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Cyclotron-Produced $^{157}\text{Dy}$ Compared with $^{18}\text{F}$ As Bone-Scanning Agent Using the Whole-Body Scanner and Scintillation Camera$^1$

Y. Yano$^2$, D.C. Van Dyke$^2$, T.A. Verdon, Jr.$^2$, and H.O. Anger$^2$


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In malignant tumors which commonly metastasize to bone (lung, breast, prostate, intestines, thyroid, kidney), the frequency of osseous involvement at the time of death is generally accepted to be 50 to 75 percent (1-4). The most common site of metastatic bone neoplasm — the spine — is unlikely to be detected early by conventional roentgenographic techniques because spongy bone such as vertebrae does not usually demonstrate roentgenographic changes unless the lesions are greater than 1.5 cm (5).

Scanning with bone-seeking radiopharmaceuticals has been shown to be a useful procedure in the early detection of metastatic bone lesions. Greenberg, who scanned with $^{47}$Ca and $^{85}$Sr, states that the time interval between abnormal scan findings and radiographic or histological confirmation varies from 34 to 164 days (6). Table I lists the bone-seeking agents $^{47}$Ca, $^{85}$Sr, $^{87m}$Sr, $^{18}$F, and $^{157}$Dy with their physical characteristics, chemical form, production method, administered dose, and radiation dose. The long half-life of $^{85}$Sr (65 days) and the high $\gamma$-ray energy of $^{47}$Ca (1.31 MeV) make these radionuclides undesirable for routine bone scanning. Nuclides more suitable for routine bone scanning are $^{18}$F (7,8) and $^{87m}$Sr (9,10). These short-lived radionuclides permit higher injected doses with greater counting rates and decreased radiation dose.

Evaluations of $^{18}$F, $^{87m}$Sr, and $^{85}$Sr for bone scanning have been made by Ronai (11), French (12), and Spencer (13). These studies generally agree with Weber's findings that $^{18}$F is the isotope of choice for bone scanning because of reduced radiation dose, increased counting rate, rapid clearance from plasma and soft tissue (4 to 5 times as fast as other bone-seeking radionuclides), and a high ratio of uptake by lesion to uptake by normal bone (14). Strontium-$^{87m}$ appears to be nearly as
good as $^{18}\text{F}$ except for a slower clearance from the plasma. The availability of $^{18}\text{F}$ is limited to areas near a cyclotron or nuclear reactor, whereas $^{87}\text{Sr}$ is obtained from its 3.3-day parent, $^{87}\text{Y}$.

At Donner Laboratory we have used both reactor- and cyclotron-produced $^{18}\text{F}$ for bone scanning with the previously described Anger Mark II Whole-Body Scanner (15) and the positron scintillation camera (16). Over a period of 7 years we have studied 270 patients. Although $^{18}\text{F}$ is useful for obtaining scans showing bone tumors, it is less than an ideal nuclide because the 110-min half-life restricts availability and the 511-keV $\gamma$-ray emissions are difficult to collimate and detect efficiently with conventional scanning equipment.

In the search for a better bone-scanning radionuclide with a more convenient half life and a more ideal $\gamma$-ray emission, we have investigated dysprosium-157, a heavy lanthanon of the rare earth group of elements. Durbin reported that the heavier lanthanons (Tb, Dy, and Lu) are taken up 50 to 60% in bone when injected intramuscularly as a citrate complex (17). O'Mara has investigated the distribution of a number of rare earth radionuclides ($^{153}\text{Sm}$, $^{171}\text{Er}$, and $^{177}\text{Lu}$) as HEDTA chelates and found about 50% of the injected dose taken up in the bone of rabbits (18).

Dysprosium-157, a cyclotron-produced radionuclide, has a half-life of 8.1 hr, which is more convenient for production, transportation, and maximum ratio of bone to blood and soft tissue (2-3 hr postinjection) than the 1.8-hr $^{18}\text{F}$. Dysprosium-157 also has a more generally useful $\gamma$-ray energy of 326 keV, 91% abundant, for use with conventional $\gamma$-ray cameras and scanners than the 511-keV annihilation gamma emission of $^{18}\text{F}$. Furthermore, the radiation dose to the patient is reduced because
Dy decays by 100% electron capture with a small internal conversion ratio.

