Anti-Carcinoembryonic Antigen Immunoscintigraphy (Technetium-99m-Monoclonal Antibody BW 431/26) and Serum CEA Levels in Patients with Suspected Primary and Recurrent Colorectal Carcinoma

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This study comprises a total of 141 patients with suspected primary and recurrent colorectal carcinomas, in whom immunoscintigraphy with ^{99m}Tc-Mab BW 431/26 was performed. Whole-body scans were done 5.5 hr and SPECT imaging of the abdominal region was done at 6 and 24 hr postinjection of 1100 MBq ^{99m}Tc-labeled Mab (1 mg). In the course of primary tumor identification (n = 65), sensitivity of anti-CEA immunoscintigraphy was 95%, specificity 91%. In the diagnosis of early recurrences (n = 76), immunoscintigraphy was the method of choice to clarify the problem (sensitivity 94%; specificity 86%). Overall sensitivity of immunoscintigraphy in patients with suspected colorectal carcinomas and early recurrences was 95%, specificity 88%. Human anti-mouse antibodies were found in 29% (80% predominantly anti-isotypic, 20% predominantly anti-idiotypic). In contrast to anti-CEA immunoscintigraphy, the results of serum CEA levels were rather disappointing. Only 18 out of the 43 surgically verified primary colorectal carcinomas and 17 out of 32 patients with recurrences showed elevated serum CEA levels. In our clinical experience with this ^{99m}Tc-labeled anti-CEA antibody, immunoscintigraphy can play an important role in the identification of early colorectal recurrences and in postoperative colorectal cancer patients it should be performed in cases with unclear transmission computed tomography.

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Colorectal cancer is one of the most frequent carcinomas in Europe (incidence 20–25 per 100,000 inhabitants) and the second most lethal cancer. Improvements of conventional diagnostic procedures such as x-ray, endoscopy, and sonography have increased early detection of primary colorectal carcinoma (PCC), but these methods are not specific. Specific methods are required in postoperative colorectal cancer care, more than in primary tumor detection because of the need to differentiate between early colorectal recurrence (CR) and scar or granulation tissue. Although the carcinoembryonic antigen (CEA) is only a tumor-associated antigen, most of the clinical studies concerning specific tumor detection deal with antibodies directed against different epitopes of CEA (*1–7*).

First attempts at immunoscintigraphy with ^{131}I-labeled polyclonal antibodies used in animals against CEA were described by Goldenberg and Mach (*5,8*). The advent of the hybridoma technique for the production of monoclonal antibodies with high specificity by Köhler and Milstein (*9*) was a major breakthrough towards clinically relevant immunoscintigraphy. Today a great number of monoclonal antibodies are available for the diagnosis of colorectal carcinomas and recurrences (*10*).

A promising antibody directed against CEA (Mab BW 431/26 - intact IgG 1) described by Bosslet et al. (*11*), binds to a specific epitope which is mainly expressed on CEA, bound to the cell membrane, or attached to a solid phase. In contrast to other anti-CEA antibodies, MAb BW 431/26 does not react with CEA in solution; therefore, this MAb is not neutralized by serum CEA (*11*). The immunreactivity to cell-bound CEA was 95%.

Recently, a special method for stable labeling of this monoclonal antibody with ^{99m}Tc has been developed by Schwarz et al. (*12*). The affinity constant of 9×10^9 1/mol allows successful immunoscintigrams 4–6 hr after intravenous application of the ^{99m}Tc-Mab immunoconjugate. In this study, the value of a ^{99m}Tc-labeled monoclonal anti-CEA antibody is described and compared to conven-

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tional methods, such as x-ray, endoscopy, transmission computed tomography (TCT), and the estimation of serum CEA levels.

PATIENTS AND METHODS

The study included 141 patients, 85 females (age: 65 ± 12 yr; range 38–87 yr) and 56 males (age: 66 ± 11 yr; range 39–90 yr). Immunoscintigraphy was performed in 65 cases for verification or exclusion of primary tumors suspected on the basis of endoscopic or x-ray findings and in 76 patients for questionable recurrences with unclear TCT or endoscopic findings (predominantly in the differential diagnosis: scar - recurrence).

After labeling of the Mab, 1 mg of the intact IgG 1 (1100 MBq ^{99m}Tc-Mab 431/26; Behring Werke, Marburg, Germany) was injected over a period of 5 min. Scintigraphic imaging was performed with an Elscint Apex 409 AG rotating gamma camera with whole-body option (Elscint, Haifa, Israel). A whole-body scan was performed in the anterior and posterior projection 5.5 hr postinjection followed by SPECT imaging of the abdominal region 6 hr and 24 hr postinjection, respectively.

The SPECT images were acquired in a 64 × 64 matrix in 6-degree steps by continuous rotation over 360 degrees. The 60 planar projections were reconstructed to transverse slices with a filtered backprojection (Hanning filter) method. An attenuation correction method ($c = 0.12\ cm^{-1}$) proposed by Chang (*13*) was used. From these corrected transverse slices, coronal slices were interpolated from ventral to dorsal and sagittal slices from right to left. The thickness of the slices (2 pixels) was 1.25 cm.

