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ORIGINAL STUDY

# Pulsed electromagnetic stimulation of regenerate bone in lengthening procedures

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**Distraction osteogenesis for limb lengthening represents the treatment of choice in patients with small stature or limb length discrepancies. Bone lengthening and callus formation requires a long therapy. Pulsed electromagnetic fields (PEMF) are normally used to enhance osteogenesis in patients with non-unions. In this study we investigated whether pulsed electromagnetic fields could be used effectively to encourage callus formation and maturation during limb lengthening procedures. Thirty patients underwent bilateral bone lengthening of the humerus, femur or tibia. At day 10 after surgery, PEMF stimulation was started on one side, for 8 hours/day. Stimulated distraction sites exhibited earlier callus formation and progression, and a higher callus density compared to non-stimulated sites. External fixation could be removed on average one month earlier in PEMF stimulated bones. Our results show that the use of pulsed electromagnetic fields stimulation during limb lengthening allows shortening the time of use of the external fixation.**

**Keywords** : bone lengthening ; pulsed electromagnetic stimulation.

## INTRODUCTION

Lengthening of bone segments in patients of small size or with limb length discrepancies has now been made possible with the currently available distraction osteogenesis techniques (*1, 5, 13*). These techniques can also be used to transport segments of bone in patients with bone defects resulting from fractures, tumours or infections (*2, 6, 10, 11, 16*).

In our experience, the pathology which most frequently requires bone lengthening is achondroplasia, which affects the four extremities symmetrically.

The discovery of the capacity of bone tissue to form new bone during the distraction of a fracture callus or a physis has resulted in the development and improvement of new effective techniques for limb lengthening. They have been implemented using various systems of external fixation, both circular and mono-lateral (*1, 3, 13*). These procedures are mainly useful in achondroplasia and hypochondroplasia, but they can also be used in other conditions causing length discrepancy of the extremities such as fracture sequelae, poliomyelitis, congenital limb discrepancies, bone transport, etc (*2, 11*).

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Nevertheless, limb lengthening and bone regeneration is a long lasting procedure often associated with muscular and articular problems, in particular joint stiffness. The combined use of techniques known to stimulate bone formation could possibly reduce the duration of the procedure.

Physical agents (electrical, electromagnetic and mechanical) have been used to enhance bone healing in patients with non-unions (*3, 4, 9, 14, 17, 20*). Direct current (*12, 18*), capacitive coupled electric fields (CC) (*14*), pulsed electromagnetic fields (PEMF) (*19*) and low intensity pulsed ultrasound (LIPU) (*15*) have been used to stimulate the healing of regenerated bone in animals.

The overall experience in the clinical use of PEMF during limb lengthening is extremely limited. Eyres *et al* (*8*) reported a positive effect of electromagnetic stimulation on bone loss adjacent to the distraction gap, but no effect on the regenerate bone as measured by bone densitometry. Dudda *et al* (*7*) reported the treatment of regenerated bone with LIPU in one patient undergoing distraction-osteogenesis of the humerus.

In our experience PEMF's have been used successfully to treat non-unions, the technique is easy to use, and no negative side effects have been described (*20*). In this study we investigated whether the stimulation of osteogenesis by pulsed electromagnetic fields, may lead to a progress in the limb lengthening field, by reducing the time the patient has to keep the fixation, and helping to prevent joint stiffness and other complications. In patients undergoing contemporary and symmetric limb lengthening, electromagnetic stimulation was applied to one limb in order to accelerate osteogenesis. We evaluated if electromagnetic stimulation could enhance bone regeneration, callus progression, mineralisation and would allow earlier removal of the external fixation device.

## MATERIALS AND METHODS

Between 1995 and 2000, we carried out a prospective randomised study in patients with bilateral short limbs who were subjected to simultaneous lengthening of two symmetric bone segments. The aetiology of the short size included achondroplasia (24 cases), metaphyseal chondrodysplasia (1 case), agenesis of the fibula (1 case) and Turner's syndrome (4 cases). The study was approved by the Institutional Review Board and parent's informed consent was obtained. We enrolled in this study 30 patients (16 boys and 14 girls, average age 11 ± 1.6 years) in whom 60 limbs were lengthened. Bone segments included 28 tibiae, 20 femurs and 12 humeri.

### Surgical procedure

In the femoral segment, a proximal metaphyseal osteotomy was performed ; soft tissue procedures included tenotomy of the hip adductors through a small incision in the groin, release of the tensor fasciae latae and the proximal sartorius tendon. In cases where the tibia was lengthened a minimally invasive tenotomy of the Achilles tendon was carried out as well as an osteotomy of the fibula in its distal third ; a 3.5-mm cortical screw was inserted below the osteotomy line, fastening fibula to tibia ; after applying the external fixator, a proximal metaphyseal osteotomy was made. The humerus was osteotomised proximally after the fixator was placed. The lengthening process started 7 days after surgery.

