesia and/or allodynia.
   d. A sensation of cold or heat can be felt on the affected region, and the skin on the affected area may appear bluish, similar in appearance to venous stasis.

A potential benefit of separation of nerves from the surrounding soft tissue with fluid (hydro) and with the fluid flushing, or enclosing the nerve to treat neuropathic pain, is the release of pressure on the "free nerves supplying the main nerves," which are called "nervi nervorum,"[16-20] outside the epineurium. These "nervi nervorum" innervate and regulate the function and discharge of the main nerves.

Additionally, "vasa nervorum," which are small blood vessels on the surface of the nerves are also present; the arteries supply nutrients to the main nerve and the veins drain away the metabolites from these main nerves [21-23]. Entrapment of the vasa nervorum would likely result in stasis and

ischemia, and the potential accumulation of toxins at the affected part of the nerve. In addition, it is postulated that lymphatic drainage might be present outside the epineurium. Therefore, the primary objective of HD is to release the entrapment of the peripheral nerves by hydrodissecting the nerves.
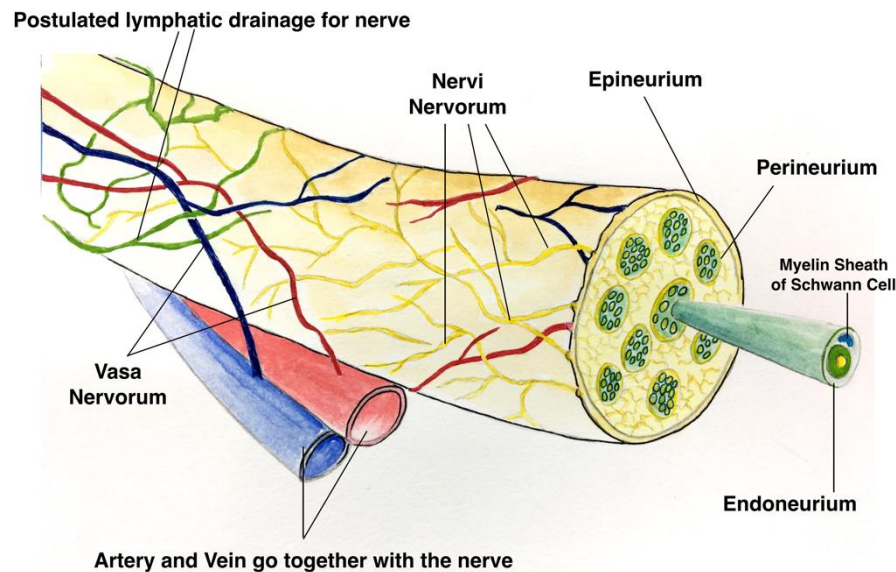
Figure 1. Diagram shows the "nervi nervorum," "vasa nervorum," and the postulated lymphatic drainage outside the epineurium [16].

2. Current Methodology

Ultrasonography (US) is usually used in nerve HD to guide needles and fluid (hydro) used to separate (dissect/release) the nerves from the surrounding entrapped soft tissues.

There are 2 methods of US-guided HD of the nervous systems. There is no literature listed and reviewed these 2 methods.

Method 1 (in-plane approach, needle perpendicular to the long-axis of the nerve)

Generally, when using method 1 for HD of nerves, the needle is perpendicular to the long-axis of the nerve and the probe is perpendicular to the short axis of the nerve. The needle is in-plane to the transducer, and the tissues above and below the nerves are hydrodissected. The needle first approaches the inferior surface of the nerve, with the needle bevel positioned up, and the pressure of the injectate is used to open the soft tissues around the nerve layer by layer until the epineurium is surrounded by the injectate. The same process is repeated with the needle approaching from the superior surface of the nerve, with the needle bevel positioned down. The hydrodissected nerve looks oval and surrounded by anechoic fluid on US. A 25-gauge, 2-inch needle or a 22-gauge, 2¾-inch needle is typically used, or a 22-gauge, 4-inch needle is used especially for performing hydrodissections of deeply-seated nerves.
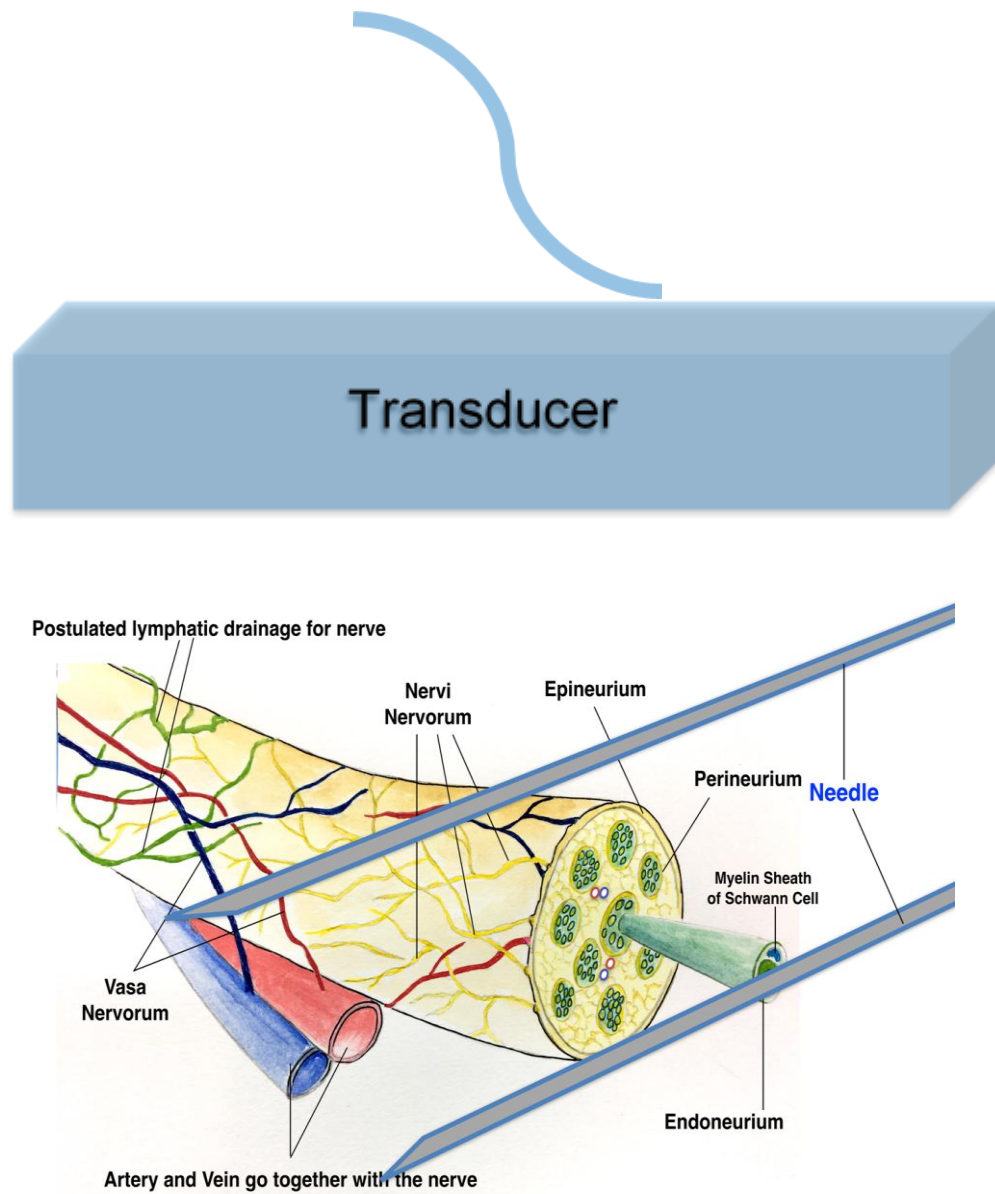
Figure 2. illustrates the needle position for method 1 of hydrodissection of nerves. With "in-plane" technique, first, the inferior surface of the nerve is hydrodissected with the needle bevel positioned up; and thereafter, the superior surface of the nerve is hydrodissected with the needle bevel positioned down.

