

# Pituitary Macroadenoma Grading Using Magnetic Resonance Imaging: A Sipap Classification Study

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## Abstract

**BACKGROUND:** Magnetic resonance imaging (MRI), which is the recommended technique, is often used to identify pituitary adenomas. All pituitary adenomas, with the probable exception of prolactinoma, must initially undergo surgery. As a result, choosing the best surgical strategy and ensuring the safest possible outcome during excision need a straightforward and reproducible MRI classification based on the primary routes of cancer growth. Based on the KNOSP-STEINER categorization of parasellar development, which now includes a classification for posterior, superior, anterior, and inferior tumour extension, the SIPAP MRI categorization for pituitary adenomas was developed.

**OBJECTIVE:** We thus advocate including the SIPAP classification in the standardized reporting format for pituitary adenomas in order to offer the best imaging definition of the tumour's delineation, connection to tumour size and juxtaseilar structure. As a result, surgical procedures and subsequent clinical treatment will have a better success rate.

**METHODS:** 49 patients with histopathology pituitary macroadenoma had their imaging retrospectively examined by two radiologists, who used the SIPAP approach to evaluate the outcomes. The study was carried out at Mayo Hospital from December 1, 2021, to November 30, 2022. Stata version 15 was used to analyze the data. Cohen's Kappa was used to determine interobserver variability. The Chi-square test was used to evaluate grades before and after therapy. In statistics, P values  $\leq 0.05$  were regarded as significant.

**RESULTS:** The patient population was 63% male and 37% female. 71.82 cm<sup>3</sup> and 49.50 cm<sup>3</sup> respectively were the largest preoperative and postoperative volumes. With a mean of 14.1 and a standard deviation of 17.7 compared to a mean of 4.5 and a standard deviation of 10.4, pre- and postoperative volumes were significantly different, with a p-value of less than 0.001. The length that differed most noticeably between pre- and post-operative lengths had a mean value of 2.4 and a standard deviation of 1.1 compared to a mean value of 1.3 and a standard deviation of 1.1, with a p-value less than 0.001. The pre-and post-operative SIPAP grading of each tumour extension varied significantly, with the exception of the anterior extension. Prior to surgery, 67.3% of patients had grade 3 suprasellar extension, but thereafter, 63.3% had grade 0. Prior to surgery, grade 2 was present in 51.0% of patients with intrasellar extension, whereas grade 0 was present in 71.4%. Grade 0 anterior, posterior, and parasellar extensions occurred more often postoperatively as compared to preoperatively. All Kappa statistical values exceeding 0.7 (p-value less than 0.001) indicated strong inter-observer agreement for the inferior, anterior, posterior, and superior extents.

**CONCLUSIONS:** We suggest adopting the straightforward and objective SIPAP categorization into standard MR reporting for the identification of the optimal pituitary tumour, its association with juxtaseilar structures, and the tumour size.

**KEYWORDS:** Tumor, SIPAP, Adenoma, MRI

**INTRODUCTION:** Pituitary lesions need immediate care since they are linked to important endocrine disorders. Pituitary adenomas (PAs) have varying prevalence estimates. They make up around 16.9% of all brain tumours, according to the most current figures from the Central Brain Tumor Registry of the USA. [1]. The detection of pituitary adenomas (PAs), which is the preferred method for the detection of pituitary adenomas, has increased with the increased usage of MRI. [2].

A surgical procedure is used to treat all pituitary adenomas initially, with the possible exception of pituitary adenoma, which is very responsive to therapy. [3] Preference is given to transsphenoidal surgery. [4] When surgically treated alone, macroadenomas with significant extrasellar extension showed remission rates of 15-37%, which was lower than the 90% remission rates of microadenomas. Surgery is often complemented by medical treatment and radiation therapy. [5] A key tool for surgical treatment is a straightforward and repeatable MR categorization based on the main directions of tumour development. In order to provide a clear road map for the best surgical approach and the safest amount of resection, it is essential to properly analyze the size of the tumour on the preoperative baseline MRI. [6] Based on the parasellar growth KNOSP-STEINER classification [8] and with the addition of a grading system for posterior, anterior, inferior, and superior tumour extension, the SIPAP MR categorization for pituitary adenomas [7] has been developed. We, therefore, suggest including SIPAP classification for the ideal radiographic portrayal of tumour bifurcation, tumour affiliation with juxtaseilar structures, and tumour volume in regular incorporates of pituitary adenomas in order to simplify a higher success rate in surgery and successive diagnosis and management (width, length, and height).

