The pituitary uptake of ^{111}In-DTPA-D-Phe^{1}-octreotide in the normal pituitary and in pituitary adenomas

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ABSTRACT. The aim of this study was to compare the pituitary ^{111}In-DTPA-D-Phe^{1}-octreotide uptake measured in 49 patients subjected to the scintigraphy for SS-R expressing tumors not located in the sellar region with that measured in 38 patients with pituitary adenomas. The 87 subjects enrolled in this study were divided into two groups: the first included SSR-expressing tumors (SS-ET), 10 thymomas, 13 differentiated thyroid carcinomas, 4 carcinoids, 5 neuroendocrine tumors, 5 insulinomas, 6 melanomas, 2 renal carcinomas, 2 pheocromocytomas, and 2 parathyroid tumors, while the second included pituitary adenomas, 25 GH-secreting, 4 GH/PRL-mixed and 9 clinically nonfunctioning adenomas (NFA). Planar and single-photon-emission tomography images of the head were obtained 2-4 and 24 hours after the injection of 77-103 MBq of ^{111}In-DTPA-D-Phe^{1}-octreotide and pituitary uptake was measured by the region of interest method. A 4 point score was used to grade the pituitary-to-blood (T-to-B) ratios: 0=negative; 1=faint (T-to-B=<1.5); 2=moderate (T-to-B=1.6-3.5); 3=intense (T-to-B=>3.5). In patients with pituitary adenomas, the percent suppression of GH and α-subunit levels after 6-12 months of octreotide treatment (0.3-0.6 mg/day) was correlated to T-to-B ratios. After 2-4 hr from injection, pituitary ^{111}In-DTPA-D-Phe^{1}-octreotide uptake was moderate/intense in 2 out of 49 SS-ET (4%), 18 out of 29 acromegalics (62%) and 6 NFA (66.6%), while a faint uptake was detected in 4 SS-ET (8%), 8 GH-secreting adenomas (27.5%) and 3 NFA (33.3%). Negative scan was detected in the remaining 43 SS-ET (87.7%) and 3 GH-secreting microadenomas (10.3%). 24 hr after injection, pituitary ^{111}In-DTPA-D-Phe^{1}-octreotide uptake was moderate/intense in SS-ET (10.2%), 21 GH-secreting adenomas (72.4%), and 9 NFA (100%) while a faint uptake was detectable in 15 SS-ET (30.6%), and 6 GH-secreting adenomas (20.7%). No uptake was visualized in 29 SS-ET, and 2 GH-secreting adenomas. By MRI a pituitary tumor was shown in the 2 SS-ET with early moderate tracer uptake. Normalization of circulating GH/IGF-I levels and suppression of α-subunit levels was achieved in 16 of 18 acromegalics (88.9%) and 5 of 6 NFA-bearing patients, respectively, with scan scored 2-3 at early images. Eleven acromegalics (37.9%) and 2 NFA (22.2%) displayed significant tumor shrinkage (≥30% of baseline size) during long-term octreotide therapy. Both in GH-secreting and in NFA, a significant correlation was found between percent GH or α-subunit suppression after 6-12 months of octreotide therapy and T-to-B ratios both in early (r=0.626; p<0.0001 and r=0.738, p=0.003, respectively) and late images (r=0.569; p=0.002 and r=0.8, p=0.01, respectively). In conclusion, the ^{111}In-DTPA-D-Phe^{1}-octreotide uptake in pituitary adenomas was significantly correlated to octreotide treatment. However, since pituitary ^{111}In-DTPA-D-Phe^{1}-octreotide uptake was clearly detectable in 40% of patients with SS-ET not located in the pituitary region at 24 hr post-injection, ^{111}In-DTPA-D-Phe^{1}-octreotide scintigraphy with late pituitary images can not be considered an useful method to predict the chronic responsiveness to octreotide in individual patients. Caution should also be taken in evaluating the results of the scintigraphy with early images in patients with scant uptake before excluding them from treatment.

