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OSTEOGENETIC STIMULATION BY EXTERNALLY APPLIED DC CURRENT

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A new, simple, safe and noninvasive technique for the electrical stimulation of fracture healing is introduced. The safety and the simplicity of the technique makes it possible to apply it almost immediately to clinical experimentation. Electrodes were applied externally to the fractured site producing current across the limb. It was observed that the current density changes the volume of callus and affects the direction of the trabecular orientation. When the trabecular orientation is completely changed from longitudinal to transverse, the larger volume of callus does not compensate for the loss of strength as compared with the callus on the control bone.

Key words: osteogenesis; callus; bioelectricity; bone

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It is a well established fact today that DC and AC electrical microcurrents have an effect on osteogenesis. The phenomenon was first observed by Yasuda et al. (1954), Iida et al. (1956) and Noguchi (1957), later by many researchers in North America and Europe and outstanding results were reported by Bassett et al. (1964 and 1975). It is also generally accepted that stimulating currents range between 5 μA and 25 μA; higher currents may produce deleterious effects.

The mechanism of electrical stimulation still remains a matter of conjecture; however, several hypotheses attempting to describe conditions in the electrically stimulated tissue environment have been proposed. It is only reasonable to accept the fact that in the presence of ionic currents, various effects of electrolysis must be present (Pilla 1974). Thus most investigators have reported, on the basis of *in vitro* (Becker & Murray 1970) and *in vivo* (Noguchi 1957 and Friedenberg et al. 1970) studies, higher osteoblastic activity on the cathode side and osteoclastic on the anode side. The ionic byproducts have also been observed in the tissue surrounding both the anode and the cathode. The puzzle which still remains unchallenged is cellular behaviour between the cathode and the anode. The conductivity in the soft and the hard tissue is predominantly ionic. Thus there are cations and anions moving through the tissue in the presence of an electrical current. Assuming that there is always a balance of positive and negative ions, the cellular environment will remain unchanged. However, there is a high probability that in the path of ions there exists selective adsorption of some ions and possible semiconductive properties of tissue (Digby 1966, 1974). The combination of the above parameters and differences in the ionic mobility would produce, according to Digby (1974), local changes in pH and thus affect precipitation of calcium salts which is highly dependent on pH. This would change the immediate cellular environment even far

removed from the electrodes. It is also reasonable to speculate that the change of the cell's environment would control its metabolic activity (Parseyian 1974).

Assuming that the above rationalization is true, the following two simple conclusions can be established.

1. The direction of the microcurrent does not have to be across the fracture site or parallel to the long axis of a bone, the way it has been attempted by Yasuda et al. (1954), Iida et al. (1956), Bassett et al. (1964, 1975), Becker & Murray (1970, Kraus & Lechner (1972), Levy (1974), Haas (1963), etc.
2. The specified magnitude of the current in electrical stimulation is an insufficient parameter. It would be more desirable to know the current density in the stimulated region.

METHODS

On the basis of the above conclusions, a new technique of electrical stimulation was designed. Electrodes were attached externally to the skin of the fractured limb using ECG gel for better coupling and the electric current density was estimated from the model illustrated in Figure 1.

The complexity of the model illustrates the difficulty of the task, especially since it was not the resistance of the tissue which was needed. In order to estimate current density, the resistivity of all elements must be known. Clearly it is not possible to obtain this information, therefore empirical methods should be used but it must always be kept in mind that the current density would change with the thickness of a limb and the proportions of various kinds of tissue in it.

MATERIALS

Three consecutive series of 12 white Australian rabbits weighing between 3 and 4 pounds were used. Prior to the actual experiment, electrical resistivity of various tissue components were measured *in vitro* and *in vivo*. An estimation was made of the magnitude of current to be applied across the limb of a rabbit which would result in approximately an equivalent of the 5–25 μA between implanted electrodes used in experiments of previous investigators. In order to verify our estimates, an insulated stainless steel wire, with a bared end, was implanted at the osteotomy site produced in the radius of the experimental animal. External electrodes made from stainless steel thumb tacks, having a contact area of 122 mm^2, were applied with ECG gel to both sides of the osteotomy. A 10-volt power supply producing 150 μA was connected to the electrodes and the current output was monitored from the implanted wire at weekly intervals for 3 weeks. The output of 8 μA remained unchanged during the whole period. The result was disappointing since it was expected that the current would diminish with the progressive growth and calcification of the callus. However, the value of 150 μA, resulting in the theoretical current density at the site of electrodes of 123 $\mu A/cm^2$, was assumed to be close for the purpose of the first experiment. The actual current density inside the limb still remained a matter of conjecture.

