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IMPACT OF BRAIN MIDLINE RESPECT DURING HIGH-DEFINITION MRI IMAGE ACQUISITION ON REAL VOXEL-BASED AND INDIRECT HIPPOCAMPAL VOLUMETRY USING THE XYZ GEO METHOD

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Abstract: Objectives: to demonstrate the impact of the acquisition of thin-slice MRI images with midline deviation on hippocampal volumetry both direct by voxels and indirect by applying the XYZ Geo¹ method. **Method:** prospective study, which took place between January 2020 and July 2022, of 100 Dominican adults, divided into a **control group** of 60 patients with normal cognition divided into 3 age groups (20-40, 41 to 60 and 61 to 80 years) and a **case group** of 40 patients complaining of cognitive problems (41 to 60 and 61 to 80 years). They were administered the Fols-tein Mini Mental State Examination (MMSE) adapted to Latino patients³. All of them benefited from a 1.5 Tesla MRI with 1-1.5 mm slices for three-dimensional reconstruction including T1 sequences without contrast, FLAIR, T2 and TOF. To determine the deviation from the midline of the MRI images, the Angulus software (May 2020 version) was used to calculate the Geometric Angulation of Anatomical Structures⁴. The hippocampi were examined morphologically to determine if there was any asymmetry in each slice when compared with each other by simple inspection by the Principal Investigator (PI). Real volumetry was performed using voxels and theoretical volumetry using the XYZ Geo method¹. The time taken for each type of hippocampal volumetry was timed. The midline deviation in the MRI images measured in degree with Angulus software, the level of asymmetry inspected in the hippocampal image on each side of the midline, the time it took to perform real and indirect volumetry of each of the 200 hippocampi studied and the percentage of approach between each type of volumetry according to the degrees of midline deviation of the MRI images were correlated. The data collected was processed using measures of central tendency and dispersion in the Microsoft Excel 2016 platform. **Results:** the data obtained showed that even

in MRIs with no midline deviation there was 37.5% asymmetry on visual inspection of the hippocampi in the same slice. No impact was found between the degree of midline deviation of the MRI image and the percentage of closeness between the real and theoretical volumetries. Neither was the degree of midline deviation of the MRI images correlated with the execution time of the real volumetry using voxels or indirect volumetry using the XYZ Geo method. The asymmetry between the hippocampi, even with significant midline deviations, did not affect the execution time of the real volumetry. **Conclusion:** There is a significant degree of morphological asymmetry between the hippocampi when inspected in the same slice, independent of the degree of midline deviation of the MRI images. Neither the degree of deviation from the midline of these images, nor the asymmetry between the hippocampi inspected in each slice impact the quality or accuracy of direct or indirect volumetry, nor its execution time.

Keywords: Midline Deviation, Magnetic Resonance Imaging, Direct Hippocampal Volumetry, Indirect Hippocampal Volumetry.

INTRODUCTION

The real direct voxel-based volumetry of any brain structure is performed by painting it slice by slice on high definition MRI images with thin slices of 1 to 1.5mm, which appear on the screen of any stereotactic image processing platform (planimetry)^{5,6,7}. When these images are provided with full respect of the midline, the conventional anatomy of a structure as important as the hippocampus is shown in its typical form, well known in classical neuroanatomy texts⁸ and can be easily compared with its counterpart on the opposite side, facilitating the assessment of its structure and allowing judgments about its trophicity to be made. This situation is very favorable for real volumetry using voxels or indirect volumetry

using the XYZ Geo method¹. The importance of assessing midline deviation in the case of brain pathologies involving mass effect is frequently cited in the literature^{10,11,12,13,14}, but we have not found any article dealing with the implications of images taken without respecting the midline in the anatomical assessment of brain structures of complex anatomy such as the hippocampus and particularly on its volumetry.

