Immunoscintigraphy of Colorectal Carcinomas and Recurrences with A Technetium-99m-Labeled Monoclonal Anti-CEA-Antibody (MAB XBW 431/26)

TO THE EDITOR: We have read the paper by Bischof-Delaloye et al. (*1*) on anti-CEA immunoscintigraphy with iodine-123 (^{123}I) labeled monoclonal Fab fragments (Mab 35) with great interest. A closer inspection of the patient population reveals that a considerable number of patients in group A (suspected primary tumors) as well as in groups B and C (probable and questionable tumor relapse, respectively) presented with metastases, predominantly in the liver. The authors do not differentiate for immunoscintigraphic detection of metastases in the liver between smaller (<1 cm) and larger (>1 cm) lesions, in contrast to a study comparing ultrasonography (US) and computed tomography (CT) (*2*), which is quoted in the paper.

Having studied the article by Bischof-Delaloye et al., we would like to ask the authors for their comments on the following questions concerning radioimmunoscintigraphy (RIS) of colorectal carcinomas and recurrences.

1. What is the rate of right-positive RIS findings in metastases of the liver (<1 cm) in comparison with US and CT? Does the use of ^{123}I-labeled Mab 35 lead to a positive visualization of larger liver metastases, or do these appear as cold lesions?
2. In view of the state-of-the-art of RIS, where do the authors see its clinical value, in other words, when should RIS be used in the follow-up of colorectal carcinomas?

We believe that these questions are of importance, since RIS, being a rather elaborate technique, should provide additional information to conventional diagnostic procedures, such as endoscopy, US, or CT, which is of clinical and therapeutical relevance for the surgeon.

According to our experience with a technetium-99m-(^{99M}Tc) labeled monoclonal anti-CEA antibody (^{99m}Tc-Mab BW 431/26, Behringwerke, Marburg, FRG), the domain of RIS is not so much the diagnosis of primary tumors or the detection of large metastases, but rather the diagnostic confirmation of early recurrences (differential diagnosis between scar tissue and locoregional recurrences) when endoscopic or CT findings are unclear (*3*).

We used ^{99m}Tc-labeled Mab BW 431/26 in a prospective study including 78 patients for detection of colorectal carcinomas (n = 37) and confirmation or exclusion of locoregional recurrences (n = 41), respectively.

Whole-body scans were obtained in all patients in anterior and posterior projection 5 hr postinjection of 1100 MBq ^{99m}Tc-Mab BW 431/26, (1 mg antibody). SPECT imaging of the abdominal region was done 6 and 24 hr postinjection (Elscint Apex 409 AG; matrix 64 × 64; Hanning filter; attenuation correction). Despite high sensitivity in the detection of colorectal carcinomas (92%), RIS did not furnish additional data for the diagnosis of primary tumors exceeding information already obtained by conventional diagnostic procedures.

On the other hand, RIS was the determining procedure for confirmation or exclusion of locoregional recurrences in cases with unclear coloscopic and/or CT findings after surgery for colorectal carcinoma. In a total of 41 patients studied, RIS detected locoregional recurrences in 23 of 25 cases and excluded a malignancy in 14 of 16 cases (scar or inflammatory tissue). All results were confirmed by biopsy and/or surgery. Interpretations of RIS were false-positive in two cases and false-negative in two cases (sensitivity 92%, specificity 87%). The serum CEA levels of patients with recurrences were clearly elevated in 10 cases, marginally elevated in 7 cases, and within the range of normal in 6 cases. In two patients, liver metastases were visualized by RIS as cold lesions with a hot margin; however, these lesions had already been diagnosed by US. According to our results obtained with ^{99m}Tc-Mab BW 431/26, RIS is the method of choice for early detection of locoregional recurrences in the follow-up of patients with colorectal carcinomas. We propose that RIS also be performed when CT findings are unclear and serum CEA levels are within the range of normal, since there is no correlation between serum CEA levels and RIS findings.

