



National Institute of Dental
and Craniofacial Research

Prediction of Skeletal Malocclusion in Non-syndromic Cleft Lip and Palate

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Introduction

- Cranial base morphology completes development at an early age, influencing the growth of the maxilla and mandible
- Craniofacial growth patterns in healthy individuals can be predicted using Geometric Morphometric Analysis (GMA) (*lab data, unpublished*)
- Non-syndromic cleft lip and palate (nsCLP) and skeletal malocclusion (SM) are complex traits that share genetic and environmental factors and may present as a combined phenotype

Hypothesis

The type of malocclusion can be predicted before puberty in individuals with nsCLP

Methods

1. Cone-beam computed tomography scans from:
 - 51 nsCLP patients at T1 (prepubertal) and T2 (skeletal maturity)
 - 307 healthy individuals with Class I, II, IIIA (maxillary hypoplasia), and IIIB (mandibular hyperplasia) skeletal Angle's Class
2. Annotation of 43 validated landmarks with sufficient coverage of the cranial base, maxilla, and mandible
3. Exporting of 3D Cartesian coordinates for the conduction of GMA
4. Principal Component Analysis to explore share variation
5. Prediction of SM at T1 with Discriminant Function Analysis (DFA)
6. Cephalometric-based skeletal diagnosis at T2 for confirmation of the T1 DFA-based prediction

Results

Table 1: Unaffected Subject Demographics

Angle's Class	N (%)	Age (years)	Sex (N)	
		Mean (range)	Male	Female
I	100 (32.6)	21.7 (13.7-58.7)	46	54
II	100 (32.6)	26.1 (14-65.4)	32	68
IIIA	29 (9.4)	26.0 (13.0-61.9)	15	14
IIIB	78 (25.4)	25.3 (12.0-58.2)	47	31
Total	307 (100)	24.5 (12.0-65.4)	140	167

Table 2: nsCLP Subject Demographics

Characteristic	N (%)	Age at First CBCT (years)*	Age at Second CBCT (years)*
		Mean (range)	Mean (range)
Left CLP	22 (43.1)	8.9 (6.0-14.0)	15.1 (12.0-19.0)
Bilateral CLP	14 (27.5)	8.7 (6.0-12.0)	15.7 (13.0-20.0)
Female	25 (49.0)	8.0 (6.0-11.0)	14.4 (11.0-18.0)
Total	51 (100)	8.6 (6.0-14.0)	15.1 (11.0-20.0)

*Confirmed via Cervical Vertebral Maturation

Table 3: Accuracy of T1 DFA-based Predictions

T2 Angle's Class	T1 Accurate	T1 Inaccurate
	N (%)	N (%)
I	0 (0)	5 (9.8)
II	7 (13.7)	1 (2.0)
IIIA	34 (66.7)	2 (3.9)
IIIB	2 (3.9)	0 (0)
Total	43 (84.3)	8 (15.7)

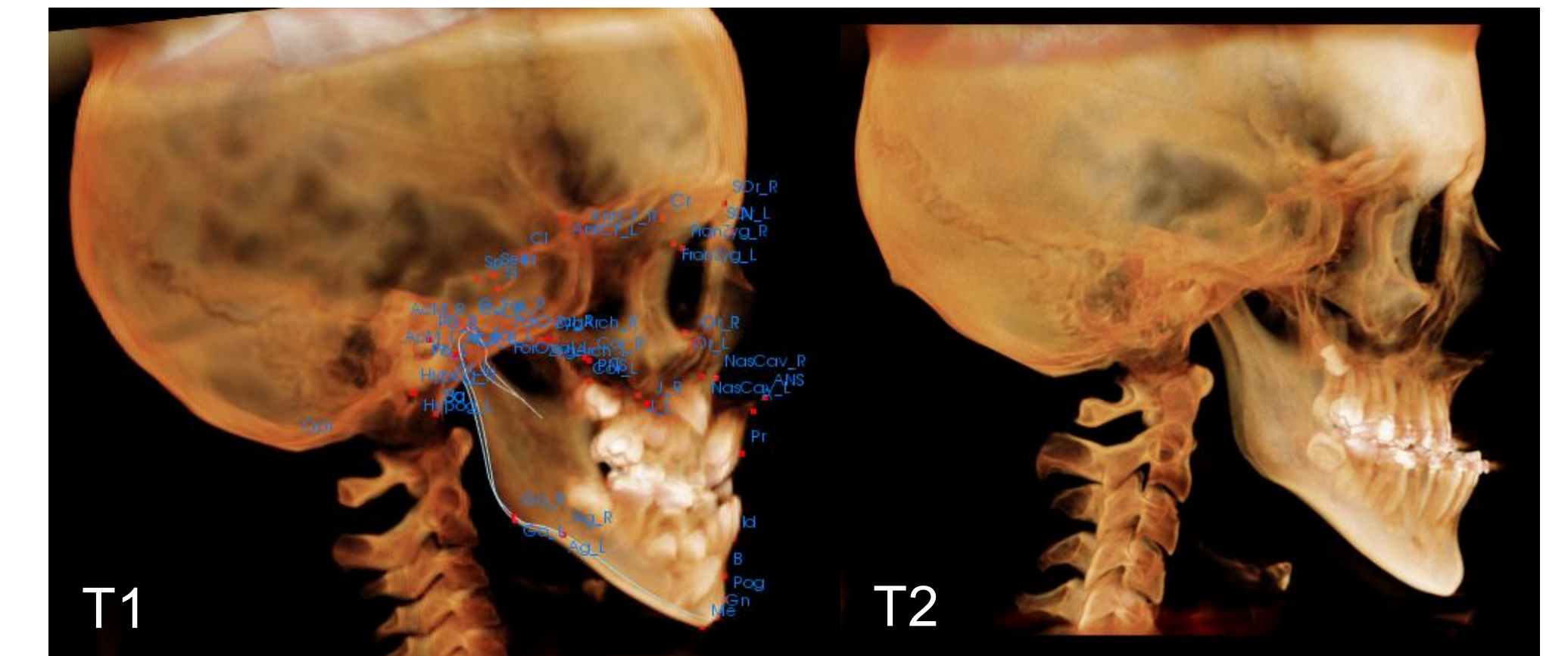


Figure 2: Subject with Class IIIB DFA classification at T1 (Left, 7 years) confirmed at T2 (Right, 13 years)

Conclusion

The malocclusion phenotype at skeletal maturity can be predicted with high accuracy (84.3%) before puberty

Recognizing the facial growth pattern can guide facial orthopedic treatment and may reduce the need for future orthognathic surgery

Currently unable to predict the final phenotype severity, and who may ultimately need orthognathic surgery after puberty

3D imaging and morphometrics demonstrate predictive capability; future work will incorporate Artificial Intelligence for model refinement and automation

Selected references

1. Liberton DK et al. Craniofacial Analysis May Indicate Co-Occurrence of Skeletal Malocclusions and Associated Risks in Development of Cleft Lip and Palate. *J Dev Biol* (2020)
2. Liberton DK et al. Development and Validation of Novel Three-Dimensional Craniofacial Landmarks on Cone-Beam Computed Tomography Scans. *J Craniofac Surg* (2019)

Acknowledgements

Research support was provided by the NIH Medical Research Scholars Program, a public-private partnership supported jointly by the NIH and contributions to the Foundation for the NIH from private donors