During the development of the research we conducted to validate the accuracy of the XYZ Geo method of indirect volumetry¹ applied to hippocampal volumetry, we had the opportunity to perform 100 MRIs in Dominican patients without and with cognitive impairment. Aware of the delicacy of the simple inspection assessment of hippocampal images on both sides of the midline, we wondered about the impact that the asymmetry generated in each MRI image slice when the images acquired are acquired with a slight, moderate or severe deviation from the midline could have on their direct or indirect volumetry. We were interested in knowing if the asymmetry with respect to the ideal, classical, expected hippocampal image could have any repercussion in the fluidity and ease with which the limits of head, body and tail of the hippocampus were painted in each slice, on each side of the midline. Also, whether this made the execution of direct voxel-based hippocampal volumetry more laborious, prolonged and time-consuming, a delicate and time-consuming process even in experienced hands. Finally, it seemed relevant to know if the degree of deviation from the midline of the MRI images and the resulting level of asymmetry between both hippocampi had any relationship with the percentage of accuracy obtained by the application of the indirect XYZ Geo volumetry method with respect to the real direct volumetry based on voxels.

MATERIAL AND METHODS

This prospective study was conducted at the Centro Gamma Knife Dominicano belonging to the Centro de Diagnostico, Medicina Avanzada y Telemedicina (CEDIMAT), located in the Plaza de la Salud in the city of Santo Domingo, Dominican Republic. A total of 100 participants were recruited, distributed in 3 age groups composed of cognitively normal individuals (20 to 40, 41 to 60, 61 to 80 years old) who attended neurology or neurosurgery outpatients for any reason, except for cognitive dysfunction. All groups were composed of 20 individuals each. They were compared with another group of 40 patients with cognitive problems, aged 41-60 and 61-80 years, periods of life in which dementia is usually detected. Before being included in the research, each patient was asked to read, understand, accept and sign an informed consent form, which was signed by a responsible family member or caregiver in case the patient had severe cognitive impairment. All patients included in the study underwent a 1.5 tesla MRI of 1 to 1.5 mm slice thickness, with capacity for three-dimensional reconstruction; obtaining in all cases the following sequences: T1 without contrast, T2, FLAIR and Time of Flight (TOF). The degree of deviation from the midline of the T1 images without contrast was immediately determined by applying the Angulus Software⁴ in the axial slice revealing the septum pellucidum (Figures 1 and 2). This was followed by the classical hippocampal slice showing the Asta of Amon (AA), the body and the temporal horn of the lateral ventricle (Figures 1 and 2). At that moment, the Principal Investigator (PI) determined whether or not there was an evident asymmetry between the two hippocampi when comparing them. After this, the real volumetry was performed using voxels (planimetry) and the indirect volumetry applying the XYZ Geo¹ method of both hippocampi, timing the time taken for

each process. We correlated the midline deviation in the MRI images measured in degrees with the Angulus software⁴, the level of asymmetry inspected in the hippocampal image on each side of the midline, the time it took to perform real and indirect volumetry of each of the 200 hippocampi studied and the percentage of approach between each type of volumetry according to the degrees of midline deviation found in the MRI images. The data collected was processed using measures of central tendency and Pearson's correlation/dispersion coefficient using the Microsoft Excel 2016 platform.

RESULTS

After analyzing 100 MRI scans during the process of direct and indirect volumetry of 200 hippocampi, determining the deviation from the midline using the Angulus software⁴ on the slice where the septum pellucidum was more clearly visible, we were able to obtain abundant information that we have summarized and simplified in Table 1, which is detailed below.

We found that an image deviation from the midline to the naked eye is discriminated only if it is greater than 2 degrees. Lower deviations are only detected by the Angulus software⁴.

The average degree of deviation was 1.56 degrees. The highest deviation was 13 degrees. Only 8 Resonances out of a total of 100 had no deviation from the midline. Towards the left 50 and towards the right 42 Resonances deviated.

With a very careful observation we were able to perceive with the naked eye 26 deviations from the midline, with an average of 3.22 degrees. Since the average degree of deviation among the 100 MRIs performed was 1.56 degrees (see Table 1) and only 8 of them showed no deviation from the midline, it can be concluded that in most cases the observer could not detect the midline deviation with the naked eye. Hence the usefulness of the Angulus software to notice this occurrence.

