A DOUBLE-BLIND TRIAL OF PULSED ELECTROMAGNETIC FIELDS FOR DELAYED UNION OF TIBIAL FRACTURES

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A total of 45 tibial shaft fractures, all conservatively treated and with union delayed for more than 16 but less than 32 weeks were entered in a double-blind multi-centre trial. The fractures were selected for their liability to delayed union by the presence of moderate or severe displacement, angulation or comminution or a compound lesion with moderate or severe injury to skin and soft tissues. Treatment was by plaster immobilisation in all, with active electromagnetic stimulation units in 20 patients and dummy control units in 25 patients for 12 weeks. Radiographs were assessed blindly and independently by a radiologist and an orthopaedic surgeon.

Statistical analysis showed the treatment groups to be comparable except in their age distribution, but age was not found to affect the outcome and the effect of treatment was consistent for each age group. The radiologist's assessment of the active group showed radiological union in five fractures, progress to union in five but no progress to union in 10. In the control group there was union in one fracture and progress towards union in one but no progress in 23. Using Fisher's exact test, the results were very significantly in favour of the active group ($p = 0.002$).

The orthopaedic surgeon's assessment showed union in nine fractures and absence of union in 11 fractures in the active group. There was union in three fractures and absence of union in 22 fractures in the control group. These results were also significantly in favour of the active group ($p = 0.02$). It was concluded that pulsed electromagnetic fields significantly influence healing in tibial fractures with delayed union.

Bassett, Pawluk and Pilla (1974) first described the use of inductively-coupled electromagnetic fields and, later (Bassett, Mitchell and Gaston 1981) their use in the treatment of fracture non-union. Since then there have been many reports of the effects of stimulation by this method, with claims of high success rates. All regimes of treatment employ immobilisation of the limb as part of the management and it has been suggested that the immobilisation itself could be largely, if not completely responsible for the healing of the ununited fracture (Barker et al 1984).

Only an adequate double-blind trial comparing treatment by immobilisation and active stimulation with similar immobilisation of a similar type of fracture with a dummy stimulator can provide evidence of the true effect of pulsed electromagnetic fields. This paper describes the results of such a trial.

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PATIENTS AND METHODS

From 1981 to 1987, 51 fractures of the tibial shaft with clinical and radiological signs of delayed union were selected for inclusion in a double-blind trial. Absence of union was demonstrated clinically by the presence of movement at the fracture site and radiologically by the presence of a fracture line.

For admission to the trial, patients had to be over 18 years old with a fracture of the tibial shaft, closed or compound, not less than 5 cm from the ankle or knee, which had not united after at least 16 weeks and not more than 32 weeks of treatment. Treatment had to have been by immobilisation in a long-leg plaster cast. Patients who had undergone surgical procedures other than those required for the initial management of a wound and open reduction (if necessary) of the initial fracture, were excluded, so as to provide a series of fractures that had

been treated as uniformly as possible. Treatment by internal or external fixation, even if temporary, led to exclusion except in two patients in whom stabilising pins were placed in the calcaneus and the upper end of the tibia and incorporated in the plaster.

After reduction, the fracture ends had to have been apposed over at least 50% of their surface, to be in acceptable alignment and to have no distraction. At the time of selection for treatment of their delayed union, patients with a gap between the bone ends greater than 0.5 cm were excluded, as were patients with any severe generalised disease, those receiving systemic steroid treatment, or those with bone disease such as Paget's disease. Severely atrophic bone with spindle-shaped bone ends, and fractures with marked hypertrophy were also excluded.

Severity of the fracture. Ellis (1958), Nicoll (1964) and Darder and Gomar (1975) have all shown that the risk that a fracture may develop delayed or non-union is related to the initial displacement and comminution of the fracture and the severity of any wound.

The severity of the fractures measured by these three criteria is shown in Table I. To be included in the trial, two or more of the factors of moderate or severe displacement or angulation, moderate or severe comminution or a moderate or severe wound had to have been present.

The cases were derived from 16 centres. The number of cases contributed by the centres varied between one and 11. Originally, it had been hoped to include 100 cases in the trial but, because of the strictness of the criteria for admission, only 51 cases had entered after six years and a decision was made to end the trial at this point.

Assessment. On admission to the trial, the clinical mobility of the fracture was assessed by manually stressing the limb and measuring the movement with a goniometer in the mediolateral and anteroposterior planes. Slight mobility was defined as 1° to 10° of movement, moderate mobility as 11° to 25° and marked mobility as more than 25° in either plane. The degree of pain on stressing the fracture was recorded, using a visual analogue scale on which the patient marked a point between 'no pain' and 'pain as severe as it could be'. The pain experienced when pressure was applied over the fracture was assessed and similarly recorded. Infection associated with a discharging sinus was rated as mild, moderate or severe according to the number of dressings needed per day.

