Experimental Fracture Healing: Evaluation Using Radionuclide Bone Imaging: Concise Communication

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Radionuclide bone imaging was performed in a rabbit model to observe the course of fracture healing and to establish criteria for distinguishing nonunion and delayed healing from normal healing. Sequential gamma-camera images (with pinhole collimator) were collected and subjected to computer analysis. Five groups were established: a) control—immobilization; b) control—immobilization plus periosteal stripping; c) simple fracture—osteotomy; d) delayed union—osteotomy plus periosteal stripping; and e) nonunion—osteotomy, periosteal stripping and polymethyl methacrylate interposed between fracture fragments.

Histographic representation of absolute count rates along rabbit tibias followed a predictable pattern in the simple-fracture and delayed-union groups. They differed only in the time of appearance of phases. The nonunion group demonstrated no recognizable sequential pattern. In this experimental model, serial bone scanning with quantitative data analysis has shown potential for indicating the course of healing in fractures and for serving as a guide to treatment.

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The use of gamma imaging in osseous trauma has so far focused largely on detection and localization of radiographically occult fractures (*1,2*). Attempts have been made to evaluate the course of fracture healing using bone-seeking radiopharmaceuticals, but studies were limited by available instrumentation and radiotracers. In 1961 Wendeberg, using Sr-85 and a 2-inch NaI(Tl) crystal, observed no difference in the activity rates at pseudoarthroses, complicated fractures, and normally healing fractures (*3*). In 1971 Green and coworkers, using rat tibia for their model, found no difference between the Tc-99m albumin and Sr-85 activity in fractures with normal union, delayed union, and nonunion (*4*). Johannsen reported similar results in a clinical study in 1973 (*5*). But Muheim reported serial quantitative Sr-87m uptake measurements in ten human lower-leg fractures. Two of the cases developed nonunion, and both demonstrated patterns of tracer uptake distinguishable from normal healing (*6*).

In 1974 John Stevenson and colleagues used Tc-99m-labeled phosphate compounds to evaluate the potential of several nonautologous bone-grafting materials. The grafts were 2 cm in length. In that study, analysis of serial radionuclide images gave information about the status of a particular graft 3–6 wk before conventional radiographs. It was suggested

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that the method might have clinical usefulness for evaluating osseous repair in other pathologic conditions (7). Velasco et al. (8) applied this approach to the early determination of bone-graft viability in a group of ten patients, with promising results.

Our project was undertaken to determine whether it was possible, using similar techniques, a) to image narrow fracture lines; and b) to distinguish the course of simple and delayed fracture healing from nonunion earlier than by radiograph.

MATERIALS AND METHODS

Adult rabbits were imaged with a gamma camera and pinhole collimator 2 hr after i.v. injection of 0.3–0.5 mCi/kg of Tc-99m-labeled methylene diphosphonate, with accumulation of 100,000 counts. A data analyzer was used to produce histograms of the collected information. Later a computer became available. The animals were divided into five groups of three each: two control groups; a simple-fracture group; a delayed-healing group; and a nonunion group.

One control group underwent surgery consisting of an axial linear incision of the skin, soft tissue, and periosteum over the midtibial shaft. Marking pins were then placed percutaneously through the distal femur and ankle. Immobilization was provided by a plaster cast from midfemur to ankle. In the second control group, periosteal stripping of the middle third of the tibial shaft was added. The simple-fracture group was subjected to transverse osteotomy through the midshaft of the tibia followed by apposition, re-alignment, pin placement, and fixation as in the control group. In the delayed-healing group, after osteotomy the periosteum was circumferentially stripped as in the second control group. The nonunion group underwent the same procedures plus surgical reaming of the endosteal canal for a short distance. After this, polymethyl methacrylate bone cement was interposed between the fracture ends. Pin placement and fixation were carried out as in the previous groups.

