Comparison of Immunoscintigraphy and Computerized Tomography in Identifying Colorectal Cancer: Individual Lesion Analysis

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ABSTRACT

Monoclonal antibody scintigraphy with $^{111}$In-ZCE025 was used in presurgical staging of 45 patients prior to abdominal exploration for primary, recurrent or metastatic colorectal carcinoma. A total of 186 lesions were identified, of which 147 were evaluated by abdominal surgery and pathology. Sensitivity was 40.5% (49 of 121) for immunoscintigraphy (IS), 61.2% (74 of 121) for computerized tomography (CT), and 72.7% (88 of 121) for IS and CT combined. The positive predictive value was 83.1% (49 of 59) for IS and 88.1% (74 of 84) for CT. Sensitivity of IS was 100% (23 of 23) for primary tumors, 17.7% (11 of 62) for hepatic metastases, and 41.7% (15 of 36) for extrahepatic abdominal metastases. Of the 50 hepatic lesions evaluated by single-proton emission computed tomography, 11 were localized by IS. Only one was visualized by planar scintigraphy. Sensitivity of CT was 87% (20 of 23) for primary tumors, 67.7% (42 of 62) for hepatic metastases, and 33.3% (12 of 36) for extrahepatic abdominal metastases. Sensitivity of IS combined with CT was 72.6% (45 of 62) for hepatic and 55.6% (20 of 36) for extrahepatic abdominal metastases. Of 24 malignant lesions measured by the pathologist to be <3.0 cm (maximum dimension), 7 (29.2%) were detected by IS and 3 (12.5%) by CT. Of 28 malignant lesions >3.0 cm, 23 (82.1%) were detected by IS and 24 (85.7%) by CT. Overall, IS and CT complemented each other in presurgical staging of colorectal carcinoma. IS was of greater value for identification of extraparenchymal and small metastases. CT was more effective for identification of hepatic metastases.

INTRODUCTION

IS$^1$ with radiolabeled monoclonal antibody specific for a tumor marker has shown potential value in cancer patient management (1–6). In colorectal adenocarcinoma, presurgical imaging has confirmed known sites of metastatic disease and has identified occult sites of disease that had not been localized previously (7–11). The sensitivity of IS for abdominal and pelvic disease has been reported to vary over a wide range, i.e., from 38% (12) to >90% (11), depending upon the antibody, the radionuclide, the disease location, and, most importantly, the method of scoring sensitivity (lesion versus region analysis). Similarly, CT has had sensitivity for abdominal metastatic disease ranging from 30% (2, 4) to >70% (13).

We previously reported our experience with two anti-CEA murine monoclonal antibodies (T84.66 and ZCE025) labeled with $^{111}$In (1, 9, 10) in patients with primary colorectal lesions, resectable hepatic metastases, or suspected resectable abdomin nal metastases. The patients were imaged prior to planned abdominal explorations, and IS results were compared to surgical and pathological findings in four clinically relevant anatomic regions. The IS was recorded as either positive or negative in each region, the presence of tumor was documented as either positive or negative in each region, and statistical analyses were performed on that basis. The clinical value of IS was in the identification of, and frequently the localization of, metastatic colorectal cancer in the abdomen outside the liver (extrahepatic) or outside the abdomen (extraabdominal). The patients benefitting from altered management based upon presurgical IS staging included (a) patients being explored for resection of hepatic metastases and (b) patients with increasing plasma CEA concentrations following resection of primary colorectal cancer in whom the suspected site of recurrence remained unknown after conventional investigations and in whom "second-look" laparotomy was planned. In these studies, IS and disease status were compared regionally in the colorectum, liver, extrahepatic abdomen, and all extraabdominal areas.

In the present study, IS and CT were compared with disease status on a lesion by lesion basis. Patients had preoperative IS with $^{111}$In-ZCE025 and CT, followed by abdominal exploration and pathological evaluation of disease sites. The sensitivity and accuracy of IS for CEA-specific identification and localization of individual sites of intraabdominal colorectal cancer was compared with CT for nonspecific identification and localization of the same individual lesions.