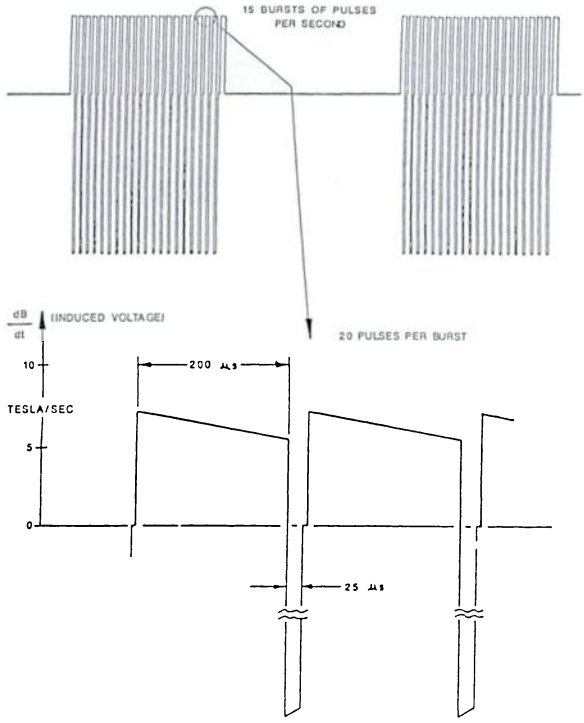

Fig. 1

The form of the signal used for pulsed electromagnetic stimulation.

Table I. Criteria of fracture severity at the time of injury

	Severity		
Criterion	**Nil or slight**	**Moderate**	**Severe**
Fracture displacement	75% to 100% apposition	25% to 75% apposition	<25% or no apposition
Fracture angulation	0° to 10°	10° to 20°	>20°
Comminution	Nil, 1 or 2 fragments	3 fragments	>3 fragments
Skin wound	Nil or <2 cm	>2 cm + contusion	Extensive wound
Soft tissue injury	Minimal	Requiring debridement Usually compound	Extensive crushing or high velocity injury + skin loss

Anteroposterior and lateral radiographs were taken. If the fracture line was not well visualised in these two pictures, one or more oblique views were taken. The parameters of radiographic exposure and the X-ray machine used were recorded so that subsequent radiographs could be made under the same conditions.

Treatment. A full-leg plaster cast was applied with the knee flexed at 20° to 30°. Patients were randomly allocated to either an active or a dummy stimulator. Neither the patient nor the surgeon knew whether the unit was an active or a dummy since they were indistinguishable in external appearance and in use. Both were provided with indicator lights and alarm signals to indicate malfunction. The units consisted of copper wire coils in two formed plastic bodies. These were positioned on a locator block placed on the plaster cast opposite the fracture site and were held in place, with one coil on each side of the fracture, in Helmholtz configuration. The coils were 35 cm long and the therapeutically effective window was 20 cm long and 11 cm wide.

Table II. Initial features of the fractures

Variable	Degree	Treatment group: Active (n = 20)	Treatment group: Control (n = 25)
Angulation or displacement	Nil/slight	2	1
	Moderate/severe	18	24
Comminution	Nil/slight	5	2
	Moderate/severe	15	23
Wound	Nil/slight	9	12
	Moderate/severe	11	13

In the active devices pulses of current were passed through the coils to produce corresponding pulses of magnetic flux through the fracture region and pulses of electric induction in the tissues. The spectral form and intensity of the magnetic pulses was calibrated with an inductive probe. The pulse form is shown in Figure 1 as the time dependence of the rate of change of magnetic flux. The magnitude of the induced electric field is proportional to the rate of change. The signal consisted of bursts of 20 individual pulses of quasi-rectangular form followed by a sharper reverse form. The bursts were repeated at 15 Hz.

In the dummy units, the coils were short-circuited so that no signal could be detected with a sensitive induction probe. As a further check on the inactivity of the dummy coil, tests were made with a model biological system as devised by Goodman, Bassett and Henderson (1983) using the glands of *Sciara coprophilia*. Stimulation by the signal used in the trial resulted in an increase in the production of RNA as compared with unstimulated controls. The dummy device gave no significant increase over controls.