Preliminary studies in animal and human subjects indicate that when Dy is administered as an HEDTA (N-hydroxy-ethylenediaminetriacetic acid) chelate, it localizes primarily in the bone (about 50% of the injected dose) and the remainder is excreted by the kidneys in much the same manner as $^{18}$F.

Materials and Methods

Radionuclides

Dysprosium-157, $T_{1/2}$ 8.1 hr, decays 100% by electron capture to $^{157}$Tb, $T_{1/2}$ 150 yr, which then decays 100% by electron capture to stable $^{157}$Gd. The gamma emission of $^{157}$Dy is essentially monoenergetic 326 keV (91% abundant). Because of the great difference in half-life between $^{157}$Dy and the daughter $^{157}$Tb, the amount of $^{157}$Tb produced by decay of $^{157}$Dy is negligible in calculating the radiation dose from $^{157}$Dy. Figure 1 shows the decay scheme and the gamma spectrum of $^{157}$Dy.

Dysprosium-157 is produced by irradiating 300 mg of $^{159}$Tb (100% abundant) as TbCl$_3$·6H$_2$O with 30-MeV protons, $^{157}$Tb(p,3n)$^{157}$Dy. The alternative nuclear reactions of (p,2n) and (p,4n) produce the stable isotopes of $^{158}$Dy and $^{156}$Dy respectively.

Contaminating radionuclides produced by the irradiation were identified by gamma-spectrum analysis using a 400-channel analyzer and a 2 x 2-in. NaI(Tl) crystal. Decay curves of the contaminating radio- nuclides were obtained over a period of 8 months to determine the half-life of radionuclides produced from the proton irradiation of $^{159}$Tb.
The production yield of $^{157}$Dy from an irradiation with 30-MeV protons and 16 $\mu$A of beam current is 2.48 mCi/$\mu$Ah or 39.6 mCi/hr (mean values from 11 production runs). Relative concentrations of nuclides that contaminate $^{157}$Dy are $< 10^{-4}$ parts of $^{156}$Tb ($T_1/2$ 3.1 d, decaying 99% by E.C. to stable $^{156}$Gd) and $< 10^{-5}$ parts of $^{160}$Tb ($T_1/2$ 72.1 d, decaying 100% by $\beta^-$ emission to stable $^{160}$Dy).

Fluorine-18, $T_1/2$ 110 min, decays 3% by E.C. and 97% by positron emission with accompanying 511-keV annihilation $\gamma$ rays. Fluorine-18 is produced by cyclotron irradiation of 50 ml of pure H$_2$O in a quartz glass target vessel with 65-MeV $\alpha$ particles by the $^{16}$O($\alpha$,pn)$^{13}$F and $^{16}$O($\alpha$,2n)$^{18}$Ne $\beta^+$ $^{18}$F reactions. The production yield of $^{18}$F from an irradiation with 65-MeV $\alpha$ particles is 19 mCi/$\mu$Ah or 116 mCi/hr (19).

Chemistry

The TbCl$_3$·6H$_2$O target material is washed from the Al target plate with 10 ml of H$_2$O and diluted to 20 ml with 1.0 N HCl acid. This solution of $^{157}$Dy·TbCl$_3$·6H$_2$O, containing about 2.3 mCi $^{157}$Dy/ml and 4.02 x $10^{-2}$ mM Tb/ml (6.4 mg Tb/ml), is filtered through 0.22-\mu Millipore filter. An aliquot of the target solution is taken to give the desired activity and HEDTA is added to give a desired molar ratio to Tb. Sodium hydroxide is added dropwise to pH 6-7 and Ca gluconate-heptonate (Abbot, sterile solution 20% W/V) is added to give a desired molar ratio of Ca to HEDTA. A typical preparation of 20:1 HEDTA to Tb and 2:1 Ca to HEDTA contains 475 \mu Ci $^{157}$Dy, 1.15 mg Tb, 40 mg HEDTA and 11.5 mg Ca per ml.