**METHODS:** Between December 2021 and November 2022, patients with pituitary macroadenomas who obtained pre- and post-operative MRI brain scans utilizing a pituitary protocol were the subjects of this cross-sectional research. The scans were read by two experienced neuroradiologists having three to eight years of experience at Mayo Hospital, Lahore, Pakistan. The inclusion criteria were a histopathologically verified pituitary adenoma and pre-and postoperative MRI with a pituitary protocol. The following conditions were not included: (1) No pretreatment scanning. (2) Previous medical intervention, radiation treatment, or chemo, and (3) An unresolved histology result. Out of 81 patients, 49 were chosen for this research based on these criteria. Typically, 161 days passed between the preoperative and postoperative scans (min 1 day and max 971 days). The Mayo Hospital's ethical review committee gave its approval and exempted this research.

Table 1: SIPAP categorization according to the 6-figure registration.

| Extension | S           | I           | P (Right)          | P (Left)          | A        | P         |
|-----------|-------------|-------------|--------------------|-------------------|----------|-----------|
|           | Suprasellar | Infrasellar | Pasasellar (Right) | Parasellar (Left) | Anterior | Posterior |
| Grading   | 0           | 0           | 0                  | 0                 | 0        | 0         |
|           | 1           | 1           | 1                  | 1                 | 1        | 1         |
|           | 2           | 2           | 2                  | 2                 |          |           |
|           | 3           |             | 3                  | 3                 |          |           |
|           | 4           |             | 4                  | 4                 |          |           |

Images were acquired using a head coil during MR investigations on 1.5- and 3-T superconducting systems. The acquisition matrix had a 180 mm field of view and was 256x256. The following imaging sequences were obtained both before and after intravenous contrast administration: coronal T1-weighted Spin Echo (SE) and sagittal T1-weighted Spin Echo (SE).

SIPAP classification is a Pituitary adenomas' expansion outside of the sella is described by a six-figure number on which this statement is based. (Table1) There are six juxtaseilar directions of relevance when reading the grades from left to right: (1) Posterior (0-1) (2) anterior (0-1), (3) parasellar left (0-4), (4) parasellar right (0-4), (5) infrasellar (0-2), and (6) suprasellar (0-4). Parasellar extension is indicated separately depending on whether it is to the right or left. Posterior, anterior, and infrasellar extensions are graded using T1 post-contrast sagittal images, whereas suprasellar

and bilateral parasellar directions of tumour development are graded using T1 post-contrast coronal Magnetic Resonance Imaging (MRI sequence). (Figures 1–5) The posterior extension was further classified as posterior inferior and posterior superior during the interpretation of the images in order to increase clarity (0-2). (Figure 4)

Left parasellar, right parasellar, infrasellar, and Suprasellar tumour expansion was assessed using post-contrast T1 sagittal parts and post-contrast T1 coronal sections. An interobserver rating was created after each examiner independently evaluated the pictures and recorded their results on two distinct excel sheets for the postoperative and preoperative MRI grading of 49 patients (a total of 98 scans). Three measurements were used to determine the size of each pituitary tumour: length (anterior-posterior dimension), craniocaudal dimension, and height (anterior-caudal dimension). The volume of each tumour was then manually computed.

The pre-and post-procedure brain tumour features of the patients' continuous variables (volume, height, length, and breadth) are reported as means with standard deviations, and differences are examined using a paired t-test. Categorical information, such as patient demographics and the grade of the tumour expansion, is provided as frequency and percentages based on the anticipated cell count distribution, and it is analyzed using the Fisher's exact or Chi-square test. We used Cohen's Kappa to determine interobserver variability. An acceptable threshold for significance was a p-value of 0.05. Using Stata version 15, data were examined.

