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FRACTURE HEALING CONTROLLED BY ^{87m}Sr UPTAKE

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Fracture healing is usually supervised by clinical and radiological examinations, which gives information about the stability of the fracture and callus formation. In this way information is obtained about the antecedent healing but not about the active process at the time of examination. The latter can be obtained by using radioisotopes which are deposited by osteoblasts in bone, and which are therefore a measure of osteoblast activity at the time of the examination (Bauer 1958, Bauer & Ray 1958, McCready et al. 1966, Bessler 1967, Bessler 1969).

The purpose of the present study was to measure by external counting the process of healing in a variety of fractures, after intravenous injection of ^{87m}Sr, to ascertain whether there was heterogeneity in the healing process, and whether complications arising during healing could be detected earlier with the method described than with the usual clinical and radiological examinations.

METHOD

After intravenous injection of 10 μc ^{87m}Sr/kg the radio-activity was measured both over the fracture and over the symmetrical position on the normal extremity.

The activity was registered continously by a point recorder for 1–1½ hours after injection. Two 3 inch sodium iodide crystal scintillators were used, each shielded with a cylindrical collimator (internal diameter 8 cm, distance from crystal to collimator edge 10 cm). The distance from the body surface to the collimator was 5 cm. To ensure consistent alignment in consecutive assays of the same patient, the position of the fracture was marked corresponding to the roentgenograms taken at the first examination.

^{87m}Sr uptake was measured at intervals during the healing process. The first measurement was made as early as possible—as a rule 2 to 3 days after the initial lesion— subsequently at 1 week and later at ½, 1, 2, 3 and 6 month intervals.

The ratio (F/N) of activity over the fracture (F) to activity over the symmetrical position in the normal extremity (N) one hour after injection, was used to evaluate the material. The activity was expressed directly in counts per second without

Table 1. Classification of the material by fracture type and type of healing.

	Number of patients	Healing		
		Uncomplicated	Complicated	Special cases
Fractura colli femoris	5	4	1 pt: caput necrosis with total collapse of caput femoris	
Fractura corporis femoris	9	6	1 pt: abscess in cicatrix after osteosynthesis	1 pt: op. for pseudoarthrosis (checked from time of operation). 1 pt: osteitis in femur (checked day 480 to day 840 after trauma).
Fractura genus	5	5		
Fractura cruris complicata	7	4	1 pt: pseudoarthrosis. Fracture consistently unstable, without callus formation. 2 ptt: Infection in cicatrix after osteosynthesis (one received skin transplantation in the area at a later date).	
Fractura cruris	7	3	1 pt: thrombophlebitis 1 pt: infection in cicatrix after osteosynthesis 1 pt: delayed healing (clinically healed day 435)	1 pt: bilateral fractures of crura
Fractura malleoli	3	2		1 pt: osteitis tali (checked day 216 to day 474 after trauma)
Fractura antebrachii	3	3		
Total	39	27	8	4

