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Functional Breathing Improvement Following Treatment with Maxillary Skeletal Expander

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Functional Breathing Improvement Following Treatment with Maxillary Skeletal Expander

A thesis submitted in partial satisfaction of the requirements for the degree Master of Science in Oral Biology

by

Boshi Zhang

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ABSTRACT OF THE THESIS

Functional Breathing Improvement Following Treatment

with Maxillary Skeletal Expander

by

Boshi Zhang

Master of Science in Oral Biology

University of California, Los Angeles, 2018

Professor Won Moon, Co-Chair

Professor Kang Ting, Co-Chair

Improving breathing for patients with obstructed airway has been heavily researched in recent years but continues to be a challenge clinically for medical practitioners including otolaryngologists, plastic surgeons, and dentists. In children with enlarged tonsils, adenotonsillectomy, partial tonsillectomy and lingual tonsillectomy are effective treatments. There are also various non-surgical treatments for obstructive sleep apnea in children including intra-nasal steroids, other anti-inflammatory medications, and oral appliances, but none of them are proven to be safe and effective.

Various forms of rapid maxillary expansion have demonstrated airway improvement but further studies are necessary to show consistent and reproducible results. The Maxillary Skeletal Expander (MSE), anchored by four palatal mini-implants, has become an increasingly more

common option for patients who may not respond to traditional RME. Additionally, expansion of the maxilla by the MSE occurs more by horizontal translation and less tipping than a RME expander. The goal of the study is to investigate the role of MSE in airway improvement using objective measurements including Peak Nasal Inspiratory Flow (PNIF) and Peak Oral Inspiratory Flow (POIF) as well as subjective measures of breathing such as the Visual Analog Scale (VAS) and Nasal Obstruction Symptom Evaluation (NOSE). Furthermore, nasal septum deviation will be measured and correlated with objective measurements of breathing.

The results indicated that MSE produced improved functional breathing. Following MSE treatment, increases in total PNIF, left PNIF and right PNIF were significant at $p<0.0001$. Increase in POIF was significant at $p<0.01$. Patients reported decreased troubled breathing based on total VAS ($p<0.01$), left VAS ($p<0.01$) and right VAS ($p<0.001$). PNIF and VAS were correlated on each side in pre- and post- MSE groups while PNIF change and VAS change were correlated on the right. Additionally, an increase in nasal septum deviation to the left was correlated with an increase in PNIF on the right although this was not seen in the contralateral side.

If treatment with an MSE indeed raises objective and subjective measurements of airway, we may conclude that MSE is a possible treatment alternative for obstructive sleep apnea. This study has the potential to reshape the current standards for treatment of OSA creating an innovative, but less invasive cure for a large proportion of the population who suffer from OSA during sleep, have loss of daytime functionality, and have a host of co-morbid conditions.

The thesis of Boshi Zhang is approved.

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Significance Statement

Current treatment with oral appliances treat the symptoms and do not cure underlying cause of disease which is rooted in anatomical abnormalities. Surgical intervention is often rejected by the patient due to its invasiveness, morbidity, and potential complications. The long-term objective of the project is to establish MSE as a treatment alternative for Obstructive Sleep Apnea. This particular study will produce data on the subjective and objective measurements of breathing. These values will be correlated with one another to establish the relationship between different measures and verify that airway improvement has indeed occurred.

However, establishing the MSE as recognized treatment modality for OSA will require all evidence from current studies to be joined together. This includes the volumetric changes in skeletal tissues of the nasopharynx and changes in the soft tissues of the oropharynx as measured by CBCT before and after MSE treatment. Soft tissue changes of the entire face as measured from 3dMD will also give insight into anatomical changes. Data from computational fluid dynamics are needed in conjunction with anatomical changes to detect areas of turbulence, which may not be explained by simple volume changes. Additionally, data from current sleep monitor studies are important in directly measuring the episodes of apnea and hypopnea. The values from all these different studies will be correlated with the values in this current study to provide a complete image of the effectiveness of MSE treatment on the airway.

If treatment with an MSE indeed raises objective and subjective measurements of airway, we may conclude that MSE is a possible treatment alternative for obstructive sleep apnea. Treatment with MSE would target the cause of disease by expanding skeletal and soft tissue structures allowing for improved airway function. Many current treatments for OSA involve oral appliances, which target the symptoms but are not able to achieve permanent airway

improvement. Treatments that do target the cause of disease including tonsillectomy and orthopedic surgery are very invasive with high morbidity. MSE could be a non-surgical alternative to achieving orthopedic movement to correct an impinged airway. If decreased NSD is indeed correlated with airway improvement following MSE treatment and MSE treatment improves NSD, NSD may be used an indication for the need for MSE. Additional studies will need to be conducted to verify the degree to which septum deviation is the cause of airway impingement. This study has the potential to redefine standard treatments for obstructive sleep apnea with a non-invasive cure for the disease that is afflicting a major portion of the world population.

Introduction

The prevalence of obstructive sleep apnea (OSA) has increased dramatically in the last 30 years as a result of increased obesity[1]. The current prevalence is 36.1% in men and 11.4% in women at the ages of 30-49 and 60.6% in men and 36.9% in women at the ages of 50-70[2]. Patients with OSA have nearly double the health care cost of patients without. The cost of medical co-morbidities is estimated to be $3.4 billion in a year[3-4]. These comorbidities include stroke, hypertension, other cardiovascular disease, insulin resistance, and atherosclerosis.[5-7]

The treatment for OSA, while heavily studied, remains problematic. There are various non-surgical treatments for obstructive sleep apnea including intra-nasal steroids, other anti-inflammatory medications, and oral appliances, but none of them are proven to be safe and effective[8]. In children with enlarged tonsils, adenotonsillectomy, partial tonsillectomy and lingual tonsillectomy are effective treatments.[9] CPAP has been shown in a Cochrane systemic review to be the gold standard for the treatment of OSA.[10] However, even this treatment requires

more long-term follow-up studies and is only able to control the symptoms rather than treat the cause of disease.

Although OSA is traditionally treated by otolaryngologist, an orthodontist who frequently sees a patient may be the first medical professional to detect OSA. The dental profession offers a range of possible treatments which have the potential to treat the cause of disease and permanently improve the airway. Rapid Maxillary Expansion (RME), which is commonly used in young patients to expand the palate, has been studied extensively. RME is shown to increase the size of the upper nasopharynx.[11] Additionally, RME increases upper middle and lower airway volume and oxygen saturation in patients with posterior crossbite.[12] Although RME has a positive effect on the apnea/hypopnea index, airway volume, and oxygen saturation, but these measures do not correlate with one another and additional studies are needed.[13] The increases the nasal cavity volume as a result of RME treatment has been shown to improve quality of life and respiratory symptoms based on questionnaires.[14]

Another potential treatment for OSA is surgically assisted rapid maxillary expansion (SARME), which is also shown to increase the volume of the nasal cavity.[15] Both Tooth-borne and bone-borne SARME showed that nasal airway volume increased after treatment.[16] SARME also increases the volume of the middle and lower pharynx.[17] Following SARME, expiratory and inspiratory flow increases over time, resistance decreases, and nasal breathing improves as measured by the Visual Analog Scale.[18]

A new innovative form of palatal expansion called micro-implant assisted rapid palatal expansion (MARPE) is beginning to be adopted in orthodontics for patients who have a fused palatal suture and have a transverse discrepancy, but want to avoid surgery. In fact, expansion of the maxilla with MARPE occurs more by horizontal translation (orthopedic movement) and less

tipping (dental movement) than a RME expander.[19-21] MARPE has may also have the potential to correct skeletal class III relationships through protraction of the maxilla when used in conjuction with facemask therapy. [22-24.]