Table 2 shows that even in MRI without any degree of deviation the symmetry between the two hippocampi was only 62.5%. This means that in a thin-slice MRI without any deviation of the midline we will face asymmetric hippocampi in 37.5% of the cases. Apparently the deviation of the midline is not the only factor for the appearance of an asymmetric hippocampus with respect to the contralateral one, given that when the deviation is to the left an average of 1.48 degrees we obtain a hippocampal symmetry of 68% and when the deviation is to the right an average of 1.63 degrees, the symmetry turns out to be equal to 88% (Table 2). It is evident that if at zero degree of deviation the percentage of symmetry obtained is lower than when there are almost two degrees of deviation from the midline, there are other causes that explain the discordant aspect on one and the other side of the midline of the hippocampal structure. Probably the morphological difference between head, body and tail to the right and to the left of the midline is more marked and frequent than it is thought.

As can be seen in graph 1, there is little or no impact of the degree of deviation from the mean line on the execution time of the real volumetry, since deviations of 13 degrees lead to an execution time of real volumetry very similar to deviations of zero degree. Therefore, it is easy to conclude that the impact of the deviation from the mean line on the indirect volumetry is zero.

Figure 2 compares the degree of deviation from the midline, the symmetry between the hippocampi and the time of execution of the real volumetry. It is noticeable that even the asymmetric hippocampi where there is a lot of deviation from the midline, the volumetry time is very similar to the cases without asymmetry and with less deviation from the midline. Looking closely at the cases on the right side of the graph, we notice that they are asymmetric hippocampi with a considerable

deviation (between 4 and 8 degrees), however, the volumetry execution time was between 5 and 10 minutes in most cases.

Figures 3 and 4 reveal the impact that midline deviation had on the accuracy of the indirect volumetry based on the XYZ Geo method applied to the head and whole hippocampus, respectively, with respect to the real voxel-based volumetry. It is noted that midline deviations as significant as 7 and 13 degrees did not alter the average accuracy of the indirect volumetry with respect to the real volumetry, which ranged between 100% +/- 10.

DISCUSSION

Despite the existence of platforms such as Elekta's Gamma Plan 11 Work Station, which can set the midline deviation of acquired images to zero, this privilege does not abound in the majority of health service centers where neuroradiology is handled. That is why we consider important to have research data to guide the therapist on the repercussion of the deviation from the midline in the interpretation of the brain slices that are handled, especially when studying structures with such a complex shape as the hippocampus. In the area of its head (Ammon's horn) which is close to the entorhinal area and from which it is necessary to differentiate it well during volumetry in order not to include it, the differentiation with the neighboring structures is quite easy, especially when we have the reference point which is the sphenoidal horn of the lateral ventricle. But when we move backwards and we find the body of the hippocampus and especially its tail, it is important to have a contralateral structural symmetry in order to be well oriented, by comparison, during the volumetry. When the images deviate a lot from the midline, it is logical to think that the asymmetry between the two hippocampi is much more important and could therefore have an impact on the volumetry execution time.

However, when analyzing Table 2 we realize that when there is no deviation from the midline the percentage of hippocampal symmetry (62.5%) is very similar to that when there is an average deviation of 1.48 degrees to the left (68%). We also observed that when there is a slightly greater deviation (1.63 degrees) to the right, the hippocampi look symmetrical on inspection in 88% of the cases. Therefore, the degree of similarity of the hippocampal image with respect to that of the opposite side that appears in the MRI slices does not only depend on the respect of the midline during the study, but also on morphological differences between both structures belonging to different hemispheres.

Figure 1 shows that the speed of the actual voxel volumetrics is not impacted by the degree of deviation from the mean line, as even the images with the largest deviation from the mean line (13 degrees) were volumetricized within the average time of 5 to 10 minutes.

A careful analysis of Figure 2 shows that the morphological asymmetry between the hippocampi on both sides of the midline does not affect the speed of hippocampal volumetry either, since the asymmetric hippocampi, even with significant deviation from the midline (7.25 degrees), were volumetrically measured in the average time of 5 to 10 minutes.

It is a legitimate concern for those who work with indirect volumetry to know if the deviation from the mean line of the images on which they are working could deteriorate the accuracy of the process. We find the answer in the analysis of graphs 3 and 4:

- When indirect volumetry of the hippocampal head is performed (Figure 3), the accuracy rate remains between the values expected when using the XYZ Geo method: 100% +/- 10.

