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PULSED SIGNAL THERAPY AND THE TREATMENT OF OSTEOARTHRITIS

Report submitted to the

Québec Minister Responsible for Research, Science and Technology

Prepared by:
Alicia Framarin

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Agence d'évaluation des technologies et
des modes d'intervention en santé (AÉTMIS)
2021, avenue Union, bureau 1040
Montréal (Québec) H3A 2S9

Telephone: (514) 873-2563
Fax: (514) 873-1369
E-mail: aetmis@aetmis.gouv.qc.ca
Web address: http://www.aetmis.gouv.qc.ca

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MISSION

To assist the Minister of Research, Science and Technology and the policymakers in Québec's health-care system, including the Ministère de la Santé et des Services sociaux, by means of health technology and intervention modality assessments, specifically, by assessing their efficacy, safety, costs and cost-effectiveness, and their ethical, social and economic implications.

To assist the Minister of Research, Science and Technology in developing and implementing scientific policy.

PULSED SIGNAL THERAPY AND THE TREATMENT OF OSTEOARTHRITIS

Osteoarthritis is a slowly and cyclically evolving disease with a high prevalence, especially among the elderly. Most often, it affects the joints in the hip, knee, cervical and lumbar spines, and fingers. Having a noninvasive and nonpharmacologic treatment that is effective in relieving pain and improving joint function is desirable.

Several studies have suggested using pulsed electromagnetic fields as a therapeutic option, one of the applications being pulsed signal therapy (PST). Since the efficacy of these methods is still debated, the Collège des médecins du Québec asked the Agence d'évaluation des technologies et des modes d'intervention en santé (AÉTMIS) to assess PST in the treatment of osteoarthritis. This assessment is essentially based on a critical review of the studies published on the subject.

The results of the studies examined strongly suggest an analgesic effect and improved joint function in osteoarthritis, but these results need to be confirmed by larger, methodologically well-designed studies and by a better understanding of the mechanisms of action at work. The role of this therapy in relation to the other available treatments may then be better defined.

However, it is difficult to consider this technology purely experimental, since it is already being used by physiotherapy clinics, physicians in private practice and private individuals in Québec and elsewhere in the world. Consequently, AÉTMIS believes that the use of pulsed signal therapy cannot be generalized and that research should continue on its efficacy and cost-effectiveness in the treatment of osteoarthritis.

In disseminating this report, AÉTMIS wishes to provide the best possible information to the policymakers concerned at different levels in Québec's health-care system.

Renaldo N. Battista
President and Chief Executive Officer

SUMMARY

Pulsed signal therapy (PST) is a therapeutic application of pulsed electromagnetic fields (PEMFs). This noninvasive technique consists in applying an extremely-low-frequency (ELF) magnetic field, either with a ring or cylinder surrounding the affected part of the body, or with electrodes applied on the skin. The most widely known application of pulsed fields is the treatment of nonhealing fractures, i.e., those that do not heal after a few weeks of standard immobilization with a cast. However, there are other possible applications. The purpose of this report, which stems from a request by the Collège des médecins du Québec, is to assess the efficacy of PST in relieving pain and improving joint function in osteoarthritis.

Osteoarthritis is a slowly and cyclically evolving disease with a high prevalence, especially among the elderly. It is characterized, among other things, by the gradual destruction of joint cartilage in pressure areas and by joint deformities. The joints most often affected are those in the hip (coxarthrosis), knee (gonarthrosis), cervical and lumbar spine, and fingers. Having a noninvasive and nonpharmacologic treatment that is effective in relieving pain and improving joint function is desirable.

A literature search revealed seven studies that had investigated the efficacy of pulsed signal therapy in the treatment of osteoarthritis, but only four of them could be used for this assessment. All of these studies have methodological weaknesses. Furthermore, it is difficult to compare the studies because the outcome measures were different and the PST techniques differed in terms of electromagnetic wave frequency, intensity and shape. Moreover, what the impact of these different parameters was on the results obtained cannot be determined.

The results of the studies examined strongly suggest an analgesic effect and improved joint function in osteoarthritis, but these results need to be confirmed by larger and methodologically well-designed studies and by a better understanding of the mechanisms of action at work. Consequently, AÉTMIS believes that this technology has almost reached the innovative stage, especially since it is already being used by physiotherapy clinics, physicians in private practice and private individuals in Québec and elsewhere in the world and since the user professionals consulted believe that pulsed electromagnetic field therapy may have a role to play in the therapeutic arsenal for osteoarthritis.

However, pulsed signal therapy should not be put into general use until research in the appropriate settings has conclusively demonstrated its beneficial effects. Furthermore, it would be desirable if this research could, as soon as possible, compare this therapy with the alternatives from the standpoint of both efficacy (including the speed of onset of action and adverse effects) and cost-effectiveness. It would then be possible to situate this therapy in relation to all the other therapeutic approaches to osteoarthritis.

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LIST OF ABBREVIATIONS

ELF	Extremely low frequency
OA	Osteoarthritis
PEMF	Pulsed electromagnetic field
PST	Pulsed signal therapy
RF	Radiofrequency
VAS	Visual analog scale
VLF	Very low frequency

GLOSSARY

Ampere (A): Unit of strength of an electric current.

Diathermia: A therapeutic method that uses high-frequency alternating electrical current to heat (medical diathermy) or destroy (surgical diathermy) tissue.

Electric field: The effect of attraction or repulsion by a given charge on another unit electric charge. It is due to voltage. The strength of an electric field is measured in volts per meter (V/m) or in kilovolts per meter (kV/m) [WHO, 1998b].