The patients were instructed to bear no weight on the plaster and to apply the coil treatment for a total of 12 hours per day, no individual session of treatment being less than one hour. Most patients used their sleeping hours for the majority of their treatment time. In infected cases, any antibiotic treatment that had been started before admission to the trial was continued if necessary. Analgesic drugs were allowed if required.

Treatment was continued for 12 weeks. The plaster cast was then removed and the mobility of the fracture, the presence of pain on stressing it and local tenderness were assessed in the same way as at the initial examination. Radiographs were taken in the same way as were the initial radiographs.

RESULTS

Of the 51 patients enroled in the trial, two were transferred from dummy devices to active devices at their request, it having been agreed initially that any patient could opt out of the trial at any stage. Both, unknown to them, had begun with dummy units. One of them transferred after 10 days and was found to be making radiological progress to union at 12 weeks; the other patient transferred after six weeks and was found to show no radiological progress to union at 12 weeks. Three patients were enrolled in error, since they were found to have had internal or external fixation. One other patient tampered with his device and broke the code.

Thus 45 patients completed the trial, 20 of whom had been given active coils and 25 dummy units.

Patient characteristics. The age of one patient in the active group had not been recorded. The mean age of the patients in the active group was 34.7 years and the median age was 28 years (range 18 to 84). In the control group the mean age was 45.4 years and the median age was 45 years (range 18 to 76). Eleven patients in the active group were less than 35 years old compared with seven in the control group; eight patients in the active group were more than 35 years old compared with 18 in the control group. There was thus a significant difference in the age distribution. There were 14 men (70%) and six women in the active group and 18 men (72%) and seven women in the control group.

Initial features of the fractures. These are shown in Table II which confirms that the fractures selected for the trial were those with a high liability to suffer delayed or non-union. A moderate or severe degree of initial angulation or displacement was present in 93% of the fractures and moderate or severe comminution was present in 84%. A moderate or severe wound was present in 53% of patients. More marked comminution was present in a greater

number of the control than the active cases but not to a significant degree and analysis showed that this did not affect the outcome.

Characteristics of the fractures on entry. These are shown in Table III. Slight movement, between 1° and 10°, was present in the mediolateral plane in 64% of fractures and in the anteroposterior plane in 60%. There was no movement in the mediolateral plane in three fractures and none in the anteroposterior plane in four. All had some movement. A few more patients showed moderate or marked mobility in the control group than in the active group but statistical analysis showed that this difference did not affect the outcome. Pain and tenderness of moderate severity was present in most patients. Seven fractures (15%) had active infection; it was slight in six and moderate in one.

Table III. Characteristics of the fractures in the two treatment groups on enrolment to the trial

Variable	Degree	Treatment group: Active (n = 20)	Treatment group: Control (n = 25)
Mediolateral movement	Nil	1	2
	Slight	14	15
	Moderate	4	8
	Marked	1	0
Anteroposterior movement	Nil	1	3
	Slight	14	13
	Moderate	3	7
	Marked	2	2
Pain	Mean	3.6	2.7
	s.d.	2.4	2.2
Tenderness	Mean	4.7	4.9
	s.d.	2.2	3.0
Infection	None	16*	21
	Slight or moderate	3	4
Radiographic findings	No healing	4	7
	Slight healing	16	18
Time since fracture (weeks)	Mean	23.3	24.2
	s.d.	5.0	4.6

* data not available for one patient

Some evidence of healing was present in the initial radiographs in 75% of the fractures and no evidence of healing in 25%. None showed marked atrophy or hypertrophy. The mean time since fracture in the whole series was 23.8 weeks with an even spread of cases over the period between 16 and 32 weeks.

Characteristics of the fractures after 12 weeks

Clinical assessment. The findings are shown in Table IV. No movement was present in the mediolateral or the anteroposterior plane in 55% of cases. Pain and tenderness also showed a significant improvement. There was, however, no statistically significant difference between the two treatment groups in any of the clinical criteria.

Radiological assessment. The radiographs were assessed independently of one another by a radiologist and an orthopaedic surgeon. Neither knew the clinical results nor the distribution of the cases in the treatment groups at the time of the reading of the radiographs. The results are shown in Table V.

