Pituitary Region Segmentation Guidelines

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Abstract

The pituitary gland, known as the master gland, regulates other endocrine glands. Pituitary adenomas are the third most prevalent intracranial tumor, and Magnetic Resonance Imaging (MRI) is the gold standard diagnostic tool for pituitary disease. However, the recent rise in automated segmentation of medical images lacks established guidelines for manual annotation, particularly for the pituitary gland and its surroundings.

This study aims to develop and validate a comprehensive methodology for manually delineating the normal pituitary gland and its surrounding structures. Furthermore, it seeks to lay the groundwork for segmenting pituitary disorders by establishing a foundational step using the developed methodology and reference data.

1 Introduction

The pituitary gland sits within the Sella Turcica of the sphenoid bone at the middle cranial fossa. Conditions of the pituitary gland have potential to encroach and disrupt the surrounding structures. The segmentation of the pituitary gland and some of the surrounding structures of interest include:

1. Pituitary Gland
2. Pituitary Stalk
3. Optic Chiasm
4. Cavernous Sinus
5. Internal Carotid Artery (supraclinoid and intracavernous part)
6. Hypothalamus

This guideline describes how to manually segment the human pituitary gland and its surrounding structures on T1 magnetic resonance images.

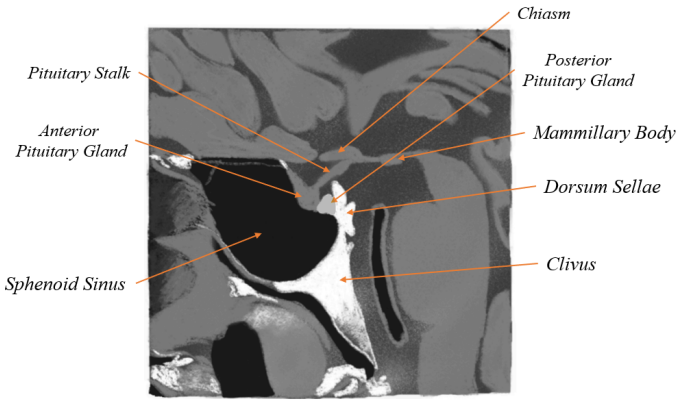
2 Segmentation

Segmentation is to be carried out on ITK-SNAP version 4.0.1 (http://www.itksnap.org)(Yushkevich et al., 2006). Image orientation should be kept as default (X axis: Left to right, Y axis: Posterior to anterior and Z axis: Inferior to superior). The mid-line of the brain MR image should coincide with the falx cerebri (inter-hemispheric fissure) and the transverse plane should also coincide with the interpupillary line. The anterior and posterior commissure (AC-PC) line should mark the horizontal orientation as described in Hammers et al., 2003. Positional normalisation can for example be achieved with posnorm (github.com/soundray/posnorm). Interpolation with 7^{th} degree B-Spline should be used for images that were not initially interpolated in their databases, for example using Statistical Parametric Mapping (SPM) package in MATLAB. There is no need for image registration as only non-contrast enhanced T1 images are to be used for the segmentation task. MRI images of the pituitary region should be segmented primarily on the coronal plane with other planes used as reference points. Segmentation should be carried out on contiguous coronal slices in the anterior-posterior (rostral-caudal) direction. The recommended approach for segmenting all these structures is sequential as listed above, starting with the pituitary gland and terminating with the hypothalamus. The basic set up for the ITK-Snap segmentation tool is to

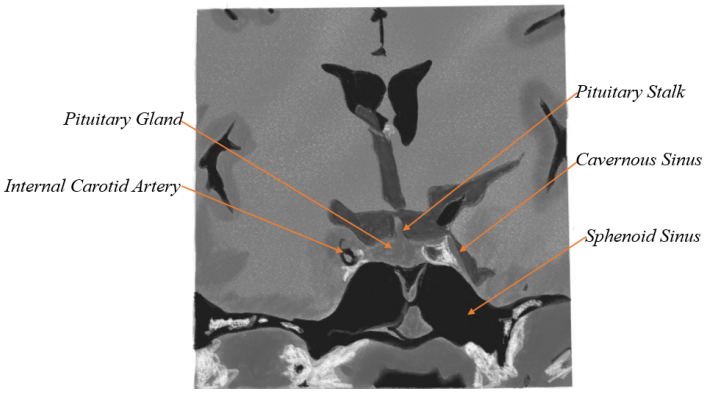
have the "Paint Over" activated and set on segment "Clear Label" to avoid clearing or overshadowing neighboring structures.

2.1 Pituitary Gland

Some landmarks to consider during pituitary gland segmentation include: optic chiasm anteriorly, sphenoid sinus inferiorly, pituitary (infundibular) stalk superiorly, cavernous sinuses laterally, and dorsum sellae posteriorly as seen in figures 1a and 1b. The tracing of the gland should be in the coronal plane with reference to other planes being made with every slide change.



(a) Diagrammatic Representation of Sella Region - Mid Sagittal Section



(b) Diagrammatic Representation of Sella Region - Coronal Section

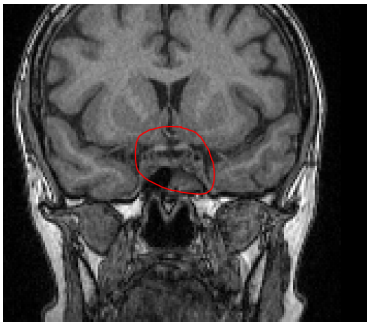
Figure 1: Sella Region and Surrounding Structures

2.1.1 Coronal Plane

Segmentation in the coronal plane should be considered as the primary reference point. The appearance of the gland is different between the anterior and posterior parts on T1 weighted images. The anterior pituitary often appears brighter than the brain grey matter but darker than the brain white matter. The posterior pituitary contains a focal bright spot which is brighter than the white matter. Generally, the size and shape of the gland has been noted to differ among age groups and sexes (Berntsen et al., 2021; Elster et al., 1990). The pituitary starts appearing as an oval-shaped light-gray structure (anterior pituitary). Starting segmentation at the most anterior extent of the gland, due to partial volume effect, only voxels with similar gray scale intensities are to be segmented (as seen in figures 2a and 2b). The appearance of the gland at these anterior slices is fairly oval in shape with different level of individual asymmetry noted. The mid slices which usually appear below the mid point of the optic chiasm, as seen in normal population (Griessenauer et al., 2014), appear like a "U" shaped structure with a depressed superior surface on this plane. Successive subsequent slices should be segmented from the lateral borders moving posteriorly (as seen in figures 2c and 2d). The posterior part of the gland is hyperintense with a good contrast against surrounding tissue and appears like a rectangular-shaped structure in most slices with the hindmost slices appearing as a square-shaped like structure. Segmentation of the last slice should include the most posterior part of the gland (posterior pituitary), as seen in figures 2e and 2f.

