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SLOW HEALING FRACTURES: CAN THEY BE PREVENTED?
(Results of electrical stimulation in fibular osteotomies in rats and in diaphyseal fractures of the tibia in humans).

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The purpose of the study was to evaluate the possibility of preventing delayed union in fractures by the use of low-frequency pulsing electromagnetic fields (PEMFs).

The study was conducted in two parts, both with control groups. Fibular osteotomies in rats and diaphyseal fractures of the tibia in humans were treated with and without electrical stimulation (PEMF). The rats were sacrificed on the 8^{th} and 23^{rd} days respectively in order to evaluate the histological picture of the repair callus and its mechanical resistance. In the human subjects, the clinical and radiological follow-up took into account various factors known to affect the rate of union in the various fracture groups.

The results obtained suggest that PEMF stimulation is capable of accelerating and modulating the physiological process of union by its favourable effect on osteogenesis.

Diaphyseal fractures of the tibia are increasingly common due to the rapid growth of road accidents and sports-related injuries. It is accepted practice that open fractures must be surgically treated urgently. The treatment of closed fractures, on the other hand, depends on a variety of factors: age of the patient, anatomical type of fracture, condition of the overlying skin, the association of local, regional or general lesions, and the surgeon’s personal preference for conservative or operative treatment.

One fact emerges from all of the reported case series. In addition to the fractures achieving consolidation in the normal time by means considered to be <<physiological>> (although a certain variability in the meaning of the term <<physiological>> must be allowed), there is another group of fractures that does not follow the <<normal>> union pattern, proceeding either very slowly or developing non-unions. By analyzing the case series reported by Watson-Jones and Coltart (1943) and by Carretti *et al.,* 1982 on diaphyseal fractures of the tibia treated conservatively with plaster cast fixation, it is seen that the time required for union follows the same pattern: 50% unite within the first 16 weeks, while 20% are not united even after 24 weeks.

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If we represent this graphically (Fig. 1) we get an asymmetrical curve with a steep ascending part (rapid union) followed by a descending part (delayed union) and a drawn out tail possibly developing into an established fibrous non-union after the 48th week.

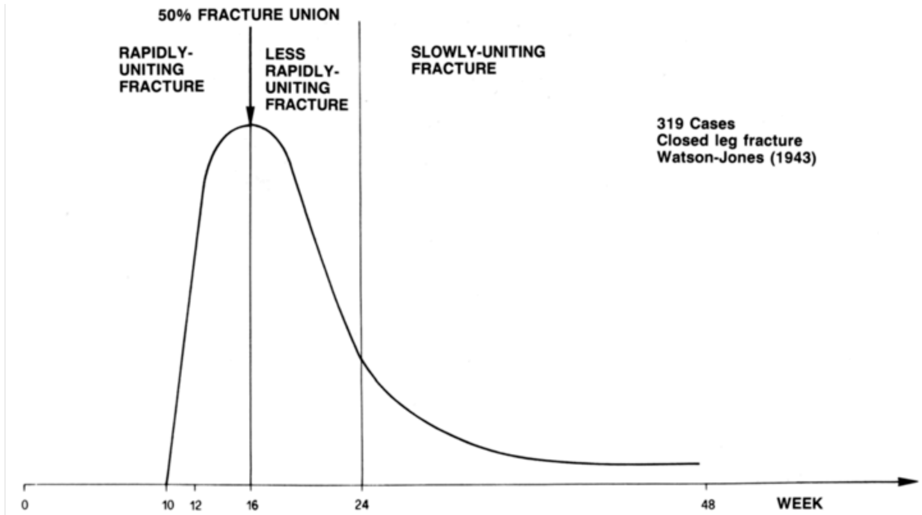

FIG. 1. – Distribution of average union times in closed diaphyseal tibial fractures treated conservatively.

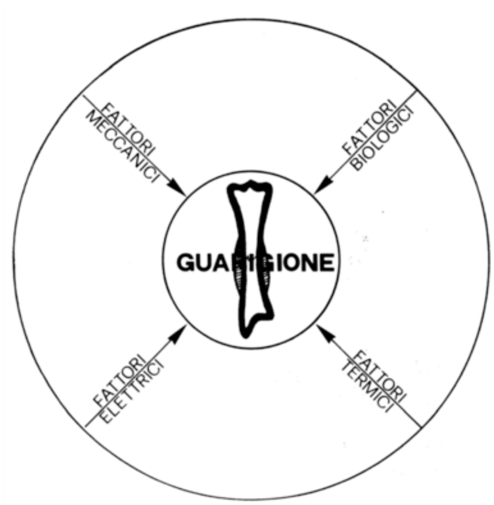

Fig. 2. – Illustration of the factors influencing fracture union. Fattori = factors: Mechanical, biological, thermal, electrical. Guarigione = healing.