Table IV. Clinical characteristics of fractures in the two treatment groups at the 12-week assessment

Variable	Degree	Treatment group: Active (n = 20)	Treatment group: Control (n = 25)	Comparison of treatment groups
Mediolateral movement	Nil	13	12	Nil against slight, moderate and marked p = 0.37*
	Slight	5	10	
	Moderate	1	3	
	Marked	1	0	
Anteroposterior movement	Nil	12	13	Nil against slight, moderate and marked p = 0.76*
	Slight	6	9	
	Moderate	1	2	
	Marked	1	1	
Pain	Mean	0.9†	1.5‡	
	s.d.	1.2	2.1	p = 0.29*
Tenderness	Mean	1.6†	2.7†	
	s.d.	2.4	3.1	p = 0.18*

* p value for movement based on Fisher's exact test and for pain and tenderness on a *t*-test
† level compared with initial findings statistically significant at $p < 0.05$
‡ level compared with initial findings statistically significant at $p < 0.01$

Table V. Radiological state of the fractures in the two treatment groups at the 12-week assessment

State of fracture	Treatment group: Active (n = 20)	Treatment group: Control (n = 25)	Comparison of treatment groups*
Radiologist's assessment			
Full union	3	0	Full union, probable union and progress to union compared with no progress p = 0.002
Probable union	2	1	
Progress to union	5	1	
No progress	10	23	
Orthopaedic surgeon's assessment			
United	9	3	United compared with improved but not united and no progress p = 0.02
Improved but not united	2	5	
No progress	9	17	

* p value based on Fisher's exact test

The radiologist (AB), defined four groups:

1. *No progress.* No change from the appearances at enrolment in the trial (Fig. 2).
2. *Progress to union.* A definite change from the earlier films, either with new subperiosteal bone, fuzziness across the fracture site or new bone peripherally across the fracture site (Fig. 3). In any case of doubt, a rating of no progress was given.

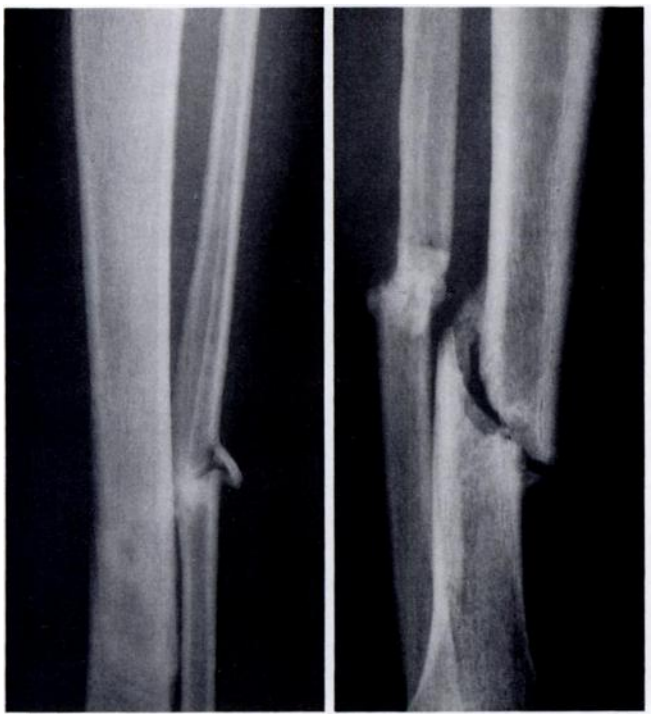

Fig. 2a

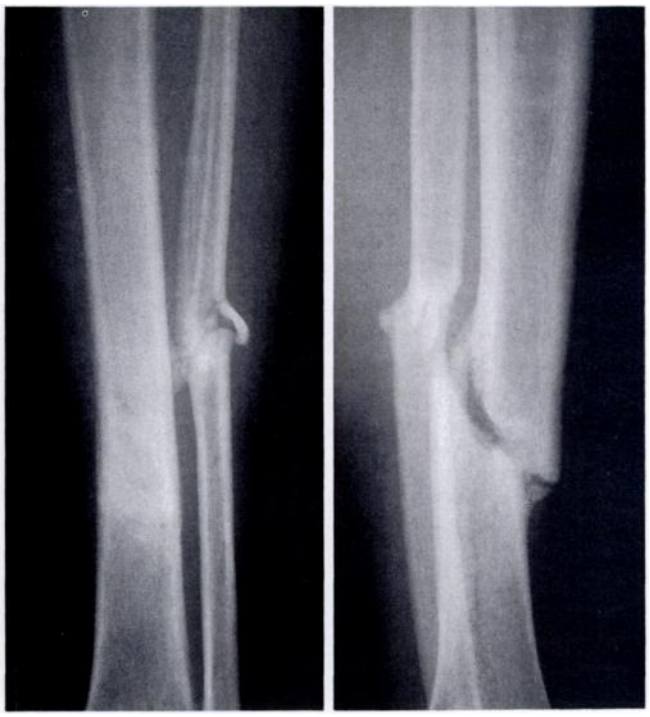

Fig. 2b

Figure 2a – Compound, moderately displaced, uncomminuted fracture of the tibia and fibula with a moderately severe wound after 21 weeks. Slightly mobile, moderately painful and tender, not infected. Radiograph shows minimal evidence of healing. Figure 2b – After 12 weeks treatment with plaster and an active unit. No movement, not painful or tender. *Radiographic assessment* – no progress (radiologist and orthopaedic surgeon).

