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Morphometric Analysis of Left & Right Tonsils in Adult Symptomatic Type 1 Chiari Patients and Healthy Controls

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Introduction

Chiari Malformation Type 1 (CMI) is a neurological disorder where the cerebellum descends from the skull crowding the spinal cord. This puts pressure on both the brain and spine causing a wide range and diverse set of symptoms.[1] Symptoms can include severe headaches, extreme pains in the neck and shoulders, respiratory problems and sleep apnea, loss of fine motor control, and trouble swallowing and sometimes speaking. Research shows that about 95% of patients experience at least 5 of these symptoms.[1] Previously, CMI has been anatomically defined when the cerebellar tonsillar descent (TD) is 5 mm or greater below the foramen magnum (FM).[2] This measurement is usually made with a single sagittal plane T1-or T2-weighted magnetic resonance imaging (MRI). Studies have obtained additional morphometric measurements to help diagnose CMI, and establish normal values.[3,4] These studies were somewhat successful in differentiating CMI patients from healthy subjects. However, results from these studies have shown that the standard TD measurement does not necessarily correlate with neurological symptom severity as patients with CMI-like symptoms have been found with a TD of less than 5 mm position below the FM.[6,7] Also, a variety of morphometric measurements have been found insufficient to differentiate disease states related to CMI such as syringobulbia.[8] Past studies have reported that the TD measurement is not a good measure for diagnosis of CMI, yet it is still being used today.[7]

The primary goal for this study is to provide a better method for diagnosing CMI. One aspect that has not been analyzed in previous work is morphometric measurement of the left and right tonsil with using a constant reference point in the mid-sagittal plane. We

hypothesize; using the proposed methodology, Cerebellar tonsil descent relative to the FM will be lower based solely on a mid-sagittal slice compared to the 7 clinical operators measurements.

Materials and Methods

For the study, 31 data sets were used consisting of CM patients and healthy volunteers. The new protocol was designed to measure the left and right tonsillar descent of the test subjects. The statistical tests used in this study included a two-tailed T-test and a frequency histogram analysis. The two-tailed T-tests were used to compare the statistical significance between the two operators of this study. The frequency histogram analysis was used to show the difference in measurements between the two operators of this study. The left and right TD measurements were obtained using a 3D image processing software known as OsiriX.

To accurately make measurements in OsiriX, a series of steps was necessary to obtain results. First, all axes needed to be oriented in the correct position. The purple line connects the anterior of the basion to the posterior of the opisthion with aspects to the foramen magnum (Image A, Figure 1). The orange line was then aligned through the subject's nasal passage (Image B, Figure 1). The blue line represents the coronal slice image of the brain (Image B, Figure 1), which allowed anterior/posterior movement of the image to better identify the lowest part of each tonsil (Image C, Figure 1). After the axes were all oriented in the correct position, measurements of each tonsil were taken relative to the purple line (Image C, Figure 1).

