Somatostatin Receptor Scintigraphy in Postsurgical Follow-Up Examinations of Meningioma

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Surgery is the treatment of choice in patients with meningioma. However, the risk of postoperative, local recurrence is well-known since total resection is not always feasible. Moreover, in these patients MRI may fail to differentiate between tumor remnants, recurrent meningioma or nonspecific hyperperfusion. In this study, the value of functional imaging using somatostatin receptor scintigraphy (SRS) was evaluated in postsurgical follow-up. **Methods:** Before and 2–3 mo after surgery, 27 patients with meningioma received MRI as well as SRS after intravenous injection of 200 MBq ^{111}In-octreotide. Planar whole-body images were obtained at 10 min, 1, 4 and 24 hr postinjection, and SPECT was performed at 4 and 24 hr postinjection. The final diagnosis was proven histologically in all patients. **Results:** Before surgery, MRI showed focal contrast enhancement in all patients, and SRS revealed focal accumulation of ^{111}In-octreotide. Thus, MRI and SRS yielded comparable results in all 27 patients. After surgery, MRI showed diffuse contrast enhancement in the area of the primary tumor site in all patients. Thus, MRI did not allow a differentiation between tumor and nonspecific hyperperfusion. In contrast, SRS revealed focal accumulation of ^{111}In-octreotide in 16 of 27 patients indicating remaining tumor tissue or relapse of meningioma. This resulted either in an operative revision or in more frequent postsurgical follow-up examinations. In 11 of 27 patients, SRS was negative. Thus, total resection of meningioma was assumed, and no further interventions were performed. **Conclusion:** Functional imaging using SRS is a highly specific imaging modality and has a significant impact in postsurgical follow-up in patients with meningioma.

Key Words: indium-111-octreotide; somatostatin receptor scintigraphy; functional imaging; meningioma; postsurgical follow-up

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Surgery is the treatment of choice in patients with meningioma. However, the risk of local recurrence is well-known. This is especially true for meningioma located near the skull base since meninges at that site are attached very closely to the bones, thus rendering total resection of meningioma difficult (*1–4*). Morphological imaging using MRI is well-established in the detection of meningioma. In the first 6 mo after surgery, in a reasonable number of patients MRI may fail to differentiate between tumor remnants or recurrent meningioma and nonspecific hyperperfusion.

Since meningioma were shown to express somatostatin receptors in nearly 100% in cell cultures (*5–9*), as well as in vivo (*10–16*), functional imaging using somatostatin receptor scintigraphy (SRS) has been suggested for differential diagnosis of meningioma versus neurinoma by several authors (*10–13*). Moreover, SRS may be helpful for differentiating between a postoperative scar and local remnants or a relapse of meningioma. Therefore, the aim of this study was to evaluate functional imaging using SRS in postsurgical follow-up in patients suffering from meningioma.

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MATERIALS AND METHODS

Patients

Between February 1996 and August 1997, a total of 27 patients (20 women, 7 men; age range 19–70 yr; mean age 53.4 ± 14.4 yr) received standard MRI as well as SRS before and 2–3 mo after surgery. Tumor volumes were calculated from MRI images under assumption of a rotational ellipsoid ranging from 0.5 ml to 43.2 ml. Patient characteristics are given in Table 1.

Histological Staining

Surgical specimens were fixed in 4% formaldehyde and embedded into paraffin for histopathological examination. Sections of 4 μm in thickness were stained both with hematoxylin-eosin and elastica van Gieson's.

Magnetic Resonance Imaging

MRI was performed either on a 1.5-Telsa Magnetom Vision (Siemens, Erlangen, Germany) or a 1.0-Telsa Magnetom Expert (Siemens). Both T1-weighted (TR = 500 ms, TE = 12 ms) and T2-weighted spin-echo sequences (TR = 3600 ms, TE = 98 ms) were acquired with a slice thickness of 6–8 mm. Gadolinium-diethylenetriamine pentaacetic acid (Schering, Berlin, Germany) was administered intravenously at a dosage of 0.1 mmol/kg body weight for contrast enhancement.