To date, there are no conclusive studies that demonstrate the effectiveness of MARPE on improving the airway. Hybrid RME, an expander anchored by posterior teeth and two anterior palatal TADs, combines dental and orthopedic movements. Studies of Hybrid RME show improved airway rhinological effects compared with traditional RME.[25] MARPE, which shows more orthopedic movement compared to RMEs, should show more significant airway improvement. One study on the effect of mini-screw implant borne expander and RME expander on the airway was inconclusive, showing variable data and unclear changes in airway volume as measured by CBCT.[26] Through subjective and objective measurements, this current study seeks to evaluate airway improvement by MSE, a newly developed form of MARPE which shows improved functionality in skeletal expansion compared with previous expanders.

There have been various subjective and objective measurements that have been validated for evaluating the effectiveness of treatments of OSA. One such measure is Peak Inspiratory Nasal Flow (PNIF), which was shown to decrease significantly for patients with nasal obstruction. There was a positive correlation seen between IPNF and VAS for nasal obstruction.[27] In addition, PNIF was significantly different among groups with different self-reported levels of nasal congestion.[28]

Another important factor in breathing is the deviation of the nasal septum. As shown in the model in Figure 1, nasal septum deviation. It has been shown that nasal septum deviation is the primary cause of impaired nasal patency, which is found in 82.5% of the patients with nasal septum deviation.[29] Nasal septum deviation was correlated with increased NOSE scores and

lower PNIF scores. PNIF scores increased and NOSE scores decreased following surgical treatment of the septum deviation.[30] Additionally, patients with nasal septum deviation had decreased quality of sleep as measured by the Pittsburgh Sleep Quality Index.[31] In terms of orthodontic treatment, nasal septum deviation improves in childhood treatment with RME, but no such results were shown in adolescents.[32] Nasal septum deviation was not shown to change after SARME.[33] The current study seeks to evaluate nasal septum changes following MSE treatment and correlate these changes to measures of airway changes.

One preliminary assessed the skeletal changes due MSE by linear measurements on the CBCT using various cross sections including an upper nasal section and lower nasal section (Figure 5). The study demonstrates that skeletal changes due to MSE involve the lateral rotation of inferior skeletal elements including the maxilla with the fulcrum at the frontozygomatico suture in coronal sections. In the axial sections, the rotation is a lateral rotation of anterior skeletal elements such as the anterior nasal spine with the fulcrum at the lateral pterygomaxillary suture. This study gives us insight to the overall skeletal changes occurring as a result of MSE which will increase the bony housing for the airway.

There are multiple other studies in progress to evaluate more specific changes due to MSE on the airway and on soft tissues although the full results are not yet available at this time. One study is measuring the volumetric changes in nasopharyngeal airway through the superimposition of Cone Beam Computed Tomography (CBCT) images of the head and neck before and after expansion. Another study, also using CBCT, is measuring these volumetric changes in the oropharyngeal airway, which is composed of soft tissues. One other study is measuring the overall soft tissue changes before and after MSE using the 3dMD imaging software.

Results

The sample included twenty-nine patients in the treatment group who underwent MSE and twenty-six patients in the control group who received no expansion treatment. Patient's PNIF, POIF, VAS, and NOSE values were collected prior to and after expansion and they were compared. The Chi-squared test determined that the values were not normally distributed. Therefore, the Wilcoxon matched-pairs signed rank test was used to determine changes in mean PNIF, POIF, VAS, and NOSE following MSE treatment. The Wilcoxon test was also used to compare the treatment group to controls and pre-treatment control to post-treatment control. Previous power analysis which was conducted based on similar studies showed an effect size of 0.877 requiring a sample size of twenty.

The results indicate a significant increase ($p<0.0001$) in PNIF from pre to post-MSE treatment (Figure 5A). Similarly, unilateral measurements showed significant improvement in PNIF on both the right ($p<0.0001$) (Figure 5A) and the left ($p<0.0001$) (Figure 5B). POIF measurements also improved but the changes were only significant at $p<0.01$ (Figure 5D). No significant differences were seen between pre-treatment, post-treatment controls, and pre-treatment MSE groups for PNIF total, PNIF right, PNIF left, and POIF (Figure 5A-D). Significant differences were found between post-MSE and post-treatment control groups (Figure 5A-D).

Following treatment with MSE, patients reported significant decrease in troubled breathing as measured by the Visual Analog Scale. Significant decreases in VAS measurements were observed for breathing through the right nostril ($p<0.01$) (Figure 6A), left nostril ($p<0.001$) (Figure 6B), and both nostrils ($p<0.01$) (Figure 6C). Similar to PNIF findings, no significant differences were found for all VAS measurement between pre-treatment control, post-treatment control, and

pre-MSE groups. Although the mean NOSE value was lower post-MSE, no significant differences were found between all four groups (Figure 6D).

The Spearman correlation coefficient was calculated to understand the relationship between objective and subjective variables in both pre-MSE or post-MSE treatment groups. While the results indicate that there is no significant correlation between total PNIF and VAS (Figure 7A), the values were significant between PNIF and VAS on each side (Figure 7A) when the patients were asked to block one nostril. The left sided PNIF and VAS correlation was significant at $p<0.05$ and the right side at $p<0.01$. Additionally, the relationship between PNIF and NOSE is significant for the post-MSE group ($p<0.05$) but not for the pre MSE group (Figure 7A). Furthermore, VAS and NOSE were strongly correlated as they were both subjective patient measurements (Figure 7A).

When evaluating the relationship between objective and subjective changes in breathing, Spearman correlation was performed between the ratio of post to pre PNIF and either VAS or NOSE changes. PNIF change was not significantly correlated with VAS change (Figure 7B). Left sided PNIF change and VAS change were also not correlated (Figure 7B). Interestingly, right sided PNIF change and VAS change showed a significant negative correlation ($r= -0.41$, $p<0.05$) indicating an inverse relationship between VAS and PNIF (Figure 7B). PNIF change and NOSE were not correlated (Figure 7B), matching our previous findings that NOSE did not improve following MSE treatment. VAS and NOSE changes were highly correlated as subjective measurements (Figure 7B).

Since many patients were not aware of possible breathing impairment prior to MSE treatment, patients were also asked to evaluate their perceived level of improvement on the VAS

scale during the post-expansion visit. However, the correlational test with PNIF, POIF, VAS, and NOSE showed no significance (Figure 7C).

Nasal septum deviation from the skeletal midline was measured for 24 of the 29 patients in the MSE treatment group. Five patients were excluded due to insufficient resolution on the CBCT to clearly demarcate the nasal septum. Relative to the midline, deviation ranged from approximately 0.5 to 3.0 mm before treatment with the majority of patients deviated to the right (Figure 8A). Following MSE treatment, septum deviation ranged from 1 to 3.5mm (Figure 8A). The absolute value of nasal septum deviation increases significantly following MSE treatment at $p<0.05$ (Figure 8B).

To evaluate whether the improvement in PNIF were related to changes in nasal septum deviation, the net change in PNIF (post-PNIF – pre-PNIF) as well as the PNIF ratio (post-PNIF / pre-PNIF) were plotted against NSD net change (post-NSD – pre-NSD) (Figure 8C-D). Spearman correlation studies showed that NSD was not significant correlated with neither PNIF net change nor PNIF ratio. Subsequently, the pool of patients was divided by the direction of NSD change to either the left or the right. The septum deviation on each side was plotted against the ipsilateral PNIF and the contralateral PNIF. Nasal septum deviation to the right was not significantly correlated with left PNIF (Figure 9A) or right PNIF (Figure 9B). However, interestingly nasal septum deviation to the left was correlated to right PNIF (Figure 9D) but not to left PNIF (Figure 9C). Nasal septum deviation to the left has a positive relationship with increased peak nasal airflow on the right ($p<0.05$, $r=0.614$).