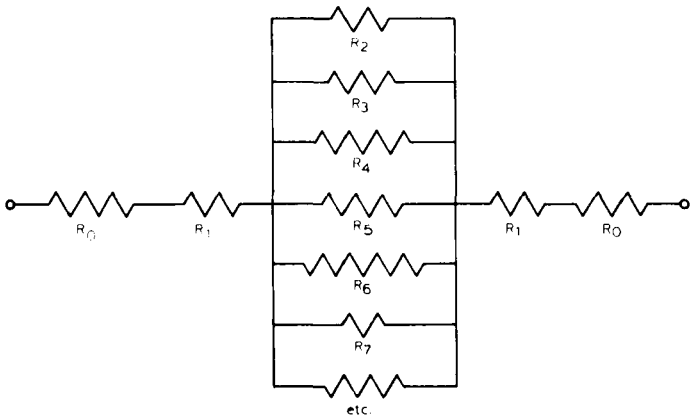


Figure 1. Electrical model of a fractured limb R_0 *and* R_1*–electrical resistance of the skin,* R_2*–*R_7 *etc. are the respective resistances of muscle, connective tissue, ligaments, periosteum, bone, haematoma, etc.*

RESULTS

Experiment 1

Bilateral osteotomies on the radii of twelve rabbits were produced using a 0.05" thick flat saw. After a 1 day postoperative recovery period, electrodes were applied externally to both radii, one pair without an electric current and the other connected to a power supply. Electrodes were positioned in such a way that the current was directed through the osteotomy site. Animals were placed in restrainers and stimulated electrically with 123 $\mu A/cm^2$ for 3 hours every day for 14 days. After 14 days, animals were sacrificed with an overdose of anaesthetic and the bones were examined for callus formation at the control and experimental sites. Two weeks of healing time proved insufficient to form a fully calcified callus. Most specimens exhibited cartilaginous gaps in the centre of the osteotomy separating bulky calcified callus. In six of the experimental bones and in two controls the osteotomy was completely bridged by fully calcified callus. Since mechanical testing, with the exception of the latter eight specimens, would not produce any results, only the size of the formed callus was examined. The bones were separated at the osteotomy and photomicrographs on the macro attachment of a metallograph were taken, showing the cross-sectional areas of the formed callus. Upon tabulating the results, it was found that the cross-sectional area of the callus of the stimulated bones was 27 per cent larger than the control side.

Experiment 2

It was evident that the postoperative healing time was not sufficient to produce fully calcified callus, therefore the second group of animals was stimulated with the same current density for 21 days.

All bones from the stimulated and controlled sides had rigid unions with fully calcified callus. The ends of the radii were mounted in acrylic resin for tensile tests and stored in saline solution at 0°C. The results of the tensile tests were completely opposite to the expected values. The tensile strength of the stimulated bones was much *lower* than on the control side and the callus was much thicker.

At this stage, it was postulated that the current density had been over-estimated and therefore the opposite adverse effect was obtained for the same reason as observed in the fully invasive techniques by Pilla (1974).

Experiment 3

The third group of animals was stimulated also for 21 days but the applied current was reduced to 50 μA, resulting in a current density of 41 $\mu A/cm^2$. This treatment produced stronger and less bulky callus on the stimulated side.

The results of mechanical testing for all three experiments are summarized in Table 1.

DISCUSSION

The interpretation of the results is reasonably simple. Experiments 1 and 2 indicated that the current density of 123 $\mu A/cm^2$ definitely produced a much more bulky callus than on the control side. The strength of the callus however was lower on the stimulated side. The comparison of values for the Ultimate Tensile Strength improved the level of significance of difference to 0.39 indicating that the quality of callus was also poorer. The larger volume of callus on the stimulated side was not able to compensate for the reduction in strength. Reducing the current density to 41 $\mu A/cm^2$ reversed the results. Although the level of significance of the load to fracture was poor, the quality of callus was better resulting in a significant improvement in strength (UTS) on the electrically stimulated side.

