

## SECTION IV

### LETTER TO THE EDITOR

#### Electrical Osteogenesis: An Analysis

Dear Sir:

Many investigators have studied the growth promoting effects of electric currents on osseous systems from  $10^{-13}$  to  $10^{-4}$  amperes (a).<sup>1-3, 5-17, 20, 21, 23-26</sup> In this communication we wish to discuss the experimental conditions which are associated with an osteogenic response (OR) in this interval, and the mechanisms involved therein.

Table 1 lists an extensive series of studies which describe attempts to produce an OR at the site of implanted electrodes. Where possible, the applied voltage and currents, and the total energy dissipated, are given. The reports have been grouped roughly in order of increasing energy dissipated.

The data in Table 1 show that an OR has been observed at currents of  $0.2 \mu\text{a}$  and  $5,000 \mu\text{a}$ , and at currents of  $3-20 \mu\text{a}$ . On the other hand, currents of  $0.7-4 \mu\text{a}$  have produced no OR, and currents above  $50 \mu\text{a}$  have produced necrosis. The data therefore suggest that different mechanisms produced the ORs in the low and high current range.

In the high range, currents of about  $3-20 \mu\text{a}$ , when applied sufficiently long that the total energy dissipated was greater than about 7 joules, generally elicited an OR. Currents of  $0.7-4 \mu\text{a}$  and less than 7 joules, generally failed to produce an OR, while currents above  $50 \mu\text{a}$  (for 10-14 days) produced necrosis. The assignment of upper and lower limits of current and energy (in the high range) which can elicit an OR is admittedly crude, but appears to have certain advantages. It clearly categorizes the

major reports dealing with ORs, regardless of type, technique of observation, or electrode material.

Electrical osteogenesis in the high range exhibits a threshold, an efficacious region, and blends directly into necrosis. The entire spectrum occurs within a current interval of less than  $50 \mu\text{a}$ . We therefore suggest that injury or tissue irritation resulting from the electrical current is the underlying physical mechanism.

The existence of an OR in bone subject to chronic or acute injury is well known.<sup>22</sup> A variety of nonspecific stimuli (mechanical, thermal, chemical) are transduced by the animal into a biological signal which initiates cellular proliferation and bone production. It appears that the most parsimonious explanation of the OR in the  $3-20 \mu\text{a}$  interval is that the applied current is simply another form of nonspecific stimuli capable of eliciting an OR. The stimulus may be electrolysis<sup>4, 18</sup> of tissue fluids, although there is some contrary evidence.<sup>17</sup>

The OR observed in the low range<sup>3, 10</sup> cannot reasonably be attributed to injury from electrical current, and may be a direct cellular effect such as that postulated to arise from the piezoelectric currents of bone.<sup>19</sup>

Sincerely yours,

ANDREW A. MARINO, PH.D.\*  
*Research Biophysicist*  
*Veterans Administration Hospital*  
*Assistant Professor*  
*Department of Orthopedic Surgery*  
*Upstate Medical Center*  
*Syracuse, New York 13210*

\* Reprint requests and correspondence to: Andrew Marino, PhD., Veterans Administration Hospital, Department of Orthopedic Surgery, Syracuse, New York 13210.

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TABLE 1. Reported Attempts to Produce Electrical Osteogenesis at Implanted Electrodes in Mammals. Occurrence (non-occurrence) of an Osteogenic Response is Indicated by a Plus (minus) Sign.

Ref.	Animal	Bone	Time (days)	Voltage (volts)	Current ( $\mu$ A)	Energy (joules)	Response	Electrode Material
10	Rabbit	Femur	14	—	0.0000002	—	(+)	Teflon
3	Rat	Humerus	3-28	—	0.005	—	(+)	Ag, Pt
2	Dog	Femur	14-21	0.35	0.7	0.3- 0.4	(+)	Pt
8	Rabbit	Femur	10	—	1.0	—	(-)	Stainless
6	Mice	Femur	14	1.35	3**	4.9	(-)	Pt
11	Rabbit	Femur	21	1.3	3	7.1	(-)	Stainless
14	Rabbit	Tibia	21	—	0.2-4.0**	—	(-)	Pt, Au
1	Rabbit	Radius	10-14	—	4-6	—	(-)	Pt
2	Dog	Femur	14-21	1.4	2-3	4.2- 6.3	(+)	Pt
21	Dog	Femur	21	1.4	3	7.6	(+)	Pt
20	Rabbit	Femur	21	1.4	3*	7.6	(+)	Pt
26	Dog	Ear	56	1.4	2.5	16.9	(+)	—
15	Rabbit	Femur	45-195	0.150	8.5**	4.9-21.5	(+)	Pt
23	Rabbit	Humerus	21	0.5**	25.0**	22.7	(+)	Pt
17	Human	Tibia	125	0.55	3.9	23	(+)	Pt
9	Rabbit	Fibula	18	—	10	—	(+)	Stainless
24	Sheep	Various	42	—	10	—	(+)	Pt
14	Rabbit	Tibia	21	—	10-20**	—	(+)	Stainless
8	Rabbit	Femur	10	—	5-20	—	(+)	Pt, Au
1	Rabbit	Radius	10-14	—	15-20	—	(+)	—
25	Rabbit	Tibia	31-77	—	5	—	(+)	Pt
16	Rabbit	Tibia	21-42	—	2.5-40	—	(+)	Pt
12	Rabbit	Femur	21	2.8	—	—	(+)	Pt
5	Human	Various	84	—	10-20	—	(+)	Stainless
13	Rabbit	Calvarium	21	—	10-50	—	(+)	Pt
7	Human	Spine	35-112	—	20	> 100	(+)	Ti
1	Rabbit	Radius	10-14	—	—	—	(+)	Pt, Au
8	Rabbit	Femur	10	—	50-100	—	(+)	Stainless

\* Estimated, based on ref. 3.

