Table 8: Cavernous Sinus Wall Invasion

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Pan (2005)[102]	Magnetic resonance imaging and biological markers in pituitary adenomas with invasion of the cavernous sinus space.	Patients with conventional MRI were prospectively analyzed for cavernous sinus invasion and compared to intraoperative findings as the gold standard. Tumors with invasion were compared to tumors without invasion in terms of F8-related antigen, Ki-67 LI, VEGF, MMP-9, c-myc, bcl2, and nm23.	45	Diagnostic / II	The sensitivity of MRI for indicating cavernous sinus invasion in this prospective study was 60%, specificity 85%, positive predictive value 83.33%, negative predictive value 62.96%. The results have shown that MVD of invasive pituitary adenomas was significantly higher than that of noninvasive ($P < .001$). There was an association between the invasion of pituitary adenomas and Ki-67 LI ($P = .039$) or the expression of VEGF ($P < .001$) and MMP-9 ($P < .001$). Parasellar extension of pituitary adenomas through the medial wall of the cavernous sinus diagnosed at surgery, can be determined by radiology with sensitive gadolinium-enhanced MRI. VEGF, Ki-67, nm23, and MMP-9 have associations with invasiveness of pituitary adenomas, but lack specificity.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Connor (2014)[103]	Magnetic resonance imaging criteria to predict complete excision of parasellar pituitary macroadenoma on postoperative imaging.	Preoperative and matched 3-month postoperative MR images were compared in patients with pituitary macroadenomas with parasellar involvement. Specifically, 12 preoperative MRI findings were compared to the presence or absence of postoperative evidence of complete resection.	49	Diagnostic / III	Depiction of the inferolateral (positive predictive value [PPV]: 0.6; negative predictive value [NPV], 0.92) and lateral (PPV: 0.65; NPV: 0.85) compartments of the cavernous sinus and the percentage of intracavernous carotid artery encasement (PPV: 0.63; NPV, 1.0 for <50% encasement) were significantly predictive of complete resection. The odds ratios indicated that depiction of the lateral venous or inferolateral venous compartments increased the likelihood of a complete resection by 6 times, whereas for every 25% reduction in intracavernous carotid artery encasement, the chance of a complete resection increased 3.4 times. Two preoperative MRI features (depiction of the lateral and inferolateral compartment of the cavernous sinus and decreasing encasement of the intracavernous carotid artery) may be useful in predicting total resection of parasellar components of pituitary adenomas.
Daniels (1988)[104]	MR imaging of the cavernous sinus: value of spin echo and gradient recalled echo images.	Clinical experience examining the utility of spin echo gradient recalled echo images in assessing the anatomy of the cavernous sinus.	25	Diagnostic / III	Correlation of coronal T1-weighted spin echo and gradient recalled echo images (the latter with high-signal-intensity vascular structures) proved to be an effective means of identifying cavernous venous spaces, connective tissue and cranial nerves, and the lateral margins of the pituitary gland, and of differentiating tumor tissue from cavernous venous spaces.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Ahmadi (1986)[105]	Cavernous sinus invasion by pituitary adenomas.	Clinical experience using CT to assess pituitary lesions with cavernous sinus invasion.	19	Diagnostic / III	CT findings included cavernous sinus expansion (17 patients) and visible encasement of the internal carotid artery (14 patients). The invasive tumor often enhanced to a lesser degree than the cavernous sinuses and ipsilateral internal carotid artery. Intracavernous cranial nerve compression, obliteration, or displacement (14 patients), invasion of the lateral wall of the cavernous sinus (7 patients), and diffuse bone destruction (7 cases) were other findings. Magnetic resonance imaging in 3 patients provided excellent demonstration of intracavernous internal carotid artery encasement, but displacement and obliteration of intracavernous cranial nerves was not shown as well as it was with CT. There was no correlation between histologic features, hormone assays, and invasiveness. This experience indicates any type of pituitary adenoma, regardless of its endocrinologic activity, can invade the cavernous sinus.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Davis (2013)[51]	Evaluation of the pituitary gland using magnetic resonance imaging: T1-weighted vs VIBE imaging.	