The process of union is conditioned by several closely related factors (Fig. 2): mechanical factors such as site, alignment, contact between the fragments, immobilization, stress; biological factors such as vitality of the fragments, integrity of nerves and main vessels, condition of the soft tissues, infections; bioelectrical factors such as electrical potentials at the site of fracture: <<current injury>>; thermal factors related to local energy consumption and muscular activity.

Even if in most cases the reason for delayed or non-unions may be mechanically related, it is also true that at times a fracture has difficulty in healing even in the best of biomechanical conditions. In these circumstances the reason is usually traceable to biological and/or bioelectric factors.

The role of electrical stimulation at the fracture site has been known for a long time and its importance in favouring the metabolic activation of osteoprogenitor cells is widely recognized (Ashihara *et al.,* 1979). Borgens (1984) demonstrated the presence of currents, measured their intensity in experimental mouse fractures and observed that these are maintained for many hours after the occurrence of the fracture. He showed that hteir intensity is equal to that of the currents used to stimulate osteogenesis, and emphasized how their absence could be correlated to delayed union. Jorghensen (1977) observed a 30% reduction of union time, as measured with a mechanical resistance test, when stimulating fresh fractures of the tibia with an electrical current directly applied to the pins of external fixators. In a comparative study on the union time required for Colles fractures treated with cast alone or with cast and PEMF stimulation, Wahlstrom (1982, 1984) was able to demonstrate by scintigraphy that in the first two weeks the union process was accelerated by 30% in the stimulated cases. Haimovici (1982) compared the results obtained in a series of patients subjected to bilateral osteotomy of the first metatarsal: one side was stimulated with PEMFs and the other was not; the union time and the incidence of non-union were clearly greater on the unstimulated side. Law *et al.*

Table 1
HISTOLOGICAL EVALUATION PARAMETERS

General characteristics	
Callus	*Numerical value*
fibrous	1
fibrous tissue and cartilage	2
cartilage only	3
cartilage and trabecular bone	4
trabecular bone	5
compact bone	18
remodelled compact bone	7
Alignment	
poor	0
fair	1
good	2
Dimensions of callus	
minimal	1
average	2
abundant	3
decreased due to remodelling	4

(1985) performed tibial osteotomy in sheep some of which were treated with PEMFs. They observed a greater accumulation of 99 Tc disphosphonate in the stimulated group during the second and third weeks after surgery. Marinozzi et al. (1985)

demonstrated that in tibial osteotomy in the rat stimulation with alternating electromagnetic fields significantly increases the resistance to traction on the 55th day.

The brilliant results obtained all over the world with PEMFs in the treatment of pseudarthrosis (Bassett *et al.,* 1977; De Haas *et al.,* 1980; De Bastiani *et al.,* 1981; Sharrard *et al.,* 1982; Fontanesi *et al.,* 1983; Bassett, 1984; Dal Monte *et al.,* 1985; Poli *et al.,* 1985; Rinaldi *et al.,* 1985) led us to use PEMFs in the treatment of fresh tibial fractures with the aim of reducing the incidence of delayed union. This paper reports the results of an experimental study on rats (fibular osteotomies) and a clinical study on humans (tibial fractures) carried out on two groups, as comparable as possible, both treated conservatively. Half the patients and rats were subjected to immediate stimulation with PEMFs, and half were used as controls.

MATERIAL AND METHOD

Rat experiments

Thirty-six male rats 21 days old were subjected to diaphyseal fibular osteotomy. Alignment of the fragments was visually controlled before suturing the skin. They were then divided into two groups, one subjected to stimulation with PEMFs and the other not. Both groups were left free to move about in their cages and were maintained in the same environment and nutritional conditions. The <<stimulated>> rats were subjected to PEMFs for 4 hours daily; the coils were positioned at the sides of the cages, activated in the stimulated group, non-activated in the control group.