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INTRODUCTION

The treatment with the somatostatin analog octreotide (OCT) improves signs and symptoms, normalizes hormonal secretion, and may produce tumor shrinkage in GH-, TSH-secreting and in some clinically nonfunctioning pituitary adenomas (NFA) (1). The therapeutic effect occurs after the OCT binding to somatostatin receptors which have been classified into 5 different subtypes: OCT binds with high affinity the SS-R subtypes 2 and 5 (1). The therapeutic success is positively correlated to the amount of receptors within tumors (2) and varies with the density of expressed SS-R (2-5). Since OCT therapy may have a long duration and is expensive, tests able to predict the response to this therapy have been investigated to spare patients from unnecessary treatment. In patients with acromegaly the acute test with OCT is considered the gold standard to address this issue (6). However, the acute test can not be perfomed in patients with NFAs and overestimates the rate of responsive patients in secreting ones (7).

Recently, the availability of labeled somatostatin analogs allowed to detect *in vivo* malignancies which express SS-R by standard γ-cameras. Besides, scintigraphy has been proposed to select candidates responsive to specific peptide treatment (8-11). In patients with pituitary adenomas this latter evidence is under debate since normal pituitary tissue can be visualized using ^{111}In-DTPA-D-Phe^1-octreotide (12, 13). Therefore, normal pituitary is hardly distinguished from a low SS-R expressing adenoma. Previous studies were based on a semi-quantitative or qualitative assessment of the radioligand uptake, measured at 24-hr (8-13) when the high gradient adenoma/background enables high quality images, but the normal pituitary tissue expressing SS-R is frequently seen (14). Whether or not the uptake in the normal pituitary influences the value of the scintigraphy with ^{111}In-DTPA-D-Phe^1-octreotide in pituitary adenomas was never investigated.

The aim of the present study was to measure the uptake of ^{111}In-DTPA-D-Phe^1-octreotide measured at 2-4 and at 24 hr in the pituitary gland both in patients with pituitary adenomas before starting long-term OCT treatment and in those undergone scintigraphy for other SS-R-expressing tumors.

PATIENTS AND METHODS

Patients

Eighty-seven patients were enrolled in this study after their informed consent had been obtained. The protocol was approved by the Ethical Committee of the National Cancer Institute of Naples. They were divided into 2 groups: the first included 49 patients (19 males, 30 females; age range: 16-74 yr) undergone scintigraphy for other SS-R-positive tumors (10 thymomas, 13 differentiated thyroid carcinomas, 4 carcinoids, 5 neuroendocrine tumors, 5 insulinomas, 6 melanomas, 2 renal carcinomas, 2 phaeochromocytomas, and 2 parathyroid tumors) who served as normal pituitary control while the second included 25 GH-secreting (12 males, 13 females; age range: 15-68 yr), 4 GH/PRL-secreting pituitary adenomas (3 males, 1 female, age range: 27-38 yr) and 9 NFA (4 males, 5 females, age range: 18-65 yr). The lesions were classified by clinical evaluation, laboratory and immunohistochemistry, when surgery was performed. At study entry, among the 38 patients with pituitary adenomas, 31 were untreated while 7 were previously operated on at least 6 months before entering the study: 5 had been previously treated with OCT but withdrew the treatment at least 15 days before the scintigraphy. CT and/or MRI documented microadenoma in 3, remnant tumor in 7 and macroadenoma in 28 patients. All patients with acromegaly had active disease at study entry.

Treatment protocol

All patients with acromegaly and NFA were treated with OCT for 6-12 months. OCT was initially administered at the daily dose of 0.05 mg thrice daily, according to patients' compliance during the acute test (0.1 mg sc), as previously reported (7). Subsequently, the dose of 0.3 mg/day was maintained throughout the follow-up in 16 acromegalic patients, while the dose was increased up to 0.45 mg daily in 10 other acromegalics and up to 0.6 mg daily in 12 patients (3 acromegalics and 9 NFA) to obtain GH/IGF-I and α-subunit suppression, improvement of clinical signs and symptoms and/or tumor shrinkage. At study entry, circulating IGF-I and α-subunit levels were assayed in a single sample while the value of serum GH was calculated as the mean of a 6 hour blood sampling (8.00-14.00 with 30 min sampling). During treatment, GH levels were calculated as the average value of at least 3 blood samples collected at 15 min intervals 2 hr after OCT administration. At this time-point, plasma IGF-I and α-subunit concentrations were assayed as single sampling. Circulating GH, IGF-I and α-subunit levels were re-evaluated 6 and 12 months after OCT treatment. The results obtained after 3 months treatment with octreotide in 23 of 29 acromegalics have been previously reported (7).