Somatostatin Receptor Scintigraphy

After an intravenous injection of 200 MBq ^{111}In-octreotide (Mallinckrodt, Petten, The Netherlands) digital whole-body acquisitions were obtained simultaneously in anterior and posterior projection at 10 min, 1, 4 and 24 hr with a scan speed of 10 cm/min. A large-field-of-view gamma camera equipped with a medium-energy, parallel-hole collimator was used (Bodyscan, Siemens). The energy window was adjusted to both ^{111}In peaks at 173 and 247 keV with a symmetric 20% window for each.

In addition, SPECT was performed at 4 and 24 hr with a single-head, large-field-of-view gamma camera equipped with a medium-energy, parallel-hole collimator (Diacam, Siemens). Data at 360° were acquired for 64 angles in a step-and-shoot mode, and projections were stored in a 128 × 128 matrix. SPECT data were reconstructed by filtered backprojection using a Butterworth filter, fifth order, and a cutoff frequency of 0.23 of the Nyquist frequency.

Quantification

Quantitative evaluation of regional uptake was performed on whole-body images by placing a circular region of interest (ROI) over the lesion and a background area located contralaterally or directly beneath the lesion, allowing the calculation of a tumor-to-background ratio (T/B) for all times of acquisition. Relative percentage of tumor uptake was measured by relating the activity within the lesion ROI to whole-body activity after correction for background activity. All quantifications were calculated as the geometric mean from anterior and posterior projections. Results are given as mean ± 1 s.d.

TABLE 1
Demographic Data, Localization and Results of Somatostatin Receptor Scintigraphy in Patients

Sex	Age (yr)	Localization	SRS (prior to)	SRS (postsurgical)	Remarks
F	59	Right temporal	Positive	Negative	ø
F	38	Right temporal	Positive	Negative	ø
F	50	Left sphenoid bone	Positive	Negative	ø
M	48	Left lateral ventricle	Positive	Negative	ø
F	68	Left lateral ventricle	Positive	Negative	ø
F	52	Falx cerebri left	Positive	Negative	ø
F	44	Left parietal	Positive	Negative	ø
F	68	Left sphenoid bone	Positive	Negative	ø
F	59	Right sphenoid bone	Positive	Negative	ø
F	53	Left parietal	Positive	Negative	ø
F	52	Left sphenoid bone	Positive	Negative	ø
F	32	Left frontal	Positive	Positive	Remnant
F	46	Left sphenoid bone	Positive	Positive	Remnant
M	20	Falx cerebri right	Positive	Positive	Remnant
F	19	Left sphenoid bone	Positive	Positive	Remnant
F	64	Left sphenoid bone	Positive	Positive	Remnant
F	47	Left cerebellopontine angle	Positive	Positive	Remnant
M	49	Optic nerve	Positive	Positive	Remnant
F	62	Multilocular	Positive	Positive	Malignant meningioma
M	57	Left falx cerebri	Positive	Positive	Malignant meningioma
F	62	Left parietal	Positive	Positive	Recurrent meningioma
F	70	Region of axis	Positive	Positive	Recurrent meningioma
F	66	Left occipital	Positive	Positive	Recurrent meningioma
M	83	Left frontal	Positive	Positive	Recurrent meningioma
M	68	Left sphenoid bone	Positive	Positive	Recurrent meningioma
F	46	Left falx cerebri	Positive	Positive	Second meningioma in right occipital area
M	59	Sellar region	Positive	Postive	Palacos right parietal

RESULTS

Before surgery, MRI showed focal contrast enhancement in the tumor area in all patients studied. Accordingly, SRS demonstrated focal tracer uptake in planar images as well as in SPECT slices in all patients before surgery. Both an increase of T/B ratio with time and an increase of the uptake of ^{111}In-octreotide (Figs. 1 and 2, open symbols; Table 2) were observed in these patients.

