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Bone Changes Due to Pulses of Direct Electric Microcurrent

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Summary. In 26 rabbits, 3 platinum electrodes (anode, cathode and control) were inserted into the medullary cavity of the humerus. In a first series, a generator produced square pulses of 50 microamperes for one second at one second intervals. In a second series, a generator produced 250 microamperes pulses for one second at 9 second intervals. During the intervals the output leads were short-circuited. An important osteogenesis was recorded around the two active electrodes. A few necrotic foci were found around the cathode.

Zusammenfassung. Bei 26 Kaninchen wurden drei Platinelektroden (Anode, Kathode und Kontrollelektrode) in den Markraum des Humerus eingesetzt. In einer ersten Gruppe erzeugte ein Generator Rechteckimpulse von 50 Mikro-Ampere Intensität während 1 sec, gefolgt von einer Pause von 1 sec. In einer zweiten Gruppe erzeugte ein Generator 250 Mikro-Ampere-Impulse während 1 sec mit einer Pause von 9 sec. Während den Pausen wurden die Elektroden kurzgeschlossen. Eine ausgedehnte Knochenneubildung konnte um beide aktiven Elektroden festgestellt werden. Begrenzte Nekrosen traten nur in der Nähe der Kathode auf.

Bone remodeling, according to one of the current theories, is the result of electric microcurrents generated within the bone tissue itself by virtue of mechanical deformation [1, 2]. This theory is supported by a number of experiments which confirm that it is indeed possible to influence osteogenesis by means of electrical stimulation [3–10]. Bassett *et al.* (1964), sent continuous currents of 1, 10 and 100 μA through dog femurs and demonstrated an osteogenic reaction around the cathode. It also became apparent that the current actually passing through the bone decreased with time because tissue resistance increased around the electrodes. Another unwanted, secondary effect that intervenes in this kind of experiment—using *direct* current—is the development of necrosis. Around the anode, necrosis already develops with currents of 3 μA. With stronger currents (of the order of 100 μA) necrosis develops simultaneously around both electrodes.

From the data available at present, it seems that optimum osteogenic stimulation occurs around the cathode with currents of 2.5 to 20 μA [4, 5]. Weigert, 1970, used induced currents of 0.5 to 400 μA and obtained a strong osteogenic reaction of the endosteum around both electrodes.

The present experiments were undertaken in order to verify the effect of microcurrents on bone, but under different conditions. We used pulses of direct current at a slow rate and allowed the tissues to discharge during intervals by short-circuiting the electrodes. This approach, as we shall see, minimizes the necrotizing effect.

Material and Methods

Electric Generator

We chose to stimulate the bone tissues of rabbits with pulses of direct constant current. Several generators were built which produce a constant current during a 1 second period.

A time interval follows (1 or 9 seconds, according to the model) during which the output leads are short-circuited to dissipate the charges accumulated during the forward current period. The fact that the tissues are short-circuited between the constant-current stimulations is the very special characteristic of these experiments (Fig. 1).

The circuit diagram on Fig. 2 shows transistor T_5 which is the constant-current generator. This current is adjusted by R_3 which is about 47 kΩ for 50 μA. Transistor T_4, driven by one leg of the multivibrator T_1 T_2, short-circuits the output at regular intervals. T_4 should have a low short-circuit resistance (30 Ω or less). Such a transistor was not available when we developed the circuit ($R_{\text{short-circuit}} = 330\ \Omega$ for a 2N 5457) so we added T_3 and T_6 to open the current loop when T_4 is shorted. The different possibilities of switching times are chosen by setting R_1, R_2, C_1 and C_2. The use of field-effect transistors in the multivibrator circuit allows low volume timing capacitors to be employed. With $C_1 = C_2 = 47$ nF and $R_1 = R_2 = 35$ MΩ, the "on" time is 1 second and equals the "off" time. The circuit remains very stable within a considerable range of temperatures. The current increases 0.4‰ per °C between +25° C and +40° C and the pulse duration decreases 0.2% per °C for the same temperature change. The battery is a 9 V. portable radio receiver battery, the stability of which is unimportant as regards the performances of the circuit. The output current decreases only 1‰ if the battery drops to 6 Volts and it remains constant within 1‰ if the output load is varied between 120 kΩ and the short-circuited state.

