Table 6: Single-Photo Emission Computed Tomography (SPECT) Imaging

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
de Herder (1999)[72]	Comparison of iodine-123 epidepride and iodine-123 IBZM for dopamine D2 receptor imaging in clinically non-functioning pituitary macroadenomas and macroprolactinomas.	Patients with nonfunctioning pituitary adenomas and prolactinomas underwent pituitary iodine-123-epide-pride single photon emission tomography (SPET) and 123I-IBZM SPET. The uptake of radioactivity was determined using a visual scoring system. The uptake index was calculated by dividing the average count rates in the pituitary region by the average count rates in the cerebellum. The uptake levels and uptake index was compared between the 2 groups of pathologies.	15	Diagnostic / III	Specific binding of 123I-epidepride was demonstrated in 9 of the 15 clinically non-functioning pituitary adenomas (60%), but specific binding of 123I-IBZM was shown in only 6 of these 15 cases (40%). The uptake of 123I-epidepride in the pituitary region was consistently higher than that of 123I-IBZM. None of the patients who showed absence of uptake of 123I-epidepride in the pituitary area showed uptake of 123I-IBZM in this area. 123I-epidepride SPET is superior to 123I-IBZM SPET for the visualization of dopamine receptor-positive pituitary adenomas. 123I-epidepride SPET potentially might serve to predict the response of clinically non-functioning pituitary adenomas to dopamine agonist therapy.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Kojima (2001)[73]	Is technetium-99m-MIBI taken up by the normal pituitary gland? A comparison of normal pituitary glands and pituitary adenomas.	Patients with and without pituitary adenomas underwent both conventional MR and technetium-99m-hexakis-2-methyoxy-isobutyl-isonitril single photon emission computed tomography (SPECT) imaging. SPECT uptake shape and location patterns were compared between patients with tumors and normal controls.	15	Diagnostic / III	Analysis of the uptake showed that 10 (67%) adenomas were C, and 5 (33%) were LO. Of the controls, 5 (33%) were C, and 10 (69%) were T/R. With regard to location, all patients with pituitary adenomas were classified as P, and all control subjects (93%) but one showed uptake in the dorsum sellae and clivus (D/C). MIBI was taken up in the dorsum sellae or clivus but not the normal pituitary gland and had a strong affinity for the pituitary adenoma. MIBI SPECT may be a useful auxiliary examination technique for the location diagnosis of pituitary adenoma.
Yamamura (2003)[74]	Differentiation of pituitary adenomas from other sellar and parasellar tumors by 99mTc(V)-DMSA scintigraphy.	Patients with pituitary adenomas and other sellar/parasellar lesions underwent pentavalent technetium-99m dimercaptosuccinic acid scintigraphy. Imaging findings were compared by differing pathology.	21	Diagnostic / III	99mTc(V)-DMSA scintigraphy showed overall sensitivity of 81% (17/21 cases) for detecting pituitary adenomas, in particular 100% for non-functioning adenomas. 99mTc(V)-DMSA may be useful for detecting pituitary adenomas, especially non-functioning adenomas, and for the differentiation of non-functioning pituitary adenomas from other sellar and parasellar lesions.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Lastoria (1995)[75]	Technetium-99m pentavalent dimercaptosuccinic acid imaging in patients with pituitary adenomas.	Patients with nonfunctioning pituitary adenomas, secretory adenomas, or non-tumor controls underwent technetium-99m-labeled pentavalent dimercaptosuccinic acid scintigraphy. Uptake levels were compared between the different groups of pathologies.	15	Diagnostic / III	Seventeen GH-secreting (81%), 7 PRL-secreting (78%), 3 ACTH-secreting (50%), 15 non-functioning (100%), and 1 (50%) mixed adenoma significantly concentrated [99mTc](V)DMSA, showing elevated tumor-to-background (T/B) ratios. Non-adenomatous lesions of the sella turcica did not concentrate [99mTc](V)DMSA in the pituitary as well as brain tumors and 8 out of 10 metastatic thyroid cancers. The [99mTc](V)DMSA scintigraphy showed an overall sensitivity of 81% (43/53) in detecting pituitary adenomas, which was increased to 95% for lesions greater than 10 mm in size. High-quality images with minimal total body radiation were obtained, enabling a good in vivo characterization of viable adenomatous tissue as well as an accurate monitoring of the effects of different therapeutic regimens. Technetium-99m DMSA may be used as a supplementary tool in the preoperative identification of pituitary adenoma.