Computer-aided facial recognition of Cornelia de Lange Syndrome (CdLS): a follow-up study

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CdLS is a genetically heterogeneous disorder, exhibiting a wide phenotypic spectrum. Approximately 70% of the clinically diagnosed CdLS patients are confirmed for a cohesin-related gene mutation. In "*Computer-aided facial recognition of Cornelia de Lange syndrome: a comparison to the recognition by human experts*" presented at the 2012 DSW workshop, the *FDNA*® technology successfully recognized facial dysmorphology associated with CdLS from 2D photos, producing results comparable with those of human experts. In this study, we collected and blindly tested 18 photos of probands with a molecularly-confirmed or clinical diagnosis of CdLS and 10 with confirmed diagnosis of various non-CdLS syndromes (e.g., *Kabuki, Aarskog, Dubowitz, etc.*). For each photo, the system produced a score above (positive) or below (negative) a threshold, determined from the results of the original study.

"*Computer-aided facial recognition of Cornelia de Lange syndrome: a comparison to the recognition by human experts*" presented at the 2012 DSW workshop

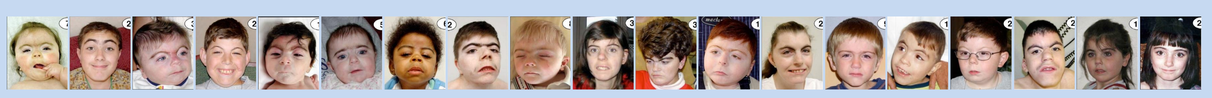
Previous Study Results

Summary

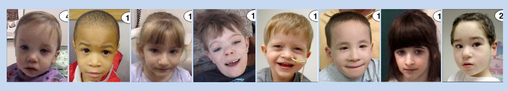
Cases	System Detection %	Human Experts Detection %
NIPBL	100	87
Mild or variant	67	54
Non - CdLS	89	90
Average	85.3	77

The computer systems accuracy places it at the 85th percentile of that of the surveyed experts

True Positives



True Negatives



False Negatives

Cases were challenging for human experts as well: three cases had SMC1L1 mutations and one was a mild familial case with no mutation.

False Positive

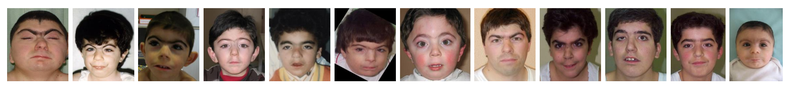
A patient with a subtelomeric 9q deletion, which can resemble CdLS

New Study Results

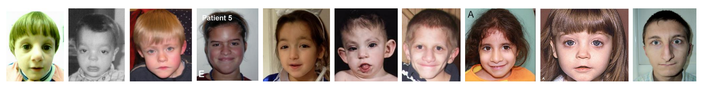
Summary

Cases	Correctly Detected/Total	System Detection% with New Threshold
NIPBL mutation (including 1 mosaic mutation)	4/5	100
SMC1L1 mutation	3/4	75
CdLS-like	5/9	80
non-CdLS	10/10	100