Discussion

As hypothesized, patients who underwent maxillary skeletal expansion showed improved breathing as measured by total PNIF. The changes in PNIF were predominantly the result of increased nasal cavity volume following expansion. Furthermore, patients saw improvements in breathing in each nostril following treatment, which suggests that expansion and nasal cavity changes were bilateral. The treatment and control groups have similar distributions for age and gender and as expected, the controls did not show improved nasal airflow following treatment.

In addition, patients showed improved POIF which indicates that the increase in nasal cavity volume is not the singular cause of breathing improvement. Maxillary skeletal expansion also results in increased oral cavity volume which may lead to improved breathing. Additionally, patients who require expansion frequently have narrow maxilla which prevents proper tongue positioning. Oral expansion would result in improved tongue posture leading to improved breathing. Furthermore, increasing both nasal and oral input with enlarged cavity volumes may result in adaptive responses in the pharynx. The pharyngeal soft tissues may accommodate the increased input by expansion of the pharyngeal space.

In additional to improved objective breathing measurements, patients also showed improved subjective measurement. The visual analog scale is a validated indicator for breathing. Values were improved following expansion, but not with non-expansion treatment. The improved VAS was seen in total breathing and both nostrils, matching our hypotheses and matching the changes observed in the objective measurements of breathing. However, the Nasal Obstruction Symptom Evaluation showed no changes following MSE treatment suggesting that patients may be less aware of their specific symptoms compared to their generalized breathing. Additionally,

patients may not be aware when asked about troubled breathing in a survey (as done in NOSE), but may become aware when asked to physically breathe in air (as done in VAS test).

One of the confounding factors in this study is that patients were not aware of their breathing problems prior to MSE. This may have resulted in decreased pre-treatment NOSE and VAS values. Interestingly, despite improvements in both PNIF total and VAS total following MSE, the values did not show a significant correlation. Due to decreased oxygen intake from plugging one of their nostrils, patients perhaps became more conscious of their breathing impairment. Correlation between PNIF and NOSE values were significant for the post-MSE group but not for the pre-MSE group suggesting that patients may become more aware of their breathing following treatment.

As expected, PNIF change was not correlated with VAS change, which matches the finding that double-sided PNIF was not correlated with double-sided VAS. If patients were indeed more aware of their breathing problems when air is constricted on one side, we would expect single-sided PNIF change to be correlated with single-sided VAS change. Surprisingly, this was the case on the right side but not on the left suggesting that additional studies may be required. PNIF change and NOSE change were not correlated, as NOSE changes were not significant after MSE treatment. VAS and NOSE changes were highly correlated as expected as both measures were subjective evaluations.

Patient measurements for improvement on the VAS scale did not correlate with any of the change in subjective and objective measurements. This finding was surprising as we would have expected PNIF and POIF change to be correlated with the improvement measure under the assumption that patients are better able to evaluate their breathing changes following expansion.

If we operate instead under the assumption that patients are able to assess their breathing accurately before and after expansion, we would see that improvement would be correlated with VAS change and NOSE change. Therefore, neither assumption is true and we can conclude that patients are not accurate in their self-assessment of breathing before or of their improvement. It is possible, however, that patients are able to correctly assess their breathing post-expansion but not their breathing improvement.

The measurements for nasal septum deviation indicate that deviation can occur both sides. The increased number of patients with deviation to the right may be due to random chance since the sample size is limited. Additionally, deviation ranges between 0.5 to 3.5 mm suggesting that most septum deviation falls within a few millimeters. Interestingly, septum deviation did not correct following MSE treatment. Instead, septum deviation increased significantly following expansion suggesting that expansion is occurring asymmetrically. It has been found in other preliminary studies that asymmetries in patients prior to MSE treatment are accentuated by expansion.

Change in nasal septum deviation was not correlated to an increase or decrease in PNIF. One may expect decreased nasal septum deviation to be correlated with increased PNIF, but a possible explanation is that a decrease in deviation improves airflow in one nostril while decreasing airflow in the other nostril. This theory is supported by the fact that there is some evidence that increased nasal septum deviation to the left results in improved PNIF on the right. However, not all the data is consistent as NSD to the left had no relationship with PNIF on the left. Furthermore, this relationship was not found for septum deviation to the right. Therefore, additional studies are necessary to fully elucidate the relationship between septum deviation and nasal airflow.

A study limitation is the fact the controls for the study are patients who undergo non-expansion orthodontic treatment. Therefore, we can conclude that the maxillary skeletal expander improves the airway relative to non-expansion treatment, but we are not able to show that the maxillary skeletal expander is superior to other forms of expansion. We were not able to use SARME for a comparison group due to the lack of a sufficient sample size of patients who underwent surgically assisted expansion as most adults in the clinic opted for MSE treatment compared to surgery. Additionally, RME was not used as a control group since RME is only performed on children and early adolescents prior to fusion of the palatal suture. Since MSE was performed predominantly on late-adolescents and adults, the two treatment samples would have a different age range preventing proper control of confounding factors.

Another important limitation is the fact that the study is retrospective and non-random. Since we must provide the patient with autonomy, it would be unethical to randomly assign patients to MSE versus non-expansion treatment. Therefore, it would not be possible to do a randomized control clinical trial. We must instead draw conclusions from previous data on the treatment of patients at UCLA. One other limitation was previously discussed, which is the fact that patients may have mild airway constriction but are not aware of their breathing difficulties prior to treatment and therefore do not show breathing improvements on the subjective measurements. These patients were generally not diagnosed with obstructive sleep apnea and were healthy making it more difficult for them to detect mild breathing impairment. Additionally, it would be not be possible to fully generalize this study to the population of patients with OSA as this was not the population used in this study.

Furthermore, a study limitation that patients will experience differences in their breathing due to variety of factors including nasal congestion from a cold, seasonal allergies, or even mild

changes in their breathing patterns throughout a day. The data was collected at a single time point before and after expansion and therefore may not be representative of the patient's overall breathing. One limitation that the study has tried to account for is the patient's improvement based on learning to use the in-check devices. Measurements were taken until the patient showed steady values and no increase in values after consecutive breathing attempts.

Finally, the nasal septum deviation studies have limitations since the septum shown on the posterior-anterior cephalogram is a 2D representation of a 3D structure. This means that multiple structures may have become superimposed into one preventing accurate measurement of the nasal septum. Additionally, nasal septum are not clearly demarcated structures. Tracing error and measurement error may be up to 0.5 mm while the septum deviations range from 0.7 to 3.2 mm. Therefore, error may account of a substantial proportion of the total values.

Conclusion & Future Direction

Based on the results of the study, treatment with MSE has indeed raised objective and subjective measurements of airway. We may conclude that MSE is a possible treatment alternative for obstructive sleep apnea. Treatment with MSE would target the cause of disease by expanding skeletal and soft tissue structures, allowing for improved airway function. Many current treatments for OSA involve oral appliances, which target the symptoms but are not able to achieve permanent airway improvement. Treatments that do target the cause of disease including tonsillectomy and orthopedic surgery are very invasive with high morbidity. MSE could be a non-surgical alternative to achieving orthopedic movement to correct an impinged airway.

Further studies are necessary to validate the findings of this study. Correlation of the objective and subjective breathing changes with changes in nasal, oral, and pharyngeal volumes as measured by CBCT would help to elucidate the skeletal changes behind the functional improvements. Additionally, correlating the findings with studies using computational fluid dynamics would provide further mechanistic explanations for improved breathing. Finally, relating these breathing changes with NOX sleep monitor or polysomnography could verify the reduction of hypopnea and apnea episodes, which is the primary goal of OSA treatment.

