Preoperative Imaging Characterization Evidence Tables

Table 7: Use of Preoperative Imaging to Differentiate NFPAs from Other Pathologies

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Amstutz (2006)[87]	Hypothalamic hamartomas: Correlation of MR imaging and spectroscopic findings with tumor glial content.	Correlate the MR imaging and proton MR spectroscopic properties of hypothalamic hamartomas with histopathologic findings.	14	Diagnostic / III	Tumors with markedly elevated mI/Cr demonstrated an increased glial component.
Freeman (2004)[88]	MR imaging and spectroscopic study of epileptogenic hypothalamic hamartomas.	Correlate the MR imaging and proton MR spectroscopic properties of hypothalamic hamartomas with histopathologic findings.	72	Diagnostic / III	MR imaging and spectroscopy suggest reduced neuronal density and relative gliosis in hypothalamic harmartomas compared with normal gray matter.

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Stadlbauer (2008)[89]	Proton magnetic resonance spectroscopy in pituitary macroadenomas: preliminary results.	Patients underwent proton MR (1H-MR) spectroscopy. Metabolite concentration of choline containing compounds was correlated to histological and surgical findings of hemorrhage as well as MIB-1 as a proliferative index.	16	Diagnostic / III	The study found a strong positive linear correlation between metabolite concentrations of Cho and the MIB-1 proliferative cell index (R = 0.819, *P* < .001). Eleven patients had a hemorrhagic adenoma and showed no assignable metabolite concentration of Cho, and the FWHM water was 13.4-24.4 Hz. In 10 patients, the size of the lesion was too small (<20 mm in 2 directions) for the acquisition of MR spectroscopy data. Quantitative 1H-MR spectroscopy provided important information on the proliferative potential and hemorrhaging of pituitary macroadenomas. These data may be useful for noninvasive structural monitoring of pituitary macroadenomas.
Sutton (1997)[91]	Proton spectroscopy of suprasellar tumors in pediatric patients.	Correlate the MR imaging and proton MR spectroscopic properties of suprasellar tumors.	19	Diagnostic / III	All craniopharyngiomas showed a dominant peak at 1 to 2 ppm, consistent with lactate or lipids, with trace amounts of other metabolites. This was confirmed using high-resolution spectroscopy. Chiasmatic gliomas showed a profile of choline, N-acetylaspartate, and creatine, and the choline:N-acetylaspartate ratio was 2.6 +/- 1.3, compared with 0.7 +/- 0.3 for samples of healthy brain (*t* test, *P* = .0003). Pituitary adenomas showed only a choline peak or no metabolites at all.
Sener (2001)[92]	Proton MR spectroscopy of craniopharyngiomas	Correlate the MR imaging and proton MR spectroscopic properties of craniopharyngiomas.	5	Diagnostic / III	Craniopharyngiomas display very prominent peaks centered at 1-1.5 ppm, which probably corresponded to lipid/cholesterol peaks.

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Faghih Jouibari (2012)[93]	Complementary effect of H MRS in diagnosis of suprasellar tumors.	Patients with suprasellar tumors underwent conventional MRI and magnetic resonance spectroscopy. A radiologist recorded the most probable diagnosis using only conventional MR imaging and then conventional MR imaging with magnetic resonance spectroscopy. These diagnoses using either a single or both modalities were compared to a pathology report as the gold standard.	23	Diagnostic / III	The information provided by MRS led the radiologist to alter his prior diagnosis that was based on the MRI in 4 patients, and the final diagnoses were in accordance with the histopathology. Wrong diagnosis was made by MRI plus MRS in 3 patients. Test efficiency of MRI was 69.6%, and it was 87% for MRI plus MRS. However, the difference was not statistically significant (*P*= .152). MRS may be useful in providing a more improved preoperative diagnosis of suprasellar tumors when used in addition to MRI.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Bladowska (2013)[60]	Usefulness of perfusion weighted magnetic resonance imaging with signal-intensity curves analysis in the differential diagnosis of sellar and parasellar tumors: preliminary report.	Patients underwent both conventional MRI and perfusion weighted MR imaging. Mean and maximum values of relative cerebral blood volume, relative peak height, and relative percentage of signal intensity recovery were calculated from the perfusion weighted MR images. These parameters were compared between different pathologies (pituitary macroadenomas, meningiomas, craniopharyngioma, hemangioblastoma, glioma, and metastasis).	23	Diagnostic / III	There were statistically significant differences in the mean and maximum rCBV values (P = .026 and P = 0.019, respectively). The maximum rCBV values >7.14 and the mean rCBV values >5.74 with the typical perfusion curve were very suggestive of the diagnosis of meningioma. Perfusion weighted MR imaging can provide supplemental information to differentiate pituitary adenomas from meningiomas. However, it is unclear how this improves the sensitivity and specificity of diagnosis of sellar/parasellar tumors.
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.