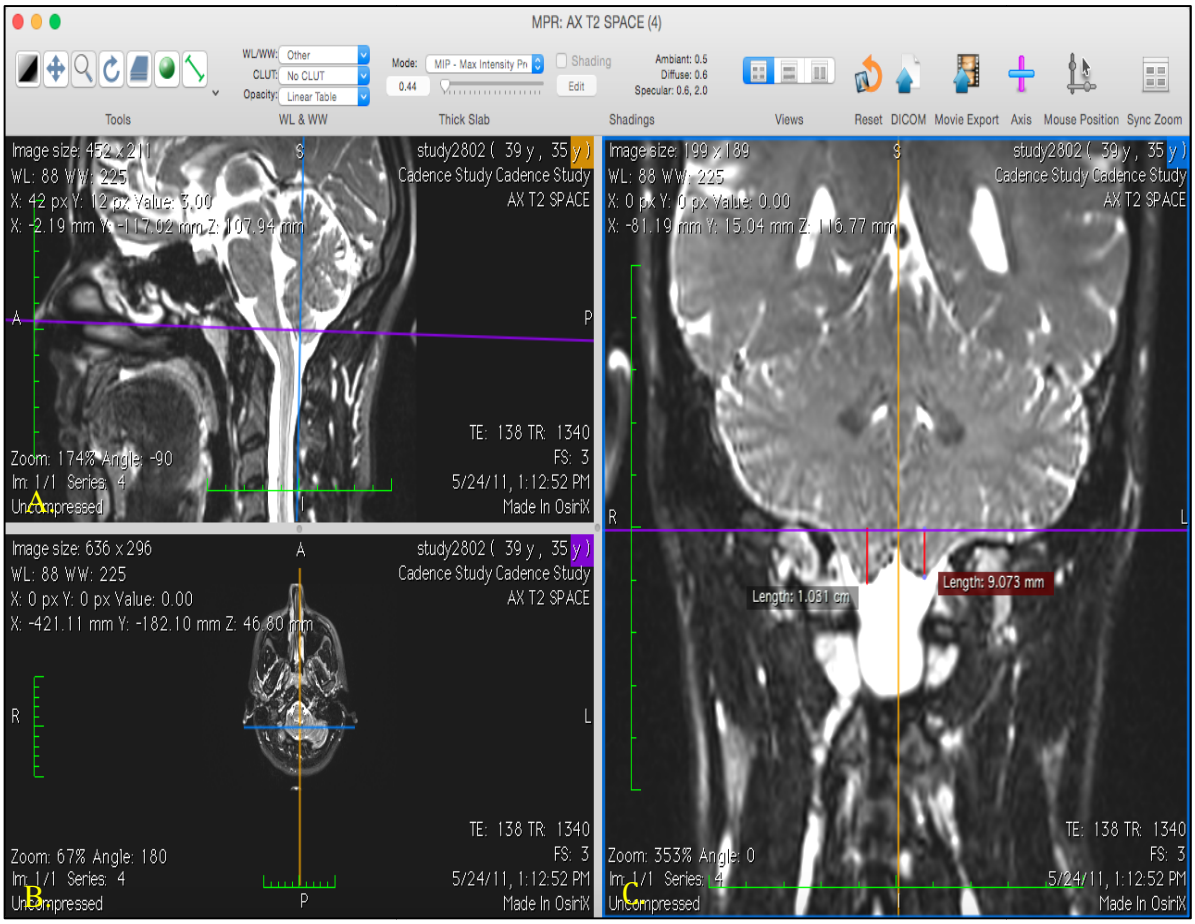

Figure 1: TD morphometric measurement made on mid-sagittal slice of a CMI case using Osirix imaging software.

After measuring the left and right tonsil, the new protocol measurements were first compared between the two operators of this study. Because there was a good correlation and agreement between both operators, their measurements were then compared with the standard practice of 7 clinical operators. Before starting this project, the 7 clinical operators were given the same 31 data sets that were used in this study and asked to make the measurements as well. However, their measurement only consisted of measuring one tonsil; compared to our study, which measured two tonsils.

Results

In this study, there were two operators, myself (LK) and VT. The comparison between LK and VT's left TD measurement resulted in a p-value of 0.9713 (Figure 2), and a histogram was used to show the difference between LK and VT left TD measurement (Figure 3).

