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Tracking Facial Mobility and Recovery in Patients with Unilateral Facial Paralysis

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Short Running Head (no more than 40 characters in length):
Facial Movement   Facial soft tissue   Facial Paralysis   Facial Symmetry

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ABSTRACT

The objective of this study was to determine the longitudinal changes in facial soft tissue movements in patients diagnosed with acute, unilateral, flaccid facial paralysis who were followed for an approximate 12-week period. The expectation was that the patients would recover their facial movements, and it was hypothesized that at the end of the recovery period the patients' movements would be similar to that of the controls. The study sample consisted of two groups of adults: 36 patients and 68 controls. Longitudinal 3D facial soft tissue movement data were collected during different facial animations and compared with similar data collected from control subjects. Mean measurements of movement displacement, velocity, and asymmetry were computed for each group. Two sample *t*-tests were used to test for significant group differences, and linear mixed models were fit to test for significant changes over time in the patient group. Visual mapping of facial movements were computed using dynamic 3D statistical modeling of mean group movements and plots of mean vectors of landmark movement. The findings were that the patients initially had significantly less displacement and velocity of movement than the controls for both the paralyzed and unaffected sides of the face, and much greater movement asymmetry. By 12 weeks, the patients' mean measurements were closer to, but fell short of, the control values; however, there was considerable individual variation. Dynamic modeling and vector plots demonstrated abnormal directional movements of the paralyzed and non-paralyzed sides of patients' faces which could be isolated to specific areas. It appeared that the paralyzed side may tether movement of the unaffected side resulting in impaired aberrant movements of the entire face. Importantly, the control 3D facial mapping and plots were used to isolate and compare regions of paralysis for diagnosis and to assess outcomes of different treatment modalities in the patients.

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INTRODUCTION

Facial paralysis in the United States affects approximately 70 cases per 100,000 new individuals per year.[1] The estimated annual health care cost to treat these patients is on the order of two billion dollars—a figure based on average fees for emergency room visits, audiologic and electroneuronography testing, MRI imaging, and surgical intervention. The paralysis results from a broad array of pathologic conditions that may be congenital or acquired,[2-3] and patients have both impaired facial soft tissue movements or function as well as facial disfigurement. Treatment varies depending on the etiology. For example, patients with permanent paralysis may require more invasive treatments that include facial reanimation surgery,[4-9] while patients expected to recover from the paralysis (e.g. those with Bells palsy) may be treated with supportive measures and drug therapy.[1] Recently, our research team developed a suite of three-dimensional (3D) measures to characterize the condition and the temporal changes as well as a method for mapping the soft tissue movements.[10] Both the measures and mapping were demonstrated to provide an objective, comprehensive analysis that can be used for surgical planning and to assess outcomes of different treatments.[10] Previous outcome measures[11-19] have been based on 2D measurements[15-19] and subjective ratings,[11-14] both of which do not provide valid assessments of movement.

Given the ability to objectively quantify the disability in these patients using the 3D analysis and modelling, the objective of this study was to determine the longitudinal changes in facial movements in patients diagnosed with unilateral facial paralysis who were followed for an approximate 12-week period. Specifically, the magnitude, velocity, and asymmetry of patients' movements were measured and modelled during this period, and compared with the movements

of control subjects who had no facial disability. It was hypothesized that at the end of the period of follow-up, the patients' facial movements would be similar to that of the control subjects.

MATERIALS AND METHODS

Two groups of participants were recruited between June 2016 and March 2018:   Patients with acute, unilateral, flaccid facial paralysis (Bell's Palsy); and a group of age- and sex-frequency matched 'normal' controls. The patients were recruited when they first presented for treatment at the Facial Nerve Center at Massachusetts Eye and Ear Infirmary (MEEI) and they were invited to participate in the study by the treating surgeons. The control subjects were invited to participate either by personal contact with research associates on the study or by responding to a posted flyer/advertisement, and they included patients being treated at Tufts University School of Dental Medicine (TUSDM). Eligible participants were screened by telephone based on selection criteria (Appendix, Table 1), and those who agreed to participate attended TUSDM Facial Animation laboratory for testing and data-collection. Study consent and HIPAA documents were approved by the Tufts Health Sciences IRB. Prior to testing, the research assistant explained the purpose of the study and written consent was obtained. The patients were tested at three time-points: Within 6 weeks of presentation for treatment at MEEI (baseline visit; Visit 1), and then at 3 weeks (Visit 2) and 12 weeks (Visit 3) after baseline. The control participants attended for one test visit since there was little expectation that their movements would change substantially over the 12-week period. Facial movement/imaging, psychosocial, and basic demographic data were collected from the subjects at each visit. Here we present the results for the facial movement data.