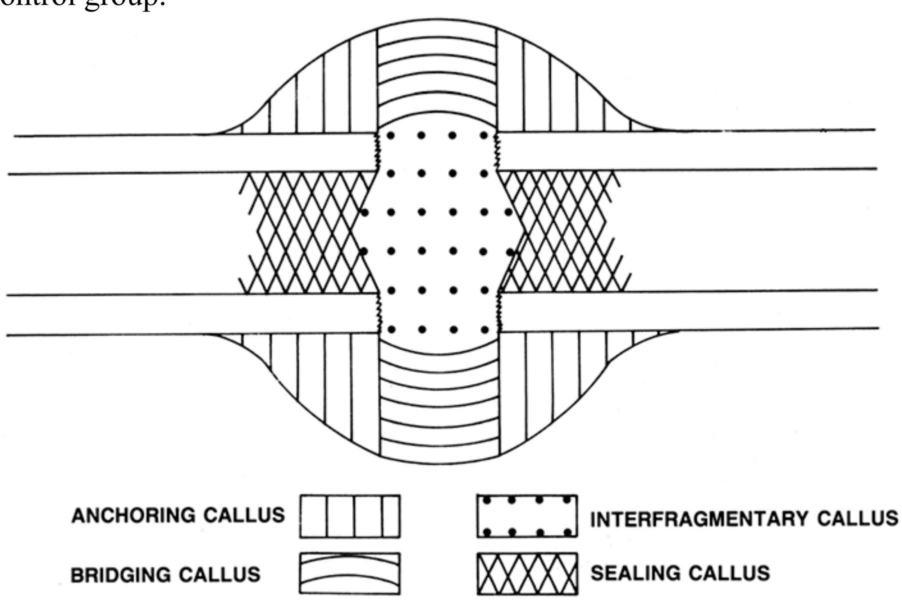

FIG. 3. – *Zonal* distribution of the repair callus.

Half the animals in each group were sacrificed on the 8th day and the segment of fibula subjected to histological evaluation according to the method proposed by Marino *et al.* (1979). The other half were sacrificed on the 23rd day, when the repair process may be considered to be complete (Connolly *et al.,* 1977). In this group, the specimens were subjected to mechanical resistance tests.

The histological evaluations were performed on a <<blind>> basis (the examiner was not aware which group he was dealing with) and two principal parameters were considered: (1) general characteristics of the callus, comprising histological quality and dimensions and alignment of the fragments (Table 1); (2) zonal characteristics of the callus (Fig. 3), defined by the presence of cartilaginous or trabecular callus in the four zones of the fracture site (Table 2). A score system was used to evaluate each parameter, the sum of which was recorded as the <<*index of union*>>. The mechanical resistance on the 23rd day was expressed as a percentage of the resistance at break point of the normal contralateral fibula. The evaluation was made by applying longitudinal and torsional stresses with an Instrom apparatus.

Table 2
HISTOLOGICAL EVALUATION PARAMETERS

Zonal features		
Numerical values	*Cartilage*	*Bone*
— anchoring callus	(0–5)	(0–5)
— bridging callus		
— interfragmentary callus		
— sealing callus		

Cartilage values: 0 = absent; 1 = small quantity; 2 = large quantity; 3 = hypertrophic small quantity; 4 = hypertrophic large quantity; 5 = wide esorption.
Osseous values: 0 = absent; 1 = thin trabeculae and cartilage; 2 = thin trabeculae without cartilage; 3 = thick lamellar trabeculae; 4 = compact bone; 5 = remodeled bone.

Clinical study

Forty patients with closed fractures of the tibial shaft (or with minimal bone exposition (Grade 1) and no infection were included in the study. Selection was confined to patients not less than 16 years of age (and in any case after closure of the epiphyses) and not exceeding 75 years; the average age was 30 years. There were 30 males and 10 females.

Treatment was the same in all cases: transkeletal traction at the heel, closed reduction of the fracture (45% with anaesthesia, 55% without) under ampliscopic control, full limb plaster cast.

The fractures were classified according to the system proposed by Johner and Wruhs (1983) Table 3). The patients were divided into two groups, one subjected to stimulation with PEMS and the other used as a control group. Stimulation was for 8 to 10 hours daily, starting 72 hours after reduction of the fracture and maintained until union was complete. Radiographic follow-up in two orthogonal projections was carried out every 40 days.

Union criteria. These were predominantly clinical (completely painless stability of the fracture) supported by radiographic findings. The evaluation of union was also assessed by different surgeons who were not aware of which group the patient belonged to. *Segmental osteoporosis:* the evaluation was subjective on the basis of a comparison of the initial and final radiographs. A value ranging from 0 to 4 was assigned depending on the degree of osteoporosis (0 = no osteoporosis). *Features of the fracture callus* (quality and quantity): values between 0 to 4 were assigned, 0 corresponding to poor quality or inadequate callus. *Index of union:* this reflects the overall clinical and radiological assessment on the rate of union, also expressed on a score system ranging rom 0 to 4 (0 = non-union).

Table 3
MORPHOLOGICAL CLASSIFICATION OF FRACTURES
(according to Johner and Wruhs)

Fracture	**Type**		
	1	**2**	**3**
A = Simple	Spiral	Oblique	Transverse
B = with third fragment	Torsional	Single	Double
C = comminuted	Torsional	Bivocal	Crush type

Table 4
CALCULATION OF THE INDEX OF UNION RESULTING FROM THE SUM OF THE NUMERICAL VALUES ASSIGNED IN THE HISTOLOGICAL EVALUATION. THE STATISTICAL ANALYSIS PERFORMED WITH STUDENT'S TEST INDICATES THAT THE DIFFERENCE BETWEEN THE CONTROL AND STIMULATED GROUP IS INSIGNIFICANT