**RESULTS:** Of the 49 patients whose data were evaluated for sellar tumour, 63.3% were male and had a mean age of 49 years (ranging from 16 to 74), while 36.7% were female and had an average age of 47 years (ranging from 24 to 66).

A total of 71.82 cm<sup>3</sup> was determined to be the maximum preoperative volume, while 49.50 cm<sup>3</sup> was determined to be the highest postoperative (residual) volume. Pituitary tumour volumes before and after surgery were seen to vary considerably as the before mean value is 14.1 with standard deviation of 17.7 and the after mean value is 4.5 with the standard deviation of 10.4 with p-value less than 0.001. The length difference between pre-and post-operative measures was observed to be most substantial for independent volumetric metrics as the before mean value is 2.4 with standard deviation of 1.1 and the after mean value is 1.3 with standard deviation of 1.1 and with p-value less than 0.001. For both pre-operative and post-operative grading prevalence, individual assessments of tumour expansions were made in accordance with the SIPAP categorization (Table 2). With the exception of the anterior extension, all extensions were determined to be statistically significant (p-value < 0.001) for both pre-and post-operative phases. 63.3% of patients who underwent suprasellar extension had post-operative grade 0 and 67.3% of patients had pre-operative grade 3. 51.0% of patients with infrasellar extension had grade 2 preoperatively, while 71.4% had grade 0 after surgery. In addition, there was a higher incidence of grade 0 parasellar, posterior, and anterior extensions in the postoperative period compared to the pre-operative stage. (Table 3)

Table 2: Volume of the pituitary tumour before and after surgery

| Brain Measurements (cm) |      | Width  | Length | Height | Volume |
|-------------------------|------|--------|--------|--------|--------|
| Post-Brain              | Mean | 1.4    | 1.3    | 1.4    | 4.5    |
|                         | SD   | 1.3    | 1.1    | 1.3    | 10.4   |
| Pre-Brain               | Mean | 2.8    | 2.4    | 2.8    | 14.1   |
|                         | SD   | 1.3    | 1.1    | 1.3    | 17.7   |
| p                       |      | <0.001 | <0.001 | <0.001 | <0.001 |

For the inferior, anterior, posterior, and superior extents of the SIPAP classification, a high level of inter-observer agreement in tumour grading was achieved. The significance p-value for each Kappa statistic was more than 0.001, showing high agreement. The inter-observer agreement for the right and left Parasellars was very high, with Kappas above 0.51 and 0.54 and a significant p-value of 0.001. (Table 4)

Table 3: Extensions of the tumour and SIPAP categorization grade

| Extensions of tumour    | Grade | Pre-operative (N) | %    | Post-operative (N) | %    | P-value |
|-------------------------|-------|-------------------|------|--------------------|------|---------|
| <b>Suprasellar</b>      | 0     | 0                 | 0    | 31                 | 63.3 | 0       |
|                         | 1     | 6                 | 12.2 | 4                  | 8.2  |         |
|                         | 2     | 6                 | 12.2 | 1                  | 2    |         |
|                         | 3     | 33                | 67.3 | 12                 | 24.5 |         |
|                         | 4     | 4                 | 8.2  | 1                  | 2    |         |
| <b>Infrasellar</b>      | 0     | 21                | 42.9 | 35                 | 71.4 | 0       |
|                         | 1     | 25                | 51   | 13                 | 26.5 |         |
|                         | 2     | 3                 | 6.1  | 1                  | 2    |         |
| <b>Anterior</b>         | 0     | 38                | 77.6 | 43                 | 87.8 | 0.1     |
|                         | 1     | 11                | 22.5 | 6                  | 12.2 |         |
| <b>Posterior</b>        | 0     | 33                | 67.3 | 41                 | 83.7 | 0       |
|                         | 1     | 12                | 24.5 | 5                  | 10.2 |         |
|                         | 2     | 4                 | 8.2  | 3                  | 6.1  |         |
|                         | 3     | 4                 | 8.2  | 3                  | 6.1  |         |
| <b>Parasellar Right</b> | 0     | 17                | 34.7 | 30                 | 61.2 | 0       |
|                         | 1     | 12                | 24.5 | 7                  | 14.3 |         |
|                         | 2     | 7                 | 14.3 | 1                  | 2    |         |
|                         | 3     | 8                 | 16.3 | 6                  | 12.2 |         |
|                         | 4     | 5                 | 10.2 | 5                  | 10.2 |         |
| <b>Parasellar Left</b>  | 0     | 23                | 46.9 | 37                 | 75.5 | 0       |
|                         | 1     | 13                | 26.5 | 3                  | 6.1  |         |
|                         | 2     | 5                 | 10.2 | 4                  | 8.2  |         |
|                         | 3     | 4                 | 8.2  | 1                  | 2    |         |
|                         | 4     | 4                 | 8.2  | 4                  | 8.2  |         |

