\( ^{111} \text{In-BLEOMYCIN KINETICS IN MICE BEARING TRANSPLANTABLE TUMORS OF LUNG, SKIN, AND BONE } \)

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Stable and chemically pure \( ^{111} \text{In-bleomycin for injection can be prepared easily from carrier-free } ^{111} \text{InCl}_3 \) and an aqueous solution of bleomycin by mixing the two at pH 1.5, adjusting the pH to 6.5–7, and autoclaving. This radiopharmaceutical shows definite tumor affinity within an hour after injection as would be predicted from its efficacy as a chemotherapeutic agent, but optimum \( ^{111} \text{In tumor-to-blood ratios in three transplantable mouse tumors are not reached for 2 days. At 48 hr postinjection, it is not known if } ^{111} \text{In is still chelated to bleomycin.} \)

Bleomycin has proven useful as an antitumor agent. It is comprised of a group of 13 polypeptides isolated from a strain of Streptomyces verticillus (1). The \( ^{57} \text{Co chelate of bleomycin has been used as a tumor-scanning agent by Nouel, et al (2). While } ^{57} \text{Co has a very favorable energy (122 keV) for the commonly available imaging devices, its very long physical half-life (270 days) imposes a necessary limitation on its use, i.e., the urine from patients who receive the agent must be collected and processed to remove the radiocontaminant (3).} \)

To avoid this limitation, we surveyed the chart of the nuclides for a gamma emitter whose chemical properties would be suitable for chelation with bleomycin and whose physical properties were also suitable for use with radionuclide imaging devices. Some of the amino acids contained in bleomycin contain the appropriate configuration and charge for chelation. These have been identified after hydrolysis of this antibiotic (4). Renault, et al (5) have tagged bleomycin with \( ^{55} \text{Co, } ^{64} \text{Cu, } ^{65} \text{Zn, and } ^{203} \text{Hg.} \) Of these, only \( ^{57} \text{Co proved useful, but its half-life appeared disadvantageous to us as noted above. Indium-111 was selected because it has a short half-life (67 hr), gamma-ray energies of 179 and 247 keV, and no beta emission. It is available commercially in a radioisotopically pure form.} \)

In this paper we describe the preparation of \( ^{111} \text{In-bleomycin, some of its physical and chemical properties, and its distribution in tumor-bearing mice compared with } ^{111} \text{InCl}_3 \) in the same mice.

\section*{MATERIALS AND METHODS}

\subsection*{Preparation of \( ^{111} \text{In-bleomycin.} \) Carrier-free \( ^{111} \text{InCl}_3 \) was purchased in the sterile, pyrogen-free form.}

1. Five milligrams of bleomycin powder† were dissolved in 3 ml of Water for Injection, U.S.P. The pH was adjusted to 1.5 with approximately 0.5 ml 0.5 N HCl.

2. Approximately 1 ml (100 Ci) \( ^{111} \text{InCl}_3 \) supplied at pH 1.5, was mixed with the bleomycin solution.

3. The solution was adjusted to pH 6.5–7 with approximately 0.6 ml 0.5 N NaOH.

4. The solution was passed through a 0.45-micron Millipore filter or sterilized by autoclaving at 121°C, 15 psi for 15 min.

The radiochemical purity and tagging yield were determined using instant thin-layer chromatography (ITLC)‡ with 10% ammonium acetate:methanol (1:1) as solvent. The \( ^{111} \text{InCl}_3 \), adjusted to pH 7, had an \( R_f \) value of 0–0.08 and the \( ^{111} \text{In-labeled bleomycin an } R_f \) value of 0.49–1.0.

\subsection*{Thermal stability.}

The thermal stability of the

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* Diagnostics Isotopes Inc., Upper Saddle River, New Jersey.

† Bristol Laboratories, Division of Bristol-Meyers, Syracuse, New York.

‡ Type SG, Gelman Instrument Co., Ann Arbor, Michigan.
$^{111}$In-bleomycin was determined by incubating the preparation for 48 hr at room temperature and at 37°C, and by autoclaving for 30 min at 121°C, 15 psi. Instant thin-layer chromatography of the radio-pharmaceutical at 1, 24, and 48 hr after preparation and before and after autoclaving was done to show the amount of free indium formed.