*Real practice of this technique:*

The video 1 shows the real practice of this technique in clinical situations.

Clinical Pearls.

a. The basic principle of US-guided HD of nervous structure is that the fluid/ injectate but not the needle is the actual tool used to separate the soft tissues. Therefore, after administering local anesthetics at the superficial entry point of the needle, it is essential to visualize the needle at all times during the procedure, particularly during needle advancement, during which time the physician will continually inject the fluid. The injectate separates the soft tissues in front of the needle and the needle just moves through and into the space separated by the fluid.

Transducer

b. If the bevel of the hypodermic needle is positioned up, the injectate points and flows upwards, whereas the tracking of the needle is downwards, especially if a long and thin needle is used.

Direction of jet
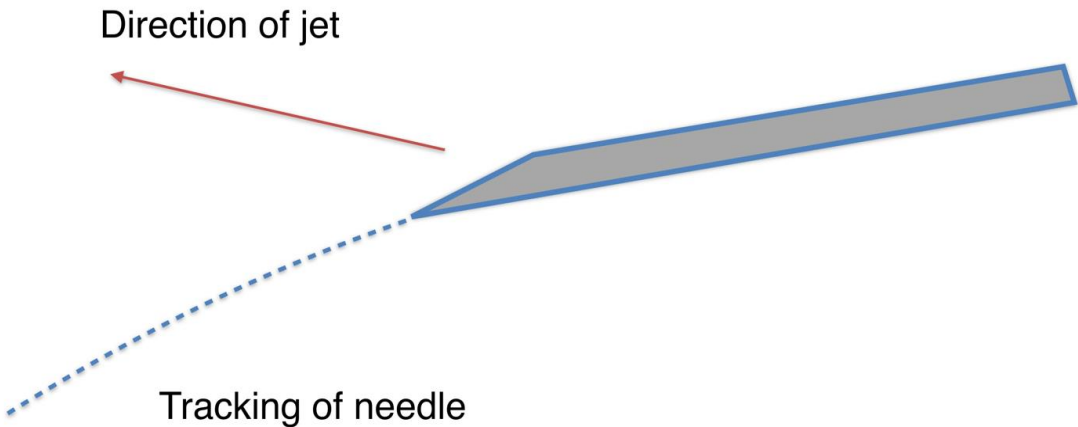
Tracking of needle

Figure 3. illustrates the effect of bevel up position on the direction of flow of the injectate and tracking of the needle.

c. If the bevel of the hypodermic needle is positioned down, the injectate points and flows downwards and the tracking of the needle is upwards, especially if a long and thin needle is used.