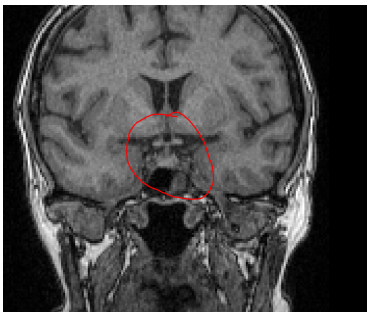
Summary

- **Start Location:** Most anterior extent of the gland (anterior pituitary).
- **End Location:** Most posterior part of the gland (posterior pituitary).

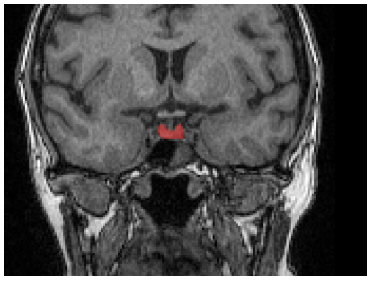


(a) Pituitary Gland Segmentation Starting Point Region of Interest

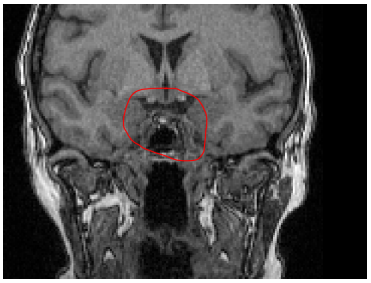
(b) Pituitary Gland Segmentation Starting Point Masked *Red*



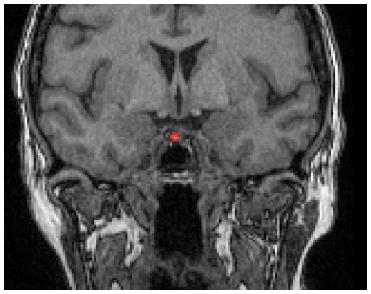
(c) Pituitary Gland Segmentation at Mid Point Region of Interest (showing stalk)



(d) Pituitary Gland Segmentation at Mid Point Masked *Red*



(e) Pituitary Gland Segmentation at End Point Region of Interest



(f) Pituitary Gland Segmentation at End Point Masked *Red*

Figure 2: Pituitary Gland Segmentation

2.2 Pituitary Stalk

The pituitary (infundibular) stalk is a structure connecting the pituitary gland and the hypothalamus. The protrusion at the mid- and posterior-superior portion of the pituitary gland refers to the insertion site of the stalk (Griessenauer et al., 2014). This is narrower compared to the wider part at the level of optic chiasm. The voxel intensities appear slightly lower than that of the pituitary gland, which gives a varying contrast to distinguish the stalk from the gland. The position of the stalk has been recognised to be either prefixed (4%-7.5%), normal (85%-88%) or postfixed (7.5%-8%) (Griessenauer et al., 2014).

2.2.1 Coronal Plane

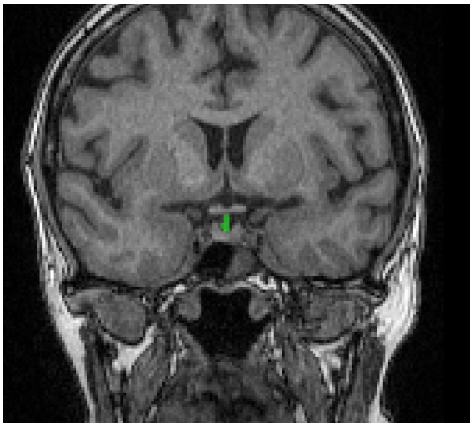
Segmentation is principally done on the coronal plane of the image and should be initiated at the insertion site and terminating at the hypothalamic median eminence (as seen in figure 3a). The pituitary gland is seen inferiorly with the optic chiasm and the start of the optic tract superiorly.

2.2.2 Sagittal Plane

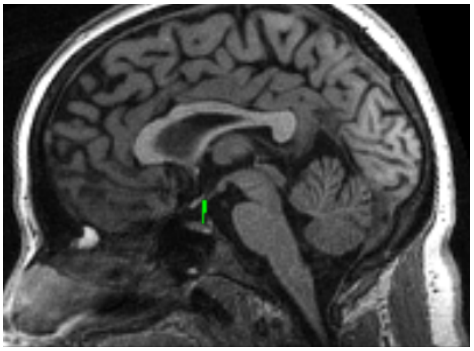
This plane is essential as a reference point to the mid-sagittal section to identify the connection to the gland. It is essential in refining the segmentation in order to identify the start and end points clearly (as seen in figure 3b). This plane reveals the anterior-posterior connection of the hypothalamus and pituitary gland.

Summary

- **Start Location:** Insertion site.
- **End Location:** Hypothalamic median eminence.