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REPLY: The aim of our study (*1*) was not to assess the detectability of liver metastases according to the size of the lesions, but to define the interest of radioimmunoscintigraphy (RIS) in the management of colorectal cancer patients with respect to the presently available diagnostic methods. In this study design, surgical confirmation of RIS findings was usually not obtained in a time interval which would have allowed estimation of tumor size at the moment of RIS. We can, therefore, only assume that liver metastases, which were detected by RIS earlier than by other methods, especially ultrasonography (US) or computer-assisted tomography (CT), were equal or smaller than 1.5 cm in diameter. In the patient

population studied here, no liver metastasis was large enough to appear as a cold lesion. Among the first patients studied with iodine-123- (^{123}I) labeled anti-CEA MAb fragments (*2*), we have observed photopenic areas in the presence of very large metastases, at least at 6 (and eventually 24) hr, but even in these patients the tumors showed uptake of MAb fragments at 48 hr.

In patients with no definite diagnosis of recurrence, we have demonstrated that RIS was able to identify 16/38 (42%) tumor sites, which could not be detected by other methods during the concomitant diagnostic work-up. Among these 16 lesions, there were 7 liver metastases and 6 local recurrences, as well as 2 lung and 1 peritoneal involvements. This seems to answer your second question. In our opinion, the present clinical value of RIS in colorectal carcinoma lies mainly in the early detection (and confirmation in case of equivocal US or CT studies) of local recurrence. To this may be added the early diagnosis of liver metastases when RIS is performed with ^{123}I labeled MAb. Our own experience with the ^{99m}Tc-labeled anti-CEA MAb BW 431/26 (*3*) is comparable to your results. We also observed excellent detection rates in primary tumors and local recurrences but did not obtain reliable data in the detection of liver metastases. With ^{99m}Tc BW 431/26 (intact MAb), we recovered in one patient 0.0001% of the injected activity (ID) per gram of liver tumor which had been resected at 24 hr. In patients studied with the ^{123}I-labeled anti-CEA MAb 25, administered as F (ab')$_2$ fragment, the order of magnitude of activity recovered in liver metastases was 0.01% ID/g.

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Starport Digital Gamma Camera

TO THE EDITOR: A recent issue of *The Journal of Nuclear Medicine* contains a report by Freitas et al. on a problem that had appeared in a Starport 500A digital camera system manufactured by General Electric Company.

The "chronology of events" recounted by the authors was accurate as far as it was reported. However, the cause of the problem was subsequently identified and its successful resolution did occur. Furthermore, the authors themselves played a key role in this successful resolution.

The first Starport digital gamma camera was installed in December 1985. More than 200 systems were in service and functioning satisfactorily when the authors notified GE about an intermittent occurrence of a display of the name of one patient with the image of another. Since this effect had been reported only by the authors' institution, it was at first believed to be the result of a hardware malfunction. After repeated unsuccessful attempts to locate the source of the problem, the entire electronics console was replaced. The paper reports that since then (i.e. April 27, 1988), ". . . the problem of switching images and patient identification text has not been observed."

The paper failed to recount subsequent developments. In May 1988, the same problem did recur, but this time a sequence of actions was identified that enabled the GE software engineers to isolate a "bug" in the management of the image memory. A revised release, provided to the authors' institution on August 4, 1988, was tested and found to have successfully resolved the problem. After further thorough testing of the new software release (designated Starport Release 4.4), it was sent to *all* Starport installations in December 1988. The release included a detailed description of the problem and its resolution.

It must be noted that even though the *Journal*'s paper was not submitted until December 1988, and later revised in April 1989, the authors chose not to include a description of the events since May 1988: namely, GE's isolation of the problem, its resolution, the validation of the solution at the authors' institution, and distribution of updated software to all users of these systems.

The lesson of all this is clear. Although GE, like other vendors, devotes considerable efforts to validating its software, some residual "bugs" may go undetected. Both hardware and software malfunctions occasionally occur. Vendors have an obligation to expeditiously work with users to bring matters such as this to a successful conclusion, which will be beneficial to the patients and to other customers.

GE thanks the authors for bringing this problem to its attention and for the confidence they expressed in GE nuclear medicine products by ordering two additional systems.

REFERENCE

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REPLY: Dr. Bernstein takes us to task for failing to continue the narrative past April 27, 1988. In May 1988, the problem of mismatched displays did recur, but modifications of the imaging protocol did not allow us to record the image on film. Thus, there was no possibility of observer misinterpretation of clinical images. Dr. Bernstein goes on to classify the image switching problem as a software malfunction that was corrected in subsequent Starport software (Version 4.4) releases received in December 1988. This information (sent in a *"Dear Customer"* letter despite our many contacts) was not brought to my attention prior to approving our April 1989 revision.