MATERIALS AND METHODS

Antibody Preparation and Administration. A murine IgG1 intact monoclonal antibody specific for CEA (ZCE025) was conjugated with diethyltertamamine pentaacetic acid (14) and labeled with $^{111}$In (dose range 2.5–7.1 mCi) using a kit provided by Hybritech Inc. (San Diego, CA). Labeling efficiency was confirmed to be 80% or greater by thin layer chromatography. Labeled $^{111}$In-ZCE025 (1 mg) was mixed with either 19 or 39 mg of unlabeled ZCE025 in approximately 50 ml of saline to produce the final $^{111}$In-ZCE025 solution which was injected i.v. during a 5- to 6-min period.

Imaging. Preoperative IS was performed at various times between 48 and 192 h following injection of $^{111}$In-ZCE025. In all patients, anterior and posterior (whole body or regional) planar scans were obtained. Prior to February 1988, a Technicare Omega 500 camera was utilized; after this date, a Toshiba 901 camera which has SPECT capability was utilized. Scintiscans used windows centered over the $^{111}$In photon energies of 172 and 247 keV. Tomographic images of the liver (SPECT) were routinely obtained in 3 planes. Other sites were selected for SPECT on the basis of the planar images or other clinical data.

Preoperative axial CT scans of the abdomen were obtained using a Synerview 1200 SX (Picker International). Chest and/or pelvis CT scans were also performed whenever possible. Each of the IS and CT scans was reviewed retrospectively for this study by an experienced diagnostic and nuclear medicine radiologist (D. Y.) and a surgeon (R. C.).

Surgery. Abdominal exploration was performed in each case. During surgery, accessible regions of the abdomen and pelvis were inspected.
with particular attention to areas of abnormality on IS scan and CT scan. Biopsy and resection of tumor and adjacent structures were undertaken as medically indicated in the best interests of the patient. Tissues were analyzed by gross visual and microscopic pathological examination. Size measurements of some resected lesions were available from the gross pathological assessment. Content of $^{111}$In in biopsy or resection tissue was measured by weighing a sample and counting it on a gamma counter (GammaTrac 1193; TM Analytic, Elk Grove, IL), expressing the results, corrected for physical decay of $^{111}$In, as the % ID/g. This latter parameter is a measure of the density of antibody within a tissue, which consequently reflects how visible it is using gamma camera scintigraphy.

Patient Selection. Between July 1986 and January 1990, all patients studied by IS using $^{111}$In-ZCE025 were eligible for consideration for this retrospective review. Patients included all had colorectal carcinoma (primary, hepatic metastasis, or known or suspected recurrence) and abdominal exploration. The $^{111}$In-ZCE025 injection for IS was performed within 2 weeks prior to surgery, and the preoperative CT scans were performed within 6 weeks prior to $^{111}$In-ZCE025 injection. The median time separation between the CT scan and operation was 19 days (range, 1-69 days). Greater than 80% of the patients had their CT scans performed within 5 weeks of surgery. Except for one patient (69 days), all had the CT scan performed within 8 weeks. This time interval was appropriate for retrospective comparison of operating room findings.

Lesion Analysis. Any area considered to represent colorectal cancer by any one of IS, CT, surgery, or pathology was defined as a lesion. On IS scan, any discrete area of relatively increased $^{111}$In uptake (“hot”) was defined as a lesion. Discrete areas of decreased uptake (i.e., cold or photopenic “lesions”) were excluded, because these were nonspecific and represented an absence of specific targeting to the CEA tumor marker. On CT scan, any noncystic lesion within the liver, nonenteric soft tissue density within the extrahepatic abdomen or pelvis, or abnormal intraluminal thickening of the bowel wall was considered a lesion.

Surgically, a discrete area of altered anatomy suggestive or suspicious of malignancy was defined as a lesion. Pathologically, a lesion was defined as histological microscopic confirmation of adenocarcinoma compatible with origin from a colorectal primary. Multiple lesions in one organ were each considered pathologically identical if they were considered identical (except for size) by surgical evaluation and at least one was microscopically evaluated.

