

**STUDY TO VERIFY THE ANALGESIC EFFECTIVENESS
OF PULSED SIGNAL THERAPY (PST)
IN GONARTHROSIS**

CLINICAL AND STATISTICAL REPORT

2nd Version, 6 April 1998

Published in Arthritis+rheuma, 22 (2002) Nr.2



CLINICAL AND STATISTICAL REPORT

TITLE OF STUDY: Study to verify the analgesic effectiveness of pulsed signal therapy (PST) in gonarthrosis.

PHASE: IV

PLACE OF STUDY: FRANCE

PROMOTER OF STUDY: PST
57 bis, Boulevard Exelmans
75016 Paris

COORDINATOR: Professeur C-J Menkès
Service de Rhumatologie A
Hopital Cochin
75014 PARIS

.....
Signature

.....
Date

INVESTIGATOR: Docteur Serge PERROT
Service de Thumatologie A
Hoptial Cochin
75014 PARIS

.....
Signature

.....
Date

PROJECT MANAGER: PST France
Docteur Jean-Louis LOMPRES
57 bis, Boulevard Exelmans
75016 PARIS

.....
Signature

.....
Date

DATA MANAGEMENT

AND STATISTICAL ANALYSIS Jean-Luc BEFFY

CLINICA & STATISTICA

52, rue Carvès

92120 MONTROUGE

Téléphone: (1) 46.56.00.49

Télécopie: (1) 46.56.70.89

.....
Signature

.....
Date

CLINICAL REPORT:

Docteur Marc MARTY

CLINICA & STATISTICA

52, rue Carvès

92120 MONTROUGE

Téléphone: (1) 46.56.00.49

Télécopie: (1) 46.56.70.89

.....
Signature

.....
Date

DURATION OF THE STUDY:

Date CCPPRB:

May 7, 1997

Date

June 23, 1997

Date

February 17, 1998

CONTENTS

Page

I	SUMMARY	1
II	INTRODUCTION	2
III	Resume of the protocol	2
III.1	Objective of the test	2
III.2	Test schedule	3
III.3	Study population	3
<i>III.3.1</i>	<i>Criteria for inclusion</i>	<i>3</i>
<i>III.3.2</i>	<i>Criteria for non-inclusion</i>	<i>3</i>
<i>III.3.3</i>	<i>Criteria for withdrawal from the study</i>	
III.4	Treatments	4
<i>III.4.1</i>	<i>Treatments within the study</i>	<i>4</i>
<i>III.4.2</i>	<i>Concomitant treatments</i>	<i>5</i>
III.5	Study procedures	5
<i>III.5.1</i>	<i>Selection of patients</i>	<i>5</i>
<i>III.5.2</i>	<i>Study procedures</i>	<i>5</i>
III.6	Criteria for evaluation of effectiveness	6
<i>III.6.1</i>	<i>Main criteria</i>	<i>6</i>
<i>III.6.2</i>	<i>Secondary criteria</i>	<i>6</i>
III.7	Criteria for evaluation of tolerance	7
III.8	Proposed statistical methodology	7
<i>III.8.1</i>	<i>Number of test subjects necessary</i>	<i>7</i>
<i>III.8.2</i>	<i>Statistical methodology and analysis plan</i>	<i>7</i>
III.9	Ethical considerations	7
IV	METHODS EMPLOYED	9
IV.1	Amendments to the protocol and/or practical modifications	9
<i>IV.1.1</i>	<i>Amendments to the protocol</i>	<i>9</i>
<i>IV.1.2</i>	<i>Practical modification</i>	<i>9</i>
IV.2	Data management	9

IV.3	Statistical analysis performed	9
<i>IV.3.1</i>	<i>Analyzed populations and analysis type</i>	<i>9</i>
<i>IV.3.2</i>	<i>Descriptive analysis</i>	<i>10</i>
<i>IV.3.3</i>	<i>Homogeneity of included groups</i>	<i>10</i>
<i>IV.3.4</i>	<i>Statistical analysis performed</i>	<i>10</i>
V	RESULTS	11
V.1	Description of the population	11
<i>V.1.1</i>	<i>Disposition of the patients</i>	<i>11</i>
<i>V.1.2</i>	<i>Deviations from the protocol</i>	<i>11</i>
<i>V.1.3</i>	<i>Characteristics of included patients</i>	<i>11</i>
V.2	Treatment during the study	12
<i>V.2.1</i>	<i>Treatment during the study</i>	<i>12</i>
<i>V.2.2</i>	<i>Concomitant treatments</i>	<i>12</i>
V.3	Results of effectiveness	13
<i>V.3.1</i>	<i>VAS of pain at rest</i>	<i>13</i>
<i>V.3.2</i>	<i>VAS of pain in motion</i>	<i>14</i>
<i>V.3.3</i>	<i>Verbal pain scale</i>	<i>15</i>
<i>V.3.4</i>	<i>Lequesne index</i>	<i>16</i>
<i>V.3.5</i>	<i>Overall assessment of effectiveness</i>	<i>17</i>
<i>V.3.6</i>	<i>Analysis based on patient response</i>	<i>20</i>
<i>V.3.7</i>	<i>SF-36 Scale of quality of life</i>	<i>22</i>
V.4	Results of tolerance	24
VI	DISCUSSION ò CONCLUSION	26