Electromagnetic field: An electromagnetic field is associated with the presence of an electric charge (electric field) and of electric current (magnetic field) [Novini, 1993].

Electromagnetic wave: Energy of natural or man-made source from oscillating electric and magnetic fields. It consists of very small packets of energy called *photons*. The energy in each photon is directly proportional to the frequency of the wave. Depending on their frequency and energy, electromagnetic waves can be classified as ionizing radiation or nonionizing radiation. Electromagnetic waves interact in different ways with biological systems [WHO, 1998a].

Extremely-low-frequency (ELF) field: An electromagnetic field with a frequency less than or equal to 300 Hz. At such low frequencies, the wavelength in air is very long (6,000 km at 50 Hz and 5,000 km at 60 Hz) [WHO, November 1998]. The most common sources of ELFs in the human environment are electricity and electrical equipment (50-60 Hz) [Novini, 1993].

Frequency: The number of complete oscillations that pass a fixed point per unit of time. It is measured in cycles per second or hertz (Hz). One cycle per second equals 1 hertz. The higher the frequency, the more energy that can be emitted when an electromagnetic field comes in contact with a body. Very-high-frequency waves, i.e., those above 10^{15} Hz, constitute the ionizing radiation [gamma rays, x-rays, certain ultraviolet (UV) rays] produced by the sun, stars, radioactive bodies, x-ray tubes, UV lamps, etc. Waves of lower frequency are said to be nonionizing. They are visible light (10^{12} Hz), the infrared, microwaves, and television and radio waves [WHO, 1998a].

Gauss (G): A unit of measure of magnetic induction (magnetic flux density) (1 G = 0.1 mT).

Hertz (Hz): A unit measure of the frequency of an electric field equal to one cycle per second.

Ionizing radiation: Extremely-high-frequency electromagnetic waves (x-rays and gamma rays) that have enough energy to produce ionization (create positively and negatively

charged atoms or parts of molecules) by breaking the bonds that hold molecules in cells together [WHO, 1998a].

Lequesne algofunctional indices: Two indices developed by Lequesne for the purpose of measuring three parameters: pain or discomfort, maximum walking distance and activities of daily living. These indices are used in diseases of the hip and knee. There are other indices, such as the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index). Little is known about the validity and reliability of these scales.

Magnetic field: The force exerted by a moving electric field (electromagnetism) or by a permanent magnet (static magnetic field). It is measured in amperes per meter (A/m) but is usually expressed in terms of the corresponding magnetic induction (magnetic flux density), which is expressed in tesla (T), millitesla (mT) or microtesla (μT). In some countries, magnetic induction is measured in gauss (G) (10,000 G = 1 T, or 1 G = 0.1 mT) [WHO, 1998b; Novini, 1993].

Nonionizing radiation: A general term for the part of the electromagnetic spectrum in which photon energy is too weak to break atomic bonds. Nonionizing radiation includes ultraviolet radiation, visible light, infrared radiation, radiofrequencies, microwaves, extremely-low-frequency (ELF) fields and static electric and magnetic fields [WHO, 1998a].

Radiofrequency: The frequency of an electromagnetic wave or an electrical signal lower than optical frequencies. The radiofrequency band is from 300 kHz to 300 MHz but can include microwaves and hyperfrequencies (up to 300 GHz), given their similar characteristics [Juutilainen, 1997].

Ritchie scale: The Ritchie scale (0 to 3) is used to assess joint pain in rheumatoid arthritis. Zero is the absence of pain or tenderness, and 1 is mild, 2 moderate and 3 severe pain or tenderness.

Tesla (T): Unit of measure of magnetic induction (magnetic flux density) (1 T = 10,000 G).

Very-low-frequency (VLF) field: An electromagnetic field with a frequency between 2 kHz and 400 kHz [Novini, 1993]. The most common sources of VLFs in our environment are televisions and video equipment.

Visual analog scale (VAS): A 10-cm-long, horizontal scale (nongraduated) on which the patient indicates the intensity of his or her pain.

Volt (V): Practical unit of force of the current that feeds a circuit.

Watt (W): Unit of measure of electric power equal to the consumption of one joule per second.

Wavelength: The distance travelled by a wave during one oscillation, or one cycle [WHO, 1998b]. It is determined by dividing the speed of propagation by the frequency. The higher the frequency, the shorter the wavelength [WHO, 1998a].

Wave generator: A device for producing electromagnetic fields. It is equipped with wave amplitude, frequency and modulation control devices.

1. INTRODUCTION

Electromagnetism was discovered in the 1800s by the English physicist Michael Faraday [Ramey, 1998] and has, for a very long time, been used in medicine for diagnostic and therapeutic purposes. One of the therapeutic applications of magnetic fields, pulsed electromagnetic field (PEMF) therapy, is used mainly in orthopedics to treat nonhealing fractures, but other indications have been proposed, such as relieving pain and improving joint function in osteoarthritis. At least two types of pulsed magnetic field generators have been approved by Health Canada.

The purpose of this Agence d'évaluation des technologies et des modes d'intervention en santé (AÉTMIS) report, which stems from a request by the Collège des médecins du Québec, is to assess the efficacy of one of the applications of pulsed electromagnetic fields, called *pulsed signal therapy* (PST), in the treatment of osteoarthritis and its use in Québec and elsewhere. It examines the available scientific literature on the technical aspects of electromagnetic fields and on the clinical applications of pulsed signal therapy. It also provides an overview of the current situation in Québec and elsewhere.

