FINAL SCRIPT: APPROVED FOR FILMING

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Title: Midface Hypoplasia and Cranial Base Morphology in Syndromic Craniosynostosis: A Comparative Analysis Study Using a Predictive Regression Model

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Author Questionnaire

1. **Microscopy**: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No**

2. **Software:** Does the part of your protocol being filmed include step-by-step descriptions of software usage? **Yes, all done**

3. **Filming location:** Will the filming need to take place in multiple locations? **no**

4. **Testimonials (optional):** Would you be open to filming two short testimonial statements **live during your JoVE shoot**? These will **not appear in your JoVE video** but may be used in JoVE's promotional materials. **yes**

Current Protocol Length
Number of Steps: 17
Number of Shots: 36

Introduction

Videographer: Obtain headshots for all authors available at the filming location.

INTRODUCTION:

~~What is the scope of your research? What questions are you trying to answer?~~

1.1. **Firdaus Hariri:** My research focuses on how age-adjusted midface and cranial base measurements improve surgical planning for syndromic craniosynostosis.

1.1.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. ~~*Suggested B.roll:3.2*~~

~~What are the most recent developments in your field of research?~~

1.2. **Firdaus Hariri :** Recent developments include morphological modeling and predictive analytics to enable more precise, personalized craniofacial surgical planning.

1.2.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

CONCLUSION:

~~What significant findings have you established in your field?~~

1.3. **Firdaus Hariri:** Age adjustment improves prediction accuracy of craniofacial morphology for better individualized surgical planning.

1.3.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. ~~*Suggested B.roll:5.6*~~

~~What research gap are you addressing with your protocol?~~

1.4. **Firdaus Hariri:** We address gaps in predictive accuracy by integrating age and cranial base measurements as a critical factor in regression models.

1.4.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

~~What advantage does your protocol offer compared to other techniques?~~

1.5. **Firdaus Hariri:** Our protocol offers improved individualized prediction by adjusting for age, unlike static cranial base models.

1.5.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. ~~*Suggested B.roll:5.2.1*~~

Videographer: Obtain headshots for all authors available at the filming location.

Testimonial Questions (OPTIONAL):

Videographer: Please capture all testimonial shots in a wide-angle format with sufficient headspace, as the final videos will be rendered in a 1:1 aspect ratio. Testimonial statements will be presented live by the authors, sharing their spontaneous perspectives.

How do you think publishing with JoVE will enhance the visibility and impact of your research?

1.6. **Professor Firdaus Hariri, Dean, Faculty of Dentistry, Universiti Malaya**: (authors will present their testimonial statements live)

Can you share a specific success story or benefit you've experienced—or expect to experience—after using or publishing with JoVE? (This could include increased collaborations, citations, funding opportunities, streamlined lab procedures, reduced training time, cost savings in the lab, or improved lab productivity.)

1.7. **Professor Firdaus Hariri, Dean, Faculty of Dentistry, Universiti Malaya**: (authors will present their testimonial statements live)

Ethics Title Card

This research has been approved by the Medical Ethics Committee at the University of Malaya

Protocol

NOTE: LAB MEDIA/SCREEN/SCOPE timestamps for protocol were added at the postshoot stage. Please contact the postshoot note integrator (Sulakshana) for queries regarding lab media.

2. Subject Selection and CT Scan Data Retrieval

Demonstrator: Ding Wen Qian

2.1. To begin, open the digital imaging archive **[1].** Retrieve retrospective cranial CT scan datasets of pediatric patients diagnosed with syndromic craniosynostosis **[2].**

2.1.1. WIDE: Talent launching the digital imaging archive on a computer.

2.1.2. SCREEN: 1.2.2.mp4 00:05-00:22

2.2. Select subjects who meet the inclusion criteria, confirmed syndromic craniosynostosis diagnosis by craniofacial surgeons, complete medical records, and are below 12 years **[2]**. Similarly select control subjects with complete cranial and facial CT scans and no history of craniofacial anomalies **[3-TXT]**.

2.2.1. SCREEN: 1.2.1.mp4 00:00-00:15

2.2.2. SCREEN: 1.3.1.mp4 00:00-00:20 **TXT: Apply exclusion criteria to remove subjects**

2.3. ~~Then, apply exclusion criteria to remove subjects aged 12 years and above, with non-syndromic or isolated craniosynostosis, incomplete clinical or imaging documentation, previous craniofacial surgery, or midface hypoplasia **[1].**~~

2.3.1. ~~SCREEN: Talent filtering and marking subject records that match any exclusion criteria.~~
NOTE: Shot deleted by authors

2.4. After receiving non-contrast CT skull datasets in DICOM *(die-com)* format, ensure imaging protocols meet departmental standards **[1-TXT]**.