\*\* Average.

and  
**ROBERT O. BECKER, M.D.**  
*Medical Investigator*  
*Veterans Administration Hospital*  
*Syracuse, New York*  
and  
*Research Professor*  
*Upstate Medical Center*  
*Syracuse, New York*

## REFERENCES

1. Anisimov, A. I.: Actions of direct current on bone tissues, *Bull. Eksp. Biol. Med.* 78:100, 1974.
2. Bassett, C. A. L., Pawluk, R. J., and Becker, R. O.: Effects of electric currents on bone *in vivo*, *Nature* 204:652, 1964.
3. Becker, R. O.: Stimulation of partial limb regeneration in rats, *Nature* 235:109, 1972.
4. Brighton, C. T. and Friedenberg, Z. B.: Electrical stimulation and oxygen tension, *Ann. N. Y. Acad. Sci.* 238:314, 1974.
5. —, —, Zemsky, L. M., and Pollis, R. P.: Direct current stimulation of non-union and congenital pseudoarthrosis, *J. Bone Joint Surg.* 57-A:368, 1975.
6. Crelin, E. S. and Dueker, D. K.: The response of the femur to trauma, a foreign body, and a direct electrical current in mice, *Yale J. Biol. Med.* 43:71, 1970.
7. Dwyer, A. F. and Wickam, G. G.: Direct current stimulation of spinal fusion, *Med. J. Aust.* 1:73, 1974.
8. Friedenberg, Z. B., Andrews, E. T., Smolenski, B. J., Pearl, B. W., and Brighton, C. T.: Bone reaction to varying amounts of direct current, *Surg. Gynecol. Obstet.* 131:894, 1970.
9. —, Roberts, P. G., Didizian, N. H., and —: Stimulation of fracture healing by direct current in rabbit fibula, *J. Bone Joint Surg.* 53-A:1400, 1971.
10. Fukada, E. and Takamatsu, T.: Callus formation by electret, *Jap. J. Appl. Physiol.* 14:2079, 1975.
11. Hambury, H. J., Watson, J., Sivyer, A., and Ashley, D. J. B.: Effect of microampere electric currents on bone *in vivo* and its measurement using strontium-85 uptake, *Nature* 231:190, 1971.
12. —, —, Toole, A., —, and —: Interdisciplinary approaches in electrically mediated bone growth studies, *Ann. N. Y. Acad. Sci.* 238:508, 1974.
13. Hassler, C. R., Rybicki, E. F., Rotaru, J. H., and Hughes, K. E.: The effects of electrode configuration and calculated current density upon electrically augmented bone healing in rabbit calvaria, *Proc. Ann. Conf. Engl. Med. Biol.* 16:297, 1974.
14. Hummel, J. C., Friedenberg, Z. B., Booth, R. E., and Brighton, C. T.: The response of non-traumatized bone to pulsed direct current of various frequencies, *Trans. Orthop. Res. Soc.* 1:204, 1976.
15. Ilfeld, F. W., Weinberg, C., Rosen, V., and August, W.: Direct current induced mosaic bone architecture, *Clin. Orthop.* 99:298, 1974.
16. Klems, H., Venohr, H., and Weigert, M.: Stimulierung des Langenwachstums von Rohrenknochen durch elektrischen Gleichstrom; Szintigraphische Untersuchungen an der Kaninchentibia, *Arch. Orthop. Unfall-Chir.* 81:285, 1975.
17. Lavine, L. S., Lustrin, I., Shamos, M., Rinaldi, R., and Liboff, A.: Electric enhancement of bone healing, *Science* 175:118, 1972.
18. —, —, —, and —: On electrical conduction in living bone, *Clin. Orthop.* 106:330, 1975.
19. Marino, A. and Becker, R. O.: Piezoelectric effect and growth control in bone, *Nature* 228:473, 1970.
20. Minikin, C., Poulton, B. R., and Hoover, W. H.: The effect of direct current on bone, *Clin. Orthop.* 57:303, 1968.
21. O'Connor, B. T., Charleton, H. M., Curry, J. D., Kirby, D. R. S., and Woods, C.: Effects of electric current on bone *in vivo*, *Nature* 222:162, 1969.
22. Pease, C. N.: Local stimulation of growth of long bones, *J. Bone Joint Surg.* 34-A:1, 1952.
23. Richez, J., Chamay, A., and Bieler, L.: Bone changes due to pulses on direct electric microcurrent, *Virchows Arch. Abt. A. Path. Anat.* 357:11, 1972.
24. Weigert, M., Werhahn, C., and Mulling, M.: Beschleunigung der knockernen Heilung von Osteotomien an Schafen durch elektrischen Strom, *Z. Orthop.* 110:959, 1972.
25. Werhahn, C. and Weigert, M.: Die Stimulierung der primären Knochenheilung durch elektrischen Gleichstrom, *Z. Orthop.* 112:1226, 1974.
26. Yarrington, C. T. and Jaquiss, G. W.: Electrical control of bone growth in ossicles, *Arch. Otolaryng.* 89:856, 1969.