Patients underwent both coronal T1-weighted and volumetric interpolated breath-hold examination imaging (VIBE). The 2 sequences were compared in terms of contrast enhancement, cavernous sinus appearance, and optic chiasm appearance. For each subject, VIBE was rated as better, equal, or worse to T1-weighted images and statistically compared using chi-square tests. These comparisons were also made while stratifying for macroadenomas and post-surgical patients.	32	Diagnostic / III	There was a trend to VIBE being superior to T1W for visualization of pituitary adenomas, but these data were not statistically significant. Visualization of chiasm in macroadenomas was similar for both techniques. VIBE was significantly superior to T1W with respect to pituitary and cavernous sinus contrast enhancement and cavernous sinus anatomy. Although not statistically significant, VIBE may improve the resolution of MR images for pre-operative visualization of pituitary adenomas, cavernous sinus invasion, and optic chiasm compression. This strength may be even larger with higher tesla magnets.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Cukiert (1998)[106]	Cavernous sinus invasion by pituitary macroadenomas. Neuroradiological, clinical, and surgical correlation.	Preoperative MR images of patients with and without intraoperative confirmation of cavernous sinus invasion were retrospectively studied. MR signs such as tumor lateral to the carotid artery, tumor within the carotid syphon, and lack of ring enhancement of the medial wall of the cavernous sinus were evaluated in the 2 groups of patients.	18	Diagnostic / III	Only 8 patients had tumor lateral to the carotid artery, 13 had tumor within the carotid syphon, and all lacked the ring enhancement of the medial wall of the cavernous sinus. In 10 patients, widening of the posterior double leaflets of the cavernous sinus could be seen. Only 3 patients disclosing the above-mentioned MRI features were identified in a series of 250 patients and did not have cavernous sinus invasion. The present criteria proved to be useful in the preoperative diagnosis of cavernous sinus invasion and patients' counselling.
Knosp (1991)[107]	Pituitary adenomas with parasellar invasion.	MR imaging of pituitary adenomas with surgically confirmed invasion into the cavernous sinus were retrospectively evaluated. MR signs were correlated to cavernous sinus invasion using surgical experience as the gold standard. Cavernous sinus invasion was also correlated with KI-67 measurements.	25	Diagnostic / III	When the adenoma encases the intracavernous internal carotid artery or reaches as far as to the lateral aspect of the artery, invasion was present in all cases. The critical area where invasion could not be predicted from MRI is the distance between the medial and the lateral aspect of the intracavernous internal carotid artery. By measurement with the monoclonal antibody KI-67, it could be shown that pituitary adenomas infiltrating the parasellar space have a statistically significant higher growth rate (*P* less than .001), compared to non-invasive adenomas. These criteria can potentially be used to identify cavernous sinus invasion.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Knosp (1993)[108]	Pituitary adenomas with invasion of the cavernous sinus space: a magnetic resonance imaging classification compared with surgical findings.	MR imaging of pituitary adenomas with surgical confirmation of invasion into the cavernous sinus space were retrospectively evaluated. Images were classified by grade 0-4 using the internal carotid artery as a radiologic landmark.	12	Diagnostic / III	Grades 0, 1, 2, and 3 are distinguished from each other by a medial tangent, the intercarotid line—through the cross-sectional centers—and a lateral tangent on the intra- and supracavernous internal carotid arteries. Grade 0 represents the normal condition, and Grade 4 corresponds to the total encasement of the intracavernous carotid artery. According to this classification, surgically proven invasion of the cavernous sinus space was present in all Grade 4 and Grade 3 cases and in all but 1 of the Grade 2 cases; no invasion was present in Grade 0 and Grade 1 cases. Therefore, the critical area where invasion of the cavernous sinus space becomes very likely and can be proven surgically is located between the intercarotid line and the lateral tangent, which is represented by our Grade 2. The monoclonal antibody KI-67 showed a statistically higher proliferation rate ($P < .001$) in adenomas with surgically observed invasion into the cavernous sinus space, as compared with noninvasive adenomas. The Knosp criteria, specifically the differentiation of grades 1/2 vs 3/4, can be used to characterize cavernous sinus invasion preoperatively.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Scotti (1988)[109]	MR imaging of cavernous sinus involvement by pituitary adenomas.	