Bone Healing During Lower Limb Lengthening by Distraction Epiphysiolysis

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A study of limb lengthening by distraction epiphysiolysis in the rabbit tibia is presented. A special external distraction device was developed that allowed 10 mm lengthening of the leg. Bone formation in the elongated zone was studied by computed tomography and [^{99m}Tc] methylene diphosphonate (MDP) scintigraphy. Computed tomography showed bone formation proceeding for several weeks after the end of the distraction period, followed by a decrease in the amount of bone during a remodeling phase leading to the formation of a solid cortical structure. The uptake of [^{99m}Tc]MDP increased parallel to, but preceeding the actual accretion of bone, followed by a decrease during the bone remodeling phase. Uptake of the tracer will partly reflect bone metabolism, but other factors, like trauma, determine much of the uptake.

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Significant inequality in limb length in childhood is a major problem in orthopedic management. Recently, remarkably good results were reported with distraction epiphysiolysis as a new method of limb lengthening (*1–5*). Applying a gradually increasing distraction force to the epiphysis will eventually result in fracturing of the cartilaginous epiphyseal plate which is the weakest site of the immature bone. Progressive continuous distraction increases the fracture gap between epiphysis and metaphysis until the desired lengthening is achieved. Ossification of the hematoma in the fracture gap occurs spontaneously. Still, the healing time is long, which poses a major problem to the young patient and his family. A way to shorten the duration of the therapy by stimulating bone formation would mean a significant break-through. To compare and validate stimulatory effects on osteogenesis, a procedure should be available allowing quantitation of bone formation, preferably in a non-invasive way. Conventional radiography is the most commonly accessible technique but is not discriminative enough to evaluate and quantitate differences in intramedullary bony structures. Besides, in the clinical practice of leg lengthening it is hard to assess cortical thickness from conventional roentgenograms.

The purpose of the present investigation was to evaluate two methods to study bone formation in the elongated zone, (a) by measuring uptake of technetium-99m methylene diphosphonate ([^{99m}Tc]MDP), and (b) by determining the roentgen absorption in serial scan planes obtained by computed tomography. Leg lengthening by distraction epiphysiolysis was studied in a lower limb lengthening model in the rabbit.

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MATERIALS AND METHODS

Distraction Procedure

By means of a specially designed device described in detail by Van Roermund et al. (*6*) distraction was applied to the proximal epiphysis of the right tibia of six female New Zealand white rabbits (each weighing ~1.5 kg). A fracture in the growth plate usually occurred after 4 days. Progressive distraction, 0.5 mm per day, increased the distance between the epiphysis and metaphysis until a separation of 10 mm was achieved. The device was kept in situ until the end of the experiment 18 wk after reaching maximal elongation. At the start of the experiment the rabbits were 18 wk old, which is near the end of their period of growth.

Bone Scintigraphy Procedure

Rabbits were injected intramuscularly with 175 MBq [^{99m}Tc]MDP. Two hours later, under general anesthesia, a scintigram was made using a gamma camera (Pho-Gamma IV, equipped with a 140 keV LEAP collimator). With the detector facing upwards the rabbits were positioned over the field of view so that both legs were clearly visible on the screen. A point source was used as a marker for the elongated leg.

