Commentary

The International Neuromodulation Society (INS) defines neuromodulation as a field of science, medicine, and bioengineering that encompasses implantable and non-implantable technologies, electrical or chemical, for the purpose of improving quality of life and functioning of humans (1).

Electrically-induced analgesia (EIA) has been noted for many centuries. Scribonius, the Emperor's physician, reportedly recommended the "sting" of the electric torpedo fish as a treatment for persistent pain after observing a freed slave, who accidentally stepped on a torpedo fish with his painful gouty foot; get an intense shock followed by significant pain relief in 15 A.D. (2).

Many centuries later Melzack and Wall (3) published their 1965 gate control theory of pain. This theory helped to promote a flurry of activity geared to neuromodulation approaches for the treatment of pain. Within 2 years from the gate control theory publication Shealy, Mortimer and Reswick reported their findings on the inhibition of pain via spinal cord dorsal column stimulation (4). That same year Wall and Sweet (5) demonstrated that pain relief could be achieved by stimulating a "painful" peripheral nerve.

Peripheral Nerve Stimulation (PNS) traditionally refers to the direct "surgical" placement of electrodes on or near an exposed nerve (e.g. radial, median, ulnar [upper extremity], sciatic, femoral, common peroneal, posterior tibial [lower extremity]). The On-Point electrode (Medtronic, Inc., Minneapolis, MN) is a quadipolar electrode with a Gor-Tex skirt which is FDA approved for PNS.

Goroszeniuk and colleagues coined the term "targeted stimulation" (TS) to refer to the targeting of peripheral distal pain receptors (rather than specific neural structures via a stimulating needle [e.g. an external nerve mapping probe connected to an impulse generator which they termed external neuromodulation (EN)]; or subcutaneous placement of a stimulating electrode array placed close to the nerves and/or fine nerve endings confined to the painful area(s) or directly in the epicenter of the painful area(s) (6-9). The author prefers to use the term, peripheral nerve field stimulation (PNFS) which others have utilized previously to refer to percutaneous subcutaneous stimulation in efforts to "cover" a painful area of skin to achieve pain relief (10-13).

The mechanisms of PNFS are uncertain, however, it is conceivable that some existing cutaneous analgesic mechanisms (14) may be "recruited" by PNFS to contribute to PNFS-induced analgesia due to the close proximity of the leads to the dermis and epidermis. In efforts to provide direct stimulation to non-dermatomal areas that are difficult to effectively cover with parasthesias from spinal cord or major nerve level, the use of peripheral nerve field stimulation appears to be increasing. In areas of skin which are allodynic, PNFS may be too painful to tolerate and may exacerbate the patient's baseline pain (although it appears that there may be exceptions where PNFS in the allodynic region may be tolerated or even provide analgesic or anti-allodynic activity). Positioning multiple leads surrounding some of the perimeter of the allodynic area (in the "border" or "transition zone" between allodynic and non-allodynic areas), in a "parenthesis-like" fashion seems reasonably suited to provide "stimulation coverage' of large allodynic skin areas. With the use of PNFS growing clinicians began to encounter patients with painful non-dermatomal skin areas that were quite large. Generally, the area of the electrode-tissue interface determines the charge and current density of the applied stimulus. Increasing the area electrode-tissue interface reduces the charge and current density of the stimulus (The current density of the applied voltage decreasing inversely with the distance from the electrode). Despite uncertainty of whether cross-talk (the creation of an electrical circuit between separate "distant" subcutaneous leads) could provide clinically effective inter-lead stimulation contributing to analgesia across large painful areas; clinicians have been utilizing multiple leads at significant distances from each other in efforts to "cover" large areas of painful skin with PNFS.

In efforts to determine if peripheral cross-talk was practical and clinically effective across large painful areas; Falco et al. studied 13 women and 5 male

patients who had undergone PNFS implantation prior to their outcome analysis (15). Additionally, Falco and colleagues demonstrated the existence of PNS cross-talk across a large area in a cadaveric model (15). This seems to provide sound initial footing to move investigative work forward surrounding PNFS for analgesia.

A body of work exists investigating neuromodulation for chronic pain with transcutaneous electrical nerve stimulation (TENS) as well as on spinal cord stimulation. Studies on supraspinal stimulation exist but are still relatively immature and not particularly robust or rigorous; however, the work evaluating peripheral nerve field stimulation is still in its infancy. It is hoped that in the future, investigators will perform large multicenter well-designed studies to analyze various patients/circumstances in which peripheral nerve field stimulation may or may not be beneficial.

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