Radiological examinations

Sellar CT scan was carried out, before and after infusion of contrast medium, with a high-resolution scan-

ner. MRI images were carried out by a superconductive magnetic resonance (0.5-1.0 Tesla) and using a superficial coil in coronal (3 sections, 3 mm thickness) and axial sections. The acquisition was fast Spin-echo before and after Gadolinium enhancement. CT and MRI studies were performed before and after 6-12 months of treatment to document, if any, adenoma shrinkage. For individual patient the same radiological technique was used to evaluate the adenoma volume which was calculated by the De Chiro and Nelson formula (volume=height x lenght x width x π/6) as previously reported (15). Reduction of tumor volume greater than 30% of baseline size was considered significant (7).

^{111}In-DTPA-D-Phe^{1}-octreotide scintigraphy

^{111}In-DTPA-D-Phe^{1}-octreotide (specific activities range: 77-103 MBq/5-10 µg of peptide) was purchased from Mallinkrodt (Petten, The Netherlands). The labeling was performed as previously described (16). Quality controls were performed on labeled peptide before the injection. More than 95% of the radioactivity was peptide-bound in injectable preparations. These doses were the true injected amount of ^{111}In-DTPA-D-Phe^{1}-octreotide measured in the syringe before and after iv administration. Lateral views of the skull were acquired between 2-4 and 24 hr after injection for 10 min: for the patients receiving lower doses longer times of acquisiton were applied. Spot images of the whole-body and tomographic acquisition were performed 4-5 hr after injection. Studies were performed by a single head gamma camera (Orbiter II, Siemens, Erlangen, Germany) equipped with a medium-energy-collimator. The photopeaks were set at 172 and 247 KeV, with a 20% symmetric function window. The images were stored in a dedicated computer (Microdelta, Siemens). Tomographic studies were acquired using a step and shoot procedure. The orbit was circular, over 360 degrees. Sixty-four images were gathered every 5° and 6' for 40-60 sec/view. Reconstruction was performed using a Hanning filter (frequency cut-off=0.5 cm^{-1}) on

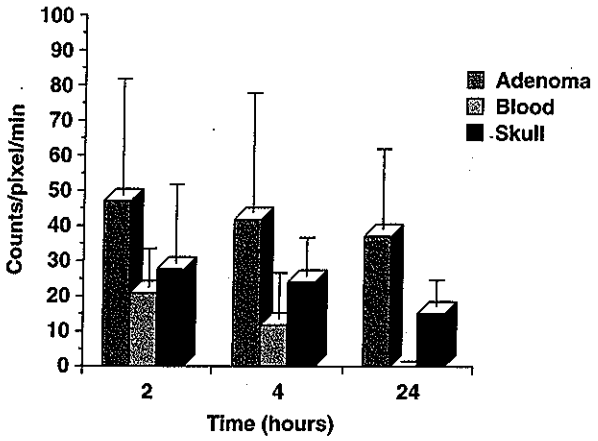

Fig. 1 - *Measurement of the levels of ^{111}In-DTPA-D-Phe^{1}-octreotide uptake in different regions of interest 2, 4 and 24 after injection.*

Table 1 - *Summary of patients' diagnosis at study entry and results of ^{111}In-DTPA-D-Phe^{1}-octreotide scintigraphy measured as uptake score.*

Patients	no.	m/f	Age-range (yrs)	^{111}In-DTPA-D-Phe^{1}-octreotide uptake score 2-4 hours images				24 hours images			
				0	1	2	3	0	1	2	3
Group 1											
Thymomas	10	4/6	22-64	6	2	2	0	4	4	2	0
Differentiated thyroid carcinomas	13	3/10	24-67	13	0	0	0	8	3	2	0
Carcinoids	4	1/3	16-62	4	0	0	0	3	1	0	0
Neuroendocrine tumors	5	2/3	18-62	3	2	0	0	2	2	1	0
Insulinomas	5	2/3	23-74	5	0	0	0	3	2	0	0
Melanomas	6	3/3	57-69	6	0	0	0	6	0	0	0
Renal carcinomas	2	2/0	42-48	2	0	0	0	2	0	0	0
Pheocromocytoma	2	1/1	33-41	2	0	0	0	1	0	0	0
Parathyroid tumor	2	1/1	32-44	2	0	0	0	0	2	0	0
Total	49	19/30	-	43	4	2	0	29	15	5	0
Group 2											
GH-secreting adenomas	25	12/13	15-68	3	8	7	7	2	6	9	8
GH/PRL mixed adenomas	4	3/1	27-38	0	0	0	4	0	0	0	4
Nonfunctioning adenomas	9	4/5	18-65	0	3	2	4	0	0	4	5
Total	38	19/19	-	3	11	9	15	2	6	13	17