Patients were asked to return for control monthly ; at the time of the visit, radiographs were taken with a grid, using the same exposure conditions in repeated examinations, depending on the bone site investigated. These radiographs were used to calculate the time of corticalisation (1 mm at least of cortical bone surrounding callus, in the AP and lateral view) of the regenerated bone. Beside monthly X-ray controls, at the time of fixator removal a millimetre scale was added to the film to eliminate the magnification effect of the beam at the site of investigation. At the end of the study, without knowing which limb was stimulated, the following measurements were made : callus thickness and cortical thickness in mm. The bone mineral density of the regenerated bone was evaluated by dual energy X-ray absorptiometry (DXA), (Lunar, Madison, USA), collimated at 1.68 mm, intensity 750 micro A, resolution $1.2 \times 1.2$ mm. The lengthening rate was 1 mm per day, in one step only. Lengthening was obtained by means of the Triax fixation device (Stryker, Geneva, Switzerland).

### PEMF stimulation

The patients were instructed on the use of the PEMF stimulator and were advised to employ it every day for 8 hours, preferably during night. The device used was BIOSTIM (IGEA, Carpi, Italy), generating pulses of

Table I. — Mean age, amount of lengthening and follow-up duration in male and female patients respectively. No significant differences were found between groups.

| | Females 14 | | Males 16 | | |
|---|---|---|---|---|---|
| | Mean | S.D. | Mean | S.D. | t-test |
| Age (years) | 10.7 | 1.6 | 11.2 | 1.6 | n.s. |
| Lengthening (mm) | 114.1 | 19.3 | 112.1 | 30.0 | n.s. |
| Follow-up (months) | 31.1 | 4.4 | 33.4 | 5.0 | n.s. |

Table II. — Mean age, amount of lengthening and follow-up duration according to lacation of the lengthening procedures.

| | Femur | | Humerus | | Tibia | |
|---|---|---|---|---|---|---|
| Patients | 10 (5M/5F) | | 6 (4M/2F) | | 14 (7M/7F) | |
| | Mean | S.D. | Mean | S.D. | Mean | S.D. |
| Age (years) | 10.4 | 1.3 | 11.3 | 0.8 | 11.2 | 1.9 |
| Lengthening (mm) | 117.6 | 19.8 | 78.7 | 16.0 | 124.4 | 18.5 |
| Follow-up (months) | 31.3 | 6.2 | 34.7 | 3.4 | 32.1 | 4.1 |

1.3 ms duration with 75 Hz frequency and an induced electric field of 3.5 ± 0.5 mV as measured in a standard coil probe (*13*). The PEMF stimulation started 10 days after surgery and was maintained during the distraction and consolidation period.

The choice of the side to treat was made by having the patient pick up a ticket from a box, where 15 tickets for the right side and 15 for the left were placed.

**Statistical analysis**

Statistical analyses were done by means of Statistical Packages for Social Science (SPSS inc., Chicago 111, USA). Statistically significant differences between groups were calculated by t-Student, paired t-Student and Wilcoxon tests when appropriate. The level of significance was set at $p < 0.05$.

## RESULTS

Among the 30 patients the average limb lengthening was 113 ± 25.2 mm (range : 53 to 153). The average follow-up was 32.3 ± 4.8 months (range : 23 to 40). No significant differences were observed in lengthening or follow-up duration between males and females (table I). Table II reports the mean age, follow-up duration and length for every segment ; in all cases the average follow-up was over 30 months. As shown in table III, there are significant differences between the stimulated and the control side regarding time to corticalisation and to fixator removal, callus thickness and density. In the stimulated bones there were no significant differences between genders for the previous variables (table IV).

Finally, table V displays those same variables for the different limb segments treated.

The positive effect of PEMF stimulation on bone regeneration was evident in all bone segments investigated.

Figures 1 and 2 illustrate the difference in callus thickness between the stimulated (the left side in both cases) and the control segment.

## DISCUSSION

The effect of pulsed electromagnetic stimulation on bone callus formation has been widely described in the literature, in patients with non-unions (*3, 17, 20*). Although PEMF stimulation has been applied to adult patients who developed non-union at the site of limb lengthening (personal experience), no extensive study of the role of PEMF stimulation in this pathology has ever been conducted.

In this study we have shown that PEMF stimulation has decreased by one month the time the patient had to keep the external fixation device and has, therefore, allowed for earlier rehabilitation. This is extremely important in view of preventing complications, such as joint stiffness, which are often noted in these patients. Regenerated bone tissue characteristics were quantified by both radiographs and DXA investigation at the end of the lengthening period. All parameters showed that PEMF stimulation favours bone mineralisation,

Table III. — Differences between stimulated and control bones regarding time to fixator removal, time to corticalisation, cortical and callus thickness, and callus density.

| | Stimulated | | Control | | |
|---|---|---|---|---|---|
| | Mean | S.D. | Mean | S.D. | Student's paired t test |
| Fixator Removal (days ) | 308.3 | 62.82 | 339.5 | 61.17 | p < 0.01 |
| Corticalisation (days) | 279.6 | 68.4 | 313.5 | 60.6 | p < 0.01 |
| Callus thickness (mm) | 31.2 | 4.41 | 21.8 | 3.96 | p < 0.01 |
| Cortical thickness (mm) | 2.73 | 0.73 | 2.63 | 0.66 | n.s |
| Density ($gr/cm^2$) | 85.7 | 5.05 | 69.8 | 7.70 | p < 0.01 |