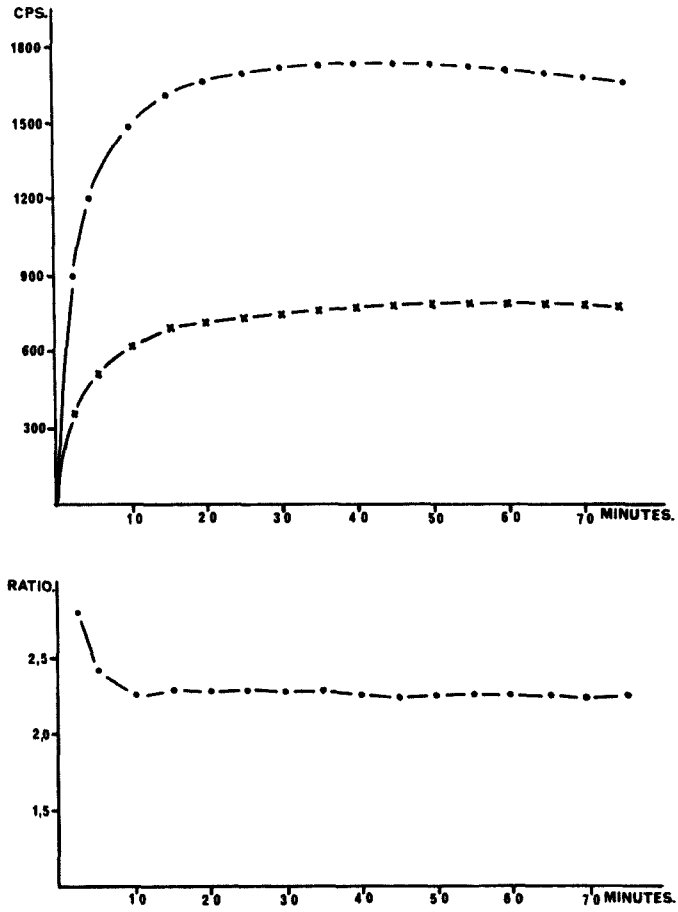

Figure 1. Top: *Activity over fracture (F) and symmetrically over the opposite normal extremity (N) during the first hour after injection with* ^{87m}Sr *(Fracture · — · Normal* × — ×*).* Bottom: *Ratio (F/N) of the activity over fracture and symmetrically over the opposite normal extremity during the first hour after injection with* ^{87m}Sr.

correction for background, which was negligible compared with the activity obtained (10^3 to 10^4 cps).

Plaster casts reduced the counts by less than 1 per cent and their effects were therefore disregarded.

Some patients were injected with ^{99m}Tc labelled albumin together with the ^{87m}Sr dose. As a dual channel system for each detector was not available, the measuring range was alternated at short intervals between ^{99m}Tc and ^{87m}Sr energy maxima (0.142 MeV and 0.388 MeV respectively).

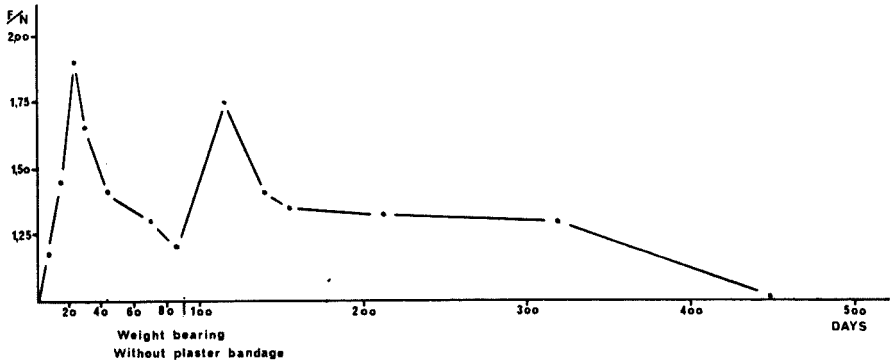

Figure 2. The ratio (F/N) of ^{87m}Sr activity over fracture and symmetrically over the opposite normal extremity 1 hour after injection during the healing period in a patient with fractura cruris.

MATERIAL

39 patients (20 women and 19 men) were studied in a total of 409 assays. The patients had an average age of 44 years (range 15 to 79 years), were followed up from 38 to 570 days (average 269 days), and assayed from 6 to 16 times. Classification of the material by fracture type together with some particulars of the healing process are given in Table 1.

RESULTS

In all 409 assays there was an increase in activity after injection of ^{87m}Sr both over the fracture and symmetrically over the normal extremity. The increase was always greatest over the fracture. The ratio (F/N) of the two activities either increased or decreased during the first 15 to 20 minutes after injection, but subsequently became constant (Figure 1).