Calculation of Index of Union (8 days)		
	Control group	**Stimulated group**
Callus	1.5	2.7
Alignment	1.87	1.5
Size	2.1	2.1
Anchoring	1.5	2.9
<<Bridging>>	0.5	2.1
Interfragmentary	0.3	0.9
Intramedullary	0.2	0.4
Index of union	7.97	12.6*

* p < 0.01 (Student's test)

Table 5
MECHANICAL RESISTANCE TEST OF RAT FIBULAE: THE STUDENT'S TEST INDICATES NO STATISTICALLY SIGNIFICANT DIFFERENCE ON THE 23rd DAY

Resistance test (23 days)			
Mechanical resistance of fibula	**Normal**	**Osteotomised**	**%**
Controls	3.73 lbs	1.93	54.5
Stimulated	3.53	1.4	50.3*

* not significant with Student's test

Features of stimulation

In both the experimental and human studies the same IGEA stimulator (Howmedica) (Fig. 4) was used. The generator of the electromagnetic field feeds a pair of coils with impulses of 75 Hz frequency; the intensity of the magnetic field generated was 2–2.8 mTesla and each impulse lasted 1.3 milliseconds. The tension induced in a calibrated probe was 2.5 ± 1 mVolt.

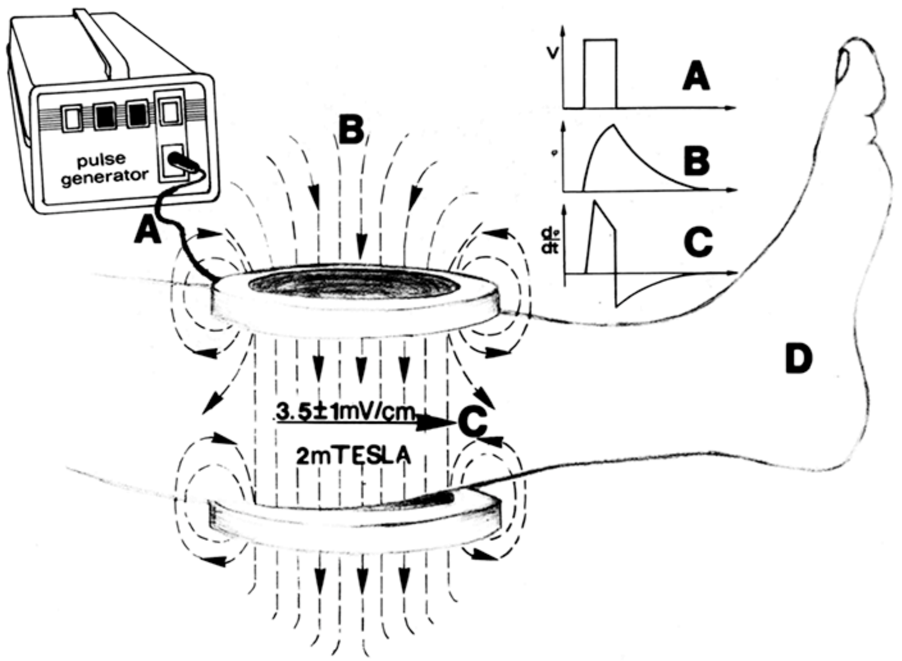

FIG. 4. – Illustration of PEMF stimulation. Upper left: stimulator. Centre: coils positioned on the leg. Upper right: stimulation characteristics. A: electrical current running from stimulator to coils. B: wave shape of the generated electromagnetic field. C: wave shape of the induced electrical current.

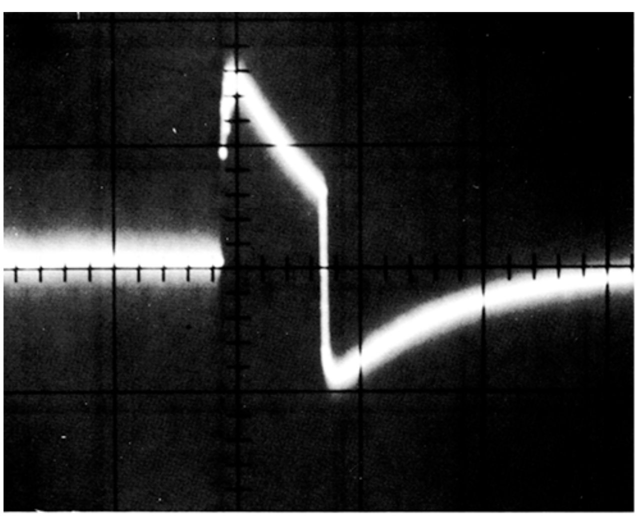

FIG. 5. – Oscilloscopic recording of the electrical current induced by the electromagnetic field in a standard pick-up coil. Scale 2 mV/cm and 2 ms/cm.

