Clinical Value of 24-Hour Delayed Imaging in Somatostatin Receptor Scintigraphy for Meningioma

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Somatostatin receptor scintigraphy (SRS) using ^{111}In-octreotide has proven useful in patients suspected of having meningiomas. Delayed imaging is regularly performed up to 24 h postinjection. However, this procedure is time consuming and expensive. Therefore, we investigated whether 24-h imaging may be omitted in these patients. **Methods:** After clinical examination and standard MRI, 71 patients were suspected of having 92 meningioma lesions. Before surgery, all patients underwent SRS after intravenous injection of 200 MBq (5.4 mCi) ^{111}In-octreotide. Planar whole-body images were obtained at 10 min and 1, 4 and 24 h, and SPECT was performed at 4 and 24 h. Results of SRS in all lesions were evaluated with respect to histology and time of image acquisition. **Results:** SRS yielded 58 true-positive, 20 true-negative and 14 false-negative results, with the false-negatives all less than 5 mL (2.3 ± 2.1 mL) in volume. In 52 of 58 true-positive lesions (89.7%), diagnosis could be established by 4-h imaging without further information by 24-h imaging. In 10 of the 52 lesions, SPECT was necessary to confirm planar findings. Imaging at 24 h was necessary in only 6 of 58 true-positive lesions (10.3%): 3 patients who had intracranial relapse of meningioma (volume < 5 mL) and 3 who had spinal meningioma. Thus, a diagnosis of intracranial meningioma could be established in 52 of 55 lesions (95%) using a 4-h imaging protocol. **Conclusion:** With a 4-h acquisition protocol that includes SPECT imaging, SRS yields sufficient information in patients suspected of having intracranial meningiomas. Delayed imaging at 24 h is recommended only for patients who have small meningiomas (volume < 5 mL), spinal localizations or negative SRS at 4 h.

Key Words: somatostatin receptor scintigraphy; ^{111}In-octreotide; meningioma; delayed imaging

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Somatostatin receptor scintigraphy (SRS) is useful both in differential diagnosis of meningioma (*1–7*) when CT or MRI were indeterminate (*8–10*) and in postsurgical follow-up to select those patients with tumor remnants or relapse of meningioma (*9,10*). Although the diagnostic impact of SRS is well documented, the best acquisition protocol still remains controversial (*2,11–16*). Several years ago, delayed images were obtained up to 48 h. However, 48-h imaging was omitted, because it could not add significant information to 24-h imaging (*17*). Thus, in differential diagnosis of meningioma, delayed imaging up to 24 h is usually recommended (*18*). On the other hand, studies have shown that in diagnosis of gastroenteropancreatic tumors (*19,20*) or liver metastases (*21*) a 24-h acquisition protocol does not provide any additional information to 4-h images. Moreover, a 24-h acquisition protocol is time consuming and expensive. Because, as studies have shown, density of somatostatin receptors is high in cell cultures (*22,23*) as well as in surgical specimens (*24*), most meningiomas are clearly detected as early as 4 h postinjection. Therefore, we investigated whether a 4-h acquisition protocol is sufficient in patients suspected of having meningiomas.

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MATERIALS AND METHODS

Patients

Between May 1994 and July 1996, 71 patients (16 men, 55 women; median age 56.1 ± 15.4 y, age range 18–85 y) were referred by the department of neurosurgery (Christian-Albrechts-University, Kiel, Germany) for SRS. In these patients, 92 lesions were either proven or suspected for meningioma by MRI. All patients underwent surgical resection, and MRI and SRS were compared with histology on a lesion-by-lesion basis. Written informed consent was obtained from all patients.

MRI

MRI was performed on a 1.5-T Magnetom Vision (Siemens, Erlangen, Germany) in a standardized manner. In short, both T1-weighted (repetition time [TR] = 500 ms, echo time [TE] = 12 ms) and T2-weighted spinecho 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. Tumor volumes were calculated from MRI under assumption of a rotational ellipsoid.