In all 27 patients with uncomplicated healing F/N increased during the first period following trauma, and then decreased uniformly, giving rise to a maximum—the initial maximum (IM). In 25 of these 27 patients a second increase and decrease was observed after weight-bearing without cast immobilisation, giving rise to a second maximum —the stress maximum (SM). Figure 2 shows as an example the variations in F/N during healing in a patient with fractura cruris.

For the material as a whole, IM occurred between day 8 and day 32 after the initial trauma or after any osteosynthesis. For the individual fracture types, IM occurred on average between day 18 and day 22 (Figure 3) and varied less than for the material as a whole. There was

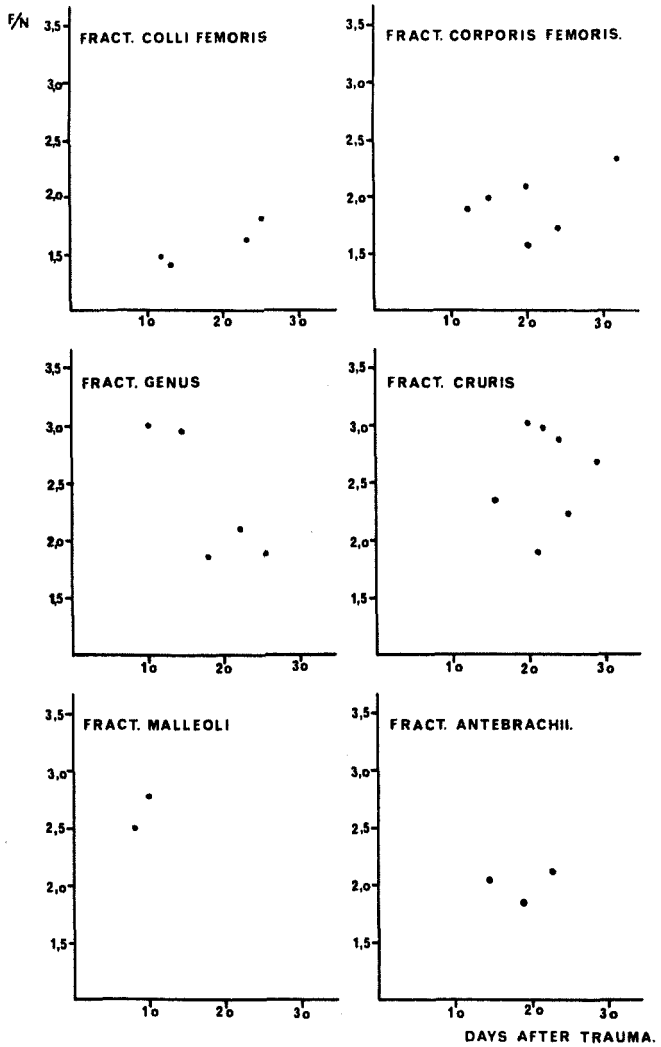

Figure 3. The ratio (F/N) of ^{87m}Sr activity over fracture and symmetrically over the opposite normal extremity 1 hour after injection, at the time for initial maximum for the various fracture types in patients with uncomplicated healing.

a clear tendency for IM to occur later with increasing complexity of the fracture (Figure 4).

The relatively large variation in IM values for the individual types of fracture can be seen in Figure 3. There was no relationship between IM values and the complexity of the fracture. On the other hand, the

Figure 4. Histograms of time for initial maximum for fractures grouped according to complexity.

average values of IM for the individual fracture types were higher the more distal the location of the fracture (Table 2).

SM occurred between day 8 and day 45 after weightbearing without plaster bandage (this rather large variation is partly due to the fact that patients, at this often late stage of healing, are only examined at one, two or even three month intervals), and the variation in SM time was considerably less for the individual types of fracture than for the material as a whole (Figure 5). No relationship was found between SM time and the time at which the patient was ambulant without weightbearing on the fracture—with either Thomas Splint, elbow crutches, perambulator or with the limb in plaster; neither were there any other maxima synchronous with these events.

As was the case with IM, SM values varied considerably for the individual types of fracture and the average values of SM were higher the more distal the location of the fracture (Table 2).