Surgical Technique

Twenty-six adult rabbits were used, weight 2.5 to 4.5 kgs, of these only 15 animals were included in this series. Others were removed for several technical reasons: infections, wire breaks, fracture, misfunction of the electric circuit, unsatisfactory topography of the histological sections.

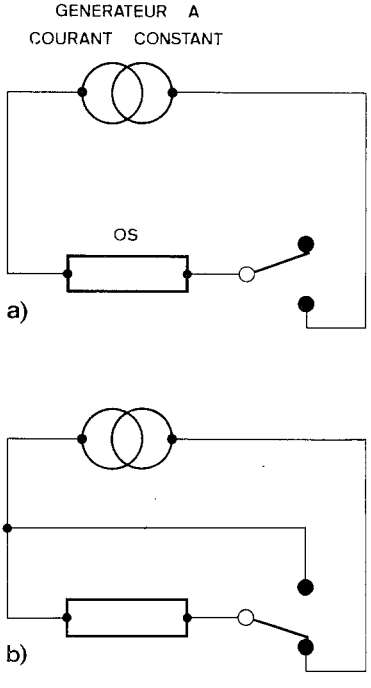

Fig. 1. Basic diagram of the constant-current generator. Type a) which is open-circuited between the stimulating periods allows tissular necrosis. b) used in our experiments provides a short-circuit between the stimulations

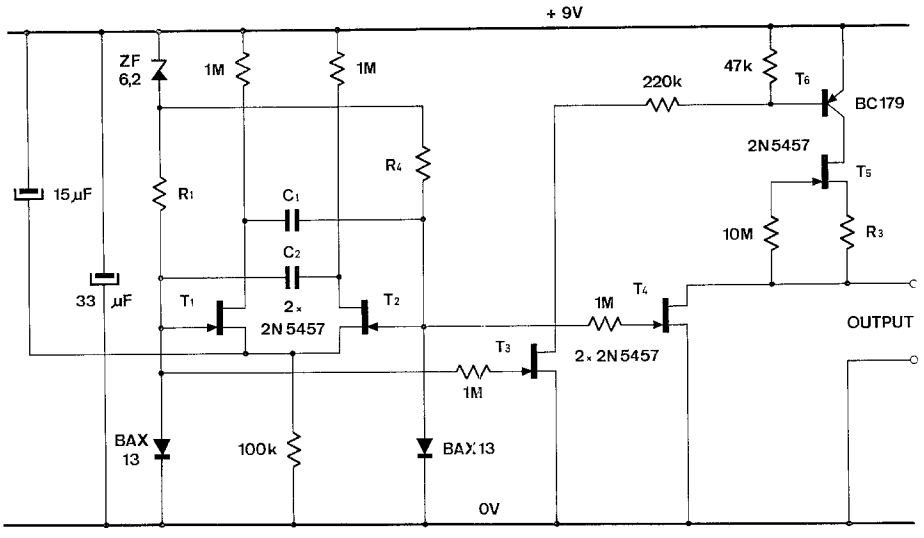

Fig. 2. Circuit diagram of the current generator

Surgical procedures were carried out under anaesthesia (Nembutal i.v. supplemented with ether), and under conditions of asepsis. The skin over a front limb was shaved, and an incision was made along the humerus, long enough to uncover the bone over a length of 5 cm, but without incising the periosteum. Three holes, 1.4 mm in diameter, were drilled into the bone, at 2 cm intervals, and penetrating into the medullary cavity. Three electrodes of 10% iridized platinum (cathode, anode, and test) were fitted into these holes, so that the tip of the electrode was located within the medullary cavity and the end of the isolating sheath was level with the outer surface of the cortex. Both active electrodes were connected to the generator by means of wires of the same metal, insulated with polyethylene and araldite. These wires were maintained tightly against the bone by means of nylon ligatures, they were then run under the skin and brought to emerge between the shoulder blades. To stabilize the wires at this point, and to minimize the hazard of infection, the wires were threaded through a plate of silicone placed under the exit to the skin. They were then connected to the current generator placed in the vicinity of the cage.

