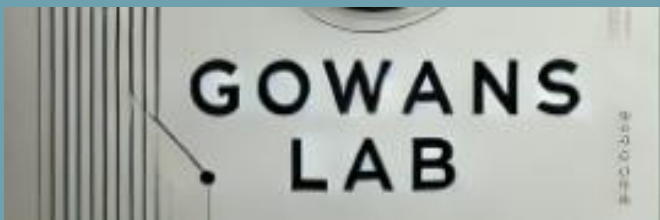




Subclinical Facial Endophenotypes in Multiplex Families with Orofacial Clefts

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INTRODUCTION

- Orofacial clefts (OFCs) are common congenital anomalies resulting from complex genetic and environmental interactions¹.
- Multiplex families are hypothesised to carry a higher burden of genetic risk factors.
- Beyond the overt clefts, evidence suggests that unaffected relatives in these families may exhibit subtle facial morphology, representing subclinical manifestations³



Figure 1: Cleft lip

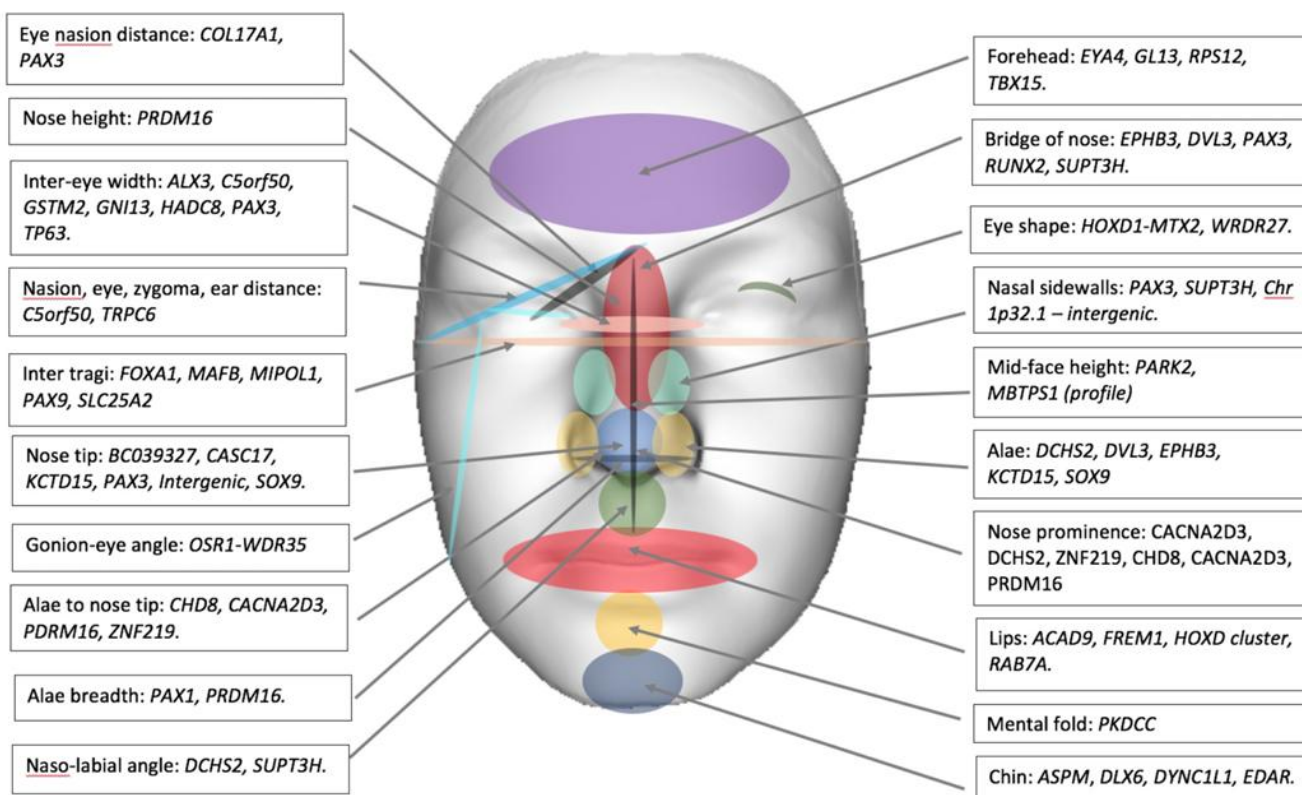


Figure 2: Genes associated with facial features in normal population. Shaffer et al. (2016)