Table 4: Inter-observer Kappa statistics for tumour grading using SIPAP classification (pre-operative)

|                    | Kappa | p- value |
|--------------------|-------|----------|
| PARASELLAR (LEFT)  | 0.545 | <0.001   |
| PARASELLAR (RIGHT) | 0.512 | <0.001   |
| POSTERIOR          | 0.724 | <0.001   |
| ANTERIOR           | 0.766 | <0.001   |
| INFERIOR           | 0.771 | <0.001   |
| SUPERIOR           | 0.769 | <0.001   |

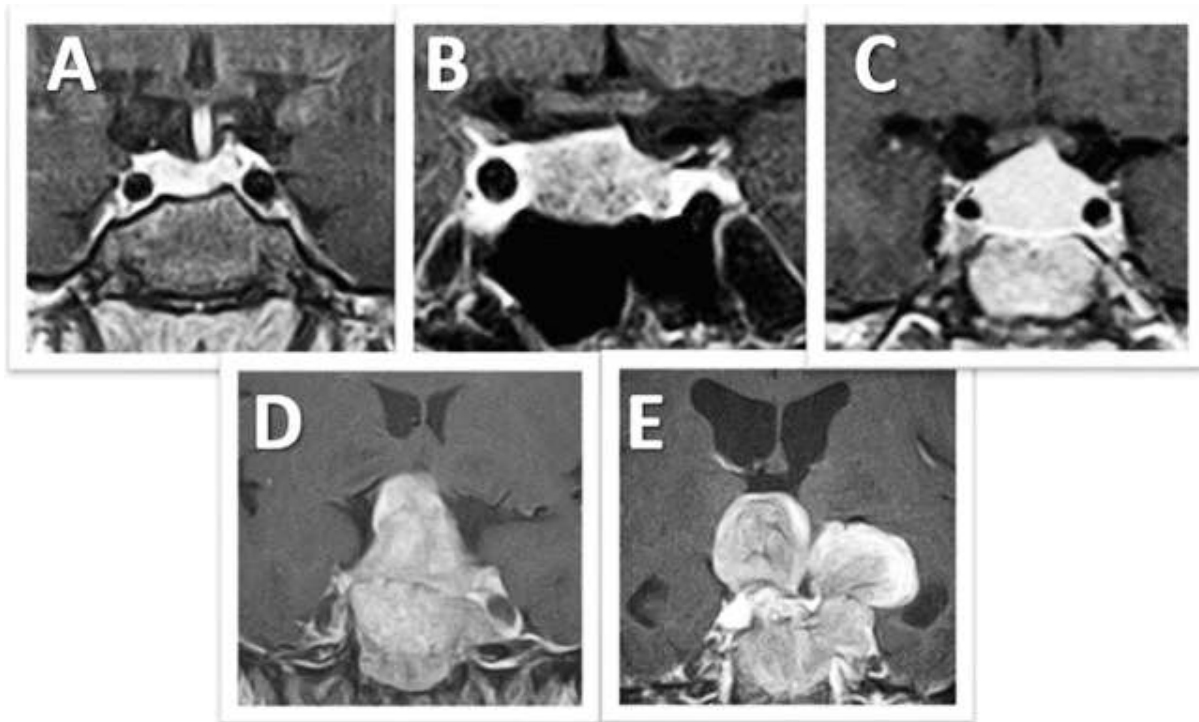


Figure 1: Coronal contrast enhanced T1 weighted MRI showing 5 grades of suprasellar extension. A) Grade 0: No bulge in the suprasellar space. B) Grade 1: Upward bulge of adenoma in suprasellar space without reaching the optic chiasm. C) Grade 2: Adenoma reaching optic chiasm but not displacing it. D) Grade 3: Adenoma displacing optic chiasm. E) Grade 5: Adenoma extension causing obstructive hydrocephalus

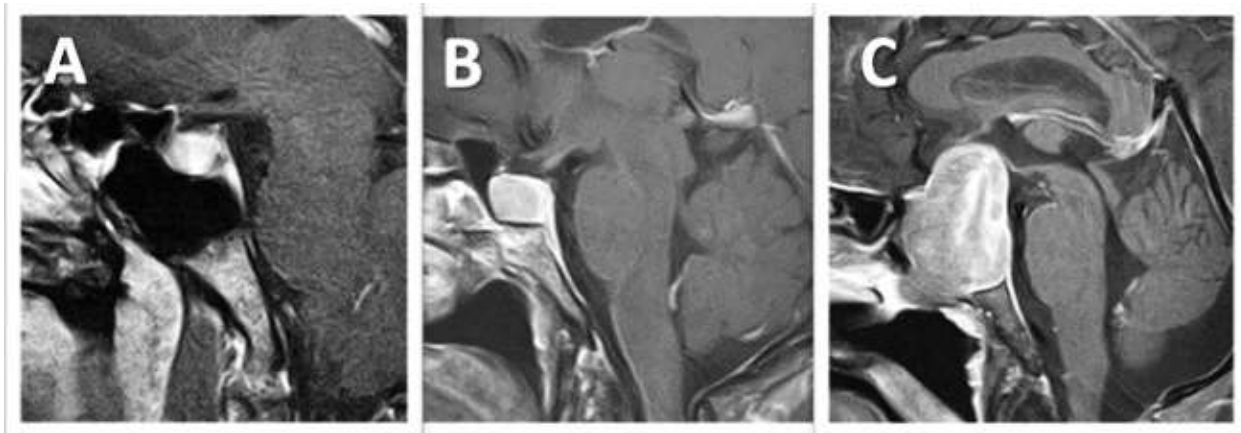


Figure 2: Sagittal contrast enhanced T1 weighted MRI showing 3 grades of infrasellar extension. A) Grade 0: No inferior bulge with intact floor of sella B) Grade 1: Focal inferior bulge of adenoma as an indirect sign of perforation of dura and floor of sella C) Grade 2: Adenoma extension beneath the sphenoid sinus.