A serum CEA was determined in all patients by CEA IRMA (Sorin: normal range 0–3 ng/ml). Human anti-mouse antibodies (Enzygnost HAMA micro, Behring, Marburg, Germany) were determined in 17 patients before and 3 mo after immunoscintigraphy. To determine the initial and HAMA-response values (IgG, IgM), the unspecific HAMA antigen (isotypic response) as well as the specific monoclonal BW 431/26 (anti-iso- and anti-idiotypic response) were used.

TABLE 1
Anti-CEA Immunoscintigraphy, Serum CEA Levels, and Tumor Stage in 25 Patients with Surgically Verified PCC and Normal Serum CEA

SPECT 6 hr/24 hr	Planar 5.5 hr	Serum-CEA ng/ml	Localization	Grading TNMGD
+++/+++	+	1.78	rectum	3/0/0/2/B
+++/+++	−	2.07	rectum	3/0/0/2/B
++/+++	−	1.73	rectum	2/0/0/2/A
+++/+++	++	1.37	sigma	2/0/0/2/A
++/++	−	2.62	rectum	2/0/0/1/A
+/+	−	1.89	rectum	1/0/0/1/A
+++/+++	+	1.23	C. trans.	2/0/0/1/A
+++/+++	+	1.57	C. asc.	3/0/0/2/B
++/+	+	0.0	sigma	3/0/0/2/B
+/+	−	1.55	rectum	1/0/0/1/A
++/++	−	1.46	sigma	2/0/0/2/A
++/++	+	3.0	sigma	inop/D
+++/+++	++	2.81	C. asc.	2/0/0/2/A
++/++	−	0.84	rectum	2/0/0/2/A
++/++	+	0.86	sigma	2/0/0/2/A
++/++	−	1.61	rectum	2/0/0/1/A
++/++	−	2.65	rectum	2/0/0/1/A
+++/+++	+	2.31	sigma	2/0/0/2/A
++/+++	−	2.37	rectum	3/0/0/2/B
++/++	−	2.70	rectum	2/0/0/2/A
++/++	−	2.07	C. trans.	2/0/0/2/A
+/+	−	0.78	sigma	1/0/0/1/A
++/++	+	1.88	C. desc.	3/0/0/1/B
−/+	−	1.78	C. trans.	3/0/0/1/B
−/−	−	1.30	C. desc.	2/0/0/1/A

TABLE 2
Anti-CEA Immunoscintigraphy, Serum CEA Levels and Tumor Stage in 18 Patients with Surgically Verified PCC and Elevated Serum CEA

SPECT 6 hr/24 hr	Planar 5.5 hr	Serum-CEA ng/ml	Localization	Grading TNMGD	Metastases
+++/+++	−	3.55	rectum	3/0/0/2/B	—
+++/+++	+	3.31	sigma	3/0/0/2/B	—
+++/+++	−	3.17	C. desc.	3/0/0/2/B	—
++/++	−	3.64	sigma	2/0/0/2/A	—
++/++	+	3.37	sigma	3/0/0/2/B	—
+++/+++	++	70	sigma	inop./D	liver
++/+++	+	56	sigma	inop./D	liver
+++/+++	++	6.36	C. asc.	3/1/0/2/C	—
+++/+++	+	37.47	C. asc.	3/0/0/3/B	—
++/+++	+	16.08	C. asc.	3/0/0/2/B	—
++/++	−	49.17	C. desc.	3/2/0/2/C	—
++/+++	++	25.07	sigma	inop./D	CP
++/++	+	6.07	C. desc.	1/0/0/2/A	—
+++/+++	+	70	C. asc.	inop./D	liver
+++/+++	++	22.26	C. desc.	3/2/0/2/C	—
+++/+++	++	70	C. asc.	inop./D	liver
+++/+++	+	6.34	C. trans.	3/0/0/2/B	—
+++/+++	+	6.34	C. asc.	3/0/0/2/B	—

CP = carcinosis peritonei.

RESULTS

Primary Tumors

Suspected primary tumors (43/65) were verified as PCC by surgery and histology (transverse colon n = 4; descending colon n = 6; ascending colon n = 8; rectum n = 12; sigmoid colon n = 13). Immunoscintigraphy showed a true-positive result in 41 patients, a false-negative result in 2 patients, a true-negative result in 20 patients, and a false-positive result in 2 patients because of antibody accumulation in the ascending colon (Tables 1 and 2, Figs. 1–3).

Sensitivity of anti-CEA immunoscintigraphy in the diagnosis of PCC was 95%, specificity 91%. Serum CEA levels were elevated in only 18 out of 43 patients with surgically verified carcinoma and in the range of normal in 25 cases (Tables 1 and 2). Serum CEA levels were slightly elevated in 5 of the 22 patients without colorectal carcinoma, and these levels were in the normal range in 17 cases.