I SUMMARY

Promoter: Bio Magnetic Therapy Systems Inc.
Name of technique: Pulsed signal therapy
Study title: Study to verify the analgesic effectiveness of pulsed signal therapy (PST) in gonarthrosis.
Coordinator: Prof. C.J. MENKES û Rheumatology Dept. A, Hopital Cochin, 75014 Paris
Centres: Dr. Serge PERROT û Rheumatology Dept. A, Hopital Cochin, 78014 Paris
Publications (references):
Duration of study: 1997 Development phase: III
Objectives: To compare the effectiveness and tolerance of pulsed signal therapy (PST) for painful gonarthrosis.
Methodology: Comparative, random, double-blind study in parallel groups.
Number of patients: 40 patients were included; 21 in the PST group and 19 in the placebo group.
Mains criteria for inclusion: aged over 50, painful gonarthrosis according to ACR arthrosis criteria with VAS pain exceeding 40 mn at rest and in motion.
Study technique and method of administration: pulsed signal therapy equipment.
Duration of treatment: 9 sessions of 1 hour on 9 consecutive days.
Reference method and method of administration: pulsed signal therapy placebo.
Criteria for evaluation:
<p>Effectiveness: main criterion : * evolution of spontaneous pain, evaluated at rest and in motion</p> <p>Secondary criteria : * spontaneous pain evaluated on a verbal scale evaluated at rest and in motion</p> <p>* LequesneÆs algofunctional index</p> <p>* questionnaire on quality of life SF-36</p>
Tolerance: overall assessment of tolerance and occurrence of undesirable events.
Statistical methods:
Analyzed population: one single population was analyzed : population with the intention of treatment (randomly selected patients, to whom a treatment number has been allocated, having been treated and re-evaluated at least once).
Analyses: 2 analyses were made for the main criteria : values received and end point. For the secondary criteria, one analysis of values received was carried out.
Tests by WILCOXON, KOLMOGOROV-SMIRNOV, analysis of variances.
Results:
This comparative, randomized and double-blind study revealed several factors which speak for the efficacy of pulsed signal therapy in the treatment of gonarthrosis. Due to the limited number of patients, some of the results may have restricted statistical significance.
The most noticeable criteria to differentiate between the two treated groups are the VAS of pain in motion (statistically significant difference at day 9 and month 3, and in the analysis of variance in repeated measurements) and the Lequesne index (statistically significant difference at month 3 and in the analysis of variances in repeated measurements).

The analysis of responses is particularly interesting with regard to the Lequesne index at month 3. The results at month 3 are reinforced by the results from SF-36 (statistically significant difference between general and emotional health). The results should be confirmed within the scope of a study embracing a greater number of patients.

Date of report: 06 April 1998

II. INTRODUCTION

Over the past few years, pulsed electromagnetic fields have been employed for a wide range of indications. In particular, they are used in orthopedics because of their effect on bones and tendons since they promote the healing of bones as well as muscles and tendons subsequent to a fracture (Bassett and coll., 1982, Binder and coll. 1984). For these orthopedic applications they received FDA approval in 1979.

Arthrosis is the most frequent osteoarticular disorder. It is responsible for pain and constitutes a major handicap requiring the application of numerous medical procedures (Wohlheim, 1996) or (Perrot and MenkΦs, 1996). In the case of arthrosis of the lower limbs, the effects of pulsed electromagnetic fields are a subject of controversy. Since 1971 Dr. Richard Markoll has developed the PST (pulsed signal therapy) treatment, which has already been applied successfully in an open study involving more than 1000 patients, without any notable side-effects. In using this technique in randomized studies with a placebo as a control, Trock and coll. (1993, 1994) demonstrated a very significant analgesic reaction in cervical and knee arthrosis. In a study using pulsed signal therapy by a different technique, the analgesic action did not seem to differ from the placebo in gonarthrosis and coxarthrosis (Klaber Moffett and coll., 1996). The osteoarticular action mechanism of pulsed signal therapy is still hardly known. Pulsed signal therapy could modify the medullary-osseous blood flow, the osteoblasts (Aaron and Ciombor, 1992). In reacting to the repair of the bone (Grande and coll., 1991), they thus diminish the mechanical pain of arthrosis of the lower limbs, related to the infection of the subchondral bones.

III RESUME OF THE PROTOCOL

III.1 Objective of the Study

The objective of this study was to compare the effectiveness and the tolerance of pulsed signal therapy (PST) in painful gonarthrosis.

III.2 Test schedule

The study was to be in the form of a double-blind test using parallel groups with direct, individual, unicentric, comparative and randomized results.

This test was to be carried out with 40 patients suffering from gonarthrosis and treated with pulsed signal therapy or with a placebo.