RESULTS

Rat experiments

Table 4 shows the average values assigned for the histological evaluation on the callus on the 8th day for the control and stimulated groups of animals. Maturation of the repair callus was more advanced in the animals subjected to PEMFs. More cartilaginous tissue and newly-formed peripheral bone trabeculae are seen throughout the entire callus (Figs. 6, 7, 8, 9).

FIG. 6

FIG. 7

FIGS. 6 and 7. – Histological picture of the repair callus on the 8th day in control rats: the fibrous component is prevalent; the cartilage component is moderately represented. No newly-formed trabeculae are observed (haematoxylin-eosin). Magnification Fig. 6 x10; Fig. 7 x20.

The statistical analysis of the union index indicates a significance of $p < 0.01$. Table 5 shows the results of resistance tests on animals sacrificed on the 23rd day. The loads required to fracture the fibula are expressed in absolute values as well as percentages of those required on the normal contralateral fibula. The differences between stimulated animals and controls were not statistically significant.

Clinical study

Table 6 reports the general data on the control patients, and Table 7 on the stimulated patients. Table 8 reports the statistical analysis comparing the two groups of patients.

It is interesting to note that, with the exception of the evaluation of the fracture callus, all the other parameters were statistically significant with the Student test. The graphic distribution of union times of the two groups of patients is represented in Figures 10 and 11.

DISCUSSION

Our data in the animal experiments are in line with what has been observed by other authors (Connolly *et al.,* 1977; Traina and Gulino, 1979; Wahlstrom, 1984; Law *et al.,* 1985). They show that while there is a difference at an intermediate stage between the stimulated osteotomies and the controls, this difference is no longer evident in the mechanical resistance tests performed on the 23rd day. The choice of the histological evaluation prior to the mechanical one was dictated by two factors. At an earlier stage, what seems more important to us is the biological aspect of cellular activity at the osteotomy site, which would lead to the organization of the callus. This stage corresponds to the <<biological anchorage>>, clearly demonstrated by Ricciardi in his echographic studies (1985). At a later stage, on the other hand, the mechanical strength of the callus is more important.

FIG. 8

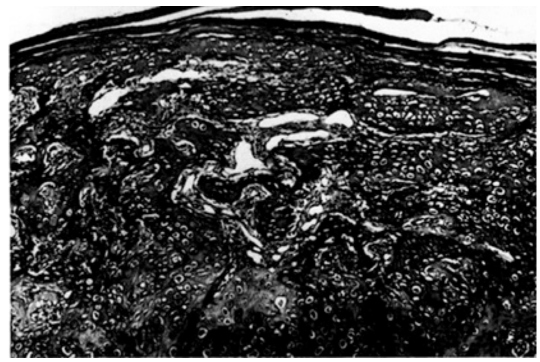

FIG. 9

FIGS. 8 and 9. – Histological picture of the repair callus on the 8th day in rats subjected to stimulation with PEMFs; showing newly-formed bone trabeculae crossing the periphery and abundant cartilage in the central areas (haematoxylin-eosin). Fig. 8 x18; Fig. 9 x25.

Our data show that although the final results are the same on the 23rd day, at an intermediate stage the maturation of the callus and therefore of the otseogenetic process seems to be more advanced and perhaps more active in the stimulated animals. The callus appears to be more organized and shows obvious elements of newly-formed peripheral bone trabeculae, something not observed in the control animals.

What does appear to be significant is the interpretation of the results obtained in the clinical experiments. It was emphasized in the introduction that the objective of the study was to evaluate the possibility of preventing delayed union. The only such case found in the 40 patients was in the control group. Although PEMFs cannot probably shorten the healing time of a rapidly healing fracture, our data demonstrate not only that in the stimulated group all the fractures were healed within 120 days, but that the average union time was reduced to 86 days compared with 109 days in the control group — an average decrease in duration of 22%.

Figures 10 and 11 show that stimulation acts not only on the right part of the curve (that is, on the slowly-uniting fractures (Figure 1), but also influences the steepness of the left side. While the distribution of union times in the control group is comparable to that observed by Watson-Jones and Coltart (1943), in the stimulated group the entire curve is shifted to the left and is clearly more homogeneous, thereby demonstrating the real possibility of shortening union time.

Table 6
SUMMARY OF THE DATA AND PARAMETERS IN THE CONTROL GROUP OF PATIENTS

Data in control group							
Patient	**Sex**	**Age**	**Type**	**Healing time**	**Osteo-porosis**	**Callus**	**Index of union**
Z.A.	M	40	A2	100	3	1	1,5
R.G.	M	17	A3	105	2	1	1,5
F.L.	M	52	B1	75	0	3	3.5
C.G.	M	16	B2	70	1,5	2,5	4
V.P.	M	18	A3	90	2	2	3
F.G.	M	25	A3	80	1	3	3
D.V.	M	35	C1	130	2	1	2,5
M.M.*	M	20	A2	130	2	1	2
B.G.	M	25	A3	105	2	3	3,5
S.A	M	30	A1	210	3	1	1,5
Z.M.	M	28	A3	70	1	3	4
B.N.	M	37	B3	120	1	2	3,5
C.P.	M	24	C2	100	2	1	1,5
G.G.	M	16	A1	100	2	1	1,5
R.L.	M	17	B3	100	2	2	2,5
N.L.	M	21	A2	110	3	3	2,5
C.A.	M	29	B1	115	4	2,5	1,5
R.B.	F	16	B3	120	1,5	3	2
M.I.*	F	28	B3	135	2,5	1,5	1,5
T.B.*	F	16	A2	120	3	2	1,5

* Point exposition (no infection).