Tracking of needle
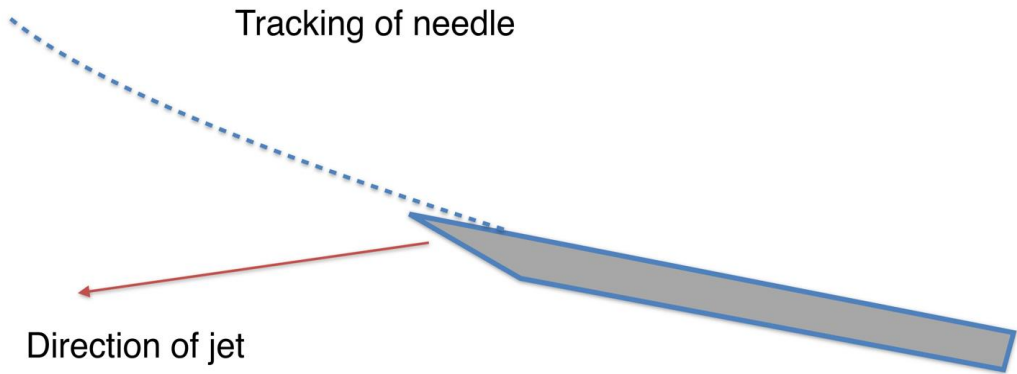
Direction of jet

Figure 4. illustrates the effect of the bevel down position on the direction of flow of the injectate and tracking of the needle.
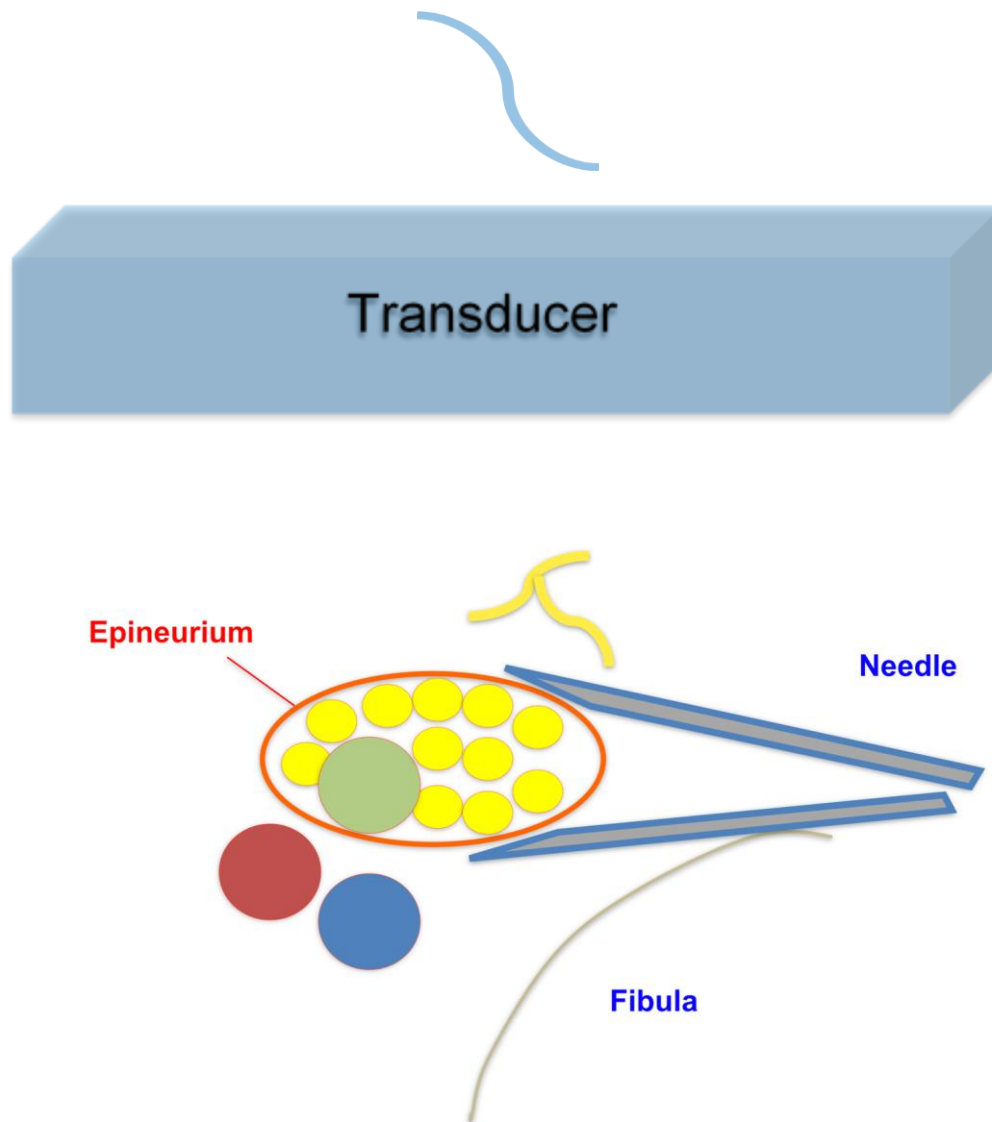
Figure 5. illustrates the needle position for method 1 of HD of the common peroneal nerve. With the "in-plane" technique, first, the inferior surface of the nerve is hydrodissected with the needle bevel positioned up, and thereafter, the superior surface of the nerve is hydrodissected with the needle bevel positioned down.

d. Usually, hydrodissection of the nerve is initiated from the site where the nerve is most severely damaged or trapped. If the diseased nerve or the damaged/entrapped part of the nerve is long, the same entry point can be used, with the transducer and needle pivoted to the proximal part of the nerve, and thereafter, to the distal part of the nerve to repeat the HD process.
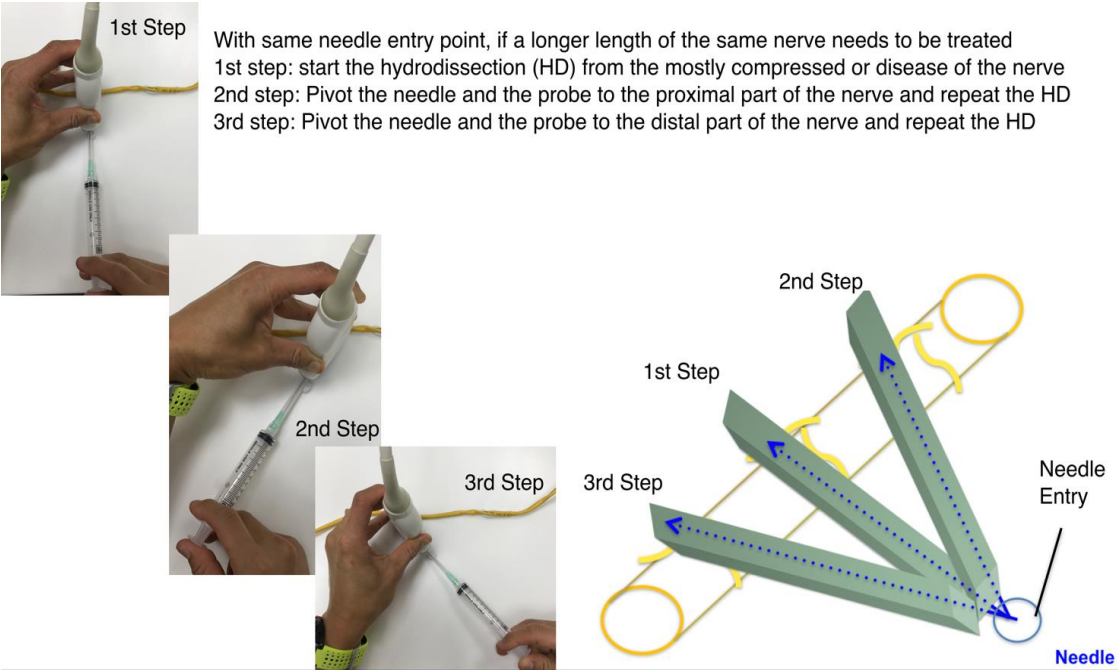
Figure 6. shows the sequence of HD of the diseased nerve using method 1. First, HD is initiated from the site where the nerve is most severely damaged or trapped, thereafter, using the same needle entry point, pivot the probe and the needle to the more proximal and/or distal part of the nerve and repeat the HD.