Diagnosis of Recurrences

Seventy-six patients were examined for clarification of early recurrence or cicatricial tissue. Immunoscintigraphy revealed an uptake in the CT or coloscopically suspicious area in 36 patients. The diagnosis of malignant recurrence

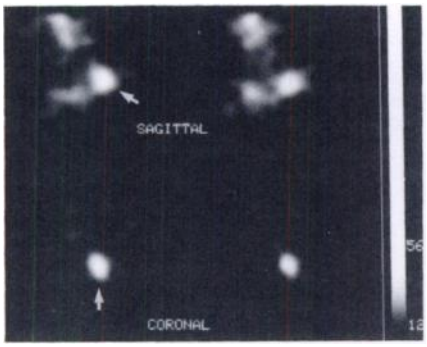


FIGURE 1. A patient with rectum carcinoma shows circumscribed uptake of ^{99m}Tc-MAb BW 431/26 in the pre-sacral area dorsal to the bladder activity (sagittal slices: upper row; coronal slices: lower row; 24 hr postinjection). Serum CEA: 1.78 ng/ml.

was verified by biopsy and/or surgery in 30 cases (true-positive) and disproved in 6 cases (false-positive). Immunoscintigraphy was interpreted to be negative in 40 patients; in 38 of them, the suspicious coloscopic or CT finding turned out to be cicatricial or inflammatory granular tissue (true-negative); in 2 patients malignant recurrence was verified by surgery and histology despite negative immunoscintigraphy. In one of these patients, histology showed tumor cells with low differentiation and without CEA expression. The second false-negative immunoscintigram was caused by a severe bladder emptying disturbance and an inability to differentiate recurrence and lymph node activity from the bladder activity (even in the SPECT images).

In comparison to immunoscintigraphy (30 true-positive, 2 false-negative), TCT was positive in 12 cases, questionably positive (no differentiation between scar and recurrences) in 10 cases, and negative in 10 cases (Table 3). In patients with TCT findings of hypodense pre-sacral lesions, malignant recurrence is very likely (Fig. 4A–B). Hyperdense lesions, however, permit no differentiation between scar or early recurrence. Figure 5A shows a patient with a hyperdense lesion, which was interpreted to be scar tissue; anti-CEA immunoscintigraphy, however, showed clear antibody uptake in this area, indicative of malignant recurrence (Fig. 5B). Second-look surgery confirmed the immunoscintigraphic finding as malignant recurrence.

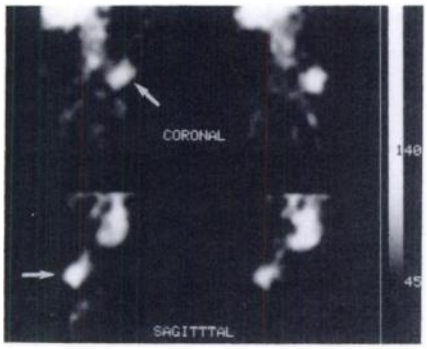
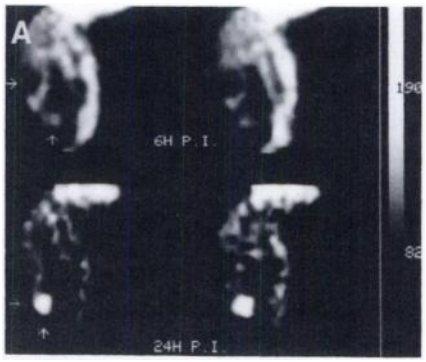


FIGURE 2. Anti-CEA immuno SPECT (coronal slices: upper row; sagittal slices: lower row, 24 hr postinjection): the circumscribed activity (arrows) demonstrates a high anti-CEA antibody uptake in the left abdomen according to a CEA expressing descending colon carcinoma. Serum CEA: 3.17 ng/ml.



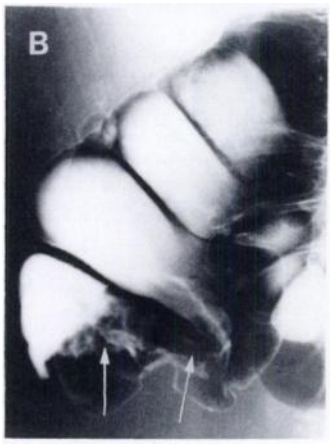


FIGURE 3. (A) Anti-CEA immuno SPECT coronal slice 6 hr postinjection (upper row) and 24 hr postinjection (lower row) shows a clear circumscribed uptake of the ^{99m}Tc labeled monoclonal antibody in the ascending colon and cold lesions in the liver. Surgery confirmed the diagnosis of ascending colon carcinoma; however, the cold liver lesions turned out to be a liver cyst. (B) Irrigoscopy findings.