The functioning of the electronic apparatus was checked daily. Rabbits were sacrificed every week up to the 6th week. The bones were fixed in 10% buffered formol, decalcified in ethylenediamine-tetra-acetic-acid, embedded in paraffin, cut, and stained with hematoxylin-eosin or according to Van Gieson.

Results

Current Wave Shapes

Fig. 3 shows the diagram of the forward and reverse current in the circuit when a 250 µA generator is used. The tissues behave like a capacitor charged with a constant current and discharged through the contact resistance of the electrodes. The charge of 250 µCoulombs injected during 1 second is restored during 9 seconds (equal shaded areas). At the end of the shorting period, a reverse current of 40 µA subsists. It represents the discharge of batteries (B_1 B_2) formed in the tissues through the contact resistances $R_{s1} + R_{s2}$ and the loss resistance R_c. A prolonged short-circuit would show a decay of this reverse current to a few µA after 4 min. During the forward-current period, this reverse current is counterbalanced by the generator which injects 250 µA to the tissues.

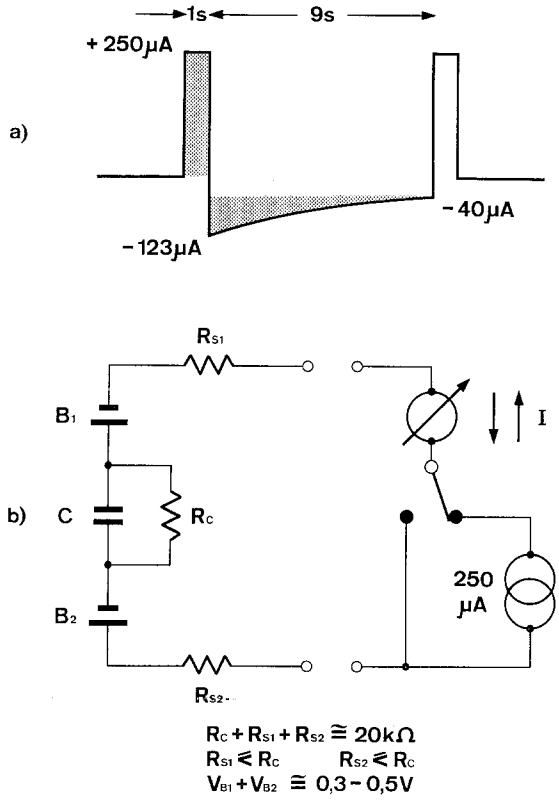

Fig. 3. a) Wave shape of the current. b) Equivalent circuit with: R_{s1} and R_{s2} contact resistance, R_c loss resistance of the capacitor, B_1 and B_2 contact batteries

We have observed similar wave shapes with a generator of 50 μA forward current during 1 second, followed by a 1 second short-circuit. The peak reverse current was —85 μA decreasing to —20 μA after 1 second short-circuit. In that case, the short-circuit time was not quite long enough to allow a full discharge of the 50 μCoulombs. Only about 32 μCoulombs are dissipated during the short-circuit. The generator "250 μA 1 second-short 9 seconds" and the generator "50 μA 1 second-short 1 second" have both the same average forward current.

Histological Changes

The *periosteum* showed a lively osteogenic reaction around both active electrodes and the test electrode as well; this was probably due to the surgical trauma and we will therefore disregard it. Osteogenesis that could be ascribed to the electrical current was observed only in the medullary cavity, and therefore this alone will be considered.