**Chemical stability.** The stability of $^{111}$In-bleomycin was challenged in vitro by incubating the $^{111}$In-bleomycin with various metal ions found in vivo as suggested by Thakur, et al (6). Excesses of Ca$^{2+}$ and Cu$^{2+}$ (CaCl$_2$ and CuSO$_4$, equivalent to 100 mg of the cation) were incubated with $^{111}$In-bleomycin at room temperature for 48 hr. Samples withdrawn at 1, 24, and 48 hr after start of incubation were chromatographed using the ITLC system described above to indicate the amount of free indium formed.

**Distribution studies in mice.** Mice (AKR strain) bearing Ridgeway osteogenic sarcoma and C57Bl/6 mice bearing Lewis lung tumor and B-16 melanoma, implanted subcutaneously 1–2 weeks before the tissue distribution studies, were kindly supplied by the Southern Research Institute of Birmingham, Alabama. Bleomycin has been shown to inhibit tumor growth in mice bearing B-16 melanoma and Lewis lung tumors (7).

Groups of mice were injected intraperitoneally with 10–80 $\mu$Ci of $^{111}$InCl$_3$ and $^{111}$In-bleomycin containing 0.2 mg bleomycin per injection. Each mouse received 0.2 ml of the $^{111}$In-bleomycin solution. The mice were sacrificed by acute trauma to the head at 1, 6, 24, and 48 hr after injection. Samples of heart blood were withdrawn immediately. Samples of the tumor, skin, fat, muscle, lung, kidneys, liver, spleen, lower and upper intestine, and heart were removed from the mice and weighed in tared counting tubes containing 2 ml saline. The $^{111}$In activity in each sample was counted in a well scintillation counter set on integral mode to count the activity from 30 keV photons and above. The counting rates were corrected for background and for decay of $^{111}$In to the time of injection. Standards were prepared in triplicate by transferring 0.2-ml doses of $^{111}$In-bleomycin to volumetric flasks and dilution to an activity level approximately equal to the sample. A 2-ml aliquot of each standard was counted in the well counter. The counting rates were corrected in the same manner as the samples. The data are expressed as percent dose per gram tissue.

**RESULTS**

The yield of $^{111}$In-bleomycin was 90–99% determined by ITLC. Figure 1 is a histogram representing the chromatography of $^{111}$In-bleomycin and $^{111}$InCl$_3$.

 Forty to 60% of the activity remained on 0.22 and 0.45-micron Millipore filters when filtration was used to sterilize the product.

As seen in Table 1, the yield of $^{111}$In-bleomycin decreased with decreasing quantities of bleomycin used in the procedure described under “Materials and Methods”.

The thermal stability of $^{111}$In-bleomycin was excellent. Samples incubated at room temperature and at 37°C for 48 hr were chromatographed using the ITLC system and showed no change during that
time. One to 2% free indium was present in both samples throughout the 48-hr incubation. Autoclaving an \(^{111}\text{In}\)-bleomycin preparation showed no change in the amount of free indium present. The presence of 1.5% free indium on the ITLC before and after autoclaving indicates that the preparation may be sterilized by this technique.

In the presence of Ca\(^{2+}\) in vitro, \(^{111}\text{In}\)-bleomycin was stable when sampled during the 48 hr-incubation. In the presence of Cu\(^{2+}\), the \(^{111}\text{In}\)-bleomycin label was destroyed in 1 hr. The ITLC of the latter sample withdrawn at 1 hr after start of incubation showed 94% of the activity in the R\(_2\) 0-0.08 region.