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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.

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Kobayashi (1994)[94]	A clinical and histopathological study of factors affecting MRI signal intensities of pituitary adenomas.	Conventional MR imaging of patients with nonfunctioning pituitary adenomas and secretory adenomas were retrospectively reviewed. MR signal intensities were calculated from the T1-weighted images and compared between the groups of different pathologies. Immunohistochemical staining allowed for calculation of the proportion of hormone positive cells. Age, maximal diameter of the tumor, cell density, and the proportion of hormone-positive cells were placed in a multiple regression analysis using signal intensity as the dependent variable.	18	Diagnostic / III	Four independent variables were used in the analysis: the age of the patient, the maximum diameter of the adenoma, the cell density, and the proportion of hormone-positive cells in the adenoma. With the signal intensity ratio as the dependent variable, a multiple regression analysis was performed. The great influence upon the signal intensities on T1-weighted images was the proportion of hormone-positive cells. This suggests signal intensities on T1W images may help with prediction of functioning versus NFPAs

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Spiller (1997)[95]	Secretory and nonsecretory pituitary adenomas are distinguishable by 1/T1 magnetic relaxation rates at very low magnetic fields in vitro.	Clinical experience using 1/T1 magnetic relaxation to discriminate between secretory and nonsecretory pituitary adenomas.	18	Diagnostic / III	Mean 1/T1 was significantly higher ($P < .02$) for hormone-secreting than for nonsecreting adenomas at fields below 0.24 T; no significant difference existed at typical MR imaging fields (0.5 to 1.5 T). Mean 1/T1 for hormone-producing and nonhormone-producing, nonsecreting adenomas were not significantly different at any field. Because 1/T1 at low fields is related to 1/T2 at imaging fields, it may be possible to detect hormone secretion of pituitary adenomas noninvasively by MR imaging.
Zada (2010)[96]	Patterns of extrasellar extension in growth hormone-secreting and nonfunctional pituitary macroadenomas.	Patients with histologically confirmed nonfunctional pituitary macroadenomas or GH secreting macroadenomas and pre-operative MR imaging had MR imaging evaluated in terms of mean maximal tumor diameter and patterns of extrasellar extension. These were compared between the two subtypes studied.	50	Diagnostic / III	The mean maximal tumor diameter in NFMAs and GH-secreting macroadenomas was 26 and 16 mm, respectively ($P < .0001$). Compared with GH-adenomas, NFMAs were more likely to develop suprasellar extension (82% vs 16%, $P < .0001$), cavernous sinus extension (40% vs 16%, $P = .04$), and isolated suprasellar extension (30% vs 4%, $P = .0145$). GH-macroadenomas had higher overall rates of infrasellar extension (72% vs 46%, $P < .05$) and isolated infrasellar extension (52% vs 6%, $P < .0001$). Substantial differences in extrasellar growth patterns were observed among varying histological subtypes of pituitary macroadenomas. Despite smaller tumor diameters, GH-macroadenomas demonstrated a proclivity for infrasellar extension, whereas NFMAs exhibited preferential extension into the suprasellar region.