Clinical experience using MR to assess macroadenomas with and without cavernous sinus involvement.	11	Diagnostic / III	In 10 of the 11 macroadenomas with surgically proved dural invasion, MR demonstrated an asymmetric increase in size and intensity of the superior and inferior cavernous sinus compartments. Noninvasive macroadenomas compressed and displaced the cavernous sinus bilaterally. The prospective MR evaluation of 30 patients undergoing surgery for pituitary tumor revealed a sensitivity for predicting cavernous sinus invasion of 55%, a specificity of 85.7%, a positive predictive value of 62.5%, and a negative predictive value of 81.8%. No feature permitted certain distinction between invasive and noninvasive microadenomas, as the medial dural wall of the cavernous sinus could not be reliably identified. MR parameters can identify cavernous sinus invasion, with the most specific sign of cavernous sinus invasion being carotid artery encasement.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Sol (2014)[110]	Evaluation of MRI criteria for cavernous sinus invasion in pituitary macroadenoma.	Coronal T2-weighted MR images of patients with pituitary adenoma with cavernous sinus invasion were retrospectively evaluated. The MR signs assessed were: presence of hypointense line suggestive of medial wall of cavernous sinus, presence of entire rim-enhancement around the intracavernous internal carotid artery, location of the tumor in relation to the lateral intercarotid lines, and angle of the tumor encasement around the intracavernous ICA. These signs were analyzed using intraoperative findings as the gold standard.	63	Diagnostic / III	CS invasion was highly probable if periarterial enhancement was not depicted (positive predictive value, 86%; $P < .001$). Valuable criteria of CS invasion by logistic regression analysis were the absence of periarterial enhancement ($P = .043$, odds ratio = 5.23) and the angle of intracavernous ICA encased by the tumor ($P = .029$, odds ratio = 1.017), with a threshold value of 136.5° with a sensitivity of 90% and specificity of 78.3%. The MRI criteria described in this study can be useful in evaluating CS invasion in pituitary adenomas.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Vieira (2006)[112]	Evaluation of magnetic resonance imaging criteria for cavernous sinus invasion in patients with pituitary adenomas: logistic regression analysis and correlation with surgical findings.	Patients with pituitary adenomas with or without cavernous sinus invasion and conventional MR imaging were retrospectively evaluated. MR imaging findings included: presence of normal pituitary gland between the adenoma and cavernous sinus, status of the cavernous sinus venous compartments, cavernous sinus size, cavernous sinus lateral wall bulging, displacement of the intracavernous internal carotid artery by adenoma, Knosp-Steiner criteria, and percentage of intracavernous internal carotid artery encased by the tumor. These findings were compared to surgical description as the gold standard.	103	Diagnostic / III	The following signs were found to represent accurate criteria for noninvasion of the CS: (1) normal pituitary gland interposed between the adenoma and the CS (PPV, 100.0%), (2) intact medial venous compartment (PPV, 100.0%), and (3) percentage of encasement of the intracavernous ICA lower than 25% (NPV, 100.0%). Cavernous sinus invasion was certain if the percentage of encasement of the intracavernous ICA was higher than 45% and 3 or more CS venous compartments were not depicted. The most valuable criterion of CSI by logistic regression analysis was the percentage of encasement of intracavernous ICA of 30% or more, with an odds ratio of 49.25. The preoperative diagnosis of CSI by PA is extremely important because endocrinologic remission is rarely obtained after microsurgery alone in patients with invasive tumors. The evaluated MR imaging criteria may be useful in patient management and in advising most of the patients preoperatively on the potential need for complimentary therapy after surgery.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Vieira (2004)[113]	Magnetic resonance imaging of cavernous sinus invasion by pituitary adenoma diagnostic criteria and surgical findings.	Conventional MR imaging of patients with and without cavernous sinus invasion were retrospectively reviewed. MR signs including presence of normal pituitary gland between the adenoma and cavernous sinus, status of the cavernous sinus venous compartments, cavernous sinus size, cavernous sinus lateral wall bulging, displacement of the intracavernous internal carotid artery by adenoma, grade of parasellar extension, and percentage of intracavernous internal carotid artery encased by tumor were assessed. These were compared using chi squared tests to intraoperative findings as the gold standard.	