Main Aim

- To investigate and characterise facial variations in multiplex families with OFCs compared to unrelated, unaffected controls.

Specific Aim

- To ascertain facial variations that may predispose affected families to OFCs, employing 3D facial morphometrics.

SUBJECTS AND METHODS

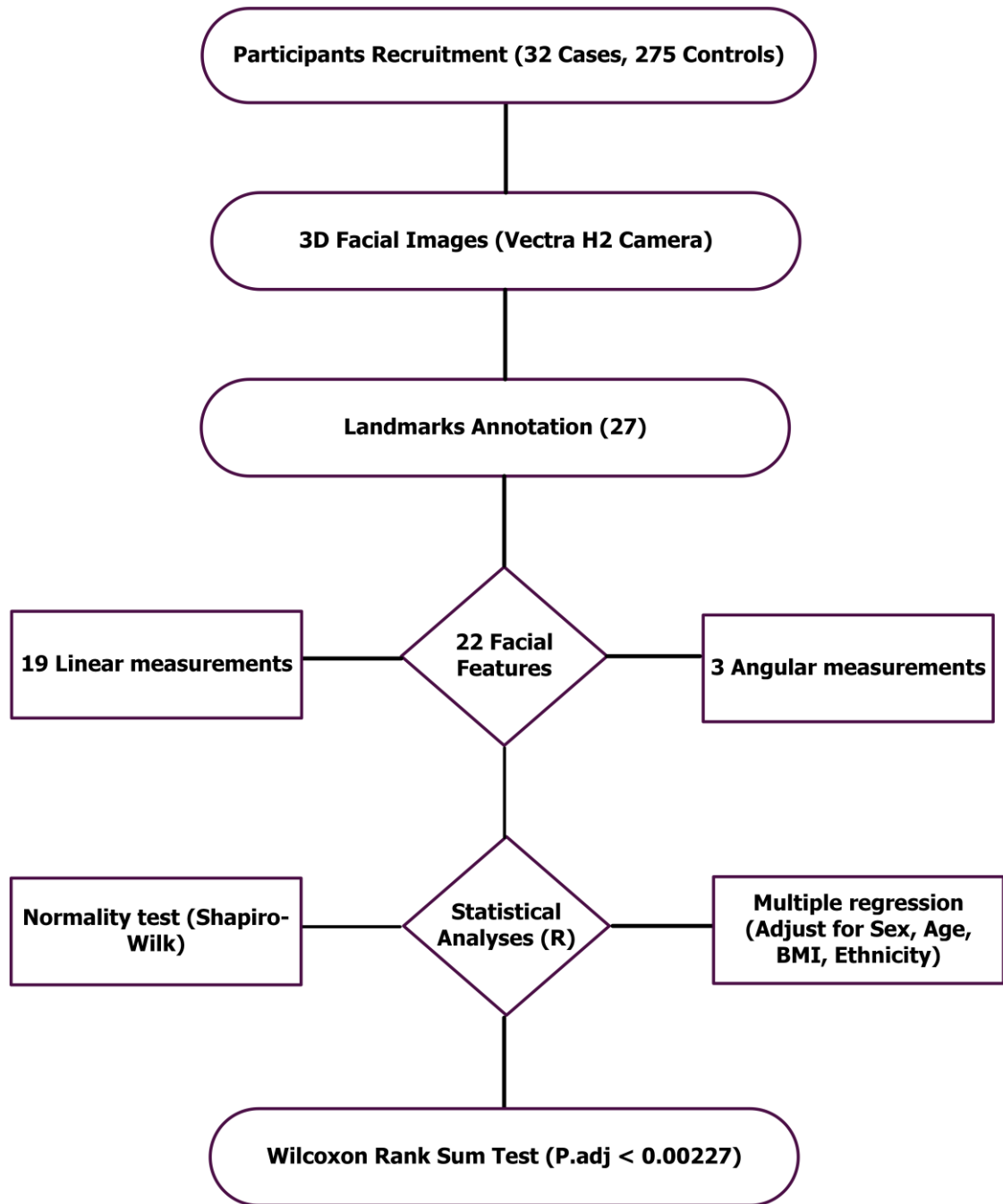


Figure 3: 3D facial morphometrics workflow

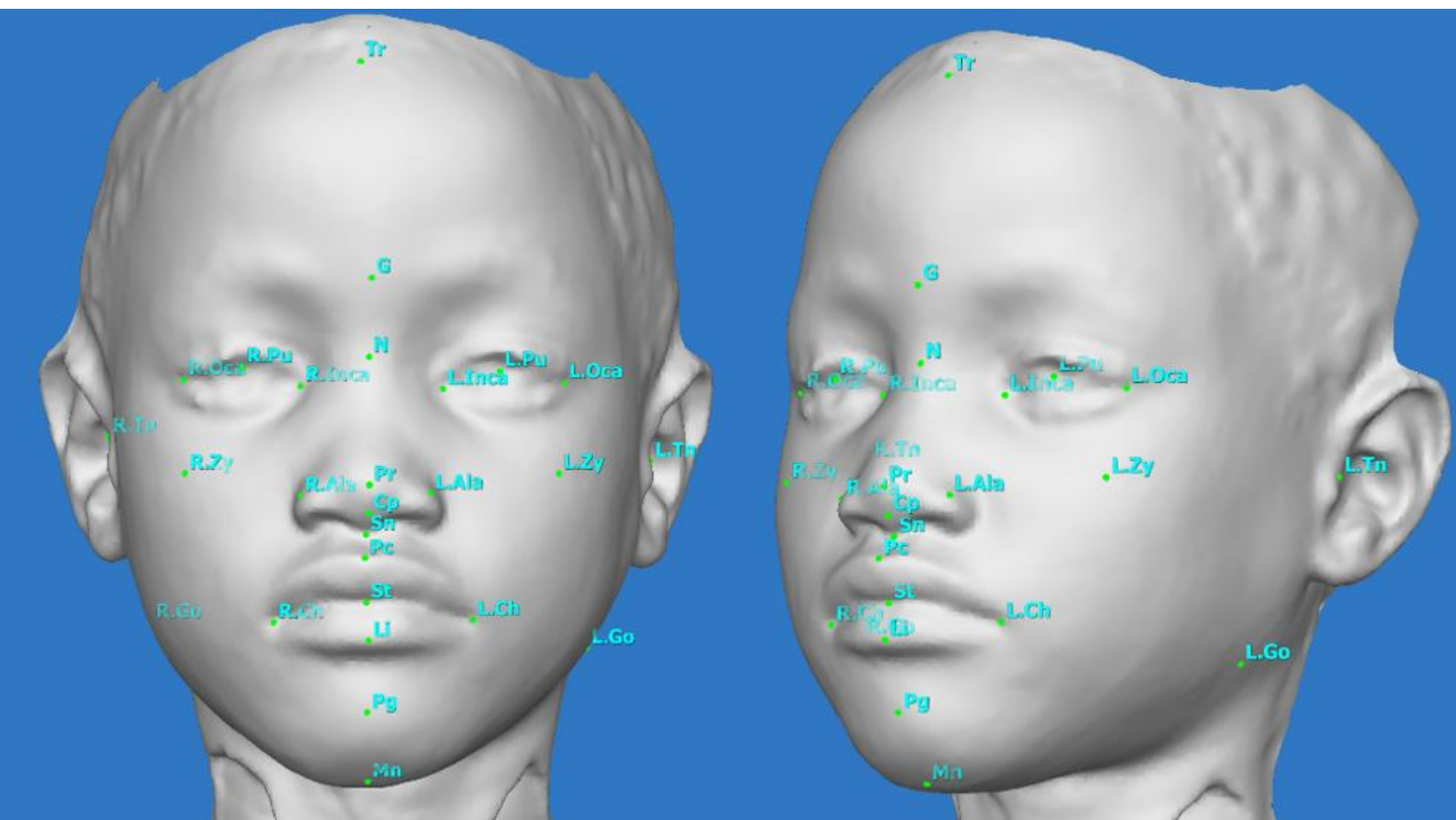


Figure 4: 3D image annotated with facial landmarks



Figure 5: 3D imaging Procedure

RESULTS AND DISCUSSION

Facial features between multiplex families and unrelated controls

Variable	Multiplex Families	Controls	P-value (adj)
Demographics			
