Developing 3D Craniofacial Morphometry Data and Tools to Transform Dysmorphology

Richard A. Spritz, M.D.
Professor and Director,
Human Medical Genetics and Genomics Program
University of Colorado School of Medicine,
Aurora, CO

Ophir Klein, M.D., Ph.D.
Chair, Division of Craniofacial Anomalies
Departments of Orofacial Sciences and Pediatrics
University of California, San Francisco
San Francisco, CA

Benedikt Hallgrimsson, Ph.D.
Alberta Children's Hospital Institute for Child and Maternal Health,
Department of Cell Biology and Anatomy,
University of Calgary, Calgary, AB, Canada

Washington Mio, Ph.D.
Department of Mathematics
Florida State University
Tallahassee, FL

Peter Hammond, Ph.D.
Institute of Child Health
University College London
London, United Kingdom

Our Current FaceBase 2 Project:

- Aim 1. Build a 3D facial scan “library” of craniofacial dysmorphic syndromes
- Aim 2. Extend the Geometric Morphometric toolkit to enhance discrimination of dysmorphic faces
- Aim 3. Validate and extend Dense Surface Modeling approaches to syndrome diagnosis
- Aim 4. Develop a prototype automated tool to assist clinical diagnosis of human syndromes

Aim 1. Build a 3D facial scan "library" of craniofacial dysmorphic syndromes

1. Initial plan 3 main sites: Denver, San Francisco, Calgary, ~~London~~
2. Current enrollment n = 620 (605 cases, 15 "familial controls)

i. 216 Chromosomal:

97 trisomy 21
31 Turner (XO)
30 4p-
17 11q-
10 12p+ (Pallister-Killian)
31 other

ii. 389 Syndromic:

33 Marfan
32 Achondroplasia
26 Pseudoachondroplasia
12 Hypohidrotic ED
17 Ectrodactyly ED
18 Stickler's
31 Loeys-Dietz
23 Cornelia deLange
13 Cohen
7 Kabuki makeup
5 Goltz
5 DiGeorge
5 Smith-Lemli-Opitz
5 Oculo-auricular-vertebral
3 Apert

etc.

Aim 1. Build a 3D facial scan "library" of craniofacial dysmorphic syndromes

Issues

1. Enrollment only ~2/3 of hoped for, largely because of loss of London and protracted IRB/hospital approval processes

Solution:

i. Adding extra clinics in Denver, SF, and Calgary
ii. Adding external sites already collecting 3D images of syndromes; reconsent for FaceBase (Brooke French, Denver, Colorado; Gareth Baynam, Australia; Chiarella Sforza, Italy; Tony Simon, Davis, CA; 33 more in current discussion)

2. Our current images taken using Creaform Gemini cameras; high quality, but require time-intensive manual image processing

Solution:

i. Purchased new 3dMD cameras for Denver, SF, Calgary
ii. Retain Gemini cameras for backup for enrollment schedule conflicts

Aim 1. Build a 3D facial scan "library" of craniofacial dysmorphic syndromes

Issues

3. Plan was to only image subjects with pre-existing molecular diagnoses. This proved impractical because:
    a. Many patients with "obvious" diagnoses never get molecular testing (availability, insurance, etc.)
    b. Most patients are coming to genetics clinics for diagnosis; once dx established, usually don't come back

Solution:

i. Image all patients with likely dx, "retrofit" images with dx if/when become available
ii. Requires time-consuming expert curation; hard to follow threads; difficult even with EMR, as clinical data and genetic data usually not linked; discussing how to achieve this now.
iii. Could Hub help, at least in building writeable database structure?

Aim 2. Extend the Geometric Morphometric toolkit to enhance discrimination of dysmorphic faces

1. Mio working to extend automated landmarking to dysmorphic faces
2. Mio and Hallgrimsson adding Monte Carlo methods that significantly enhance shape discrimination
3. Mio is learning generalized shape metrics and developing hierarchical methods to enhance dysmorphic syndrome discrimination
4. Plan to prioritize 32 pseudoachondroplasia images first (requested by Jaqui Hecht; will obtain through FaceBase)

Aim 3. Validate and extend Dense Surface Modeling approaches to syndrome diagnosis

1. Issue: This was to be done by Hammond, who has been deleted from FaceBase

Solution:

i. Mio has begun implementing dense surface modeling to quantitatively distinguish facial shape variation that changes with age, which cannot be obtained only from 3D landmark data.

ii. Mio is developing a method related to the Claes "Dysmorphometrics" method, but that learns from data using a generalized Procrustes metric that optimally discriminates a given set of syndromes, rather than requiring an ad hoc choice of metric.

Aim 4. Develop a prototype automated tool to assist clinical diagnosis of human syndromes

1. It was anticipated this might require collaboration with a commercial entity to produce a polished product with clinical utility.
2. An Israeli company, FDNA, has produced a free iPhone app (Face2Gene) that clinicans can use to take 2D photos and reference a private database for syndrome diagnosis; clinicians can also upload images of unknowns for private use.
3. We have begun discussion with Dekel Gelbman (President, FDNA) regarding collaboration in principal to:
    a. assess whether 3D might be better than 2D for syndrome discrimination
    b. assess whether 3D might be combined with 2D, the 3D "anchoring" the 2D to provide better syndrome discrimination