Somatostatin Receptor Scintigraphy

After intravenous injection of 200 MBq (5.4 mCi) ^{111}In-octreotide (Mallinckrodt, Petten, The Netherlands), digital whole-

TABLE 1
Tumor-to-Background Ratio with Percentage of Uptake of ^{111}In-Octreotide

Time of scan post-injection	T/B*			Uptake (%)*		
	TP (n = 58)	FN (n = 14)	TN (n = 20)	TP (n = 58)	FN (n = 14)	TN (n = 20)
10 min	1.54 ± 0.50	1.17 ± 0.22	1.16 ± 0.24	0.18 ± 0.19	0.02 ± 0.02	0.02 ± 0.01
1 h	1.89 ± 0.73	1.15 ± 0.20	1.26 ± 0.35	0.28 ± 0.48	0.02 ± 0.02	0.02 ± 0.02
4 h	2.36 ± 1.92	1.25 ± 0.27	1.22 ± 0.24	0.31 ± 1.97	0.02 ± 0.02	0.01 ± 0.01
24 h	3.66 ± 1.98	1.33 ± 0.37	1.34 ± 0.32	0.54 ± 0.60	0.02 ± 0.01	0.02 ± 0.02

*Results are given as mean ± SD.
T/B = tumor-to-background ratio; TP = true-postive; FN = fase-negative; TN = true-negative.

body acquisitions in anterior and posterior projection were obtained at 10 min and 1, 4 and 24 h with a scan speed of 10 cm/min. The large-field-of-view gamma camera (Bodyscan; Siemens) was equipped with medium-energy, parallel-hole collimators. The energy window was adjusted to both photopeaks of ^{111}In at 173 and 247 keV with a symmetric 20% window each.

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

Quantitative Evaluation

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 ROI located contralaterally or directly beneath the lesion, allowing the calculation of a tumor-to-background ratio (T/B). The percentage of tumor uptake was measured by relating the activity within the lesion to whole-body activity after correction for background activity. All quantification was calculated as geometric mean of anterior and posterior projection.

Statistics

Results are given as mean ± 1 SD (*25*). True-positive, true-negative and false-negative results were calculated for uptake of ^{111}In-octreotide versus histologically proven presence or absence of meningioma.

RESULTS

SRS yielded 58 true-positive, 20 true-negative and 14 false-negative results with respect to histological evaluation. T/B and percentage of tumor uptake with time are given in detail (Table 1). T/B and percentage of tumor uptake