e. This method can be used for HD of 2 to 3 nerves running parallel to each other and if all nerves require treatment simultaneously.
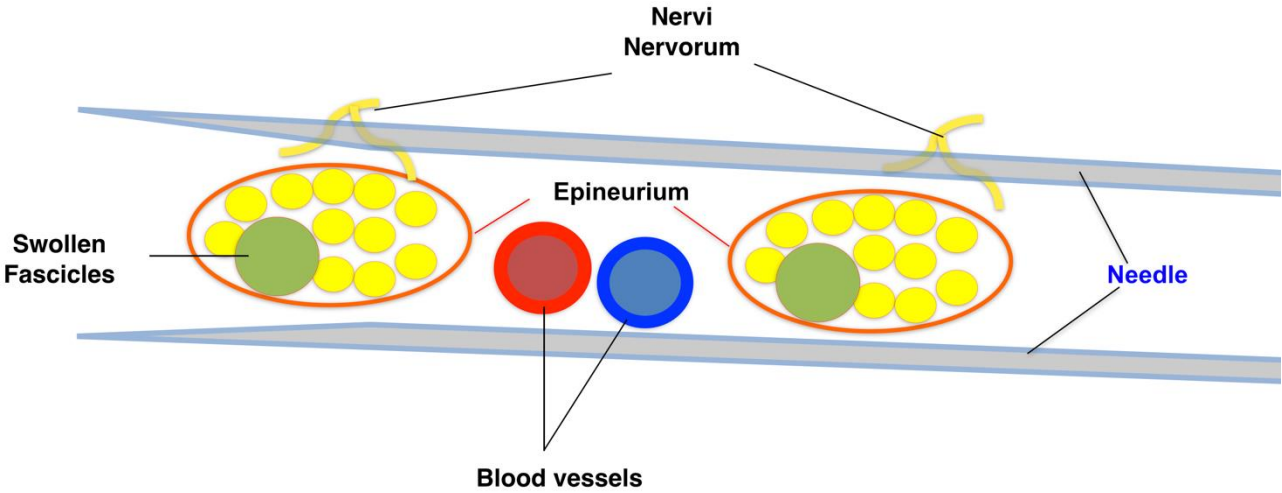

Figure 7. showing the method for using 1 needle entry for HD of 2 nerves running parallel to each other, when both need to be treated simultaneously, e.g., the common peroneal nerve lateral to the tibial nerve, at the level of the distal hamstring.

The video 2 shows the use of method 1 to treat 2 or 3 diseased nerves running parallel to each other in real clinical practice.

Method 2 (Out-of-plane with subsequent in-plane approach)

The needle is parallel to the long axis of the nerve, the probe is first perpendicular and thereafter parallel to the long axis of the nerve. First, an "out-of-plane" technique is used for HD of the nerve from the surrounding tissues. The nerve should be confirmed to be freed from the surrounding soft tissues by visualizing the anechoic fluid surrounding the nerve (both above and below the nerve). Thereafter, the needle is guided back to the top of the nerve, and the probe is turned "in-plane" towards the nerve to inject the fluid above it, with the bevel positioned down when approaching the nerve to avoid making accidental contact with the nerve. The injected fluid should be visualized to be tracking above and below the nerve.
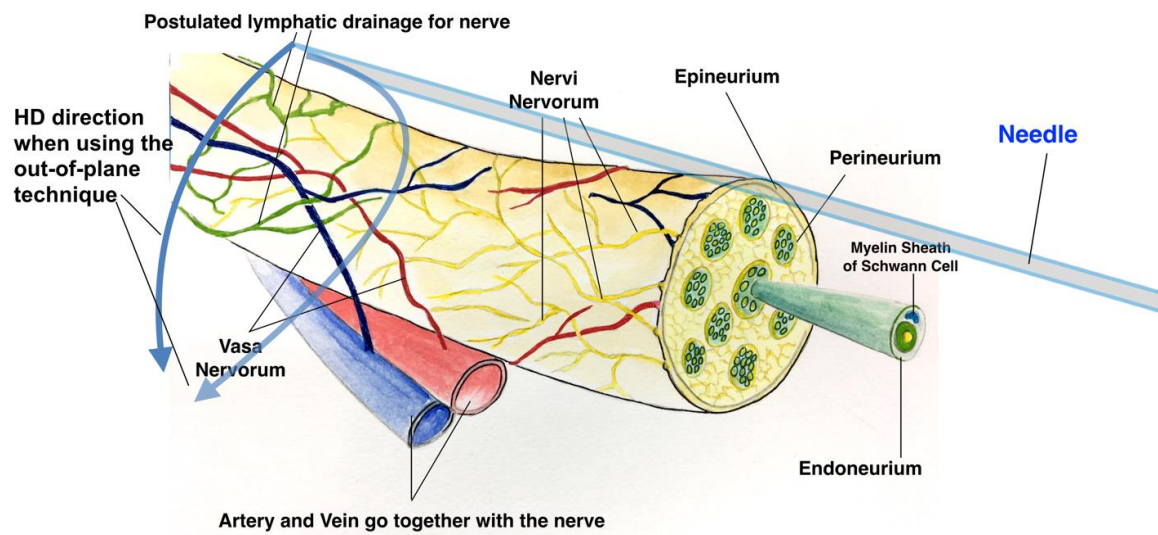
Figure 8. Diagram shows the relative direction and movement of the needle with the nerve with method 2 for HD of nerves.

The video 3 and 4 showing the real clinical practice of method 2 for HD of nerves.