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Luo (2000)[97]	Imaging of invasiveness of pituitary adenomas.	CT and/or MR imaging of patients with pituitary tumors were retrospectively reviewed. The images were assessed for tumor size, extension, and direction of tumor spread.	135	Diagnostic / III	One hundred and seventeen patients (87%) had suprasellar extension with compression of optic apparatuses, and 12 patients (9%) had extension of tumor upward to hypothalamus and third ventricle. Infrasellar extension via the floor of the sella and sphenoid sinus was found in 38 patients (28%), and further downward extension to ethmoid sinus, nasopharynx, and/or skull base was depicted in 5 patients (4%). Twenty-two patients (16%) had lateral invasion to the cavernous sinus and associated cranial nerves. Temporal and frontal extensions were depicted in 7 patients (5%) and 6 patients (4%), respectively. Five patients (4%) had posterior subtentorial extension to posterior fossa. Histologically, only 2 patients showed microscopic invasive features. There was no correlation between histologic features and imaging invasiveness. Pituitary adenomas have the potential of multi-directional extension. This experience indicated any type of pituitary adenoma could invade surrounding structures. Suprasellar invasion was the most common direction of pituitary adenoma spread, followed by infrasellar, lateral, anterior, and posterior routes.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Lundin (1992)[98]	MRI of pituitary macroadenomas with reference to hormonal activity.	Patients with nonfunctioning pituitary adenomas and secretory adenomas underwent conventional MR imaging. Signal intensity patterns, relaxation times, and ratios of signal intensity and proton density relative to the corpus callosum were calculated and compared between the different groups of pathologies.	64	Diagnostic / III	Invasiveness was more common in PRL- and GH-secreting adenomas than in the nonsecreting ones. Diffuse invasion of the base of the skull was most common in prolactinomas and associated with a lower frequency of suprasellar tumor extension. In prolactinomas, a correlation was found between the maximum serum PRL level and tumor size. Hemorrhagic, cystic, or necrotic areas were less common in GH-secreting tumors than in the other types. Hemorrhage was more common in prolactinomas than in nonsecreting tumors. MR parameters were similar in prolactinomas and nonsecreting adenomas but indicated a smaller amount of water in GH-secreting tumors. MR parameters may be used to identify histology of different pituitary adenomas.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Chang (2000)[99]	Computed tomography and magnetic resonance imaging characteristics of giant pituitary adenomas.	CT and/or MR imaging of patients with pituitary tumor were retrospectively reviewed. The tumor appearances and patterns of extension were recorded.	14	Diagnostic / III	Thirteen tumors (93%) extended upward to the suprasellar cistern and/or hypothalamus and third ventricle. Infrasellar extension through the sellar floor and sphenoid sinus to the skull base, or to the ethmoid sinus or the nasopharynx, was identified in 7 patients (50%). Eight patients (57%) had lateral invasion to the cavernous sinus. Temporal and frontal extension was apparent in 7 patients (50%) and 6 patients (43%), respectively. Five patients (36%) had posterior subtentorial extension to the posterior fossa. Histologically, only 2 GPAs showed invasive features. There was no correlation among histologic features, pituitary hormone concentrations, and evidence of tumor aggressiveness on CT and MRI scans. Any type of pituitary adenoma, regardless of its endocrinologic activity, may invade surrounding structures. Suprasellar invasion is the most common pathway of tumor spread, followed by infrasellar, lateral, anterior, and posterior routes.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Cazabat (2014)[100]	Silent, but not unseen: multimicrocystic aspect on T2-weighted MRI in silent corticotroph adenomas.	Preoperative T2-weighted MR images were retrospectively evaluated in patients with histologically proven (1) silent corticotroph adenomas, (2) corticotroph macroadenomas, and (3) nonfunctional gonadotroph macroadenomas by a single radiologist blind to histologic/clinical diagnosis.	77	Diagnostic / III	Multiple microcysts were present in 76% (13/17) of SCAs, 21% (3/14) of CSMs, and 5% (3/60) of NFGMs. The presence of MMs in clinically nonfunctioning macroadenomas had a sensitivity of 76% and a specificity of 95% for predicting SCA. The presence of MMs in T2-weighted MRI is a potential diagnostic tool to suggest the histologic subtype in NFPAs.
Nishioka (2012)[101]	Correlation between histological subtypes and MRI findings in clinically nonfunctioning pituitary adenomas.	Patients with conventional MR imaging and classification of histological subtype of nonfunctioning pituitary adenomas were retrospectively analyzed. MR findings were correlated to different histological subtypes as well as MIB-1 index and patient age.	390	Diagnostic / III	Three MRI findings were less common in NCA/SGA than in the other groups ($P < .0001$): giant adenoma (>40 mm), marked cavernous sinus invasion (Knosp grade 4), and lobulated configuration of the suprasellar tumor. When these MRI findings were negative in patients older than 40 years old, 91.0% (212/233) were NCA/SGA. NFPA subtypes including silent corticotroph and other silent adenomas are associated with certain radiologic signs.