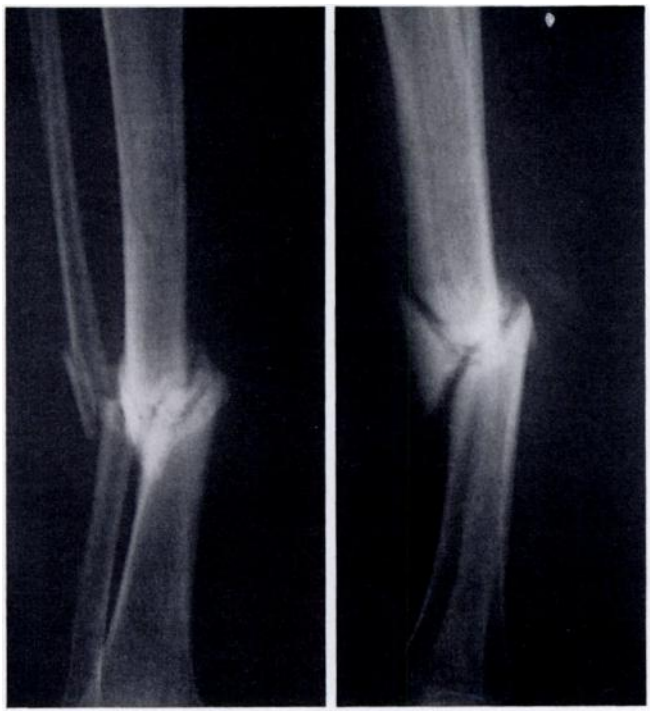

Fig. 3a

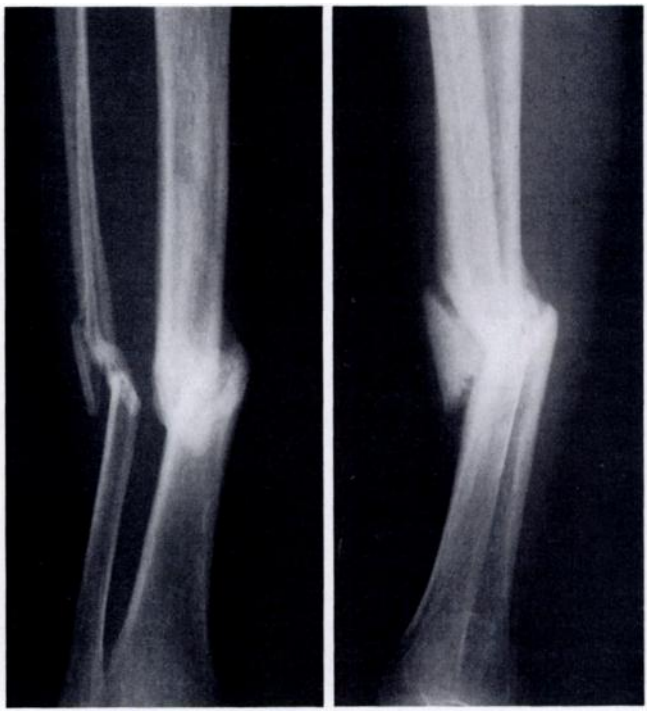

Fig. 3b

Figure 3a – Compound, moderately severely displaced, comminuted fracture of the tibia and fibula with a moderate wound after 26 weeks. Moderately mobile anteroposteriorly, minimally painful or tender, not infected. Radiograph shows slight evidence of healing. Figure 3b – After 12 weeks treatment with plaster and a dummy unit. Slightly mobile anteroposteriorly, not tender or painful. *Radiographic assessment* – progress to union (radiologist), improved but not united (orthopaedic surgeon).

3. *Probable union.* A marked change with thicker denser bone across at least two cortices and fuzziness across the fracture site (Fig. 4). Union was thought to be present.
4. *Full union.* Dense and extensive new bone formation union across involving the fracture site and at least three of the four cortices visible on the two films (Fig. 5).