Materials & Methods

Data will be collected from patients receiving treatment at the University of California at Los Angeles School of Dentistry Department of Orthodontics. The experimental group will be patients at the Orthodontic Clinic who are treated with Maxillary Skeletal Expansion. The control groups will include a subset of patients in the UCLA clinic who are treated with a conventional Rapid Maxillary Expander and patients who undergo orthodontic treatment without expansion. Prior to delivery of the Rapid Maxillary Expander, patients undergo subjective and objective measurements of the airway.

Subjective measurements include the Nasal Obstruction Symptom Evaluation (NOSE) and the patient's reported breathing impairment on the VAS. The Nasal Obstruction Symptom Evaluation (Figure 6) involves asking the patient to evaluate their problems associated with breathing in the last month. The following items are listed: 1) Nasal congestion or stuffiness, 2) Nasal blockage or obstruction, 3) Trouble breathing through my nose, 4) Trouble sleeping, 5) Unable to get enough air through my nose during exercise or exertion. The items are rated on a

scale of 0 (not a problem), 1 (very mild problem), 2 (moderate problem), 3 (fairly bad problem), 4 (severe problem).

The patient is then asked to breathe through both nostrils and asked to rate their current level of breathing impairment using a 100cm Visual Analog Scale ruler (Figure 7) with faces to demonstrate the level of impairment with 1 being no trouble breathing to 5 being severe trouble breathing. They are asked to repeat the exercise when blocking out their right nostril with their finger to evaluate breathing in the left nostrils. This is followed by blocking out the left nostril to evaluate breathing in the right nostril.

Objective measurements of airway include the Peak Nasal Inspiratory Flow (PNIF) and Peak Oral Inspiratory Flow (POIF), which are measured with the In-Check medical device. For the PNIF, the patients are asked to stand and inhale using the In-Check medical device with the nasal mask attachment. With the mouth closed and the mask fully sealed, the patient is instructed to exhale and inhale as quickly with maximum force through the nose. The measurement is taken three times. Subsequently, the measurements will be taken with individual nostrils. The right nostril measurement is taken with the left nostril sealed by a cotton roll. The opposite is done to measure breathing through the left nostril. Measurements for each nostril is also repeated three times.

Peak Oral Inspiratory Flow is measured with the oral attachment using the same In-Check medical device (Figure 8). The patient is again asked to exhale and inhale quickly with maximum force with their lips fully sealed on the oral attachment. The measurement is again taken three times.

Each patient subsequently undergoes treatment with and Maxillary Skeletal Expander at the UCLA Orthodontic Clinic. Immediately following expansion and at 6 months after

expansion, the subjective and objective measurements of airway (NOSE, VAS, PNIF, and PNOF) are repeated. In the repeated VAS measurement, one modification is made: the patient is asked to evaluate any changes in breathing on the VAS with the middle of the ruler (3) as no change, (1) defined as large improvement in breathing, and (5) defined as large reduction in breathing.

Subjective and objective airway measurements will be compared between the time points using a paired T-test to detect any significant differences arising from expansion treatment. Preliminary testing using the Chi-squared test indicated that the data was not normally distributed for PNIF, PNOF, VAS, and NOSE. Therefore, the differences between time points was tested using the Wilcoxon matched-pairs rank test, which is indicated for non-parametric data. Correlational statistics will be run between the PNIF, PNOF, VAS, and NOSE values to determine whether changes in multiple breathing measurements occur in the same individuals. The Spearman correlation coefficient was calculated for each correlational study as opposed to the Pearson coefficient since the data was non-parametric as previously shown.

Based on similar studies[27] on patients with obstructive sleep apnea and anterior nasal septum deviation, corrected by nasal septoplasty, quantified peak nasal inspiratory flow, significant differences were observed between pre- and post-operative measurements with an effect size of 0.877. Thus, based on power analysis calculations with α=0.05 and power=0.8, significance should be observed with N=17 and therefore, initial patient numbers for Aim1b (N=20 per treatment group) have been determined to be sufficient to determine significance.

Prior to expansion, a full volume Cone Beam Computed Tomography (CBCT) is taken of the head and neck using a NewTom machine for diagnostic purposes to determine whether MSE

is an appropriate treatment for the patient. A new CBCT is taken immediately following the end of expansion to verify sutural opening, measure the magnitude of expansion, and rule out any abnormal skeletal changes. Finally, a CBCT is taken at 6-months after expansion to verify retention and again rule out any skeletal abnormalities due to treatment.

The CBCTs are oriented laterally on Frankfort horizontal and frontally using the orbits as reference. PA cephalograms are generated using Dolphin and basic tracing is performed. The skeletal midline is generated based on tracing. The longest linear distance from nasal septum to midline is measured. The chi-squared test determined that the data on nasal septum deviation was not normally distributed. Subsequently, pre- and post-MSE septum deviation are compared using the non-parametric Wilcoxon matched-pairs rank test. The changes in nasal septum position are correlated to the changes in objective (PNIF) and subjective (VAS) measurements in the left and right nostril using the non-parametric Spearman correlation coefficient.

Figures

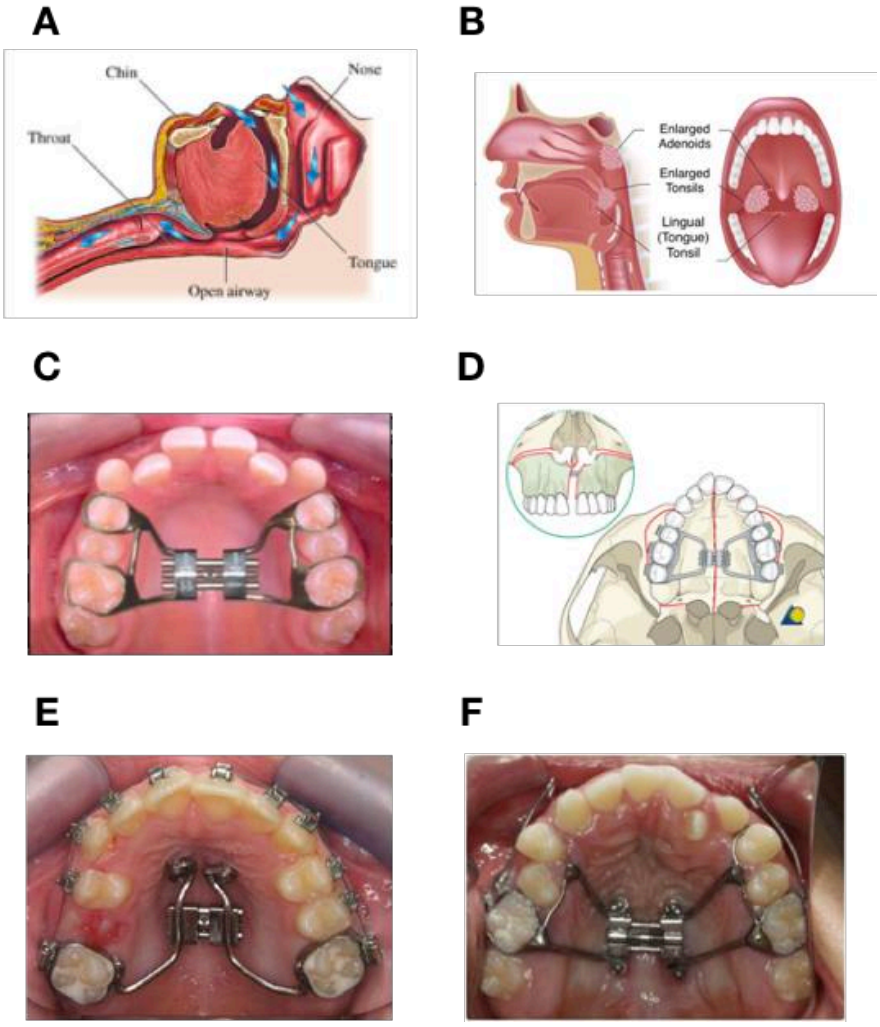

Figure 1. Airway impingement and maxillary expansion. (A) Image[34] illustrates the anatomical relationship between the soft tissues of the airway. Tongue and soft palate position may cause obstruction of the airway. **(B)** Image[35] illustrates enlarged tonsils which will cause airway impingement. Surgical treatment may alleviate the symptom. **(C)** A Hyrax Expander, a type of Rapid Maxillary Expander, is shown[36]. **(D)** Diagrammatic representation of a Surgically Assisted Rapid Maxillary Expander is seen on the right[37]. **(E)** A Hybrid Rapid Maxillary Expander is shown on the Left.[25] **(F)** A Mini-implant Assisted Rapid Palatal Expander with buccal extension arms for maxillary protraction is shown.[23]