Only abdominal lesions with pathological confirmation were utilized in the statistical lesion analysis. Lesion size (in cm) and lesion location (primary colorectal, hepatic metastasis, or extrahepatic abdominal metastasis/recurrence) were included in the analyses. Pathological classification was used as the absolute status (“gold standard”) of all lesions. Relative to the pathological status, the IS and CT scans (alone and combined) were scored for each lesion as one of: TP, TN, FP, and FN.

Statistical Methods. The sensitivity, PPV, and accuracy for the two imaging modalities were calculated using standard statistical formulas (15). To examine the correlation between lesions within a subject, the intraclass correlation coefficient was estimated using the one-way random effect model, in which the dependent variable is a binary variable indicating the degree of agreement between the two imaging modalities (16, 17). For these data, the intraclass correlation coefficient was found to be extremely low and was not statistically significantly different from zero (using the $F$ test from the one-way analysis of variance). Consequently, multiple lesions from the same subject were treated as independent measurements. McNemar's test of symmetry was used to compare the sensitivities and accuracies from the imaging modalities. While the formula for accuracy was used for statistical purposes, this parameter would be more appropriately considered as “correct classification” of lesion (i.e., benign versus malignant). Statistical significance was considered as $\leq 0.05$. All hypothesis tests were two sided unless otherwise indicated.

On the basis of the study inclusion criteria, both patients and lesions were selected for the presence of adenocarcinoma. Therefore, the sampling of normal tissue was uncommon. The usual cause for biopsy of normal tissues occurred when one test detected a lesion which proved to be FP, while a second diagnostic test identified no lesion (TN). As a result, specificity (TN/TN + FP) would have been biased, based upon very few numbers, and was not included in our analysis.

RESULTS

Of 111 patients having IS at City of Hope National Medical Center between July 1986 and January 1990, 45 fulfilled all the patient selection criteria. In these patients, 186 lesions were identified. Seven of these were extraabdominal (4 malignant, 3 benign) and were excluded from further analysis. A total of 141 lesions were evaluated by abdominal surgery and were pathologically confirmed. In one patient there were 6 lesions that were unquestionably benign hepatic hemangiomas; these were not biopsied for safety reasons but were included in the analysis and coded as nonmalignant. These six hemangiomas were interpreted on CT scan as sites of metastasis (FP) but were not visualized on IS scan (TN). Thus, there were 147 lesions included in the analysis, 121 (82.3%) malignant and 26 (17.7%) benign. Twenty-three (19.0%) of the malignant lesions were primary colorectal carcinomas; 62 (51.2%) were hepatic metastases and 36 (29.8%) were extrahepatic abdominal metastases. The median number of lesions/patient was 2 (range, 1-9).

Both IS and CT were documented to contribute to the diagnosis of primary and metastatic colorectal cancer (Figs. 1-6). Some malignant lesions were identified using both IS and CT (Fig. 1). Other malignant lesions were identified using CT but not using IS (Fig. 2). As defined above, nonspecific photopenic areas on IS, usually in the liver, were noted and considered untargeted lesions for purposes of the data analysis. Several malignant lesions were identified using IS but not using CT (Fig. 3). Hepatic lesions poorly visualized using planar IS were often clearly identified using SPECT (Fig. 4). Some lesions identified using IS were localized surgically but did not contain CEA-bearing carcinoma pathologically (Fig. 5). Other lesions were only appreciated after surgical resection and pathological evaluation (Fig. 6). Only one lesion identified by surgical exploration to be grossly compatible with carcinoma was biopsied and not confirmed to be malignant by pathological evaluation.

Sensitivity of IS imaging for colorectal adenocarcinoma was 40.5% (49 of 121), of CT was 61.2% (74 of 121) ($P = 0.0006$), and of IS and CT combined was 72.7% (88 of 121) (Table 1). PPV of IS and CT were similar (83.1 and 88.1%, respectively). Accuracy of CT (61.2%) was higher than IS (44.2%) ($P = 0.0013$).