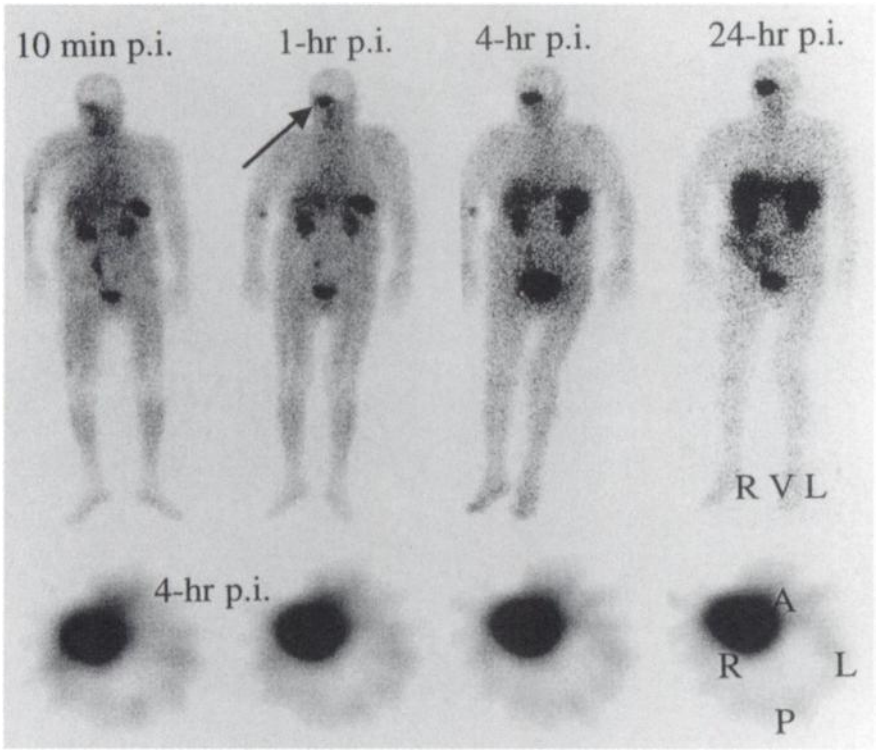

FIGURE 1. (Top row) Planar whole-body images at 10 min and 1, 4 and 24 h in anterior projection. (Bottom row) Corresponding transverse SPECT slices at 4 h. Note intense focal tracer uptake in area of right sphenoid bone on 4-h whole-body image, indicating meningioma tissue in patient. p.i. = postinjection.

significantly increased with time in SRS-positive lesions; this was not the case in SRS-negative lesions. SRS-positive lesions showed higher values of both T/B and percentage of tumor uptake at 10 min compared with SRS-negative lesions at 24 h.

True-Positive SRS

In 52 of 58 true-positive lesions (89.7%), diagnosis could be established by 4-h images without further consideration of 24-h images (Fig. 1). In 10 of the 52 lesions, additional SPECT was necessary to confirm planar findings (Fig. 2). In only 6 of 58 true-positive lesions (10.3%) were 24-h images necessary to establish the diagnosis (Fig. 3).

In 52 of 58 lesions for which SPECT images were not required at 4 h, the T/B was 2.72 ± 1.00, and the percentage of tumor uptake amounted to 0.41 ± 0.36. In contrast, in 6 lesions in which SPECT images were necessary, T/B and the percentage of tumor uptake were lower, with 1.51 ± 0.26 and 0.04 ± 0.02, respectively (Table 2). Moreover, in 6 lesions in which 24-h imaging was necessary, a low T/B of 1.41 ± 0.30 was observed at 4 h, whereas at 24 h, T/B increased to 1.88 ± 0.54. Mean tumor volume was 22.8 ± 26.0 mL in these 58 meningiomas.

Histology of lesions diagnosed at 4 h without additional SPECT revealed secretoric (n = 2), fibroblastic (n = 2), malignant (n = 8), transitional cellular (n = 7) and meningotheliomatous (n = 23) meningioma. Four fibroblastic, 4 malignant, 1 transitional cellular and 1 meningotheliomatous meningioma were detected at 4 h by additional SPECT images. Thus, no correlation was found between histology and imaging time when final diagnosis of meningioma could be established. All 52 meningiomas were located intracranially. Six patients for whom 24-h imaging was necessary had 3 intracranial relapses of meningioma with a mean tumor volume less than 5 mL and 3 meningiomas located within the spine. A diagnosis of intracranial meningioma could be established in 52 of 55 patients (95%) using only a 4-h imaging protocol.

