TABLE 2
Technetium-99m-MDP Apposition onto Fracture Site as a Function of Time*

Component	b	k
I	1.06	0.345
II	8.32E-11	7.75

* for, $y = b(x^k)$

resorption, might indicate that it is a marker of bone formation and that ongoing resorption does not necessarily have to be present for the increased uptake of ^{99m}Tc to occur." We previously reported the relative rates of resorption and apposition of radiolabeled phosphonates in a rat fracture model (*2*). In our opinion, these data demonstrate the concomitant tracer resorption and apposition at the healing tibial fracture site when compared to normal bone. For example, Table 1 illustrates the biexponential resorption constants for ^{125}I-labeled phenylphosphonic acid as calculated from an activity versus time semilog plot. The fraction of fracture to normal retention (FR) exhibits a biexponential relationship as a function of time in days (t) as follows:

$$FR = 0.31\ e^{-0.347t} + 0.69\ e^{-0.0125t}$$

$$\text{By Day 10, } FR = 0.31(0.0311) + 0.69(0.882)$$

$$= 0.00964 + 0.608$$

$$FR = 0.617, \text{ then } 1 - 0.617 = 0.383 \text{ resorbed.}$$

$$\text{By Day 30, } FR = 9.34E - 6 + 0.47$$

$$= 0.47, \text{ then, } 1 - 0.47 = 0.53 \text{ resorbed.}$$

The release of ^{125}I-phenylphosphonic acid from normal bone, after tracer equilibrium, has a monoexponential biologic half-time of 962 days (*3*).

Table 2 lists the biexponential constants associated with the ^{99m}Tc-MDP time-dependent apposition pattern at the fracture site relative to normal bone. The rate of increase as a function of time follows the mathematical law of allometric growth; $y = b(x^k)$, where b is the y intercept and k is an exponent of a power function (*4*).

By Day 10, the fraction of ^{99m}Tc-MDP uptake relative to normal bone (FA) is:

$$FA = (b)(x^k)_I + (b)x^k)_{II}$$

$$FA = (1.06)[(10)(\hat{}0.345)] + [8.32E - 11)[(10)(\hat{}7.75)]$$

$$\text{By 30 days, FA becomes:}$$

$$FA = (1.06)[(30)(\hat{}0.345)] + 8.32\ E - 11)[(30)(\hat{}7.75)]$$

$$FA = 3.43 + 23.32$$

$$FA = 26.75.$$

The ratio of apposition-to-resorption after 10 days equals 2.36/0.383 = 6.16, and after 30 days; 26.75/0.526 = 50.86. This biologic behavior undoubtedly plays a major role in bone healing.

As shown above, the apposition is significantly greater than resorption for the healing fracture in our rat model. This pattern continued to increase at the time the investigation was terminated at 30 days. The results of Shani et al. show a return to uniform uptake (treatment/control) by approximately 15 days, after a maximum treatment/control uptake of approximately 1.75 after 6 days for ^{99m}Tc-MDP. By Day 6, this ratio, as calculated by the allometric growth equation, is equal to $(1.06)[(6)(0.345)] + (8.32E - 11)[(6)(\hat{}7.75)] = 1.97$. This value agrees with that reported by Shani et al., which was 1.75.

Why our tibial rat fracture continued to exhibit increased ^{99m}Tc-MDP uptake relative to normal at 30 days, while that of Shani et al. showed uniform uptake by Day 15 is presently unknown. It has been documented, however, that human fractures are positive on bone scans for an extended period of time after their induction and that this time period is a function of fracture type (*4*).

REFERENCES

1. Shani J, Amir D, Soskolne WA, et al. Correlations between uptake of technetium, calcium, phosphate, and mineralization in rat tabial bone repair. *J Nucl Med* 1990;31:2011–2014.
2. Castronovo FP Jr, Strauss HW. Dual-tracer resorption and apposition in a rat fracture model. *Nucl Med Biol* 1988;15:181–185.
3. Castronovo FP Jr, Strauss HW, McKusick KA, et al. Iodine-125-labeled phenylphosphonic acid: a new radiopharmaceutical for long term investigations of the skeleton. *Skeletal Radiology* 1982;7:233–237.
4. Merrick MV. Review article—bone scanning. *Br J Radiol* 1975;48:327–351.

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REPLY: We would like to express our appreciation in allowing us the opportunity to respond to Dr. Castronovo's letter. It is indeed gratifying to note that our results are in agreement with the results of Drs. Castronovo's and Strauss' study.

The differences in the sequence of events between the two studies was expected. The model of tibial bone fracture used by the authors is a complex sequence of events through blood clot formation, primary callus formation including cartilage formation, calcification and then reorganization of the callus through primary to mature bone. These events take 30 to 60 days before completion of the process. In our model, the process is far more rapid as there is no bone fracture. The healing process goes through the organization of the initial blood clot directly to primary bone formation. After this, the primary bone is completely resorbed and replaced by bone marrow. In fact, by the 14–21st day, no more bone formation occurs.

Thus, we believe that the difference referred to in Dr. Castronovo's letter can be explained by the difference in the sequence of events, while both models confirm the similarity in the ^{99m}TC-MDP uptake during their respective periods of bone apposition.

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