Sensitivity. Primary colorectal lesions were well visualized using both IS and CT imaging with sensitivities of 87.0 (CT) and 100% (IS) for either modality or both modalities combined (100%) (Table 2). On the other hand, CT was more sensitive (67.7%) than IS (17.7%) for identification of hepatic metastases ($P < 0.0001$). However, IS targeted 3 hepatic lesions not identified by CT and yielded no false-positive localizations in the liver. Both IS and CT images contributed to the localization of extrahepatic abdominal lesions. While 55.6% of extrahepatic metastases were visualized using IS and CT, 41.7% were targeted using IS, and only one third were visualized using CT.

PPV. For colorectal and hepatic lesions, PPV of both IS and CT imaging was very good (88-100%), but for extrahepatic lesions PPV was somewhat lower (68-80%) (Table 2).

Accuracy. Scan accuracy, a reflection of scan utility for correctly identifying the nature of lesions (benign or malignant), varied with the region. Accuracy of both IS and CT imaging was high for primary colorectal lesions (85-89%). For hepatic
Lesion size. Lesion size information obtained from the pathology report was available for 66 (44.8%) of lesions (19 colorectal, 17 hepatic, 30 extrahepatic). Both IS and CT methodologies showed a low (<40%) sensitivity and accuracy for smaller lesions (≤3.0 cm), but for larger lesions (>3.0 cm) sensitivity and accuracy were both >80% (Table 2). Of the 19 colorectal lesions, 18 were >3.0 cm. All 18 were visualized using IS and 16 were identified using CT. Of 8 hepatic metastases ≤3.0 cm, only one was localized using IS and none using CT. Two of 7 hepatic metastases >3.0 cm were visualized using IS and 6 were visualized using CT. Of 16 extrahepatic abdominal metastases ≤3.0 cm, 6 were localized using IS (37.5%) and 3 using CT (18.8%). Five of the 6 lesions identified by IS alone were <1.5 cm. Only 3 extrahepatic abdominal metastases >3 cm were evaluated, 3 were localized using IS, and 2 were localized using CT.

SPECT. Of the 147 lesions evaluated using both planar IS and abdominal CT, 96 were also evaluated by SPECT (Table 4). In this group, 58 (60.4%) were hepatic and 30 (31.3%) were extrahepatic abdominal lesions. Little difference was seen between planar IS and SPECT imaging, except in the liver. Of 50 hepatic metastases, only one (2.0%) was localized using planar IS (Fig. 3), while 11 (22%) were localized using SPECT (Figs. 3 and 6). The SPECT modality was used to visualize 3 hepatic metastases not observed using planar IS or CT imaging.

**DISCUSSION**

In the current study, patients who were selected were staged presurgically with both 111In anti-CEA antibody (ZCE025) IS and with conventional CT. Criteria were applied retrospectively regarding preoperative testing by IS and CT to make the group as homogenous as possible. Both IS and CT scans were re-reviewed emphasizing identification of individual lesions in the abdomen. All patients had abdominal exploration with documentation of the individual sites of disease. There were 186 lesions identified using IS, CT, or the surgical procedure in the 45 patients evaluated. Seven extraabdominal lesions and 32 lesions that were surgically documented but that did not have pathological confirmation were excluded from analysis. Thus, this comparison of IS and CT was based upon an analysis of 147 surgically explored and pathologically confirmed lesions in the abdomen using uniform patient and lesion selection criteria.

Primary colorectal cancer lesions were identified correctly in a high percentage of cases by both IS and CT. Almost all of these lesions were large (>3.0 cm) and had previously been identified by other tests (barium enema, colonoscopy). The ability to detect smaller primary lesions in the colorectum using IS prior to their identification by conventional modalities remains untested.