2. METHOD

A search was conducted in Medline and the Cochrane Database for the relevant published literature, using the following keywords: *pulsed signal therapy*, *pulsed electromagnetic fields*, and *electromagnetic fields* in combination with *osteoarthritis*. We did not impose any cut-off with regard to the date of publication. We chose, for our review, studies published in English, French, German, Spanish and Italian, and those involving human subjects. The literature search was complemented by hand-searching the bibliographies in the articles consulted. We also consulted the lists of publications from the International Network of Agencies for Health Technology Assessment (INAHTA). Unpublished studies were identified by Web searches and by gleaning lists of references and articles provided by the manufactures. In several cases, the authors were contacted.

3. DESCRIPTION OF THE TECHNOLOGY

3.1 TECHNICAL ASPECTS

Therapeutic devices based on electromagnetic fields can be classified into three main categories according to their frequency band: 1) radiofrequency (RF) generators (which usually operate at 27 MHz); 2) low-frequency (VLF and ELF) electromagnetic field generators (1 Hz to 10 kHz); and 3) sources of static magnetic fields [Barker, 1993].

Radiofrequency generators are used in physiotherapy to treat soft-tissue lesions. The technique is known as *shortwave diathermy*. The devices generate up to 100 watts of electrical power and produce a thermal effect responsible for physiological responses such as increased blood flow and increased tissue oxygenation. RF fields with frequencies greater than about 1 MHz cause heating because of the movement of ions and water molecules in the medium in which they flow. At frequencies below 1 MHz, RF fields induce electrical charges and currents that can stimulate cells in certain tissues, such as nerves and muscles [Barker 1993].

There are many sources of static magnetic fields. They include bracelets, collars, insoles and other devices that one can apply on the skin. There is a wide variety of clinical applications, but their efficacy has not been demonstrated [Aymerich et al., 1996].

Generators of extremely-low-frequency (ELF) fields produce pulsed electromagnetic fields (PEMFs), which are said to have a nonthermal beneficial effect. These are noninvasive techniques in which the magnetic field is applied from a ring or a cylinder surrounding the affected part of the body or by means of skin surface electrodes. The most widely known application of pulsed fields is the treatment of nonhealing fractures, i.e., those that do not heal after a few weeks of standard immobilization with a cast. There are other potential applications. For each one, the characteristics of the recommended magnetic waves are different both with regard to frequency and wavelength.

PEMF therapy, which is used mainly to treat nonhealing fractures, and pulsed signal therapy (PST) both use electromagnetic fields, although some authors make a distinction between the two approaches on the basis of technical characteristics. The main differences are presented in Table 1 [Trock et al., 1993; Cossu et al., 1999].

The U.S. Food and Drug Administration (FDA) has approved a certain number of electromagnetic field generators for the following three applications: 1) the stimulation of osteogenesis in cases of nonhealing fractures; 2) congenital pseudoarthrosis; and 3) spinal fusion. Three of these devices generate low-frequency pulsed electromagnetic fields. No device has been approved by the FDA for accelerating fracture healing or treating osteoarthritis [Polk, 1996]. However, there at least two devices on the list of medical devices approved by Health Canada [Health Canada, 2000]. The cost of the devices is estimated at about $5,000 CDN [Health Canada, 1998].

Table 1: Characteristics of pulsed electromagnetic fields and pulsed signal therapy

	PEMFs	PST
Engery source	Alternating current	Unidirectional current
Field intensity	2 G	12.5 G (0.15 -1.5 mT)
Frequency	44-77 Hz	1-30 Hz
Pulsation	Constant	Alternating
Wave type	Sinusoidal	Quasirectangular
Duty cycle	< 50 %	> 50 %
Pulse frequency	Continuous	Modulated
Frequency source	Fixed	6 frequency sources

Source: Documentation provided by a manufacturer and Cossu et al., 1999.

3.2 MECHANISM OF ACTION

Exposure to static or pulsed magnetic fields has effects on cell and organ function. The effects of PEMFs depend on the intensity of the electric field produced in the tissues. Magnetic induction of 1 A/m^2 or more can cause acute and potentially harmful effects. At lesser intensities, various effects occur, some reversible, some not. The effects occur at different frequencies, intensities and durations of exposure [Czerski et al., 1986]. PEMFs produce three types of effects: an analgesic effect, a stimulating effect on chondrocytes and a stimulating effect on osteocytes.

The analgesic effect attributed to PEMFs is apparently due to a change in the electrical potential across the cell membrane, which has the effect of altering the release of chemical transmitters in the synaptic space and thus causing a change in the reaction to pain. When joint cartilage is subjected to the stress of physical activity, the electrical potential created promotes chondrocyte replication and joint cartilage regeneration. A pulsed magnetic field apparently acts on joint cartilage by generating an electrical potential similar to that produced during the normal functioning of a joint.

3.3 COMPLICATIONS AND ADVERSE EFFECTS

Although the debate over the safety of magnetic fields and their effects in terms of the development of cancer continues, exposure to low-intensity fields over short periods of time is probably safe. However, treatment with pulsed electromagnetic fields is contraindicated in patients with cancer, pregnant women and pacemaker wearers [Trock, 2000]. The long-term effects on tissues in the exposed area are not documented in the currently available literature.

3.4 STATUS OF THE CURRENT PRACTICE

Two pulsed magnetic field generators are on the list of medical devices approved by Health Canada. In Québec, it appears that four companies market magnetic field generators and that one of them is an Ontario firm. Most of those generators have been

purchased and are being used by physiotherapy clinics, physicians in private practice and private individuals. To our knowledge, the costs associated with PEMF therapy are not specifically covered by the different health insurance plans but may be covered indirectly when included in physiotherapy.