(a) Pituitary Stalk Segmentation on Coronal Masked *Green*



(b) Pituitary Stalk Segmentation on Sagittal Masked *Green*

Figure 3: Pituitary Stalk Segmentation

2.3 Optic Apparatus

This structure consists of the optic nerve, optic chiasm and optic tract and spans a considerable distance from anterior to posterior parts of the brain. The optic nerve is the most anterior and the longest. It measures about 50mm and is divided into intraocular ($\tilde{1}$mm), intraorbital ($\tilde{3}$0mm), intracanalicular ($\tilde{6}$-9mm) and prechiasmatic ($\tilde{1}$0mm)(Gala, 2015; Zwerling and Carter, 2021). The intraocular part is the region of attachment of the nerve to the globe of the eye, as it emerges through the scleral opening. The intraorbital part of the nerve is surrounded by cerebrospinal fluid and extraocular muscles. The intracanalicular part has the ophthalmic artery in its close proximity as they exit through the bony optic canal and run into the middle cranial fossa. The prechiasmatic part, which is the last part of the nerve, is seen within the vicinity of the suprasellar cistern and appears voluminous in respect to the other parts. The second region of the optic apparatus is the optic chiasm, it is the point of decussation of nerve fibers and resembles an "X" shaped structure or H-shaped structure (Bosler et al., 2021). The optic tract is a continuation of the decussated nerve fibers from the optic chiasm and runs to the right and left lateral geniculate bodies (Smith and Czyz, 2022). Each segment of the optic apparatus has a relatively uniform voxel intensity (the entire optic nerve sheath complex) which can be delineated against other surrounding structures. For ease of segmentation, an axial slice can be used to place markers as guides and indicate the location of the optic apparatus. This is very helpful for segmenting the intracanalicular part of the nerve, at the optic canal, as it aids in distinguishing other surrounding structures and aids with the visualisation of the whole length of the anterior optic pathway (as seen in figures 4a and 4b). The entire optic apparatus is to be delineated using the same label.

2.3.1 Axial Plane

Reference markers should initially be placed on this plane to aid the subsequent segmentation in the coronal plane. After segmentation on the coronal plane, the axial plane can again be used to refine the X-shaped region of the chiasm (as seen on 5d).

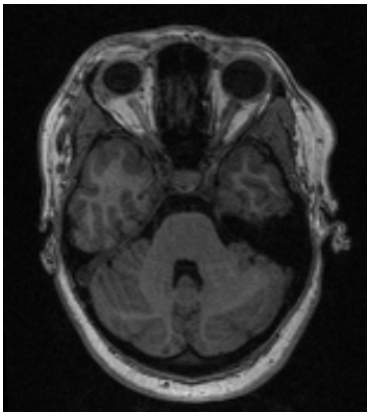
2.3.2 Coronal Plane

Segmentation should commence on the coronal plane and start from the optic nerve at the intraocular part (as seen in figures 4c, 4d and 4e). Due to anatomical asymmetry of the brain and its structures, the start point for the two eye balls might not necessarily be on the same slice. The chiasm

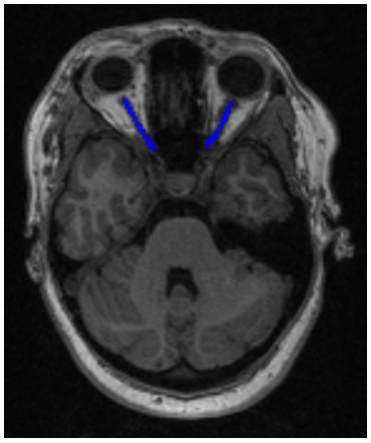
should be traced through the entire X- shaped region (as seen in figure 4f). The optic tract converging into the brain parenchyma (the lateral geniculate body) should be the end point (as seen in figures 5a 5b and 5c).

Summary

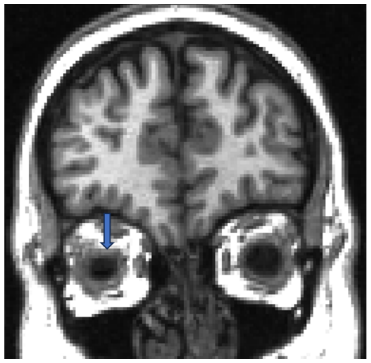
- **Start Location:** Optic nerve at the intraocular part.
- **End Location:** Lateral geniculate body.



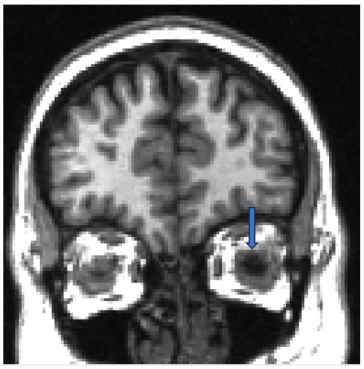
(a) Intracanalicular region of Optic Nerve



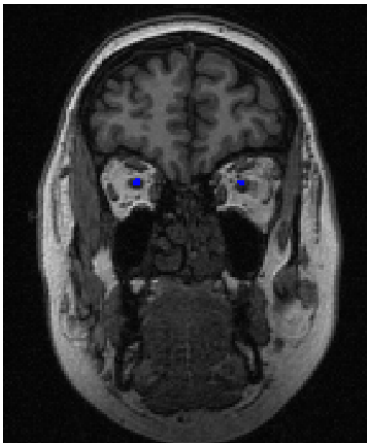
(b) Intracanalicular region of Optic Nerve Masked *Dark Blue*



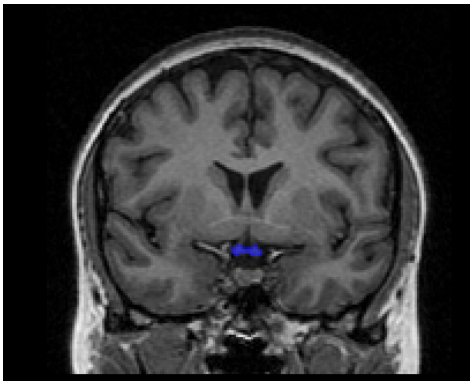
(c) Start Point of Right Optic Nerve *Arrow*