Based on the above observations, it is not possible for this pilot project to claim quantitative results. However, a general qualitative but also very significant observation can safely be made: The current density controls the strength, the amount and the porosity of the forming callus. Larger

Table 1. Results of mechanical testing

	Control bones	Stimulated bones	Percent of difference	Level of significance of difference*
Experiment 1				
Av. cross-sectional area ($m^2 \times 10^{-6}$)	15.68	19.98	+ 27	0.11
Experiment 2				
Av. maximum load to fracture (N)	158.50	142.79	− 10	0.58
Av. cross-sectional area ($m^2 \times 10^{-6}$)	29.95	33.54	+ 12	0.09
Av. UTS (MPa)	5.56	4.45	− 20	0.39
Experiment 3				
Av. maximum load to fracture (N)	180.84	185.56	+ 3	0.89
Av. cross-sectional area ($m^2 \times 10^{-6}$)	37.2	34.3	− 8	0.34
Av. UTS (MPa)	4.64	5.26	+ 13	0.52

* *t*-test for nonindependent samples.

current densities produce larger amounts of callus with higher porosity and poor strength.

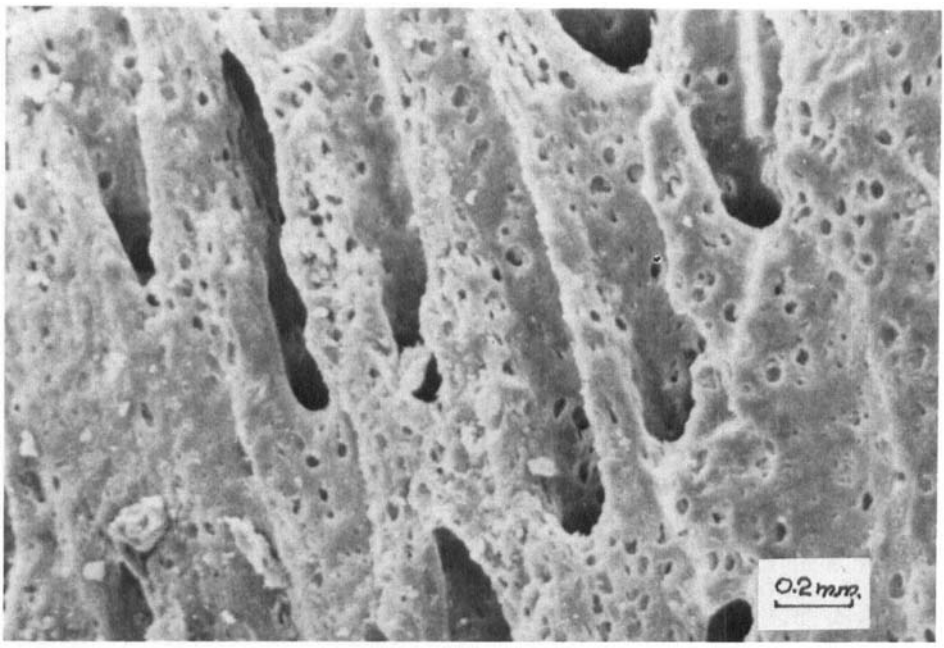
In order to get one step closer to the explanation of this phenomena, the morphology of the formed callus was examined. The fractured ends of the bones were treated with Hydrazine (95 per cent) immersed in the bath of an ultrasonic cleaner. This treatment removed the organic phase, cleaned the remaining debris and left only fully calcified trabeculae. Control and stimulated callus were examined under the scanning electron microscope for the porosity and morphological formation of trabeculae.

Figures 2a and 2b show the typical formation of trabeculae in the callus of the control bones in all three experiments. Figure 2a is the transverse view and Figure 2b is the longitudinal view of the same callus. Both photomicrographs show a preferred orientation of trabeculae parallel to the long axis of the radius. Figure 3 shows a side view of a callus electrically stimulated for 2 weeks with the current of 123 $\mu A/cm^2$. The arrangement of trabeculae is longitudinal away from the fractured surface, but right at the fractured site it changes to the transverse orientation corresponding to the direction of the current flow through the haematoma. Figure 4 is a side view of the callus on the fractured side stimulated with the current of 41 $\mu A/cm^2$. Most of the callus has a longitudinal orientation of trabeculae with the exception of occasional protrusions with distinctly transverse trabecular orientation.

Conclusions

The fact that osteogenesis is stimulated by DC current has been documented before. This research may indicate that local stimulation depends on the local current density which in turn is dependent on the resistivity of the materials through which the current passes. The dramatic illustration of this fact is shown in Figure 4. It may be speculated that the large lumps of callus on otherwise smooth surfaces were the areas of higher current denstiy resulting in a large amount of deposition of bone. The comparative results of the cross-sectional area of control and stimulated bones in Experiments 1 and 2 show that the higher current produces much more callus.