In the *medullary canal*, osteogenesis was observed around both active electrodes. This osteogenesis was of the same order of magnitude with both generators, A and B (it should be kept in mind that in both cases the number of Coulombs administrated is the same), but, on the whole, it seemed that generator A (50 μA

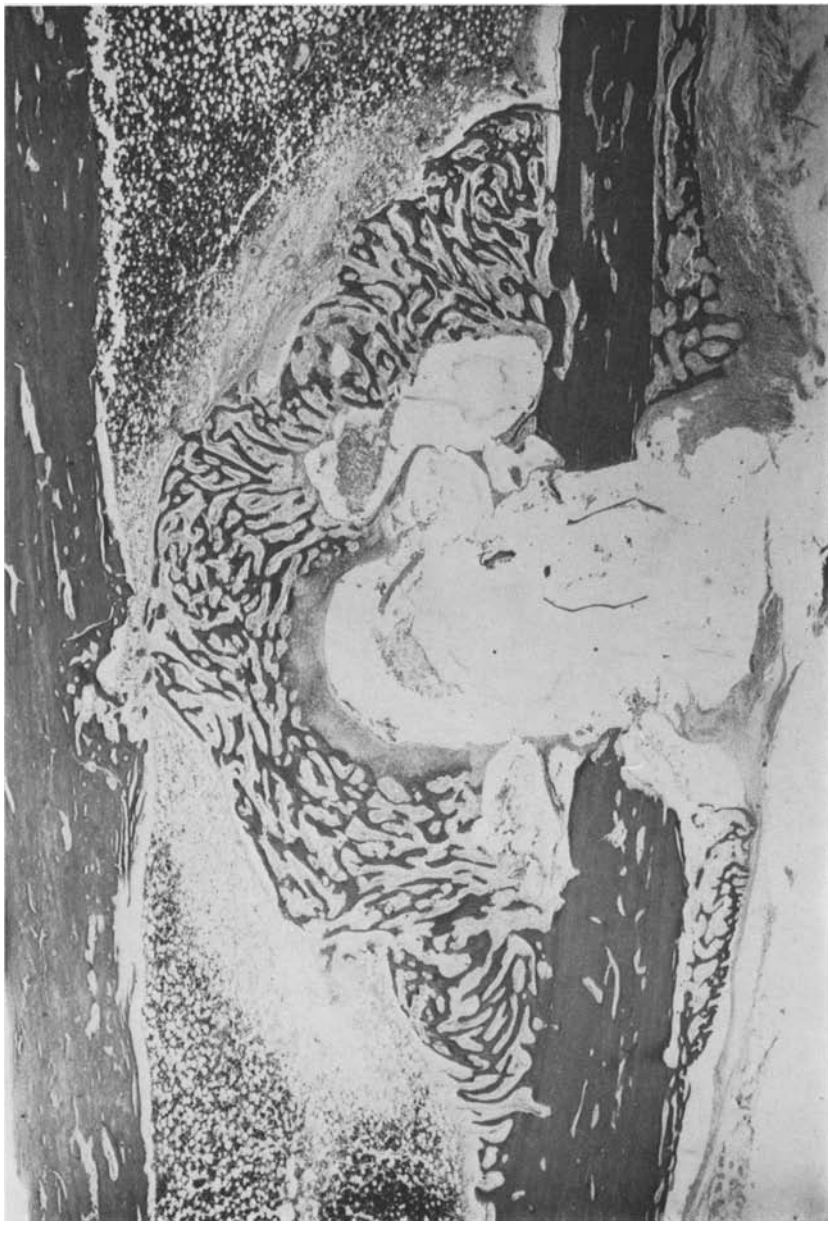

Fig. 4. Endosteal spongious bone formation surrounding the negative electrode. Big holes optically empty are situated in the new cancellous bone near by the central zone occupied by the cathode. These holes corresponded to necrobiosis of the medullary tissue. (Rabbit, 21 days of discontinuous electrical stimulation, 50 microamperes, 1 sec./1 sec. Stain: Van Gieson)

for 1 sec., with 1 sec. interval) induced a more efficient osteogenic stimulation than generator B (250 μA for 1 sec., with 9 sec. interval). The difference was not great; therefore, in describing the histological changes, there will be no need to separate the results obtained with each individual type of generator.