In France, use of PEMF is restricted to private centres, and the treatment is not covered by insurance, according to a personal communication from Dr. Perrot, Rheumatologist Unit and Pain Centre, Hôpital Cochin (November 1999). PEMF therapy is also used at private centres in Germany and Italy, but it was not possible to determine the extent of such use.

4. THE USE OF PULSED ELECTROMAGNETIC FIELDS IN THE TREATMENT OF OSTEOARTHRITIS

4.1 DESCRIPTION OF OSTEOARTHRITIS

Osteoarthritis is a disease characterized by the gradual destruction of joint cartilage in pressure areas, subchondral bony sclerosis, joint deformities and the formation of osteophytes. It is a frequent health problem, and its prevalence increases with age [Felson et al., 2000]. The prevalence of osteoarthritis after the age of 65 is estimated at 68% in women and 58% in men (all sites combined) [Altman, 1994]. The disease manifests mainly as pain and a loss of joint function. The joints most often affected are those in the hip (coxarthrosis), knee (gonarthrosis), cervical and lumbar spine, and fingers [Pinals, 1996; Jackson, 1998].

The etiology of osteoarthritis is not known with certainty. For a long time, it was associated with aging. However, aging cartilage has different biochemical characteristics than osteoarthritic cartilage [Sack, 1995; Schwartz et al., 1999]. The disease is probably due to a set of factors that cause a loss of joint cartilage integrity [Bagge, 1995], including joint injury, heredity, female gender, estrogen deficiency during menopause, and obesity [Jackson, 1998; Sack, 1995; Jordan et al., 2000].

4.2 THERAPEUTIC APPROACHES

Osteoarthritis is a slowly evolving disease, with successive flare-ups and with periods of remission. The main objective of treatment is to relieve pain and improve joint function. The conventional approaches include, among others: 1) nonpharmacologic measures, such as an orthosis with support (cane), physiotherapy, occupational therapy, physical activity, weight loss and support groups; 2) pharmacologic measures (analgesics, nonsteroidal antiinflammatories, intra-articular injections); and 3) surgical treatments (osteotomy and arthroplasty).

New developments are giving hope for interventions that might protect deficient osteoarthritic cartilage and that might even permit cartilage regeneration. The administration of glucosamine or chondroitin sulfate could have effects on cartilage regeneration [Hochberg et al., 2000]. Although a recent meta-analysis of 15 randomized, double-blind, comparative trials with placebo control groups evaluating the efficacy of glucosamine and chondroitin sulfate in the treatment of osteoarthritis showed a positive effect, the American College of Rheumatology believes that it is too early to make any specific recommendations regarding the use of these compounds because of the studies' methodological bias [McAlindon et al., 2000; American College of Rheumatology, 2000].

Pulsed signal therapy is part of conventional physiotherapy care in the treatment of osteoarthritis. Recent reviews of nonpharmacologic approaches to treating osteoarthritis discuss the use of electromagnetic fields for pain relief. The use of pulsed electromagnetic fields (PEMFs or PST) for relieving gonarthrotic pain is

considered relatively expensive, given the results obtained [Perrot et al., 1996], and an approach whose efficacy has not been demonstrated [Schwartz 1999].

4.3 DESCRIPTION AND ANALYSIS OF HARD DATA

We identified six published studies and one unpublished study on the effects of pulsed electric and magnetic fields in the treatment of osteoarthritis. Five of them were double-blind, comparative trials with placebo groups. The other two involved longitudinal cohorts with no comparison group, although one of them also included a comparison with a placebo group. In the studies with placebo groups, the patients in those groups were exposed to simulations similar to the exposure in the experimental group, using the same type of device but in the inactive mode, i.e., without the generation of a magnetic field. It should be noted that the generating of a magnetic field does not produce any noise or sensations that can be perceived by the patient. Neither the patient nor the attending physician knew whether the device was in the active or inactive mode during the treatment sessions. However, the device's active or inactive status during application was known to the person responsible for applying the treatment.

All the studies were methodologically flawed. In most of them, the samples were small, and there is no discussion of the calculation of the sample size required to ensure sufficient statistical power. The outcome variables were based on subjective observations. In most of the comparative studies, improvement in the clinical variables was calculated only in relation to baseline in both groups, not by comparing the experimental group with the placebo group. In those studies that were not comparative and randomized, the observed improvement could have been the result of the cyclic course of the disease, which can exhibit periods of spontaneous remission. Lastly, most of the studies were financially supported by the companies that manufactured the devices being tested.

Three of the seven studies were excluded from our review. In two of them, a technique other than PST was used, one employing pulsed electrical stimulation via skin surface electrodes [Zizic et al., 1995], the other pulsed magnetic shortwaves [Van Steenbrugghe et al., 1988]. The third study excluded was a pilot study with a randomized, double-blind, comparative design [Trock et al., 1993]. It was excluded because of the small sample size (27 patients, 15 in the experimental group and 12 in the placebo group), the loss to follow-up, which was 26% (33% in the experimental group and 17% in the placebo group) and the heterogeneity of the experimental and placebo groups, as they included patients with different affected joints (knee, hand and ankle). The subjective evaluation of pain and the difficulty performing the activities of daily living can vary according to the affected joint. The features and the results of the three excluded studies are shown in Table A.1 in Appendix A.