In some preparations chemical separation of the Tb target material from $^{157}$Dy was done by ion-exchange separation, using cation-exchange
resin AG 50 x 4 (Bio-Rad) and \( \alpha \)-hydroxyisobutyric acid (0.4 M, pH 3.4) as the eluant solution. The reagent solutions and glassware used for the preparation of \( \text{\textsuperscript{157}} \text{Dy-HEDTA} \) are sterilized either by Millipore filtration or by autoclaving.

\( \text{\textsuperscript{157}} \text{Dy-HEDTA} \) was prepared in different molar ratios of HEDTA to Tb (which acts as a Dy "carrier ion") and different molar ratios of Ca to HEDTA to determine the concentrations of Tb, HEDTA, and Ca which give the best ratio of bone to blood and soft tissue for \( \text{\textsuperscript{157}} \text{Dy} \).

Results and Discussion

Animal Studies

\( \text{\textsuperscript{157}} \text{Dy-HEDTA} \) uptake in rat tissue was determined in 200-g Sprague-Dawley rats. Figure 2 shows the distribution of \( \text{\textsuperscript{157}} \text{Dy-HEDTA} \) in rat tissue [blood, lungs, liver, kidneys, spleen, muscle over sternum, muscle over femur, and bone (femur)]. The results are expressed as percent per gram of tissue 2 hr after intravenous administration of 5:1, 10:1, 20:1, and 30:1 molar ratios of HEDTA to Tb. The preparations were injected at pH 6-7 with an excess of Ca to HEDTA. In rats the higher ratio of HEDTA to Tb enhances clearance from the blood and uptake in bone while minimizing the uptake in liver. When the HEDTA ratio is 5:1, the uptakes are 1.02% of the injected dose of \( \text{\textsuperscript{157}} \text{Dy} \) per gram of blood, 0.69% per gram of liver, and 0.72% per gram of bone. When the HEDTA ratio is increased to 30:1 the uptakes are 0.003% per gram of blood, 0.016% per gram of liver, and 1.58% per gram of bone. An excess of HEDTA is necessary to prevent the deposition of \( \text{\textsuperscript{157}} \text{Dy-Tb} \) in the reticulo-endothelial system and to allow the \( \text{\textsuperscript{157}} \text{Dy} \) to be extracted at the bone binding sites. The molar ratio of
HEDTA to $^{157}$Dy-Tb which enhances bone uptake also favors excretion by the kidneys.

Preparations of $^{157}$Dy-HEDTA were also studied in beagle dogs and rhesus monkeys. "Carrier free" (i.e., no Tb) $^{157}$Dy-HEDTA was administered to a beagle dog and a rhesus monkey. Blood clearance half times were determined and compared with blood clearance half times for $^{157}$Dy-HEDTA with Tb "carrier" present as well as for varying amounts of HEDTA and Ca. The clearance of $^{157}$Dy from the blood was determined by taking 1-ml blood samples periodically after administration of the isotope and counting in a deep-well counter with NaI(Tl) crystal and multichannel analyzer. Blood disappearance half times were obtained from a semi-logarithmic plot of the data.

Table II presents a summary of the blood-disappearance half times for $^{157}$Dy-HEDTA in beagle dogs and rhesus monkeys for molar ratios of 10:1 and 20:1 for HEDTA to Tb and 1:1, 2:1, and 3:1 for Ca to HEDTA. The weight in mg of Tb, HEDTA, and Ca injected for each study is given together with the half times obtained from analysis of the two-component blood clearance curves from 1 to 180 min postinjection. It can be seen from the data that in beagle dogs, with a constant molar ratio of 20:1 for HEDTA to Tb and an increasing Ca-to-HEDTA ratio, there is an increasing clearance half time from blood for $^{157}$Dy-HEDTA from 50 min at 1:1 Ca:HEDTA to 85 min at 2:1 Ca:HEDTA and 96 min at 3:1 Ca:HEDTA. In monkeys at 10:1 HEDTA to Tb and 1:1 Ca to HEDTA the slow component of the clearance half-time curve is 265 min compared with a constant blood activity at 10:1 HEDTA to Tb and 2:1 Ca to HEDTA. When the HEDTA-to-Tb ratio is increased to 20:1 and the Ca-to-HEDTA ratio is 1:1, the half time for
blood clearance is 30 min. When the ratio of Ca to HEDTA is increased to 2:1 the clearance half time is 26 min.