^{111}In-DTPA-D-Phe^{1}-octreotide uptake score: 0=negative; 1=faint (T-to-B=<1.5); 2=moderate (T-to -B=1.6-3.5); 3=intense (T-to-B=>3.5).

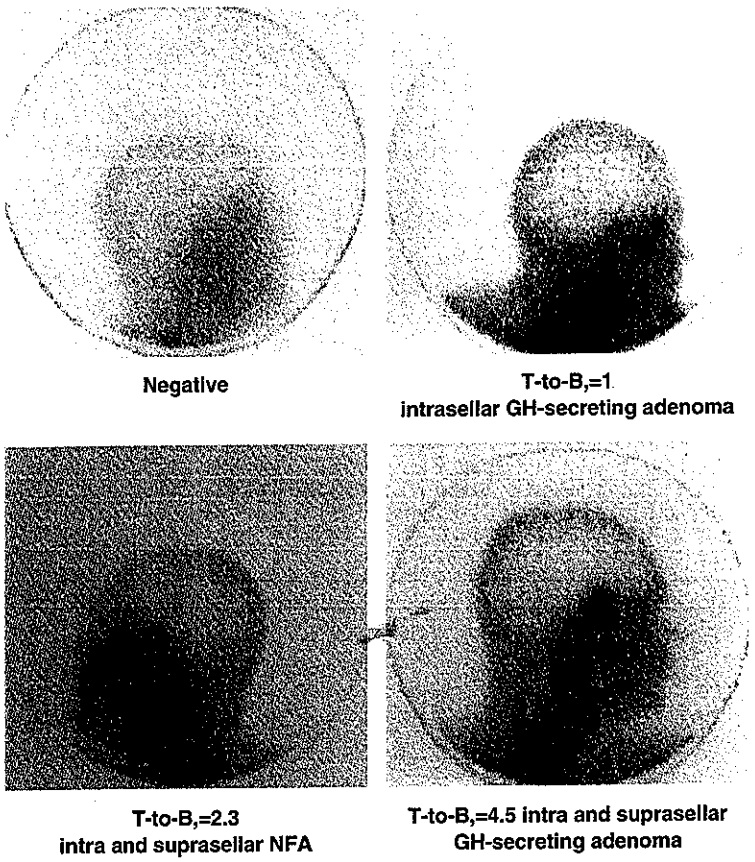

Fig. 2 - *The scintigraphic patterns corresponding to the uptake scores are shown. Negative ^{111}In-DTPA-D-Phe^1-octreotide uptake (score 0); GH-secreting adenoma with faint uptake (score 1); Clinically nonfunctioning adenoma with well defined uptake (score 2); mixed GH-secreting adenoma with very high uptake (score 3).*

backprojected images. No attenuation correction was applied.

Image analysis and ^{111}In-DTPA-D-Phe^1-octreotide uptake score

In individual patients, irregular regions of interest (ROI) were manually drawn on planar images as well as in SPECT reconstruction by three independent observers (S.L., P.V., W.A.) blinded for the results of the hormonal evaluation. By the ROI method were delineated the following areas: pituitary or pituitary adenoma (T), blood pool in transversal sinus (B), and skull (S). The degree of ^{111}In-DTPA-D-Phe^1-octreotide uptake within the pituitary region was studied on the planar images or spect acquired after 2-4 and 24 hr from injection. This time was selected after performing the analysis of the activity time curves during the whole study, which included three experimental time-points. The choice was based upon the following evidences: no significant changes of uptake occurred between 2 and 4 hours, visualization only in very early scans (2-hr) of still circulating activity in the transversal sinus. The selection of a vascular structure as background was based upon the rationale that this activity represents the still circulating, unbound radioligand. Conversely, activity in the normal brain is not recognizable (unless blood brain barrier leakage occurs), whereas the activity within the skull is often greater than that measured within adenoma and drastically reduces from early to late (24 hr) images (Fig. 1). The average counts/pixel measured within T was divided for the average counts/pixel measured in B to obtain the T-to-B ratios. Using the 2-4 hr T-to-B ratios, the images were graded using the following four point score: 0=negative; 1=faint uptake, T-to-B ratios below 1.5; 2=moderate uptake, T-to-B ratios ranging from 1.6 to 3.5; 3=intense uptake, T-to-B ratios above 3.5. Evaluation of planar and SPECT images was performed separately to allow for independent interpretation.