At the beginning of the second week, patches of osteogenesis began to be noticed in the medullary cavity, around anode and cathode, but, not around

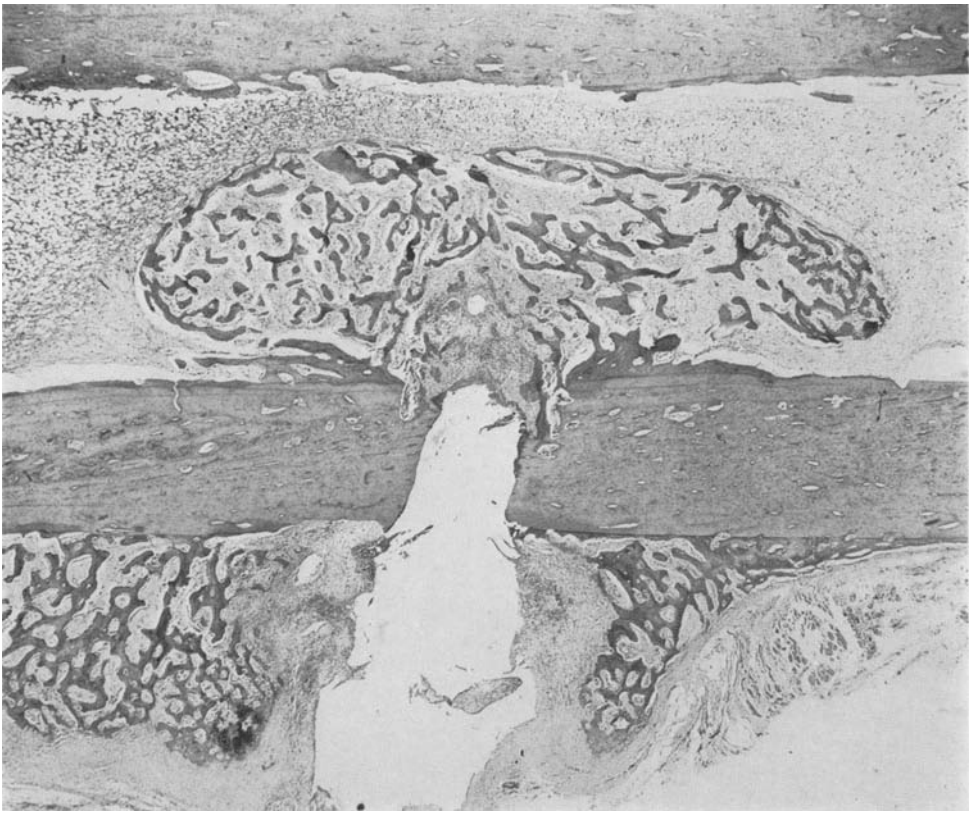

Fig. 5. Around the positive electrode, we note an osteogenic reaction of the endosteum. The periosteal reaction is also important. (Rabbit, 21 days of discontinuous electrical stimulation, 50 microamperes, 1 sec./1 sec. Stain: Van Gieson)

the test electrode. About the third week, this osteogenic reaction reached its maximum; at that time it appeared as a cap of young, cancellous bone, 5–6 mm in diameter around the cathode, 3–4 mm around the anode. This newly formed bone consisted of thin trabeculae without any particular orientation, surrounded by osteoblasts and separated by loose, richly vascularized connective tissue.

The histogenesis of this newly formed bone tissue appeared to follow three patterns:

1. Proliferation of the previously existing endosteal layer.

2. Metaplastic ossification arising in the connective tissue of the bone marrow around active electrodes.

3. Enchondral ossification, arising within a small mass of hyaline cartilage surrounding the tip of the electrode (Fig. 4).

Occasionally, the young trabeculae were reinforced by a superficial layer of lamellar bone, much as in any normal callus.

Around the cap of newly formed bone, the bone marrow appeared mostly hematopoietic, sometimes oedematous and fibrillar. Around the test electrode