Two-to-three months after surgery, MRI yielded diffuse contrast enhancement in the region of the previous meningioma in all patients. Therefore, MRI failed to differentiate between nonspecific hyperperfusion and tumor remnants or recurring meningioma.

Additional information was provided by SRS. In 11 (1 man, 10 women) out of 27 patients, SRS was negative and total tumor resection was assumed. Thus, no further interventions were performed so far (Fig. 3).

In contrast, postsurgical SRS revealed focal accumulation of ^{111}In-octreotide in 16 of 27 patients (6 men, 10 women). In all 16 patients, an increase both in T/B ratio (Fig. 1, filled circles) and uptake of ^{111}In-octreotide (Fig. 2, filled circles) was

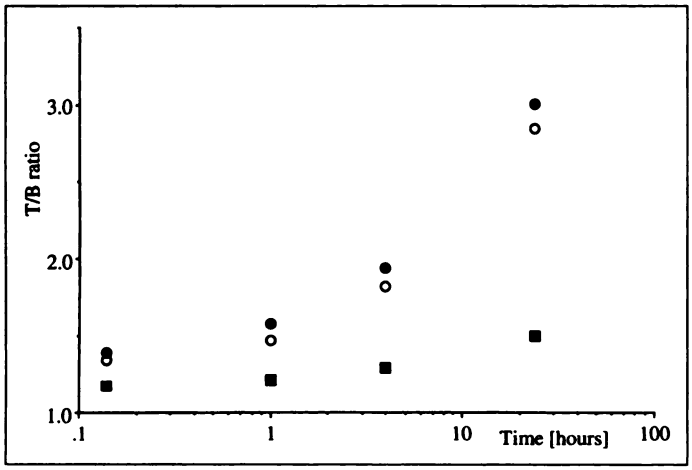

FIGURE 1. Geometric mean of T/B ratio derived from anterior and posterior projection of somatostatin receptor scintigraphy in 27 patients with suspected meningioma versus logarithm of time postinjection in hours. Open circles = SRS-positive before surgery, n = 27; filled circles = SRS-positive 2–3 mo postsurgery, n = 16; and filled squares = SRS-negative 2–3 mo postsurgery, n = 11.

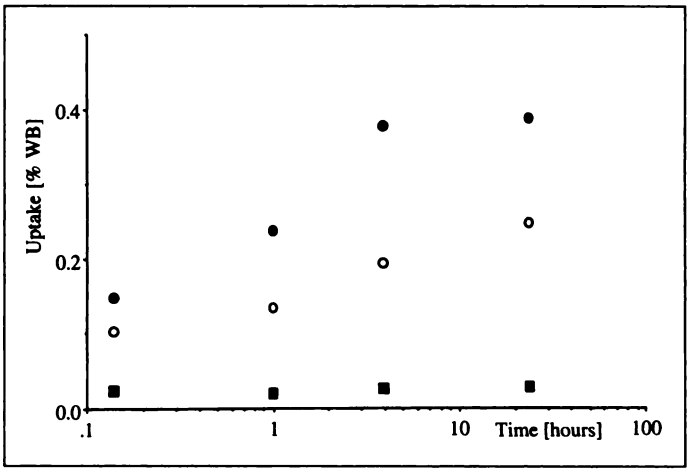

FIGURE 2. Geometric mean of uptake in percentage of whole-body activity derived from anterior and posterior projection of somatostatin receptor scintigraphy in 27 patients with suspected meningioma versus logarithm of time postinjection in hours. Open circles = SRS-positive before surgery, n = 27; filled circles = SRS-positive 2–3 mo postsurgery, n = 16; and filled squares = SRS-negative 2–3 mo postsurgery, n = 11.