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Colao (1999)[76]	The pituitary uptake of (111)In-DTPA-D-Phe1-octreotide in the normal pituitary and in pituitary adenomas.	Clinical experience using The (111)In-DTPA-D-Phe1-octreotide for assessment of pituitary lesions.	38	Diagnostic / III	The (111)In-DTPA-D-Phe1-octreotide uptake in pituitary adenomas was significantly correlated to octreotide treatment. Pituitary (111)In-DTPA-D-Phe1-octreotide uptake was clearly detectable in 40% of patients with SS-ET not located in the pituitary region at 24 hours post-injection. (111)In-DTPA-D-Phe1-octreotide scintigraphy with late pituitary images cannot be considered a useful method to predict the chronic responsiveness to octreotide in individual patients.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Oppizzi (1998)[77]	Scintigraphic imaging of pituitary adenomas: an in vivo evaluation of somatostatin receptors.	Patients with nonfunctioning pituitary adenomas, GH-secreting adenomas, or no tumor underwent pituitary scintigraphy with somatostatin analog pentetreotidean. The accumulation of this analog was expressed as an activity radio between the uptake of radioactivity by the adenoma to that of normal brain tissue. Activity ratios were compared between the different groups of pathologies.	22	Diagnostic / III	In 15 out of the 17 patients with GH-secreting adenoma, an accumulation of the radioligand was shown. Median activity ratio was 3.8 (range 1-6.9; in 14 AR were greater than 2.2) and ARs were directly correlated (r = 0.54; *P* < .05) with the suppressibility of plasma GH levels by octreotide (OC) acute administration. In 2 patients who repeated scintigraphy during chronic OC treatment, AR values were reduced. In all the 22 patients with NFPA, an accumulation of 111In-P at the pituitary level was observed and median AR was 3.0 (range 1.5-20; in 14 greater than 2.2). In vitro autoradiography of surgical specimens in 6 NFPA patients revealed SS-R in 4 cases with high scintigraphic AR and negative results in 2 cases with low AR. Scintiscan was repeated during chronic OC treatment in 5 patients with high score: AR decreased in 1 patient, increased in 3, and did not change in the other patient. No changes in tumor size were shown in any of these patients. A total of 8 patients (3 GH secreting and 5 NFPA) had "normal" AR values. In acromegaly scintigraphy with 111In-P visualizes functioning pituitary SS-R coupled to intracellular events that control hormonal hypersecretion and tumor growth. In contrast, in spite of the positivity of 111In-P imaging in most patients with NFPA, their receptors might have a defect in the coupling-transduction process, as they are not inhibited by OC treatment and no tumor shrinkage is observed.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Broson-Chazot (1997)[78]	Somatostatin receptor imaging in somatotroph and non-functioning pituitary adenomas: correlation with hormonal and visual responses to octreotide.	Patients with nonfunctioning pituitary adenomas and GH-secreting adenomas underwent somatostatin receptor scintigraphy. Uptake index was calculated and a threshold for a positive test was calculated using non-tumor controls. Uptake index data was compared in the different groups of pathologies.	29	Prognostic / III	In non-functioning pituitary adenomas, somatostatin receptor scintigraphy was positive in 62%. Based on visual effects, the positive predictive value was 61% and the negative predictive value was 100%. A wide distribution of somatostatin binding sites was found in 8 non-functioning pituitary adenomas with expression of sst2 only. In patients with non-functioning pituitary adenomas, negative somatostatin receptor scintigraphy predicts that there will be no visual improvement during octreotide treatment.