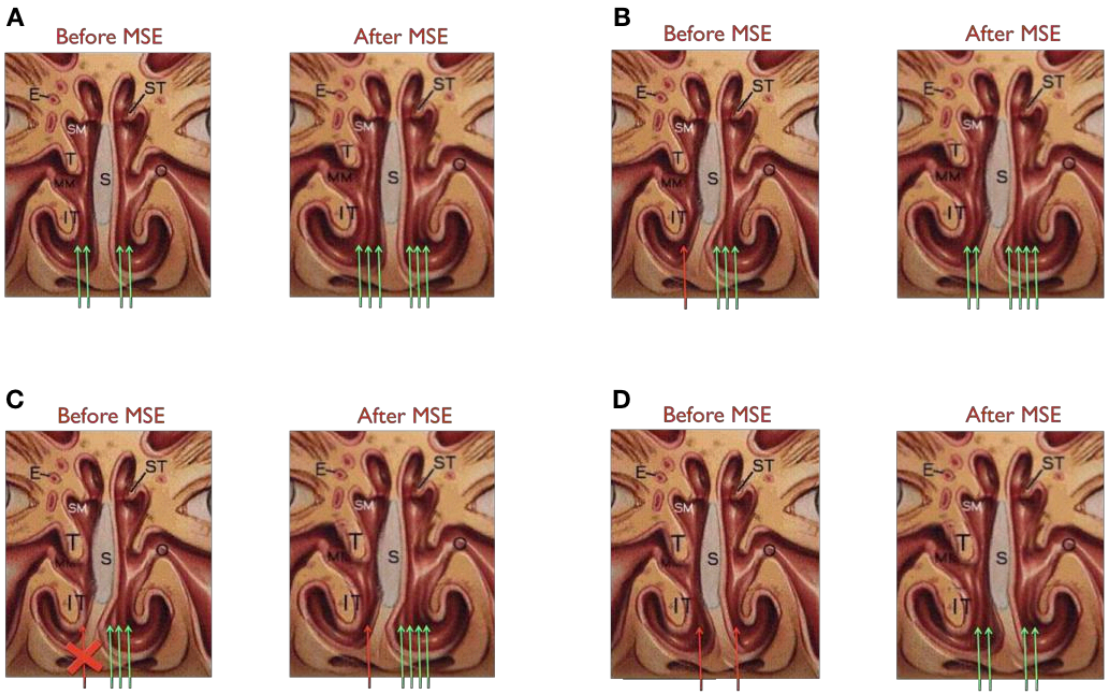

Figure 2. Diagramatic representation of nasal septum deviation and the effects of MSE. Diagmatic respresenation of the effects of MSE on nasal septum devation.[38-39] **(A)** Normal nostrils show increase airflow following MSE treatment. **(B)** In cases of nasal septum deviation, decreased flow in one nostril is also relieved by MSE treatment. **(C)** When nasal septum deviation is combined with ipsilateral hypertrophic hard tissue in the turbinates, one nostril is completely obstructed and MSE results in partial relief. **(D)** When septum deviation is combined with contralateral hard tissue hypertrophy, both nostrils have decreased flow which is relieved by MSE.

A Results for lateral displacement of ANS and PNS and width of opening in pterygoid processes

		Before expansion		After expansion		Treatment change		*P* value	
		Mean	sd	Mean	sd	Mean	sd		
1	Rt ANS to maxillary sagittal plane	0.00	0.00	2.59	1.70	2.59	1.70	<.0001	**
2	Lt ANS to maxillary sagittal plane	0.00	0.00	2.16	1.27	2.16	1.27	<.0001	**
3	Rt PNS to maxillary sagittal plane	0.00	0.00	2.34	1.32	2.34	1.32	<.0001	**
4	Lt PNS to maxillary sagittal plane	0.00	0.00	1.99	0.90	1.99	0.90	<.0001	**
5	Lateral displacement of Rt ANS + Lt ANS	0.00	0.00	4.75	2.59	4.75	2.59	<.0001	**
6	Lateral displacement of Rt PNS + Lt PNS	0.00	0.00	4.33	1.74	4.33	1.74	<.0001	**
7	Width of opening in Rt pterygoid process	0.00	0.00	1.35	1.79	1.35	1.79	0.011	*
8	Width of opening in Lt pterygoid process	0.00	0.00	2.17	2.45	2.17	2.45	0.004	**

All measures are expressed in mm
Rt ANS right half of anterior nasal spine, *Lt ANS* left half of anterior nasal spine, *Rt PNS* right half of posterior nasal spine, *Lt PNS* left half of posterior nasal spine, *Rt* right, *Lt* left
*$P < .05$; **$P < .01$

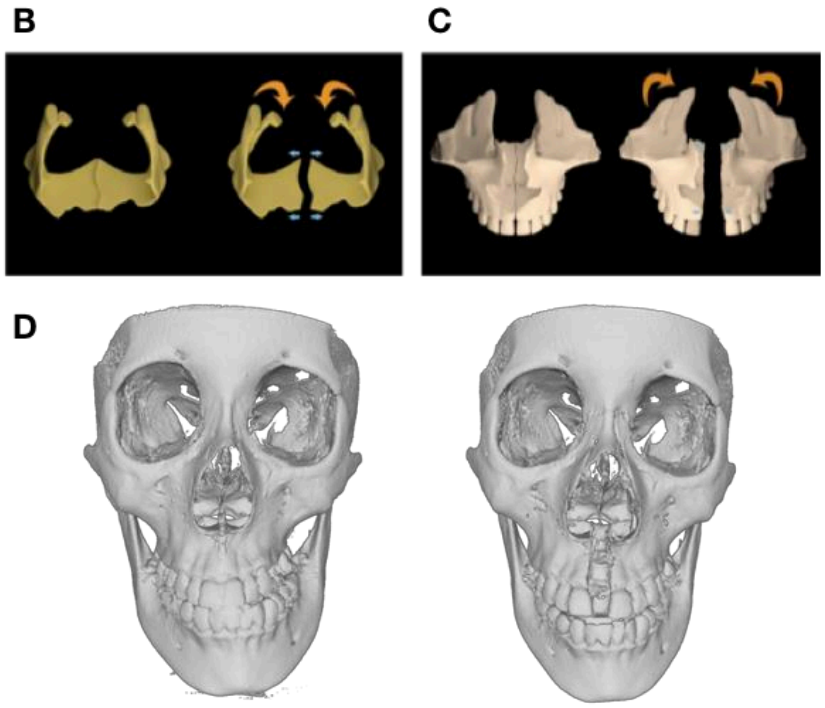

Figure 3. The effects of MSE on skeletal tissues. An increase in the inclination of the palatine bone is seen following both Hyrax and MSE treatment. The rotation of the palatine bone **(B)** and maxilla **(C)** are depicted in diagrams. Segmented skulls from Cone Beam CTs of a patient who underwent treatment with Maxillary Skeletal Expander (MSE). Pre-treatment **(D)** and post treatment **(E)** skull is shown on right. As depicted, patient shows significant expansion of the midface and nasal cavity resulting in increased volume of the airway.