Table IV. — Differences between stimulated and control bones, in male and female patients.

| | Females (14) | | | Males (16) | | |
|---|---|---|---|---|---|---|
| | Stimulated | Control | Wilcoxon Test | Stimulated | Control | Wilcoxon Test |
| Fixator Removal (days) | 308.0 ± 49.0 | 341.9 ± 49.5 | 0.01 | 308.6 ± 74.5 | 338.1 ± 71.4 | p < 0.01 |
| Corticalisation (days) | 273.8 ± 49.4 | 312.6 ± 52.5 | 0.01 | 284.7 ± 83.0 | 314.4 ± 68.7 | p < 0.01 |
| Callus thickness (mm) | 32.7 ± 4.6 | 23.4 ± 3.6 | 0.01 | 30.0 ± 4.0 | 20.4 ± 3.9 | p < 0.01 |
| Cortical thickness (mm) | 2.9 ± 0.8 | 2.6 ± 0.6 | 0.05 | 2.6 ± 0.7 | 2.7 ± 0.7 | n.s. |
| Density ($g/cm^2$) | 0.849 ± 0.041 | 0.675 ± 0.082 | 0.01 | 0.866 ± 0.058 | 0.718 ± 0.069 | p < 0.01 |

Table V. — Differences between stimulated and control bones, for lengthening of femur, tibia and humerus respectively.

| | **Femur** | | | | |
|---|---|---|---|---|---|
| | Stimulated | | Non stimulated | | |
| | Mean | S.D. | Mean | S.D. | p |
| Fixator removal (days) | 321.4 | 57.6 | 349.4 | 63.0 | <0.01 |
| Corticalisation (days) | 295.1 | 55.6 | 325.5 | 59.1 | <0.01 |
| Callus thickness (mm) | 30.4 | 2.8 | 24.4 | 3.4 | <0.01 |
| Cortical thickness (mm) | 3.3 | 0.7 | 3.3 | 0.5 | n.s. |
| Density ($g/cm^2$) | 0.816 | 0.035 | 0.620 | 0.037 | <0.01 |
| | **Humerus** | | | | |
| | Stimulated | | Non stimulated | | |
| | Mean | S.D. | Mean | S.D. | p |
| Fixator removal (days) | 239.2 | 45.4 | 276.5 | 47.1 | < 0.05 |
| Corticalisation (days) | 210.5 | 39.3 | 249.3 | 32.1 | 0.05 |
| Callus thickness (mm) | 26.5 | 2.9 | 17.0 | 3.4 | < 0.05 |
| Cortical thickness (mm) | 2.5 | 0.5 | 2.5 | 0.5 | n.s. |
| Density ($g/cm^2$) | 0.933 | 0.024 | 0.817 | 0.015 | < 0.05 |
| | **Tibia** | | | | |
| | Stimulated | | Non stimulated | | |
| | Mean | S.D. | Mean | S.D. | p |
| Fixator removal (days) | 328.6 | 54.1 | 360.2 | 48.8 | < 0.01 |
| Corticalisation (days) | 298.1 | 70.5 | 332.6 | 54.5 | < 0.05 |
| Callus thickness (mm) | 33,9 | 4.0 | 22.0 | 2.6 | < 0.01 |
| Cortical thickness (mm) | 2.4 | 0.6 | 2.2 | 0.4 | n.s. |
| Density ($g/cm^2$) | 0.855 | 0.025 | 0.703 | 0.032 | < 0.01 |

***Fig. 1.*** — This radiograph shows the difference in callus thickness between stimulated (left) and the control bone, in a patient who underwent a bilateral femoral lengthening procedure.

***Fig. 2.*** — This radiograph shows the difference in callus thickness between stimulated (left) and the control bone, in a patient who underwent a bilateral tibial lengthening procedure.

maturation and corticalisation, so that the external fixator can be removed earlier.

In the humerus, corticalisation was observed earlier than in the tibia and femur ; the external fixator was therefore used for a shorter time compared to the other segments.

Regarding callus thickness, PEMF stimulation was effective in all cases, particularly at the tibia.

DXA showed that, in all treated segments, the bone callus density was higher on the side where PEMF stimulation was applied. The humerus was the segment where a greater bone callus density was measured ; in the control humerus group, mean bone mineral density was 0.86 rng/cm$^2$, i.e. approximately 87% of the opposite side (stimulated).

Contrary to Eyres *et al* (*8*), we have observed a positive effect of PEMF stimulation on bone mineral density of the regenerated bone. In their study, bone mineral density was lower at the distraction gap in controls compared to the stimulated side, however the difference did not reach statistical significance.

PEMF was well tolerated in all patients ; nevertheless the treatment requires the patient's commitment. Six months after the external fixator was removed, 3 fractures (all femoral) were registered ; one in the stimulated group and two in the control. This study demonstrates that in patients undergoing limb lengthening, PEMF stimulation favours maturation of regenerate bone, so that the external fixator could be removed one month earlier, allowing for earlier rehabilitation.

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