In another patient with extensive hyperdense lesions detected with TCT (Fig. 6a), anti-CEA immunoscintigraphy was negative at 6 and 24 hr postinjection (Fig. 6B–C); these findings also were confirmed as scar tissue by computer-assisted biopsy. Since the aim of this study was to detect early local recurrence, only 11 of the 76 patients investigated presented metastases (7 patients with lymph node metastases, 4 patients with liver metastases). Immunoscintigraphy demonstrated a positive result in five out of seven patients with lymph node metastases. Of the four patients with liver metastases, one patient showed positive Mab accumulation (hot spots), one patient hot and partially cold lesions with marginal elevated uptake (compared to the high nonspecific liver uptake, using the intact IgG1), and two patients presented liver metastases as cold lesions (Fig. 7). Sensitivity of anti-CEA immunoscintigraphy in patients with suspected colorectal recurrence was 94%, specificity 86%. In patients with verified recurrence, serum CEA-levels were clearly elevated in 14, slightly elevated in 3, and in the normal range in 15 (Table 3).

HAMA Response After Anti-CEA Immunoscintigraphy

We measured HAMA in 17 patients before and 3 mo after immunoscintigraphy. Only one patient in this group developed predominantly anti-idiotypic, while four pa-

TABLE 3
Anti-CEA Immunoscintigraphy TCT Findings and Serum CEA Levels in 32 Patients with Verified Colorectal Recurrences

SPECT 6 hr/24 hr	Planar	TCT	Serum-CEA ng/ml	Localization (preop)	TNMGD (preop)	Recurrence
++/+++	(+)	+	2.24	rectum	3/1/0/2/C	pre-sacral
+/++	−	+	1.31	rectum	3/1/0/2/C	pre-sacral/LN
++/++	(+)	+	1.75	rectum	2/1/0/2/C	pre-sacral
+/++	−	±	2.34	rectum	2/1/0/2/C	pre-sacral
++/++	(+)	−	2.07	rectum	2/1/0/3/C	pre-sacral/CP
++/++	−	−	2.24	rectum	3/1/0/2/C	pre-sacral
++/++	++	±	2.77	C. asc.	2/1/0/2/C	anastomosis
++/++	−	−	2.17	rectum	2/1/0/3/C	pre-sacral
++/++	−	−	1.28	rectum	2/1/0/2/C	pre-sacral
++/++	−	−	0.54	rectum	3/1/0/2/C	pre-sacral
+/+	−	−	2.39	rectum	3/0/0/2/B	pre-sacral
+++/+++	++	−	2.63	rectum	3/1/0/2/C	pre-sacral
++/+	(+)	+	1.56	sigma	3/2/0/2/C	anastomosis
++/++	−	−	2.88	rectum	2/0/0/2/B	pre-sacral
−/−	−	±	0.80	rectum	3/0/0/2/B	per-sacral
++/++	−	−	3.07	rectum	2/1/0/2/C	pre-sacral
++/++	+	+	30.98	C. desc.	3/2/0/2/C	anastomosis/LN
+++/+++	++	+	70	rectum	3/1/0/2/C	pre-sacral/liver
++/++	+	±	3.04	C. asc.	3/0/0/2/B	anastomosis
++/+++	(+)	−	3.82	sigma	4/0/0/2/B	pre-sacral
++/++	−	±	3.01	rectum	3/0/0/2/B	pre-sacral
+++/+++	++	+	70	rectum	3/1/0/2/C	pre-sacral/CP
++/+++	++	+	64.39	rectum	3/1/0/2/C	pre-sacral/LN/CP
+/++	+	+	70	C. desc.	3/1/0/3/C	anastomosis/LN
++/++	−	+	30.36	rectum	2/0/0/2/A	pre-sacral
+++/+++	++	±	18.25	rectum	2/0/0/2/A	pre-sacral/LN
+++/+++	++	±	16.80	C. desc.	2/0/0/2/A	pre-sacral/liver
+++/+++	++	+	12.47	C. desc.	3/2/0/2/C	pre-sacral/LN
++/++	+	+	70	C. desc.	2/1/0/3/C	anastomosis/liver
+++/+++	+	±	16.35	sigma	3/1/0/2/C	anastomosis/liver
++/+	−	±	12.47	rectum	2/1/0/2/C	pre-sacral
−/−	−	±	13.80	rectum	3/1/0/2/C	pre-sacral/LN

Preop. = preoperative findings; CP = carcinosis peritonei; and LN = lymph node metastases.

tients developed predominantly anti-isotypic antibodies. Table 4 shows the original and HAMA response values (IgG, IgM) after anti-CEA immunoscintigraphy (1 mg antibody) in five patients with positive HAMA response.

DISCUSSION

Several studies describe immunoscintigraphy with antibodies directed against CEA (*14–21*). With the initial use of anti-CEA immunoscintigraphy, ^{131}I-polyclonal antibodies and planar imaging resulted in low sensitivities. Therefore, this method was not acceptable for clinicians and surgeons as an additional investigational tool in colorectal cancer care.

