# ELECTRICAL STIMULATION OF ARTICULAR CARTILAGE REGENERATION*

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The fact that bone is stress electrogenic is well substantiated.[1] Becker and colleagues[2] have proposed that this property is the biological signal that regulates Wolff's law, whereas others[1,2] have observed osteogenic responses to electrical voltages and currents. Becker and Murray[3] detected electrical control signal characteristics in fractured long bones. The above findings and the work of Smith,[25] which involved the use of galvanic stimulation, led to the use of bimetallic devices in rats by Becker and Spadaro.[4] Amputated rat extremities at the midhumeral level responded to electrochemical stimulation with partial limb regeneration. The regenerates demonstrated distal growth of an epiphysis and growth plate, with evidence of developing articular cartilage (FIGURE 1). It was believed that similar devices might be used to stimulate the regrowth of specific damaged tissues, such as articular cartilage.

When joint surfaces are damaged in mammals, the common repair response is to fill the defect with fibrocartilage.[9,17,20–22] Some authors have reported limited attempts at repair by proliferation of surviving articular cartilage cells[5,6,8] and by metaplasia of marrow elements.[12,23,24] The increased biochemical activity of hyaline cartilage cells[11,13,18,26] subjected to arthritic changes and the proliferation of hyaline cartilage cells *in vitro*[10,14,15,19] support the latter observations.

It seemed reasonable, therefore, to attempt to stimulate the repair tissue that responds to articular cartilage defects by electrochemical means. This communication describes preliminary results of attempts at the stimulation of articular cartilage repair by electrical means.

## METHODS AND MATERIALS

The initial experiments involved the implantation of a bimetallic silver platinum electrochemical device similar to that used by Becker and Spadaro[4] (FIGURE 2).

Four-millimeter, circular, full-thickness defects were created through the articular cartilage to subchondral bone on the weight-bearing surface of the lateral femoral condyles of 6-week-old male New Zealand white rabbits. Retrograde drill

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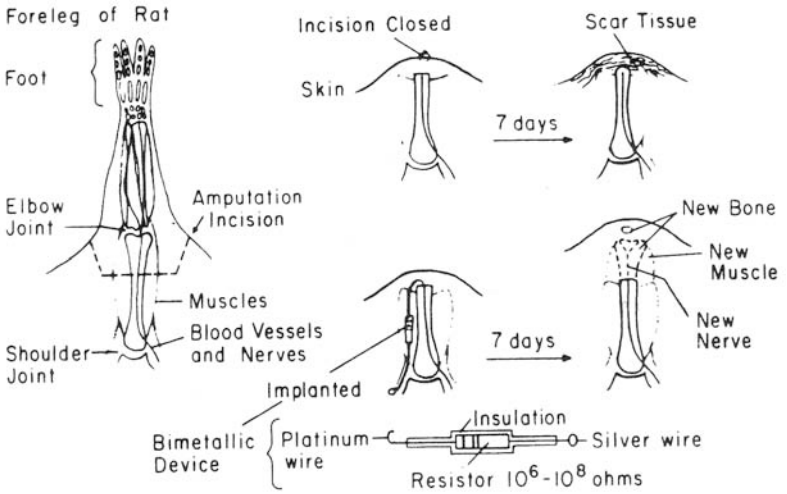


FIGURE 1. *(Left)* Sketch of a rat forelimb that demonstrates the level of amputation through the humerus; *(upper right)* representation of control that shows progression of healing at one week; *(middle right)* experimental model that depicts progression of healing with regeneration at one week; *(lower right)* silver-platinum bimetallic device used for this work. (From Becker & Spadaro.[4])