The results of the tissue distribution studies in mice are given in Tables 2–5. Table 2 presents results from the study of \(^{111}\text{In}\)Cl\(_3\) in C57B1/6 mice with Lewis lung tumors; while Tables 3–5 show the results from \(^{111}\text{In}\)-bleomycin injected into C57B1/6 mice bearing Lewis lung tumors, C57B1/6 mice bearing B-16 melanoma, and AKR mice bearing Ridgeway osteogenic sarcoma, respectively. Table 6 gives a comparison of ratios of tumor to blood, lung, skin, kidney, liver, muscle, and fat in the C57B1/6 mice bearing Lewis lung tumors for both \(^{111}\text{In}\)-bleomycin and \(^{111}\text{In}\)Cl\(_3\). Tables 7 and 8 provide similar data for \(^{111}\text{In}\)-bleomycin only for C57B1/6 mice bearing B-16 melanoma and AKR mice bearing Ridgeway osteogenic sarcoma.

It is apparent that the \(^{111}\text{In}\)Cl\(_3\) tumor concentration is considerably greater than that of \(^{111}\text{In}\)-bleomycin but is cleared more slowly from the blood. By 48 hr postinjection the tumor-to-blood ratios exceed 9 with both agents (Table 6). In fact, the ratios of tumor to kidney, liver, lung, and muscle are remarkably similar by 48 hr.

**DISCUSSION**

The cumulative human therapeutic dose of bleomycin has been limited to 3 mg/kg, and with a single dose of 0.1 mg/kg some febrile responses...
TABLE 4. DISTRIBUTION OF $^{111}$In-BLEOMYCIN IN C57B1/6 MICE BEARING B-16 MELANOMA (PERCENT DOSE/GM TISSUE ± 1 S.D.)*

<table>
<thead>
<tr>
<th>Organ</th>
<th>1 hr</th>
<th>6 hr</th>
<th>24 hr</th>
<th>48 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor</td>
<td>7.28 ± 1.61</td>
<td>4.28 ± 1.05</td>
<td>4.19 ± 1.05</td>
<td>3.48 ± 0.95</td>
</tr>
<tr>
<td>Skin</td>
<td>6.06 ± 0.94</td>
<td>2.72 ± 0.21</td>
<td>1.67 ± 0.65</td>
<td>1.42 ± 0.73</td>
</tr>
<tr>
<td>Fat</td>
<td>2.36 ± 0.45</td>
<td>1.38 ± 0.20</td>
<td>1.26 ± 0.68</td>
<td>1.48 ± 0.80</td>
</tr>
<tr>
<td>Muscle</td>
<td>6.56 ± 4.09</td>
<td>1.29 ± 0.73</td>
<td>0.54 ± 0.22</td>
<td>0.61 ± 0.25</td>
</tr>
<tr>
<td>Lung</td>
<td>8.06 ± 2.42</td>
<td>2.75 ± 0.33</td>
<td>1.16 ± 0.50</td>
<td>1.40 ± 0.38</td>
</tr>
<tr>
<td>Kidneys</td>
<td>27.30 ± 3.14</td>
<td>19.73 ± 4.89</td>
<td>16.51 ± 4.90</td>
<td>17.44 ± 1.08</td>
</tr>
<tr>
<td>Liver</td>
<td>4.42 ± 0.66</td>
<td>2.47 ± 0.44</td>
<td>3.12 ± 1.13</td>
<td>4.29 ± 1.12</td>
</tr>
<tr>
<td>Spleen</td>
<td>3.55 ± 1.16</td>
<td>1.69 ± 0.20</td>
<td>2.09 ± 1.14</td>
<td>2.07 ± 0.53</td>
</tr>
<tr>
<td>Blood</td>
<td>3.85 ± 0.79</td>
<td>2.99 ± 0.54</td>
<td>0.72 ± 0.30</td>
<td>0.33 ± 0.18</td>
</tr>
<tr>
<td>Heart</td>
<td>2.48 ± 0.33</td>
<td>1.00 ± 0.19</td>
<td>0.49 ± 0.18</td>
<td>0.45 ± 0.05</td>
</tr>
</tbody>
</table>

* Three mice in each group; average value ± 1 s.d.