(d) Start Point of Left Optic Nerve *Arrow*

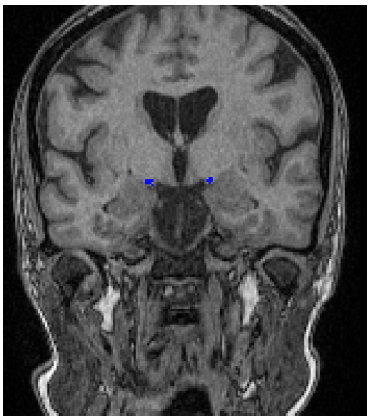


(e) Optic Nerve Segmentation Masked *Dark Blue*

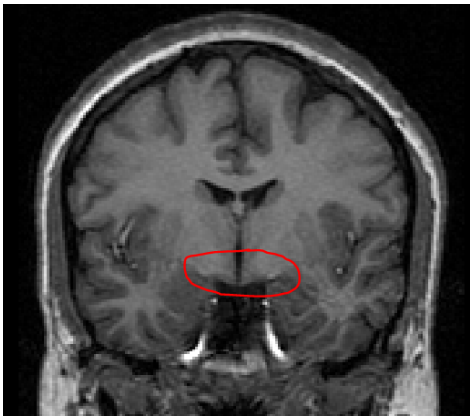


(f) Chiasm Segmentation Masked *Dark Blue*

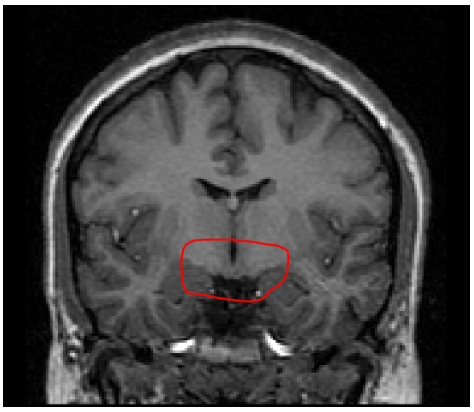
Figure 4: Optic Apparatus Segmentation: Nerve and Chiasm



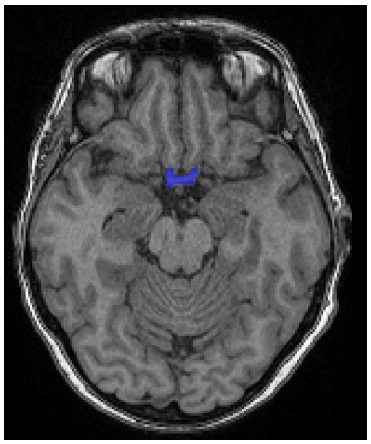
(a) Optic Tract Segmentation Masked *Dark Blue*



(b) Region of Interest Showing Last Slice with Optic Tract



(c) Region of Interest with No Optic Tract Visible (Stopping Point)



(d) Chiasm Segmentation Masked *Dark Blue*

Figure 5: Optic Apparatus Segmentation: Optic Tract and Chiasm Refinement

2.4 Internal Carotid Artery (ICA)

The carotid arteries are seen on either side of the sphenoid sinus and the pituitary gland. There are two distict parts of the artery seen within the para-sellar region; the intracavernous part and the supraclinoid part as seen in figures 6a and 6b. The blood within the arteries appear as hypointense with a hyperintense thin wall (subject to MR image spatial resolution) on non-contrast enhanced images. This inherent contrast distinguishes the ICA from surrounding structures.

2.4.1 Axial Plane

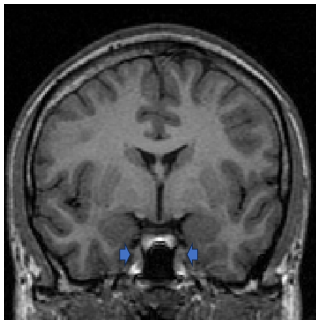
Marker slices placed at the starting point for segmentation of the ICA at the curvature of the intracavernous part as it runs into the supraclinoid part is best done on this plane (as seen in figure 6h)

2.4.2 Coronal Plane

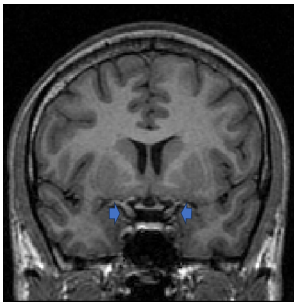
The segmentation of the intracavernous part of the artery should be done along the medial part of the inferior temporal gyrus, starting at the most superior part of the carotid canal as seen in figures 6c and 6d. The supraclinoid part is also traced on this plane and the tracing should terminate at the beginning of the middle cerebral artery (MCA) (as seen in figure 6g). This point can be identified by the difference in caliber of the arteries with the MCA being smaller than the ICA (Gunnal et al., 2019; Krejza et al., 2006). There is some variability in where exactly the MCA starts (Gunnal et al., 2019) but this can be identified by the bifurcation of the ICA into the middle cerebral and anterior cerebral arteries as seen in figures 6e and 6f.

Summary

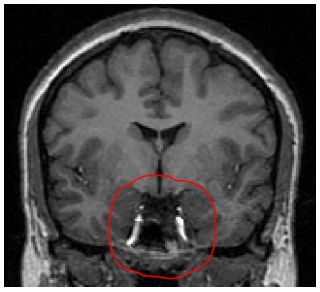
- **Start Location:** Most superior part of the carotid canal.
- **End Location:** Beginning of the middle cerebral artery (MCA).



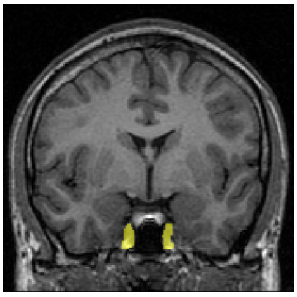
(a) ICA Intracavernous part: Segmentation on coronal plane *Arrow Head*



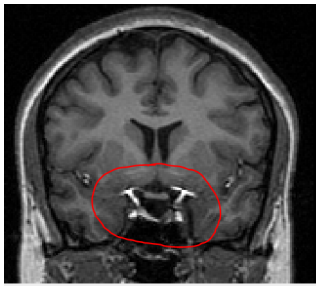
(b) ICA Supraclinoid part: Segmentation on coronal plane *Arrow Head*



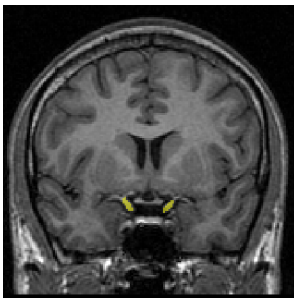
(c) ICA Intracavernous Part Region of Interest: Segmentation on coronal plane



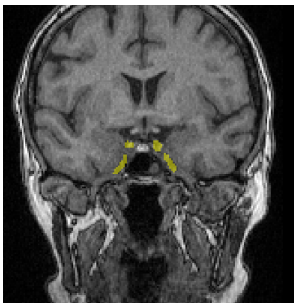
(d) ICA Intracavernous Part Region of Interest: Segmentation on coronal plane *Masked Yellow*



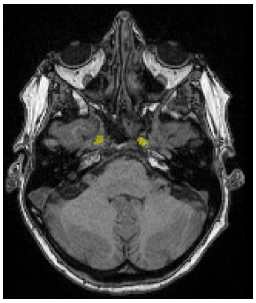
(e) ICA Supraclinoid part Region of Interest: Segmentation on coronal plane