Table 2: Breakdown of the published and unpublished studies, included in our review, on the efficacy of pulsed electromagnetic fields in the treatment of osteoarthritis according to the strength of the evidence

Strength of evidence	Description of study	Number of studies	Number of patients
High - Level 1	Meta-analysis of randomized, comparative trials	0	-
Level 2	Randomized, double-blind, comparative trial with a placebo group	2	167 [Trock et al, 1994] 40 [Menkès, 1998]
Level 3	Randomized, comparative trial	0	-
Level 4	Prospective, nonrandomized, comparative trial	0	-
Level 5	Case-control study	0	-
Low - Level 6	Clinical series, descriptive studies	2	233 [Dal Conte, 1986] 34 [Cossu, 1999]

Four studies (three published, one unpublished) on the efficacy of PEMFs in the treatment of osteoarthritis were included in this review. Table 2 shows the evaluation of the available literature on the subject according to the strength of the evidence and indicates the number of articles in each category.

The three published studies included in the analysis are a randomized, double-blind, comparative trial with a placebo group [Trock et al., 1994], a study with a double design (longitudinal cohort comparison) [Dal Conte et al., 1986] and a descriptive, longitudinal cohort study with no comparison group [Cossu et al., 1999]. The latter two studies involved a follow-up of 6 and 12 months, respectively. Table A.2 (Appendix A) shows the features of these three studies.

Trock et al. studied the effects of PST in 86 patients with osteoarthritis of the knee (42 in the experimental group and 44 in the placebo group) and 81 patients with osteoarthritis of the cervical spine (42 in the experimental group and 39 in the placebo group). The following variables were measured: 1) pain (10-cm VAS); 2) the difficulty performing the activities of daily living; 3) pain on motion and tenderness (measured by the physician using a modified Ritchie scale); and 4) a global assessment of improvement by the patient and by the physician. In the case of cervical osteoarthritis, limitation of flexion-extension and rotation was measured as well. Improvement was measured by the percent change observed at the midpoint of therapy, at the end of treatment and one month after the end of treatment in relation to baseline.

A significant improvement of between 29 and 36% in the measured variables was observed at the end of treatment in the treated patients with osteoarthritis of the knee. The improvement varied from 11 to 19% in the placebo group patients. One month after the end of treatment, the percent improvement was between 21 and 31% in the experimental group and between - 0.3

and 16% in the placebo group. In the case of cervical osteoarthritis, the improvement was between 30 and 35% at the end of treatment and between 20 and 39% one month later in the experimental group. In the placebo group, the improvement varied from 17 to 27% at the end of treatment and from 0 to 18% one month later. Although the improvement was greater in the treated patients (experimental group), there was also significant improvement in the placebo group for most of the variables, whether at the end of treatment or one month later compared to baseline [Trock et al., 1994].

The comparative results between the treated and placebo groups showed significant improvement in pain in the case of osteoarthritis of the knee and cervical spine at the end of treatment and one month later. Table B.1 (Appendix B) shows the comparative results between the two groups for each of the measured variables and for the different periods of time.

The second study had a double design. One part of the study involved evaluating changes in a group of 233 patients with cervical (n = 144) or lumbar (n = 89) spondylosis treated with a PEMF device. The results with regard to joint pain and joint function were evaluated at the end of treatment, and three months and six months after the end of treatment and were compared with baseline. The observed improvement was significant ($p < 0.005$) for all the variables and between each measurement and baseline. The second part of the study compared the results obtained in 29 patients who underwent three weeks of sham treatment (treatment session with the PEMF device but without the passage of current) with the results obtained in the same 29 patients treated for three weeks with PEMF after a period of three months with no treatment. The patients were not selected randomly, and the sample was small. The improvement observed in the treated patients was significant ($p < 0.005$) at the end of treatment and three months and six months after the end of treatment compared to the pretreatment data, while no significant improvement was observed in the placebo group [Dal Conte et al., 1986].

A longitudinal cohort study with no comparison group was conducted in Italy for the purpose of assessing the effect of pulsed signal therapy (PST) on 34 patients (8 men and 26 women) with osteoarthritis of the knee [Cossu et al., 1999]. The patients underwent a cycle of nine 1-hour sessions with intervals of less than 48 hours between the sessions. The outcome variables were pain, as measured on a VAS of 1 to 10, pain present during functional tests (range of 0 [absence of pain in all the tests] to 10 [presence of pain during all the tests]) and functional difficulty (assessed by means of a questionnaire). Measurements were made at the start of treatment (time 0), at the end of treatment (time 1), and two weeks (time 2) and one year after the end of treatment (time 3). None of the patients had undergone physiotherapy, and five had taken nonsteroidal antiinflammatories sporadically for fewer than two consecutive days during the year of follow-up. On average, the pain index decreased from 7.12 to 2.38 (on a scale of 10) from time 0 to time 3, the difference between the measurements being significant ($p = 0.01$). Pain on motion decreased as well, from 7.15 (time 0) to 1.47 (time 3). The fact that there was no comparison group makes it difficult to interpret the results, given that the disease evolves cyclically, with periods of spontaneous remission. Other studies are underway in Italy, but this one is the only one published thus far (according to information from Christine Rosichelli, PST Italia Srl, May 19, 2000).

The analgesic efficacy of PEMFs in knee osteoarthritis was examined in a randomized, double-blind, comparative study involving 40 patients (21 in the experimental group and 19 in the placebo group) conducted in France in 1998 [Menkès et al., 1998]. This study, whose results have not been published, found some evidence indicating that PEMFs are effective in the treatment of knee osteoarthritis. The significant differences between the two groups were observed on the VAS for pain on motion (measured on day 9 and three months after the end of treatment) and the Lequesne indices measured three months after the end of treatment [Menkès et al., 1998]. The authors state that the study was of an exploratory nature and that the results need to be confirmed by a study including a larger number of patients (written personal communication from Dr. Perrot, November 1999). A description of the study is provided in Table A.2 (Appendix A).