TABLE 5. DISTRIBUTION OF $^{111}$In-BLEOMYCIN IN AKR MICE BEARING RIDGEWAY OSTEOSARCOMA (PERCENT DOSE/GM TISSUE ± 1 S.D.)*

<table>
<thead>
<tr>
<th>Organ</th>
<th>1 hr</th>
<th>6 hr</th>
<th>24 hr</th>
<th>48 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor</td>
<td>4.93 ± 3.23</td>
<td>2.88 ± 1.15</td>
<td>2.15 ± 0.01*</td>
<td>1.61 ± 0.43</td>
</tr>
<tr>
<td>Skin</td>
<td>4.56 ± 1.87</td>
<td>2.26 ± 0.28</td>
<td>1.29 ± 0.41</td>
<td>1.64 ± 0.26</td>
</tr>
<tr>
<td>Fat</td>
<td>2.14 ± 1.50</td>
<td>1.00 ± 0.15</td>
<td>0.73 ± 0.25</td>
<td>1.22 ± 0.13</td>
</tr>
<tr>
<td>Muscle</td>
<td>3.93 ± 2.06</td>
<td>1.14 ± 0.31</td>
<td>0.74 ± 0.23</td>
<td>0.81 ± 0.07</td>
</tr>
<tr>
<td>Lung</td>
<td>3.79 ± 1.43</td>
<td>2.32 ± 0.87</td>
<td>1.24 ± 1.00</td>
<td>0.84 ± 0.32</td>
</tr>
<tr>
<td>Kidneys</td>
<td>12.05 ± 7.31</td>
<td>9.59 ± 4.11</td>
<td>7.88 ± 0.71</td>
<td>8.91 ± 2.09</td>
</tr>
<tr>
<td>Liver</td>
<td>1.99 ± 0.49</td>
<td>1.53 ± 0.23</td>
<td>1.62 ± 0.85</td>
<td>5.70 ± 6.23</td>
</tr>
<tr>
<td>Spleen</td>
<td>1.61 ± 0.54</td>
<td>1.17 ± 0.23</td>
<td>1.32 ± 0.66</td>
<td>1.71 ± 0.37</td>
</tr>
<tr>
<td>Blood</td>
<td>4.00 ± 0.63</td>
<td>3.35 ± 0.56</td>
<td>0.84 ± 0.54</td>
<td>0.38 ± 0.14</td>
</tr>
<tr>
<td>Heart</td>
<td>1.65 ± 0.41</td>
<td>0.95 ± 0.16</td>
<td>0.46 ± 0.25</td>
<td>0.44 ± 0.03</td>
</tr>
</tbody>
</table>

* Three mice in each group; average value ± 1 s.d.
† Tumors from 2 mice; average value ± one-half the range of the individual values.

have been noted (8). The diagnostic dose, therefore, should be as low as practicable. In our labeling procedure, a 5-mg quantity was the smallest amount of bleomycin that would give a yield better than 90%. Therefore, this quantity has been used throughout our study. The preparation contains 1 mg/ml. At this concentration an average patient given a nominal 1-ml volume would receive 0.014 mg/kg. This is well below the level mentioned above which has produced febrile responses in patients. The decreasing yield with decreasing quantity of bleomycin employed is an indication of the capacity of bleomycin to complex trivalent cations as discussed by Renault (5,9).

Millipore filtration of $^{111}$In-bleomycin would be the most convenient method of sterilizing the preparation. However, since 0.45 and 0.22-micron filters reduce the quantity of $^{111}$In-bleomycin obtained, sterilization by autoclaving is the method preferred. The thermal stability at autoclave temperature and pressure permits the autoclave method to be used. The material that is filtered from the $^{111}$In-bleomycin solution is some of the tagged polypeptide. The material on the filter could not be insoluble indium hydroxide since a strong chelate is formed with bleomycin. Thin-layer chromatography confirmed the high tagging yield (90–99%).

The thermal stability at room temperature indicates that this radiopharmaceutical can be prepared several hours in advance of its use. The stability at body temperature (37°C) indicates the suitability of $^{111}$In-bleomycin for use in the human.

The exchange of Cu$^{2+}$ with the $^{111}$In-bleomycin that occurred in the in vitro experiment suggests possible dissociation of the $^{111}$In-bleomycin chelate when this metal is encountered in vivo. This is not unexpected since it is known that Cu$^{2+}$ forms more stable chelates than In$^{3+}$ with bleomycin (9).