Rieger (1997)[79]	Somatostatin receptor scintigraphy in patients with pituitary adenoma.	Clinical experience using somatostatin receptor scintigraphy for the assessment of pituitary lesions.	42	Diagnostic / III	No specific binding of 111In-octreotide was found. Five patients showed a weak positive, 5 had a positive, and 9 a strong positive signal in the region of interest. Uptake of octreotide was significantly correlated with tumor size and age ($P < .01$).

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
de Herder (1996)[80]	In vivo imaging of pituitary tumours using a radiolabelled dopamine D2 receptor radioligand.	Patients with nonfunctioning pituitary adenomas and secretory adenomas underwent pituitary dopamine D2 receptor scintigraphy with (S)-2-hydroxy-3-123I-iodo-6-methoxy-N-[(1-ethyl-2-pyrrolidinyl) methylbenzamide and single photon emission tomography. Imaging findings were compared for the different groups of pathologies.	17	Diagnostic / III	Single-photon emission tomography (SPECT) showed significant uptake of 123I-IBZM in the pituitary region in 3/5 macroprolactinoma patients. In 4/17 patients with NFPA, significant uptake of the radioligand in the pituitary region was observed. In 2/3 scan-positive NFPA patients who were treated with quinagolide, shrinkage of the pituitary tumors was observed. Treatment with quinagolide resulted in stabilization of tumor growth in the other scan-positive patients. Four out of 17 patients with NFPA and a negative SPECT were treated with quinagolide. Tumor growth was observed in 1 patient, and tumor size did not change in the other 3 patients. The pituitary region of none of the 12 acromegaly patients showed significant uptake of 123I-IBZM. Sensitivity of the GH-secreting adenomas to quinagolide was demonstrated in 8/12 patients in vivo by an acute test, and in 6/9 of the tumors in vitro. Pituitary SPECT was negative in the patient with the TSH-secreting macroadenoma, and this tumor also showed no sensitivity to quinagolide in vivo or in vitro. 123I-IBZM is a ligand for in vivo imaging of dopamine agonist-sensitive macroprolactinomas, but not for microprolactinomas or GH-secreting adenomas. The technique potentially provides a means of predicting the dopamine agonist-responses of non-functioning pituitary adenomas in vivo.

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Luyken (1996)[81]	Clinical relevance of somatostatin receptor scintigraphy in patients with skull base tumours.	Patients with pituitary adenomas and other sellar/parasellar lesions underwent somatostatin receptor scintigraphy with octreotide. Results were compared between different groups of pathologies.	18	Diagnostic / III	All of the meningiomas (unifocal and multifocal tumors in various locations) showed a high density of SBS, whereas in none of the examined neurinomas SR were found. Pituitary adenomas revealed in only 50% SR in different concentrations and independent of the endocrine activity. A dural infiltration with meningioma tissue ("meningeal sign") may be discriminated from a reactive hypervascularisation in lesions with a diameter >0.5 cm. SRS can help in the differential diagnosis between meningiomas and other tumors, postoperative scar, or radionecrosis at the skull base.