The patients were to be treated one hour per day on 9 consecutive days, excluding week-ends and public holidays.

The duration of the study was 3 months for each patient.

The patients were to be evaluated before treatment on the first inclusion visit, then at day 9, month 1 and month 3.

III.3 Study population

In order to be included, patients had to exhibit all the criteria for inclusion and none of the criteria for non-inclusion.

III.3.1 Criteria for inclusion

The criteria for inclusion were as follows:

- * Male or female patients, aged over 50.
- * Patients exhibiting painful gonarthrosis according to ACR criteria:
 - * knee pain and presence of osteophyte (radiography of articulation no more than six months old) and at least one of the three following elements:
 - * over 50 years of age,
 - * morning joint stiffness >30 minutes,
 - * cracking of the joint on movement,
 - * pain clearly predominant at the joint,
 - * initial pain measured by VAS > 40 mn at rest and in motion,
 - * patient has filled in the signed form of consent.

III.3.2 Criteria for non-inclusion

The criteria for non-inclusion were as follows:

- * pacemaker,
- * pregnancy,
- * association with a further rheumatic disorder : gout, rheumatoid polyarthritis, psoriatic rheumatism, infectious rheumatism, algodystrophy,
- * recent intra-articular injection into the knee to be studied, less than 1 month ago,
- * consumption of non-steroidal anti-inflammatories and non-stable analgesics in the 7 days preceding the study,
- * introduction of a basic treatment for arthrosis (Jonctum«, ART50«, Piascledine«, Chondrosulf«) in the month preceding inclusion.
- * treatment by physiotherapy, kinesitherapy or non-conventional medicine (mesotherapy, osteopathy, sophrology),
- * surgery scheduled within the next three months,
- * painful homolateral coxarthrosis,
- * other current attempts at therapy.

III.3.3 Criteria for withdrawal from the study

There may be premature withdrawal from the study when a patient who enters the study ceases to participate before the end of the study as defined in the protocol, regardless of the circumstances.

A patient may withdraw from the study for the following reasons:

- * at his or her request,
- * if in the opinion of the investigator the patient's health could be compromised by an undesirable event occurring subsequent to his or her entry into the study,
- * occurrence of a serious incident,
- * if the patient is not cooperative after inclusion or has repeatedly refuse to recognize the constraints stipulated in the protocol,
- * if the patient manifests one or more exclusion criteria during the course of the study.

III.4 Treatments

III.4.1 Treatments within the study

III.4.1.1 Presentation, composition

The PST equipment was supplied by Bio-Magnetic Therapy Systems Inc. It comprised a magnetic field generator, an electronic surface and a ring surrounding the joint to be treated, attached to a seat for positioning the patient's knee in the axis of the machine.

The physical characteristics of the equipment were as follows:

- * output : < 2A, 120 V
- * frequency : from 2 to 60 Hz.
- * duration of pulse : 1.0 second; pause: 0.1 second.

III.4.1.2 Therapeutic scheme

The person responsible for supervising the treatment was instructed to install the patient in the equipment. With the aid of a chip card established for the patient and randomized for the type of treatment given, the PST equipment was run for one hour.

Nine sessions of 1 hour of treatment were to be given on 9 consecutive days, not including week-ends and public holidays.

A random number was allocated to each patient in accordance with a pre-determined randomized list. **The allocation of random numbers was not to be carried out before the patient's inclusion visit and not before confirming that the patient satisfied the criteria for inclusion and non-inclusion.**

III.4.2 Concomitant treatments

No treatment was forbidden for the duration of the study.

III.5 Study procedures

III.5.1 Selection of patients

The patients were to be informed verbally about the course of the study and receive an information sheet before giving their written consent to participation in the study. They received the opportunity to ask any questions they deemed necessary before giving their written consent.

The collection of medical information was restricted to the patients included in the study.

III.5.2 Study procedures

Four evaluation visits were proposed: visit 1 (inclusion), visit 2 (day 9), visit 3 (month 1) and visit 4 (month 3).

The procedure on each visit is described below.

Visit 1 (inclusion): for the purpose of

- * obtaining the consent of the patient, the patient receiving a copy thereof,
- * verifying that the patient satisfies the criteria for inclusion and non-inclusion,
- * recording:
 - date of birth,
 - history of pains,
 - concomitant treatments (analgesic, AINS, antiarthrosis medicine and other),
 - pain intensity (VAS and verbal pain scale) at rest and in motion,
 - LequesneÆs algofunctional index
 - SF-36

Visits 2 (day 9), 3 (month 1) and 4 (month 3):

- * for the purpose of recording:
 - pain intensity (VAS and verbal pain scale) at rest and in motion,
 - LequesneÆs algofunctional index
 - SF-36
 - assessment of effectiveness and tolerance as judged by doctor and patient.

III.6 Criteria for evaluation of effectiveness

III.6.1 Main criteria

The main criterion for evaluating efficiency was the development of spontaneous pain at rest and in motion. The development of pain is determined by VAS, which is normally used in clinical tests on analgetics, notably in rheumatology.