Sex (M/F)	15 (46.9%) / 17 (53.1%)	101 (37%) / 172 (63%)	
Age (years)	22.94 ± 16.77	13.24 ± 1.5	
BMI (kg/m ²)	20.25 ± 16.77	19.26 ± 1.5	
Facial Features			
Intercanthal Width	36.54 ± 2.17	35.58 ± 0.66	0.065133
Interpupillary Distance	64.31 ± 3.01	63.27 ± 0.89	0.180216
Facial Height	128.2 ± 5.48	125.96 ± 2.51	0.019497
Upper Facial Height	84.1 ± 4.6	82.3 ± 1.74	0.032106
Lower Facial Height	70.66 ± 3.14	69.94 ± 1.82	0.072219
Mid Facial Width	92.57 ± 5.07	90 ± 1.82	0.063605
Lower Facial Width	115.92 ± 8.2	111.47 ± 3.04	0.03262
Alar Width	39.42 ± 3.23	37.53 ± 1.53	0.000713
Philtrum length	13.55 ± 1.44	12.81 ± 0.84	0.002388
Nasal protrusion	15.81 ± 1.08	15.25 ± 0.46	0.012984
Nasal Bridge length	52.13 ± 3.01	50.67 ± 1.54	0.019387
Nasal Height	62.18 ± 4.07	61.49 ± 2.47	0.595599
Labial Fissure length	50.92 ± 4.34	48.46 ± 1.41	0.023453
Facial Convexity	145.22 ± 1.72	145.67 ± 1.34	0.123227
Nasolabial Angle	94.06 ± 3.14	93.79 ± 2.75	0.565134
Nasofrontal Angle	141.07 ± 1.02	141.71 ± 1.55	0.000776
Palpebral fissure length	30.38 ± 1.26	31.04 ± 0.78	0.007106
Upper facial depth	116.05 ± 7.42	113.76 ± 4.65	0.048429
Low facial depth	140.03 ± 9.21	134.65 ± 3.23	0.012305
Alar length	23.3 ± 2.08	22.3 ± 0.87	0.010389
Outer canthal Width	95.12 ± 3.26	95.6 ± 2.94	0.821479
Mid facial depth	123.86 ± 6.8	120.82 ± 2.44	0.026462