Hormone assays

Serum GH and PRL levels were assessed by IRMA using commercially available kits: the normal ranges were below 2.5 µg/l and 5-2 µg/l respectively. Plasma IGF-I levels were assessed after extraction

using commercial kits: the normal range for adults aged 20-30, 31-40, 41-50 and over 51 yrs, was respectively 110-502, 100-494, 100-303 and 78-258 µg/l. Serum α-subunit levels were assessed by a RIA monoclonal antibody (Biomerica, IMC, Newport Beach, CA, USA), the normal range was 0.1-1.5 for male and pre-menopausal female and 0.7-4.4 IU/l for post-menopausal female.

Statistical analysis

Correlation between ^{111}In-DTPA-D-Phe^{1}-octreotide uptake in early and late images, measured as T-to-B ratio, and response of serum GH and α-subunit levels after 6-12 months of OCT treatment, expressed as percent decrease of baseline values, was performed by the Spearman's Rank correlation. The significance was set at 5%.

RESULTS

Imaging results in patients with SS-R expressing tumors (Table 1)

At 2-4 hr images, among the 49 patients with SS-R expressing tumors, 4 showed a faint uptake and 2 others a moderate uptake in the pituitary region, in absence of any endocrine sign of pituitary disease. In the remaining 43 patients the scintigraphic scan was negative. At 24 hr images, a faint uptake was detected in the pituitary region of 15 controls (30.6%), a moderate uptake was detected in 5 controls, respectively (10.2%, Table 1). MRI of the sellar region performed in these 20 patients was negative in all patients, but the 2 patients with moderate uptake in early images. An intrasellar adenoma (5 mm in size the first and 12 mm the second, final diagnosis NFA) was found.

Imaging results in patients with pituitary adenomas (Table 1)

The scintigraphy was negative both in early and late images only in 2 GH-secreting microadenomas. The 4 uptake scores measured in early images are exemplary shown in Figure 2.

After 6-12 months of treatment with OCT, normalization of circulating GH and IGF-I levels was achieved in 20 of 29 acromegalics: 1/3 with score 0, 3/8 with score 1, 6/7 with score 2 and 10/11 with score 3 at early images. Moreover, significant tumor shrinkage was documented at CT scan and/or MRI in 2 patients with score 1, 4 with score 2 and 7 with score 3 (Table 2). Among the 9 patients with NFA, 4 had high circulating α-subunit levels before treatment (Fig. 3). The normalization of α-subunit levels was achieved in all patients: 1 had score 2 while 3 had score 3. In 2 out of 4 patients with intense ^{111}In-DTPA-D-Phe^{1}-octreotide, significant tumor shrinkage was documented at CT scan and/or MRI.

In the 29 patients with GH-secreting pituitary adenoma, a significant correlation was found between the percent inhibition of serum GH after 6-12 months of OCT treatment and the T-to-B ratios of ^{111}In-DTPA-D-Phe^{1}-octreotide uptake both in early (r=0.626; p<0.0001) and late images (r=0.569; p<0.02). Similarly, in the 9 patients with NFA, a significant correlation was found between inhibition of serum α-subunit after 6-12 months of OCT treatment and the T-to-B ratios of ^{111}In-DPTA-D-Phe^{1}-octreotide uptake both in early (r=0.738; p<0.003) and late images (r=0.8; p<0.01).