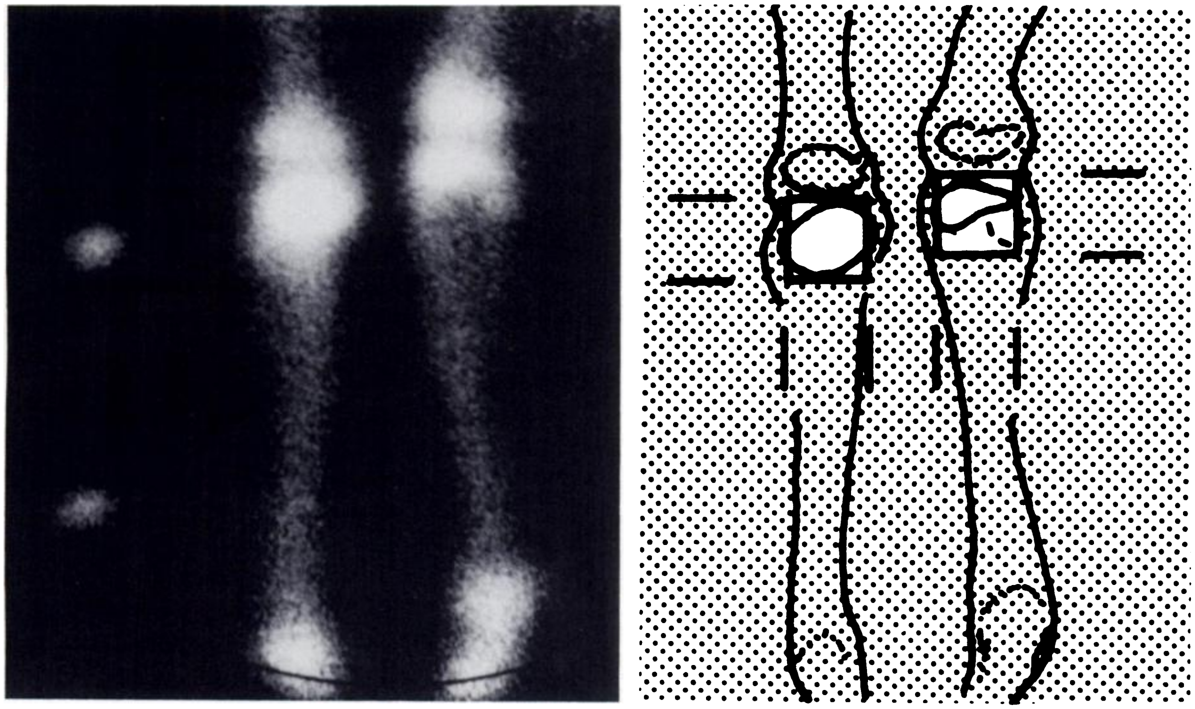

FIGURE 1
Scintigram of a rabbit's tibiae. The elongated tibia (left) is marked by point sources. The diagram illustrates the regions of interest to measure uptake of radioactivity.

Regions of interest of 15 × 15 mm were selected over the elongated zone, and over the corresponding area on the contralateral tibia (Fig. 1). The radioactivity in these regions was measured. The uptake ratio (UR) of radioactivity was calculated as: UR = (Ua−Ub)/(Ua+Ub), where Ua is the radioactivity in the region over the elongated zone, and Ub is the radioactivity in the region over the contralateral tibia. Scintigrams were made weekly, starting 1 wk after the operation till 10 wk after reaching maximal elongation.

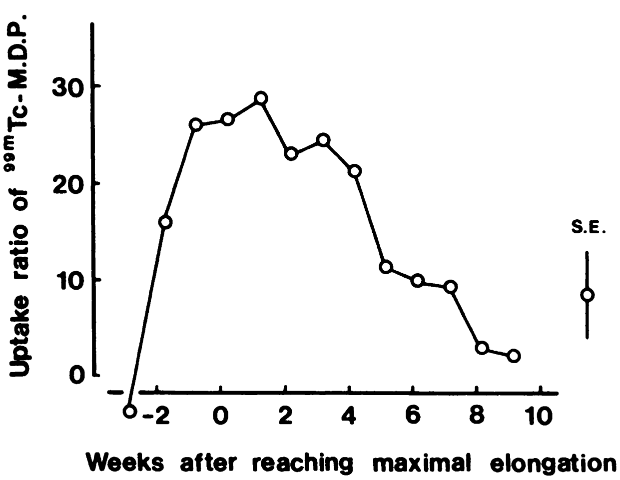

FIGURE 2
Uptake ratio of [^{99m}Tc]MDP in the elongated zone of the tibia. The uptake ratio is defined under Materials and Methods. The indicated standard error represents the pooled standard errors from the individual time points (six animals).

Computed tomography procedure

The procedure was described in detail by Van Roermund et al. (*6*). Using a Philips Tomoscan 350, scans were made weekly for 18 wk after the end of the distraction period. From the epiphyseal pins down, a series of 1.5-mm slices was obtained perpendicular to the long axis of the tibia. The roentgen absorption in the 5–6 scan planes covering the length of the elongated zone was averaged to represent the mean roentgen absorption in the elongated zone.

Statistics

The data in Figure 2 and Figure 3 were statistically evaluated by analysis of co-variance to validate the significance of

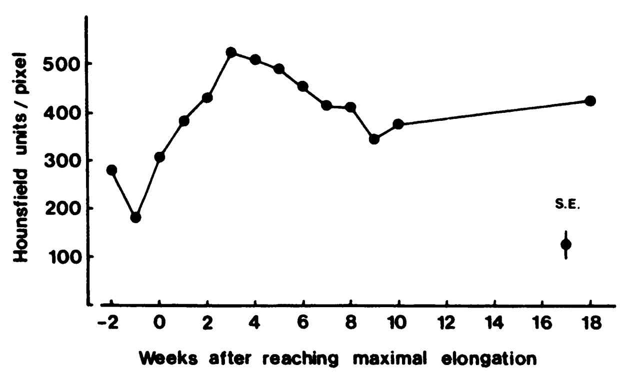

FIGURE 3
Mean roentgen absorption in the elongated zone of the tibia calculated from transverse computed tomography scans covering the length of the elongated zone. The indicated standard error represents the pooled standard errors from the individual time points (six animals).

increase and decrease in the curves. The slope of the curve between −3 and −1, and between 1 and 9 weeks in Figure 2, between −1 and 3, and between 3 and 10 wk in Figure 3 was significantly different from zero (correlation coefficients: 0.80, −0.68, 0.84, and −0.70, respectively; $p < 0.001$).

