

Computer-aided facial recognition of individuals with FG (Opitz-Kaveggia) syndrome caused by p.Arg961Trp mutation in MED12

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FG (Opitz-Kaveggia) syndrome is an X-linked recessive syndrome characterized by relatively large head, frontal upsweep, hypertelorism, ptosis, small ears, broad and flat thumbs, imperforate anus, hypotonia, agenesis of the corpus callosum and moderate intellectual disability. The classical form of FG syndrome is caused by a recurrent p.Arg961Trp mutation in the MED12 gene. FG syndrome is misdiagnosed and recent literature confirmed that several patients with similar features had microdeletion/microduplication syndromes and syndromes caused by FLNA mutations.

With the advent of novel automatic face analysis techniques, our ability to analyze facial morphology from photographs has improved significantly. In this study we examined whether a computer-based dysmorphological analysis can be used in order to discern between FG patients and non-FG patients that present superficially similar facial features. For this, we used a collection of 18 genetically verified FG cases and 18 non-FG cases that were clinically suspected to be FG but do not carry mutations in the MED12 gene.

A modern face analysis system that was developed specifically for dysmorphological analysis was used. The system is fully automatic and starts by detecting the face in the image. Then, 130 facial fiducial points are localized and various measurements are taken. The final classification is based on these measurements as well as on a global "gestalt" detector that estimate the probability of the subject having FG based on the appearance of the entire facial image. A statistical technique called cross validation was used to estimate the recognition capability of the computer system. At each one of 20 rounds, the data was split randomly to training and testing data, each comprising of 50% of the samples.

The system was trained to separate between the two classes using the train dataset, and evaluated on the test data. The statistical power of the test in correct recognition of FG patients with the p.Arg961Trp mutation was estimated using the conventional recognition metric of average area under the ROC curve and was 90%, which is considered very high. The gestalt of the face as captured by multiple local patterns of facial texture contributed significantly to the correct recognition of the individuals with FG syndrome.

Overall, we have demonstrated that computer-based analysis can be successfully used in supporting experts for the correct recognition of patients with FG syndrome.

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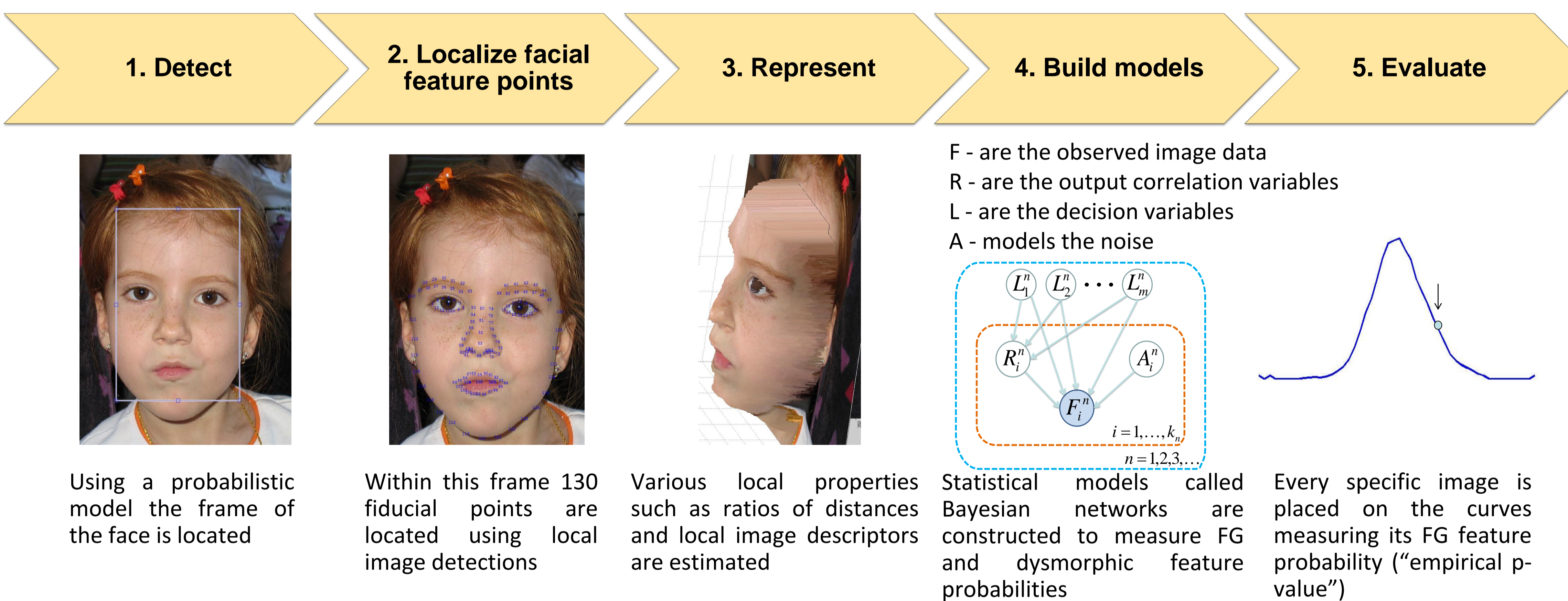
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General Image Analysis Pipeline