- When indirect volumetry of the entire hippocampus is performed (Figure 4), most cases are within the expected percentage

when using the XYZ Geo method, being notorious the fact that even deviations as important as 13 degrees from the mean line were very close to 100% accuracy.

CONCLUSIONS

Respecting the midline should be a priority in the acquisition of brain CT and MRI images to facilitate accurate and smooth interpretation of each slice and to achieve optimal results when implementing indirect volumetry using the XYZ Geo Method. In experienced hands and using sophisticated imaging pla-

tforms, the midline deviation and subsequent asymmetry that will be found in structures as delicate in their interpretation as the hippocampus, does not make much difference in the imaging evaluation and the results of real and indirect volumetry. However, this variable is still one to be taken into account if you want to optimize diagnostic and therapeutic results, especially if you are working on ordinary platforms such as an ordinary laptop and an MRI CD with the usual software capable of tracing diameters in the 3 planes of space, as it happens in many medical offices and hospital institutions throughout the world.

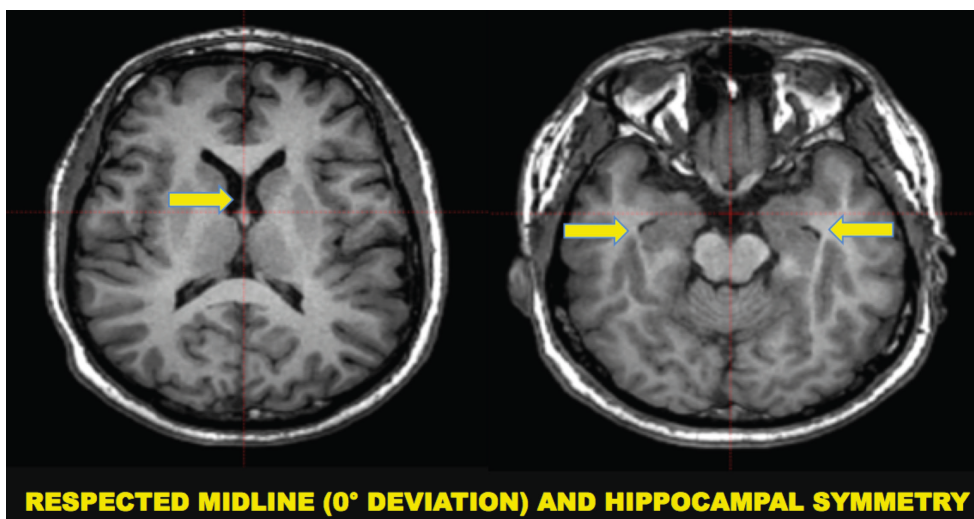


Figure 1:

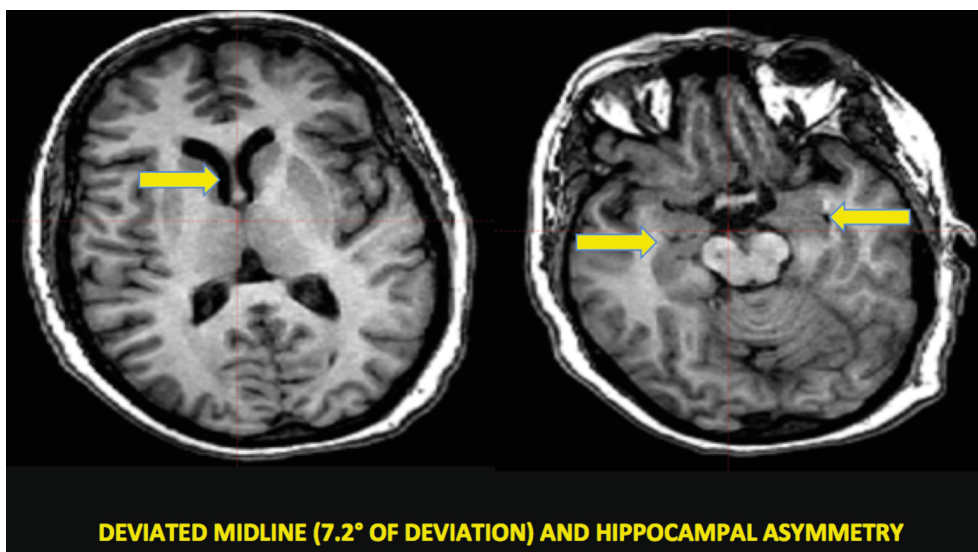


Figure 2:

DEGREES OF DEVIATION FROM THE MIDLINE (DEVIATION PERCEPTIBLE TO THE EYE OF THE OBSERVER: ≥ 2 DEGREES)

SAMPLE	100 PACIENTS
Mean Degree of Deviation from the midline	1,56 Degrees
Predominant direction of deviation from midline	Left
Deviations to the left of the midline	50
Deviations to the right of the midline	42
MRI without Deviation from the midline	8
Images with deviations perceptible to the naked eye from the midline	26 (Mean Degrees of Deviation= 3,22 degrees)
Highest degree of Deviation recorded from the midline	13 degrees
Perception of deviation from the midline to the naked eye	≥ 2 degrees

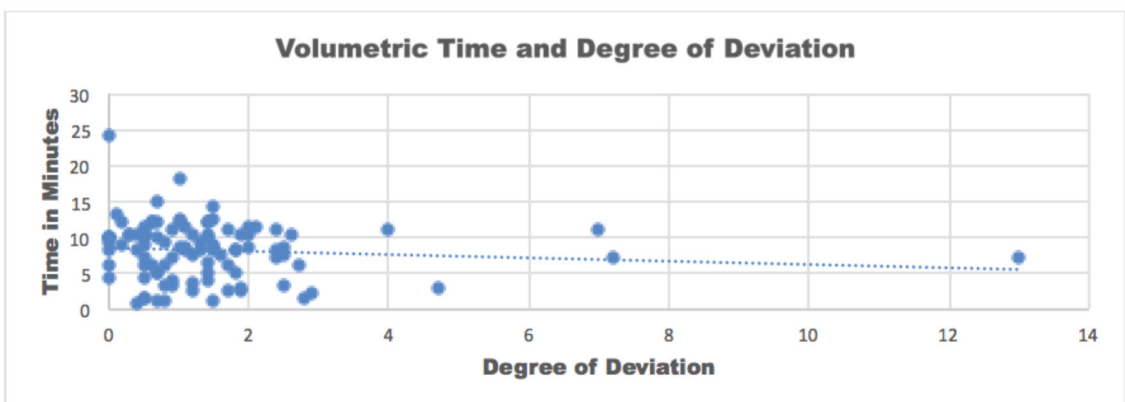
TABLE 1:

Hippocampal Symmetry / Midline Deviation

	Deviation	Degree	Symmetry
Left	50	1.48 Degree	34 (68%)
Right	42	1.63 Degree	37 (88%)
Straight	8	0 Degree	5 (62.5%)

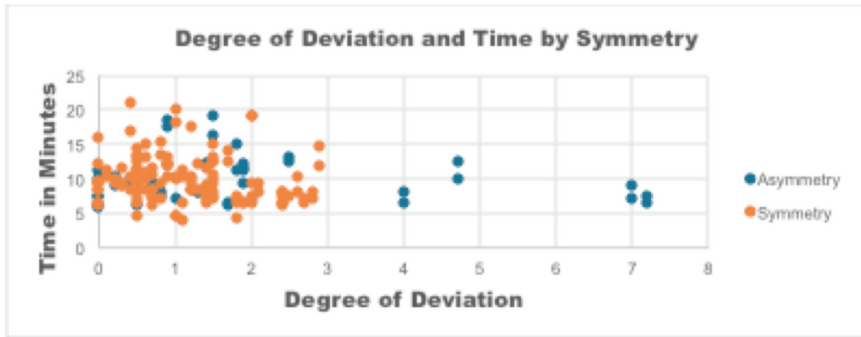
TABLE 2:

Relationship between Real Volumetry Time and Degree of Deviation.