RESULTS

Figure 2 shows the uptake ratio of [^{99m}Tc]MDP. Uptake of radioactivity increased during the distraction period. In the weeks following maximal elongation the uptake ratio decreased to a near basal level.

Figure 3 shows the mean roentgen absorption in the elongated zone. The roentgen absorption derived from the formation of bony structures increased till 3 wk after reaching maximal elongation. Subsequently, a gradual but significant decrease in roentgen absorption was observed, which leveled off at 8–10 wk after maximal lengthening.

DISCUSSION

Uptake of [^{99m}Tc]MDP is the resultant from a number of factors including the affinity of the tracer for bone mineral, metabolic activity of osteogenesis, local alterations in blood flow and blood supply, and effects of trauma in general (*7–12*). These factors determine the uptake of the tracer during the distraction period (Fig. 2), when fracturing of the growth plate and continuous distraction induce a major trauma to the tissue. The uptake ratio reached a maximal level around the end of the distraction period.

The result of osteogenesis is accretion of bone, which is reflected by an increase in roentgen absorption (Fig. 3). The amount of bone in the elongated zone reached maximal values ~4 wk after maximal elongation (Fig. 3). The peak in bone accretion occurred ~3 wk later than maximal uptake of the tracer was reached. Apart from other explanations, this difference in time may illustrate a sequence of events, where tracer uptake reflects the cellular metabolism of osteogenesis, which preceeds the presence of bone seen in computed tomography.

As we demonstrated before (*6*), the decrease in roentgen absorption in Figure 3 is caused by resorption of intramedullary bony structures and formation of a solid cortex (Fig. 4). The decrease in uptake of [^{99m}Tc]MDP might be caused by this change in bone metabolism from net formation to remodeling. However, it may be assumed that, in addition, during this period effects of trauma from progressing distraction gradually subsided.

In fact, it is likely that effects of trauma largely determine the shape of the tracer-uptake curve. This is illustrated in the Figures 5 and 6 showing the uptake ratio's from two rabbits excluded from the test series. In one animal (Fig. 5) the distraction rate was 1.0 mm instead of 0.5 mm per day. Therefore, the distraction period was half the normal period. Maximal roentgen absorption was reached at the same time as shown in Figure 3, indicating that bone formation in the elongated zone was not influenced by the increase in distraction rate. The time to reach maximal uptake of [^{99m}Tc]MDP was longer than that in Figure 2 and uptake continued to increase after the end of the distraction period. The prolonged increase in uptake of [^{99m}Tc]MDP after maximal elongation may result from enhanced and prolonged effects of trauma due to the higher distraction rate. In Figure 5 the time between maximal uptake of the tracer and maximal roentgen absorption was markedly shorter than in Figure 2 and Figure 3. In this case, either the time between the onset of osteogenesis and the roentgenographic detection of bony structures was reduced—which seems highly unlikely, because the rate of bone formation is comparable to that in Figure 3—or the prolonged increase in uptake of the tracer obscures what would otherwise have been a longer difference in time to reach maximal roentgen absorption and maximal uptake of the tracer. In a second animal (Fig. 6), after maximal elongation had been reached, the distracted length was erroneously decreased by 0.5 mm. This caused a roentgenographically detected delayed union at the site of the growth plate. The uptake ratio remained at the maximal level during the period of observation.

It is noteworthy that the peak uptake ratio in Figure

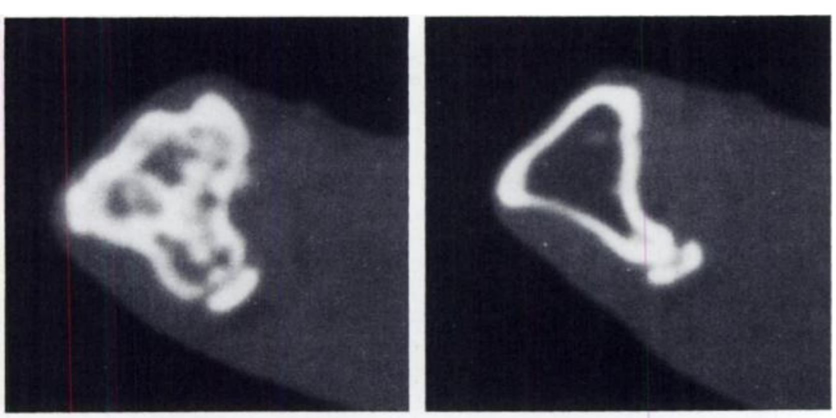

FIGURE 4
Scan planes at the center of the elongated zone at 3 (left) and 9 (right) wk after reaching maximal elongation. At 3 wk the medullary region is filled with bony structures. At 9 wk a solid cortex is present.