These results in dogs indicate that a molar ratio of 20:1 HEDTA to Tb-\(^{157}\)Dy is sufficient to bind the \(^{157}\)Dy to HEDTA in preference to binding to the blood plasma, in contrast to the results with monkeys at 10:1 ratios. The Ca-to-HEDTA ratio appears to influence the extraction of \(^{157}\)Dy from the HEDTA binding sites into bond-binding sites, as shown by the increasing blood-clearance half times with increasing Ca ratios in dogs. This effect can also be seen in the monkeys: an increase in Ca ratio prevents the \(^{157}\)Dy from being extracted by bone and at the 10:1 HEDTA and 2:1 Ca ratios the \(^{157}\)Dy appears to be bound to proteins in the blood plasma and remains in the blood pool.

The removal of "carrier" Tb did not enhance the clearance half time of \(^{157}\)Dy from the blood. This result is contrary to expectation, since Tb and Ca are very likely to be in competition with \(^{157}\)Dy for the bone binding sites. However, the competition of Tb, Ca, and \(^{157}\)Dy for binding sites on the blood plasma proteins would explain the unexpected enhancement of \(^{157}\)Dy clearance from the blood when Tb "carrier" is present.

Toxicity studies were done by administering 100 times the proposed human dose of Tb, HEDTA, and Ca gluconate in two rats, one dog, and one monkey. There were no visible adverse reactions.

Scintillation-camera pictures and whole-body scans were taken 2 to 3 hr after intravenous administration to determine the distribution of \(^{157}\)Dy-HEDTA and Na\(^{18}\)F.

Figure 3 shows the distribution of 1 mCi \(^{157}\)Dy-HEDTA (20:1) and 150 \(\mu\)Ci \(^{18}\)F in a dog with a lesion in the left tibia produced by curetting.
the inside of the bone. Increased uptake at the lesion site is demonstrated with both radionuclides. Although the same dog is used for both studies, the composite picture on the right is larger because of the magnification effect of the positron scintillation camera compared with the $^{157}$Dy picture on the left, made without magnification by using a parallel-hole multichannel collimator. The bladder was emptied prior to imaging in both cases.

**Patient Studies**

Twenty-two patients were studied at Donner Laboratory from June 6, 1970 to December 21, 1970. Further studies of patients were also done with the cooperation of Dr. Paul Weber at Kaiser Hospital, Oakland, California, and Dr. Joseph Kriss, Stanford University Medical Center, Stanford, California. A typical administered dose to humans of 1.0 mCi of $^{157}$Dy-HEDTA in a volume of 2.1 ml contained 2.4 mg Tb, 84.5 mg HEDTA, and 24.2 mg Ca.

The radiation dose to a 70-kg human subject from 1.0 mCi of $^{157}$Dy-HEDTA, assuming 50% uptake in bone, 50% excretion by the kidneys, and an effective half-life equal to the physical half-life in bone and 1 hr in the bladder and kidneys, is 0.158 rad to kidneys, 0.316 rad to bladder, and 0.144 rad to bone.

The distribution of $^{157}$Dy-HEDTA as a function of time after intravenous administration is seen in Fig. 4, which shows whole-body scans taken at 15 min (top) and 5 hr (bottom) of a female patient with known metastases to the lumbar vertebrae. Note the rapid excretion by the kidneys in the early scan and the increased uptake in bone and at the
lesion site in the late scan.

Comparisons were made of $^{157}$Dy-HEDTA and $^{18}$F distribution in 9 of 22 patients with established malignancy. They were given 500 to 600 $\mu$Ci of $^{18}$F, and 3 hr later 22-min whole-body scans were obtained from the posterior view. In some patients positron scintillation-camera pictures were also obtained. One week later the patients returned to receive 1.0 mCi $^{157}$Dy-HEDTA and were scanned under the same conditions as with $^{18}$F. In some cases scintillation camera pictures were taken using the $^{131}$I (2.2 in thick) lead collimator. Each field of view was exposed for 5 min.