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Data Collection and Processing

The data collection methods and analyses specific for facial paralysis were described in a previous publication,[10,20-27] and a brief summary is provided here. A video-based motion tracking system (Motion Analysis ™, Motion Analysis Corporation, Santa Rosa, CA, USA) was used to record the movement during eleven facial animations of 64, retro-reflective markers placed on specific facial soft tissue landmarks. The animations were gentle eye closure (gec), natural smile (nsm), and the following maximum movements— brow raise (br), tight eye closure (tec), "ee" sound (eeee), "oo" sound (oooo), smile (msm), grimace (gr), lip purse (lp), check puff (cp), and mouth opening (mo). Each animation was repeated ten times by the subjects. The raw data were tracked off-line. The tracked data consisted of a time series of 3-D vectors defined by x, y, z where x, y and z represented the position in space at 60 frames per second (60 Hz) for 4 seconds. Then, mean measurements of the displacement, velocity, and asymmetry of the landmarks were computed for each animation. For these calculations, patients' faces were standardized using reflection with the paralyzed side on the right, and for the purposes of comparison with the controls, a similar standardization was made of the control subjects' faces. To control for differences in facial size, the faces were scaled to the average facial size for the entire sample of patients and controls. To control for head motion of each subject, Procrustes rotation was used to fit the frames of data collected during each animation onto a standardized template.

Maximum Displacement. For a given subject and visit, the initial rest frames of each of the repeated movements from the eleven animations were selected and an average 'rest' frame with the positions of the landmarks was computed. The differences between the landmarks in the

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averaged rest frame and the landmarks in the frame at the maximum Procrustes distance from rest for each movement then was measured to give the average 'maximum' landmark displacement (mm) or the maximum average distance moved per landmark. The maximum Procrustes distances or displacements of the facial landmarks then were averaged over the ten repeated movements of each animation per subject to give a final mean movement score for each animation, and then the mean displacement for the patient and control groups was calculated per animation. *Movement Velocity.* For each repeated movement of an animation, and between successive frames of data, the unscaled Procrustes distances were measured in millimeters (mm) and the 99th percentiles of these distances computed. The velocity (mm/sec) then was measured and averaged over the ten repeated movements of each animation per subject, and the mean patient and control group velocity was calculated for each animation. *Mean Asymmetry.* For each animation, each subject's facial landmarks were measured at the position of maximum displacement. The faces then were reflected left to right and ordinary Procrustes analysis was used to match the landmarks in original and reflected faces, and the distances (mm) between the original and reflected landmarks were calculated. Distances increasing from '0' represented increasing asymmetry. The mean asymmetry for each subject, and subsequently, the mean asymmetry for each patient and control group was calculated.

Power Analysis.

Preliminary data to inform sample size determination for patients with facial paralysis using our methodological approach were not available. Therefore, sample size calculations were conducted from previous work on patients with unilateral cleft lip/palate (age range 5 to 21 years) and based on the maximum displacement measurement for the smile and cheek puff

animations (smile: patient mean=46.4mm, S.D.=2.3mm, control mean=55.7 mm S.D.=10.2;

cheek puff: patient mean=21.8mm S.D.=9.8, control mean=33.7mm S.D.=10.3). It was

anticipated that at baseline, patients with facial paralysis would have substantially greater

restriction in facial movement than patients with cleft lip/palate, and that their improvement

would be substantially greater. Given this background, it was determined that a sample size of

34 subjects per group, which is sufficient to detect a large effect size (ES >=0.80) using an

unpaired *t*-test approach at a level of significance of 0.05 and 90% power, would be adequate.