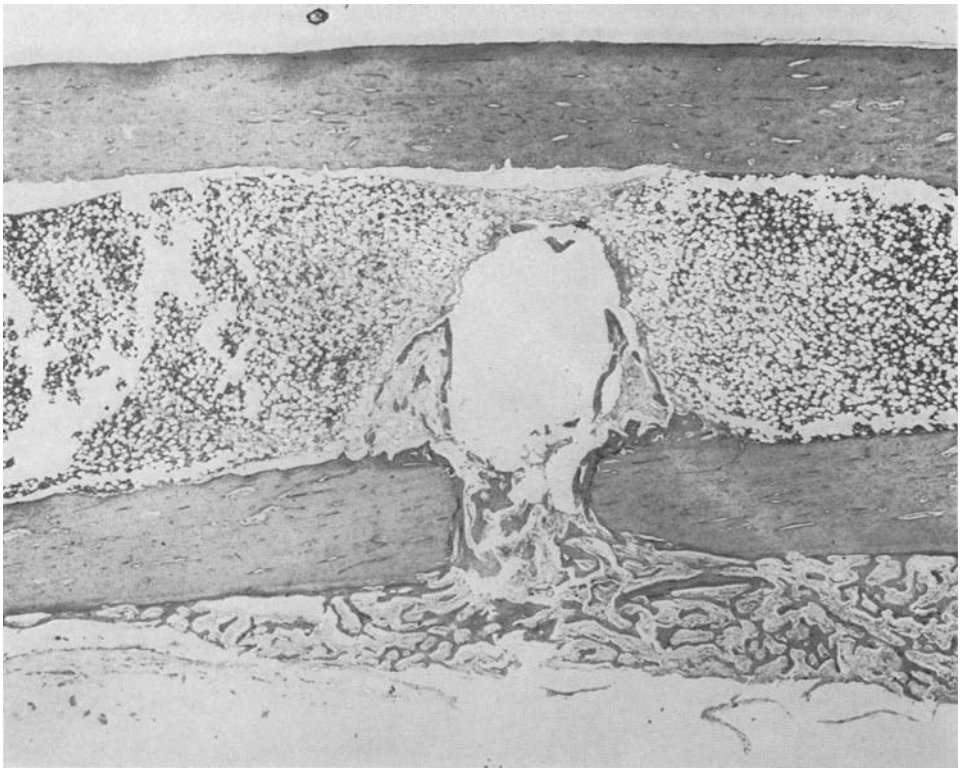

Fig. 6. Around the reference electrode (without any current) of the same animal, no osteogenic reaction is visible

there was only a thin layer of fibrous tissue, surrounded by normal—appearing bone marrow.

Foci of necrosis were observed in the bone marrow in the vicinity of the two active electrodes. These foci of hemorrhagic necrosis appeared after one week as blood filled lacunae or as empty holes located in the osteogenic patch around the cathode. Around the anode, in a few cases, we found a narrow band of granulous necrosis. Those foci of necrosis were slightly more important with 250 μA impulses than with 50 μA impulses.

Discussion

Since Bassett's original experiments (1964) all attempts to produce osteogenesis by means of an electric current have been performed with direct current [3–10]. The principal finding has been that osteogenesis develops only around the cathode, whereas some necrosis occurs around both electrodes.

The principal feature of our experiments has been the use of pulses of direct current, separated by periods during which the tissues were short-circuited. During the rest period, a reverse current appears, which represents approximately 80% of the current supplied during the previous pulse. This means that the bone

marrow (and possibly the surrounding tissues) act as a capacitor. In essence, then, the rationale of the rest period is to give time to this capacitor to discharge. It should be noted that the discharge of the capacitor is not complete, and therefore the electrodes never exchange their polarity. Hence, the fact that we obtained osteogenesis around both electrodes cannot be explained by an alternating function of the electrodes.

When a continuous, direct current is used, osteogenesis appears only around the cathode [3–5] (Bassett, 1964; Friedenberg, 1970). In our system, both electrodes induce osteogenesis, though the cathode induces a slightly greater osteogenic reaction, perhaps 30% greater. This greater "efficiency" of osteogenic induction may be of interest in view of possible practical applications of this technique as a therapeutic procedure.

Another advantage of our system should be noticed. It appears to reduce considerably the extent of necrosis; in our preparations, necrotic tissue was much less prominent than in the material published by other authors [3–6].

On the whole, judging from the efficiency in inducing osteogenesis, and from the extent of necrosis, our circuit type A (50 μA) was preferable to circuit B.

It should also be noticed that we did not observe any stimulation of bone destruction, while Friedenberg *et al.* found an osteoclasia around the anode [5].

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