Figure 5 shows whole-body scans with $^{157}$Dy-HEDTA (top) and $^{18}$F (bottom) of the same patient as in Fig. 4. Both $^{157}$Dy and $^{18}$F demonstrate increased uptake at the lesion site on the lumbar spine.

A 43-year-old female patient with cancer of the breast and metastases to the liver is shown in an anterior whole-body view (right) and posterior or spinal view (left), Fig. 6, which are composites of scintillation camera pictures. There is good uptake of $^{157}$Dy-HEDTA in the spine and pelvis. There is also some uptake in the right chest area and increased uptake in the distal end of the left femur.

A male patient, age 57 years, with osteopetrosis and an old fracture in the left femur was scanned with $^{18}$F, Fig. 7, top, and with $^{157}$Dy, Fig. 7, bottom. Both nuclides show increased uptake at the fracture site and the same overall normal skeletal distribution.

Figure 8 shows the whole-body scan distribution of $^{18}$F (top), $^{157}$Dy (middle), and $^{85}$Sr (bottom) in a 55-year-old male patient with cancer of the lungs. All three radioisotopes show increased uptake in the right
shoulder and right lateral rib cage, which corresponds to a fracture site. Increased uptake is also seen in the upper thoracic area near the spine and near the left rib cage. The increased uptake in the right lateral thoracic area corresponds to an incision site for thoracotomy.

Figure 9 is a whole-body scan with $^{157}$Dy showing increased uptake in the lumbar spine of a female patient with cancer of the breast.

Table III summarizes the results for patients scanned with $^{18}$F and $^{157}$Dy at Donner Laboratory.

In three patients, two with normal and one with abnormal extraction of $^{157}$Dy-HEDTA by the bone, the percent of $^{157}$Dy-HEDTA/liter of blood, percent excreted in urine, and clearance half times from the blood 3 hr after intravenous injection are shown in Table IV. In the two normals the mean excretion value is 44.5% of the injected dose; this compares with 22.5% excreted in urine at 3 hr for $^{18}$F (20). In the abnormal (more rapid uptake in bone) the excretion of $^{157}$Dy-HEDTA is 37.5%. In the two normals the percent of $^{157}$Dy-HEDTA/liter of blood at 3 hr ranged from 0.91%/liter to 1.92%/liter; the value for the abnormal was 0.72%/liter. The average clearance half times for $^{157}$Dy-HEDTA from the blood of the two normals are 13 min for the rapid phase and 95 min for the slow phase. In the abnormal case the rapid phase $T_{1/2}$ is 8 min and the slow phase $T_{1/2}$ is 64 min.

These data of the kinetics of $^{157}$Dy-HEDTA in humans seem to indicate that relatively high blood levels and high excretion rates are compatible functions with normal bone uptake, whereas abnormal or high bone uptake is reflected by low blood levels and reduced excretion of $^{157}$Dy.
Summary

Dysprosium-157 can be produced in 100-mCi amounts by cyclotron irradiation of $^{159}$Tb. Some of the advantages of $^{157}$Dy for scanning are (1) 8.1-hr half-life, (2) high yield of 326-keV photons, and (3) decay by electron capture. When $^{157}$Dy is administered as an HEDTA chelate in a molar ratio of 20:1 of HEDTA to Tb, there is uptake of activity primarily in the bone, but an increased uptake in bone lesions.

Fluorine-18 has the advantage of more rapid clearance from the blood and soft tissues (2 to 3 hr) after intravenous administration, as compared with 3 to 5 hr for $^{157}$Dy-HEDTA.

Metastatic bone lesions were visualized with both $^{157}$Dy and $^{18}$F. Twenty-two-minute whole-body scans with the Donner Laboratory Whole Body Scanner were usually sufficient to demonstrate the lesion sites.

Acknowledgments

The authors gratefully acknowledge the valuable technical assistance of Patricia Chu, Dianne Peterson, Mary Lou Nohr, and William Hemphill. Our appreciation also goes to the LRL 88-inch cyclotron group for carrying out the irradiations.
References


Table I. Physical characteristics of bone-seeking radionuclides.