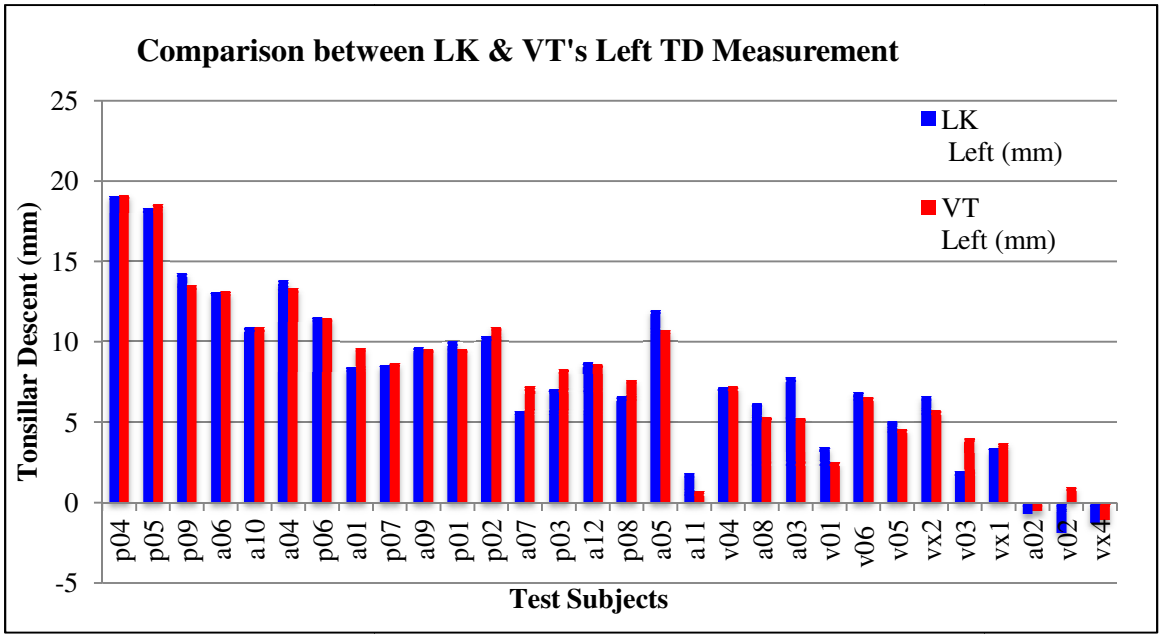

Figure 2: Comparison between LK & VT's Left TD Measurement

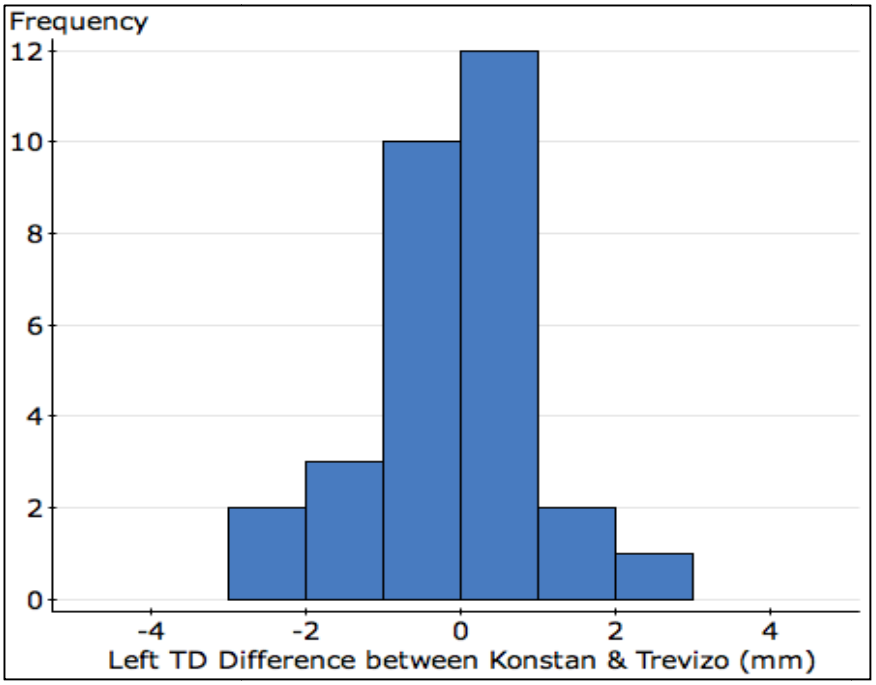

Figure 3: Left TD difference between LK and VT

The comparison between LK and VT's right TD measurement resulted in a p-value of 0.8507 (Figure 4), and histogram was used to show the difference between LK and VT's right TD measurement (Figure 5).