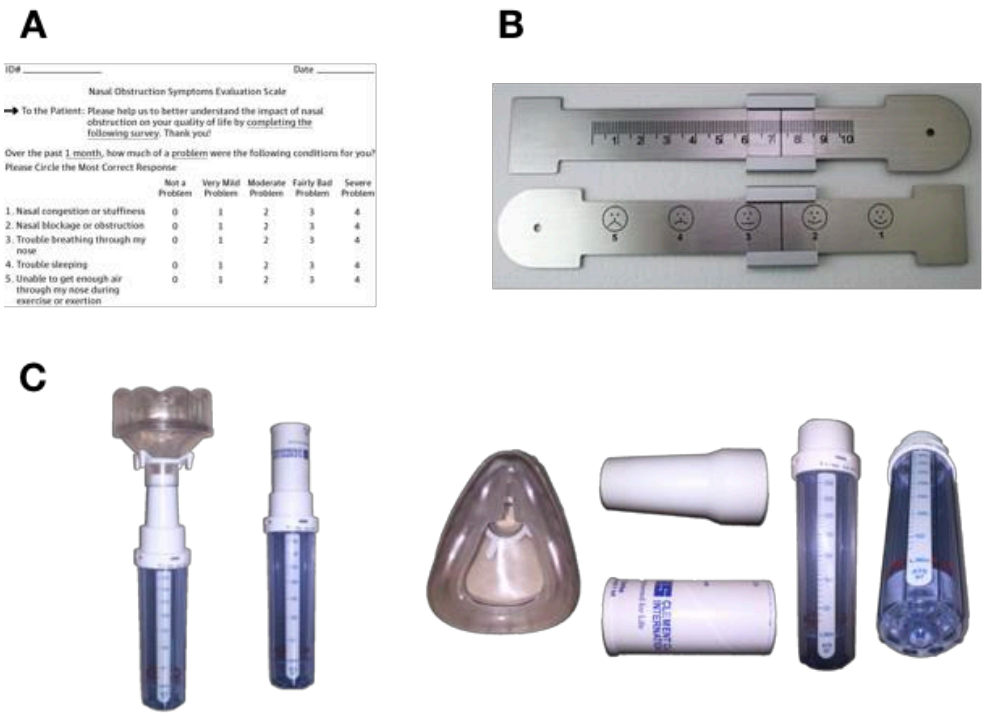

Figure 4. Subjective and objective measurements of airway. (A) Image[40-41] shows the ruler used for the measurement of the Visual Analog Scale. **(B)** Image shows Nasal Obstruction Symptom Evaluation form which is filled out by each patient before and after expansion[42]. **(C)** Left shows the assembled In-Check medical devices for PNIF and PNOF measurements. Right picture shows disassembled parts of the In-check medical devices.

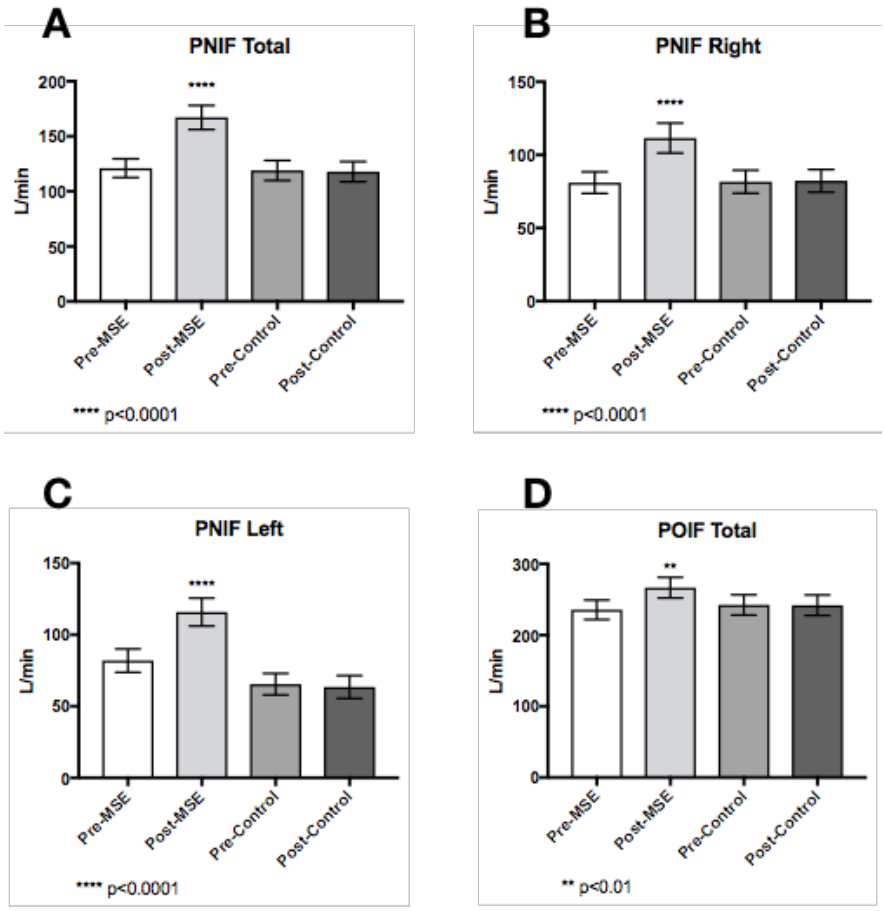

Figure 5. Objective measurements of airway before and after MSE treatment. Mean Peak Nasal and Oral Inspiratory Flow for pre- and post- MSE and control groups. Total PNIF **(A)**, left nostril PNIF **(B)**, right nostril PNIF **(C)**, and total POIF **(D)** were measured.
*p≤0.05 post-MSE compared to pre-MSE. **p≤0.01 post-MSE compared to pre-MSE. ****p≤0.0001 post-MSE compared to pre-MSE.