Of the 25 fractures in the control group, none showed full union and only one probable union. One showed progress to union and 23 showed no change. These results reflect the severity of the fractures that had been selected. Of the 20 fractures in the active group, three showed full union and two probable union. Five showed progress to union and 10 showed no change. There was a statistically significant difference in favour of the active group ($p = 0.002$).

The orthopaedic surgeon's assessment defined three groups:
1. *No progress.* No change from the appearances at enrolment in the trial (Fig. 2).
2. *Improved but not yet united.* Some change in the region of the fracture line with increased density visible, but either insufficient to be considered as full cancellous healing or across an insufficient width of bone (Fig. 3).
3. *United.* Evidence of bony continuity across at least half the width of the fracture confirmed on at least two views (Figs 4 and 5). Restoration of cortices, though often present, was not, in itself, necessary for a diagnosis of union; continuity of cancellous bone was required.

Of the 25 fractures in the control group, three showed union, five showed improvement but not union and 17 showed no change. Of the 20 fractures in the active group, nine showed union, two showed improvement but not union and nine showed no change. There was a statistically significant difference in favour of the active group ($p = 0.02$).

Differences between the radiologist's and the orthopaedic surgeon's assessments arose more from differences

Table VI. Comparison of radiological results (radiologist's assessment) in lower and higher age sub-sets

Age group	Outcome	Active*	Control	Significance of difference†
< 35 years	Union or progress	7	1	p = 0.07
	No progress	4	6	
> 35 years	Union or progress	3	1	p = 0.07
	No progress	5	17	

* age of one patient in active treatment group not known
† p value based on Fisher's exact test

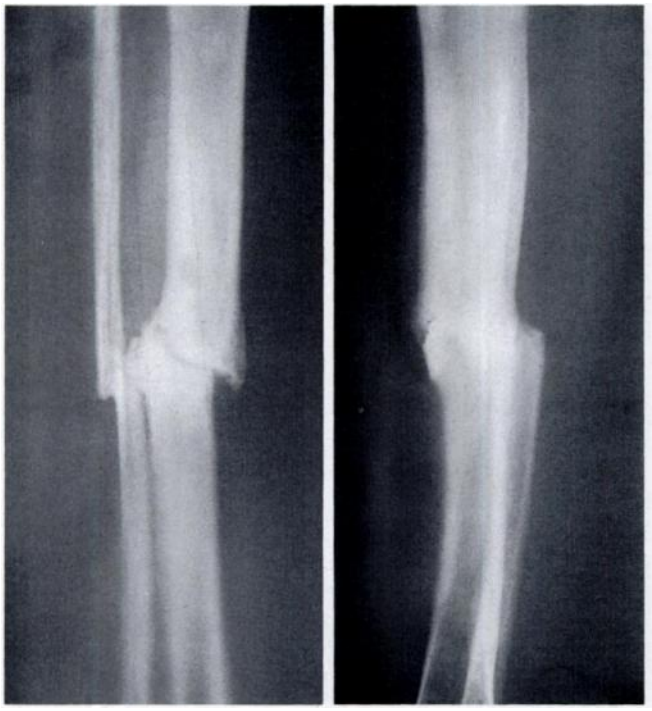

Fig. 4a

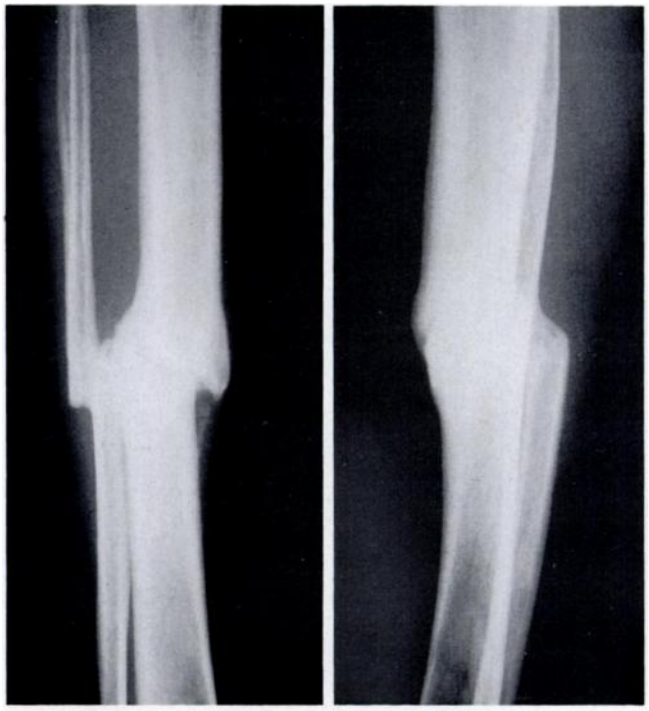

Fig. 4b

Figure 4a - Closed, moderately angulated, comminuted fracture of tibia and fibula after 31 weeks. Moderately mobile, slightly painful, markedly tender. Radiograph shows some evidence of healing. Figure 4b - After 12 weeks treatment with plaster and an active unit. No movement, slightly painful, moderately tender. *Radiographic assessment* - probable union (radiologist), united (orthopaedic surgeon).