Clinical Pearls:

Method 2 for HD of nerves requires good "out-of-plane" and "in-plane" techniques. Therefore, we suggest extensive practice of this technique on fresh cadavers. Generally, method 2 for HD can separate a comparatively longer length of nerves from the surrounding soft tissues. The end target is the separation of the nerve from the surrounding soft tissues and visualization of the anechoic injectate above, below, proximal, and distal to the hydrodissected nerve.

Identification of nerve(s) indicated for treatment:

1. The pathologic nerves/entrapped nerves are usually more swollen compared to the healthy counterpart. The cross-sectional areas of the entrapped nerves are usually found to be double or even triple in size in comparison to the healthy nerves.
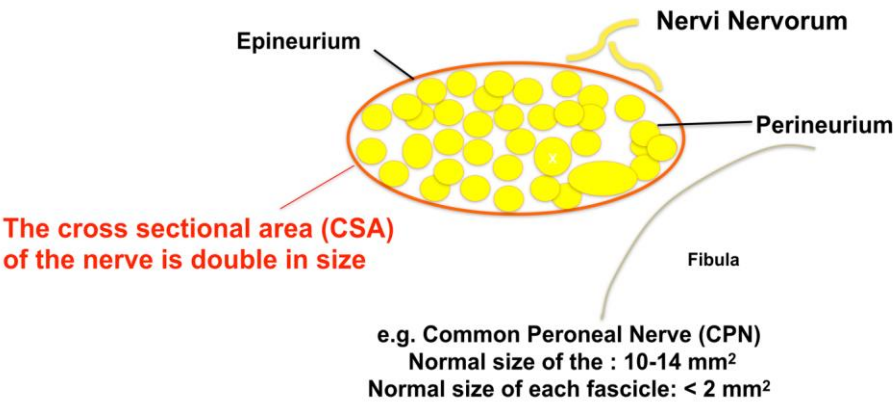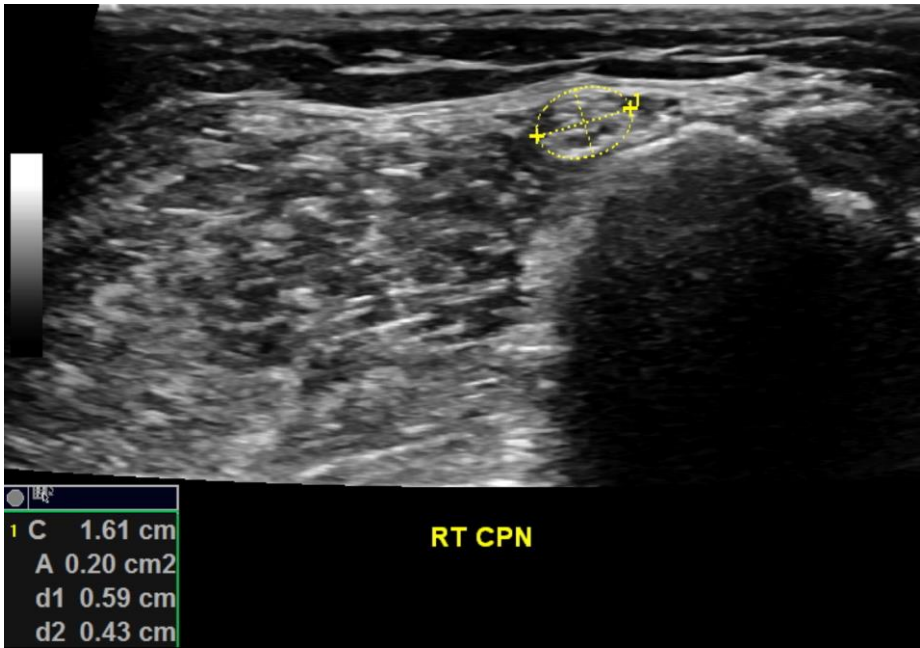
Figure 9. illustrates the common peroneal nerve as a representative example. The pathologic nerve is usually swollen with twice the cross-sectional area of the healthy fibular nerve.
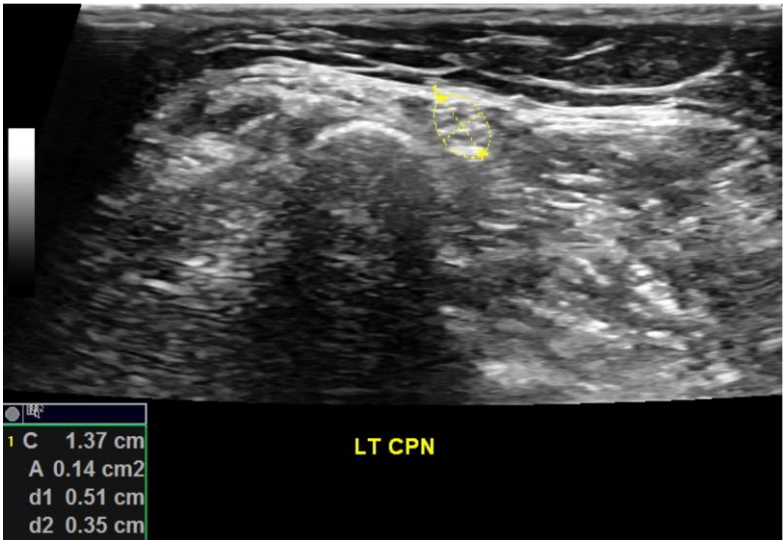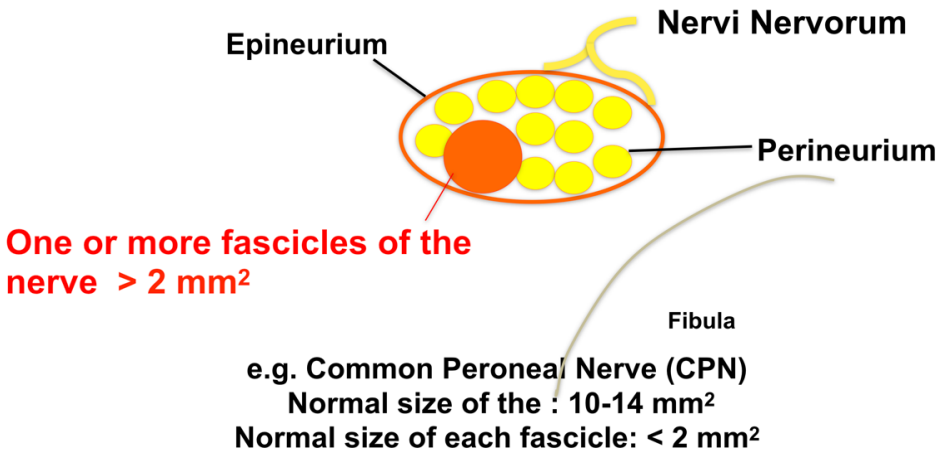

Figure 10. shows normal common peroneal nerve with a normal cross-sectional area of 14 mm^2.