III.6.2 *Secondary criteria*

The secondary criteria for evaluating effectiveness were as follows:

- * spontaneous pain evaluated on a verbal scale at rest and in motion. The scale consisted of 5 points: without, slight, moderate, serious, extremely serious,
- * the algofunctional Lequesne index: this investigates pain or discomfort in everyday life, maximum step and difficulties encountered in the course of a normal day. The score varies from 0 (no obstacle) to 24 (maximum hindrance),
- * the SF-36 questionnaire on quality of life. This questionnaire on quality of life was devised in the USA within the scope of a Medical Outcome Study. It is a generic instrument for the purpose of evaluating quality of life by means of a questionnaire filled in by the patient him/herself. It comprises 36 questions relating to 8 components of daily life : physical function (10 questions), physical work (2 questions), physical pain (2 questions), general health (5 questions), vitality (4 questions), social functioning (2 questions), emotional functioning (3 questions), emotional health (5 questions). Each component is expressed in a score from 0 (poor) to 100 (good).

III.7 **Criteria for evaluation of tolerance**

Tolerance was evaluated on the basis of overall assessment of tolerance.

III.8 **Proposed statistical methodology**

III.8.1 *Number of subjects necessary*

The number of patients required was fixed at 40.

III.8.2 *Statistical methodology and analysis plan*

- * Data collection and database management : not specified in the protocol.
- * Analyzed populations : not specified in the protocol.
- * Statistical analysis : in the protocol it was proposed that the demographic characteristics of the patients be described, and that t or Wilcoxon tests be used for quantitative variables and Chi2 tests for qualitative variables.

III.9 Ethical considerations

At its meeting on 7 May 1997, the Advisory Committee for the Protection of Persons in Biomedical Research (CCPPRB) at the Hopital COCHIN gave a favourable assessment of the study. The promoter was notified of this approval before the start of the study.

All patients included in the study have signed a declaration of consent which summarizes the objective, methodology, duration of the study, constraints and hazards, the statement of the CCPPRB and their right to refusal participation or to withdraw at any time without incurring any liability. Patients received a copy of the document; the researcher is obliged to keep the original on file for a legally stipulated period of 15 years. The promoter must also keep a copy under the condition of confidentiality as prescribed by law.

This test was conducted in conformance with the Declaration of Helsinki dated 1964, amended in Tokyo in 1975, Venice in 1983 and Hong Kong in 1989. Every researcher undertakes to carry out this study in compliance with Law No. 88-1138 dated 20 December 1988 pertaining to the protection of persons who make themselves available for biomedical research and its decree of application. PST had taken out an insurance policy for possible damages resulting from the research project.

IV METHODS EMPLOYED

IV.1 Amendments to the protocol and/or practical modifications

IV.1.1 Amendments to the protocol

The protocol was not the subject of any amendment.

IV.1.2 Practical modification

No practical amendment was carried out.

IV.2 Data Management

Data management and statistical analysis were entrusted to Clinica & Statistica (52, rue CarvΦs - 92129 Montrouge).

Data was extracted from the observation notes. A verification of data was performed between the listing and the observation notes.

Logical checks were made on the database. The final data bank was achieved in March 1998.

The statistical analysis was carried out using a PC with the aid of SAS« software version 6.12 for Windows.

IV.3 Statistical analysis performed

IV.3.1 Analyzed populations and type of analysis

The analysis of effectiveness was performed for the population of all patients treated : randomly selected patients who had received a treatment number and who had been treated and re-evaluated at least one further time.

For this population 2 analyses were performed for the main criterion:

- * analysis of the values obtained (observed cases): only patients informed on each visit about the main criteria for effectiveness were taken into account.
- * end point analysis (last observation carried forward : LOCF) : in the case of patients who had not been informed on each visit about the main criteria for effectiveness, the last values observed were carried forward to the subsequent visits.

For the secondary criteria only the analysis of obtained results was performed.

IV.3.2 Descriptive analysis

A description was compiled of the number of patients included and the number of patients present at each visit.

Quantitative variables were described in terms of the average and the standard deviation.

Qualitative variables were described in terms of the frequency tables specifying the percentage and actual numbers.

IV.3.3 Homogeneity of included groups

The homogeneity of the included groups was verified for all included patients.

For the non-ordered qualitative variables, the comparison of the groups was made with the aid of a Chi2 test, or an exact Fischer test if the conditions for application of the Chi2 test were not fulfilled. For the ordered qualitative variables, the comparison of groups was made by Kolmogorov-Smirnov test. For the quantitative variables, the comparison of groups was made using a Wolcoxon test.

IV.3.4 Statistical analysis performed

Because of the limited numbers, a non-parametric approach was preferred over a parametric approach. The quantitative variables were compared each time using a Wilcoxon test.

The ordered quantitative variables were compared each time by Kolmogorov-Smirnov test.

Evaluations of quantitative variables received from the two groups in the course of time were compared by analysis of variance by rank, taking into account the effect of time, the effect of treatment and the interaction of time/treatment.