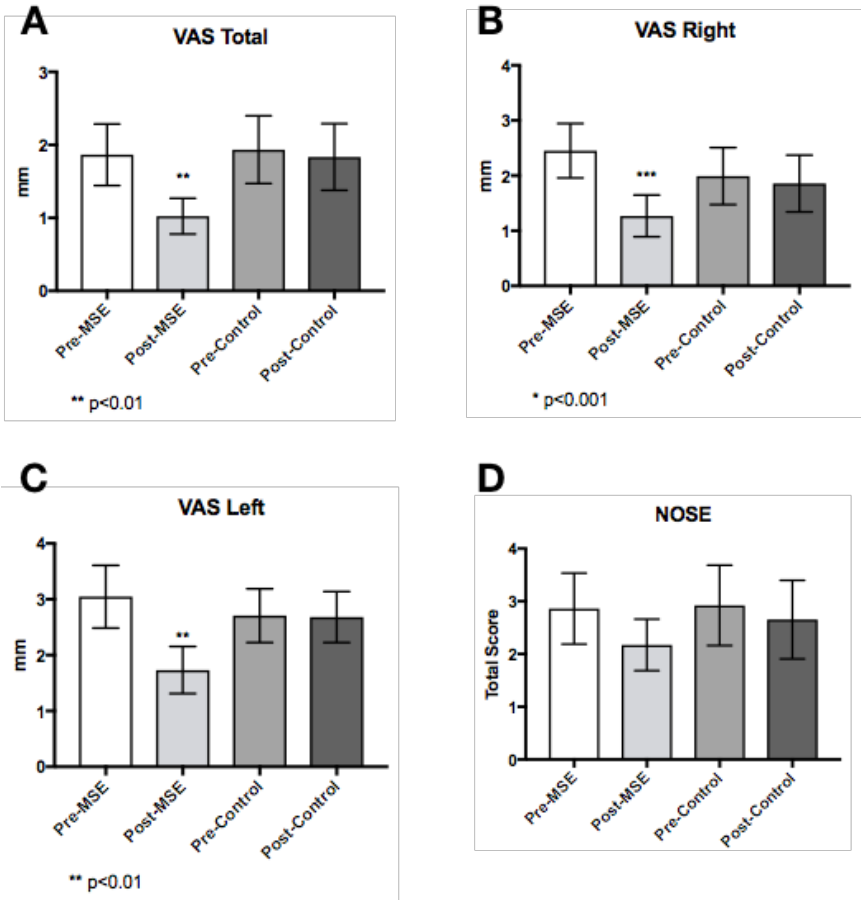

Figure 6. Subjective measurements of airway before and after MSE treatment. Mean scores on VAS and NOSE evaluation for pre- and post- MSE and control groups. Total VAS **(A)**, right nostril VAS **(B)**, left nostril VAS **(C),** and NOSE **(D)** are shown.
*p≤0.05 post-MSE compared to pre-MSE. **p≤0.01 post-MSE compared to pre-MSE. ***p≤0.001 post-MSE compared to pre-MSE.

A

	PRE	POST
PNIF TOTAL vs VAS Total	p=0.0533	p=0.3388
PNIF left Vs VAS left	p=0.0243*	p=0.0146*
PNIF right vs VAS Right	p=0.0030**	p=0.0044**
PNIF vs NOSE	p=0.3850	p=0.0246*
VAS vs NOSE	p<0.0001****	p=0.0005***

B

	Correlation
PNIF Ratio vs VAS Change	p=0.4085
PNIF left Ratio vs VAS left Change	p=0.4314
PNIF right Ratio vs VAS right change	p=0.0145*
PNIF ratio vs NOSE change	p=0.3608
VAS vs NOSE change	p<0.0001****

C

	Correlation
PNIF ratio Vs Improvement	p=0.2203
VAS vs Improvement	p=0.2264
Nose vs improvement	p=0.1896
POIF vs Improvement	p=0.2614

Figure 7. Correlation between subjective and objective measurements of airway. Tables of p-values for Spearman correlation studies including: **(A)** Correlation between objective and subjective breathing measurements in pre- and post- MSE groups. **(B)** Correlation between net changes in objective measurements and subjective measurements. **(C)**Correlation between changes in each value and measurement of improvement.
*p≤0.05; **p≤0.01; ***p≤0.001; ****p≤0.0001

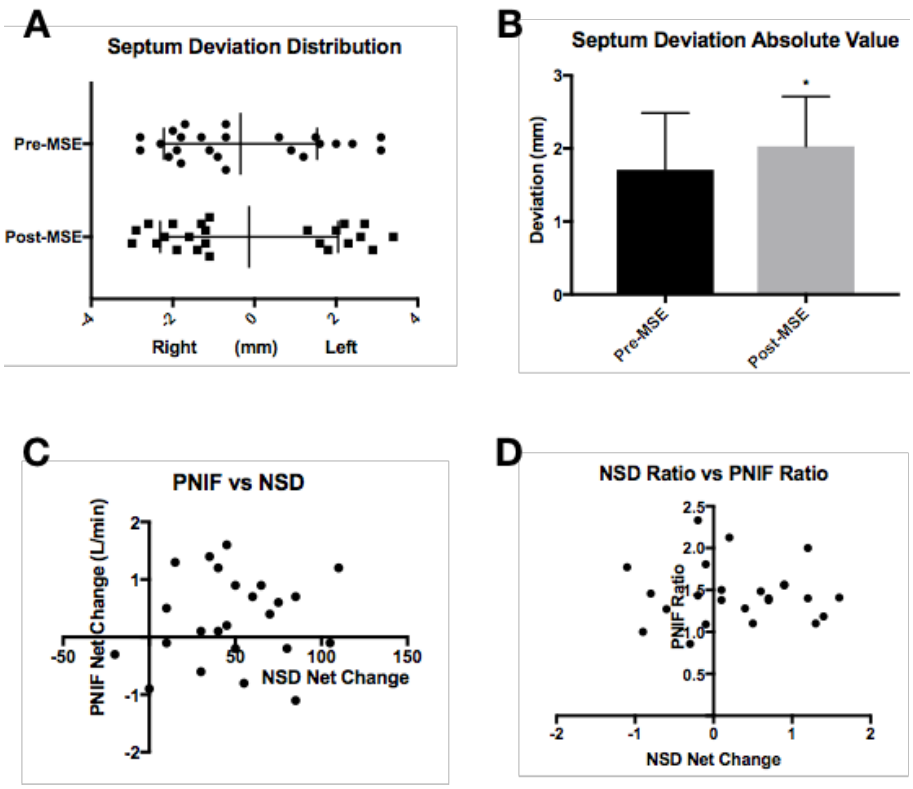

Figure 8. Relationship between nasal septum deviation and peak nasal inspiratory flow. **(A)** The distribution of nasal septum deviation from the skeletal midline before and after MSE treatment. **(B)** Comparison of the average absolute value of deviation before and after MSE. **(C)** Correlation of PNIF net change (pre to post) with nasal septum deviation. **(D)** Correlation of PNIF post/pre ratio with nasal septum deviation. Spearman correlation was calculated for (C) and (D) and both were not significant.

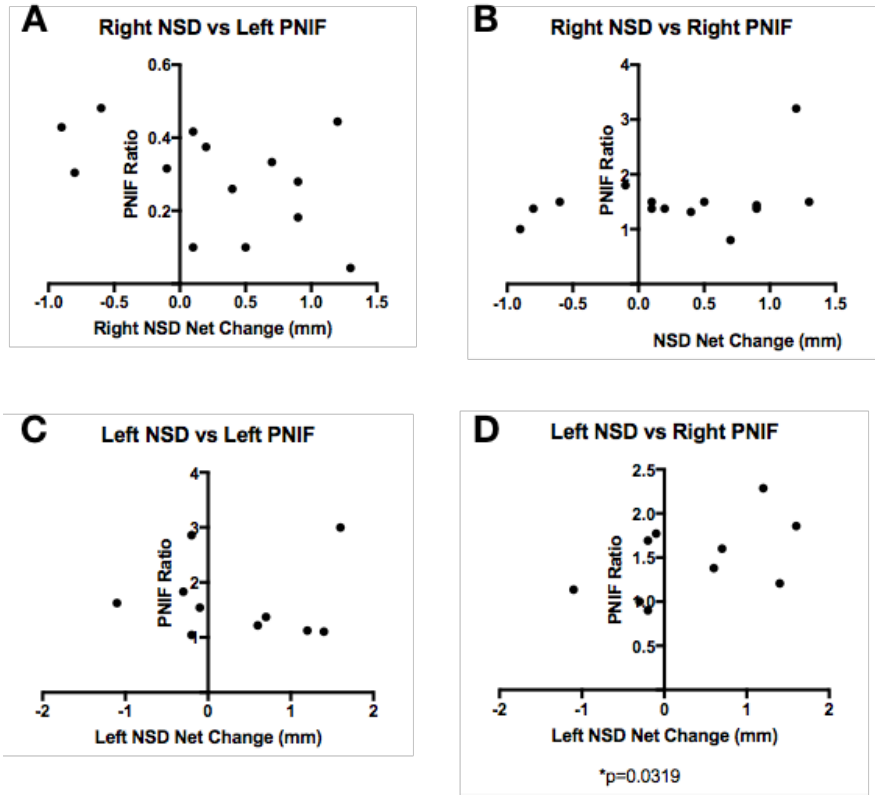

Figure 9. Relationship of nasal septum deviation with ipsilateral and contralateral peak nasal inspiratory flow. Net change in right NSD was correlated with left PNIF **(A)** and right PNIF **(B)**. No significant correlations were found. Net change in left NSD was correlated with left PNIF **(C)** and right PNIF **(D)**. Significant correlation between left NSD and right PNIF (r=0.614 p=0.0319). *p≤0.05