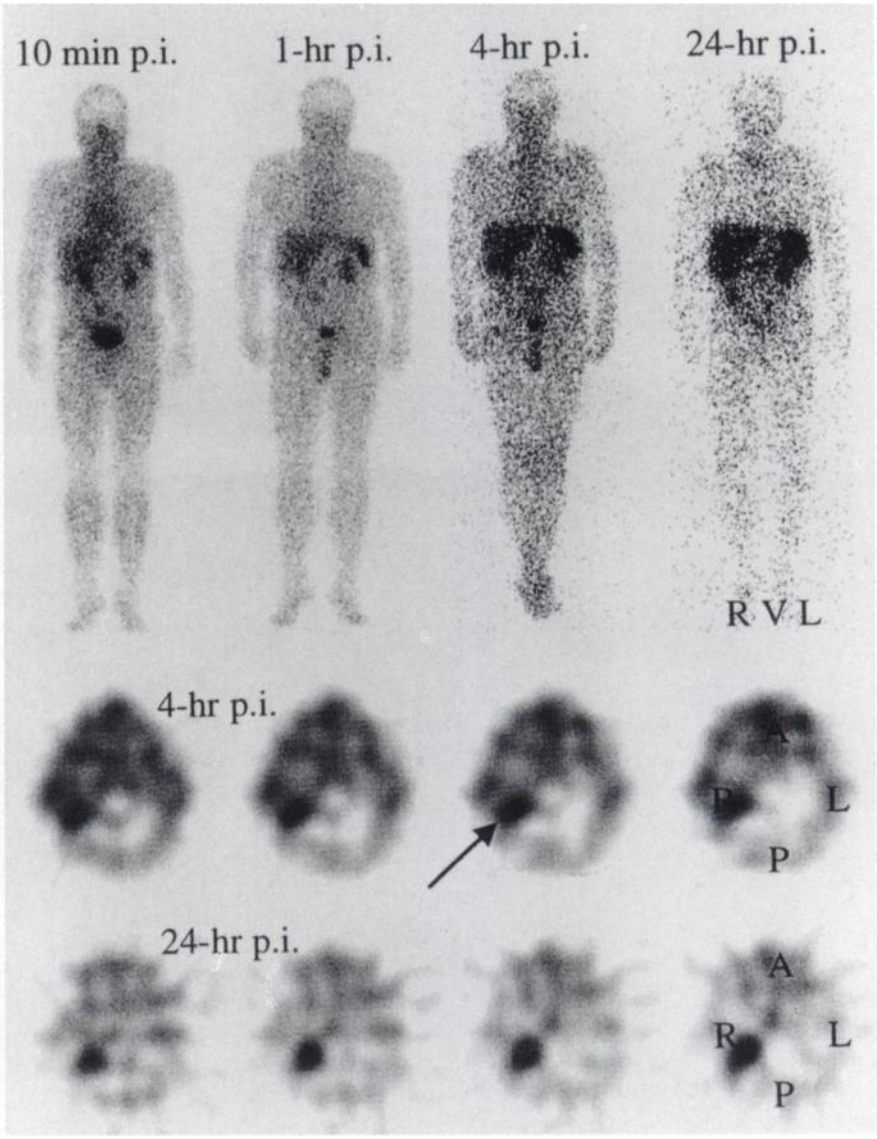

FIGURE 2. (Top row) Planar whole-body images at 10 min and 1, 4 and 24 h in anterior projection. (Bottom rows) Corresponding transverse SPECT slices at 4 and 24 h. SPECT imaging at 4 h was necessary to confirm planar findings in right posterior cranial fossa. p.i. = postinjection.