2.4.1. SCREEN: 1.4.1.mp4 00:00-00:19

TXT: Verify dataset completeness, absence of artifacts before dataset release

2.5. Archive all verified datasets securely and prepare them for import into a three-

dimensional medical image processing software for reconstruction and analysis **[1]**. Select 30 subjects and assign them equally into three cohorts: non-operated syndromic craniosynostosis, operated syndromic craniosynostosis, and normal control, with 10 subjects in each group **[2]**.

2.5.1. SCREEN: 1.5.1.mp4 00:01-00:08

2.5.2. SCREEN: 1.5.2.mp4 00:02-00:08

3. 3D Reconstruction and Landmark Identification

Demonstrator: Lantian Zheng

3.1. Display all imported datasets simultaneously in axial, sagittal, and coronal planes along with a three-dimensional preview **[1]**.

3.1.1. SCREEN: 3.1-new.mp4 00:03-00:07

3.2. To begin three-dimensional volumetric reconstruction, ~~create a bone mask.~~ ~~Select **Segment** and~~ click **New Mask** ~~in the Mimics software~~ to generate the initial reconstruction **[1]**. Check the boxes for **Fill Holes** and **Keep largest** then press **OK [2]**.

3.2.1. SCREEN: 3.2-new.mp4 00:00-00:05

3.2.2. SCREEN: 3.2-new.mp4 00:06-00:11

3.3. Now, resolve segmentation issues caused by inappropriate Hounsfield Unit ranges by applying the standard **Bone** threshold preset **[1]**. Refine the segmentation mask further using the **Edit Mask** function to remove artifacts and ensure structural continuity **[2]**.

3.3.1. SCREEN: 3.3-new.mp4 00:01-00:12

3.3.2. SCREEN: 3.3-new.mp4 00:13-00:20

3.4. ~~Navigate to **Masks** and click on **Calculate Part** to generate the mask **[1].** Then, use the **Create Point** tool under **Measurements** to mark anatomical landmarks on the 3D model **[2]**. Rotate and magnify the reconstruction to enhance visibility, then click once to place each point directly on the anatomical site **[2].**~~ Navigate to the **Analyse** tab and click on **Measure and Analyse [2].** Mark the landmarks the **Sella (S)** *(Stella-S)* at the midpoint of the sella turcica, the **Nasion (N)** *(Nasion-N)* at the frontonasal suture junction, the **Basion (Ba)** *(Basion-B-A)* at the anterior midpoint of the occipital bone at the spheno-occipital synchondrosis, and **right and left zygomaticomaxillary sutures (ZMR, ZML)** *(Right-and-Left-Zygomaticomaxillary-sutures-Z-M-R-Z-M-L)* at the infraorbital rim **[3]**.

3.4.1. ~~SCREEN: 3.4,3.5-new.mp4 00:10-00:17, 00:25-00:30~~

3.4.2. SCREEN: 3.4,3.5-new.mp4 00:03-00:05

3.4.3. SCREEN: 3.4,3.5-new.mp4 00:24-00:30, 02:46-02:50, 01:04-01:10, 02:20-02:26, 01:39-01:47

3.5. To confirm each landmark, view it from multiple angles and compare it with the axial, sagittal, and coronal planes for accuracy **[1-TXT]**. Store all marked landmarks automatically in the **Measurements** section of the project tree **[2]**. Export the coordinates and labels of each landmark using the **Export Measurements** function to generate datasets in .csv *(C-S-V)* or .xls *(X-L-S)* format **[3]**.

3.5.1. SCREEN: 3.4,3.5-new.mp4 01:50-02:00
TXT: Store all landmarks automatically in the Measurements section then export in .csv format

3.5.2. SCREEN: 3.7-new.mp4 00:40-00:53
AND
TEXT ON PLAIN BACKGROUND:
SN: anterior cranial base length between the sella and nasion landmarks
SBa: posterior cranial base length between the sella and basion
NBa: total cranial base length between the nasion and basion
ZMR–ZML: maxillary width between the right and left zygomaticomaxillary
Video Editor: Please play both shots side by side in a split screen

3.5.3. SCREEN: 3.8-new.mp4 00:10-00:32, 00:42

3.6. ~~Now, navigate to **Analyze, Measurements,** and **Distance between points** to open the distance measurement tool **[1].**~~ Select any two anatomical landmarks manually on the 3D reconstruction, allowing the software to automatically calculate and display the Euclidean distance between them in the **Measurements Results** window **[2]**.