The growth of callus in the direction of applied electric potential was observed by Yasuda (1974). The remarkable observation in



(a)

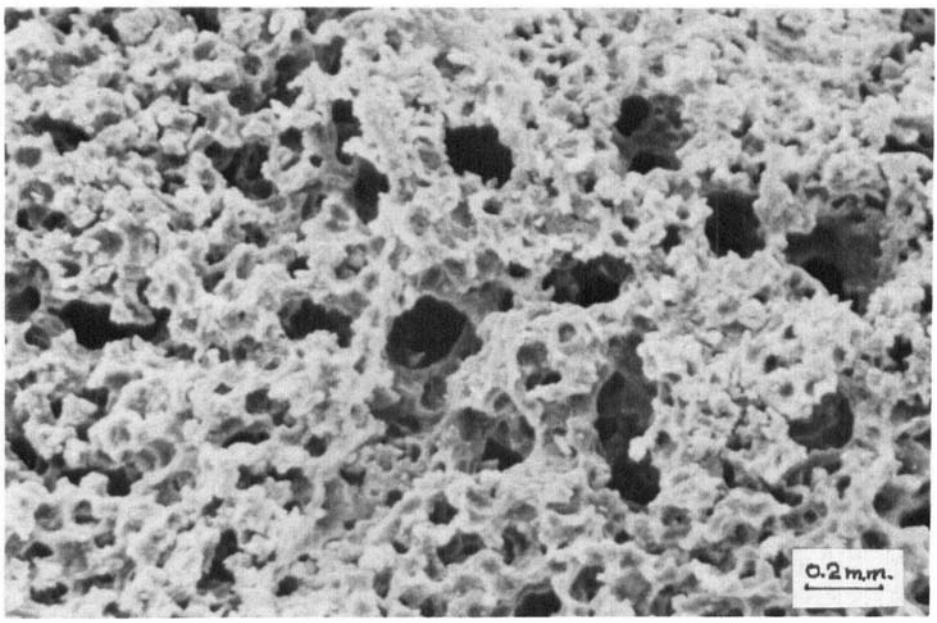


Figure 2. Transverse (a) and longitudinal (b) view of callus on the control side.

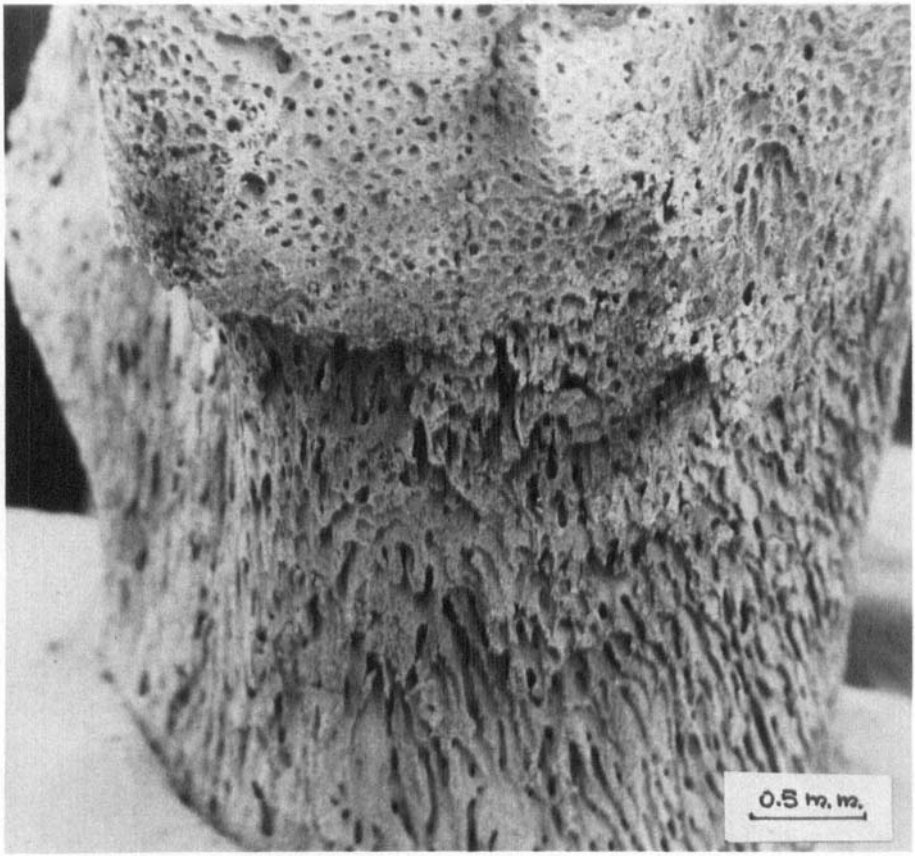


Figure 3. Side view of a callus electrically stimulated for 2 weeks with the "current density" of 123 $\mu A/cm^2$.