Because the estimation of change within each group had the advantage of each patient serving as

his own control, a sample size of 34 in the patient group was judged to be sufficient to detect a

lower effect size (ES >=0.60) with 90% power at 0.05 level. The power was set at a high level

given the use of estimates from a different patient population.

Statistical Analysis

The mean displacement, velocity, and asymmetry measures were compared between the

paralyzed (right) side of the face and the similar (right) facial side of the control face, and

between the unaffected (left) side of the face and the same (left) side of the controls. This

comparative side-to-side approach versus a full facial comparison was shown to produce similar

but more sensitive results.[10] Results for the full facial comparison are available upon request.

To test for significant mean differences in maximum displacement, velocity, and asymmetry

between the patients and controls, two sample *t*-tests were used. To test for significant mean

changes in the patients' measures over time, separate linear mixed models were fit with 'visit' as

a fixed effect, 'patient' as a random effect, and the response variables set as displacement,

velocity, and asymmetry.

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Dynamic 3D statistical modelling of the control group mean movements for each animation as well as vector plots were computed. These control computations serve as a comparison with similar mean computations (modelling and vector plots) of the patient group. The methodology was developed previously by Dr. Julian Faraway[25] and the software is available from https://github.com/julianfaraway/facer.

Because patients presented for their initial test at different times from almost immediately after the paralysis symptoms were first noticed to six weeks, a separate analysis was conducted to determine the effect of this variation in presentation for initial testing on the measures. The approximate date of first onset of symptoms was based on patient self-report. Separate plots for each animation were made of the date of baseline testing (or Visit 1) minus the approximate date of first onset of symptoms termed 'Days since Onset' versus (a) patients' Initial Displacement, (b) patients' 'Initial Velocity'; and (c) patients' Change in Displacement over the 12-week period, and (d) patients' Change in Velocity over the 12-week period. Simple linear models were used to check for a relationship between the variables in each plot.

RESULTS

During the recruitment period, 42 patients were eligible to participate in the study and six declined to participate. Of those who declined, five did not give a reason and one gave 'lack of time' as the reason. The final sample consisted of 36 patients (mean age = 43.3 yrs. ±12.9) and 68 control participants (mean age = 42.7 yrs. ±14.5). Of the 36 patients, two did not attend for the Visit 3 test and were lost to follow-up. Therefore, complete data were available for 34 patients. There were 18 males and 18 females. Five patients self-identified as Hispanic, one as

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Black, two as Asian, and 28 as Caucasian. Treatment involved non-invasive therapies except for one patient who had an eyelid weight placed: a procedure that the physician considered minimally invasive. Of the controls, four self-identified as Hispanic, five as Black, six as Asian, and 53 as Caucasian.

(1) Baseline (Visit 1) maximum displacement & velocity.

For the paralyzed side of the face, the mean measures of displacement and velocity (Appendix, Figures 1 & 2) were significantly less for the patients compared with the controls for all animations except gentle eye closure (gec) and mouth opening (mo). For the unaffected side, the mean displacement was significantly less for the patients during brow raise (br), cheek puff (cp), lip purse (lp), maximum smile (msm), and natural smile (nsm) (Appendix, Figure 3); and the mean velocity was significantly less during cheek puff (cp), 'ee' sound (eeee), lip purse (lp), maximum smile (msm), natural smile (nsm), and tight eye closure (tec) (Appendix, Figure 4). As expected, there were strongly significant differences in asymmetry between the patients and controls (Appendix, Figure 5). The asymmetry scores were greater for patients during all animations and ranged between 1.30 (gec) to 4.94 (msm) versus 0.90 (gec) to 1.62 (nsm) for the controls. Also, the variability in asymmetry on repeated movements was much greater for the patients.