3.6.1. ~~SCREEN: Show the user accessing Analysis, selecting Measurements, then choosing Distance between points.~~
NOTE: This was merged with 3.6.2 to prevent redundancy

3.6.2. SCREEN: 3.6-(1).mp4 00:45-01:04

3.7. ~~Now, measure the SN *(S-N)* distance as the anterior cranial base length between the sella and nasion landmarks on the 3D model **[1].** Measure the SBa *(S-B-A)* distance as the posterior cranial base length between the sella and basion **[2].** Then, measure the NBa *(N-B-A)* distance as the total cranial base length between the nasion and basion **[3]**. Measure the maxillary width between the right and left zygomaticomaxillary sutures as the ZMR–ZML *(Z-M-R-Z-M-L)* distance **[4-TXT].**~~
NOTE: Step converted to on-screen text in 3.5.2

3.7.1. ~~SCREEN: 3.7-3.8.mp4 00:01-00:10 Show the SN distance being measured~~

~~directly on the 3D model with a line connecting the sella and nasion.~~

3.7.2. ~~SCREEN: 3.7-3.8.mp4 Show the SBa distance being measured between the sella and basion with the model slightly rotated.~~

3.7.3. ~~SCREEN: 3.7-3.8.mp4 Show the NBa distance line drawn between the nasion and basion in a zoomed-in view.~~

3.7.4. ~~SCREEN: 3.7-3.8.mp4 Show the ZMR–ZML distance being measured as a horizontal line between the zygomaticomaxillary sutures. **TXT: Use zoom and rotation tools for precise point selection**~~

3.8. Next, allow the software to automatically update the measurement list within the project tree upon completion **[1]**. Export the complete dataset using the **Export Measurements** function and save it in .xls format ~~including all landmark labels and their corresponding linear values. Use these exported values for subsequent statistical analysis~~ **[2]**.

3.8.1. SCREEN: 3.8-new.mp4 00:04-00:10

3.8.2. SCREEN: 3.8-new.mp4 00:11-00:15, 00:39-00:42

4. Regression Model Application

Demonstrator: Norli Anida

4.1. Import the exported linear measurement dataset into a spreadsheet program for analysis **[1-TXT]**. Apply the Hariri Ros-Nor regression formula to calculate predicted values for total cranial base length and maxillary width **[2-TXT]**.

4.1.1. SCREEN: 69176_-4.1.1.mp4 00:11-00:28
TXT: Apply the Hariri Ros-Nor regression formula to calculate predicted values for total cranial base length and maxillary width
Video Editor: please freeze frame here

4.1.2. SCREEN: 69176_4.1.2.mp4 00:00-00:19
TXT: $-NBa$ = − 1.554 + 1.021 (SN) + 0.753 (SBa); $-ZMRZML$ = 5.762 + 0.920 (NBa)

4.2. Compare the predicted values with the measured values for each subject to evaluate consistency and morphological deviation **[1]**. Calculate the standard deviation of the differences between measured and predicted values to quantify variability in the dataset **[2]**. Then, prepare the finalized dataset for downstream statistical analysis **[3]**.

4.2.1. SCREEN: 69174_4.2.1.mp4 00:00-00:09

4.2.2. SCREEN: 69176_4.2.2.mp4 00:24-00:57

4.2.3. SCREEN: 69176_4.2.3-(1).mp4 00:00-00:12

4.3. After compiling all measured and predicted values into a single dataset, import them into statistical analysis software **[1]**. Calculate descriptive statistics to summarize cranial base and midfacial measurements across all subject groups **[2]**.

4.3.1. SCREEN: 4.3-(4.3.1,-4.3.2).mp4 00:05-00:21

4.3.2. SCREEN: 4.3-(4.3.1,-4.3.2).mp4 01:15-01:50
Video Editor: Please speed up the file

4.4. Use the non-parametric **Mann–Whitney U test** to assess differences in cranial measurements between groups **[1]**. Conduct a **Pearson correlation analysis** to determine the relationship between age and cranial measurements within each group **[2-TXT]**.

4.4.1. SCREEN: 4.4.1.mp4. 00:36-00:58

4.4.2. SCREEN: 4.4.2.mp4 00:05-00:22 **TXT: Generate boxplots and line graphs for results interpretation**

Results

5. Results

5.1. A strong positive correlation was found between NBa *(N-B-A)* and ZMR–ZML *(Z-M-R-Z-M-L)* in the normal group, as shown in the scatter matrix **[1]**, supported by a Pearson correlation of 0.992 **[2]**.

5.1.1. LAB MEDIA: Figure 1. *Video editor: Emphasize the top right panel showing clustered diagonal scatter of "Normal NBa" vs. "Normal ZMR–ZML".*

5.1.2. LAB MEDIA: Table 2. *Video editor: Highlight the Pearson Correlation value of 0.992 between "Normal NBa" and "Normal ZMR–ZML".*

5.2. Measured NBa values were consistently higher than predicted values across all groups, with the greatest deviation observed in the operated syndromic craniosynostosis group **[1]**. Measured ZMR–ZML values were significantly lower than predicted values in all groups, demonstrating considerable variability **[2]**.