A qualitative analysis was performed in terms of patients' responses. The reaction to treatment was studied in terms of pain VAS at rest, pain VAS in motion, Lequesne index, both pain EVAs and the three criteria combined. A patient was considered a respondent if at each visit he or she manifested at least a 30% reduction in comparison to the initial values.

V RESULTS

V.1 Description of the population

V.1.1 *Disposition of the patients*

Forty patients were included (21 patients received pulsed signal therapy (PST group) and 19 were treated with placebo (placebo group)).

All patients received their treatment. No-one discontinued the treatment sessions.

The number of patients present at each visit is shown in Table 1.

Table 1: Disposition of patients in the course of the study

		PST (effective)	PLACEBO (effective)
Number of patients included		21	19
Number of patients evaluated at	Day 9	21	19
	Month 1	20	16
	Month 3	13	12
Number of patients at month 3 (ITT analysis – end point)		21	19

V.1.2 *Deviations from the protocol*

No major deviation from the protocol was registered during the study.

V.1.3 *Characteristics of included patients*

The average age of the patients was 69.0 years \pm 7.6 (n=19) in the placebo group and 68.8 years \pm 9.4 (n=21) in the PST group (p=0.89).

95.5% (2/21) of the patients in the PST group and 89.5% (17/19) in the placebo group were taking at least one analgesic, one AINS or one antiarthrosis medication (Table 2).

Table 2: Treatment at time of inclusion : analgesics, anti-inflammatory or antiarthrosis medicine.

	PST % (effective)	PLACEBO % (effective)	p
Analgesics	61.9% (13/21)	68.4% (13/19)	0.66
Anti-inflammatory medicine	14.3% (3/21)	15.8% (3/19)	1.00
Antiarthrosis medicine	33.3% (7/21)	52.6% (10/19)	0.22

87.7% (18/21) of the patients in the PST group and 78.9% (15/19) in the placebo group were receiving other treatment (p=0.69).

The mean history of pain was 6.9 years [SD] 5.4 (n=21) for the PST group and 7.6 years [SD] 10.3 (n=19) for the placebo group (p=0.53).

There was no statistically relevant difference between the two groups with regard to clinical characteristics on inclusion (see 'Results' section).

V.2 Treatment during the study

V.2.1 Treatment during the study

All patients received their nine treatment sessions.

V.2.2 Concomitant treatments

Table 3: treatment during the study : comparison of the frequencies of patients who started taking an analgetic, an AINS or antiarthrosis medicine after the inclusion visit.

	PST % (effective)	PLACEBO % (effective)	p
Analgesics	25% (2/8)	33.3% (2/6)	1.00
Anti-inflammatory medicine	---	25% (4/16)	0.04
Antiarthrosis medicine	7,14% (1/14)	---	1.00

Five patients from the placebo group and two from the PST group withdrew from the study in order to receive an infiltration.

V.3 Results of effectiveness

V.3.1 Pain VAS at rest

The analysis of variance with regard to repeated measurements (day 0, day 9, month 1, month 3) of the population to be treated revealed no statistically significant difference, neither in terms of values recorded ($p=0.27$) nor end-point values ($p=0.28$), (see Tables 3 and 4).

Table 4 : Pain VAS at rest (values recorded) (ITT)

	Group PST % (effective)	Group PLACEBO % (effective)	p
Day 0	31.0 ± 24.8 n = 21	33.2 ± 25.3 n = 19	0.75
Day 9	17.8 ± 19.0 n = 21	24.9 ± 24.7 n = 19	0.18
Month 1	18.0 ± 23.8 n = 20	26.0 ± 24.6 n = 16	0.26
Month 3	17.9 ± 22.7 n = 13	29.6 ± 30.7 n = 12	0.26

Table 5 : Pain VAS at rest (end-point) (ITT)

	Group PST % (effective)	Group PLACEBO % (effective)	p
Day 0	31.0 ± 24.8 n = 21	33.2 ± 25.3 n = 19	0.75
Day 9	17.8 ± 19.0 n = 21	24.9 ± 24.7% n = 19	0.18
Month 1	17.1 ± 23.5 n = 21	27.4 ± 24.9 n = 19	0.17
Month 3	19.7 ± 27.8 n = 21	27.3 ± 29.3 n = 19	0.25

V.3.2 Pain VAS in motion

The analysis of variance with regard to repeated measurements (day 0, day 9, month 1, month 3) of the population to be treated revealed a statistically significant difference, both in terms of values recorded ($p=0.0.0001$) and end point values ($p=0.0002$), (see Tables 5 and 6).