in emphasis and definition than from important differences in opinion about the state of union. All the fractures considered by the radiologist to show full union or probable union were thought by the orthopaedic surgeon to have united and all those considered by the orthopaedic surgeon to have shown no progress were also regarded as showing no progress by the radiologist.

Because of the statistically significant differences in the mean age of the active and the control groups, an analysis was made to show whether or not age might have been responsible for the results. The findings are shown in Tables VI and VII. Table VI compares the results in patients of 35 years or less with those over 35 years of age. In both age groups the results are better for active than for control cases, though the p values were a little above 0.05. This result reflects the small numbers in the sub-sets. The age differences between active and control groups do not account sufficiently for the preference for the active group. Table VII, using categorical modelling, indicates that age group had no effect on the outcome ($p = 0.23$) and that the effect of treatment was consistent for each age group ($p = 0.99$). The effect of treatment was, again, shown to be highly significant ($p = 0.009$).

Combined radiological and clinical assessment. Table VIII shows the relationship between absence of movement in

Table VII. The use of categorical modelling to indicate the effects of age on the outcome of treatment

Factor	p value
Age group	0.23
Treatment group	0.009
Age by treatment group	0.99

Table VIII. Comparison of radiological findings and clinical mobility in 45 cases

	Clinical findings	
Radiological appearances	**No movement**	**Movement**
Radiologist's assessment		
Union and probable union	6	0
Progress to union	3	3
No progress	13	20
Orthopaedic surgeon's assessment		
United	12	0
Improved and no progress	10	23