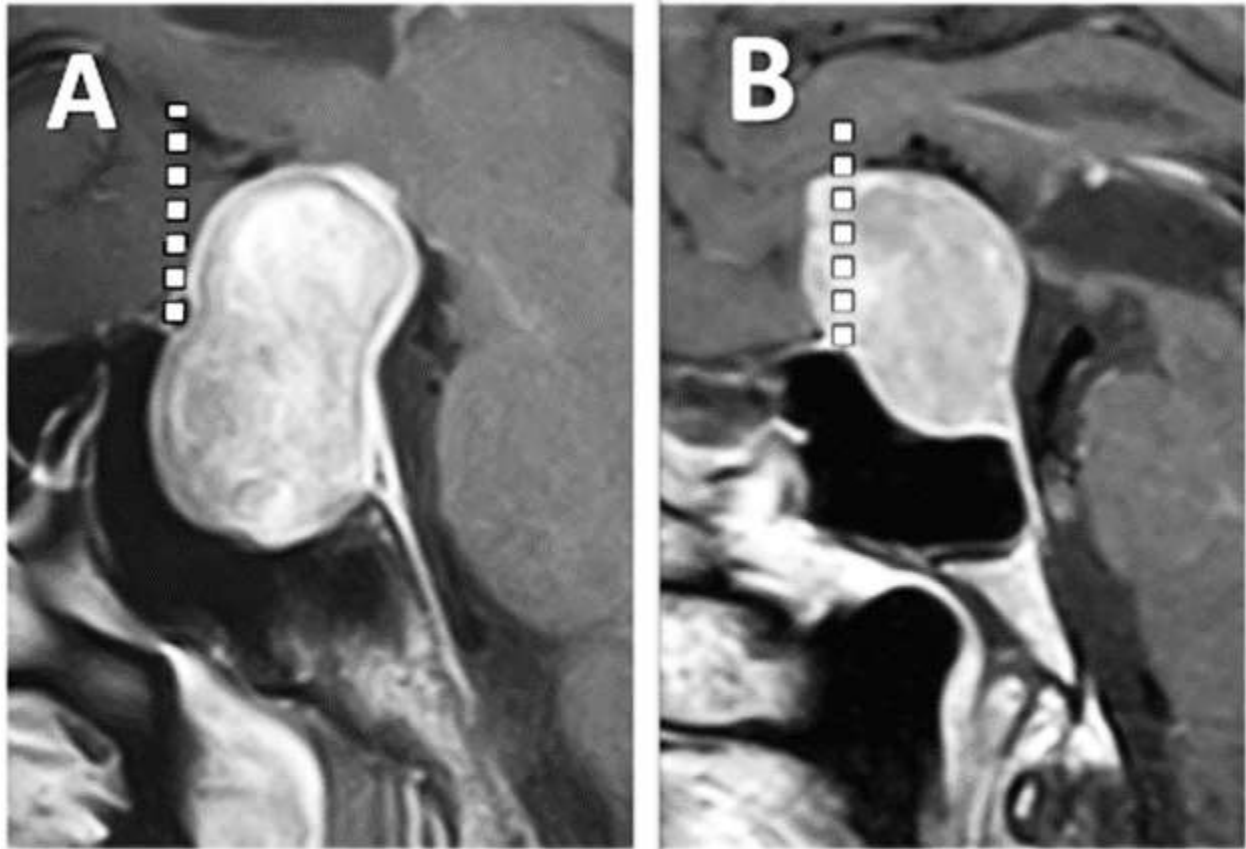


Figure 3: Sagittal contrast enhanced T1 weighted MRI showing 2 grades of anterior extension. Dotted line represents perpendicular line to the tubercle of sella A) Grade 0: No extension into anterior cranial fossa B) Grade 1: Extension into anterior cranial fossa