Twenty-five patients with uncomplicated healing were followed up after the fractures were healed clinically. The majority were followed for 60 to 180 days—a few even longer. Figure 6 shows F/N at the final check, in relation to time after the fractures were healed clinically.

Complications in fracture healing occurred in 8 patients (Table 1). Large increases in activity over the fracture zone occurred in conjunction with infections in osteosynthetic cicatrices, thrombophlebitis and

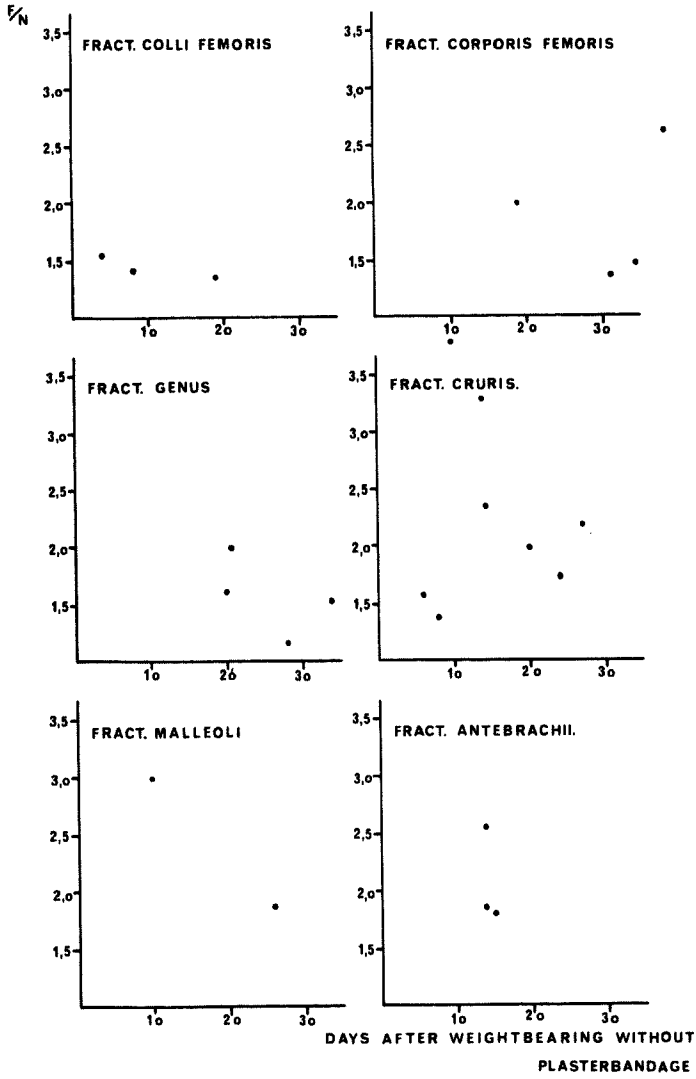

Figure 5. The ratio (F/N) of 87mSr activity over fracture and symmetrically over the opposite normal extremity 1 hour after injection, at the time for stress maximum for the various fracture types with uncomplicated healing.

after skin transplantation. Only in one patient, who developed caput necrosis after fractura colli femoris, was no initial maximum found. Apart from these cases, the same relationships were found for patients with complicated healing as for patients with uncomplicated healing.