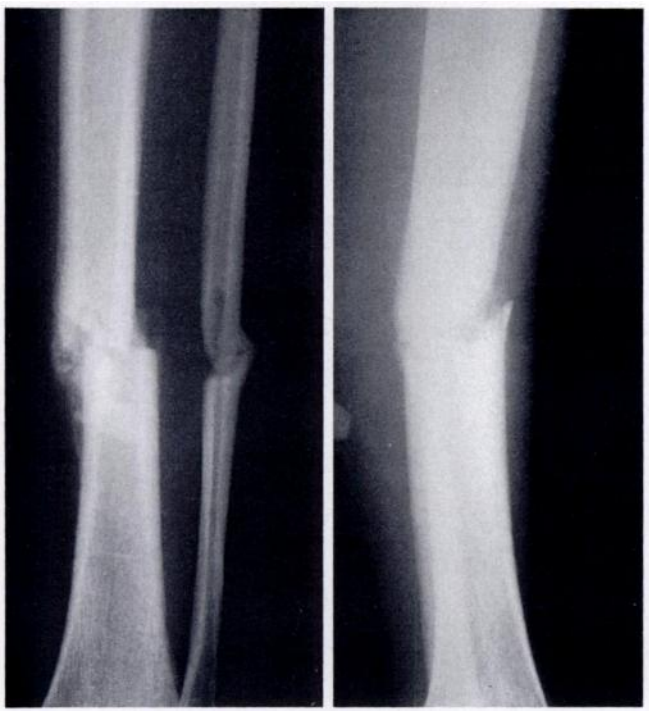

Fig. 5a

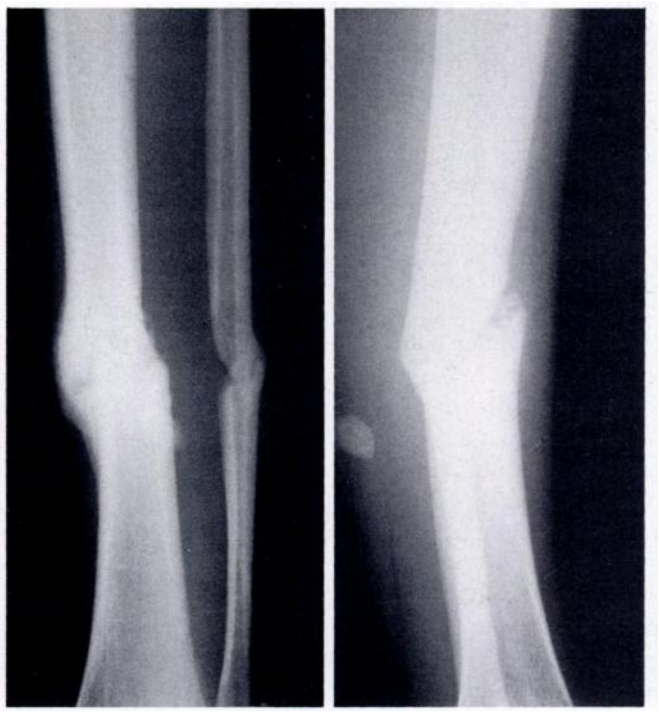

Fig. 5b

Figure 5a – Closed, moderately displaced and angulated comminuted fracture of tibia and fibula after 20 weeks. Moderately mobile, painful and tender. Radiograph shows some evidence of healing. Figure 5b – After 12 weeks treatment with plaster and active unit. No movement, no pain, not tender. *Radiographic assessment* – full union (radiologist), united (orthopaedic surgeon).

both planes and the presence of radiological signs of union. Although movement at a fracture is, a priori, indicative of failure of union, absence of movement was not a reliable indicator of union. It is suggested that this is why clinical assessment alone did not demonstrate a statistically significant difference between the control and active groups. However, radiographic union was always supported by clinical evidence of union whether the films were interpreted by a radiologist or an orthopaedic surgeon. Absence of movement on clinical examination combined with radiological evidence of union seems, therefore, to be a reliable indicator of bony union.

DISCUSSION

It is a necessary requirement for a valid double-blind trial of any method of treatment that the cases to be compared should be as much alike as possible. Double-blind trials of fracture treatment are especially difficult to carry out because of the wide spectrum of bone and soft tissue injury that may occur and the varieties of treatment that may be used. For this reason, the trial was limited to fractures of the tibial shaft that had received only conservative management. Many simple undisplaced tibial fractures are likely to be united or to be approaching union by 16 weeks and would not be in need of supplementary measures to achieve union. Fractures that had initially been moderately or severely displaced or angulated, comminuted, or associated with soft tissue injury, and which were making no progress or minimal progress to union, were selected because of their recognised tendency to delayed union or non-union. The low rate of union in the series as a whole is an indication that the strict selection did identify fractures with a very poor prospect for union.

Although tibial fractures are among the commonest of major limb fractures, the limitations imposed by our protocol meant that a multi-centre trial had to be instituted to obtain enough case material and, even then, a six-year period was needed. The base from which the 45 cases was obtained is estimated to be approximately 2 000 tibial fractures treated in the 16 centres during this time. The number of patients was adequate to produce two treatment groups that did not differ significantly except in their age distribution.

Because of the difficulty of diagnosing bony union from radiographs, it was thought to be important to have an independent opinion from a radiologist and an orthopaedic surgeon. In the event, both gave statistically significant results in support of the efficacy of pulsed electromagnetic fields.

No comparable trial has been found in a review of the literature. A double-blind study of the effects of electromagnetic fields on fractures ununited for more than a year (Barker et al 1984), in which the present author took part, cast considerable doubt on their value. It may be that such fractures do not respond as well or in the same way as those at an earlier stage of fracture healing, though the clinical results of non-randomised series (Bassett, Valdes and Hernandez 1982; Sharrard et al 1982; Fontanesi et al 1983; Hinsenkamp, Ryaby and Burney 1985) have suggested that such fields are effective. The number of cases in our earlier trial (Barker et al 1984) was small, and, in consequence, the cases in the two treatment groups were, in some important respects, not fully comparable. The fractures had also received previous treatment of very varied kinds. It is also possible that the method of defunctioning the dummy coils could have allowed some stimulatory effect to continue to act.

It is not the purpose of this paper to attempt to show how pulsed electromagnetic fields produce their effect on bone. It will suffice to mention several contributions indicating effects on calcium and calcification (Bassett et al 1979; Bassett et al 1982; Norton and Rovetti 1988), on angiogenesis (Yen-Patton et al 1988) and on collagen and proteoglycans (Farndale and Murray 1985; Norton 1985). Whilst it would be misleading to suggest that pulsed electromagnetic fields as such produce bony union, since their application requires the concomitant use of immobilisation, as does a bone graft, it is important that the claims made for their clinical effects in stimulating bone formation should have been investigated by an adequate double-blind clinical trial. Their proven value in this series justifies their continued use for delayed or non-union of fractures, especially where surgical measures are inappropriate or invite the risk of infection.

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