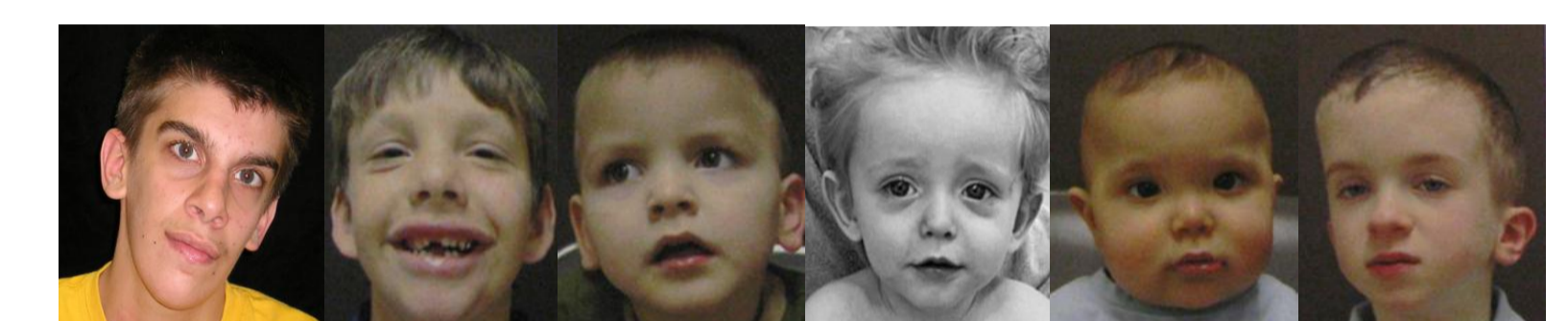
Training the System

Positive samples:



A collection of 18 genetically verified FG cases

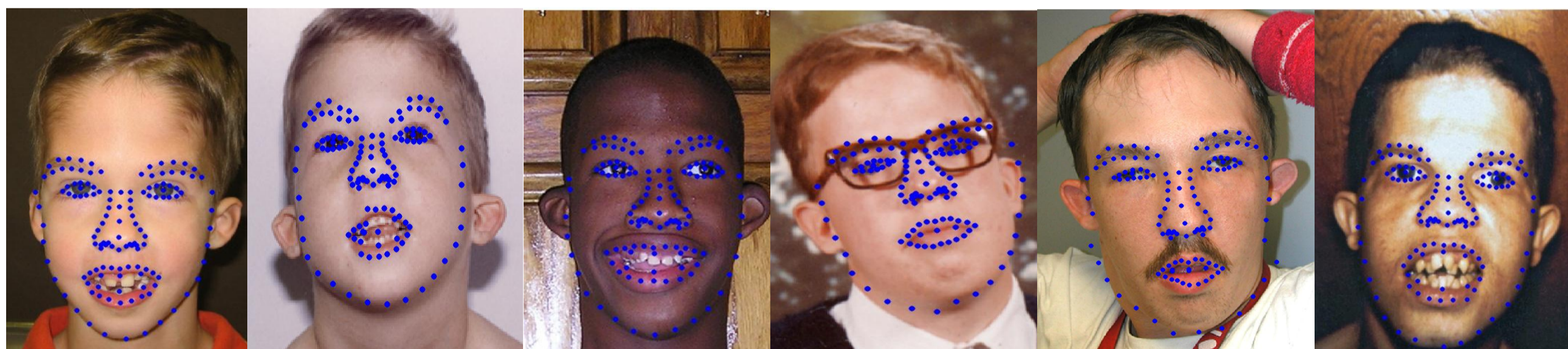
Negative samples:



A collection of 18 non-FG cases that were clinically suspected to have FG, but do not carry mutations in the MED12 gene.