Hepatic metastases of colorectal cancer were most effectively identified and localized using CT. The ineffectiveness of planar IS (sensitivity, 2%) was increased by using SPECT (sensitivity, 22%) and could be made to appear better by accepting photopenic lesions (sensitivity, 36%). However, the high retention of 111In in the normal liver remained a major problem. It was previously documented in the nude mouse model that liver accumulation was due to parenchymal accumulation of a low molecular weight break-down product of the 111In-antibody (18, 19). Using size exclusion HPLC analysis of homogenized normal liver, we have demonstrated the same low molecular weight substance in humans. The use of a novel transition metal chelate technology recently reported by Hawthorne et al. (20) has led to lower liver accumulation of radioisotope and no low molecular weight material on HPLC.

Current explanations for the photopenic nature of most hepatic lesions in this study include (a) the high uptake of free 111In and nonspecific 111In-labeled antibody by histologically normal liver, (b) central necrosis of large hepatic metastases, (c) damage to the liver parenchyma by the high accumulation of antibody, and (d) the inability of the liver to properly clear the antibody.

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4 J. D. Beatty and R. G. Beatty, unpublished data.
A 62-year-old female presented with anemia and constipation. A constricting lesion in the ascending colon was found on barium enema. Plasma CEA was 53 ng/ml. Surgery and pathology revealed a primary ascending colon adenocarcinoma and three hepatic metastases. A, planar anterior scintiscan 72 h following injection of ZCE025 (40 mg, 5.59 mCi) demonstrated three photopenic hepatic areas. No SPECT was done. B, a sketch of the scintiscan in A depicting 3 photopenic hepatic areas. Dashed horizontal lines, planes of the 2 axial CT views selected in C and D. C, axial CT view showing lesion 1. D, axial CT view showing lesions 2 and 3.

(c) interstitial transport distances and high interstitial pressure in tumors (21), and (d) clearance of antigen-antibody complexes of CEA-\(^{111}\)In monoclonal antibody by the histologically normal liver (19). As the problem of high liver background is solved in humans, we anticipate that IS will play a greater role in the identification of hepatic metastases.

Extrahepatic metastases of colorectal cancer were identified using both IS and CT with intermediate sensitivity (42 and 33%, respectively). The two modalities were found to visualize two distinct overlapping populations of metastases. Used in combination, IS and CT were complementary to one another, correctly identifying and localizing 56% of the extrahepatic abdominal metastases. In both the liver and the abdomen outside the liver, IS tended to be more sensitive than CT for smaller lesions. In the liver the only metastasis <3.0 cm that was documented prior to surgery was visualized using IS only. In the extrahepatic abdomen, 5 of 10 metastases <1.5 cm were visualized using IS and only 2 of 10 using CT.

While IS was more effective for localization of smaller metastases, it was disappointing in its assessment of lymph nodes status. Often grossly and histologically malignant nodes were not localized, while histologically uninvolved nodes draining known tumor masses had high \(^{111}\)In content and were therefore readily visualized. We have observed that these false-positive nodes contained a radiolabeled low molecular weight substance when homogenized and run on HPLC.* Labeling techniques that result in less accumulation of radiolabeled low molecular weight catabolites in lymph nodes also may aid in reducing this problem. However, the reason for this accumulation in normal nodes is not fully understood. We have found that these lymph nodes contained a higher concentration of CEA than normal background tissue, and this was possibly related to the antigen-filtering effect of antigen-processing cells (i.e., macrophages) that reside in lymph nodes (22). These antigen-processing cells are known to engulf the antigen, degrade the antigen in fragments (8-200 amino acids), and recycle the antigen fragments to the cell membrane (23). These membrane-bound fragments may provide the appropriate binding site for \(^{111}\)In anti-CEA.
Fig. 3. A 59-year-old male 21 months following resection of cecal carcinoma presented with an increasing plasma CEA (20.7 ng/ml). Surgery and pathology demonstrated multiple hepatic and extrahepatic foci of metastatic colon adenocarcinoma. Planar anterior scintiscan 72 h following injection of ZCE025 (40 mg, 5.63 mCi) showed one distinct focus within the right abdomen at level L2 (arrow) and a less distinct focus in the mid-lower abdomen, overlying approximately L5 (arrow). Axial CT images (not shown) were normal.