Table 2 - *Response to long-term octreotide treatment in patients with pituitary adenomas in agreement with the results of ^{111}In-DTTA-D-Phe^{1}-octreotide score.*

Pituitary adenoma histotype (patient no.)	m/f	Age range (yr)	Serum GH levels (µg/l) basal	Serum GH levels (µg/l) nadir	Plasma IGF-I levels (µg/l) basal	Plasma IGF-I levels (µg/l) nadir	Serum α-subunit levels (U/l) basal	Serum α-subunit levels (U/l) nadir	Tumor shrinkage
Score 0, negative									
GH-secreting adenomas (3)	3/0	17-57	26.3±8.9	8.6±4.8	574.3±158	242.7±17	-	-	0/3
Score 1, faint uptake									
GH-secreting adenomas (8)	3/5	42-52	27.1±5	7±2.4	442±51	240±30	-	-	2/8
NFA (3)	2/1	33-65	0.9±0.2	0.3±0.1	-	-	1.3±0.1	1.1±0.1	1/3
Score 2, moderate uptake									
GH-secreting adenomas (7)	4/3	23-68	42±12	2.7±1.3	440±36	152±13	-	-	4/7
NFA (2)	0/2	18-54	0.2±0	0.2±0	-	-	2.6±1.9	0.2±0.1	0/2
Score 3, intense uptake									
GH-secreting adenomas (7)	2/5	15-45	63±21	3±1.7	582±102	189±14	-	-	4/7
GH/PRL-secreting adenomas (4)	3/1	27-38	59±8	1.2±0.4	793±57	162±16	-	-	3/4
NFA (4)	3/1	38-65	1.1±0.3	0.1±0.02	-	-	4.8±1.5	0.6±0.3	2/4

Normal ranges: GH=<25 µg/l; IGF-I=110-502, 100-494, 100-303 and 78-258 µg/l respectively in 20-30, 31-40, 41-50 and over 51 yrs adults; α-subunit, 0.1-1.5 (male and premenopausal female), 0.7-4.4 mIU/ml (postmenopausal female).

Table 3 - *Sensitivity, specificity, positive and negative predictive value of scintigraphic results using ^{111}In-DPTA-D-Phe^1-octreotide with images collected after 2-4 and 24 hr in patients with pituitary adenomas.*

	2-4 hr images	24 hr images
Sensitivity (%)	86.6	88.7
Specificity (%)	83.3	41.7
Positive predictive value (%)	91.7	76.7
Negative predictive value (%)	71.4	62.5

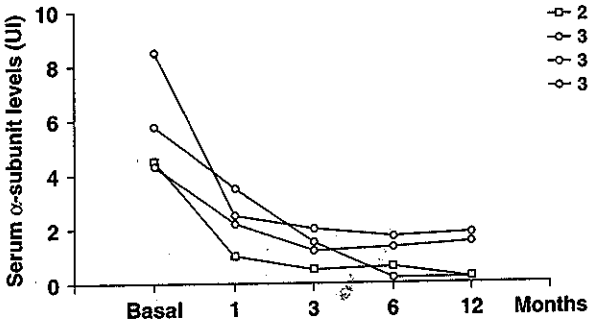

Fig. 3 - Serum α-subunit levels in 4 patients with clinically non-functioning pituitary adenomas displaying high levels before treatment with octreotide and effect of treatment on hormone levels. The legend shows the ^{111}In-DTPA-D-Phe^1-octreotide uptake score in early images.

The evaluation of the accuracy of the scintigraphy (Table 3), revealed that in late images specificity, positive and negative predictive values were lower than in early ones: the sensitivity remained similar. The ^{111}In-DTPA-D-Phe^1-octreotide uptake in early images correctly predicted a positive response to OCT treatment in 21 of 24 patients with moderate/intense uptake while it wrongly predicted a negative response in 4 of 15 patients with negative-scant uptake. Tracer uptake measured in late images correctly predicted a positive treatment response in 22 of 30 patients with moderate/intense uptake while it wrongly predicted a negative response in 3 of 8 patients with negative-scant uptake.

DISCUSSION

The results of the present study show that pituitary ^{111}In-DTPA-D-Phe^1-octreotide uptake occurred in 40% and 12% of control subjects after 24 and 2-4 hr from injection, respectively. Since in patients with secreting pituitary adenoma the effectiveness of OCT treatment can be easily monitored by serial serum hormone assays, the potential value of the scintigraphy with ^{111}In-DTPA-D-Phe^1-octreotide mainly resides in its ability to select patients with NFA who can benefit from OCT treatment, although controversial data have been reported (12, 13, 17-20). Since a number of patients without pituitary tumors may have a significant uptake of this tracer when the images were collected after 24 hr, this is a serious shortcoming in the evaluation of the usefulness of the scintigraphic test in patients with pituitary adenomas.