103	Diagnostic / III	The following signs have been found to represent accurate criteria for non-invasion of the CS: 1, normal pituitary gland interposed between the adenoma and the CS (PPV, 100%); 2, intact medial venous compartment (PPV, 100%); 3, percentage of encasement of the intracavernous ICA lower than 25% (NPV, 100%); and 4, medial intercarotid line not crossed by the tumor (NPV, 100%). Criteria for CSI were: 1, percentage of encasement of the intracavernous ICA higher than 45%; 2, occlusion of 3 or more CS venous compartments; and 3, occlusion of the CS lateral venous compartment. The CS was very likely to be invaded if the inferior venous compartment was not detected (PPV, 92.8%), if the lateral intercarotid line was crossed (PPV, 96.1%), or if a bulging lateral dural wall of the CS was seen (PPV, 92.3%). The above-mentioned MR imaging criteria may be useful in advising most of the patients preoperatively on the potential need for complimentary therapy after surgery.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Cottier (2000)[114]	Cavernous sinus invasion by pituitary adenoma: MR imaging.	Patients with conventional MR imaging were retrospectively reviewed. Nine MRI signs of cavernous sinus invasion were assessed on preoperative images. These signs were compared with chi squared tests using surgical findings as the gold standard.	106	Diagnostic / III	Invasion of the cavernous sinus was certain (PPV, 100%) if the percentage of encasement of the internal carotid artery (ICA) by tumor was 67% or greater. It was highly probable if the carotid sulcus venous compartment was not depicted (PPV, 95%) or the line joining the lateral wall of the intracavernous and supracavernous ICAs was passed by the tumor (PPV, 85%). It was definitely not invaded (NPV, 100%) if the percentage of encasement of the intracavernous ICA was lower than 25% or the line joining the medial wall of the intracavernous and supracavernous ICAs was not passed by the tumor. The radiologic diagnosis of cavernous sinus invasion by pituitary adenoma can be aided by the criteria in this study.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Steiner (1994)[40]	MR-appearance of the pituitary gland before and after resection of pituitary macroadenomas.	Clinical experience using MR to assess pituitary macroadenomas prior to and after surgical excision.	30	Diagnostic / III	On preoperative MR images, contrast administration increased the detectability of the anterior lobe from 30% to 80%. Depending on the size and extension of the adenoma, the pituitary gland was displaced to the suprasellar space (53%) and/or deformed to a club-shaped (27%) or sickle-shaped (47%) configuration. In 6 patients, the sickle-shaped pituitary gland was interposed between the cavernous sinus and the adenoma ("rim-sign"), which was seen only on gadopentetate dimeglumine-enhanced images. In these cases, there was no infiltration of the cavernous sinus at surgery. Postoperatively, descent of the pituitary gland was found in 63%, and re-expansion in 54%. We conclude that contrast administration improves the detectability of the pituitary gland on preoperative MR images, and that the displacement and deformation of the pituitary gland depend on the size, location, and extension of the adenoma. Preoperatively, demonstration of the pituitary gland interposed between the cavernous sinus and the adenoma ("rim-sign") is a very useful sign for exclusion of cavernous sinus infiltration, best seen on contrast-enhanced coronal MR images.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Daita (1995)[115]	Cavernous sinus invasion by pituitary adenomas—relationship between magnetic resonance imaging findings and histologically verified dural invasion.	Clinical experience using MR to assess pituitary lesions with dural invasion.	26	Diagnostic / III	All patients were classified according to MR imaging findings into 3 types. Type I showed a gadolinium-enhanced stripe medial to the carotid artery (5 patients), none of which showed dural invasion. Type II showed no enhanced stripe (17 patients), 6 of which showed dural invasion. Within this type, tumor size and dural invasion showed no correlation. Type III showed displacement or encasement of the carotid artery by the tumor with or without extracranial extension (4 patients), all of which showed massive infiltration of the tumor cells into the dura mater. This study shows that preoperative MR imaging can provide information for assessment of invasion into the cavernous sinus in patients with pituitary adenoma.