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>$^{47}$Ca</th>
<th>$^{85}$Sr</th>
<th>$^{87m}$Sr</th>
<th>$^{18}$F</th>
<th>$^{157}$Dy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical half-life</td>
<td>4.5 days</td>
<td>65 days</td>
<td>2.8 hr</td>
<td>110 min</td>
<td>8.1 hr</td>
</tr>
<tr>
<td>Primary gamma energy (No./100 disintegrations)</td>
<td>1.31 MeV (76)</td>
<td>0.513 MeV (100)</td>
<td>0.388 MeV (78)</td>
<td>0.511 MeV (97, β+)</td>
<td>0.326 (91)</td>
</tr>
<tr>
<td>Chemical form</td>
<td>Chloride</td>
<td>Nitrate</td>
<td>Chloride</td>
<td>Sodium fluoride</td>
<td>HEDTA</td>
</tr>
<tr>
<td>Production method</td>
<td>$^{46}$Ca(n,γ)$^{47}$Ca</td>
<td>$^{84}$Sr(n,γ)$^{85}$Sr</td>
<td>$^{87}$Y → $^{87m}$Sr (Generator)</td>
<td>$^{16}$O(α, pn)$^{18}$F</td>
<td>$^{159}$Tb(p, 3n)$^{157}$Dy</td>
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<tr>
<td>Admin. activity</td>
<td>100 μCi</td>
<td>100 μCi</td>
<td>1 mCi</td>
<td>1 mCi</td>
<td>1 mCi</td>
</tr>
<tr>
<td>Dose to bone (rads)$^a$</td>
<td>6.3</td>
<td>5.2</td>
<td>0.14</td>
<td>0.26</td>
<td>0.144$^b$</td>
</tr>
</tbody>
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$^b$ New data.
Table II. Dy$^{157}$-HEDTA ($T_{1/2}$ blood disappearance) for various concentrations of HEDTA, Tb, and Ca in dogs and monkeys.

<table>
<thead>
<tr>
<th>Ratio HEDTA:Tb</th>
<th>Ratio Ca:HEDTA</th>
<th>Tb (mg)</th>
<th>HEDTA (mg)</th>
<th>Ca (mg)</th>
<th>Blood $T_{1/2}$ (min)</th>
<th>Animal</th>
<th>Approx. weight (lb)</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>20:1</td>
<td>1:1</td>
<td>2.68</td>
<td>93.5</td>
<td>13.5</td>
<td>8.5 50</td>
<td>Beagle dog</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>20:1</td>
<td>2:1</td>
<td>2.14</td>
<td>75.5</td>
<td>21.8</td>
<td>17.0 85</td>
<td>Beagle</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>20:1</td>
<td>2:1</td>
<td>4.65</td>
<td>162</td>
<td>46.5</td>
<td>14 69</td>
<td>Beagle</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>20:1</td>
<td>2:1</td>
<td>7.98</td>
<td>279</td>
<td>78</td>
<td>9 78</td>
<td>Beagle</td>
<td>12</td>
<td></td>
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<tr>
<td>20:1</td>
<td>3:1</td>
<td>2.2</td>
<td>76</td>
<td>33</td>
<td>11.5 96</td>
<td>Beagle</td>
<td>12</td>
<td></td>
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<tr>
<td>0.4:1</td>
<td>C.F.¹</td>
<td>13.8</td>
<td>0.9</td>
<td>5</td>
<td>80</td>
<td>Beagle</td>
<td>12</td>
<td></td>
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<tr>
<td>2.2:1</td>
<td>C.F.</td>
<td>3.8</td>
<td>1.2</td>
<td>15</td>
<td>77</td>
<td>Beagle</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>10:1</td>
<td>1:1</td>
<td>8.5</td>
<td>149</td>
<td>21.4</td>
<td>15 265</td>
<td>Rhesus monkey</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>10:1</td>
<td>2:1</td>
<td>6.85</td>
<td>120</td>
<td>34.5</td>
<td>blood activity constant</td>
<td>Rhesus monkey</td>
<td>8</td>
<td>in blood pool</td>
</tr>
<tr>
<td>20:1</td>
<td>1:1</td>
<td>3.2</td>
<td>111</td>
<td>16</td>
<td>4 30</td>
<td>monkey</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>20:1</td>
<td>2:1</td>
<td>3.2</td>
<td>111</td>
<td>32</td>
<td>7 26</td>
<td>monkey</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>0.69:1</td>
<td>C.F.</td>
<td>14.1</td>
<td>1.37</td>
<td>increases for 60 min, then 265</td>
<td>monkey</td>
<td>30</td>
<td>poor injection</td>
<td></td>
</tr>
</tbody>
</table>