(2) Changes over time (patients only)

Appendix, Tables 2 to 6 give the mean values for displacement, velocity, and asymmetry for each animation at baseline (Visit 1), three weeks (Visit 2), and twelve weeks (Visit 3) as well as the changes that were significant between Visits 1 to 2 and Visits 1 to 3. Appendix Figures 6 to

8 is a graphical display of these changes. The tables and figures show that at Visit 2, the patients' mean values for the three measures moved closer to the control means. Ultimately, at 12 weeks, the values for maximum displacement and velocity were closer to, but still less, than the control values. For asymmetry, the patients' mean scores also were closer too, but remained greater than, the control means for all animations. Furthermore, observation of the difference in the slope of the lines in Appendix, Figures 6-8 between the two time periods (Visits 1 to 2 and Visits 2 to 3) demonstrated that for most of the animations, the changes occurred at a faster rate during the first three weeks when compared to the subsequent nine weeks.

(3) Dynamic 3D statistical modelling and vector plots

The dynamic modeling for the mean maximum smile movement of the control group (control-msm.mov) is seen at: https://tufts.box.com/s/f8yqq27zycrxk8wgvb2pc5ibepdkmyzr and Figure 9 shows the mean control vector plots for the smile generated from the 68 control subjects. The control dynamic modeling and vector plots for all eleven animations are provided at: (https://tufts.box.com/s/rta28ylpz03bif7eint7skr1g5kasbta). A patient's mean facial movements can be statistically and dynamically modeled and compared to these mean control movements and plots. For example, consider patient 003 (Figure 10 a & b) the dynamic modeling seen at: (https://tufts.box.com/s/0tanhg3zzn0u8azzw5towcfe9ric8bry) shows the mean maximum smile movement for this patient (open red circles) superimposed on the mean control smile movement (solid black circles) at Visit 1 (FP003v1msm.mov), Visit 2 (FP003v2msm.mov), & Visit 3 (FP003v3msm.mov). Figure 11 gives the frontal views of the mean vector plots for the maximum smile movement of the patient at each Visit which can be compared with frontal view of the mean control smile in Figure 9.

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(4) Days since onset of symptoms of paralysis

For all the animations, there was a significant relationship (p≤0.05) between the 'Days since Onset' versus the 'Change in Displacement' for the brow raise (br), maximum smile (msm), and the natural smile (nsm) animations. A similar significant relationship was seen for the 'Change in Velocity' but the cheek puff (cp) and lip purse (lp) animations also demonstrated a significant relationship. The relationship indicated that the change in displacement and velocity was slightly less the longer the delay of the initial test. The results for the linear fit of the plots of 'Days since Onset' versus the 'Initial Displacement', and 'Days since Onset' versus the 'Initial Velocity' demonstrated no significant relationship.

Commented [JF5]: I would characterize this relationship as weak. Although some of the animations are significant, others are not. There is something but it's not a large effect. Would not oversell this.

DISCUSSION

Patients presented with unilateral facial paralysis of varying severity. As expected, the magnitude and velocity of their facial soft tissue movements were affected by the paralysis, and the facial impairment and asymmetry was greatest when they first presented for testing. These baseline findings were similar to those reported previously by our research group using a smaller subset of ten patients and control subjects,[10] and confirmed with this much larger subject sample. Recovery over the 12-week period was substantial but the patients remained with residual impairment, a finding that did not support full recovery by 12 weeks. There was, however, considerable variability in recovery ranging from minor to substantial. Other investigators have reported similar variability. For example, Patterson and Adams (2012) found that patients may notice improvements in symptoms after two to three weeks but complete recovery may take three to six months.[28] Murthy and Saxena (2011) reported that about two-thirds of patients with Bell's palsy recovered completely within six months while the remaining one third had incomplete

recovery with residual effects.[29] In addition, patients who did not show signs of recovery by six

weeks were more likely to have severe nerve damage and very delayed recovery.[28] We found no

relationship between the days since symptoms were first noticed and patients' initial movement

probably because the patients had varying degrees of paralysis on entering the study. When the

days since symptoms were first noticed was related to recovery (Appendix, Figure 12), those

patients who had their initial testing at 10 to 20 days after the onset of their symptoms, which

was the vast majority of patients, experienced a wide range of recovery from minimal to

substantial. Six patients had their initial testing at 20 to 30 days after the onset of symptoms, and

they had less of a range of recovery but the recovery was moderate to substantial. Of the four

patients tested greater than 30 days after symptom onset, three had minimal recovery, and these

latter three patients (denoted by X in Figure 12) had minimal movement on initial resting. This

finding may suggest that these three patients had more severe paralysis and/or had additional co-

morbidities that negatively affected their recovery necessitating a longer recovery time.