monoclonal antibody. The above hypothesis is supported by immunohistological documentation that the CEA in hot lymph nodes is localized in the histiocytes.6

In this report, the focus has been the comparison of the IS and CT modalities for individual lesion identification in contrast to previous studies which concentrated on region, organ, or whole body analysis. The present sensitivity measure was based on an individual lesion by lesion analysis. Specifically, if only one of 3 lesions was visualized in the liver, the sensitivity was 33% by lesion analysis, whereas it would be 100% by region, organ, or whole body analysis. Regional analysis would consider only the presence or absence of disease in the region and the presence or absence of a positive finding by the IS and CT modalities. Thus, it is less rigorous than the lesion by lesion analysis, which accounts for the increased sensitivity and accuracy reported using a regional method (9, 10).

This report was based on an analysis of individual lesions and excluded photopenic liver lesions. A photopenic area does not reflect marker-specific targeting of the radiolabeled antibody and, thus, has been excluded in this analysis. Again, this approach decreased the efficacy of IS for indicating the presence of tumors in the liver. Interestingly, inclusion of photopenic lesions and analysis of data by region or organ did not alter the conclusions of the study for identification of abdominal metastases. For example, accepting photopenic lesions resulted in an increase of liver IS from 17.7 to 35.5% and of liver IS+CT from 72.6 to 74.2%. Accuracy was similarly increased from

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*J. D. Beatty and J. Esteban, unpublished data.*

Fig. 4. A 70-year-old male was evaluated 17 months following resection of rectal carcinoma. Surgery and pathology confirmed a 6-cm hepatic adenocarcinoma metastasis. A, planar anterior scintiscan 72 h following injection of ZCE025 (40 mg, 6.60 mCi), demonstrating a hot lesion within the liver (arrow). B, coronal SPECT view of the same photophilic liver lesion. C, axial CT view demonstrating a lesion (6 x 5 cm) in the right lateral lobe of the liver (arrow).
Fig. 5. A 53-year-old female evaluated 19 months following resection of a cecal cancer presented with an elevated CEA (61.5 ng/ml). Surgery and pathology confirmed metastatic mucinous adenocarcinoma in the omentum (lesion 1) and in the pelvis (lesion 2). A, planar anterior scintiscan 72 h following injection of ZCE025 (40 mg, 7.12 mCi) demonstrating 2 lesions (arrows). B, coronal SPECT scan demonstrating these same lesions (arrows). C, axial CT view showing the anterior midline periumbilical lesion (1). D, axial CT view of the pelvis showing the lesion at the level of the inferior portion of the iliac bone (2).

28.2 to 43.7% and from 67.6 to 69.0% for IS and IS+CT, respectively.

We excluded photopenic lesions from the positive category because we thought IS was intended to localize specifically to tumors with the appropriate tumor marker; thus, it would not be fair to include lesions that were visualized simply because they were nonspecific space-occupying foci seen in relief against a background of intense uptake (i.e., the liver). On the other hand, we accepted any abnormal-appearing lesion on CT because this modality was much less specific, reflecting only the presence of a mass that was not clearly a benign cyst. Thus, we believe IS had more potential for identifying the presence and nature of a lesion and we had a higher expectation for its performance. This decision is also consistent with our eventual intention of using radiolabeled monoclonal antibodies for radioimmunotherapy, but it does tend to favor CT over IS in terms of sensitivity.

Previous reports (9, 10) focused upon the clinical value for
Table 1 Sensitivity, positive predictive value, and accuracy of IS and CT on a lesion by lesion basis

<table>
<thead>
<tr>
<th>Image modality</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
<th>Sensitivity (%)</th>
<th>Positive predictive value (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS</td>
<td>49</td>
<td>10</td>
<td>72</td>
<td>16</td>
<td>40.5⁺</td>
<td>83.3⁺</td>
<td>44.2²⁺</td>
</tr>
<tr>
<td>CT</td>
<td>74</td>
<td>10</td>
<td>47</td>
<td>16</td>
<td>61.2⁺</td>
<td>88.1⁺</td>
<td>61.2⁺</td>
</tr>
<tr>
<td>IS + CT</td>
<td>88</td>
<td>18</td>
<td>33</td>
<td>8</td>
<td>72.7⁺</td>
<td>83.0⁺</td>
<td>65.3⁺</td>
</tr>
</tbody>
</table>

⁺ P = 0.0006.  
² P < 0.003.  
* P = 0.0001 (one sided).