The similarity of the tumor-to-kidney, liver, lung, and muscle ratios at 48 hr for $^{111}$InCl$_3$ and $^{111}$In-bleomycin (Table 6) suggests dissociation of the bleomycin label. Thakur, et al have shown that the $^{111}$In of $^{111}$In-bleomycin is found on transferrin within 4 hr postinjection in man (6), which suggests
TABLE 6. TUMOR:ORGAN RATIOS FOR $^{111}$InCl$_3$ AND $^{111}$In-BLEOMYCIN IN C57B1/6 MICE BEARING LEWIS LUNG TUMORS

<table>
<thead>
<tr>
<th>Time after injection</th>
<th>1 hr</th>
<th>6 hr</th>
<th>24 hr</th>
<th>48 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In*</td>
<td>BLM</td>
<td>In*</td>
<td>BLM</td>
</tr>
<tr>
<td>Tumor:Blood</td>
<td>0.33</td>
<td>0.62</td>
<td>1.20</td>
<td>0.92</td>
</tr>
<tr>
<td>Tumor:Lung</td>
<td>0.67</td>
<td>0.83</td>
<td>0.72</td>
<td>1.02</td>
</tr>
<tr>
<td>Tumor:Skin</td>
<td>2.99</td>
<td>0.37</td>
<td>2.74</td>
<td>0.88</td>
</tr>
<tr>
<td>Tumor:Kidney</td>
<td>0.14</td>
<td>0.23</td>
<td>0.06</td>
<td>0.16</td>
</tr>
<tr>
<td>Tumor:Liver</td>
<td>0.86</td>
<td>1.44</td>
<td>0.56</td>
<td>0.73</td>
</tr>
<tr>
<td>Tumor:Muscle</td>
<td>1.03</td>
<td>1.04</td>
<td>—</td>
<td>1.00</td>
</tr>
<tr>
<td>Tumor:Fat</td>
<td>0.43</td>
<td>1.44</td>
<td>0.73</td>
<td>2.09</td>
</tr>
</tbody>
</table>

* In = $^{111}$InCl$_3$.
† BLM = $^{111}$In-bleomycin.

TABLE 7. TUMOR:ORGAN RATIOS FOR $^{111}$In-BLEOMYCIN IN C57B1/6 MICE BEARING B-16 MELANOMA

<table>
<thead>
<tr>
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<th>48 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In*</td>
<td>BLM</td>
<td>In*</td>
<td>BLM</td>
</tr>
<tr>
<td>Tumor:Blood</td>
<td>1.24</td>
<td>1.43</td>
<td>5.82</td>
<td>10.55</td>
</tr>
<tr>
<td>Tumor:Lung</td>
<td>0.90</td>
<td>1.56</td>
<td>3.61</td>
<td>2.49</td>
</tr>
<tr>
<td>Tumor:Skin</td>
<td>1.05</td>
<td>1.57</td>
<td>2.51</td>
<td>2.45</td>
</tr>
<tr>
<td>Tumor:Kidney</td>
<td>0.27</td>
<td>0.32</td>
<td>0.25</td>
<td>0.20</td>
</tr>
<tr>
<td>Tumor:Liver</td>
<td>1.65</td>
<td>1.73</td>
<td>1.34</td>
<td>0.81</td>
</tr>
<tr>
<td>Tumor:Muscle</td>
<td>1.11</td>
<td>3.32</td>
<td>7.76</td>
<td>5.20</td>
</tr>
<tr>
<td>Tumor:Fat</td>
<td>3.22</td>
<td>3.26</td>
<td>3.33</td>
<td>2.35</td>
</tr>
</tbody>
</table>