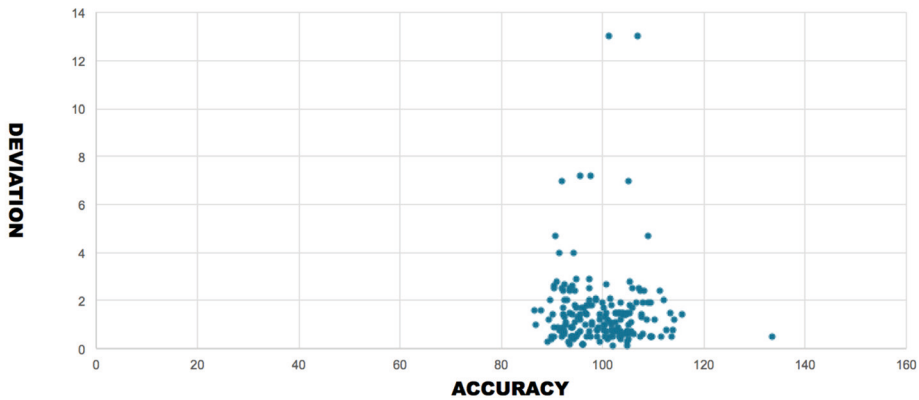
GRAPHIC 1:

Relationship between the Degree of deviation angle and the time in minutes of volumetry according to Hippocampal symmetry



GRAPHIC 2:

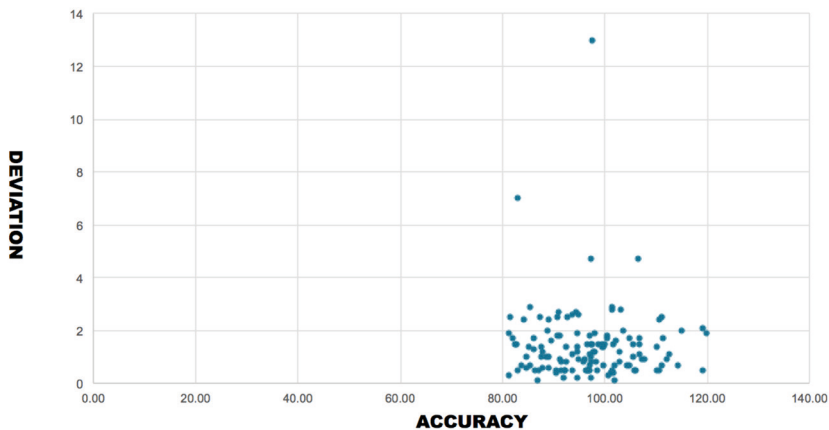
ACCURACY OF INDIRECT/XYZ Geo VOLUMETRY OF THE HEAD OF THE HIPPOCAMPUS RELATED TO THE DEVIATION FROM THE MIDLINE



THE DEGREE OF DEVIATION DOES NOT AFFECT THE ACCURACY OF INDIRECT/ XYZ Geo VOLUMETRY OF THE HEAD OF THE HIPPOCAMPUS WITH AN OR 1.4 (0.3-2.4) P = 0.94, INDICATING THAT THERE IS NO STATISTICAL DIFFERENCE BETWEEN THE GROUPS

GRAPHIC 3:

ACCURACY OF INDIRECT/XYZ Geo VOLUMETRY OF ENTIRE HIPPOCAMPUS RELATED TO THE DEVIATION FROM THE MIDLINE



THE DEGREE OF DEVIATION DOES NOT AFFECT THE ACCURACY OF THE INDIRECT/XYZ Geo VOLUMETRY OF THE ENTIRE HIPPOCAMPUS, WITH AN OR 1.1 (0.6-1.5), P = 0.54. INDICATING THAT THERE IS NO STATISTICAL DIFFERENCE BETWEEN THE GROUPS

GRAPHIC 4:

REFERENCES

1. Valenzuela Sosa, S., Peralta, I., Valenzuela, M.A., Fermin, R., Speckter, H., Bido, J., Hernandez, G., Suazo, E., Rivera, D., Garcia, J., Marmol, F. New Option for Reliable Fast Indirect Volumetry: The XYZ GEO Method. *International Journal of Health Science*. v. 3, n. 99, 2023.
2. Valenzuela Sosa, S., Marmol, F., Coats, C., Jimenez, O., Peralta, I., Valdez, J. Rapid Indirect Hippocampal Volumetry Using the XYZ GEO Method: a Useful Tool in the Diagnosis of Cognitive Impairment. *International Journal of Health Science*. V. 4, n. 13, 2024.
3. Crum R. Population-Based Norms for the Mini-Mental State Examination by Age and Educational Level. *JAMA: The Journal of the American Medical Association* [Internet]. 1993 [cited 20 January 2019];269(18):2386. Available from: <https://jamanetwork.com/journals/jama/article-abstract/405973>
4. <https://angulus-measure-angles-on-images-videos.softonic.com>
5. Boccardi M, Bochetta M, Ganzola R, Robitaille N, Redolfi A, Duchesne S, Jack CR, Frisoni GB. Operationalizing protocol differences for EADC-ADNI manual hippocampal segmentation. *Alzheimers Dement*. 2015 Feb;11(2):184-94. doi: 10.1016/j.jalz.2013.03.001. Epub 2013 May 21.
6. Boccardi M, Bocchetta M, Apostolova LG, Barnes J, Bartzokis G, Corbetta G, DeCarli C, deToledo-Morrell L, Firbank M, Ganzola R, Gerritsen L, Henneman W, Killiany RJ, Malykhin N, Pasqualetti P, Pruessner JC, Redolfi A, Robitaille N, Soinen H, Tolomeo D, Wang L, Watson C, Wolf H, Duvernoy H, Duchesne S, Jack CR Jr, Frisoni GB;(2015) EADC-ADNI Working Group on the Harmonized Protocol for Manual Hippocampal Segmentation. Delphi definition of the EADC-ADNI Harmonized Protocol for hippocampal segmentation on magnetic resonance. *Alzheimers Dement*.11(2):126-38.
7. Li X, Li D, Li Q, Li Y, Li K, Li S, Han Y. Hippocampal subfield volumetry in patients with subcortical vascular mild cognitive impairment. *Sci Rep*. 2016 Feb 15;6:20873. doi: 10.1038/srep20873.
8. Amaral, D; Lavenex P. "Ch 3. Hippocampal Neuroanatomy". In Andersen P; Morris R; Amaral D; Bliss T; O'Keefe J (eds.). *The Hippocampus Book*. Oxford University Press. (2006).
9. Wang, H.; Ho, S.; Xiao, F.; Chou, J. A Simple, Fast and Fully Automated Approach for Midline Shift Measurement on Brain Computed Tomography. (2017). <https://doi.org/10.48550/arXiv.1703.00797>
10. Qi, Xuguang & Belle, Ashwin & Shandilya, Sharad & Chen, Wenan & Cockrell, Charles & Tang, Yang & Ward, Kevin & Hargraves, Rosalyn & Najarian, Kayvan. (2013). Ideal Midline Detection Using Automated Processing of Brain CT Image. *Open Journal of Medical Imaging*. 03. 51-59. <https://doi.org/10.4236/ojmi.2013.32007>
11. McKeown ME, et al. Midline shift greater than 3 mm independently predicts outcome after ischemic stroke. *Neurocrit. Care*. 2021 doi: 10.1007/s12028-021-01341-x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
12. Liao CC, Chen YF, Xiao F. Brain midline shift measurement and its automation: A review of techniques and algorithms. *Int. J. Biomed. Imaging*. 2018;2018:4303161. doi: 10.1155/2018/4303161. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
13. Yang WS, et al. Defining the optimal midline shift threshold to predict poor outcome in patients with supratentorial spontaneous intracerebral hemorrhage. *Neurocrit. Care*. 2018;28:314–321. doi: 10.1007/s12028-017-0483-7. [PubMed] [CrossRef] [Google Scholar]
14. Tu PH, et al. Postoperative midline shift as secondary screening for the long-term outcomes of surgical decompression of malignant middle cerebral artery infarcts. *J. Clin. Neurosci*. 2012;19:661–664. doi: 10.1016/j.jocn.2011.07.045. [PubMed] [CrossRef] [Google Scholar]