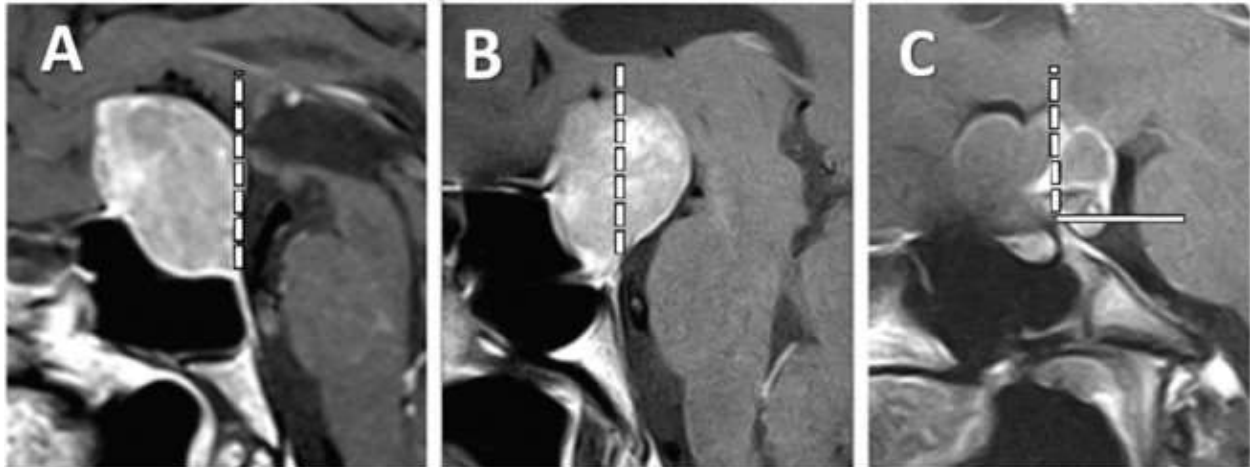


Figure 4: Sagittal contrast enhanced T1 weighted MRI showing 3 grades of posterior extension. Dotted line represents perpendicular line to the dorsum sella. Solid line represents horizontal line to dorsum sella A) Grade 0: No posterior extension B) Grade 1: Posterior-superior growth C) Grade 2: Posterior-inferior growth.