TABLE 2
Tumor-to-Background Ratio (T/B) and Uptake with Time of Indium-111-Octreotide in Patients with Suspected Meningioma Prior to and 2–3 Months Postsurgical

	Prior to surgery	Postsurgical, 2–3 mo	
	SRS-positive	SRS-positive	SRS-negative
T/B	n = 27	n = 16	n = 11
10 min	1.33 ± 0.20	1.39 ± 0.24	1.17 ± 0.21
1 hr	1.46 ± 0.28	1.57 ± 0.68	1.20 ± 0.17
4 hr	1.82 ± 0.58	1.94 ± 0.88	1.28 ± 0.22
24 hr	2.85 ± 1.47	3.01 ± 1.90	1.49 ± 0.38
Uptake (% WB)			
10 min	0.102 ± 0.111	0.148 ± 0.117	0.024 ± 0.037
1 hr	0.134 ± 0.163	0.236 ± 0.453	0.018 ± 0.026
4 hr	0.192 ± 0.233	0.376 ± 0.326	0.025 ± 0.028
24 hr	0.346 ± 0.455	0.388 ± 0.404	0.027 ± 0.029

Data represent mean ±1 s.d. SRS = somatostatin receptor scintigraphy; WB = whole body.

observed over time. Details of the 16 SRS-postive patients are given in Table 1.

Since total tumor resection was not feasible intraoperatively, the presence of residual tumor was confirmed by positive SRS 2 to 3 mo postsurgically in 9 out of these 16 patients (Fig. 4). In 2 out of the latter 9 patients, multilocular malignant meningioma was proven histologically.

In 5 out of 16 patients, positive SRS demonstrated meningioma tissue in the tumoral area despite attempted total tumor resection. In 2 out of the latter 5 patients, positive SRS resulted in an operative revision. The remaining 3 patients received more frequent follow-up examinations.

In the remaining 2 out of 16 SRS-positive patients, focal accumulation of ^{111}In-octreotide was detected at a different location when compared with tracer accumulation observed before surgery. In 1 out of these 2 patients, postoperative tracer accumulation was located in the right parietal area, while SRS performed before surgery yielded focal tracer uptake in the sellar region (Fig. 5). In the second patient with preoperative tracer accumulation in the right sinus sphenoidalis, postoperative SRS yielded a focus in the right occipital area. Positive SRS in this patient resulted in an operative revision with resection of a second meningioma.

DISCUSSION

Meningioma and neurinoma are tumors with similar predilection sites, e.g., cerebello pontine angle or cavernous sinus. However, standard neuroimaging using morphologically orientated MRI may fail to differentiate between meningioma and neurinoma (*17*). Since preoperative discrimination is demanded by the neurosurgeon, functional imaging, e.g., SRS may be helpful in the preoperative diagnostic work-up. Meningioma have been shown to express somatostatin receptors in nearly 100% in cell cultures (*5–9*), as well as in vivo (*10–16*), whereas neurinoma do not express somatostatin receptors on their cell surface (*9,17*). Consequently, uptake of ^{111}In-octreotide with an increasing T/B ratio provides the basis to exclude neurinoma (*10–13*).

Between June 1996 and August 1997, a total of 27 patients with suspected meningioma underwent SRS, as well as MRI, before and 2–3 mo after surgery. Presurgically, morphological imaging using MRI showed focal contrast enhancement indicating meningioma in all patients studied. Accordingly, focal tracer uptake of ^{111}In-octreotide with an increase of T/B ratio was shown in all of them. Positive SRS obtained preoperatively demonstrated the presence of somatostatin receptors, and final diagnosis of meningioma was proven by histology in all 27 patients. The diagnostic benefit of both SRS and MRI in the preoperative work-up of all patients studied was comparable.