Initial clinical experiences with a ^{99m}Tc-labeled monoclonal antibody (Mab BW 431/26) demonstrated that its high sensitivity, specificity and image quality, coupled with a reduced radiation exposure (to 5% of the ^{131}I dose) will possibly make this method part of the standard armamentarium of procedures in the follow-up of patients with

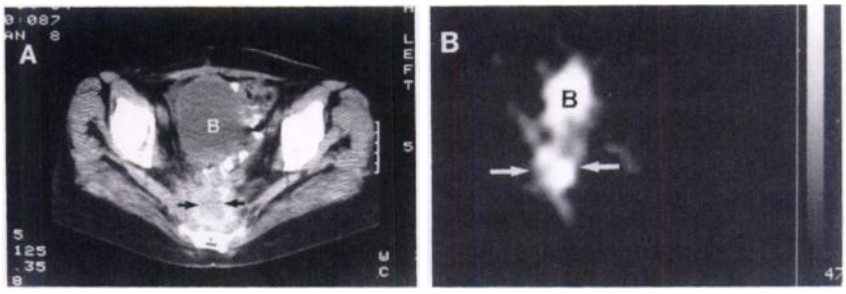


FIGURE 4. TCT 1 yr after surgery of rectum carcinoma. The hypodense lesion behind the bladder was interpreted as suspicous recurrence (B = bladder activity); the CEA serum level was in the range of normal (2.24 ng/ml). (B) Anti-CEA immuno SPECT (transaxial slice 24 hr postinjection). Despite normal serum CEA, there is circumscribed uptake of anti-CEA antibody (arrow), confirming the diagnosis of malignant recurrence that was verified by computer-assisted biopsy and surgery (B = bladder activity).

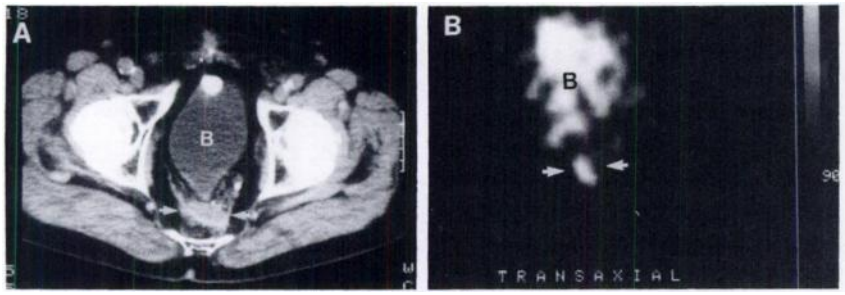


FIGURE 5. (A) CT (transaxial slice) shows a small hyperdense lesion in the pre-sacral area. This lesion was interpreted to be scar tissue (B = bladder activity). (B) Anti-CEA immuno SPECT (transaxial slice 24 hr postinjection). Dorsal to the bladder activity (bladder emptying disturbance after surgery), there is circumscribed antibody uptake in the pre-sacral area (B = bladder activity); serum CEA level: 2.17 ng/ml. Second-look surgery and histology confirmed the immunoscintigraphic diagnosis of early malignant recurrence.

colorectal carcinomas (22–24). Since, however, immunoscintigraphy is technically more elaborate and time-consuming when compared to coloscopy, the questions arise: what are the indications for clinical additional diagnostic information and what are the resultant therapeutic consequences.

Our investigations reveal that in patients with PCC immunoscintigraphy does not furnish additional data for this diagnosis above that already obtained by conventional diagnostic procedures [although sensitivity is very high (95%)]. On the other hand, immunoscintigraphy is helpful for confirmation or exclusion of early locoregional recurrences with unclear coloscopy and/or TCT findings after surgery.

Computed tomographic hypodense lesions accompanied by rising CEA levels always suggest tumor recurrences, however, an unequivocal differentiation from cicatricial or granular tissue is not possible (*25*). With the specific demonstration of CEA-expressing tumor cell complexes, a differentiation from cicatricial tissue is possible via immunoscintigraphy in most cases. In the diagnosis of pelvic recurrences, however, a non-overlapping demonstration by means of a SPECT technique is imperative to avoid missing lesions located behind the bladder. Of the 75 tumors and recurrences verified by surgery or biopsy in our study, 71 were correctly localized with SPECT, whereas with planar scintigraphy the result was definitely positive in only 34 cases, questionably positive in 8 cases, and negative in 33 cases. This high rate of false-negative planar scans in our study was mainly caused by the fact that many of the primary tumors were rectum carcinomas and most of the recurrences were pre-sacral in close vicinity to the bladder activity.

False-positive results were due to nonspecific activities in the ascending colon 24 hr postinjection or to urine activity in patients with cicatricial dislocation of the bladder after surgery. After rectum surgery, urine activity in dislocated bladder areas may cause false-positive results and reduce the specificity of this method for early detection of recurrences. Therefore, we propose urine catheterization immediately before immunoscintigraphy in order to prevent false-positive results in the pre-sacral area.