Nakasu (2001)[116]	Tentorial enhancement on MR images is a sign of cavernous sinus involvement in patients with sellar tumors.	Patients with pituitary adenomas and other sellar/parasellar lesions underwent conventional MR imaging. Enhancement patterns of the dura around the tumors were compared with levels of tumor invasion or compression of the cavernous sinus, where intraoperative experience was the gold standard.	64	Diagnostic / III	For evaluation of cavernous sinus invasion ipsilateral to the enhancement, sensitivity and specificity of the asymmetric tentorial enhancement sign were 81.3% and 86.3%, respectively. Sensitivity and specificity of the sign were 42.9% and 93.6% for cavernous sinus involvement, including compression and invasion. Asymmetric tentorial enhancement is a useful sign in the diagnosis of invasion or severe compression of the cavernous sinus by sellar tumor. The sign may represent venous congestion or collateral flow in the tentorium due to obstructed flow in the medial portion of the cavernous sinus.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Cattin (2000)[117]	Dural enhancement in pituitary macroadenomas.	Patients with and without pituitary adenomas underwent conventional MR imaging. Dural enhancement patterns of the sellar region were analyzed and noted if abnormal. Differences in dural enhancement patterns between the 2 groups were compared.	20	Diagnostic / III	Dural enhancement appeared to be usually abnormal in 20 patients with pituitary macroadenoma compared with 20 control patients, mainly at the planum sphenoidale and carotid sulcus. However, dural changes are subtle and their recognition requires knowledge of the normal enhancement patterns. Dural changes may also be seen in pituitary macroadenomas, although this is not a specific finding.
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.

Author (Year)	Title	Study Description	Number of Patients	Evidence Class	Conclusions
Kunishio (2006)[118]	Technetium-99m sestamibi single photon emission computed tomography findings correlated with P-glycoprotein expression in pituitary adenoma.	Patients underwent technetium-99m sestamibi single photon emission computed tomography (SPECT). SPECT characteristics were compared to cavernous sinus invasion, proliferative potential, and multidrug resistance gene product P-glycoprotein expression.	10	Diagnostic / III	The pituitary adenomas specimens were examined by immunohistochemistry using anti-Pgp and MIB-1 monoclonal antibodies. (99m)Tc-MIBI SPECT findings were not related to MIB-1 labeling index or cavernous sinus invasion. (99m)Tc-MIBI SPECT RI (-38.55+/-20.77) of the Pgp-positive group was significantly lower than that (-15.78+/-19.40) of Pgp-negative group *(P* = .0494). No significant difference was observed in the ER and DR of (99m)Tc-MIBI SPECT between Pgp-positive and negative groups. This study suggests that although (99m)Tc-MIBI SPECT is not useful to evaluate the proliferative potential or cavernous sinus invasion of pituitary adenomas. (99m)Tc-MIBI SPECT could predict anti-cancer drug resistance related to the expression of Pgp in pituitary adenomas.
Nakano (2001)[119]	Use of 201Tl SPECT for evaluation of biologic behavior in pituitary adenomas.	Patients with pituitary adenomas underwent 201 Tl chloride SPECT studies. 201 Tl uptake indices were calculated, and these data were compared between invasive and noninvasive pituitary adenomas as well as monoclonal antibody labeling index.	22	Diagnostic / III	In comparison with noninvasive pituitary adenomas, invasive pituitary adenomas exhibited significantly higher 201Tl uptake indices on both the early and the delayed images (*P* = .0010 and .0019, respectively). A significant correlation was found between the 201Tl uptake index on the delayed image and the MIB1 labeling index (*P* = .0107). 201Tl SPECT can be useful for detecting biologic aggressiveness in pituitary adenomas.