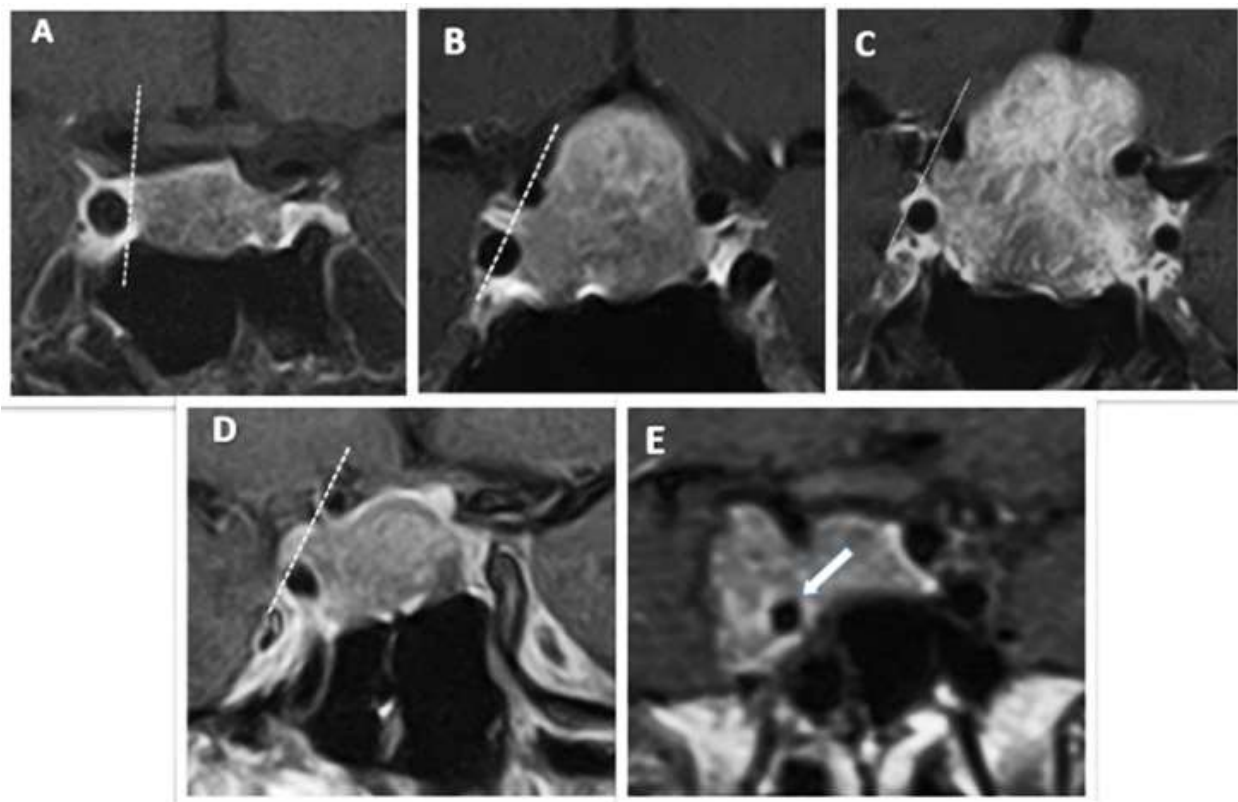


Figure 5: Coronal contrast-enhanced T1 weighted MRI showing 5 grades of parasellar extension. Dotted lines drawn at the intra and supra cavernous internal carotid arteries A) Grade 0: Extension not beyond the medial tangent. B) Grade 1: Extension up to inter-carotid line. C) Grade 2: Extension up to lateral tangent. D) Grade 3: Extension beyond the lateral tangent E) Grade 4: Total encasement of intra-cavernous carotid artery. (solid arrow)

**DISCUSSIONS:** Pituitary adenomas were initially commonly classified radiographically using the HARDY classification, which included a pneumoencephalographic indirect measurement of suprasellar extension [8,9]. As the uni-direction of tumour development was taken into consideration, this categorization was inappropriate for the computed tomography (CT) modality. However, it was crucial from a neurosurgical standpoint to define different extrasellar tumour expansions. As a result, WILSON offered a modified grading system based on the extent of extrasellar extension (stage) and sellar damage (grade), with an emphasis on the size of the tumour and its expansions. This categorization showed a strong predictive value and was useful in developing therapies. [10-12]

A high level of diagnostic performance was attained with the introduction of MRI, high-resolution scanning, and higher soft tissue contrast [12]. Prior to surgical planning, anatomical information and a sufficient topographical assessment must be reported [14,15]. The best way to show the relationship between neighbouring parasellar structures and the lateral expansion of pituitary macroadenomas, particularly the internal carotid arteries, which are most susceptible to damage after surgery, is using MRI post-contrast coronal sections [16]. KNOSP provided a very useful and straightforward grading system that has been utilized to date to forecast parasellar tumour development into the cavernous sinus [17].

A categorization system called SIPAP was presented [18], attempting to merge the KNOSP- HARDY-WILSON categories. They were able to precisely describe tumour development in all directions using this combination, including lateral, upward, and downward orientations as well as forward and backward extensions. [19,20]