Table 6: Pain VAS in motion (recorded values) (ITT)

	Group PST % (effective)	Group PLACEBO % (effective)	p
Day 0	68.4 ± 16.0 n = 21	75.3 ± 17.2 n = 19	0.24
Day 9	41.8 ± 23.6 n = 21	59.5 ± 24.2 n = 19	0.02
Month 1	42.0 ± 29.4 n = 20	55.6 ± 23.7 n = 16	0.14
Month 3	32.2 ± 23.8 n = 13	59.9 ± 34.0 n = 12	0.03

Table 7: Pain VAS in motion (end point) (ITT)

	Group PST % (effective)	Group PLACEBO % (effective)	p
Day 0	68.4 ± 16.0 n = 21	75.3 ± 17.2 n = 19	0.23
Day 9	41.8 ± 23.6 n = 21	59.5 ± 24.2 n = 19	0.02
Month 1	40.60 ± 29.4 n = 21	57.5 ± 23.7 n = 19	0.06
Month 3	37.4 ± 29.3 n = 21	64.1 ± 30.1 n = 19	0.009

V.3.3 Verbal pain scale

No statistically significant difference in values emerged between the two treated groups in the verbal scale of pain at rest and in motion (Table 7 and 8).

Table 8: Verbal pain scale at rest (recorded values)

		Day 0	Day 9	Month 1	Month 3
Nulle None/Never	PST	20.0% (4/20)	35.0% (7/20)	35.0% (7/20)	53.9% (7/13)
	PLACEBO	15.8% (3/19)	21.1% (4/19)	25.0% (4/16)	41.7% (5/12)
Faible Slight/seldom	PST	30.0% (6/20)	40.0% (8/20)	50.0% (10/20)	38.5% (5/13)
	PLACEBO	47.4% (9/19)	47.4% (9/19)	37.5% (6/16)	25.0% (3/12)
Modérée Moderate/sometimes	PST	35.0% (7/20)	25.0% (5/20)	5.0% (1/20)	7.7% (1/13)
	PLACEBO	21.1% (4/19)	15.8% (3/19)	25.0% (4/16)	---
Importante Important	PST	15.0% (3/20)	---	5.0% (1/20)	---
	PLACEBO	15.8% (3/19)	15.8 (3/19)	12.5% (2/16)	33.3% (4/12)
Extrem. importante Very important	PST	---	---	5.0% (1/20)	---
	PLACEBO	---	---	---	---
		p = 0.99	p = 0.97	p = 0.76	p = 0.49

Table 9: Verbal pain scale in motion (recorded values)

		Day 0	Day 9	Month 1	Month 3
--	--	-------	-------	---------	---------

Nulle None/never	PST	---	5.0% (1/20)	5.0% (1/20)	15.4% (2/13)
	PLACEBO	---	5.3% (1/19)	---	16.7% (2/12)
Faible Slight/seldom	PST	5.0% (1/20)	25.0% (5/20)	45% (9/20)	38.5% (5/13)
	PLACEBO	---	10.5% (2/19)	12.5% (2/16)	16.7% (2/12)
Modérée Moderate/some- times	PST	30.0% (6/20)	35.0% (7/20)	20.0% (4/20)	38.5% (5/13)
	PLACEBO	21.1% (4/19)	26.3% (5/19)	37.5% (6/16)	25.0% (3/12)
Importante Important	PST	50.0% (10/20)	35.0% (7/20)	30.0% (6/20)	7.7% (1/13)
	PLACEBO	63.2% (12/19)	47.4% (9/19)	37.5% (6/16)	8.3% (1/12)
Extrem. importante Very important	PST	15.0% (3/20)	---	---	---
	PLACEBO	15.85 (3/19)	10.5% (2/19)	12.5 (2/16)	33.3% (4/12)
		p = 0.99	p = 0.69	p = 0.16	p = 0.47

V.3.4 Lequesne index

The analysis of variance with regard to repeated measurements (day 0, day 9, month 1, month 3) for the population to be treated showed a statistically significant difference in the values recorded ($p=0.0001$) (Table 9).

Table 10: Lequesne index (recorded values) (ITT)

	PST	PLACEBO	p
Day 0	10.4 ± 2.6 n = 21	11.2 ± 2.8 n = 19	0.20
Day 9	8.5 ± 3.6 n = 21	10.3 ± 3.9 n = 19	0.09
Month 1	6.7 ± 4.3 n = 20	9.2 ± 4.6 n = 16	0.07
Month 3	4.9 ± 3.6 n = 13	9.7 ± 5.1 n = 13	0.02

V.3.5 Overall assessment of effectiveness

Only the difference in overall assessment of effectiveness by the doctor on day 9 is statistically significant between the two treated groups (Tables 10, 11, 12 and 13).