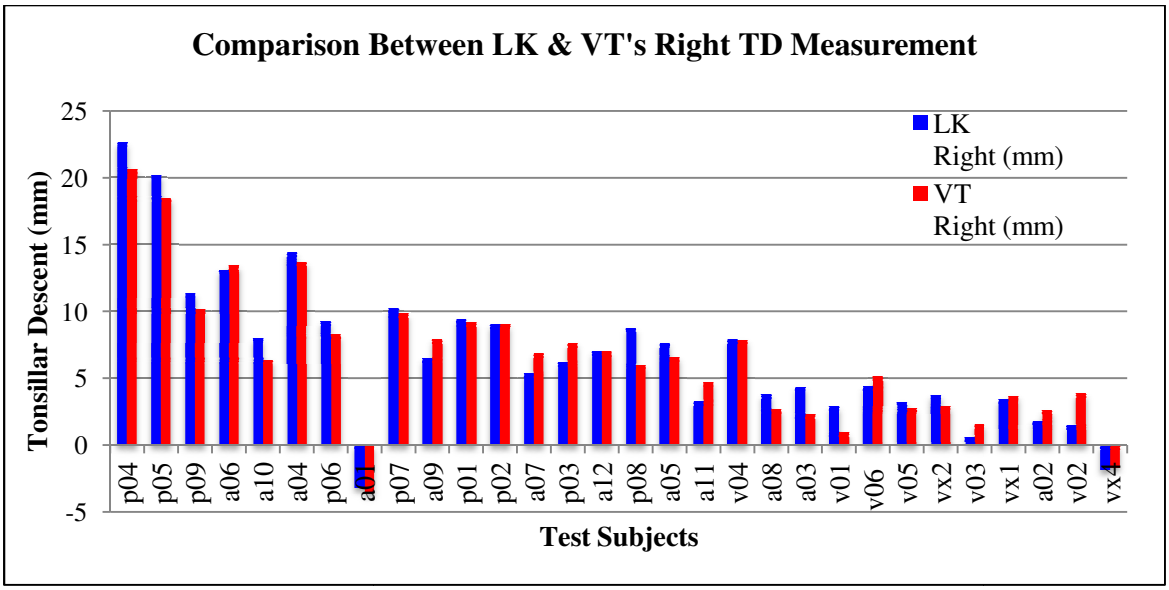

Figure 4: Comparison Between LK & VT's Right TD Measurement

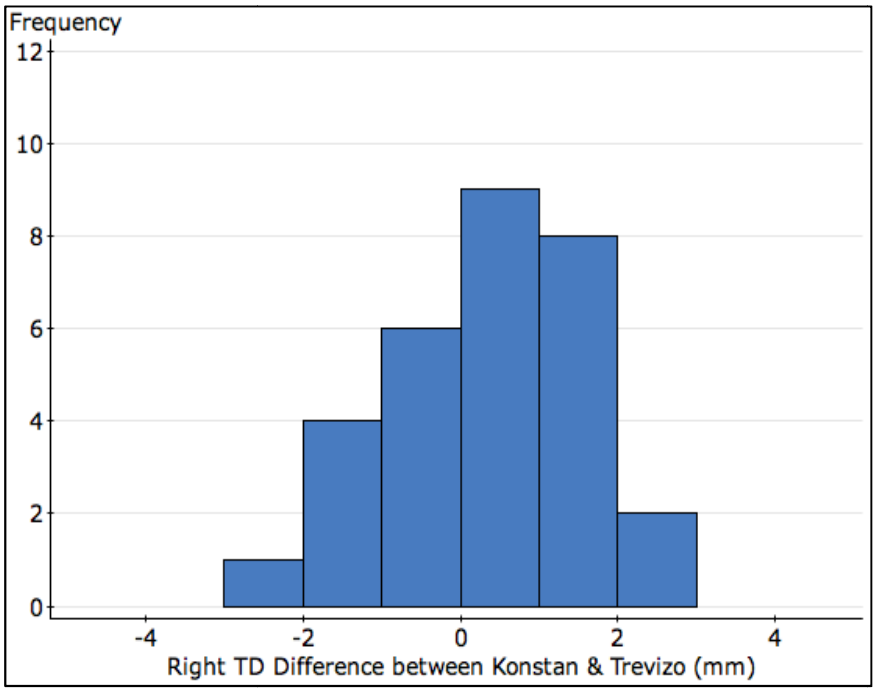

Figure 5: Right TD difference between LK and VT

The average left TD, combination of both operators' left measurement, was 7.838 mm and the average right TD, combination of both operators' right measurement, was 6.702 mm (Figure 6).