Two-to-three months after surgery, MRI yielded a diffuse contrast enhancement in the primary tumor site in all 27 patients. Since the blood-brain barrier is disrupted normally for several months after surgery, contrast enhancement allows, in principle, no discrimination between tumor remnants or relapse of meningioma and postoperative hyperperfusion. Morphological imaging such as MRI failed in postsurgical follow-up of meningioma. In contrast, SRS provided additional information.

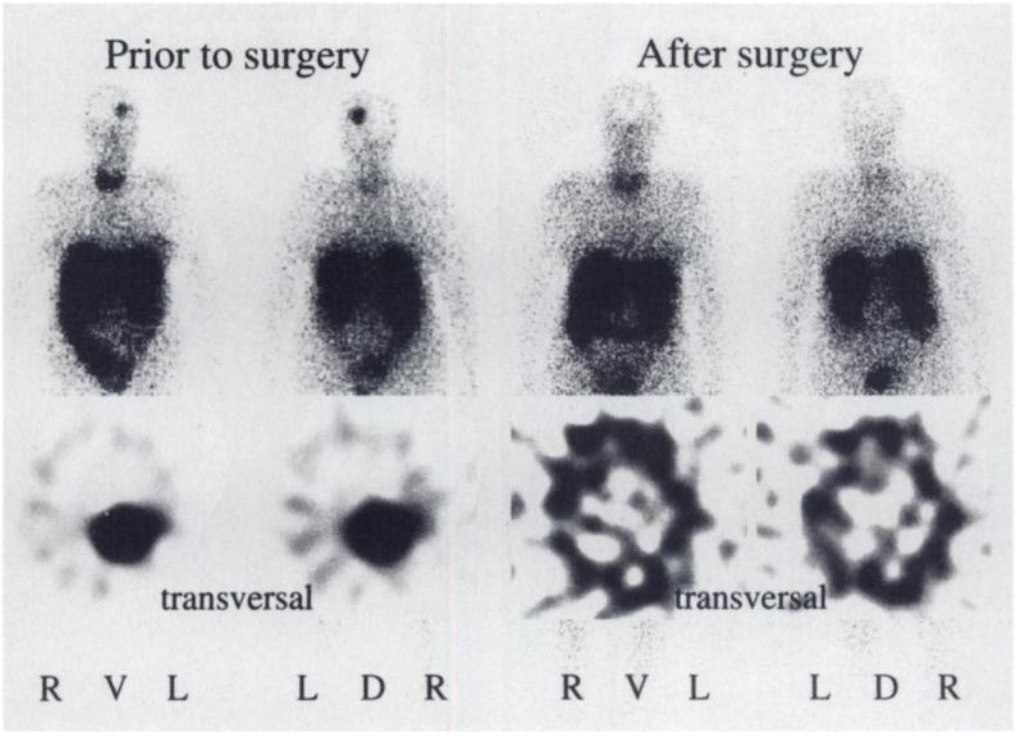

FIGURE 3. Example of postoperative SRS-negative patient (woman, 68 yr). Planar somatostatin receptor scintigraphy 24 hr postinjection in anterior and posterior projection and corresponding transverse SPECT slices (inset). Preoperatively, focal accumulation of ^{111}In-octreotide localized in region of left lateral ventricle. Histologically-proven transitional cell meningioma.