**Figure 11.** shows an abnormal/swollen common peroneal nerve with a cross-sectional area of 20 mm^2.
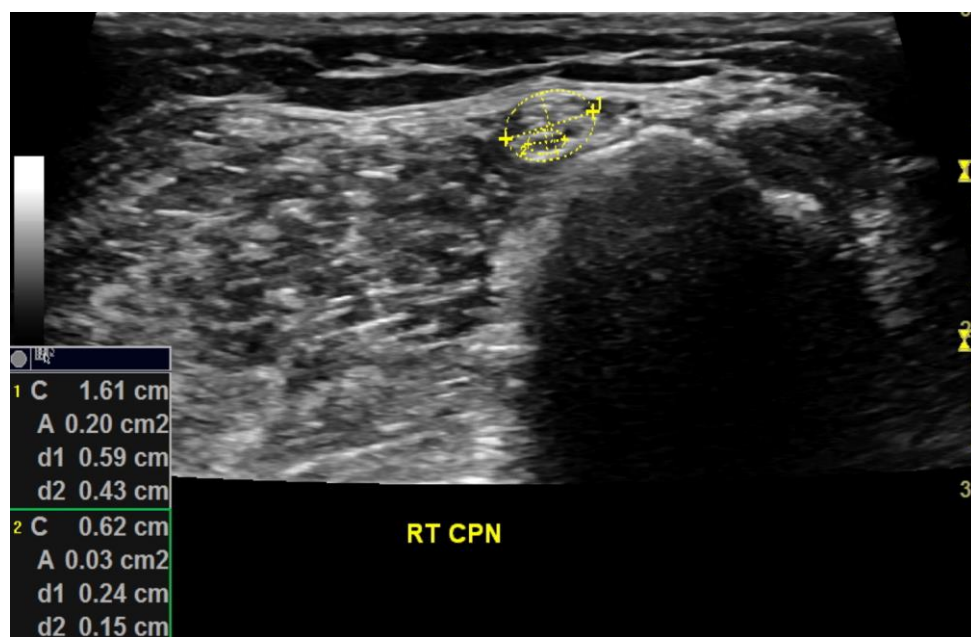
2. One of the fascicles of the entrapped/diseased nerve is swollen and much bigger than the rest of the fascicles within the same nerve.

Figure 12. Diagram shows one or more of the fascicles with a cross-sectional (CSA) of more than 2 mm^2; the whole nerve may have a normal CSA or may be slightly swollen.
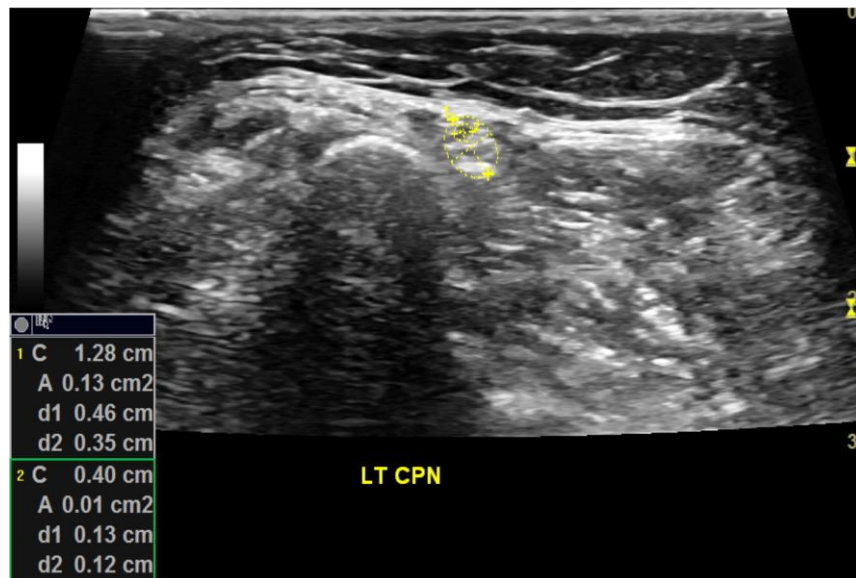
Figure 13. shows the normal nerve with normal fascicles.

Figure 14. shows slightly swollen nerve with swollen nerve fasicle with a cross-sectional area of 3 mm^2.

The video 5 shows the tracking of common peroneal nerve (CPN) from the distal to proximal end and shows a swollen fascicle.

3. Direct digital palpation of the suspected swollen nerve or suspected nerve with swollen fascicles reproduces the neuropathic pain experienced by the patient.

4. Using continuous dynamic US, a snapping/ sudden motion of a nerve against a surrounding bone, ligament, or tendons is observed, and it reproduces the neuropathic pain experienced by the patient.

The video 6 shows direct digital palpation and snapping of the CPN against the fabella when the knee is flexed and extended.

5. Dynamic US of the nerves shows lost relative movement of the some of the nerves to the surrounding structures. The major example is the loss of the "seesaw sign" of the tibial nerve and common peroneal nerve in the sciatic nerve sleeve during the ankle-planter flexion and dorsiflexion [24].

The video 7 shows the dynamic US visualization of the loss of the "seesaw sign" of the tibial nerve and the CPN in the sciatic nerve sleeve during the ankle-planter flexion and dorsiflexion.