Specificity, positive and negative predictive values of the scintigraphy with ^{111}In-DTPA-D-Phe^1-octreotide were greater in early than in late images. Therefore, the discrepancy reported in literature on the predictive effect on ^{111}In-DTPA-D-Phe^1-octreotide in patients with pituitary adenomas, can be explained taking into consideration the different time of images acquisition. In fact, either the presence (7-11) or the absence (12, 13) of significant correlation between ^{111}In-DTPA-D-Phe^1-octreotide uptake and GH, IGF-I and α-subunit suppression after OCT treatment were reported. On the other hand, scant data are available so far on the pituitary uptake of ^{111}In-DTPA-D-Phe^1-octreotide in subjects not bearing a pituitary tumor. Recently, in healthy volunteers the accumulation of the radiotracer in the pituitary was shown to be highly variable (up to 5-times) and best visualized 24 hr after injection (14). Patients with pituitary adenoma had an ^{111}In-DTPA-D-Phe^1-octreotide uptake greater than healthy volunteers (14). In order to limit the variability in the reading of the images, van Royen *et al.* (14) suggested to perform the scintigraphy matching the CT or MRI images with the SPECT results and drawing the ROI accordingly. However, this appears a rather complex procedure particularly in patients with remnant tumors. Since the measurement of tumor-to-background ratios in early images is supposed to mirror the bound-to-free ratios and assess the bioavailability of SS-R, we evaluated the early tracer uptake in the pituitary gland of patients with and without pituitary adenoma. Clearly, the use of a semiquantitative analysis of scintigraphic results may better characterize the SS-R content within adenomas, which is the basic requirement to obtain a tumor response, and is an information otherwise not obtainable. Using only 24-hour images the majority of lesions could be considered positive, and there was no distinct cut-off to differentiate adenomas from normal pituitary. The ^{111}In-DTPA-D-Phe^1-octreotide uptake was detected in 12% of our controls in early images (8% faint and 4% moderate uptake) and in 40% (30% faint and 10% moderate uptake) in late images. However, in most controls tracer uptake was faint and in the two controls with early moderate uptake, a pituitary tumor was demonstrated at MRI. No pituitary lesion was shown so far in the remaining 18 controls with ^{111}In-DTPA-D-Phe^1-octreotide uptake.

In addition, in patients with pituitary adenoma and moderate-to-intense tracer uptake, GH, IGF-I or α-subunit levels were normalized in the great majority of patients (16 of 18 acromegalics and all 4 NFAs with high α-subunit levels) with a relevant proportion of patients displaying tumor shrinkage. However, it should be also noted that 4 acromegalic patients normalized their GH and IGF-I levels after OCT treatment despite the evidence of a negative-faint ^{111}In-DTPA-D-Phe^{1}-octreotide uptake. Therefore, although a significant correlation was present between tracer uptake score and percent hormone suppression in a rather large series of 38 patients with pituitary adenoma, a small (10.5%) but not negligible proportion of patients would be excluded from the treatment on the basis of the results of the scintigraphy.

In conclusion, ^{111}In-DTPA-D-Phe^{1}-octreotide uptake was clearly detectable in 12% and 40% of controls without any known pituitary disease, at 2-4 and 24 hr post-injection, respectively. In patients with pituitary adenoma, the scintigraphic results analyzed in early *vs* late images showed that specificity, positive and negative predictive values were reduced (83.3 *vs* 41.7%, 91.7 *vs* 76.7% and 71.4% *vs* 62.5%) while the sensitivity was unchanged (86.6 *vs* 88.5%). Although, tracer uptake measured in early images correctly predicted a positive response to long-term OCT in 22 out of 24 patients with evident uptake, it wrongly predicted a negative response in 4 out of 14 patients with negative-scant uptake.

Thus, ^{111}In-DTPA-D-Phe^{1}-octreotide scintigraphy with late pituitary images can not be considered an useful method to predict the chronic responsiveness to octreotide and even the results based on early images in patients with scant uptake should be considered with caution before excluding them from treatment. In these patients a short-term treatment with OCT could be advisable (7, 21).

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