Other unpublished studies have been carried out in Italy and Germany for the purpose of evaluating the efficacy of pulsed signal therapy in the treatment of osteoarthritic pain. The studies were uncontrolled and involved small numbers of patients. Also, a multicentre study for evaluating the effects of pulsed signal therapy on knee osteoarthritis has just ended in Germany, but the results have not yet been published. Preliminary results show an improvement in pain (VAS) and joint function (Lequesne algofunctional index) of 50% after six months of follow-up ($p < 0.0001$), according to a personal communication with Dr. Rainer Breul, May 16, 2000. This study has still not been published. We do not have any more-detailed information at this time.

4.4 SYNOPSIS ON EFFICACY

The published studies are few in number and are methodologically flawed. The only published randomized, double-blind study with a placebo-group used in this assessment [Trock et al., 1994] showed a considerable effect in the placebo group. Although osteoarthritis evolves cyclically, with periods of spontaneous remission, the longitudinal cohort studies showed an improvement in pain and joint function after PEMF therapy. These beneficial effects persisted for several months and even up to one year. It is difficult to compare the studies because the outcome measures were different, even for the same variable. Additionally, the studies used PST techniques that vary in terms of electromagnetic wave frequency, intensity and shape. What the impact of these different parameters might have been on the results obtained cannot be determined.

If the main effect of PEMF therapy is pain relief, such treatment will have to be situated in relation to the other forms of osteoarthritis treatment that can relieve pain, such as nonsteroidal antiinflammatories and intra-articular treatments (corticosteroid infiltration, hyaluronic acid injections and joint debridement and lavage). These therapies are less expensive and have a faster speed of onset of action, although they may have some untoward or adverse effects. However, such an analysis cannot be performed until the efficacy of PEMF therapy is conclusively confirmed by rigorous studies.

5. THE STATUS OF PULSED ELECTROMAGNETIC FIELD THERAPY

The classification adopted by the Agence d'évaluation des technologies et des modes d'intervention en santé for designating the status of a given technology is as follows:

1) An **experimental** technology is one whose efficacy has not yet been established. Such a procedure should therefore not be used by health professionals or in health-care facilities, except in the context of research projects.

2) An **innovative** technology is one that has moved beyond the experimental stage and whose efficacy has been established. However, because of a lack of experience, certain indications for its use and various aspects of its application are not yet clearly defined. In addition, data on the technology's cost-effectiveness may be lacking or even nonexistent. To gain further knowledge of the technology, it would be important to systematically gather all the data acquired from its use and to communicate them to the medical community in the form of a clinical research report or systematic review or an appropriate register. To further these objectives and to prevent its premature widespread use, the technology should be restricted to certain authorized centres with the necessary resources and knowledge.

3) An **accepted** technology is one that is well established and for which there is lengthy utilization experience and a knowledge of, or failing that, universal acceptance of its efficacy and cost-effectiveness in all its applications.

Because of the small number of studies currently available on the results of the use of pulsed electromagnetic field therapy in the treatment of osteoarthritis, no firm conclusions can be drawn as to its efficacy. Although the technology seems to be effective for certain indications, for example, the treatment of nonhealing fractures, the mechanisms of action that promote osteogenesis in this specific case are different from those that act on pain and joint function in osteoarthritis. This technology is already being used by physiotherapists and physicians in Québec, and private medical clinics in Canada and elsewhere in the world offer this service. It is therefore difficult to consider this technology purely experimental. We are of the opinion that its use in osteoarthritis should be considered between experimental and innovative and that it should not be generalized until high-quality studies have demonstrated its efficacy and explained the mechanisms of action at work in the treatment of osteoarthritis.

6. CONCLUSION

Osteoarthritis is a disease with a high prevalence, especially among the elderly. Having a noninvasive and nonpharmacologic treatment that is effective in relieving pain and improving joint function is desirable. Several studies have suggested using pulsed electromagnetic fields as a therapeutic option, one of the applications being pulsed signal therapy, whose efficacy had previously been demonstrated for other indications, such as the treatment of nonhealing fractures.

In light of its assessment, AÉTMIS believes that pulsed signal therapy has almost achieved the status of innovative technology. Although no firm conclusions can be drawn from the available scientific data, the latter strongly point to an analgesic effect and improved joint function in osteoarthritis. Furthermore, this technology cannot be considered purely experimental, since it is already being used by physiotherapy clinics, physicians in private practice and private individuals in Québec and elsewhere in the world and since the user professionals consulted believe that pulsed electromagnetic field therapy may have a role to play in the therapeutic arsenal for osteoarthritis.

However, the use of pulsed signal therapy cannot be generalized until larger, methodologically well-designed studies have confirmed its efficacy and until its mechanism of action is understood. Research should therefore continue in the appropriate areas.

Lastly, it would be advisable for research to be conducted as soon as possible to compare pulsed electromagnetic field therapy with the alternatives, both in terms of efficacy (including the speed of onset of action and untoward or adverse effects) and cost-effectiveness. It will then be possible to situate this therapy among all the other therapeutic approaches to osteoarthritis.