Tumiati (1995)[82]	Scintigraphic assessment of pituitary adenomas and several diseases by indium-111-pentetreotide.	Clinical experience using indium-111-pentetreotide for the assessment of pituitary lesions.	21	Diagnostic/ III	In vivo scintigraphy showed pentetreotide receptors only in large GH-secreting adenomas and several macroadenomas. Concerning the endocrine activity of the adenomas, 111In-octreotide showed a good sensibility in detecting GH-secreting tumors.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Boni (1995)[83]	[111In-DTPA-D-Phe]-octreotide scintigraphy in functioning and non-functioning pituitary adenomas.	Patients with non-functioning pituitary adenomas and secretory adenomas underwent [111In-DTPA-D-Phe]-ocretotide scintigraphy. Uptake levels were compared between the different groups of pathologies.	12	Diagnostic / III	Only 2/12 patients with non-functioning pituitary adenoma showed a positive scan while 12/13 with GH secretion and 2/2 TSH macroadenomas had positive scans. [111In-DTPA-D-Phe]-octreotide scintigraphy is a useful tool to confirm the presence of somatostatin receptors in selected patients with GH- and TSH-secreting pituitary adenoma. The role of [111In-DTPA-D-Phe]-octreotide scintigraphy in non-functioning pituitary tumors remains to be established, but it could be useful for octreotide treatment in patients who refuse surgery or who are poor surgical candidates.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Duet (1994)[84]	Somatostatin receptor imaging in non-functioning pituitary adenomas: value of an uptake index.	Patients with nonfunctioning pituitary adenomas, GH-secreting adenomas, or no tumor underwent pituitary scintigraphy with somatostatin analog pentetreotidean. The accumulation of this analog was expressed as an activity radio between the uptake of radioactivity by the adenoma to that of normal brain tissue. Activity ratios were compared between the different groups of pathologies.	22	Diagnostic / III	In 15 out of the 17 patients with GH-secreting adenoma, an accumulation of the radioligand was shown. Median activity ratio was 3.8 (range 1-6.9; in 14 AR were greater than 2.2) and ARs were directly correlated (r = 0.54; *P* < .05) with the suppressibility of plasma GH levels by octreotide (OC) acute administration. In 2 patients who repeated scintigraphy during chronic OC treatment, AR values were reduced. In all the 22 patients with NFA, an accumulation of 111In-P at the pituitary level was observed, and median AR was 3.0 (range 1.5-20; in 14 greater than 2.2). In vitro autoradiography of surgical specimens in 6 NFA patients revealed SS-R in 4 cases with high scintigraphic AR and negative results in 2 cases with low AR. Scintiscan was repeated during chronic OC treatment in 5 patients with high score: AR decreased in 1 patient, increased in 3, and did not change in the other patient. No changes in tumor size were shown in any of these patients. A total of 8 patients (3 GH secreting and 5 NFA) had "normal" AR values. In acromegaly scintigraphy with 111In-P visualizes functioning pituitary SS-R coupled to intracellular events that control hormonal hypersecretion and tumor growth. In contrast, in spite of the positivity of 111In-P imaging in most patients with NFA, their receptors might have a defect in the coupling-transduction process, as they are not inhibited by OC treatment and no tumor shrinkage is observed.

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Colombo (1996)[85]	Three-step immunoscintigraphy with anti-chromogranin A monoclonal antibody in tumours of the pituitary region.	Patients with nonfunctioning pituitary adenomas and secretory adenomas underwent immunoscintigraphy with antichromogranin A monoclonal antibody and/or [111In]pentetreotide scintigraphy. Results were compared between the two modalities and the different groups of pathologies.	11	Diagnostic / III	Positive immunoscintigraphy with anti-chormogrnain A antibody was obtained in 9/11 (82%) non-functioning, but less in hormone-secreting adenomas. In conclusion, ISG is able to image pituitary tumors and particularly non-functioning pituitary adenomas. In this respect, it may be helpful in discriminating non-neuroendocrine masses of the pituitary region from non-functioning pituitary adenomas.
Kurtulmus (2007)[86]	The value of Tc-99m tetrofosmin in the imaging of pituitary adenomas.	Patients with and without pituitary adenomas underwent single-photon emission computed tomography (SPECT) imaging. Tc-99m uptake indices were compared statistically via Mann-Whitney U test between pituitary adenomas and normal controls.	15	Diagnostic / III	The average tetrofosmin uptake index of pituitary adenoma is 2.44+/-1.54 for the patients and 1.69+/-0.71 for the control group. Any significant difference was not observed between the groups (*P* = .3). The average index was calculated as 3.04+/-2.15 for invasive adenomas and 1.92+/-0.33 for the non-invasive group, and there was no significant difference between the 2 groups regarding uptake of the agent (P = .53). Furthermore, it was determined that the invasive and non-invasive adenomas displayed an uptake of Tc-99m TF similar to normal pituitary tissue. Since the pituitary adenoma and normal pituitary tissue gave similar results regarding Tc-99m TF uptake, it was concluded that this agent would not be useful in the diagnosis of pituitary adenoma.