5.2.1. LAB MEDIA: Figure 2. *Video editor: Highlight the orange and dark green boxplots under "SC operated" group showing "Measured Nba" and "Predicted Nba" values.*

5.2.2. LAB MEDIA: Figure 2. *Video editor: Highlight the blue and purple boxplots across all groups showing "Measured ZMR–ZML" and "Predicted ZMR–ZML" values.*

5.3. In the normal group, Pearson correlation analysis revealed strong associations between age in both NBa **[1]** and ZMR–ZML **[2]**.

5.3.1. LAB MEDIA: Table 3. *Video editor: Highlight the Pearson Correlation value of 0.917 for "Observed NBA" under "Normal" group.*

5.3.2. LAB MEDIA: Table 3. *Video editor: Highlight the Pearson Correlation value of 0.728 for "Observed ZMRZM" under "Normal" group.*

5.4. In the SC non-operated group, a strong correlation was observed only for ZMR–ZML, while the SC operated group showed weak correlations across all variables **[1]**.

5.4.1. LAB MEDIA: Table 3. *Video editor: Highlight the Pearson Correlation value of 0.772 for "Observed ZMRZM" in the "SC Non-Operated" group.*

5.5. Greater variability and wider interquartile ranges were observed in both NBa and ZMR–ZML values compared to the normal group in the SC operated cohort **[1]**.

5.5.1. LAB MEDIA: Figure 2. *Video editor: Highlight the taller boxplots for "Measured Nba" and "Measured ZMR–ZML" in the "SC operated" group compared to "Normal control".*

5.6. The ratio distributions for the normal control group were clustered around central values **[1],** while the operated and non-operated SC groups showed broader distributions with extreme values **[2]**.

5.6.1. LAB MEDIA: Figure 3. *Video editor: Highlight the boxplots for all four ratios under "Normal control".*

5.6.2. LAB MEDIA: Figure 3. *Video editor: Highlight the boxplots under both "SC operated" and "SC non-operated" groups.*

5.7. The SC operated group displayed a lower median ratio and reduced spread compared to the SC non-operated group **[1]**.

5.7.1. LAB MEDIA: Figure 3. *Video editor: Highlight the "SC operated" boxplots and the "SC non-operated" group.*

Pronunciation Guide:

 Sella (as in “sella turcica”)
Pronunciation link: https://www.merriam-webster.com/dictionary/sella
IPA: /ˈsɛlə/
Phonetic Spelling: SEH-luh
 Turcica (as in “sella turcica”)
Pronunciation link: https://www.merriam-webster.com/dictionary/turcica
IPA: /tərˈsɪkə/
Phonetic Spelling: ter-SIH-kuh
 Nasion
Pronunciation link: https://www.merriam-webster.com/dictionary/nasion
IPA: /ˈneɪʒən/
Phonetic Spelling: NAY-zhun
 Basion
Pronunciation link: https://www.merriam-webster.com/dictionary/basion
IPA: /ˈbeɪziən/
Phonetic Spelling: BAY-zee-uhn
 Zygomaticomaxillary
Pronunciation link: https://www.howtopronounce.com/zygomaticomaxillary
IPA: /ˌzaɪgəˌmætɪkoʊˈmæksɪˌlɛri/
Phonetic Spelling: zy-go-matih-ko-MAX-ih-lair-ee
 Hypoplasia
Pronunciation link: https://www.merriam-webster.com/dictionary/hypoplasia
IPA: /ˌhaɪpoʊˈpleɪʒə/
Phonetic Spelling: hy-po-PLAY-zhuh
 Craniosynostosis
Pronunciation link: https://www.merriam-webster.com/dictionary/craniosynostosis
IPA: /ˌkreɪniˌoʊsɪˈnɒstəsɪs/
Phonetic Spelling: KRAY-nee-oh-si--NOS-toe-sis
 Morphology
Pronunciation link: https://www.merriam-webster.com/dictionary/morphology
IPA: /mɔrˈfɒlədʒi/ or in American /mɔrˈfɑlədʒi/
Phonetic Spelling: mor-FOL-uh-jee
 Regression (as in “regression model”)
Pronunciation link: https://www.merriam-webster.com/dictionary/regression
IPA: /rəˈgrɛʃən/
Phonetic Spelling: reh-GRESH-uhn
 Euclidean (as in “Euclidean distance”)
Pronunciation link: https://www.merriam-webster.com/dictionary/Euclidean
IPA: /juˈklɪdiən/
Phonetic Spelling: yoo-KLIH-dee-uhn