APPENDIX A:
FEATURES OF THE STUDIES EXCLUDED FROM AND INCLUDED IN THE ASSESSMENT

Appendix A: Features of the studies excluded from and included in the assessment

Table A.1: Features of the studies excluded from the assessment

	Van Steenbrugghe et al., 1988	Trock et al., 1993	Zizic et al., 1995
Reason for exclusion	Pulsed shortwave therapy	Small sample size (n=27). 27% lost to follow-up one month after the end of treatment (33% in the experimental group and 17% in the placebo group). Heterogeneity of the experimental and placebo groups, as they included patients with different affected joints (knee, hand, ankle).	Electrical stimulation with skin surface electrodes.
Objective	To assess the efficacy of pulsed electromagnetic-field shortwaves in tendon or osteoarticular disease.	To evaluate PEMFs in the treatment of osteoarthritis.	To evaluate the safety and efficacy of pulsed electrical stimulation in the treatment of osteoarthritis of the knee.
Design	Controlled and double-blind, with a placebo control group.	Randomized, double-blind, comparative trial with a placebo control group.	Randomized, double-blind, comparative trial with a placebo control group.
Equipment used	27-mHz shortwave oscillator, power of 1 kW, emission of 400 µsec pulsed at a low frequency (26 Hz) for the first 5 sessions, then gradually at a higher frequency (200 Hz).	Extremely-low-frequency PEMF generator (< 30 Hz), 10-20 G of magnetic energy on average at a coil current of up to 2 A drawn from a power source of 120 V AC. Pulse phase duration: 67 ms, including 15 micropulses with a pause duration of 0.1 s.	Electrical impulses generated by a portable device producing a low-frequency (100 Hz), low-amplitude, monophasic signal, which was applied via skin surface electrodes, one on the knee, the other on the thigh.
Treatment	Ten 20-minute sessions at the rate of two sessions per week.	Eighteen 30-min sessions at the rate of 3 to 5 times a week for one month	6 to 10 hours a day for four weeks
Study population	141 patients: cervicalgia (n=58), lumbalgia (n=42), knee osteoarthritis (n=16), shoulder tendon pain (n=13), various tendon problems (n=12).	21 patients with osteoarthritis of the knee. 5 patients with osteoarthritis of the hands. 1 patient with posttraumatic osteoarthritis of the ankle.	78 patients with osteoarthritis of the knee.
Lost to follow-up	3%	27%	9%

Appendix A: Features of the studies excluded from and included in the assessment

Table A.1 (Cont'd): Features of the studies excluded from the assessment

	Van Steenbrugghe *et al.*, 1988	Trock *et al.*, 1993	Zizic *et al.*, 1995
Inclusion criteria	Not specified.	a) > 18 years. b) Altman's criteria for osteoarthritis. c) Symptoms of at least one year's duration. d) Symptoms incompletely relieved with nonsteroidal anti-inflammatory drugs (NSAIDs), other analgesics and physical therapy.	a) > 20 years. b) Osteoarthritis diagnosed and treated. c) Patient consent.
Exclusion criteria	Not specified.	a) Patient started a new treatment, including NSAIDs, during the previous month. b) Osteoarthritis of an isolated joint in the hand or osteoarthritis of the spine c) Pacemaker or unstable medical illness.	Presence of another disease: aseptic necrosis of the femoral condyle, juxta-articular Paget's disease, chondrocalcinosis, hemochromatosis, inflammatory arthropathy, etc.
Results	Significant improvement in pain and functional limitation in the cases of cervicalgia. No significant difference in the other cases.	23 to 61% improvement in the clinical variables in the treated patients. 2 to 18% improvement in the placebo group.	Significant improvement: physician assessment ($p = 0.023$); patient assessment of pain ($p = 0.04$); functional evaluation by patient ($p = 0.045$). Decrease in duration of morning joint stiffness of 20 minutes in the treated group and 2 minutes in the placebo group ($p < 0.05$). No difference between the groups in terms of walking time, flexion, extension, joint tenderness or swelling.

Appendix A: Features of the studies excluded from and included in the assessment

Table A.2: Features of the studies included in the assessment

	Dal Conte et al., 1986	Trock et al., 1994	Menkès et al., 1998	Cossu et al., 1999
Objective	To evaluate the efficacy of PEMFs in reducing pain and functional limitation due to cervical and lumbar spondylosis.	To evaluate PEMFs in the treatment of osteoarthritis of the knee and cervical spine.	To compare the efficacy and tolerance of pulsed magnetic fields (PST technology) in painful knee osteoarthritis.	To evaluate, in the long term, the efficacy of PST in the treatment of osteoarthritis of the knee.
Design	Descriptive and comparative (small sample, comparison between the same cohort of 29 patients who received placebo treatment and PST therapy three months later). 6-month follow-up after the end of treatment.	Randomized, double-blind, comparative trial with a placebo group.	Randomized, double-blind, comparative trial with a placebo group.	Longitudinal cohort. 12-month follow-up after the end of treatment.
Equipment used	A Ronefor. Frequency: 50 Hz. Sinusoidal wave. Maximum intensity of 33 G for the cervical spine and 58 G for the lumbar spine.	ELF magnetic field generator using a coil current of < 2 A drawn from a power source of 120 V AC. Energy applied stepwise: 5 Hz, 10-15 G (10 min); 10 Hz, 15-25 G (10 min); 12 Hz, 15-25 G (10 min). Number of pulses/burst determined by the frequency; max.: 20.	Intensity: < 2A, 120 V. Frequency: 2 to 60 Hz. Pulse duration: 1.0 second; pause: 0.1 second.	PST generator; intensity: 12.5 G. Extremely low frequency (ELF) of 1 to 30 Hz with amplitude and duration modulation. Quasirectangular wave [Cossu et al., 1998]
Treatment	30 min per day, 4 weeks (open trial) and 3 weeks (controlled trial).	Eighteen treatment sessions, each 30 minutes long, 3 to 5 times a week for one month.	Nine 1-hour sessions during 9 consecutive days.	Nine 1-hour sessions, with one session a day and a break of no more than 48 hours.
Study population	144 patients with cervical spondylosis. 89 patients with lumbar spondylosis.	86 patients with osteoarthritis of the knee (EG, n = 42 ; PG, n = 44). 81 patients with osteoarthritis of the cervical spine (EP, n = 42; PG n=39).	40 patients: 21 in the PST group and 19 in the placebo group.	34 patients with osteoarthritis of the knee. .