True Positives



True Negatives



False Negatives

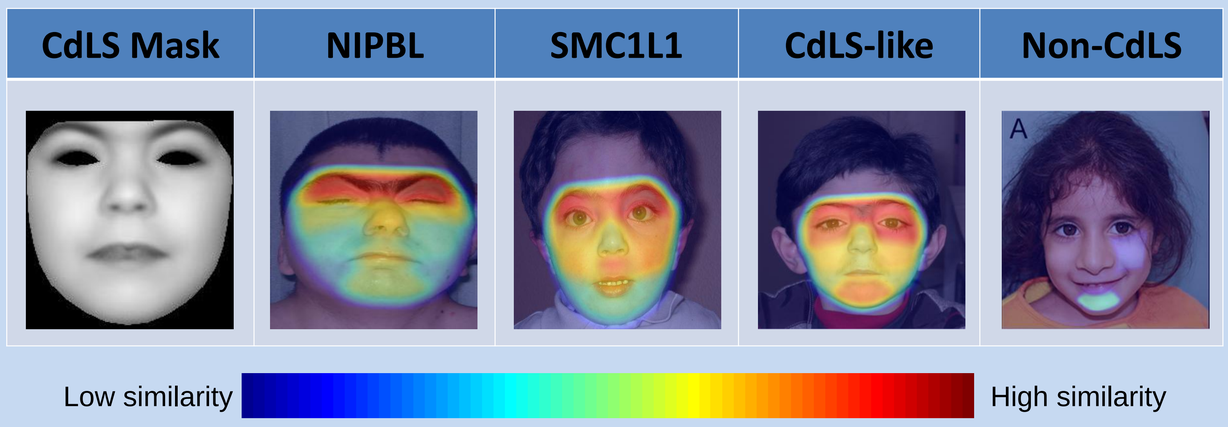
3 cases scored immediately below the threshold computed in the previous study

The remaining false negatives had a mild phenotype or did not meet clinical diagnostic criteria

Using the threshold computed in the previous study, the system achieved 67% sensitivity and 100% specificity. Decreasing the threshold increases the systems sensitivity to 83% while maintaining 100% specificity

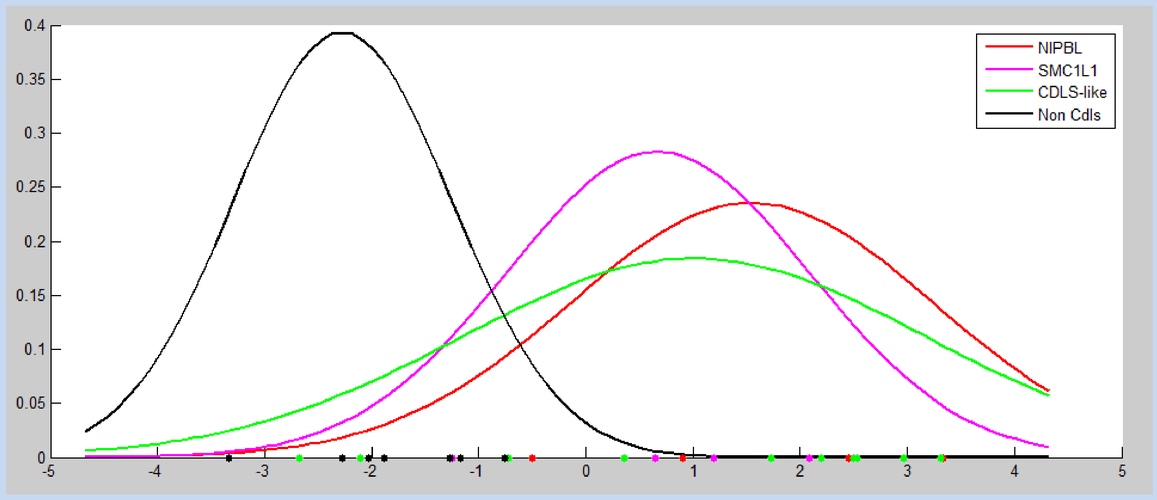
Study Analysis

FDNA® Heat Map Technology Analysis



- In CdLS, the most distinguishable gestalt feature is the eyebrow region
- CdLS similarity of the eyebrows in the non-CdLS patient was not detected

Distribution Curves for Detection Scores



Conclusions

Cases	System Detection% in Previous Study	System Detection% in New Study
NIPBL	100	100
Mild or variant	67	**75** (SMC1L1) **80** (CdLS-like)
Non - CdLS	89	100
Average	85.3	88.8

- Recognition of patients with a milder phenotype increased from 67% to 77.5%
- Detection of non-CdLS increased to 100%
- Correct detection increased 3.5% so now the computer-based recognition is **11.8% better than experts**

The results of the new study, show consistency with a slight improvement from previous study, suggesting that Computer-based analysis may be a helpful tool to support clinicians in the recognition of CdLS patients