On the other hand, false-negative results are rare with the SPECT technique. The lack of CEA expression within the tumor cells or the low background/tumor ratio in some cases are regarded as possible causes of false-negative immunoscintigraphic results (*26*). Most of the patients in our postoperative group were investigated for confirmation or exclusion of early local recurrences. Therefore only a few patients presented with extensive metastatic disease. For the detection of liver metastases, anti-CEA immunoscintigraphy with the intact monoclonal antibody is inferior to morphologic methods such as sonography or CT because of high nonspecific liver uptake. The use of the anti-CEA antibody fragment may overcome this problem because of lower nonspecific uptake in the liver (*27*). However, the high excretion of the fragment via the kidneys and the resulting high bladder activity, especially in

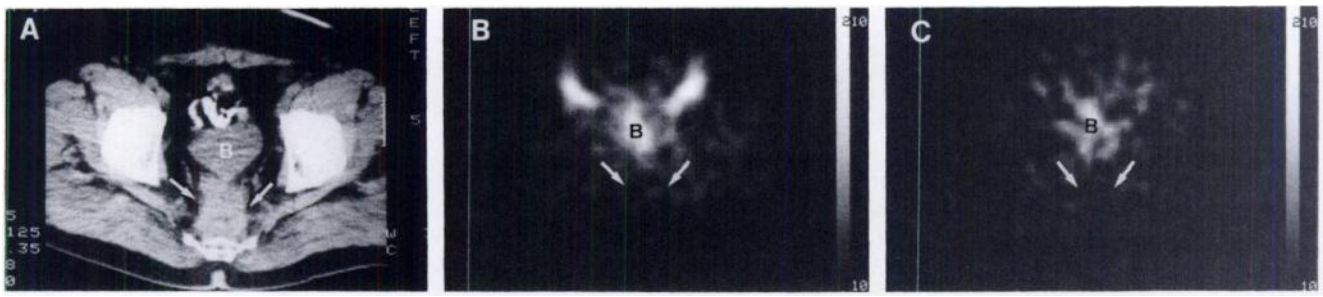


FIGURE 6. (A) CT (transaxial slice) image shows an extensive hyperdense lesion in the pre-sacral area 2 yr after rectum surgery (B = bladder activity). (B) Anti-CEA immuno SPECT (transaxial slice 6 hr postinjection). There is no antibody accumulation in the pre-sacral area (B = bladder activity). Immunoscintigraphy gave evidence that the extensive hyperdense TCT lesion might be scar tissue after surgery; computer-assisted biopsy confirmed the diagnosis of "scar tissue." (C) Anti-CEA immuno SPECT (transaxial slice 24 hr postinjection). There is no antibody accumulation in the pre-sacral area.

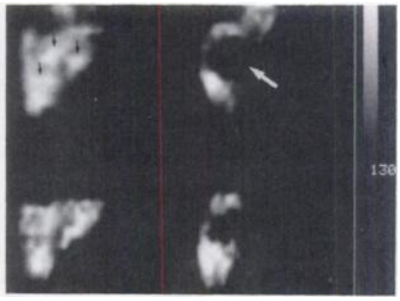


FIGURE 7. Anti-CEA immuno SPECT of the liver (coronal slices 6 hr postinjection upper row; coronal slices 24 hr postinjection lower row). The images show several hot lesions ventral in the right lobe (arrows) and a cold lesion dorsal in the right liver lobe in a patient with liver metastases after surgery of an ascending colon carcinoma.

the postoperative dislocated bladder, may increase false-positive results in early pre-sacral recurrence compared to the intact IgG1.

The support of serum CEA in detecting primary or early recurrent colorectal malignancy was low in our study. Nearly all cases with elevated serum CEA were caused by advanced or metastatic tumor stages; in 16 out of 27 patients, carcinosis peritonei or metastases were present. Moreover, in 39 patients with normal serum CEA, PCC or early CR was present. Therefore, a normal serum CEA level does not exclude positive immunoscintigraphic demonstration of tumor. As shown in our study, positive immunoscintigraphy and elevated CEA levels need not necessarily correlate. Because of the poor correlation between serum CEA levels and positive anti-CEA immunoscintigraphy, we propose that anti-CEA immunoscintigraphy should also be performed in patients with unclear TCT findings despite normal CEA levels.

In cases of repeated immunoscintigraphy, HAMA (anti-iso- and anti-idiotypic) should be measured. Although no allergic reactions occurred in any of our patients (even in cases of repeated investigations), the value of the investigation in cases with positive HAMA (especially with predominantly anti-idiotypic response) is very poor because the demonstration of the CEA epitope is markedly reduced and almost all the activity is concentrated in liver, spleen, and bone marrow.

In conclusion, our clinical experiences with a ^{99m}Tc-labeled anti-CEA antibody show that anti-CEA immunoscintigraphy provides important additional information in the early diagnosis of colorectal recurrences and should therefore be a firm part in the diagnostic follow-up of patients with suspected recurrences.