TABLE 8. TUMOR:ORGAN RATIOS FOR $^{111}$In-BLEOMYCIN IN AKR MICE BEARING RIDGWAY OSTEOSARCOMA

<table>
<thead>
<tr>
<th>Time after injection</th>
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<th>48 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In*</td>
<td>BLM</td>
<td>In*</td>
<td>BLM</td>
</tr>
<tr>
<td>Tumor:Blood</td>
<td>1.23</td>
<td>0.86</td>
<td>2.56</td>
<td>4.24</td>
</tr>
<tr>
<td>Tumor:Lung</td>
<td>1.30</td>
<td>1.24</td>
<td>1.73</td>
<td>1.92</td>
</tr>
<tr>
<td>Tumor:Skin</td>
<td>1.08</td>
<td>1.27</td>
<td>1.66</td>
<td>0.98</td>
</tr>
<tr>
<td>Tumor:Kidney</td>
<td>0.41</td>
<td>0.30</td>
<td>0.27</td>
<td>0.18</td>
</tr>
<tr>
<td>Tumor:Liver</td>
<td>2.47</td>
<td>1.86</td>
<td>1.33</td>
<td>0.28</td>
</tr>
<tr>
<td>Tumor:Muscle</td>
<td>1.25</td>
<td>2.53</td>
<td>2.91</td>
<td>1.99</td>
</tr>
<tr>
<td>Tumor:Fat</td>
<td>2.30</td>
<td>2.88</td>
<td>2.94</td>
<td>1.32</td>
</tr>
</tbody>
</table>

competition by transferrin for the $^{111}$In label and/or exchange of serum cations for the chelated indium. Studies using $^{14}$C-labeled bleomycin compared with $^{111}$In-bleomycin to resolve these two suggestions are contemplated. The absolute uptake of activity by the tumor (Tables 2 and 3) and the tumor-to-organ ratios (Table 6) for $^{111}$InCl$_3$ and $^{111}$In-bleomycin suggest that $^{111}$InCl$_3$ is a superior scanning agent to $^{111}$In-bleomycin.

In agreement with the original studies of Umezawa on unlabeled bleomycin in mice bearing Ehrlich carcinoma (10), we find tumor concentration at a maximum 1 hr postinjection. But, at variance with his data, Tables 3–5 indicate concentrations of $^{111}$In-bleomycin in many tissues at 1 hr at a level close to that of the tumors we studied. We find persistently high kidney activity at 48 hr while the renal concentration of Umezawa's unlabeled preparation fell to levels lower than those found in tumor within 5 hr. Apparently $^{111}$In-bleomycin as a chelate is metabolized differently from the material studied by Umezawa.

The highest ratios of tumor to blood in this study clearly occur at 48 hr for the three tumors studied (Tables 6–8) but the ratios of tumor to liver, skin, kidney, muscle, and fat are higher at 24 hr for the Ridgway osteosarcoma. The data suggest optimum scanning time at 24–48 hr. We studied no animals beyond 48 hr.

ACKNOWLEDGMENT

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REFERENCES

Accepted Articles To Appear in Upcoming Issues

Distribution and Retention of the Anti-tumor Agent Cis-dichlorodiammine-
platinum (II) in Man (Concise Communication). Accepted 11/21/73.

Use of $^{111}$ In-labeled Leukocytes in the Diagnosis of Cerebral Aneurysms (Concise Communication). Accepted 11/30/73.

J. P. McKeigan, G. Muehlethaler, and R. A. Moyer
Detection of Abnormalities Produced by Electroencephalographic Procedures (Case Report). Accepted 12/3/73.

R. W. Morris and F. H. DeLand
An Automated System for Measurement of Leucocyte Metabolism (Concise Communication). Accepted 11/21/73.

J. F. Hoffer, K. Lahroup, C. Bekeruam, V. S. Frank, and S. Refetoff
Safety of Yb-DTPA in Cisternography (Letter to the Editor). Accepted 11/21/73.

J. B. Hands and D. M. Taylor
An Automated Technique for the Detection of Subphrenic Abscesses Using $^{99m}$ Tc (Preliminary Note). Accepted 11/30/73.

R. M. Bein, J. R. Damron, and T. Hafner
Histogram in the Diagnosis of Cerebral Aneurysms (Case Report). Accepted 11/30/73.

F. J. DeLand and F. Garcia
Detection of Abscesses with $^{99m}$ Tc-labeled Leukocytes (Letter to the Editor). Accepted 11/30/73.

