CALMARE® PAIN THERAPY TECHNOLOGY

The Calmare® Pain Therapy Treatment (Model MC-5A) medical device utilizes basic research and technological development published in the scientific literature as “Scrambler Therapy”, developed by Professor Giuseppe Marineo (D.Sc., M.S.) which is based on Information Theory and complex systems. TENS and other implanted devices are based on the “Gate Control” theory. This strategy is based on "blocking" pain by action outside the pain pathways. For this reason the conventional electroanalgesia uses the tactile A-Beta fibers.

The Gate Control theory assumes the existence of an interneuron in the jelly substance that differentiates the signal coming from C-fibers (pain pathways) and the signal coming from the A-Beta fibers (tactile sensitivity). If the activity of the C-fibers prevails then pain passes, whereas, if the activity of the tactile fibers prevail then pain is reduced or blocked. This strategy of stimulating only the tactile A-beta fibers is the normal function of TENS and implanted devices. This approach is ideal for the treatment of acute pain. However, the Gate Control theory and TENS devices have not proven effective in the treatment of chronic pain and cancer pain. The main reason is that chronic and cancer pain is associated frequently with a neuropathic injury.

The technology behind the Calmare® is specifically for the treatment of chronic neuropathic and oncologic pain. Whereas acute pain in itself is not considered a pathology because it has a beginning, an end and a protection function. In chronic pain the cause and effect relation is not clear and definitely not linear, as with acute pain. An example is allodynia. The Gate Control theory cannot explain the non-linear pain response in allodynia, because there is "no reason" to stimulate tactile fibers and feel terrible pain. Oncologic pain can also be considered a type of neuropathic pain when it does not respond to morphine and opioids, typically because the cancer infiltrates or compresses the nerves.

The differences between the Calmare® and TENS are considerable. Basic functions of each device operate differently, including different stimulations. First, TENS uses square and triangular signals or others linear waveforms that do not exist in the CNS naturally. These signals have been specifically created for TENS and implants. The Calmare® creates synthetic action potentials (non-linear) similar to endogenous action potentials waveforms. These synthetic action potentials are dynamically assembled and processed by an innovative algorithm which creates strings of non-pain information and an artificial neuron. This provides a high level of compatibility to allow the brain to recognize the new artificial signal as “self” with the non-pain information. The Calmare® stimulates the C-fibers. Technically these fibers react to the stimuli width of an impulse. The non-myelized fibers are slower and need wider impulses, while the myelized fibers respond to very short impulses. A-Beta fibers are easily isolated with a TENS device because they are larger and are responsive to short impulses in the micro-second range (µsec). The TENS standard impulse of 50 µsec is specifically used to excite only A-Beta fibers. When the impulse width gets longer they involve the C fibers. Even at width longer than 5 milli-seconds, like in the Calmare®, the stimulation of A-Delta fibers is unavoidable, but the physiological perception effect of this is annulled when you stimulate the C fibers.

This is noticeable as a feeling similar to a "sting" (bee sting) during the early fine-tuning stage of treatment with the Calmare® which is specific to the insufficient and lower intensity stimulation. When the intensity level of the Calmare® is increased, and all the non-pain information is transmitted through the C-fibers, the sting feeling disappears and the patients feels a different and variable sensation that signals the start of the analgesic effect. Only after this phase does the patient then describe a more comfortable feeling, which must coincide with the immediate pain relief.

Note that a known issue to the TENS and implanted stimulators, even if initially useful, is the loss of efficacy over time. Because their stimulation signal is consistently the same the patient eventually becomes desensitized to it, and therefore they experience a drop-off or complete loss of treatment efficacy.

Calmare® incorporates 16 synthetic action potentials, which are dynamically organized according to a specific algorithm (not randomly selected) in sequences and packets of time, and which prevents the brain from adapting to the non-pain message. In fact, over consecutive treatment sessions the Calmare® increases in therapeutic efficacy and which then is relational to reduced perceived pain by the patient.

A doctor at Massachusetts General had shared the following description – chronic pain is a bad memory which provides no benefit but is replayed as a continuous loop by the brain. Whereas with successive treatments the Calmare displaces the chronic memory with new information of non-pain, and this becomes the predominant memory with additional treatments. Clinical studies have validated that patients with mono neuropathies have experienced no-pain periods of up to 1-year without drugs, and polyradicular neuropathy patients have no-pain periods ranging from several weeks to 3 months before additional booster treatments are recommended.

SYSTEM SIMPLIFICATION

From a high level, the Calmare° system can be described in terms of inputs, outputs, and internal functionality. Other than main power input, the system can be represented as illustrated:

Operator (User) Input is intended to be as simple as possible, to minimize the possibility of operator error. In the therapeutic program, the user can:

- modify treatment time within pre-set limits (if necessary)
- initiate therapy
- adjust output intensity
- select end-of-therapy tone (on / off)
- abort therapy
- respond to system prompts in case of case of anomalies

Intended Use Environment

The Calmare° device has been designed for hospital and outpatient facility by physicians and trained medical personnel. The device is indicated for:

- Symptomatic relief of oncological pain
- Symptomatic relief of chronic neuropathic pain non-responsive to morphine and opioid drug protocol