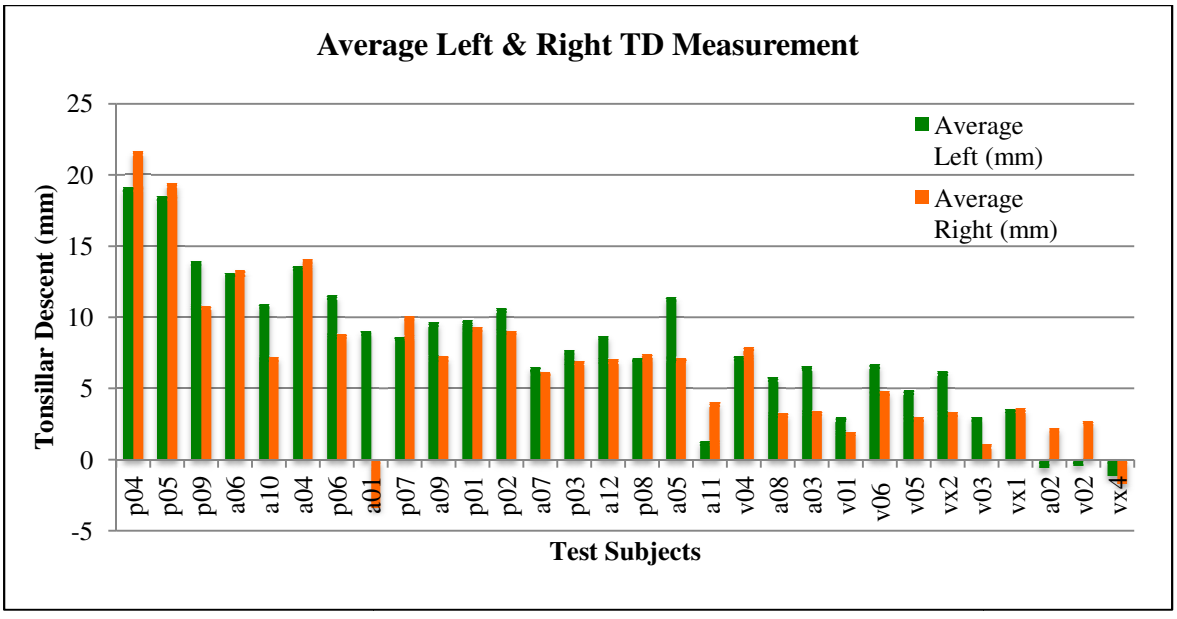

Figure 6: Average Left & Right TD Measurement

On average, our tonsillar descent's length (mm) using two operators was lower than that of the mean of the 7 clinical operators in relation to the FM. The lowest TD measurement recorded for this study was 21.635 mm. The lowest TD measurement recorded for the 7 clinical operators was 18.195 mm (Figure 7).