this investigation is the effect of current on the directionality of trabecular formation. It appears that the electrical potential predetermines the orientation of forming trabeculae in callus. In the normal healing process of bone there exists an electrical potential between the fractured ends which presumably controls the orientation of callus. Such a control results in the orientation of callus parallel to the long axis of the bone, which is observed in Figures 2a and 2b. When a higher potential, resulting in a higher current density, is applied across the fracture site as in Experiments 1 and 2, the trabecular orientation on the fracture side, where the conductivity through the haematoma was high, is perpendicular to the long axis of the bone as though this were an overriding effect on the natural currents between fractured ends. Figure 4 shows the effect of both potentials. The trabecular orientation seemed to change according to the localized current density. The path of the high current, which presumably found a low resistivity in some parts of the haematoma, formed channels of trabeculae oriented at right angles to the rest of the callus. The localized higher density current still has not produced any adverse biological conditions except for the change in the trabecular orientation. Thus, it appears that a theoretical current density of about 40 $\mu A/cm^2$ is quite safe and the technique may have immediate clinical applications.

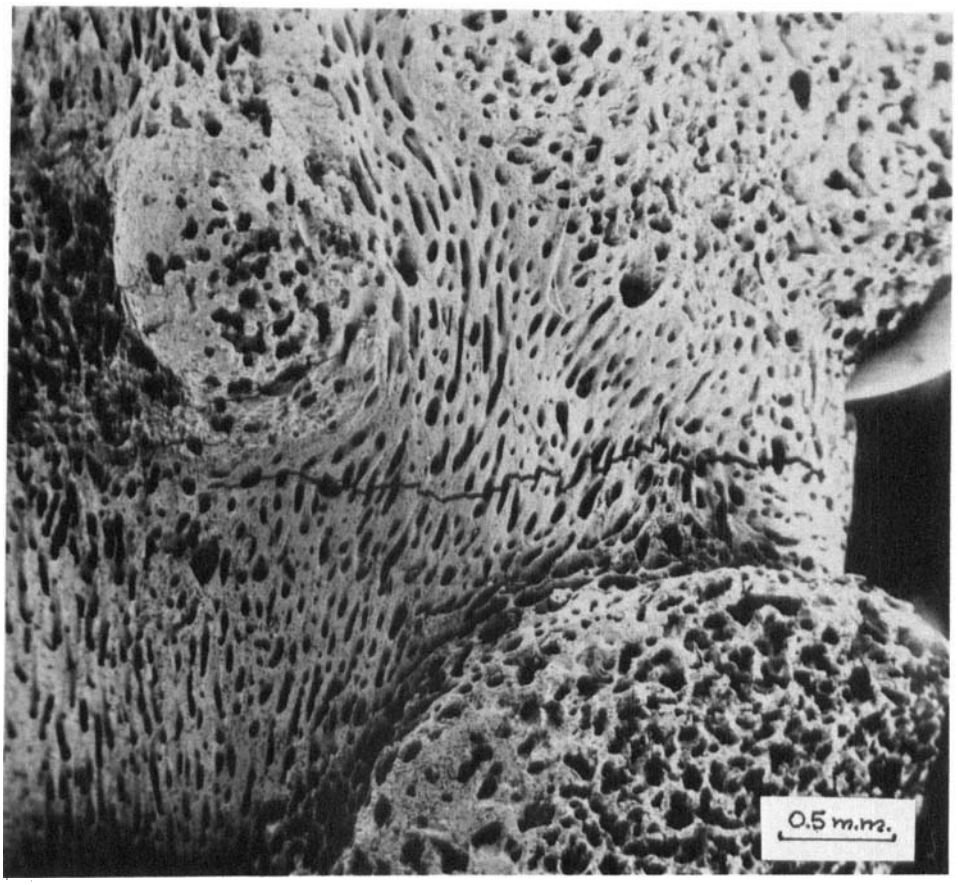


Figure 4. Side view of a callus electrically stimulated for 3 weeks with the "current density" of 41 μA/cm².

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