After standard scans, histographic representations of the count rates along the axis of the limb were generated. The X axis of the histogram represents the axial length of the tibia from knee to ankle. The Y axis represents the count rate at each point along the bone. The fractures were situated in the midtibial shaft, approximately at the midpoint between knee and ankle activity spikes. Reproducible orientation of scan images was insured by the use of an external fixation device that was keyed to the pins in the immobilizing plaster cast. Corresponding radiographs of the limb were obtained at the time of each scan to assess the spatial relationship of fracture fragments and to determine whether calcified callus was present. Baseline preoperative images were obtained. Initially, the first postoperative image was recorded 3–4 days after surgery, but the hyperemia associated with the procedure made it impossible to distinguish the radioactivity in the bone from that in the surrounding soft tissues. Successful imaging was carried out 7 days after surgery and at 7- to 10-day intervals until healing or nonunion was established clinically. At the completion of the investigation, the rabbits were autopsied to confirm this clinical impression.

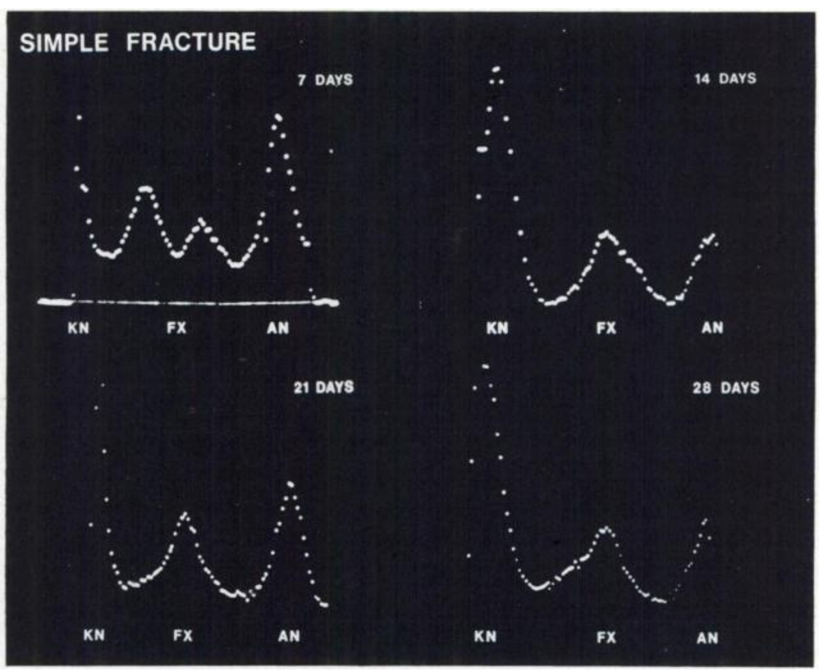

FIG. 1. Histograms along tibia at 7, 14, 21, and 28 days following fracture. There is prompt coalescence of two peaks at fracture site into single peak indicating successful bridging of fracture by healing bone. KN = knee, FX = fracture, AN = ankle.

RESULTS

In both control groups, no increase in radionuclide localization was observed along the tibial shafts in any of the subjects. In the simple-fracture group a recognizable pattern of histographic changes was observed (Fig. 1). At approximately 7 days, a double peak of increased tracer activity was noted at the site of osteotomy. By 14 days the two peaks had coalesced into a single peak in two of the group's three rabbits. Radiographs of the limb did not reveal any calcified callus at the same time. By 21 days the histographic peaks were slightly narrower and calcified callus was present in two rabbits. At 28 days there was little alteration in the radionuclide image pattern, and calcified callus was present in all three rabbits. Healing was judged adequate clinically at 28 days in all the rabbits. Bony union was confirmed postmortem. The third animal in the group—the rabbit exhibiting relative delay in appearance of calcified callus—showed a persistent biphasic tracer activity peak at the osteotomy site at 28 days, but there was a clear trend toward coalescence of the peaks.

In the delayed-healing group, which was subjected to periosteal stripping at the osteotomy site, a similar pattern of tracer activity was observed. In two of the rabbits there was a 7-day delay in the appearance of the biphasic activity peaks, and a similar delay was seen in the time of appearance of calcified callus. The third rabbit in this group began to show a biphasic peak at 24 days and demonstrated the characteristic pattern at 35 days. Calcified callus was not observed until 56 days. At the time of cast removal, bony union had occurred in all three rabbits.