(f) ICA Supraclinoid Part Region of Interest: Segmentation on coronal plane *Masked Yellow*



(g) ICA Intracavernous and supraclinoid parts: Segmentation on coronal plane masked *Yellow*

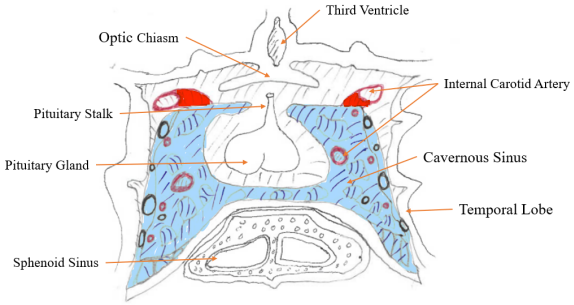


(h) Marker at ICA start point on axial plane masked *Yellow*

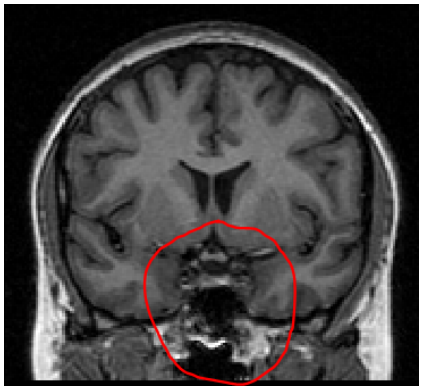
Figure 6: Carotid Artery Segmentation

2.5 Cavernous Sinus

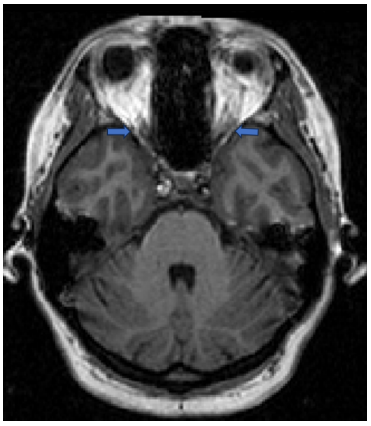
The cavernous sinus is a complex structure of the dural venous sinuses (dural walls). The linings of the dural walls are seen on both sides of the sphenoid bones within the para-sellar area creating a cavity called the lateral sellar compartment which has important neurovascular structures coursing through it (Renn and Rhoton, 1975). It is recommended that the internal carotid artery should be segmented before the cavernous sinus. Again, the ITK-SNAP segmentation tool "Paint Over" should be set to only segment "Clear Label". This is to avoid overshadowing of the two structures. The cavernous sinus typically lies along the lateral borders of the sphenoid sinus. The boundary formations of the cavernous sinus include; basal cisterns (cerebrospinal fluid spaces) form the roof, superior orbital fissure forms a narrow anterior wall, pituitary gland and sphenoid bone form the medial wall, temporal lobe forms the lateral wall, and the posterior cranial fossa forms the posterior wall as seen in figures 7a and 7b (Yasuda et al., 2008).



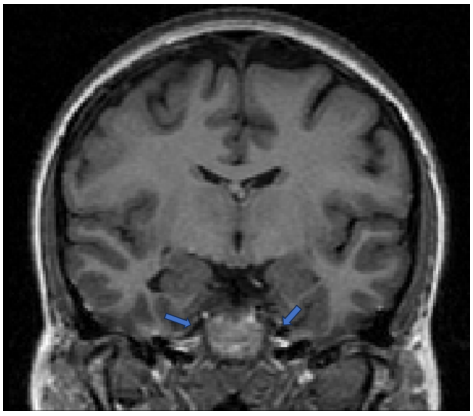
(a) Cavernous Sinus Schematic Representation



(b) Cavernous Sinus Region of Interest



(c) High-Intensity Fat Signal Area *Blue Arrows*

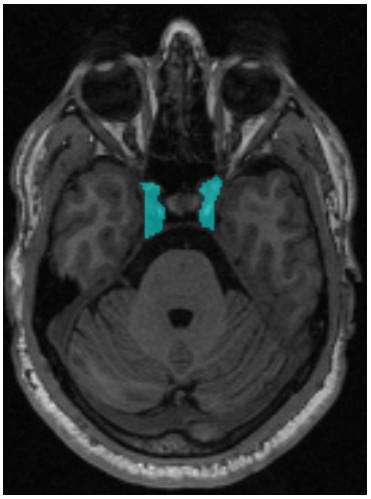


(d) Region of Meckel's Cave *Blue Arrows*

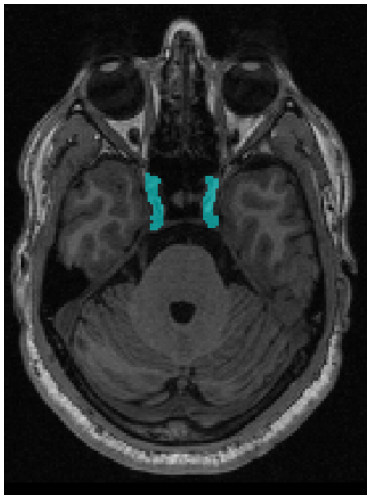
Figure 7: Cavernous Sinus Region

2.5.1 Axial Plane

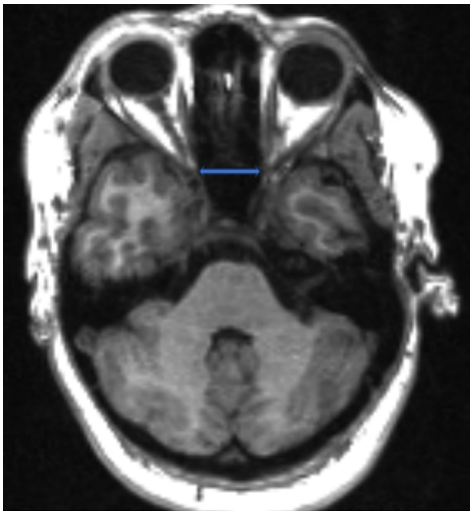
Marker slices should be placed on the axial slices to aid in localization of the boundaries of the cavernous sinus during segmentation. The most anterior point should be considered to be the orbital apex (as seen in figures 8a and 8c). Please note; do not include high-intensity fat signal related to the superior orbital fissure (as seen in figure 7c). The most posterior part should be the region of Meckel's cave (as seen in figure 8b), dorsum sellae and prepontine cistern, which also corresponds to the site of entry of the oculomotor nerve after it exits the brain stem and traverses the prepontine cistern as seen in figure 8d. The lateral margins are distinguishable from the low voxel intensities of the temporal lobe gray matter (as seen in figure 9a). The medial borders are identifiable from the low signal areas of the sphenoid bone and sinus. A clear contrast of the most superior part is noted due to the fluid intensity of the basal cisterns (as seen in figure 9a). The inferior point should not be beyond Meckel's cave.