6.   Elastography may show the whole or part of the nerve with fibrosis or the hardened nerve [8].
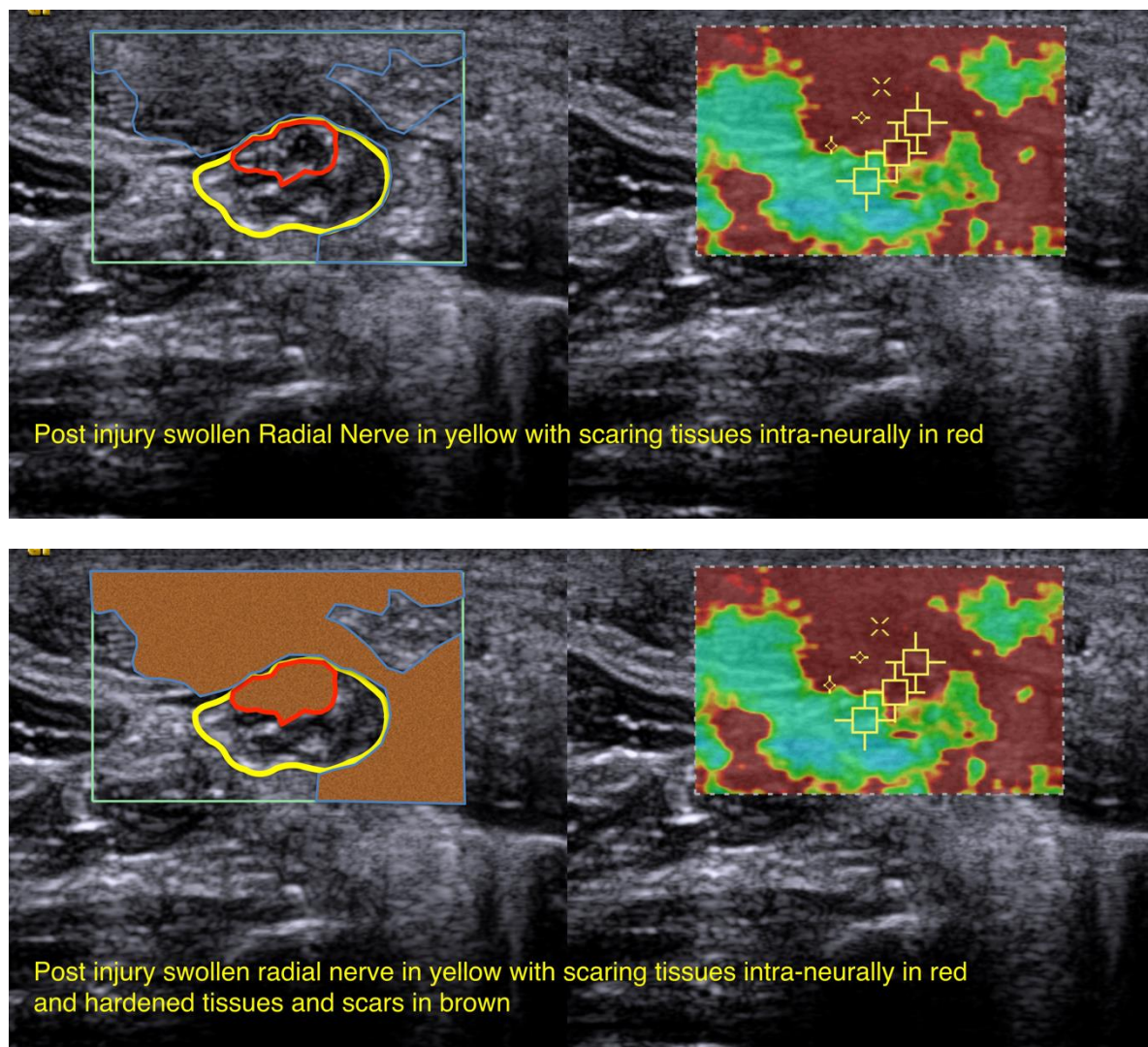
Figure 15. Elastography image of the swollen radial nerve after injury with scar tissues. Figure 15a shows the left-side B-mode image; the yellow circle outlines the swollen radial nerve with the swollen fascicles in red circle; the panel on the right is the elastography image showing the relative hardness of the tissues enclosed in the square under the present scanning conditions, corresponding to the B mode image on the left; the brown regions show that the scanned structure has a high density, and

the green regions represent soft tissues. Figure 15b; the red circular part of the radial nerve shows similar hardness as compared to the scar tissue near the swollen radial nerve.

7. If the patient has no phobia of needles, US-guided dry needling can be utilized. The dry needle is placed as close as possible to the diseased part of the nerve and stimulate by vibration or electricity to assess the reproducibility of neuropathic pain experienced by the patient.

The video 8 shows the dry needle stimulation of the pathologic nerve under US guidance.

Injectate for HD:
Traditionally, a large volume of normal saline and a small volume of steroids and local anesthetic solution is used for HD of nerves [5, 7].

HD alone appears to be beneficial, as shown in a clinical trial of patients with mild-to-moderate carpal tunnel syndrome (CTS), which compared the effect of HD with saline injected to the intracarpal region and to the subcutaneous injection of saline, which significantly improved the Boston Carpal Tunnel Syndrome Questionnaire score and CSA in the interventional group [4]. Wu et al. also compared HD with 5% dextrose and HD with saline in patients with CTS and found HD with 5% dextrose to be more effective in treating media nerve entrapment [2]. In addition, Wu et al. also showed that HD with 5% dextrose is more effective than steroid injection in the carpal tunnel for treating CTS [1]. The 20th edition of Harrison's Principles of Internal Medicine textbook also lists injection of 5% dextrose as an alternative local treatment that do not have the side effects of corticosteroids.