Table 7
SUMMARY OF THE DATA AND PARAMETERS IN THE PEMF STIMULATED GROUP

Data in control group							
Patient	**Sex**	**Age**	**Type**	**Healing time**	**Osteo-porosis**	**Callus**	**Index of union**
E.M.	M	18	A3	70	0	2	3,5
L.F.	M	58	A3	60	0	1	2
P.G.	M	71	B1	70	1	2	4
F.T.	M	70	A3	70	1,5	1	3
D.B.	M	62	A3	90	0	2	4
B.A.	F	68	B2	90	2	3	4
B.N.	M	64	A2	110	1	3	3,5
C.O.B.	M	18	B2	75	2	4	4
C.C.	F	24	A3	75	0	2	3
C.T.*	F	25	C2	120	3	3	3,5
T.P.	M	18	B2	60	1	2	3
F.A.	M	18	B3	90	1	3	4
A.G.	M	16	B1	60	1	2	3,5
M.S.	M	50	C3	90	1	1,5	3
R.R.	M	30	B3	90	1	1,5	2,5
T.D.	M	16	A3	100	2	2	3
S.M.*	F	20	A1	90	0	3,5	4
M.N.	F	18	A3	115	0	1	2,5
A.R.	F	21	A3	85	1,5	3	3,5
F.M.	F	17	A3	105	0	2,5	3

* Point exposition (no infection).

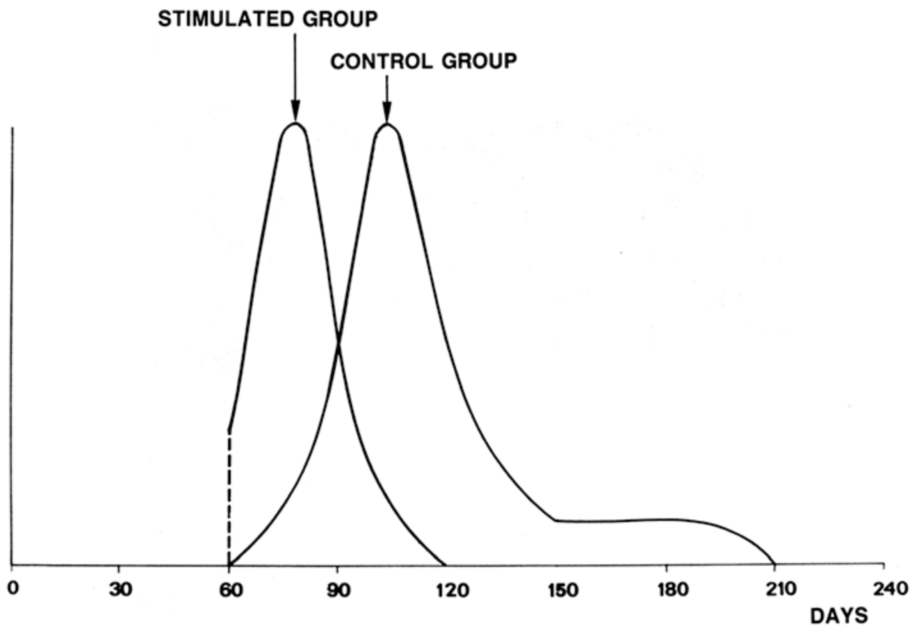

FIG. 10. – Distribution of the union time in the control and stimulated groups of patients: the arrow indicates the time required for union in 50% of the patients.