Testing the System

Automatic facial contours analysis is used to extract relative measurements, fiducial points and dysmorphic feature evaluation



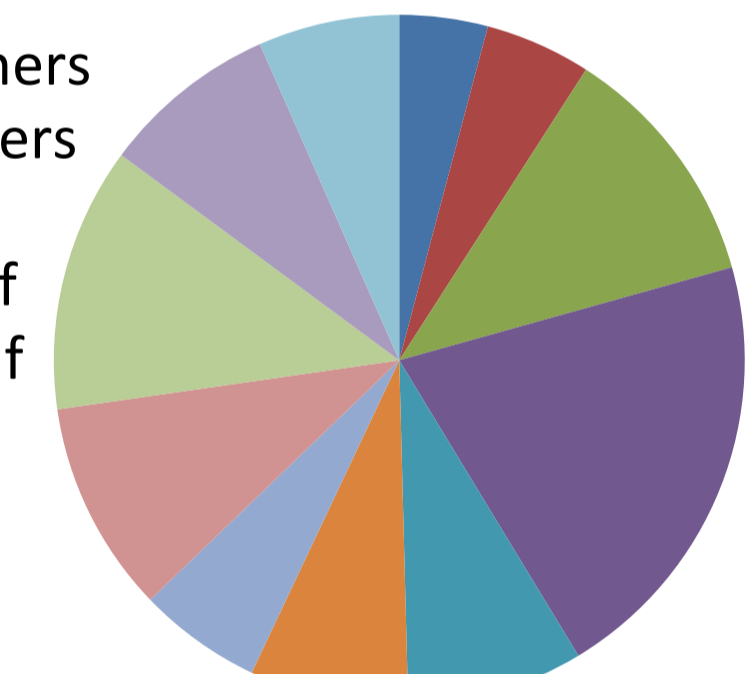
Facial points automatically located and used for feature detection and other measurements

A "gestalt" description of the face is used to evaluate the entire images at once



A heat map displaying distinguishable regions of FG patients

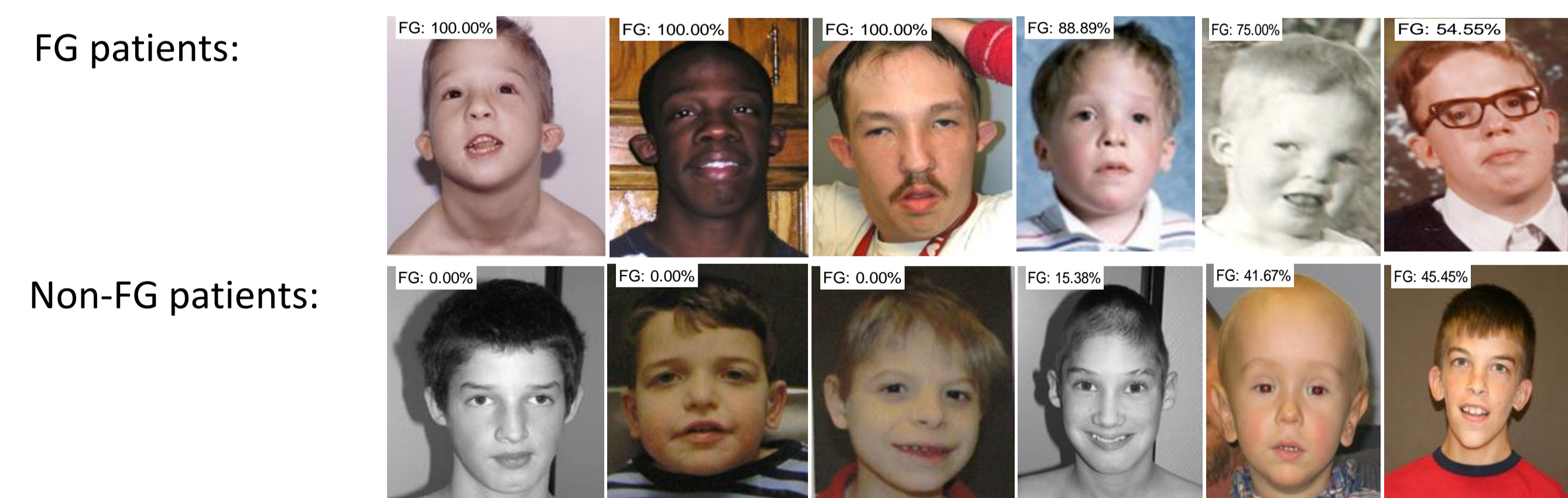
- Outer eye corners
- Inner eye corners
- Entire face
- Face lower half
- Face upper half
- Eyebrows
- Chin
- Ears
- Mouth