The nonunion group demonstrated a less uniform pattern of tracer localization (Fig. 2). In two of the rabbit limbs, activity peaks of variable intensity developed along the tibial shafts at sites distant from the plane of osteotomy. These peaks corresponded to areas of intense periosteal reaction demonstrated by radiograph. The wide separation of activity peaks, and marked variation in their intensity, persisted until 60 days when the animals were killed and nonunion confirmed clinically and by postmortem examination. In a third rabbit in the nonunion group, multiple low-intensity spikes of tracer activity developed along the tibial shaft. Location of peaks was not constant and there was no observable trend toward coalescence. Nonunion was also confirmed in this animal at the completion of the study.

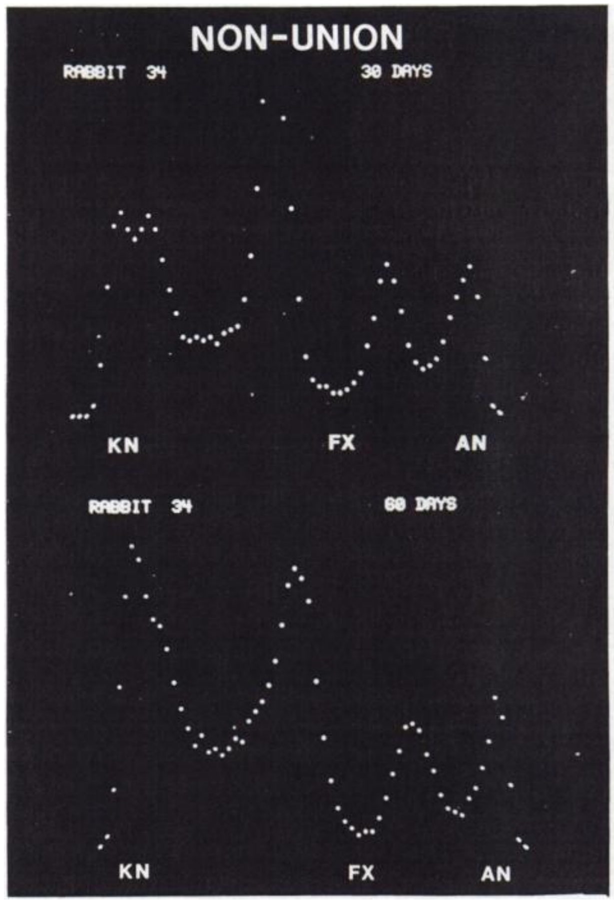

FIG. 2. Histograms through tibia in nonunion animal, 34 and 60 days after surgery. Note persistence of two peaks at the fracture ends and failure of healing bone to bridge the gap. Abbreviations as in Fig. 1.

DISCUSSION

In the animal model studied, the surgically produced fractures that healed by bony union followed a reproducible sequence of radiotracer localization. The pattern was similar for models of simple fracture and delayed healing. The latter differed only in time of appearance of the various stages. This is in contrast to the pattern in the nonunion model. The appearance of a double activity peak at the fracture site, subsequently coalescing, was a predictor of healing that preceded the appearance of radiographically observable signs.

Although this technique has not yet been studied in a clinical setting, it seems to have excellent potential for investigation of the rate of spontaneous repair of fractures, as well as influences on osseous healing in general. For example, it may be possible using serial radiotracer examination to offer predictive information in cases of suspected post-traumatic nonunion. If borne out in clinical trials, the finding of a double activity pattern that is coalescing should suggest that the fracture is likely to heal by bony union. Conversely, no dominant activity peaks, or a noncoalescing pattern in serial examinations, may be an indicator of eventual nonunion. In such cases, early therapeutic intervention should reduce associated morbidity. Likewise, therapeutic expedients that have been proposed to accelerate healing (such as electrical stimulation) could be objectively evaluated using this simple noninvasive technique (*9*). Also, mechanical, humoral or other factors that delay or prevent healing could be similarly studied.

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