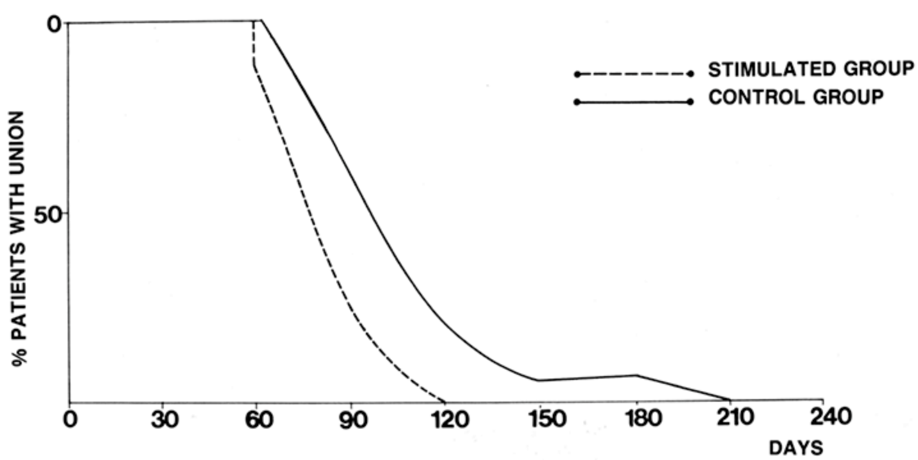

FIG. 11. – Percentage of united fractures in relation to time following injury.

Both osteoporosis and union were considerably improved by stimulation. However, it must be admitted that these assessments, even if done <<blind>>, are parameters related to the observer and therefore m ore difficult to evaluate precisely.

The x-ray analysis of tibial bone callus formation does not appear to be particularly significant at the time of healing, similarly to what was observed in rat experiments.

More favourable results in the stimulated group cannot be attributed to age differences in the two groups; in fact, the average age in the PEMF group was higher than in the control group (35.2 years as compared to 25.5 years). As a logical conclusion, on average the time needed for total functional recovery was shorter in the group of patients subjected to stimulation, and the healing union index was better.

Table 8
STATISTICAL ANALYSIS OF THE DATA RELATED TO PATIENTS IN THE STIMULATED GROUP AND THOSE IN THE CONTROL GROUP. THE ANALYSIS IS SIGNIFICANT FOR VALUES EXCEEDING OR EQUAL TO $p < 0.05$.

	Average in control group	**Standard deviation**	**Average in stimulated group**	**Standard deviation**	**Student's test**
Union time in days	109.2	30.7	85.7	18.1	$p < 0.005$
Osteoporosis	2.0	0.9	0.9	0.8	$p < 0.002$
Quality of callus	2.0	0.8	2.2	0.8	$p < 0.25$*
Index of union	2.4	0.9	3.3	0.5	$p < 0.002$

* Not statistically significant

The interpretation of the data reported above is confirmed and biologically supported by experimental observations conducted in vitro. It has been shown that PEMF stimulation is capable of favourably influencing cellular activity and proliferation (Cadossi *et al.,* 1985; Emilia *et al.,* 1985). This seems in part to be mediated by an increased Ca^{++} influx, which is considered to be an aspecific proliferative signal common to all eukaryotic cells (Hesketh *et al.,* 1985). The same in vitro studies on PEMF exposure showed that, although favouring cellular proliferation by recruiting more cells, PEMFs do not seem to affect the rate of the metabolic processes. Exposure to PEMFs favours skeletal development in the chick embryo at an intermediate stage while at the end of development there are no longer

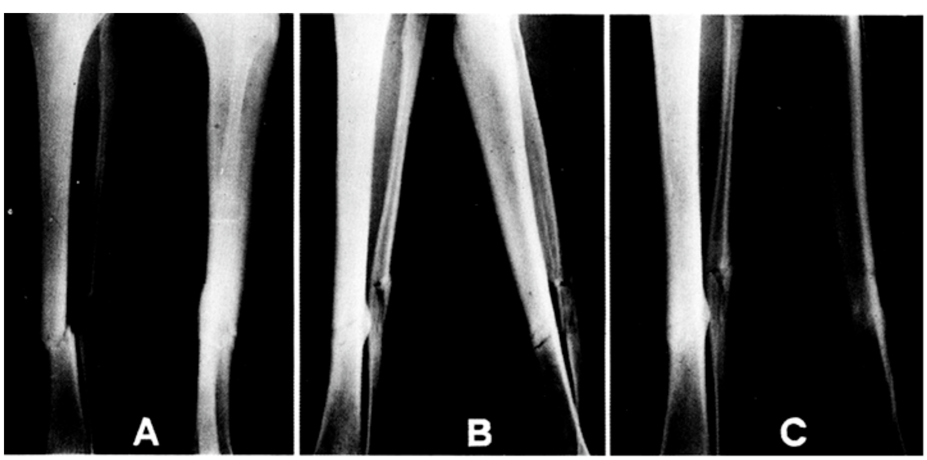

FIG. 12. – A.R. female aged 21 years. (A) Fracture of the lower third. (B) Follow-up 6 weeks after stimulation with PEMFs. (C) Total clinical and radiographic consolidation after 12 weeks. Index of union 3.5.

any differences between chick embryos exposed to PEMFs and those not so exposed (Rooze, 1984). All these observations indicate that exposure of a fresh fracture to PEMFs may favour an early and increased recruitment of osteoprogenitor cells capable of guaranteeing successful repair, but the times required and the phases of maturation through which the callus must necessarily pass remain unchanged.