TABLE 4
HAMA Factor (IgM, IgG) Before (Basal I) and 3 Months After (Response II) Application of 1 mg Mab BW 431/26

	MAb BW 431/26				HAMA-antigen (IgG1)			
Patient	IgM		IgG		IgM		IgG	
no.	I	II	I	II	I	II	I	II
1	1.33	2.70	1.03	5.96	1.31	2.06	1.86	5.73
2	2.02	7.09	2.00	5.39	1.74	1.94	1.30	3.68
3	2.32	5.49	1.54	8.91	1.87	7.05	1.28	10.66
4	2.02	3.09	2.00	16.11	2.33	2.65	3.63	4.65
5	1.84	1.91	1.97	25.58	1.70	1.84	1.53	22.81

Total HAMA response when using the specific (Mab BW 431/26) and antiisotypic HAMA response when using the nonspecific (HAMA antigen) antibody is shown.

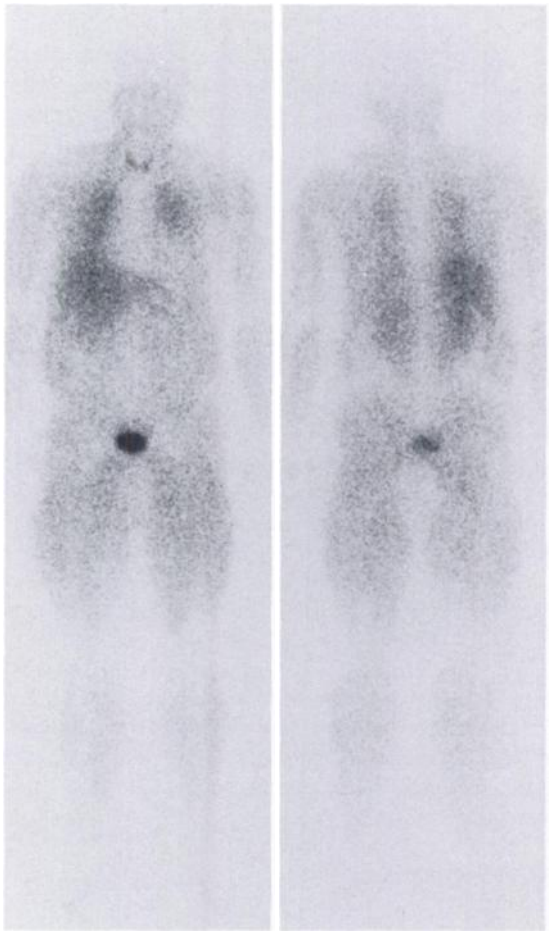
REFERENCES

1. Mach JP, Buchegger F, Forni M, et al. Use of radiolabeled monoclonal anti-CEA antibodies for the detection of human carcinomas of external photoscanning and tomoscintigraphy. *Immunol Today* 1981;2:239–249.
2. Mach JP, Carrell S, Merenda C, et al. In vivo localization of anti-CEA antibody in colon carcinoma. Can the results obtained in the nude mice model be extrapolated to the patient situation? *Eur J Cancer* 1978;1(suppl):113–120.
3. Goldenberg DM, Kim EE, DeLand FH, et al. Radioimmunodetection of cancer with radioactive antibodies to carcinoembryonic antigen. *Cancer Res* 1980;40:2984–2992.
4. Goldenberg DM, Kim EE, Bennett SJ, et al. Carcinoembryonic antigen radioimmunodetection in the evaluation of colorectal cancer and in the detection of occult neoplasms. *Gastroenterology* 1983;84:524–532.
5. Goldenberg DM, DeLand F, Kim E, et al. Use of radiolabeled antibodies to carcinoembryonic antigen in the detection and localization of diverse cancers by external photoscanning. *N Engl J Med* 1978;298:1384–1388.
6. Wahren B, Hammarström S, Harmenberg U, et al. Polyclonal and monoclonal anti-CEA antibodies in immunolocalization of colorectal cancer. *Tumour Biol* 1986;7:361–369.
7. Delaloye B, Bishof-Delaloye A, Buchegger F, et al. Detection of colorectal carcinoma by emission-computerized tomography after injection of ^{123}I-labeled Fab or F(ab')2 fragments from monoclonal anti-carcinoembryonic antigen antibodies. *J Clin Invest* 1986;77:301–311.
8. Mach JP, Carrel S, Forni M, et al. Tumor localization of radiolabeled antibodies against carcinoembryonic antigen in patients with carcinoma. *N Engl J Med* 1980;303:5–10.
9. Köhler G, Milstein C. Continuous cultures of fused cells secreting antibody of predefined specificity. *Nature* 1975;256:494–497.
10. Baum RP, Lorenz M, Senekowitsch R, et al. Klinische Ergebnisse der Immunszintigraphie und Radioimmuntherapie. *Nucl Med* 1987;26:68–78.
11. Bosslet K, Lüben G, Schwarz A, et al. Immunohistochemical localization and molecular characteristics of three monoclonal antibody-defined epitops on carcinoembryonic antigen (CEA). *Int J Cancer* 1985;36:75–84.
12. Schwarz A, Steinsträsser A. A novel approach to Tc-99m-labeled monoclonal antibodies. *J Nucl Med* 1987;28:721.
13. Chang LT. A method of attenuation correction in radionuclide computed tomography. *IEEE Trans Nucl Sci* 1978;25:638–643.
14. Mach JP, Forni M, Ritschard J, et al. Use and limitations of radiolabeled anti-CEA antibodies and their fragments for photoscanning detection of human colorectal carcinomas. *Oncodev Biol Med* 1980;1:49–69.
15. Serafini AN, Goldenberg DM, Higginbotham-Ford EA, et al. A multicenter trial of cancer imaging with fragments of CEA monoclonal antibodies [Abstract]. *J Nucl Med* 1989;30:748.
16. Siccardi AG, Buraggi GL, Callegaro L, et al. Immunoscintigraphy of adenocarcinomas by means of radiolabeled F(ab')2 fragments of an anti-carcinoembryonic antigen monoclonal antibody: a multicenter study. *Cancer Res* 1989;49:3095–3103
17. Buraggi G, Turrin A, Bombardieri E, et al. Immunoscintigraphy of colorectal carcinoma with F(ab')2 fragments of anti-CEA monoclonal antibody. *Cancer Detect Prevent* 1987;10:335–345.
18. Riva P, Moscatelli G, Paganelli G, et al. Antibody-guided diagnosis: an Italian experience of CEA-expressing tumours. *Int J Cancer* 1988;(suppl 2):114–120.
19. Beatty JD, Duda RB, Williams LE, et al. Preoperative imaging of colorectal carcinoma with ^{111}In-labeled anticarcinoembryonic antigen monoclonal antibody. *Cancer Res* 1986;46:6494–6502.
20. Baum RP, Lorenz M, Hör G. Radioimmunszintigraphie bei kolorektalen