Four patients were regarded as special cases. One patient, who was

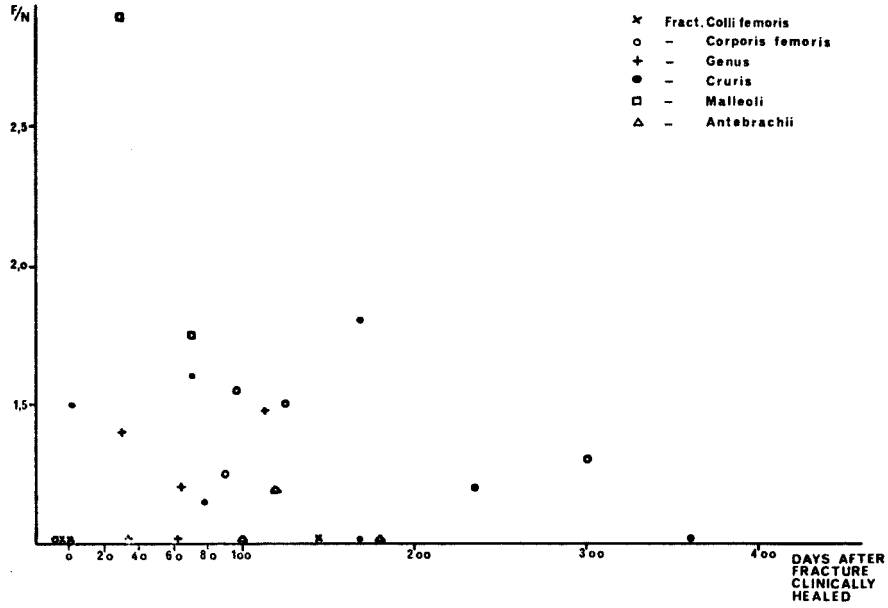

Figure 6. The ratio (F/N) of ^{87m}Sr activity over fracture and symmetrically over the opposite normal extremity 1 hour after injection, at different times after the fracture clinically was healed.

operated for pseudoarthrosis and supervised from the time of operation, exhibited the typical curve (F/N versus time) of a new trauma. Similarly, one patient with a medial fracture in one leg and a distal fracture in the other leg, exhibited the typical curve with distinct maxima, although the values of the maxima were lower than those of patients with fractures on one side only. Finally, two patients with,

Table 2. Average values for initial maximum and stress maximum for the various fracture types in patients with uncomplicated healing.

	Initial maximum	Stress maximum
Fractura colli femoris	1.65	1.45
- corporis femoris	1.90	1.95
- genus	2.35	1.60
- cruris	2.60	2.30
- malleoli	2.65	2.45
- antebrachii	2.00	2.15

respectively, osteitis femoris and osteitis tali arising from fractures, had uniformly decreasing values of F/N at the same time as radiologically increasing sclerosis of the bones.

In addition to the increases in F/N described, increases of unknown origin were observed at various times in five patients with uncomplicated healing.

Nine patients in 14 assays were injected with 1 mc ^{99m}Tc labelled ablumin together with the ^{87m}Sr dose. The curves of the activities F and N and the ratios for the two compounds during the first hour after injection were displaced relative to each other, but were otherwise parallel. When patients were checked several times, changes in the ratios for the two compounds were closely related.

DISCUSSION

A considerable haemorrhage usually occurs about the broken surfaces of a fracture. The haematoma is rapidly invaded by capillaries and osteoblasts. The osteoblasts form trabeculae about central canals—hereby forming the osteogenic tissue in which calcium salts are deposited (Watson-Jones 1952, Boyd 1961). This proliferation of osteoblasts can be observed in studies using bone-seeking isotopes—which are metabolised in the organism in the same manner as calcium—as an increase in activity measured over the fracture zone (Bauer & Wendeberg 1959).

The ratio of activity over the fracture to activity symmetrically over the normal extremity varied during the process of healing, having two distinct maxima.

The first maximum was found within the first weeks after trauma, corresponding to an especially large proliferation of osteoblasts at this time (Watson-Jones 1952). This increase in activity shortly after the occurrence of a fracture has also been observed by Myers & Olejar (1963) in a study with ^{87m}Sr healing of tibia and fibula fractures in rats.

The increase in activity is localised in a relatively restricted region (Bauer & Wendeberg 1959), so that it was possible to follow variations during the healing process in a patient with bilateral fractures, one located medially on the one side and the other distally on the opposite side.