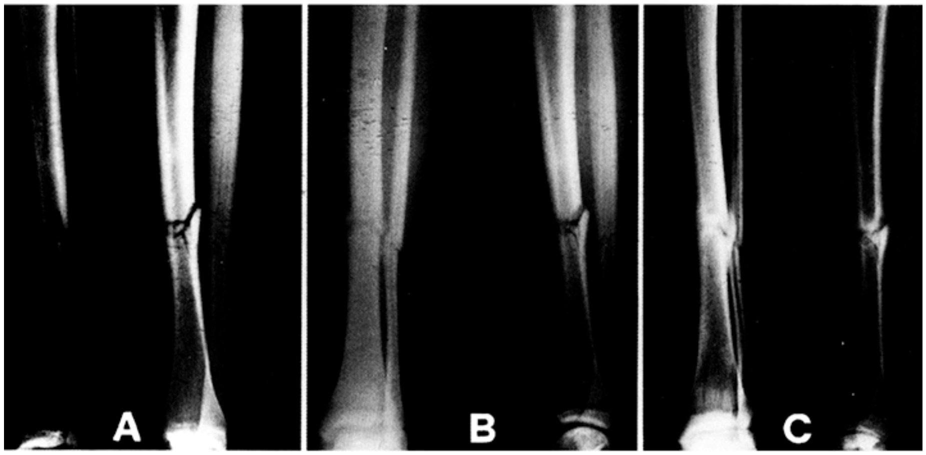

FIG. 13. – B.G. male aged 25 years. (A) Fracture of the middle third tibia and fibula in the control group. Type A3 fracture. (B) Follow-up at 8 weeks. (C) At 15 weeks. Index of union 3,5.

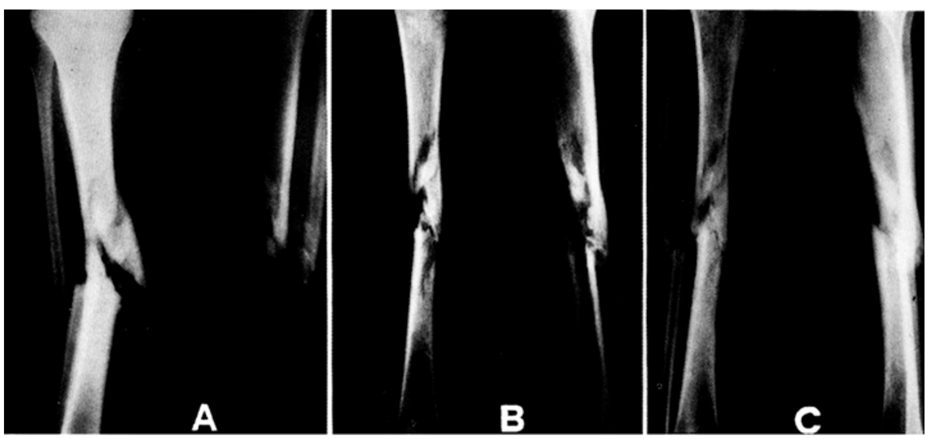

FIG. 14. – F.A. male aged 18 years. (A) Fracture of the middle third of the tibia and fibula. Type B3 fracture. (B) After 6 week stimulations with PEMFs union is advanced. (C) Union is complete at 13 weeks. Index of union 4.

In conclusion, or data suggest that in optimum conditions fracture healing occurs in the same time independently of exposure to PEMFs, but stimulation would favour the establishment of such optimum conditions in a greater percentage of cases, with consequent shortening of average union time and an increased incidence of rapidly-uniting fractures.

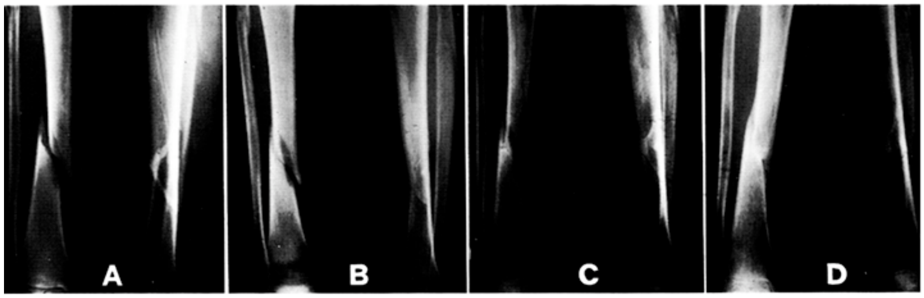

FIG. 15. – Control group. S.A. male aged 30 years. (A) Fracture of the lower third of the tibia and upper third of the fibula. Type A1 fracture. (B) Follow-up at 13 weeks. (C) Union took 30 weeks but with inadequate callus. (D) Even after 1 year union is not really satisfactory. Index of union 1.5.

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