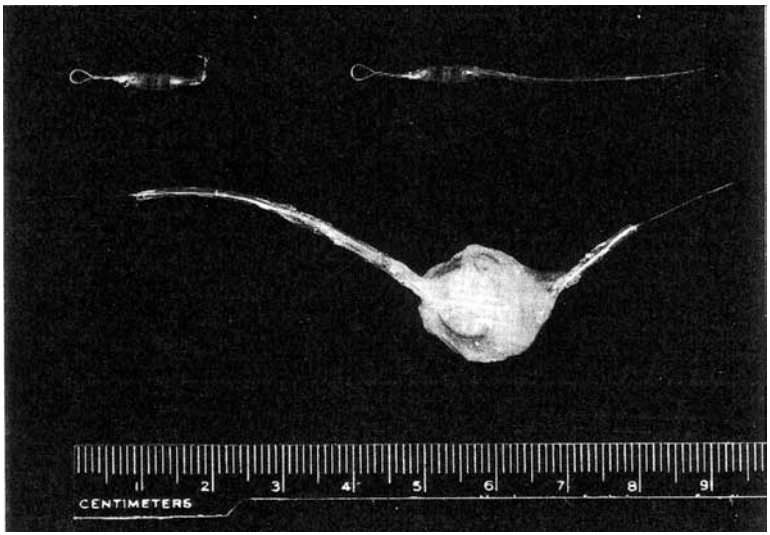


FIGURE 2. *(Upper left)* Bimetallic device used in limb regeneration studies; *(upper right)* bimetallic device used in articular cartilage studies; *(middle)* dc battery-operated device used in articular cartilage studies.

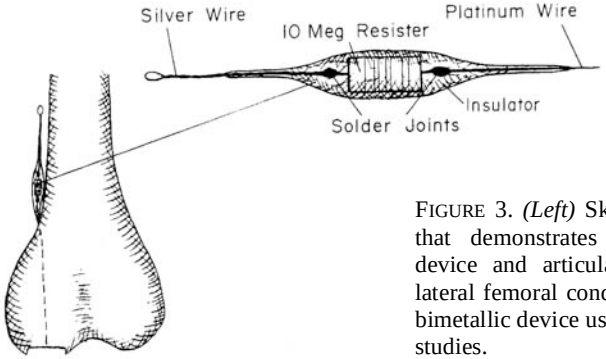


FIGURE 3. *(Left)* Sketch of a distal femur that demonstrates implanted bimetallic device and articular cartilage defect of lateral femoral condyle; *(above)* sketch of bimetallic device used in articular cartilage studies.

holes through the center of the defect were made exiting at the flare of the condyle. The bimetallic devices were inserted with 1-2 mm of uninsulated platinum wire exposed at the surface of the defect (FIGURE 3). The remainder of the device was deep to the musculature and superficial to the cortex of the femur. *In vitro* and *in vivo* studies indicate a potential difference of about 70 mV and an approximate amperage of 6 nA. The specimens were recovered at intervals of 1-9 weeks and compared to control specimens that consisted of defects without metallic implantation but with comparable healing time.

Subsequent experimentation has involved the use of dc battery-operated devices in comparable defects in New Zealand white rabbits. These devices were manufactured from 1.35-V nickel-plated batteries, with silver electrodes soldered to each end of the circuitry. Insulation was accomplished with epoxy lacquer and polyethylene tubing. The circuitry was modified to achieve a range of constant voltage from 15 to 500 mV. These devices were inserted into the 4-mm full-thickness defects in a manner similar to the bimetallic devices. The methods of evaluation included gross inspection, light microscopy, scanning electron microscopy, and transmission electron microscopy after appropriate preparation.

## RESULTS

The controls demonstrated a repair response that consisted of fibrous tissue in the central defect, with progression of the healing tissue to fibrocartilage as healing time progressed from I to 9 weeks (FIGURES 4-6). The defect margins exhibited some cellular proliferation and matrix production, and an occasional specimen displayed encroachment of proliferating hyaline cartilage from the margins of the defect. The specimens treated with bimetallic devices showed an increase in marginal cellular response, as evidenced by increased proliferation and matrix production. Seventy-one percent of the experimental specimens revealed evidence of hyaline cartilage growing from the remaining articular cartilage rim, with as much as 0.5-1 mm of advancement at 3 weeks (FIGURE 7). Scanning electron micrographs of the experimental models demonstrated evidence of peripheral encroachment of advancing repair tissue from the marginal articular cartilage rim, with rounding and thickening of the cartilage rim. These findings were compatible with the image created by serial sectioning of the specimens and evaluation with light microscopy. Transmission electron micrographs of the repair tissue growing from the margin in