¹. Carrier-free.
Table III. Results from scanning 22 patients at Donner Laboratory with \( ^{157} \text{Dy-HEDTA} \) and \( ^{18} \text{F} \); (+) abnormal bone scan, (-) normal bone scan.

<table>
<thead>
<tr>
<th>Patient/Sex</th>
<th>Condition</th>
<th>( ^{157} \text{Dy} )</th>
<th>( ^{18} \text{F} )</th>
<th>85Sr</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.B./M</td>
<td>Hepatoma? metastases</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
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<tr>
<td>V.M./F</td>
<td>Postoperative CA of breast</td>
<td>-</td>
<td></td>
<td></td>
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<tr>
<td>N.J./M</td>
<td>Multiple myeloma, ?osteoporotic disease</td>
<td>-</td>
<td></td>
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<tr>
<td>L.W./F</td>
<td>Bone tumor</td>
<td>+</td>
<td></td>
<td></td>
<td>Increased uptake R anterior thoracic</td>
</tr>
<tr>
<td>L.S./F</td>
<td>CA esophagus, back trauma</td>
<td>+</td>
<td></td>
<td></td>
<td>Increased uptake in three areas</td>
</tr>
<tr>
<td>C.D./F</td>
<td>Old CA lung</td>
<td>+</td>
<td>+</td>
<td></td>
<td>Increased uptake T9-10; also in wrist due to sprain; increased uptake in thoracic spine</td>
</tr>
<tr>
<td>J.A./M</td>
<td>CA lung--alcoholic</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Increased uptake in R shoulder, R lateral ribcage, hip and thoracic spine--( ^{157} \text{Dy}, 85 \text{Sr}, 18 \text{F} )</td>
</tr>
<tr>
<td>S.H./F</td>
<td>Hodgkin's</td>
<td>+</td>
<td></td>
<td></td>
<td>Heavy concentration in sacroiliac joints -- more in R</td>
</tr>
<tr>
<td>M.H./F</td>
<td>Paget's</td>
<td>+</td>
<td></td>
<td></td>
<td>Increased uptake in sacroiliac joints</td>
</tr>
<tr>
<td>J.E./M</td>
<td>Osteopetrosis</td>
<td>+</td>
<td>+</td>
<td></td>
<td>Increased uptake in old fractured R femur</td>
</tr>
<tr>
<td>E.J./F</td>
<td>L radical mastectomy--supraclavicular lymph nodes</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G.Z./F</td>
<td>Skeletal metastases from CA breast</td>
<td>+</td>
<td></td>
<td></td>
<td>Good visualization of lesions (lumbar spine)</td>
</tr>
<tr>
<td>M.H./F</td>
<td>'61 mastectomy &amp; oophorectomy; '70 L-4 collapse</td>
<td>+</td>
<td>+</td>
<td></td>
<td>Increased uptake: L-4 R of midline</td>
</tr>
<tr>
<td>R.T./F</td>
<td>Hodgkin's</td>
<td>+</td>
<td></td>
<td></td>
<td>Increased uptake L knee, uptake L temporal skull and L scapula</td>
</tr>
<tr>
<td>G.P./M</td>
<td>? R/o bone metastasis; CA of R lung</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.C./F</td>
<td>Breast CA; liver metastasis</td>
<td>-</td>
<td>-</td>
<td></td>
<td>Increased lumbar spine (normal after radiation therapy)</td>
</tr>
<tr>
<td>H.G./M</td>
<td>Lymphosarcoma, pain hips and lower spine</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.M./F</td>
<td>Osteoporosis</td>
<td>-</td>
<td>-</td>
<td></td>
<td>Decreased bone blood flow</td>
</tr>
<tr>
<td>M.B./F</td>
<td>Early myeloma</td>
<td>-</td>
<td></td>
<td>No abnormal regional uptake</td>
<td></td>
</tr>
<tr>
<td>K.C./M</td>
<td>Possible lesion T6-9</td>
<td>-</td>
<td></td>
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</tr>
</tbody>
</table>
Table IV. Percent $^{157}$Dy-HEDTA per liter of blood, percent excreted in urine, and fast and slow half times for clearance from blood 3 hr after intravenous injection in humans.

