The Calmare® Pain Therapy Treatment (Model MC-5A) medical device utilizes "Scrambler Technology" developed by Professor Giuseppe Marineo (D.Sc., M.S.) which is based on Information Theory. Typical 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. Using the tactile A-Beta fibers, according to the Gate Control theory, there is an interneuron in the jelly substance that differentiates the signal coming from C-fibers and the signal coming from the A-Beta fibers. If the activity of the C-fibers prevails then pain passes, whereas, if the activity of the tactile fibers prevail then pain is interrupted or blocked. This strategy of stimulating only the tactile A-beta fibers is the 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 difference is due to that chronic pain and cancer pain are associated with a neuropathic injury.

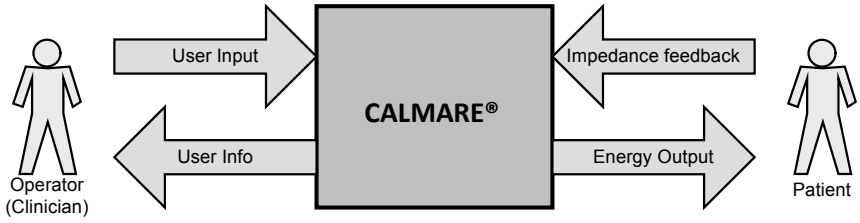
The technology behind the Calmare® is specifically for the treatment of chronic neuropathic and oncologic pain. Whereas acute pain in itself is not a pathology because it has a beginning, an end and a protection function. In chronic pain the cause and effect relation is not clear and definitely not linear, as with acute pain. An example is allodynia, which the Gate Control theory cannot explain the non-linear response to chronic pain, 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, because the cancer filters 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 (waveforms) that do not exist in the CNS naturally. These signals have been specifically created for TENS and implants. The Calmare® uses the natural action potentials and artificially creates action potentials which are irregular shaped like the natural waveforms. This provides a high level of compatibility to allow the brain to recognize the new artificial signal as "self" with non-pain information. The Calmare® stimulates not only C-fibers but also partially A-Delta fibers. (This is unavoidable.) 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 shorter 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. The TENS standard impulse of 50 µsec is specifically used to excite only A-Beta fibers. When the impulse width gets longer they involve other type of slower fibers, however even at 5 milli-seconds, like in the Calmare®, the stimulation of A-Delta fibers is unavoidable. This is noticeable as a feeling similar to a bee sting during the early fine-tuning stage of treatment with the Calmare® which is specific to lower intensity stimulation of the A-Delta fibers. When the intensity level of the Calmare® is increased, and all the no-pain information is transmitted through the C-fibers, which is during the excitation of the C-fibers and wider pulse width, the sting feeling disappears and the patients feels a tingle sensation that signals the start of the analgesic effect. This is an important identifier with the Calmare® technology that until the patient feels the sting the analgesic effect cannot start. Only after this phase does the patient then describe a more comfortable feeling, sometimes a wave-like feeling, which indicates the analgesic effect has begun.

It is important to note that the electrical stimulation signal produced by TENS and other implants is always the same. The signal does not vary and because the brain is adaptive it then over a period of time perceives the signal as noise and therefore the therapeutic activity is lost. The patient becomes desensitized to TENS and other implant treatments. Whereas, the Calmare® incorporates 16 synthetic, naturally perceived waveforms which are dynamically and randomly assembled in sequences and packets of time, and which prevents the brain from adapting to the no-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 polyneuropathy patients have no-pain periods ranging from several weeks to 3 months before additional booster treatment is 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
- 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