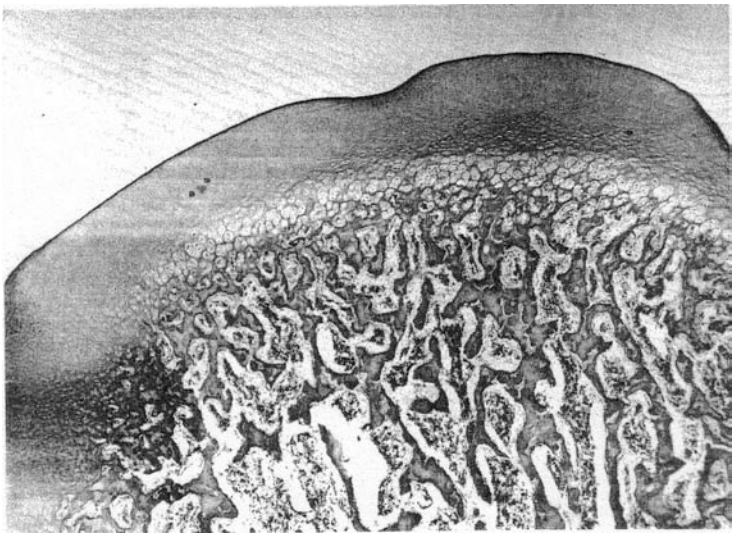

FIGURE 4. Section through unoperated lateral femoral condyle of rabbit that demonstrates rim of articular cartilage over subchondral bone. Stained with hematoxylin and eosin. x 20.

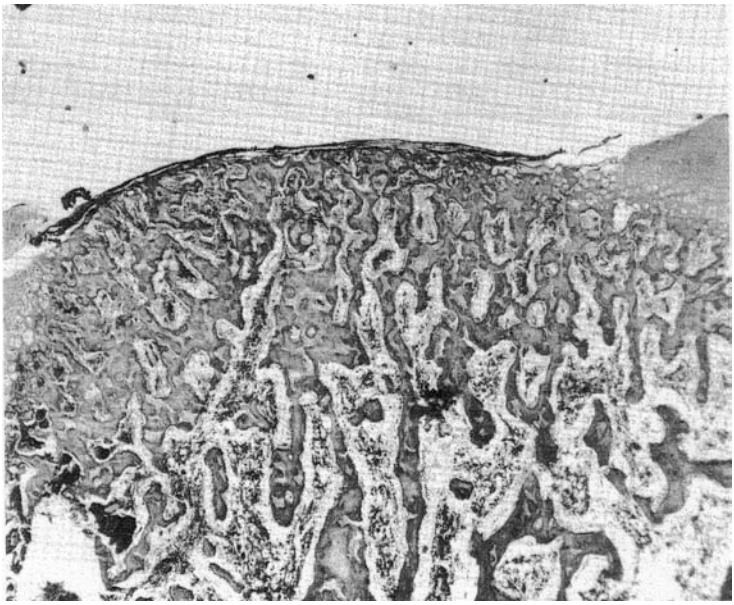

FIGURE 5. Immediate postoperative specimen that demonstrates full-thickness removal of articular cartilage to subchondral bone. Stained with hematoxylin and eosin. x 25.

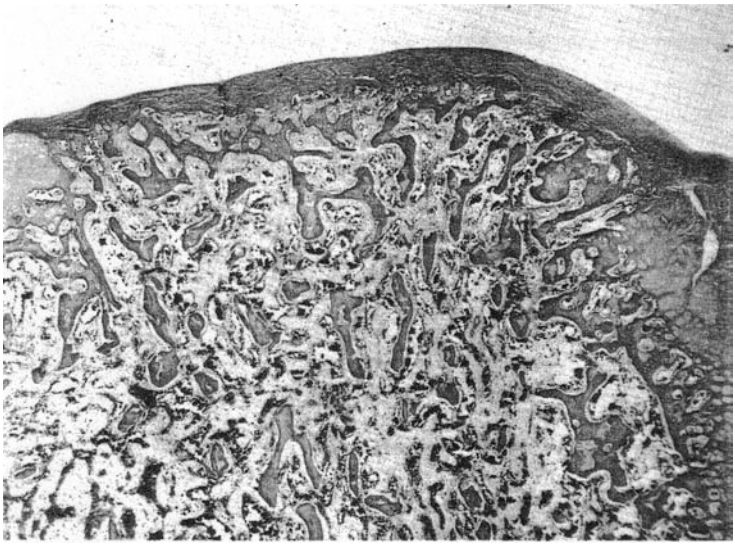

FIGURE 6. Day-14 response seen in controls with fibrous covering of subchondral bone at the base of the defect. Stained with hematoxylin and eosin. x 20.