Table 11: Effectiveness assessed by doctor at day 9

	Group PST	Group PLACEBO
None	19.1% (4/21)	31.6% (6/19)
Slight	14.3% (3/21)	52.6% (10/19)
Medium	33.3% (7/21)	5.3% (1/19)
High	23.8% (5/21)	5.3% (1/19)
Very high	9.5% (2/21)	5.3% (1/19)

p = 0.011

Table 12: Effectiveness assessed by patient at day 9

	Group PST	Group PLACEBO
None	14.3% (3/21)	42.1% (8/19)
Slight	28.6% (6/21)	26.3% (5/19)
Medium	23.8% (5/21)	21.1% (4/19)
High	19.1% (4/21)	5.3% (1/19)
Very high	14.3% (3/21)	5.3% (1/19)

p = 0.42

Table 13: Effectiveness assessed by doctor at month 1

	Group PST	Group PLACEBO
None	31.6% (6/19)	41.2% (7/17)
Slight	15.8% (3/19)	23.5% (4/17)
Medium	---	23.5% (4/17)
High	21.1% (4/19)	5.9% (1/17)
Very high	31.6% (6/19)	5.9% (1/17)

p = 0.1

Table 14: Effectiveness assessed by patient at month 1

	Group PST	Group PLACEBO
None	31.6% (6/19)	41.2% (7/17)
Slight	10.5% (2/19)	29.4% (5/17)
Medium	10.5% (2/19)	11.8% (2/17)
High	42.1% (8/19)	11.8% (2/17)
Very high	5.3% (1/19)	5.9% (1/17)

p = 0.41

Table 15: Effectiveness assessed by doctor at month 3

	Group PST	Group PLACEBO
None	23.1% (3/13)	50.0% (6/12)
Slight	23.1% (3/13)	16.7% (2/12)
Medium	---	8.3% (1/12)
High	23.1% (3/13)	16.7% (2/12)
Very high	30.8% (4/13)	8.3% (1/12)

p = 0.68

Table 16: Effectiveness assessed by patient at month 3

	Group PST	Group PLACEBO
None	23.1% (3/13)	45.5% (5/11)
Slight	7.7% (1/13)	18.2% (2/11)
Medium	15.4% (2/13)	---
High	30.8% (4/13)	27.3% (3/11)
Very high	23.1% (3/13)	9.1% (1/11)

p = 0.54

V.3.6 Analysis of patient responses

Table 17: Comparison of groups with regard to frequency of responding patients for pain VAS at rest at different visits.

	Group PST % (effective)	Group PLACEBO % (effective)	p
Day 9	61.9% (13/21)	50.0% (9/18)	0.455
Month 1	75.0% (15/20)	60.0% (9/15)	0.467
Month 3	69.2% (9/13)	41.7% (5/12)	0.165

Table 18: Comparison of groups with regard to frequency of responding patients for pain VAS in motion at different visits.

	Group PST % (effective)	Group PLACEBO % (effective)	p
Day 9	57.1% (12/21)	42.1% (8/19)	0.342
Month 1	55.0% (11/20)	37.5% (6/16)	0.296
Month 3	46.2% (6/13)	33.3% (4/12)	0.688

Table 19: Comparison of groups with regard to frequency of responding patients for the Lequesne index at different visits.

	Group PST % (effective)	Group PLACEBO % (effective)	p
Day 9	42.9% (9/21)	15.8% (3/19)	0.062
Month 1	55.0% (11/20)	25.0% (4/16)	0.070
Month 3	76.9% (10/13)	30.8% (4/13)	0.018

Table 20: Comparison of groups with regard to frequency of responding patients for pain VAS at rest and pain VAS in motion at different visits.

	Group PST % (effective)	Group PLACEBO % (effective)	p
--	----------------------------	--------------------------------	---

Day 9	42.9% (9/21)	31.6% (6/19)	0.462
Month 1	55.0% (11/20)	31.3% (5/16)	0.154
Month 3	46.2% (6/13)	33.3% (4/12)	0.688

Table 21: Comparison of groups with regard to frequency of responding patients for pain VAS at rest, pain VAS in motion and the Lequesne index at different visits.

	Group PST % (effective)	Group PLACEBO % (effective)	p
Day 9	23.8% (5/12)	11.1% (2/18)	0.418
Month 1	50.0% (10/20)	13.3% (2/15)	0.024
Month 3	46.2% (6/13)	25.0% (3/12)	0.411

V.3.7 SF-36 Scale of quality of life

By virtue of the analysis mode of the SF-36 and the limited numbers it is advisable to exercise caution in the interpretation of the results. Indeed, the use of a normalization of the scores between 0 and 100 results in substantial variations in certain dimensions, particularly when the dimension includes a limited number of items and limited possibilities for response. In the course of the study, statistically significant differences arose at month 3 in the dimension “general health” and “emotional health”.

Table 22: Results of the 8 dimensions of SF-36

		Day 0	Day 9	Month 1	Month 3
Fonction physique Physical function	PST	43.7 ± 23.4 n = 21	52.1 ± 21.7 n = 21	56.8 ± 25.3 n = 20	52.2 ± 30.0 n = 13
	PLACEBO	39.9 ± 19.7	38.6 ± 17.1	47.9 ± 22.2	55.4 ± 24.4

		n = 19	n = 19	n = 17	n = 12
	p	0.63	0.04	0.31	0.96

		Day 0	Day 9	Month 1	Month 3
Fonctionnement physique Physical functioning	PST	21.4 ± 30.9 n = 21	45.2 ± 42.3 n = 21	62.5 ± 41.0 n = 20	63.5 ± 37.7 n = 13
	PLACEBO	18.4 ± 26.1 n = 19	28.9 ± 31.5 n = 19	45.6 ± 36.7 n = 17	50 ± 41.3 n = 12
	p	0.80	0.31	0.19	0.48