Tumour size is not included in the SIPAP classification; however, it may be included as an addition for correct recording and reporting. In a phantom investigation, the tumour volume was recommended to be assessed in length, height, and width the formula supplied for this purpose being  $0.5 \times \text{height, length, and width}$ . [21] When pharmacological treatment of functional adenomas is needed, it is crucial to take the tumour volume into consideration. Tumour extensions, on the other hand, are more crucial for providing a surgical management road map, and by default, the tumour volume is intended to decrease postoperatively as a result of debulking.

There are different methods for scanning pituitary adenomas, but post-contrast coronal and sagittal T1-weighted MR imaging provides the basis for the SIPAP classification. [22, 23] It is a useful follow-up technique with good diagnostic precision and dependability in determining tumour growth. [24]

Our study's evaluation of the tumour's anterior, posterior, suprasellar, and infrasellar extension was mostly agreed upon. We think the intercarotid section, medial tangent, and lateral tangents' close closeness and thin line are to blame for the moderate interobserver rating for parasellar extension. This component can be made better with practice.

This classification may be used for pharmacologically treated tumours as well as pre and post-operative tumour assessment. In our research, there were 39 cases of maximum safe resection (MSR) with a residual tumour, compared to 10 cases of gross total resection (GTR).

We think the SIPAP classification may provide neurosurgeons a full analysis of tumour extension and help them prepare for possible challenges after surgery.

Before beginning this surgical intervention, it is essential to ascertain the extent of parasellar extension because the window for the endoscopic transsphenoidal approach is narrow. This is so that the carotid arteries are protected. [25]

**CONCLUSIONS:** Incorporating the SIPAP grading system into MRI findings of pituitary adenomas is an effective and reliable method to detect tumour growth prior to treatment, which is often surgery. This provides the surgeon with a good road map and reduces problems. Additionally, it may be helpful in monitoring the recurrence of tumours over time.

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