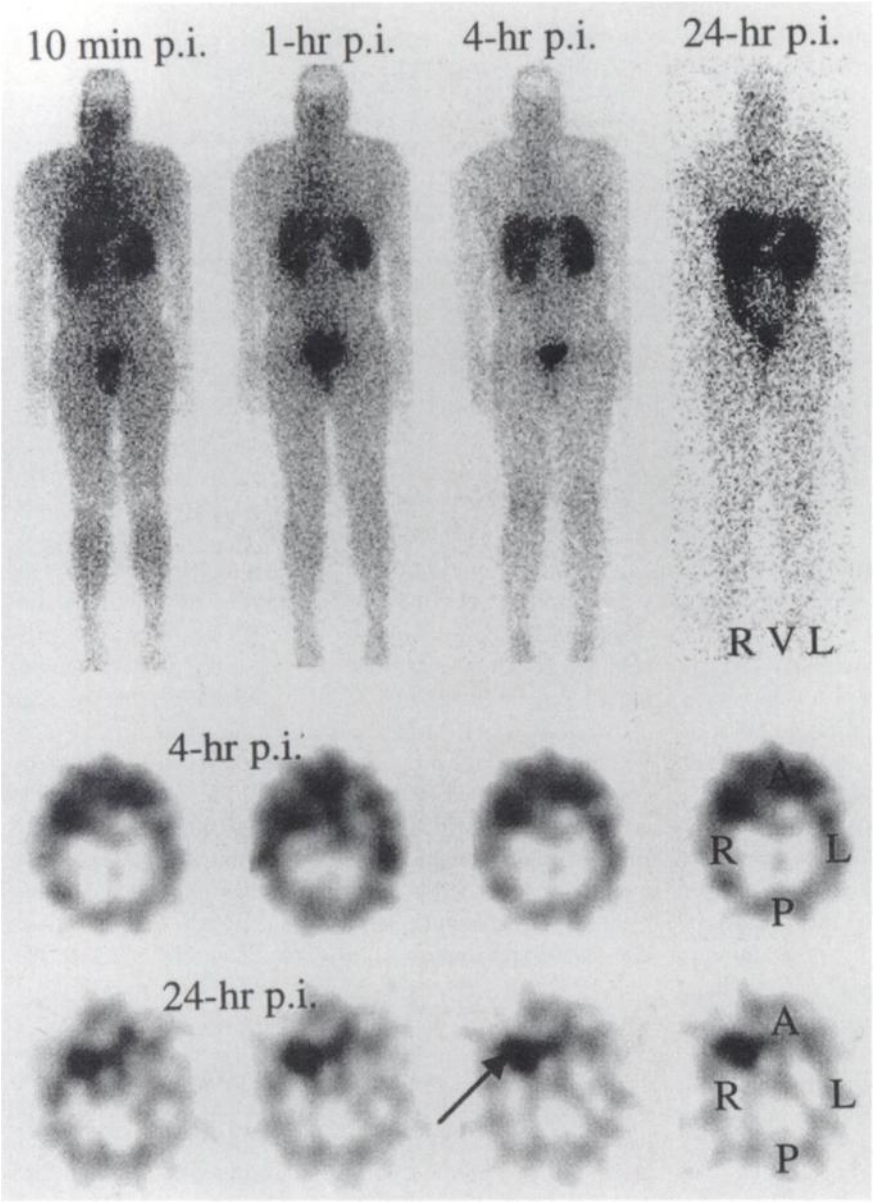

FIGURE 3. (Top row) Planar whole-body images at 10 min and 1, 4 and 24 h in anterior projection. (Bottom rows) Corresponding transverse SPECT slices at 4 and 24 h. Note focal tracer uptake in area of right sphenoid bone at 24 h, indicating meningioma tissue in patient and negative SRS at 4 h in planar whole-body image as well as in SPECT slices. p.i. = postinjection.

False-Negative SRS

In 14 localizations, SRS was false-negative. Eight meningiomas were located intracranially, 6 within the spine. Mean tumor volume of all SRS-negative meningiomas was 2.3 ± 2.1 mL with the largest tumor volume being 6.8 and 4.9 mL intracranially and within the spine, respectively.

True-Negative SRS

As confirmed by histology, a total of 20 lesions were found not to express somatostatin receptors. Pathological findings revealed 8 neurinomas, 3 adenomas of the hypophysis, 2 ependymomas, 1 dermoid cyst and 1 mucocele. In 5 patients with suspected relapse of meningiomas, SRS was negative, confirming total tumor resection. Four of the 20 lesions (20%) were located within the spine, whereas the remaining 16 (80%) were located intracranially.

DISCUSSION

Although the diagnostic impact of SRS is well documented in both differential diagnosis (*4*) and postsurgical follow-up of meningioma (*8–10*), the optimum acquisition protocol still remains controversial (*2,11–16*). In the last few years, delayed images obtained up to 48 h were abandoned in most clinical settings (*17*) because no additional information could be obtained. Studies have shown that a 24-h acquisition protocol with ^{111}In-octreotide is not helpful in the diagnosis of gastroenteropancreatic tumors (*19,20*) or liver metastases (*21*). However, in differential diagnosis of meningioma, delayed imaging up to 24 h is still recommended (*18*). However, a 24-h protocol is time consuming and expensive. Because, as studies have shown, density of somatostatin receptors is high in cell cultures (*22,23*) and in surgical specimens (*24*), most meningiomas are clearly

TABLE 2
Tumor-to-Background Ratio with Percentage of Uptake of ^{111}In-Octreotide in True-Positive Lesions Diagnosed by Planar Whole-Body Imaging