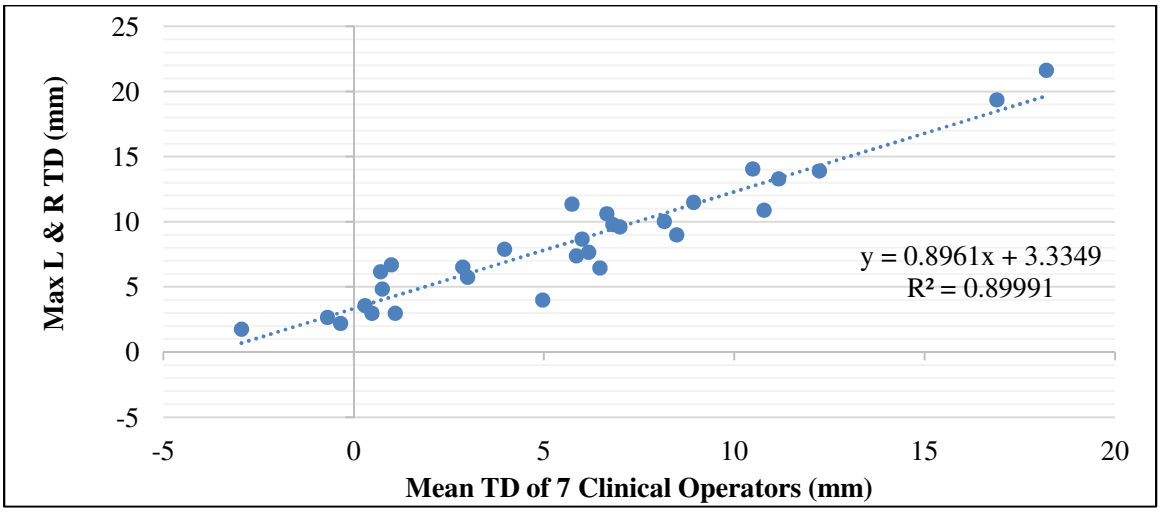

Figure 7: Max left and right TD compared to the mean TD of the 7 clinical operators.

Discussion

The comparison between the two operators, LK and VT, had very good agreement. A statistical two-tailed T-test was used to compare LK's left TD measurement to that of VT's left TD measurement. The level of significance for this study was set at 0.05. The outcome resulted in a p-value of 0.9713, which was greater than 0.05 indicating that there was no significant difference and data was random between the two operator's left TD measurements. A histogram was made to find the difference between LK and VT's left TD measurement. Results indicated that there was not much difference between the two operator's left TD measurements. The histogram is

symmetric showing that the two operators differed mostly by 1 mm with a frequency of 12 (Figure 3).

Again, the comparison between the two operators, LK and VT, had very good agreement. A statistical two-tailed T-test was used to compare LK's right TD measurement to that of VT's right TD measurement. The level of significance was again set at 0.05. The outcome resulted in a p-value of 0.8507, which was greater than 0.05 indicating that there was no significant difference and data was random between the two operator's right TD measurements. A histogram was made to find the difference between LK and VT's right TD measurement. Results indicated that there was not much difference between the two operator's right TD measurements. The histogram is symmetric showing that the two operators differed mostly by 1 mm with a frequency of about 9 (Figure 5).

After discovering both LK and VT agreed in their measurements of the left and right TD, the average of the two operators left and right measurements were taken. On average, the left tonsil was found to be lower than the right tonsil. The average left TD, combination of both operators' left measurement, was 7.838 mm and the average right TD, combination of both operators' right measurement, was 6.702 mm (Figure 6).

When the two operators from this study were compared to the 7 clinical operators, there was a significant difference between the two when the TD was relatively small (most important range). The results of the linear equation identify the slope, m, as 0.8961 and the y-intercept as 3.3349 (Figure 7). For example, when the 7 clinical operators measured "Patient XYZ's" TD at 3.96 mm; our operators measured "Patient's XYZ's" TD at 7.899 mm. The reason for this outcome is due to the shape of the foramen

magnum (FM). The geometry of the FM is not a perfectly flat circular opening, because the bones are curved. Therefore, to make this measurement, it requires the midline sagittal slice to be moved off axis (Figure 8). This will make the McRae line shorter and the width of the FM smaller. Since all other morphometric measurements are relative to the McRae line, there is a systemic error in all other measurements. Our study used a more precise and accurate method using the coronal plane to determine the left and right tonsil. It is a better indicator since the left and right tonsils can both be measured compared to just one tonsil, which was done in the previous study by the 7 clinical operators. We expected these results.