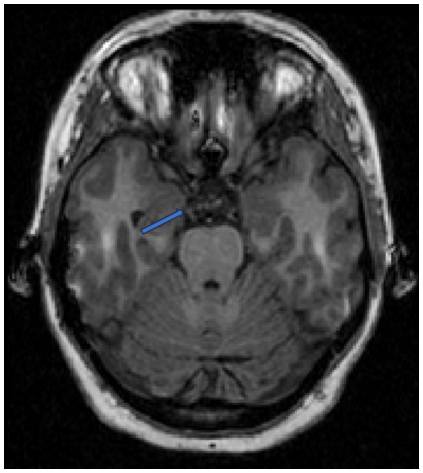
(a) Cavernous Sinus: Marker slice *Sky Blue* showing anterior and posterior limits at mid portion



(b) Cavernous Sinus: Marker Slice *Sky Blue* showing anterior and posterior limit at superior portion



(c) Cavernous Sinus: Right and Left Orbital Apices *Double-Headed Blue Arrow*



(d) Cavernous Sinus: Occulomotor site of entry *Blue Arrow*

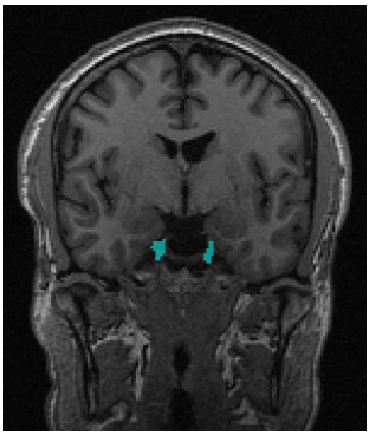
Figure 8: Cavernous Sinus Region: Axial Points

2.5.2 Coronal Plane

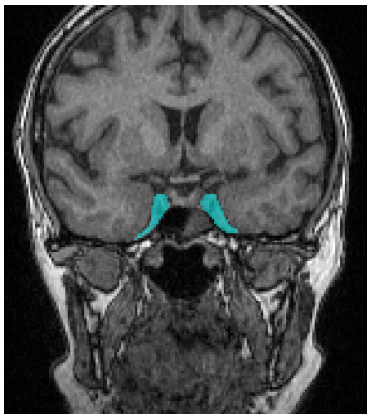
After placing the axial markers, the cavernous sinus is segmented on the coronal plane in anterior-posterior (rostral-caudal) direction. The intracavernous part of the ICA is not overwritten within the sinus (make sure ITKsnap is set to only painting over clear labels) as seen in figures 9b 9c and 9d. The markers placed on the axial slices should provide a guide to the start and end points of the region as seen figure 7d

Summary

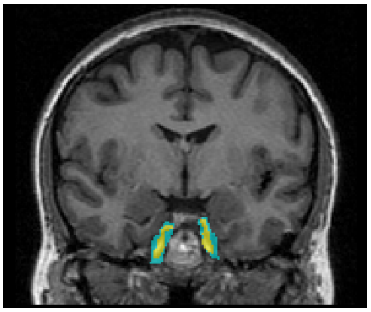
- **Start Location:** Orbital apex.
- **End Location:** Region of Meckel's cave.



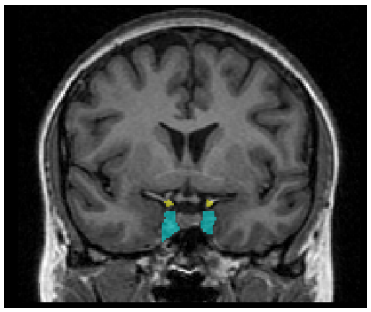
(a) Cavernous Sinus: Marker is Slice *Sky Blue* showing posterior limits with Mickel's cave as Posterior inferior boundary



(b) Cavernous Sinus Masked *Sky Blue* showing lateral and medial limits with temporal lobe and sphenoid sinus boundaries respectively



(c) Cavernous Sinus (*Sky Blue*) and Intracavernous part of Internal Carotid Artery (*Yellow*)

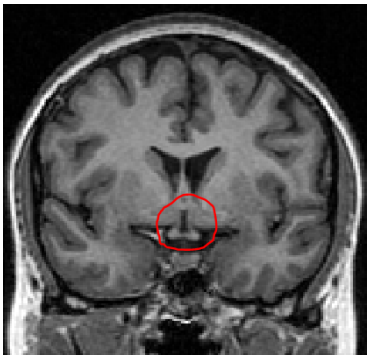


(d) Cavernous Sinus (*Sky Blue*) and Supraclinoid part of Internal Carotid Artery (*Yellow*)

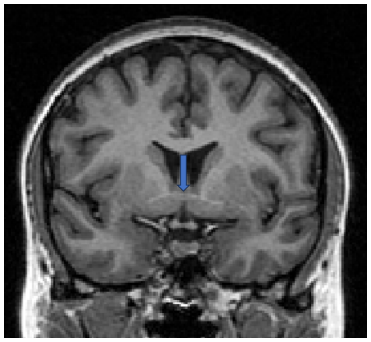
Figure 9: Cavernous Sinus Segmentation: Coronal Points