Karzinomen—Stellenwert in der Rezidivdiagnostik nach 2 Jahren Klinischer Erfahrung. *Nuklearmedizin* 1987;10:219–234.
21. Bischof-Delaloye A, Delaloye B, Buchegger F, et al. Clinical value of immunscintigraphy in colorectal carcinoma patients: a prospective study. *J Nucl Med* 1989;30:1646–1656.
22. Lind P, Langsteger W, Költringer P, et al. Tc-99m-labeled monoclonal anti-carcinoembryonic antigen antibody (MAb BW 431/26): clinical results in the detection of colorectal carcinomas and recurrences. *Scand J Gastroenterol* 1989;24:1205–1211.
23. Kroiss A, Schüller J, Tuchmann A, et al. Immunoscintigraphy in patients with colorectal cancer recurrences. In: Schmidt HAE, Chambron J, eds. *Nuclear medicine.* Stuttgart, New York: Schattauer Verlag; 1990:570–572.
24. Lind P, Langsteger W, Költringer P, et al. Immunoscintigraphy with Tc-99m-labeled monoclonal anti-CEA antibodies (MAb BW 431/26) in the follow-up of patients with colorectal carcinomas. In: Schmidt HAE, Chambron J, eds. *Nuclear medicine.* Stuttgart, New York: Schattauer Verlag; 1990;567–569.
25. Freeny PC, Marks WM, Ryan JA, et al. Colorectal carcinoma evaluation with CT: preoperative staging and detection of postoperative recurrences. *Radiology* 1986;158:347–353.
26. König B, Röhle R, Köhn H, et al. Ergebnisse der quantitativen Messung des CEA-Antikörper-uptake (BW 431/26) im Tumor. *Workshop Immunoscintigraphie, Acta Med Austr* 1989;(suppl):25–28.
27. Goldenberg DM, Goldenberg H, Ford EH, et al. Initial clinical imaging results with a new Tc-99m-antibody method [Abstract]. *J Nucl Med* 1989;30:809.

(continued from page 5A)

FIRST IMPRESSIONS



PURPOSE:
A 50-yr-old male with a history of hypertension was admitted for evaluation. Iodine-123-MIBG scintigraphy was performed to identify a possible pheochromocytoma. The ^{123}I-MIBG scan (24 hr postinjection) shows, in addition to some uptake in the thyroid, diffuse uptake in the soft tissue (muscular compartment, liver, lung). The heart and bone structures are relatively photopenic. The parotid and submandibular glands are not visualized.

At the time of his admission, the patient was taking multiple antihypertensive drugs, including labetolol which depletes the storage vesicles and inhibits the uptake I mechanism.

Another acquisition was made 48 hr after the injection of the tracer. At that time, the intake of labetolol had been interrupted for 22 hr. These images were identical with those obtained 24 hr after the tracer injection, when the patient was still taking labetolol.

TRACER:
Iodine-123-MIBG

ROUTE OF ADMINISTRATION:
Intravenous injection after blocking of thyroid

TIME AFTER ACQUISITION:
24 hr, whole-body acquisition

INSTRUMENTATION:
Siemens Whole-Body Scanner

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