Interestingly, patients also demonstrated impaired movements in terms of limited

displacement and velocity as well as movement vectors of the non-paralyzed side of the face.

This impairment was most apparent during movements concentrated in the middle and lower

facial regions that involved the use of larger muscle groups, movements such as the smile, lip

purse, and cheek puff. A possible explanation for this finding may be due to altered behavior of

the patients who themselves may limit their movements to lessen the effect of the paralysis;

however, this explanation is very unlikely as the patients were instructed to, and did, perform

maximum animations. A more likely explanation relates to the anatomy of the facial muscles.

For example, consider the orbicularis oris which spans both sides of the face and is connected to

the levator muscles on each side. Contraction of the levators on one side of the face affects movement on the opposite side via the orbicularis oris. It is likely that the paralyzed side of the face may act as a weight and tether or limit the muscle movement of the unaffected side. Thus, in patients with unilateral facial paralysis, the muscles on both sides of the face are impaired and there is no 'normal' functioning side.

As an example, the dynamic modeling comparisons demonstrated clearly that Patient 003 had severe paralysis of the right side of the face at the Visit 1 (baseline). The lack of movement on the paralyzed side is shown by the difference between the red (mean patient movement) and black (mean control movement) circles during the smile movement. It is clearly apparent that the unaffected side of the face also shows abnormal movements. At Visit 2, this patient shows substantial improvement in movement, and by Visit 3, the movement is almost similar to that of the controls. Figure 11 are the mean vector plots of this patient's smile at Visits 1, 2, and 3 which should be compared with the mean vectors for the control smile (Figure 9). These plots provide an alternative way to localize the patient's movement deficits. This vector analysis provides a very sensitive quantification of an individual patient's facial paralysis and can be targeted to specific zones or regions of the face.

The velocity of movement is an important addition to displacement as an outcome measure of facial soft tissue impairment especially for patients that require facial reanimation surgery particularly to effect the smile. The surgical approaches for smile reanimation are perhaps the most disjointed, least systematic, and most controversial with no fewer than ten muscles described for reconstruction[30-31] and varied choices for the donor nerve, for example, the facial

(cross face nerve graft), trigeminal, and/or hypoglossal to name a few. Surgeons must clearly identify superior neurorrhaphy techniques and routes across the face during cross face nerve grafting. Recent studies support very positive outcomes with gracilis muscle transfer, and these outcomes are markedly different depending on the choice of innervation for the transplanted muscle.[32-37] Trigeminal innervation tends to produce greater magnitude of movement during smiling but lacks spontaneity while facial nerve innervation via a cross-face nerve graft produces good to excellent spontaneity with less movement magnitude leading surgeons to perform dual innervation grafts to produce the desired outcome—magnitude and spontaneity. As such, a measure of movement velocity is vital to assess spontaneity of movement. In addition, multi-vector muscle insertion techniques during gracilis muscle insertion[37] have become a clinical reality heightening the importance of dynamic 3D modeling and vector analyses of movement, as described in this study, to objectively assess surgical outcomes.

More recently, a novel treatment has been proposed that utilizes biomimetic implantable, real-time, closed-loop facial pacing devices that mimic movements in the paralyzed side of the face.[38-40] These devices record and process a biopotential signal when the presumed healthy side of the face moves which can be processed in real-time to create a train of electrical pulses that would initiate an artificial movement on the paralyzed side. A concern for some patients is undesirable facial activity due to aberrant neural regeneration or nerve transfer procedures.[40] Jowett et al. (2019)[40] demonstrated 'proof of principle' for a similar implantable neuroprosthetic device that provided the needed stimulation to the paralyzed side of the face while blocking undesirable muscle activity. Importantly, the longitudinal mapping of both normal facial movements and movements of patients with unilateral facial paralysis as demonstrated in this

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study, in addition to aiding in surgical planning and outcome assessment, can be used to support the development and training of these implantable, facial pacing devices by informing clinicians on their precise placement and the signal strength needed to facilitate movements in the required 'paralyzed' facial zones until the recovery process has been completed.