Statistical significance

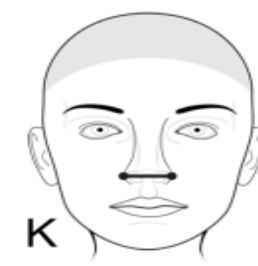


Figure 6: Alar width

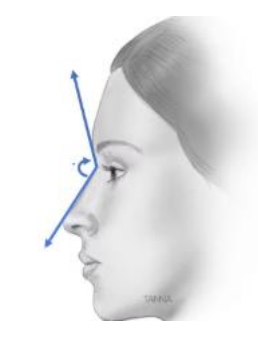


Figure 7: Nasofrontal Angle

RESULTS AND DISCUSSION

Facial features between unaffected family members and unrelated controls

Variable	Unaffected	Controls	P-value
Demographics			
Sex (M/F)	11(55%) / 9(45%)	101 (37%) / 172 (63%)	
Age (years)	26.95 ± 18.02	13.24 ± 1.5	
BMI (kg/m ²)	21.29 ± 4.74	19.26 ± 1.5	
Facial Features			
Intercanthal Width	37.1 ± 2.23	35.58 ± 0.66	0.001322
Interpupillary Distance	65.02 ± 3.12	63.27 ± 0.89	0.01037
Facial Height	129.66 ± 5.59	125.96 ± 2.51	0.001322
Upper Facial Height	85.3 ± 4.67	82.3 ± 1.74	0.002868
Lower Facial Height	71.42 ± 3.07	69.94 ± 1.82	0.024698
Mid Facial Width	93.76 ± 5.38	90 ± 1.82	0.001627
Lower Facial Width	117.91 ± 8.85	111.47 ± 3.04	0.00079
Alar Width	40.36 ± 3.28	37.53 ± 1.53	1.15E-05
Philtrum length	13.98 ± 1.36	12.81 ± 0.84	8.11E-05
Nasal protrusion	16.05 ± 1.17	15.25 ± 0.46	0.004881
Nasal Bridge length	52.87 ± 3.18	50.67 ± 1.54	0.001523
Nasal Height	62.42 ± 4.37	61.49 ± 2.47	0.643051
Labial Fissure length	51.88 ± 4.74	48.46 ± 1.41	0.001248
Facial Convexity	144.85 ± 1.75	145.67 ± 1.34	0.058306
Nasolabial Angle	94.6 ± 3.16	93.79 ± 2.75	0.134409
Nasofrontal Angle	140.87 ± 1.04	141.71 ± 1.55	0.000962
Palpebral fissure length	30.4 ± 1.24	31.04 ± 0.78	0.067584
Upper facial depth	118.03 ± 7.26	113.76 ± 4.65	0.006126
Low facial depth	142.4 ± 9.87	134.65 ± 3.23	0.000377
Alar length	23.88 ± 2.13	22.3 ± 0.87	0.000287
Outer canthal Width	95.78 ± 3.1	95.6 ± 2.94	0.278327
Mid facial depth	125.66 ± 7.1	120.82 ± 2.44	0.001769

Statistical significance

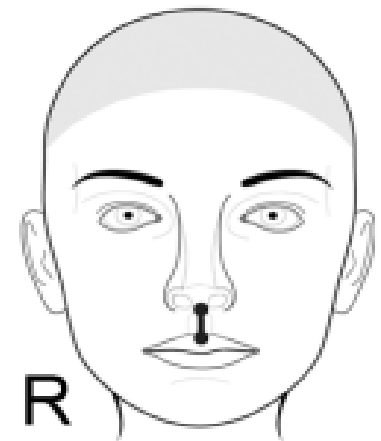


Figure 8: Philtrum length

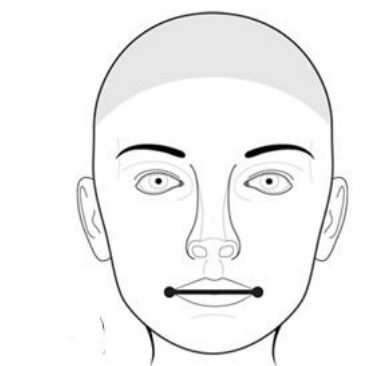


Figure 9: Labial fissure length

CONCLUSION AND RECOMMENDATION

- Multiplex families (MF) have relatively longer Alar width and a narrow nasolabial angle.
- Unaffected members of MF have sub-clinical phenotypes including longer philtrum, which may predispose them to OFCs.
- Our results on specific facial phenotypes in MF emphasize the value of a multifactorial approach in understanding OFC risk.
- Larger sample size is required to support observations on 3D facial features.

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