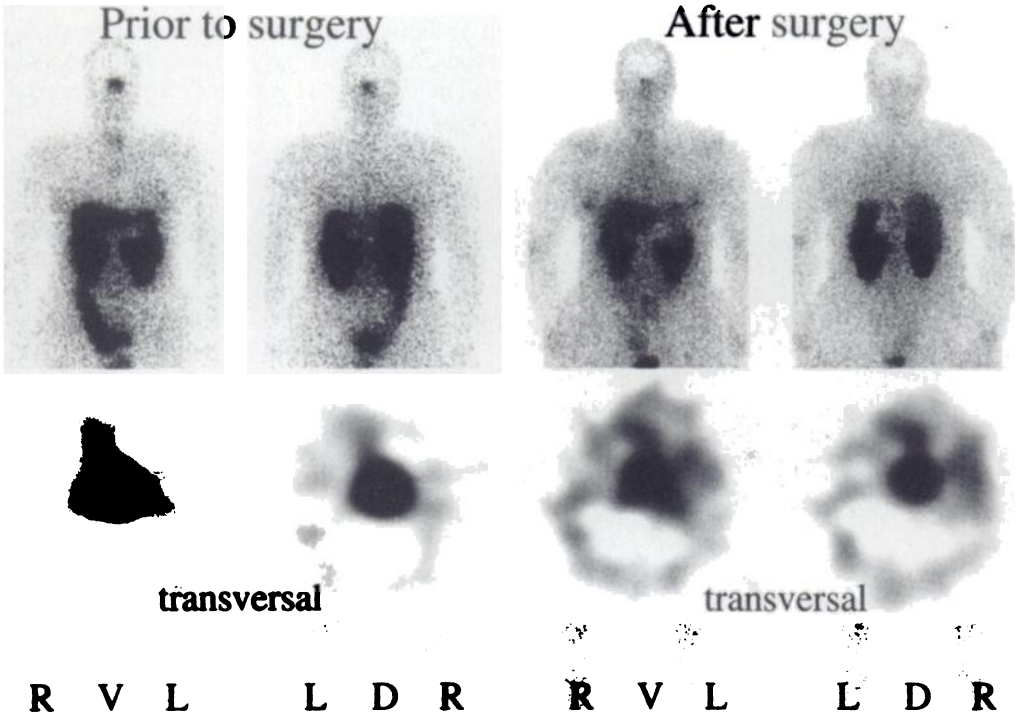

FIGURE 4. Example of postoperative SRS-positive patient (woman, 19 yr). Planar somatostatin receptor scintigraphy 24 hr postinjection in anterior and posterior projection and corresponding, transverse SPECT slices (inset). Preoperatively, focal accumulation of ^{111}In-octreotide localized in region of left sphenoid bone. Histologically proven menigotheliomatous meningioma. Total tumor resection was not feasible.

Postoperative SRS yielded a negative result in 11 patients. Although previous studies showed that small meningioma with a volume below 5 ml may present as SRS-negative (*18–21*), there is no evidence that once a meningioma has been proven SRS-positive a loss of somatostatin receptors will occur later. Consequently, these 11 negative SRS results can be considered as true-negative confirming pathological findings of total tumor resection, and no further interventions were performed. Clinical follow-up up to 1 yr after surgery confirmed the absence of meningioma.

Two-to-three months after surgery, positive SRS was found in 16 patients. In 9 out of these 16 patients, total tumor resection was not feasible. This was proven by focal tracer accumulation of ^{111}In-octreotide demonstrating remaining meningioma tissue.

In 5 out of 16 SRS-positive patients, somatostatin receptors were detected, and total tumor resection was assumed. In 2 out of these 5 patients, positive SRS resulted in an operative revision with histologically proven meninigioma tissue. The remaining 3 patients were referred for more frequent follow-ups, but results of SRS could not be proven histologically. Nevertheless, in these patients positive SRS directly influenced either treatment or diagnostic follow-up.