W. C. Harvey
Limitations of Orthogonal Tangent Correction (Letter to the Editor). Accepted 11/30/73.

J. W. Keys
Section Scanning Using Orthogonal Tangent Correction (Letter to the Editor). Accepted 11/30/73.

G. D. S. Neill
The Authors’ Reply to Letters to the Editor. Accepted 11/30/73.

D. E. Kuhl and R. Q. Edwards
Blomycin as a $^{99m}$ Tc Carrier in Tumor Visualization. Accepted 12/3/73.

M. S. Lin, D. A. Goodwin, and S. L. Kruse
Brain Scan Abnormalities Produced by Electroencephalographic Procedures (Case Report). Accepted 12/3/73.

E. H. Harris, J. W. Fletcher, E. Solaric-George, and R. M. Donati
Use of $^{111}$ In and $^{111}$ Inm as Sources for Bone Mineralization Studies. Accepted 11/30/73.

A. M. Friedman, B. G. Olitman, J. Kastner, F. K. Eckerman, and L. S. Goodman
Localization of a Metastatic Adenocarcinoma Using $^{111}$ In-19-Iodocholesteryl. Accepted 12/3/73.

B. L. Forman, M. A. Amin, R. J. Touloukian, P. J. Mullrow, and M. Gehl
Effects of Capsular Blockage with $^{99m}$ Tc-Iron Hydroxide: A Histopathologic Study (Concise Communication). Accepted 12/3/73.

M. S. L. Lin, D. A. Goodwin, and S. L. Kruse
Clinical Evaluation of Radiolabeled Blomycin for Tumor Detection. Accepted 12/3/73.

R. B. Groves, R. C. Reba, W. C. Eckerman, and M. Goodyear
Use of $^{99m}$ Tc-DTPA for Measuring Gastric Emptying Time. Accepted 12/6/73.

T. K. Chaudhuri
Tomography Using An Unmodified Anger Camera (Concise Communication). Accepted 12/11/73.

J. T. Payne, D. Reinke, and M. K. Loken

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Ga-Citrine Imaging in Untreated Primary Lung Cancer: Preliminary Report of Cooperative Group. Accepted 12/31/73.

Quality Control of $^{99m}$ Tc-DTPA by Double Tracer Clearance Technique (Concise Communication). Accepted 12/31/73.

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Radionuclide Cisternography—Prediction of Clinical Results of Neurosurgical Shunting in Patients with Communicating Normal Pressure Hydrocephalus—Fact or Fantasy (Letter to the Editor). Accepted 12/31/73.

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$^{111}$ In Transmission Source (Concise Communication). Accepted 12/31/73.

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Uptake of $^{99m}$ Tc-Sulfur Colloid During Liver Scanning (Case Report). Accepted 12/31/73.

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Tumor Blood Flow Study to Measure Response to Treatment (Case Report). Accepted 12/31/73.

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Cross Reaction of Schwarz/Mann Antibody with a Normal Control Serum (Letter to the Editor). Accepted 12/31/73.

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Radionuclide Contamination of Eluates from Fission-Product Molybdenum-Technetium Generators (Letter to the Editor). Accepted 12/31/73.

M. H. Briner, C. C. Harris
Anger Camera Deadtime (Letter to the Editor). Accepted 12/31/73.

M. Hutti
The Authors’ Reply. Accepted 12/31/73.

R. Adams and D. Zimmerman
Peristalsis Activity of Carcinoma Tumors Used in Radioummunodiagnosis. Accepted 1/16/74.

A. R. Hunter, S. Gutcho, J. Johnson, and T. Dodd
Distribution of $^{60}$ Co and $^{99}$ Sr-Heterotocicin in Dogs and Toadfish. Accepted 1/16/74.

U. R. Yoo, W. H. Beierwaltes, P. Feehan, and R. D. Ice
Scan Demonstration of Delayed Splenic Rupture (Case Report). Accepted 1/16/74.

J. D. Slavin, T. F. Minehan, and R. P. Spencer
Renal Uptake of $^{99m}$ Tc-Sulfur Colloid, Accepted 1/16/74.

C. B. Higgins, R. M. Takeda, A. Taylor, S. E. Halpern, and W. L. Ashburn