2.6 Hypothalamus

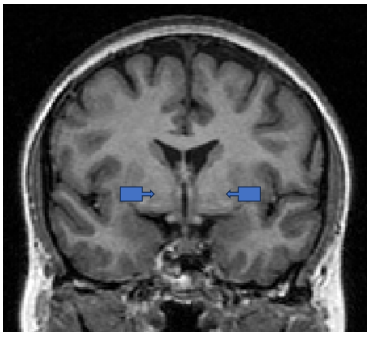
We took note of several existing protocols describing the hypoyhalamus (Billot et al., 2020; Bocchetta et al., 2015; Makris et al., 2013). This is a part of the forebrain that sits superior-posterior to the pituitary gland and inferior to the thalamus. The anterior part of hypothalamus forms the wall of the third ventricle, with the inferior-lateral border at this level corresponding to the beginning of the optic tracts and cerebral peduncles (as seen in figures 11a and 10b). Caudally, the hypothalamus is demarcated inferiorly by the pituitary stalk and superiorly by the hypothalamic sulcus of Monro. The lateral hypothalamic border is well delineated by the sharp contrast of the internal capsule. In the mammillary region (as seen in figures 10c and 10d, however, it has similar intensities with the internal capsule. The hypothalamus is bounded ventrally by the cerebral exterior (i.e. cerebrospinal-fluid filled cisterns), posteriorly by the hypothalamic sulcus and inferior thalamic peduncle, inferomedially by the mammillary bodies which can be distinguished by their shape, and laterally by the zona incerta and cerebral peduncle.



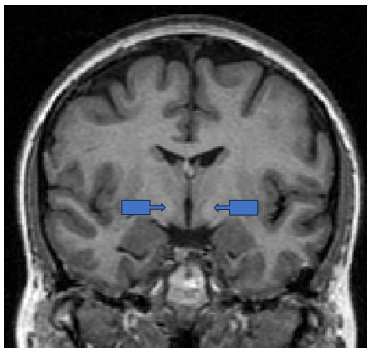
(a) Hypothalamus Region of Interest



(b) Hypothalamus: Anterior commisure *Blue Arrow*



(c) High Intensity Region of Internal Capsule: Proximal Slices *Blue Box Arrow*



(d) High Intensity Region of Internal Capsule: Distal Slices *Blue Box Arrow*

Figure 10: Hypothalamus Region and Boundaries

2.6.1 Coronal

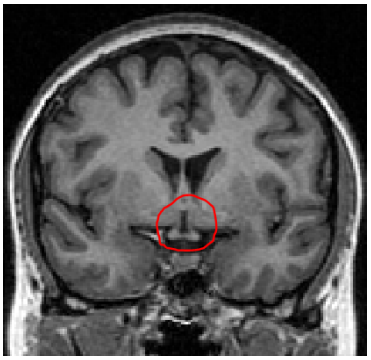
Segmentation should be done for right and left hypothalami seperately, on either side of the third ventricle. Segmentation should begin at the very first slice where the anterior commissure appears continuous through the right and left brain hemispheres with the optic apparatus inferiorly (as seen in figure 11c. The mid slices have a highly asymmetric appearance of the right and left hypothalami (as seen in figure 11d. Segmentation should end at the beginning of the mammillary bodies. Distinguished by the consistent hyperintensity, the mammillary bodies exhibit a uniform appearance and are observed in close proximity to one another (as seen in figure 11e).

2.6.2 Axial

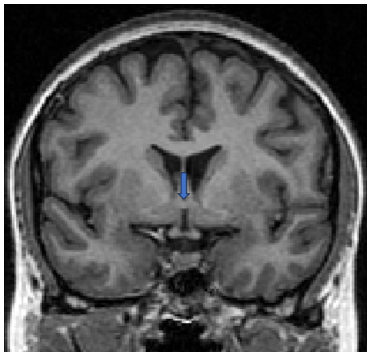
This plane should be considered for refining segmentation and selecting the end point of segmentation with markers (as seen in figure 11f). The start point of the mammillary bodies is easily depicted on this plane with the hypointense appearance of the cerebrospinal fluid within the third ventricle providing a clear contrast.

Summary

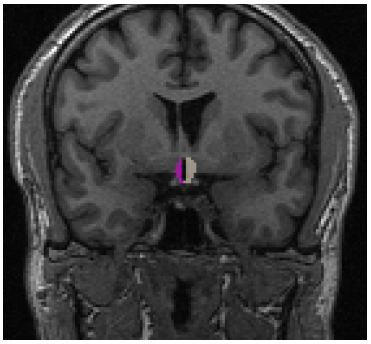
- **Start Location:** First slice where the anterior commissure appears continuous through the right and left brain hemispheres.
- **End Location:** Beginning of the mammillary bodies.



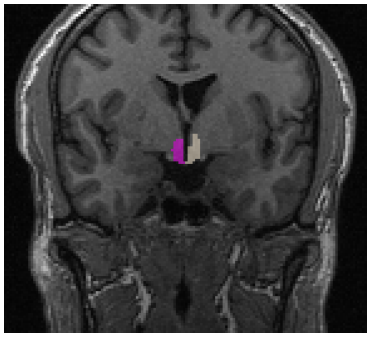
(a) Hypothalamus Region of Interest



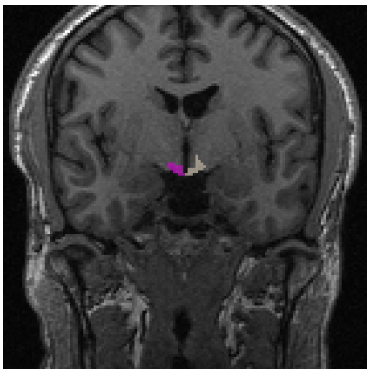
(b) Hypothalamus: Anterior commissure *Blue Arrow*



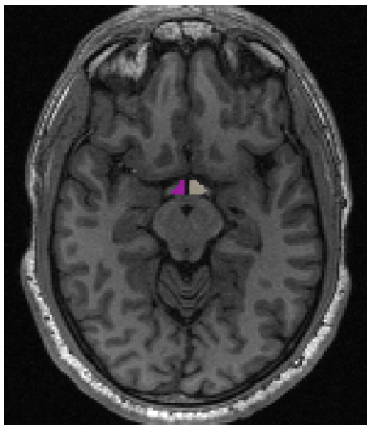
(c) Hypothalamus: Coronal segmentation at anterior commissure point