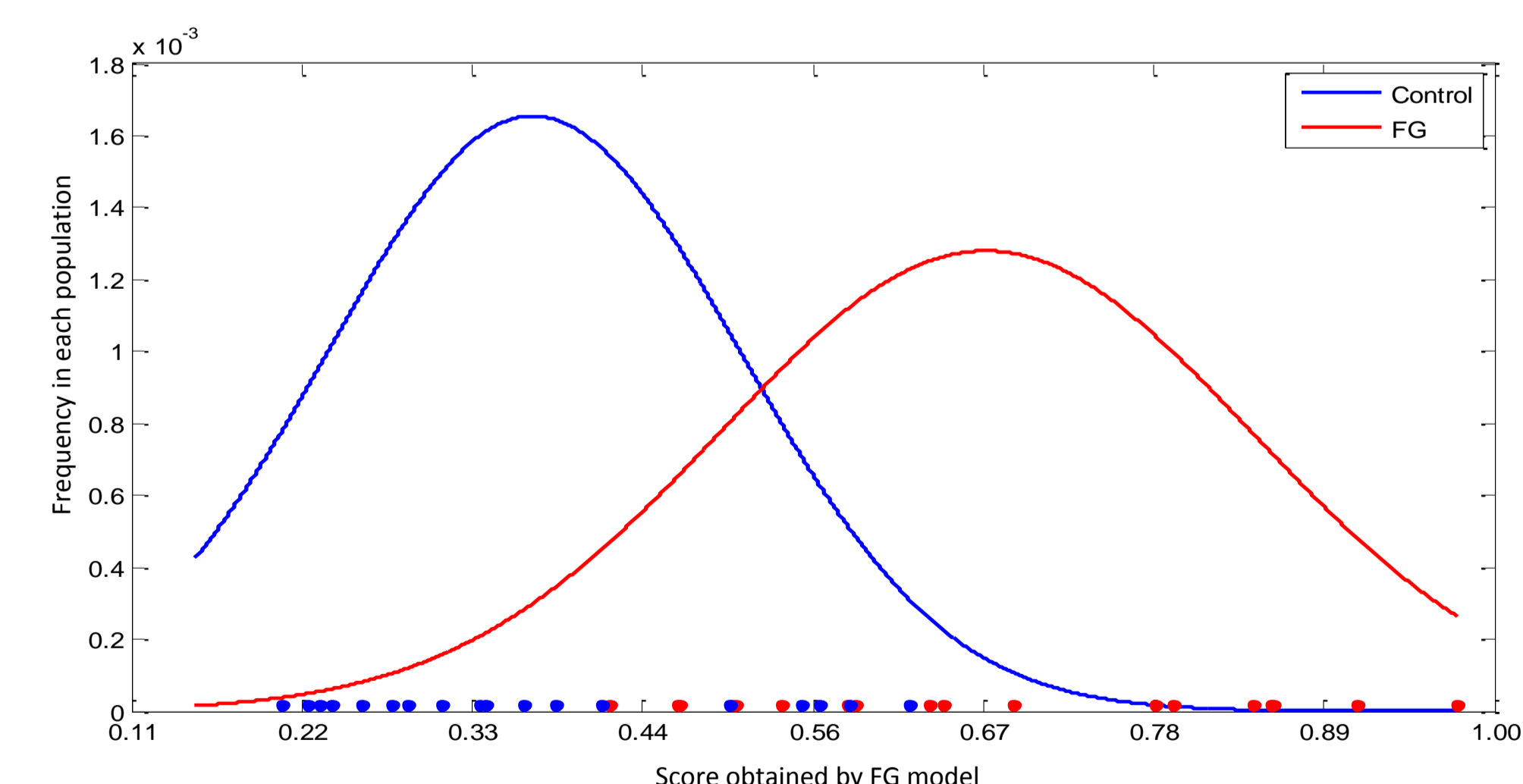
Relative contribution of each facial region

Results

The average ratio of the "Hit-Miss" (in %) in the cross validation process



Detection scores obtained for FG patients and non-FG control



The statistical power of the test in correct recognition of FG patients with the p.Arg961Trp mutation was estimated using the conventional recognition metric of average area under the ROC curve and was 90%, which is considered very high.

This demonstrates that computer-based analysis can be successfully used in supporting experts for the correct recognition of patients with FG.