<table>
<thead>
<tr>
<th>Subject</th>
<th>$^{157}$Dy/liter blood (%)</th>
<th>$^{157}$Dy in urine (%)</th>
<th>Blood $T_{1/2}$ (min) (fast)</th>
<th>Blood $T_{1/2}$ (min) (slow)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1.92</td>
<td>47.5</td>
<td>14</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Avg. 13</td>
<td>Avg. 95</td>
</tr>
<tr>
<td>Normal</td>
<td>0.91</td>
<td>41.5</td>
<td>12</td>
<td>92</td>
</tr>
<tr>
<td>Abnormal</td>
<td>0.72</td>
<td>37.5</td>
<td>8</td>
<td>64</td>
</tr>
</tbody>
</table>
Figure Captions

Fig. 1. Decay scheme and gamma spectrum of $^{157}$Dy.

Fig. 2. Distribution of $^{157}$Dy-HEDTA in rat tissue 2 hours after intravenous administration of 5:1, 10:1, 20:1, and 30:1 molar ratios of HEDTA to Tb.

Fig. 3. Posterior views of dog with lesion in left tibia; $^{157}$Dy-HEDTA (20:1) scintillation camera pictures (left) and $^{18}$F positron camera pictures (right).

Fig. 4. Whole-body scans with $^{157}$Dy taken at 15 min (top), showing excretion, and at 5 hr (bottom), showing bone uptake. Note the increased uptake in the lumbar vertebrae.

Fig. 5. Whole-body scans with $^{157}$Dy (top) and $^{18}$F (bottom), showing increased uptake at the lesion site of female patient with metastases to the lumbar spine.

Fig. 6. $^{157}$Dy-HEDTA scintillation camera picture of female patient with cancer of breast and metastases to liver. Anterior whole-body view (right) and posterior view of spine (left); note improved resolution of spine from posterior aspect.

Fig. 7. Whole-body scans of male patient with osteopetrosis and old fracture in left femur; $^{18}$F scan (top) and $^{157}$Dy scan (bottom).

Fig. 8. Whole-body scan of male patient with cancer of the lungs; $^{18}$F scan (top), $^{157}$Dy scan (middle), and $^{85}$Sr scan (bottom). Note increased uptake in lumbar spine and at fracture site in right femur.

Fig. 9. $^{157}$Dy whole-body scan showing increased uptake in lumbar spine of a female patient with cancer of breast.
$^{157}$Dy DECAY SCHEME

$^{157}$Dy $\rightarrow$ $^{157}$Tb (91%)

$^{157}$Dy $\rightarrow$ $^{156}$Dy (5.0%)

$^{157}$Dy $\rightarrow$ $^{157}$Gd (0.061)

$^{157}$Dy GAMMA SPECTRUM

2'' $\times$ 2'' NaI (TI)

326 keV

Fig. 1
Fig. 2
DOG: LESION LEFT LEG

\[ ^{157}\text{Dy-HEDTA (20:1)} \]
\[ 1 \text{ mCi} \]

\[ ^{18}\text{F} \quad 130 \mu\text{Ci} \]

Posterior

Posterior

XBB 709-3977

Fig. 3
$^{157}$Dy-HEDTA

BO-70-179

15 min post injection

5 hr post injection

XBB 709-3981

Fig. 4
$^{157}$Dy-HEDTA

Fig. 5
$^{157}$ Dy-HEDTA

Fig. 9
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