	Pre				Post					Pre			Post					Pre	Post		Pre	Post	
Treat	PNIF	PNIF	PNIF	POIF	PNIF	PNIF	PNIF	POIF		VAS	VAS	VAS	VAS	VAS	VAS	Impr		NOS	NOS		NSD	NSD	Net
1	40	45	105	330	55	50	145	330		2.9	4	4.9	2.4	3.2	1.3			3	1		-1.1	-1.2	0.1
2	35	55	95	165	45	100	130	190		5.5	6.9	6.2	2.4	4	2.2			4	2		-3.5	No	
3	110	40	110	290	125	65	195	290		0	5.2	2.5	0	4.7	2.5			0	0		3.1	2	-1.1
4	80	90	115	310	115	125	180	310		0	0	0	0	0	0			0	0		-0.7	-1.6	0.9
5	40	40	90	180	40	70	90	190		2.4	2.4	0.2	0.3	0.3	0			4	1		-2.8	-1.9	-0.9
6	25	50	100	250	80	90	140	310		6.2	5	2.5	1.1	0.7	1.1			5	4		-1.8	-3	1.2
7	40	45	100	350	60	50	110	350		7.4	7.4	3.8	4.4	2.8	3.2			7	3		-0.7	-1.2	0.5
8	150	175	225	335	240	240	310	330		1.4	1.4	1.4	0	0	0			3	0		0.9	1.6	0.7
9	40	25	40	140	55	40	85	170		2.5	5	7.5	2.8	6.3	4.2			12	9		-1.8	-2	0.2
10	70	30	110	170	130	90	155	265		2.5	0	0	0	1.5	0			3	3		0.6	2.2	1.6
11	130	125	170	210	160	160	205	235		0	0	0	0	0	0			0	0			No	
12	100	60	140	180	100	110	120	220		0	0.7	0	0.7	0	0			0	0		1.6	1.3	-0.3
13	40	30	70	110	60	55	135	150		0	5	2.5	0	0	0			4	1		1.7	No	
14	50	65	110	230	90	95	120	230		1.5	1.5	0.5	0.5	0	0			1	2		-2.3	-2.2	-0.1
15	145	145	190	300	175	160	225	330		0	0	0	0.3	0	0			0	0		1.2	2.6	1.4
16	100	110	115	400	90	115	165	400		5.6	5.8	6.6	2.3	2.9	3	0		8	3		2	1.8	-0.2
17	60	110	150	175	90	115	165	400		1.7	1.6	0	0.7	0.7	0.7	4.5		0	8		-2.1	3.4	1.3
18	110	120	130	220	195	185	235	160		3.7	2.2	1.1	1.2	2.6	2	0.6		0	2		2.4	2.3	-0.1
19	40	35	60	90	60	60	90	120		5.1	5.1	4.1	2.6	3.8	2.4	7.8		13	4		-2.8	-2.9	0.1
20	175	185	250	305	230	250	320	350		0	0	0	0	0	0	0		0	0		-0.9	-1.3	0.4
21	145	115	155	205	200	140	230	235		2.6	3.1	2.4	2.2	2.9	0.9			0	0		-2	-2.6	0.6
22	65	35	60	200	110	100	140	230		1	0	0	1.3	0.2	1.1	8.1		1	2		3.1	2.9	-0.2
23	80	80	120	230	110	115	175	295		0	0	0	0.3	0.5	0.1	5.3		0	1		-1.9	-1.1	-0.8
24	75	120	150	285	60	180	210	235		10	2.2	2.5	10	0.9	3.8	8.5		7	9		-0.7	-1.4	0.7
25	70	120	110	270	160	135	220	400		4.6	3.8	2.5	1.3	2.5	1.2	7.5		2	3		1.5	2.7	1.2
26	80	90	90	200	110	110	140	215		0	0	0	0	0	0	4.3		0	0		-1.3	-2.4	0.9
27	100	100	110	205	105	135	140	225		0	0	0	0	0	0	3.6		0	0		0.9	No	
28	70	70	110	205	105	135	140	225		3.9	1	0.6	0	0	0	8.4		1	1		-1.7	-1.1	-0.6
29	85	65	130	275	80	85	135	340		0.5	0.6	1.3	0	0	0	2.7		5	4			No	
	Pre				Post					Pre			Post					Pre	Post				
Cont	PNIF	PNIF	PNIF	POIF	PNIF	PNIF	PNIF	POIF		VAS	VAS	VAS	VAS	VAS	VAS			NOS	NOS				
1	75	65	160	330	75	5	165	340		1.4	1.2	0.3	1.7	1.7	0.3			1	1				
2	75	50	110	150	75	50	100	150		0	1.4	0	0	1.9	0			2	1				
3	40	40	100	350	40	45	95	350		7	7	3.4	7.5	7.3	3.9			7	5				
4	110	40	110	290	110	40	110	290		0	5.2	2.5	0	5	2			0	0				
5	80	90	115	310	80	90	115	310		0	0	0	0	0	0			0	0				
6	50	70	90	250	55	65	95	245		2.2	2.2	0	1.4	2.5	0			0	0				
7	40	40	80	180	45	40	80	180		2.4	2.4	0.2	2.3	2.2	0.2			3	2				
8	40	20	40	140	45	20	50	150		2	4.8	7	2.3	4	6			12	9				
9	140	105	170	345	135	105	175	345		8	3.8	6.7	8.2	5.4	7.5			10	12				
10	155	175	225	330	160	180	225	330		2	1.4	1.7	1.4	1.2	1.8			3	3				
11	135	120	210	340	145	120	215	340		3	1	1	2.5	0.5	0.5			3	3				
12	35	50	100	250	30	50	100	250		6	4	4	6	5	2.5			5	5				
13	75	30	110	175	80	30	110	170		1	0	0	1	0	0			3	3				
14	60	60	90	185	60	65	100	185		2	1	2	2	2	2			3	3				
15	130	120	170	215	125	125	170	215		0	0	0	0	0	0			0	0				
16	110	40	110	290	100	45	105	285		0	5.5	2.5	0	4.0	2			0	0				
17	50	65	110	230	45	60	100	230		1.5	0	0.5	0	1.5	1			1	0				
18	150	145	190	300	145	145	190	300		0	0	0	0	0	0			0	0				
19	30	40	50	150	30	35	50	150		0	0	0	0	0	0			1	0				
20	95	60	140	190	100	60	130	190		0	0.7	0	0	0	0			0	0				
21	50	55	65	235	45	50	60	245		7.8	5	6.8	7	4	7.5			14	14				
22	35	50	95	165	45	45	100	165		5.5	6.9	6.2	5	6	5			4	4				
23	100	60	140	190	100	65	135	185		0	0.7	0	0	0	0			0	0				
24	110	40	110	290	115	40	110	290		0	6	2	0	5.5	1			0	0				
25	40	30	75	120	45	35	70	110		0	6	2	0	5	2.5			4	4				
26	115	40	130	300	110	40	110	290		0	5	1.5	0	5	2			0	0				

Figure 10. Data table on each patient's objective and subjective measurements of breathing. Treatment group is shown above and control group is shown below. PNIF and POIF values are measured in L/min. VAS, Improvement, and NSD are measured in mm. Pre and post treatment groups are labeled appropriately. NSD and Improvement was not measured for the control group. Improvement data was missing from patients prior to protocol change.

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