A Gamma-detecting Probe for Radioimmune Detection of CEA-producing Tumors
Successful Experimental Use and Clinical Case Report

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The detection of tumors with radiolabeled antibodies against CEA is possible; however, current nuclear medicine scanning cameras rarely detect tumors smaller than 2 cm in diameter. One of the limitations to tumor detection is the inability to place a detecting camera near a deeply seated intra-abdominal tumor. A hand-held gamma-detecting probe, suitable for intraoperative use, was designed to locate radioactive tumors. Experimental work with CEA-producing colon tumor xenografts in nude mice suggests this probe is more sensitive than external scanners in detecting small tumors. A case report documents the clinical use of this new intraoperative probe. [Key words: Radioimmune detection; CEA; Carcinoembryonic antigen; Gamma-detecting probe; Nuclear medicine tumor scanning; Radiolabeled antibodies]

The identification of CARCINOEMBRYONIC ANTIGEN (CEA) in 1965† gave rise to the hope that screening for this specific antigen would detect digestive tract cancers at a preclinical stage and survival would improve. Unfortunately, CEA has not proved to be specific, and its therapeutic usefulness has been limited. A decreased CEA level following tumor resection indicates operative success. The primary clinical benefit of serum CEA evaluation is the monitoring of serial levels. An increase following a postoperative drop indicates residual or recurrent tumor growth and is an indication for a second-look operation to accomplish a possibly curative resection. Adherence to this sequence has resulted in the earlier detection of resectable tumors, but prolonged survival has not yet been established.‡

Use of the basic immunologic principles of antigen-antibody interaction holds promise for new therapeutic advances by both surgeons and chemotherapists. The presence of antibodies capable of recognizing tumor-associated antigens can be used to localize tumors and to deliver chemotherapy directly to them.¶

Several investigators have injected radiolabeled antibodies in various forms, as polyclonal antisera, monoclonal antibody fragments, into oncology patients and have used scintillation camera imaging to localize sites of primary and metastatic tumors and to stage disease. In some instances this technique has identified tumor sites...
not detected by conventional methods. The advantage of radioimmune detection (RID) is obvious to surgeons; preoperative localization of tumor would aid in operative planning, and the detection of widely disseminated tumor would indicate only palliative procedures.

Although the RID of tumors has been proven possible, there are still some limitations to its clinical use. Only relatively large tumors, 2 cm or greater in diameter, can be detected. Failure to detect smaller tumors leads to an underestimation of the tumor burden and distribution in many patients. Better tumor definition by external scanning cameras is hampered by various properties of the tumor such as location, size, blood supply, and in vivo tumor antigen expression; by the radionuclide energy-emitted and radiolabeling problems; and by scintillation camera resolution capabilities.

One major limitation is defined by the inverse square law, \( S = S_0 / D^2 \), where \( S \) signifies sensitivity and \( D \) distance. This indicates that the sensitivity of a detecting device varies inversely with the square of the distance separating it from the source of radioactivity. In patients, it is frequently impossible to get a scintillation camera close to a deeply seated tumor. If the detector could be placed directly over a radioactive site, the number of counts detected would increase dramatically.

A small, hand-held gamma-detecting probe (GDP) has been designed to detect radioactivity in tumors in animals and patients after injection of radiolabeled antibody against CEA.

**Materials and Methods**

**Probe:** The GDP consists of a cadmium telluride scintillation crystal, a preamplifier, and an amplifier with a digital read-out displaying the radioactive counts. (Radiation Monitoring Devices, Watertown, MA). The scintillation crystal is housed in a 16-mm diameter lead collimator with a 4-mm aperture (Fig. 1).

**Tumor Model:** Swiss nude mice (supplied by the Animal Production and Genetics Branch of the National Cancer Institute) had a CX-1 human colon adenocarcinoma implanted in the right flank. The tumor xenograft produced CEA.

**Radiolabeled Antiserum:** An affinity-purified baboon antiserum against CEA (CEA-As)\(^9\) was labeled with iodine \( ^{131}I \) using the chloramine-T reaction.

**Tumor Activity Determination:** The radiolabeled \(^{131}I\)-CEA-As (40 \( \mu Ci \)) was injected intraperitoneally into the mice (Fig. 2). The GDP was used to measure activity over the subcutaneous flank tumor, the contralateral flank without tumor (control site), the liver, and the thyroid. Each reading was for a 20-second period and was repeated four times at one-half hour, 24, 48, and 72 hours following injection. The mean and standard deviation of each reading was calculated.

The degree of \(^{131}I\)-CEA-As localization in the tumor at each reading was derived from the following ratio of radioactive count activity: tumor flank counts/nontumor flank counts. Following the 72-hour readings, the mice were killed humanely and various tissues were placed in a gamma well counter to determine their activity.

**Scintillation Camera Imaging:** Selected mice were imaged each day following the injection of escalating doses of radiolabeled antisera.

**Results**

Preferential localization of tumor radioactivity was noted as early as 24 hours following intraperitoneal \(^{131}I\)-CEA-As injection (Table 1). This pattern continued until death. Localization was apparent even though the number of detected counts at the various sites decreased over three days. The daily drop in radioactivity was due to both physical decay and biologic elimination.

The gamma well-determined activity in the tumors was increased over that in other tissues, except that the activity in the blood was nearly equal to that in the tumor (Table 2).

Although preferential radioactivity lateralization was detected with injection of 40 \( \mu Ci \), it was not until the injected dose was increased to 200 \( \mu Ci \) that imaging with a scintillation camera was possible.

After the reliability of the GDP to detect radioactivity in

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**Table 1. Gamma-detecting Probe Count Ratios Comparing Tumor Flank (TF) Counts to Non-tumor (NTF) Counts**

<table>
<thead>
<tr>
<th>Time After Injection of (^{131}I)-CEA-antisera (Hours)</th>
<th>Count Ratio: TF/NTF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2</td>
<td>1.04 ± 0.14, 0.88-1.12</td>
</tr>
<tr>
<td>24</td>
<td>1.44 ± 0.33, 1.10-1.75</td>
</tr>
<tr>
<td>48</td>
<td>1.58 ± 0.07, 1.50-1.60</td>
</tr>
<tr>
<td>72</td>
<td>1.80 ± 0.43, 1.20-2.21</td>
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