Time of scan post-injection	T/B* 4-h WB (n = 42)	T/B* 4-h WB plus 4-h SPECT (n = 10)	T/B* Additional 24-h WB plus 24-h SPECT (n = 6)	Uptake (%)* 4-h WB (n = 42)	Uptake (%)* 4-h WB plus 4-h SPECT (n = 10)	Uptake (%)* Additional 24-h WB plus 24-h SPECT (n = 6)
10 min	1.66 ± 0.53	1.24 ± 0.13	1.23 ± 0.07	0.23 ± 0.21	0.03 ± 0.04	0.11 ± 0.07
1 h	2.07 ± 0.73	1.32 ± 0.19	1.24 ± 0.15	0.35 ± 0.52	0.03 ± 0.02	0.07 ± 0.05
4 h	2.72 ± 1.00	1.51 ± 0.26	1.41 ± 0.30	0.41 ± 0.36	0.04 ± 0.02	0.08 ± 0.06
24 h	4.24 ± 1.96	2.04 ± 0.68	1.88 ± 0.54	0.69 ± 0.62	0.07 ± 0.05	0.11 ± 0.08

*Results are given as mean ± SD.
T/B = tumor-to-background ratio; WB = whole body.

detected as early as 4 h postinjection (*16*). Therefore, we investigated whether a 4-h protocol of SRS is sufficient in patients suspected of having meningiomas.

In 52 of 58 true-positive lesions (approximately 90%), final diagnosis could be established using a 4-h acquisition protocol only. In 10 of the 52 lesions, additional SPECT images were necessary to clarify findings of planar scintigrams, because tomographic technique provides better spatial resolution and anatomic orientation. Localization, histology and tumor volume of these 10 meningiomas did not differ from those of the 42 meningiomas diagnosed by planar imaging at 4 h only. Thus, we found no parameters that might be used to predict the necessity of additional SPECT imaging. Therefore, planar imaging, as well as SPECT imaging, at 4 h is necessary in every patient suspected of having a meningioma.

With regard to tumor localization, it is noteworthy that all tumors detected at 4 h were localized intracranially. In contrast, 3 of 6 meningiomas in which 24-h imaging was necessary were localized within the spine. The remaining 3 meningiomas within the cranium were rather small (mean volume < 5 mL, diameter 1.7 cm); this may explain their late demarcation. This is in agreement with the findings of other investigators who reported a correlation between the amount of tracer uptake and the tumor volume (*4,5*). Thus, for accurate detection of meningiomas, a 24-h acquisition protocol was necessary for meningiomas located within the spine as well as for tumors less than 5 mL in volume. In 14 of 92 lesions, SRS was false-negative. SRS-negative lesions were significantly smaller (mean tumor volume 2.3 ± 2.1 mL) than SRS-positive lesions (mean volume 22.8 ± 26 mL). These findings are consistent with studies demonstrating that uptake of ^{111}In-octreotide in meningiomas depends on tumor volume (*4,5*). Moreover, 6 of 14 false-negative lesions were located within the spine. Thus, a total of 9 meningiomas located within the spine either were found by 24-h imaging (n = 3) or could not be detected (n = 6).

Technical reasons for negative findings could be excluded for several reasons. First, whole-body imaging performed in our SRS-negative patients showed typical distribution of ^{111}In-octreotide. Second, our study group included a patient with simultaneous exhibition of SRS-positive and SRS-negative meningiomas. Because the SRS-positive meningioma proved to express somatostatin receptors in high density on its cell surface, a lack of somatostatin receptors within the second site meningioma as demonstrated by negative SRS seemed to be reliable. Third, a relationship between size and detection of uptake might be expected from straightforward physical principles. However, the quality of our SPECT system is demonstrated by our smallest SRS-positive meningioma, which was 0.5 cm in diameter corresponding to a volume of approximately 1 mL.

CONCLUSION

SRS yields sufficient information in patients suspected of having an intracranial meningioma using a 4-h acquisition protocol including SPECT imaging. Only in small meningiomas (volume < 5 mL), spinal localizations or negative SRS at 4 h is delayed imaging at 24 h recommended. Thus, 24-h delayed imaging is useful for a clearly defined subset of patients with meningiomas.

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