		Day 0	Day 9	Month 1	Month 3
Doleurs physiques Physical pains	PST	36.5 ± 11.1 n = 21	41.6 ± 8.7 n = 21	40.1 ± 11.8 n = 20	37.9 ± 14.8 n = 13
	PLACEBO	37.5 ± 10.3 n = 19	38.1 ± 9.9 n = 19	40.0 ± 18.8 n = 17	42.2 ± 5.0 n = 12
	p	0.47	0.15	0.56	0.49

		Day 0	Day 9	Month 1	Month 3
Santé générale General health	PST	45.7 ± 11.1 n = 21	43.3 ± 15.8 n = 21	43.9 ± 19.6 n = 20	50.2 ± 12.6 n = 13
	PLACEBO	42.8 ± 14.2 n = 19	42.3 ± 16.6 n = 19	44.9 ± 16.8 n = 17	33.1 ± 21.0 n = 12
	p	0.35	0.88	0.79	0.04

		Day 0	Day 9	Month 1	Month 3
Vitalité Vitality	PST	39.8 ± 13.6 n = 21	45.2 ± 9.4 n = 21	42.8 ± 7.9 n = 20	45.4 ± 13.9 n = 13
	PLACEBO	33.4 ± 14.4 n = 19	38.9 ± 14.9 n = 19	36.5 ± 16.0 n = 17	36.3 ± 15.2 n = 12

p	0.28	0.19	0.27	0.09
---	------	------	------	------

		Day 0	Day 9	Month 1	Month 3
Fonction sociale Social function	PST	47.7 ± 13.3 n = 21	41.1 ± 10.6 n = 21	45.0 ± 12.4 n = 20	44.2 ± 9.7 n = 13
	PLACEBO	41.5 ± 13.9 n = 19	42.8 ± 7.6 n = 19	36.8 ± 16.8 n = 17	37.5 ± 10.7 n = 12
	p	0.71	0.78	0.07	0.14

		Day 0	Day 9	Month 1	Month 3
Fonctionnement émotionnel Emotional function	PST	54.0 ± 44.1 n = 21	68.3 ± 38.7 n = 21	76.7 ± 32.6 n = 20	76.9 ± 37.0 n = 13
	PLACEBO	24.6 ± 33.0 n = 19	33.3 ± 40.1 n = 19	45.8 ± 43.7 n = 17	41.7 ± 45.2 n = 12
	p	0.03	0.01	0.04	0.04

		Day 0	Day 9	Month 1	Month 3
Santé morale Moral health	PST	52.6 ± 15.4 n = 21	59.8 ± 10.1 n = 21	57.2 ± 10.4 n = 20	59.1 ± 14.1 n = 13
	PLACEBO	46.8 ± 18.1 n = 19	51.6 ± 15.1 n = 19	48.8 ± 18.8 n = 17	40.0 ± 20.4 n = 12
	p	0.30	0.07	0.23	0.05

V.4 Results of tolerance

In the course of the 9 treatment sessions none of the patients described an undesirable event.

The overall assessment of tolerance by patient and doctor at day 9, month 1 and month 3 revealed no statistically significant difference between the two treated groups.

On each visit, tolerance was assessed by the doctor to be very good in the case of all patients, with the exception of one patient from the placebo group at month 1 (medium) and one patient from the PST group at month 3 (good).

Tolerance as assessed by the patients is shown in Tables 22, 23 and 24.

Table 23: Tolerance patient at day 9

	Group PST	Group PLACEBO
Very high	85.7% (18/21))	84.2% (16/19)
High	14.3% (3/21)	15.8% (3/19)

p = 1.0

Table 24: Tolerance patient at month 1

	Group PST	Group PLACEBO
Very high	94.8% (18/19)	82.4% (14/17)
High	5.3% (1/19)	11.8% (2/17)
Insufficient	---	5.9% (1/17)

p = 0.99

Table 25: Tolerance patient at month 3

	Group PST	Group PLACEBO
Very high	76.9% (10/13)	90.9 (10/11)
High	23.1% (3/13)	9.1% (1/11)
Insufficient	---	---

p = 0.99

VI DISCUSSION - CONCLUSION

This comparative, randomized, double-blind study has brought to light a number of aspects which speak for the effectiveness of pulsed signal therapy in the treatment of gonarthrosis. Due to the limited number of patients, not all the results are statistically significant.

The most notable criteria for differentiating between the two treated groups are the pain VAS in motion (statistically significant difference at day 9 and month 3 and in the analysis of variations in

repeated measurements) and the Lequesne index (statistically significant difference at month 3 and in the analysis of variations in repeated measurements).

The analysis with regard to responses is particularly interesting in the Lequesne index at month 3.

The results at month 3 are supported by the results obtained from the SF-36 (statistically significant difference between general health and emotional health).

These results merit confirmation within the framework of a further study including a greater number of patients.