With the commencement of stressing, a functional adaptation to the primary bone tissue takes place, with a reorganisation of the bone lamellae. In conjunction with this rearrangement of the bone structure,

a further proliferation of osteoblasts occurs. A renewed increase in activity over the fracture is observed in the first examination after weightbearing without cast immobilisation, indicating that reorganisation first starts at this time, no increase in activity occurring when the patient supports on a cast-immobilised fracture.

The reorganisation of bone structure is a very long process; in most patients activity over the fracture was higher than activity over the normal extremity for more than 6 months after the fracture was healed clinically.

Complications in fracture healing could not be detected earlier with the isotopic method described than with the usual clinical and radiological examination. Activity relationships for patients with delayed healing and pseudoarthrosis were of special interest, but were found to be similar to those for patients with uncomplicated healing and gave no information which could help in the prediction of complications. However, according to Segmüller et al. (1970) isotopic methods are able to distinguish between a pseudoarthrosis caused by inadequate osteogenesis and one caused by insufficient fixation.

^{87m}Sr has a relatively short half-life (2.8 hours) and measurements of activity have to be taken shortly after injection. One hour after injection, the blood system still contains 50–70 per cent of the injected quantity (Charkes 1969), and consequently there is a strong secondary radiation from the blood system at this time. This may explain why the average values for the two maxima for the individual fracture types were increasingly lower with more proximal fracture location, since the proportion of soft tissue, relative to bone, is greater proximally than distally (Bauer & Wendeberg 1959).

In patients with cicatrix infections after complicated fractures or osteosynthesis, as well as in one patient with thrombophlebitis, a sharp increase in activity over the fracture zone was found at the time of infection. This indicated that variations in activity were not caused by a change in the quantity of osteoblasts alone, but could be caused by other factors such as changes in blood flow in the vicinity of the fracture.

Certain patients were therefore injected with ^{99m}Tc labelled albumin as well as ^{87m}Sr. The labelled albumin, which is a macromolecule, remains in the blood vessels and capillary bed and ^{99m}Tc activity is thus a measure of the blood space. An increased blood flow in the fracture zone was found in all cases, and the variations in F/N for the two compounds were always found to be parallel.

Since studies with injection of both ^{87m}Sr and ^{99m}Tc were restricted to a few patients, there is little basis for definite conclusions; but part of the rise in activity over the fracture zone after ^{87m}Sr injection can probably be attributed to increased blood flow, and part of the variation in the ratio F/N is thought to be due to altered blood flow. It is therefore necessary to elucidate the effects of changes in circulation before studies of the control of fracture healing with ^{87m}Sr uptake can be continued.

SUMMARY

Thirty-nine patients with a variety of fractures, mainly in the lower extremities, were injected intravenously with 10 μc ^{87m}Sr/kg in 409 separate assays, with the intention of supervising fracture healing by external counting; 27 fractures healed without complications, 8 with complications and 4 patients were regarded as special cases. Patients were followed up for an average of 269 days and were checked from 6 to 16 times.

In all patients an increased activity was observed over the fracture. The ratio of activity over the fracture to activity symmetrically over the opposite normal extremity varied during the healing process. Two maxima occurred consistently; one between day 8 and day 32 after the initial lesion, the other between day 8 and day 45 after weightbearing without plaster fixation. The initial maximum was delayed in proportion to increasing complexity of the fracture. The average values of both maxima were higher the more distal the location of the fracture.

Complicated fracture healing could not be detected earlier with isotopic examination than with the usual clinical and radiological examination. Large increases in activity over the fracture zone were observed in cases of infection in the vicinity of the fracture.

The effects of blood flow were investigated in a number of cases by injecting patients with ^{99m}Tc labelled albumin together with ^{87m}Sr. In all cases an increased blood flow was found in the vicinity of the fracture, and part of the variation in the ratio of activities over the fracture and symmetrically over the other extremity after injection of ^{87m}Sr, could be attributed to changes in blood flow in the vicinity of the fracture.

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