Other studies have supported the use and efficacy of dextrose solution to treat neuropathic pain. Injection of 5% dextrose into the caudal epidural space has been demonstrated by Smigel et al. to result in prompt and consistent multi-segmental post-injection analgesia and a cumulative analgesic effect in patients with chronic low back pain with radiation to buttock or leg [25]. In a retrospective data collection of consecutive patients with severe neuropathic pain, Lam et al. demonstrated both the safety and efficacy of 5% dextrose solution without the use of lidocaine to treat neuropathic pain caused by nerve roots or plexi in consecutive patients [9]. This is of particular interest as in the absence of lidocaine, optimal HD volumes can be utilized without the concern for lidocaine toxicity. Given the benefit of injection at the nerve root and plexi level, a mechanism of action of 5% dextrose injection at the somatosensory system at the dorsal root level has been proposed[25]

Several hypotheses have been proposed to explain the effect of dextrose solution on treating neuropathic pain such as:

Downregulation of the transient receptor potential vanilloid receptor-1 (TRPV1) ion channel.

The TRPV1 ion channel has been postulated to be associated with chronic neuropathic pain [26]. Its upregulation is directly associated with persistent of chronic neuropathic pain, and dextrose may directly or indirectly antagonize the TRPV1 upregulation effects. The TRPV1 ion channel was previously called the capsaicin receptor because it is the only capsaicin receptor-containing TRP ion channel [27]. Capsaicin causes characteristic burning sensation by upregulating the TRPV1 channel. Mannitol, a 6-carbon-atom sugar has been found to reduce the burning sensation after exposure to capsaicin, suggesting an antagonistic (calming) effect on TRPV1 upregulation. Dextrose, similar in structure to mannitol, has empirically been observed to have similar effect, although it has not been formally tested using the capsaicin model developed by Bertrand et al [28].

Chronic neuropathic pain may signify glycopenia around the corresponding nerve(s). Injecting dextrose may promptly correct this glycopenia and consequently reduce neuropathic pain. Moreover, 40% of our peripheral somatosensory nervous system are small capsaicin-sensitive nerves (nerves with the TRPV1 ion channels on their surface), which are predominantly C fibers, and have an apparent homeostatic role in monitoring the level of systemic dextrose [29]. Both the brain and peripheral nerves have high and constant requirement for glucose [11]. When isolated C fibers are exposed to a hypoglycemic environment by substituting D-glucose with non-metabolizable L-glucose, it demonstrated a dramatic (653±23%) increase in discharge frequency, within 5 minutes and maximized after 15 minutes [30]. Hypoglycemia results in the reduction of high energy substrates, e.g., ATP, leading to reduced activity of the ATP dependent Na+-K+ pump, resulting in progressive nerve depolarization and hyperexcitability. Replacement of D-glucose can rapidly correct the above-said effects. [30].

Dextrose injection may hyperpolarize nerve cells responsible for neuropathic pain, and reduce their depolarization and pain generating ability. There are both potassium channels and TRVP1 channels localized on capsaicin sensitive nerves [31]. These potassium channels have receptors for dextrose. The attachment of dextrose to the receptor leads to opening of the potassium channel, and thence transports potassium out from the cell, and hyperpolarize the nerve cell [31].
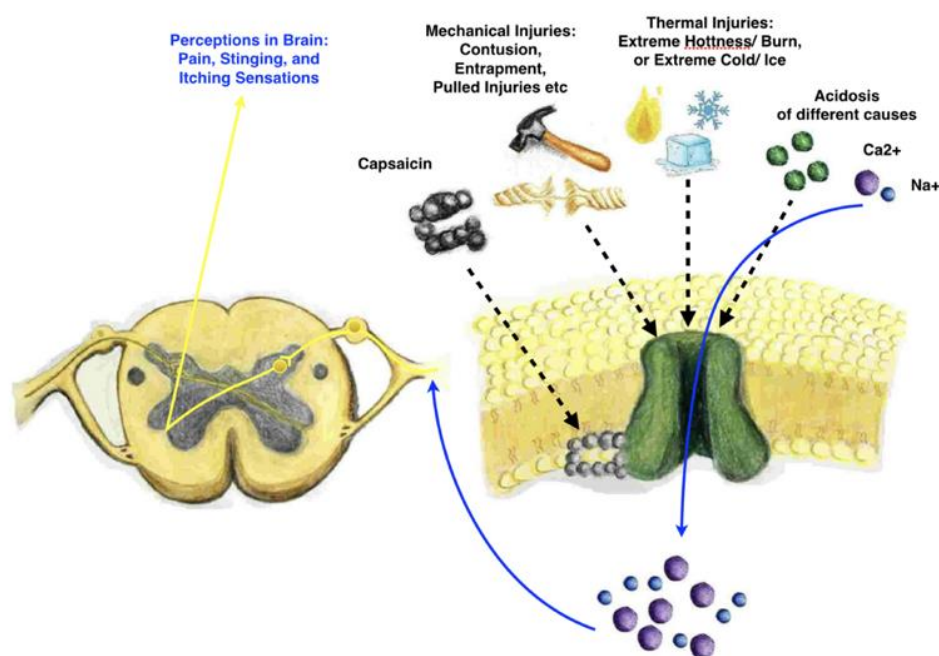
Figure 16. Figure showing different stimuli including mechanical stimuli (which include: entrapment, pulled injuries, direct trauma), heat, ice, acidosis, capsaicin, will cause influx of sodium and calcium and thence depolarization of the nerves, leading to signal perceived in the brain.

In summary, when performing HD of nerves, the needle is guided by US to approach the nerves. The skin is anesthetized by skin bleb by administering local anesthetics. Once the needle is under skin, the patient usually does not feel the needle movement if continuous HD with 5% dextrose solution is maintained. A key feature of the technique is that the advancement of the injectate/solution dissects the soft tissues in front of the needle, without the involvement of the needle. It is the injectate that opens the fascia or spaces in front of the needle.. Needle advancement ceases just outside the epineurium and the injectate dissects and releases the entrapped soft tissues around the nerves. It is crucial to have the nervi nervorum and vasa nervorum fully released from the entrapment or abnormal external stimuli, and to be surrounded by the injectate. Therefore, the soft tissues surrounding the nerve will be hydrodissected layer by layer until the epineurium has no further layers of fascia surrounding it. A key observation here is that the nerve should appear rounded rather than fusiform and is free floating. Along with the release of the nerve, the injection of dextrose is

expected to induce a calming effect on the effects of TRPV1 upregulation, and improves the vascular supply and venous drainage (may be lymphatic drainage as well) of the main nerves.

Conflicts of Interest: The authors declare no conflict of interest.

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