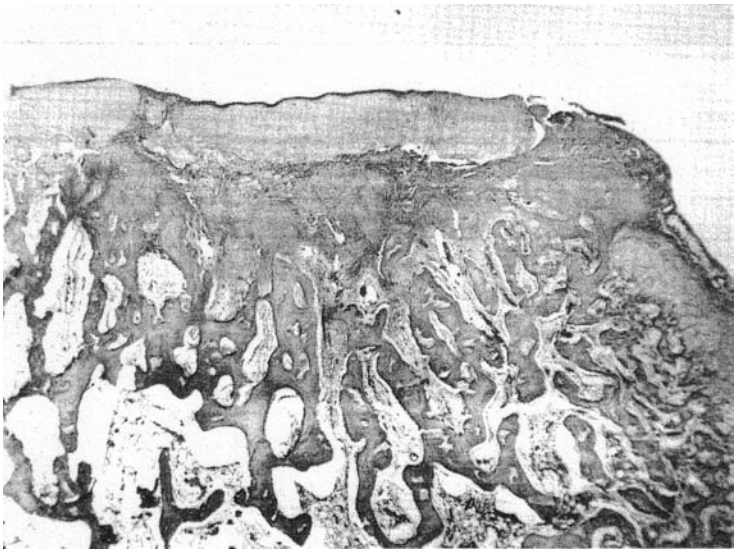

FIGURE 7. Bimetallic device at Day 14 that illustrates a cap of encroaching hyaline cartilage from the margin of the defect. The repair appears to be growing over an area of fibrous tissue covering the subchondral bone. Stained with hematoxylin and eosin. x20.

experimental animals demonstrated chondrocytes and matrix compatible with normal articular cartilage. The initial work with bimetallic devices showed enhancement of the latent potential for repair of articular cartilage defects with hyaline cartilage. The repair response was not totally efficient, however, as revealed by the lack of total healing with articular cartilage.

The dc battery-operated devices have subsequently been used. Preliminary results indicate an increased stimulation of the repair tissue, as evidenced by total healing of two of the experimental defects with hyaline cartilage (FIGURES 8-10). The other specimens demonstrated increased articular cartilage repair response as compared to the control specimens. Work with these devices is currently being continued in our laboratories in an attempt to define electrical parameters and techniques that will allow consistent enhancement of total repair of articular cartilage defects with hyaline cartilage.

## DISCUSSION

Articular cartilage defects characteristically heal with the production of a repair response of fibrocartilage. Various authors[12,23,24] have reported hyaline cartilage repair to a limited extent in a few experimental animals. Our results with bimetallic devices inserted into full-thickness articular cartilage defects demonstrate enhancement of this latent potential for repair with hyaline cartilage. The repair response appears to derive from proliferating chondrocytes at the defect margin, with encroachment over the surface of the central defect. A base of fibrous tissue appears to grow in from the subchondral elements below the capping articular car

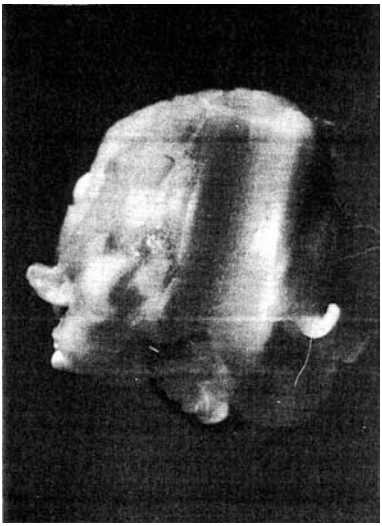

FIGURE 8. Photograph of distal femur with a lateral condyle *(left)* that shows complete closure of the defect. Specimen is from an animal treated with the dc device.