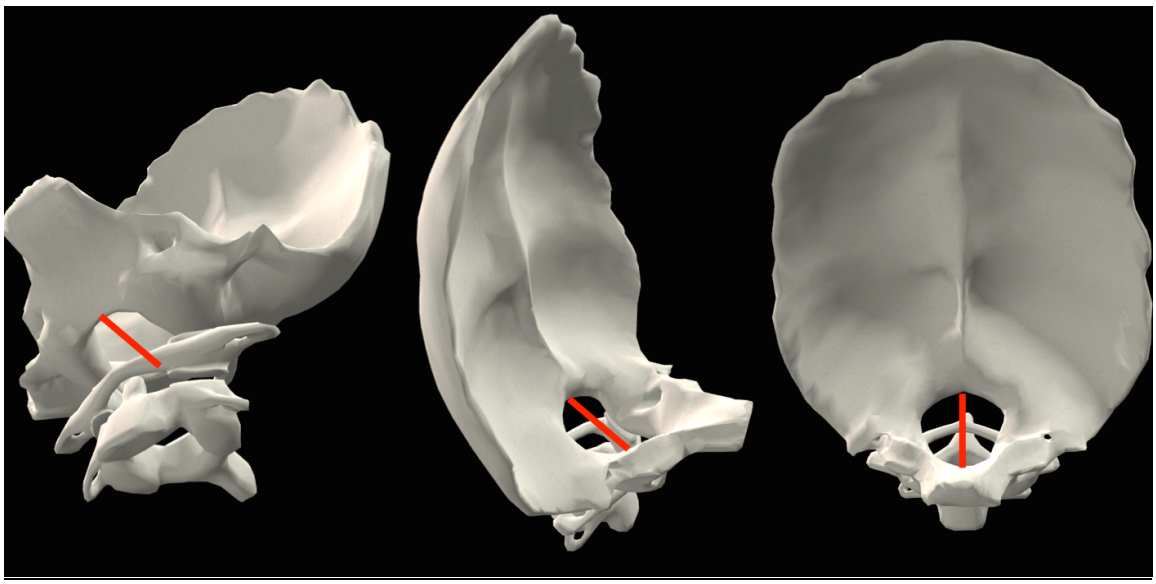

Figure 8: The Geometry of the arc shape of the foramen magnum (FM). It is not a straight line, bones are curved, which displaces the angulation of the FM. Red line refers to the McRae line.

Limitations

There were multiple limitations in this research study that included having only 31 test subjects, 2 operators who were inexperienced, the quality of MRI images, and difficulty lining up all axes in correct positions in Osirix. Also, the mean TD made by the 7 clinical operators was performed using different software than what was used in this study, and they only measured one tonsil.

Conclusion

Chiari Malformation Type I diagnosis still appears to be a challenging task for both researchers and physicians to make. It is obvious that that tonsillar descent measurement is critical in making a proper diagnosis. The goal of this study was to observe how much of an operator dependence there was for making the tonsillar descent measurements. We wanted to improve the methodology by measuring the left and right tonsil by a constant reference point in the mid-sagittal plane. The results indicated that when measuring the left and right tonsil with a consistent mid-sagittal slice, the outcome was significantly different than that of the clinical operators. This occurs because the basion and opisthion change due to the curvature of the foramen magnum. The difference is so significant that it could impact the diagnosis of these test subjects. We were not able to differentiate between asymptomatic and symptomatic Chiari patients in this study.

Because our study included very few data sets and only two operators were involved with this project, our results are not to be interpreted as finding an accurate way to diagnose CMI. However, it did provide potential research projects and ideas that could

lead to improving future diagnoses. Future research should focus on trying to differentiate asymptomatic from symptomatic Chiari patients.

Acknowledgements

I would like to thank Dr. Bryn Martin and the Conquer Chiari Research Center for providing me the opportunity to be a part of this research team. Dr. Martin has been a great mentor, providing me with knowledge about Chiari and the importance of research. Lastly, I would like to thank my honors project reviewers, Richard Mostardi and John Kunz, for their contribution to this project.

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