In 2 out of 16 postoperative SRS-positive patients, localiza-

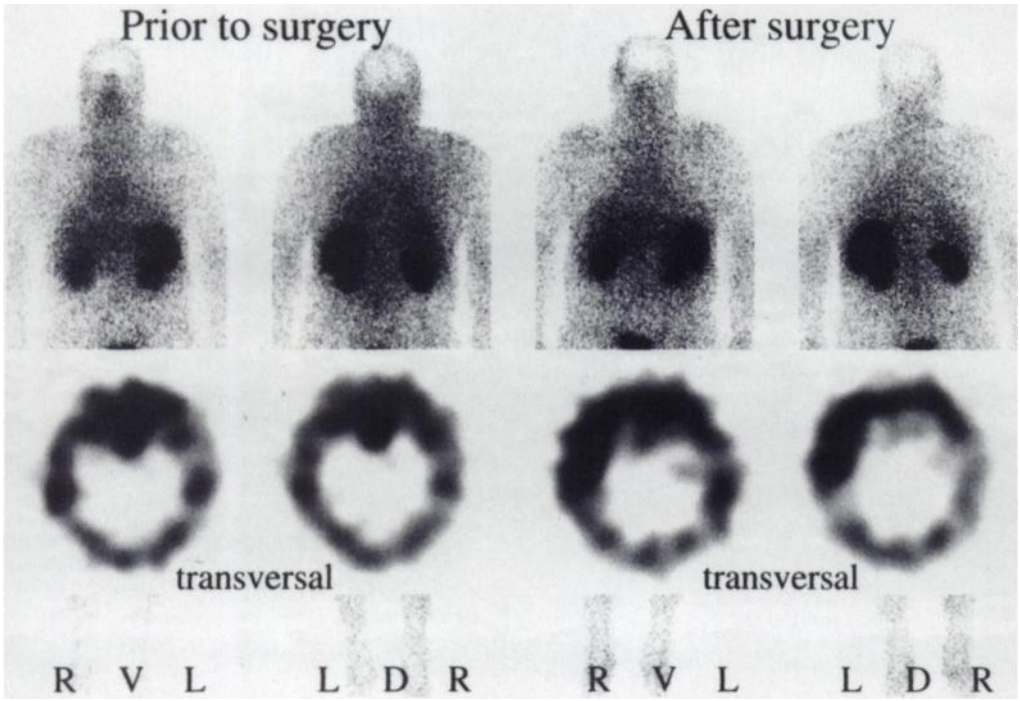

FIGURE 5. Example of postoperative SRS-positive patient (man, 59 yr). Planar somatostatin receptor scintigraphy 4 hr postinjection in anterior and posterior projection and corresponding, transverse SPECT slices (inset). Preoperatively, focal accumulation of ^{111}In-octreotide localized in sellar region. Histologically proven meningotheliomatous meningioma. Postoperatively, focal tracer accumulation in right parietal area corresponding to localization of craniotomy and implantation of palacos.

tion of postoperative focal tracer accumulation was not consistent with localization of preoperative tracer uptake. Before surgery, one patient showed focal tracer uptake in the sellar region while postoperative tracer uptake was localized in the right parietal area, and the neurosurgeon ascertained total tumor resection. In this patient, craniotomy and implantation of palacos, i.e., artificial bone substance, was localized in the same region where an increase of ^{111}In-octreotide was observed postsurgically. Therefore, SRS was primarily noted as false-positive but turned out to be consistent with nonspecific tracer accumulation, probably due to an unspecific lymphocyte accumulation in the palacos area. This emphasizes the necessity to assess the results of SRS with a thorough knowledge of both the complete history of the individual patient and the results of complementary imaging.

As shown in Table 2, all SRS-positive patients demonstrated a progressive increase of T/B ratio with time. This implied that the most important imaging time would be 24 hr postinjection and suggested that other imaging times could be eliminated totally. If patients show a positive SRS within 4 hr postinjection, further imaging times, e.g., 24 hr postinjection, are eliminated, and time is saved for these patients. However, SRS-negative patients at 4 hr postinjection should be regularly imaged again at 24 hr postinjection, since a reasonable number of patients assumed to be SRS-negative at 4 hr postinjection will show a rather slow increase of T/B ratio; thus, these patients finally become SRS-positive at 24 hr postinjection.

CONCLUSION

Functional imaging using SRS is a highly specific imaging modality that has a significant impact on postsurgical follow-up in patients with meningioma. It provides the basis for selecting those patients who need more frequent follow-up examinations.

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