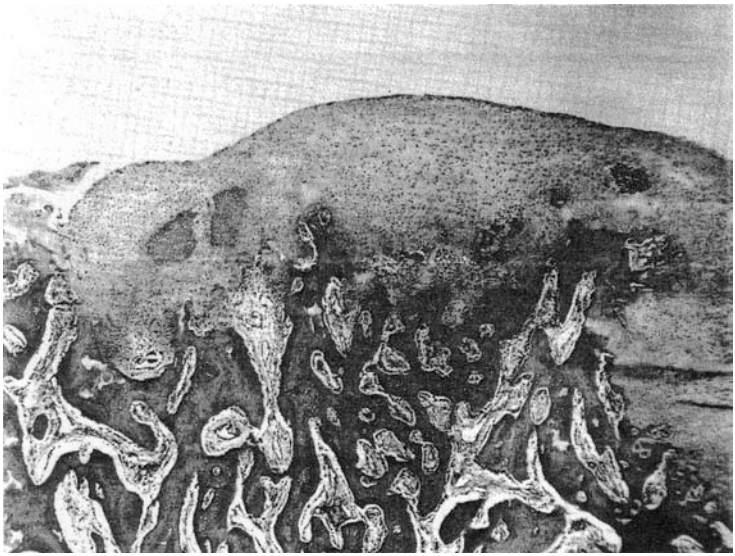

FIGURE 9. Section through specimen treated with dc battery-operated device with complete healing of the defect at Day 17. This section reveals repair tissue compatible with hyaline cartilage. Stained with hematoxylin and eosin. x20.

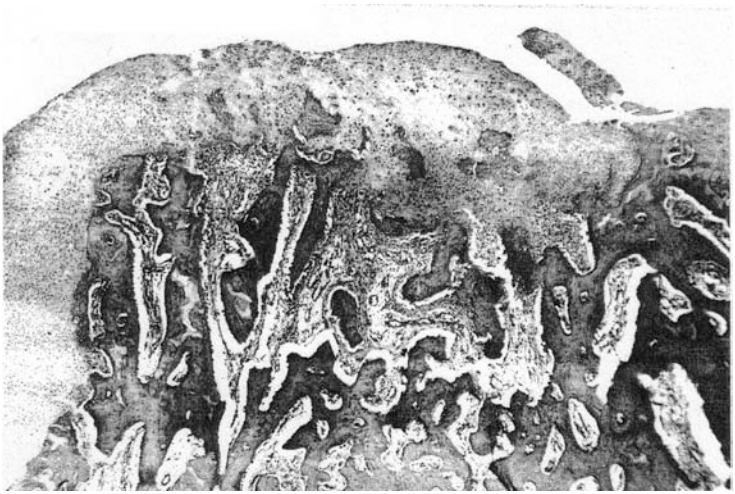

FIGURE 10. Additional section through specimen treated with a dc battery. The specimen again shows complete healing of the defect with hyaline cartilage at Day 17. Stained with hematoxylin and eosin. x20.

tilage. The potential for healing through metaplasia of cells from the subchondral elements has been suggested by another author[24] but not demonstrated in our initial results.

A more efficient means of enhancing repair appears to be possible through the use of dc energy sources. Preliminary results with do devices demonstrate total healing in several specimens, with a repair response that consists of articular cartilage. The evaluation of articular defects and the effect of various electrical devices

on this healing response is still under investigation in our laboratories. We are attempting to define the electrical parameters and techniques that will allow consistent and total repair of articular defects with hyaline cartilage.

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## DISCUSSION

DR. E. L. RADIN: Could you clarify the controls?

DR. BAKER: The majority of the controls showed a fibrous response, sometimes with progression, to fibrocartilage for as long as nine weeks, and there was also some evidence of hyaline repair and proliferation. Roughly 10-15% of the animals demonstrated 1-2 mm of encroachment, but there was never total repair of the defect. The defect is 4 mm, which is essentially the full width of the condyle in these animals.