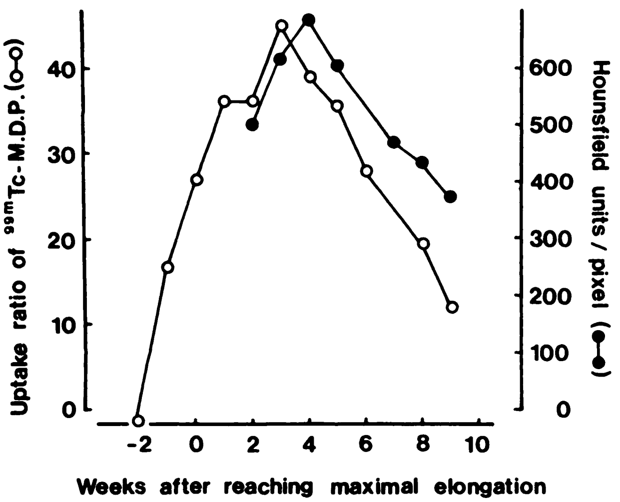

FIGURE 5
Uptake ratio of [^{99m}Tc]MDP and the mean roentgen absorption in the elongated zone of the tibia of one animal, where the distraction rate was 1 mm per day instead of 0.5 mm, and, thus, the distraction period 1.5 instead of 3 wk.

5 and the final level in Figure 6 are higher than the peak level in Figure 2.

The data in Figure 5 and Figure 6 suggest that the trauma induced by fracturing of the growth plate and distraction forces exerted on the tissue largely determine the level of uptake of [^{99m}Tc]MDP. An indication of the contribution of changes in vascularity to the extent of uptake of [^{99m}Tc]MDP, in trauma and during the healing process, may be assessed by dynamic flow studies. The influence of high osteogenic activity and callus

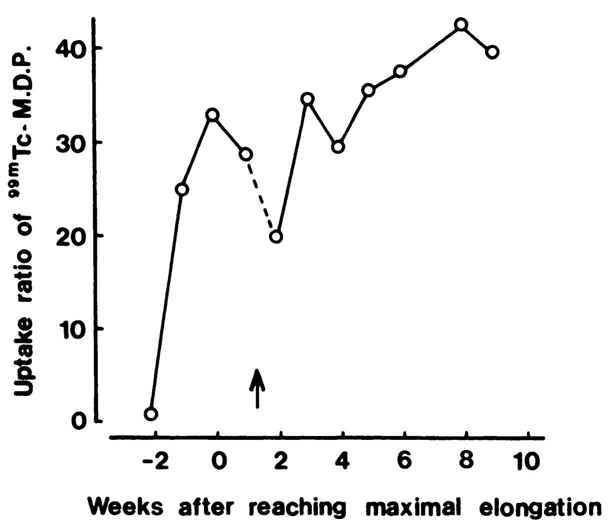

FIGURE 6
Uptake ratio of [^{99m}Tc]MDP in the elongated zone of the tibia of an animal, where a delayed union had developed at the growth plate fracture site. The arrow indicates when erroneously the distracted length was decreased by 0.5 mm.

accretion on the uptake of the tracer may be obscured by the dominating effects of trauma.

The objective of this study was to evaluate the uptake of [^{99m}Tc]MDP and roentgen absorptiometry on computed tomography scans as methods to quantitate bone formation in distraction epiphysiolysis. Computed tomography adequately and quantifiably illustrates the bone formation processes resulting in elongation of a pipe bone. A serious drawback for using computed tomography in a clinical setting at present is that most clinically used external distraction devices contain metallic parts in the scanning zone, which interfere with the image formation. The present study shows that measuring uptake of [^{99m}Tc]MDP during leg lengthening by distraction epiphysiolysis provides important data on the healing process, but will probably not allow quantitation of relatively small differences in rate or extent of bone formation in the elongated zone. Therefore, [^{99m}Tc]MDP scintigraphy was not found suitable to compare and validate stimulatory effects on osteogenesis.

In a pilot study we tested magnetic resonance imaging of the elongated zone. Imaging did not provide more information than computed tomography. However, the possibility offered by magnetic resonance spectroscopy in combination with imaging to correlate images with metabolic data will open a vast new field of research.

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