(d) Hypothalamus: Coronal segmentation at mid point



(e) Hypothalamus: Coronal segmentation at end point

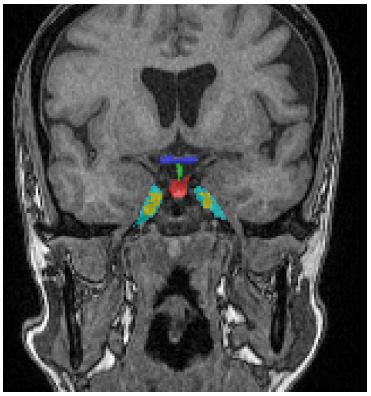


(f) Axial slice used to verify the segmentation end point

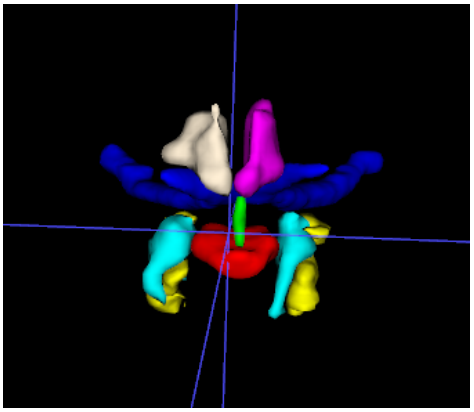
Figure 11: Right and Left Hypothalamus Segmentation

3 Conclusion

Segmenting the pituitary gland and its surrounding structures on MRI images requires careful and precise delineation of the different structural intensities but can be achieved (see figures 12a & 12b and table 1). Adjacent structures do not always appear distinct on a single plane and thus require visualization on other planes to have a better delineation.



(a) Coronal View of Pituitary Gland and Surrounding Structures



(b) 3D Volume-Rendered Masks Showing the Posterior View of the Pituitary Gland and Surrounding Structures

Figure 12: Segmentation of pituitary gland and surrounding structures on coronal plane masks. Legend: red = pituitary gland, green = pituitary stalk, blue = optic apparatus, yellow = internal carotid artery, teal (blue+green) = cavernous sinus, purple = right hypothalamus and gray = left hypothalamus

Label	Region	Colour
1	Pituitary Gland	Red
2	Pituitary Stalk	Green
3	Optic Apparatus	Blue
4	Internal Carotid Artery	Yellow
5	Cavernous Sinus	Teal
6	Right Hypothalamus	Purple
7	Left Hypothalamus	Gray

Table 1: Labels, Regions, and Colours for Segmentation

References

Berntsen, E. M., Haukedal, M. D., & Håberg, A. K. (2021). Normative data for pituitary size and volume in the general population between 50 and 66 years. *Pituitary*, *24*(5), 737–745.

Billot, B., Bocchetta, M., Todd, E., Dalca, A. V., Rohrer, J. D., & Iglesias, J. E. (2020). Automated segmentation of the hypothalamus and associated subunits in brain mri. *Neuroimage*, *223*, 117287.

Bocchetta, M., Gordon, E., Manning, E., Barnes, J., Cash, D. M., Espak, M., Thomas, D. L., Modat, M., Rossor, M. N., Warren, J. D., et al. (2015). Detailed volumetric analysis of the hypothalamus in behavioral variant frontotemporal dementia. *Journal of Neurology*, *262*, 2635–2642.

Bosler, N. S., Ashton, D., Neely, A. J., & Lueck, C. J. (2021). Variation in the anatomy of the normal human optic chiasm: An mri study. *Journal of Neuro-ophthalmology*, *41*(2), 194–199.

Elster, A. D., Chen, M., Williams 3rd, D., & Key, L. L. (1990). Pituitary gland: Mr imaging of physiologic hypertrophy in adolescence. *Radiology*, *174*(3), 681–685.

Gala, F. (2015). Magnetic resonance imaging of optic nerve. *Indian Journal of Radiology and Imaging*, *25*(04), 421–438.

Griessenauer, C. J., Raborn, J., Mortazavi, M. M., Tubbs, R. S., & Cohen-Gadol, A. A. (2014). Relationship between the pituitary stalk angle in prefixed, normal, and postfixed optic chiasmata: An anatomic study with microsurgical application. *Acta neurochirurgica*, *156*, 147–151.

Gunnal, S. A., Farooqui, M. S., & Wabale, R. N. (2019). Study of middle cerebral artery in human cadaveric brain. *Annals of Indian Academy of Neurology*, *22*(2), 187–194.

Hammers, A., Allom, R., Koepp, M. J., Free, S. L., Myers, R., Lemieux, L., Mitchell, T. N., Brooks, D. J., & Duncan, J. S. (2003). Three-dimensional maximum probability atlas of the human brain, with particular reference to the temporal lobe. *Human brain mapping*, *19*(4), 224–247.

Krejza, J., Arkuszewski, M., Kasner, S. E., Weigele, J., Ustymowicz, A., Hurst, R. W., Cucchiara, B. L., & Messe, S. R. (2006). Carotid artery diameter in men and women and the relation to body and neck size. *Stroke*, *37*(4), 1103–1105.

Makris, N., Swaab, D. F., van der Kouwe, A., Abbs, B., Boriel, D., Handa, R. J., Tobet, S., & Goldstein, J. M. (2013). Volumetric parcellation methodology of the human hypothalamus in neuroimaging: Normative data and sex differences. *Neuroimage*, *69*, 1–10.

Renn, W. H., & Rhoton, A. L. (1975). Microsurgical anatomy of the sellar region. *Journal of neurosurgery*, *43*(3), 288–298.

Smith, A. M., & Czyz, C. N. (2022). Neuroanatomy, cranial nerve 2 (optic). In *Statpearls [internet]*. StatPearls Publishing.

Yasuda, A., Campero, A., Martins, C., Rhoton Jr, A. L., de Oliveira, E., & Ribas, G. C. (2008). Microsurgical anatomy and approaches to the cavernous sinus. *Neurosurgery*, *62*(6), SHC1240–SHC1263.

Yushkevich, P. A., Piven, J., Hazlett, H. C., Smith, R. G., Ho, S., Gee, J. C., & Gerig, G. (2006). User-guided 3d active contour segmentation of anatomical structures: Significantly improved efficiency and reliability. *Neuroimage*, *31*(3), 1116–1128.

Zwerling, C. S., & Carter, L. (2021). Unilateral traumatic optic neuropathy case report: A rarity or a pattern. *Ann Rev Research*, *6*(5), 555699.