Table A.2 (Cont'd): Features of the studies included in the assessment

	Dal Conte et al., 1986	Trock et al., 1994	Menkès et al., 1998	Cossu et al., 1999
Lost to follow-up	3% at the evaluation done 6 months after the end of treatment.	Different according to the variables; maximum: 19% (one month after the end of treatment).	10% one month after the end of treatment and 37% three months after the end of treatment.	No subjects lost to follow-up.
Inclusion criteria	Radiologic diagnosis of grade III or IV spondylosis and the presence of cervical or lumbar pain syndrome.	a) > 35 years. b) Altman's criteria for osteoarthritis. c) Symptoms of at least one year's duration. d) Symptoms persistent despite conventional treatment. e) If osteoarthritis of the cervical spine: x-ray showed disk space narrowing.	a) > 50 years. b) Painful knee osteoarthritis according to ACR criteria with rating greater than 40 mm at rest and on motion on a pain VAS.	Pain for at least three months that persisted, despite the usual treatment, plus radiologic criteria [Cossu et al., 1998].
Exclusion criteria	a) Pacemaker wearer. b) Presence of severe liver or kidney disease, cardiocirculatory failure, severe osteopenia, even in a single vertebra.	a) Patient began a new treatment, including nonsteroidal anti-inflammatories, or changed treatments in the previous month. b) Pregnancy. c) Patient with pacemaker or unstable medical illness.	a) Pacemaker. b) Pregnancy. c) Coexisting rheumatic disease: gout, rheumatoid arthritis, psoriasic rheumatism, infectious arthritis, algodystrophy. d) Recent intra-articular injection (less than one month). e) Having taken nonsteroidal anti-inflammatories and analgesics in the 7 days prior to the study. f) Initiation of a disease-modifying treatment for osteoarthritis in the month prior to inclusion. g) Treatment in the form of physiotherapy, kinesiotherapy or alternative medicine. h) Surgery scheduled within 3 months. i) Painful homolateral osteoarthritis of the hip. j) Other therapeutic trial in progress.	a) No pain at the time of recruitment, even if there were episodes of pain in the previous 3 months. b) Presence of neoplastic disease. c) Unstable disease (hepatic cirrhosis, decompensated diabetes, etc). d) Patient with pacemaker [Cossu et al., 1998].

Table A.2 (Cont'd): Features of the studies included in the assessment

	Dal Conte et al., 1986	Trock et al., 1994	Menkès et al., 1998	Cossu et al., 1999
Outcome variables	• Spontaneous pain. • Provoked pain. • Joint function. • If cervical osteoarthritis: nocturnal acroparesthesia, brachialgia, dizziness, headache. • If lumbar osteoarthritis: hip pain, nighttime cramps. • Global assessment by patient. • Assessment by physician.	• Pain (VAS). • Difficulty performing activities of daily living. • Pain on passive motion. • Tenderness. • Global assessment by patient. • Global assessment by physician.	• Evolution of spontaneous pain (VAS) at rest and during movement. • Spontaneous pain assessed with a verbal scale at rest and on motion, by the Lequesne algofunctional index and a quality-of-life questionnaire (SF-36).	• Pain at rest. • Pain on motion. • Evaluation by motor function questionnaire.
Results	Improvement in pain and joint function in relation to baseline. The improvement peaked in the 3 months following the therapy and persisted at least until the follow-up examination at 6 months. A follow-up of one year may be too long for assuming that the improvement is attributable to the treatment.	Osteoarthritis of the knee: significant improvement in the treated patients compared to the placebo group for all the variables, except pain on passive motion. Cervical osteoarthritis: significant improvement in spontaneous pain and in pain on passive motion in the treated patients compared to the placebo group. No significant difference between the two groups for the other variables.	The most sensitive criteria for differentiating between the two groups were the VAS for pain on motion (significant difference at the end of treatment and 3 months after the end of treatment) and the Lequesne indices (significant difference 3 months after the end of treatment). A significant difference was observed for general health and mental health (SF-36) 3 months after the end of treatment.	Gradual decrease in pain at rest (on average, 7.12 at the start of treatment and 2.38 one year after the end of treatment) and on motion (on average, 7.15 at the start of treatment and 1.47 one year after the end of treatment).

APPENDIX B: ADDITIONAL INFORMATION ON THE STUDY BY TROCK ET AL., 1994

Table B.1: Results of the study by Trock et al., 1994: p value for the difference observed between the treated and placebo groups for each variable and for each time period (significant if p ≤ 0.1).

Variable	Period		
	Mid-treatment (p)	End of treatment (p)	1 month after (p)
Osteoarthritis of the knee			
Pain (mm)	NS	0.04	0.08
Difficulty performing the activities of daily living	NS	0.04	NS
Pain on passive motion	NS	NS	0.07
Tenderness	NS	0.05	0.03
Patient's assessment of his/her improvement	NS	0.02	NS
Physician's global assessment	-	0.04	0.1
Osteoarthritis of the cervical spine			
Pain (mm)	0.1	0.004	0.1
Difficulty performing the activities of daily living	NS	NS	NS
Pain on passive motion	NS	0.03	0.0004
Tenderness	NS	NS	0.02
Patient's assessment of his/her improvement	NS	NS	NS
Physician's global assessment	-	NS	NS

NS: Not significant
- : Figure not available

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