Table 2 Analysis of Imaging Modality by Region of Localization

<table>
<thead>
<tr>
<th>Region</th>
<th>Sensitivity (%)</th>
<th>Positive predictive value (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary colorectal (n=26)</td>
<td>IS 33</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>CT 20</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>IS+CT 23</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Hepatic metastasis (n=71)</td>
<td>IS 11</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>CT 42</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>IS+CT 45</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Extraphepatic abdominal metastases (n=50)</td>
<td>IS 15</td>
<td>7</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>CT 12</td>
<td>3</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>IS+CT 20</td>
<td>9</td>
<td>16</td>
</tr>
</tbody>
</table>

⁺ P < 0.0001.  
² P < 0.0001 (one sided).  
* P = 0.04 (one sided).

¹¹¹In-anti-CEA murine monoclonal antibodies in the presurgical staging of patients with known (or suspected) recurrent (or metastatic) colorectal cancer. Identification or confirmation of recurrent or metastatic disease in the liver, the extrahepatic abdomen, or extraabdominally had a major impact upon clinical decisions. Sensitivity of IS for the presence of metastases in the abdomen (excluding the liver) using a regional analysis was 48% and for the presence of metastasis outside the abdomen was 80%. In half of the patients with previously unsuspected extrahepatic metastases, the presence of extrahepatic disease was picked up using IS. Overall, ¹¹¹In-labeled anti-CEA (9) and ¹¹¹In-labeled anti-CA 19-9 antibodies (11) have been reported to benefit half of a carefully selected population of colorectal cancer patients.

Irrespective of the method of data analysis (lesional or regional), the basic objective of the IS technique has been the use of a radiolabeled antibody directed against a tumor marker for specific targeting to tumor bearing the marker. The ability to visualize the tumor depends on a number of factors including the physical characteristics of the radionuclide, the pharmacokinetics of the agent, the size and depth of the tumor, and the relative uptake of the radionuclide in tumor and normal background tissue (24). In general, visualization by gamma camera scintigraphy is dependent upon T/NT ratios of isotope uptake. This ratio may be obtained from tissue analysis expressed as unit % ID/kg using a well gamma counter or from apparent

Fig. 6. A 60-year-old male 6 months following resection of a transverse colon carcinoma presented with an abdominal wall mass, two liver lesions suspicious for metastases, and an increasing plasma CEA level at 21 ng/ml. Pathology of resected right hepatic lobe revealed 10 separate foci of metastatic colon carcinoma. A hot portal lymph node was also resected which was normal by pathology but contained a high level of ¹¹¹In (47.9% ID/kg). No hepatic lesion contained more than 3.3% ID/kg of ¹¹¹In. A, axial SPECT view 72 h following injection of ZCE025 (40 mg, 5.91 mCi) demonstrating one of the hepatic lesions (arrow) which was not visualized on planar images. B, axial CT scan through the dome of the right hepatic lobe, presumably demonstrating the same lesion (arrow). C, axial SPECT view 72 h demonstrating hot portal lymph node (arrow).
 contrast values (count density per pixel in the tumor divided by the count density in adjacent normal tissue) using gamma camera scintigraphy. Minimal T/NT ratios for visualization of the radionuclide in adjacent background tissue. The sensitivity and accuracy of the two modalities varied with the site of metastasis. CT was more effective for visualization of lesions >3 cm were effectively localized by both modalities, while IS tended to be more sensitive for identification of smaller lesions. SPECT dramatically improved IS identification of hepatic metastases. As this technology is refined, we expect to see further improvements in performance of IS as an imaging modality, particularly for “occult” disease.

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