Group 4: Brow Symmetry Project Final Report

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Abstract. *This paper deals with a study of ptosis surgery patients. In particular, ptosis surgeons and researchers have noted the frequency of brow asymmetry among ptosis surgery patients and this recurring incidence is the focus of our study. Our exploratory approach preceding logistical and multiple linear regression modeling serves to explore the data and then provide an interpretable model for brow asymmetry as our response variable. From the logistic model, we conclude that the odds of a patient starting with brow asymmetry resulting in brow asymmetry after the surgical operation is 17.80 times more likely than those who began the operation with brow symmetry; the logistic model's predictive accuracy was 87.12%. From our multiple linear regression model, we conclude that the most important predictor is the variable representing the preoperational Pupil-to-Brow difference measured in millimeters, coded as `PrePTBDiff` (P-value = 2e^-16, R^2 = .5455, Adj. R^2 = 0.5354).*

1. Research problem

The research question we are interested in is the relationship between eyelid asymmetry and eyebrow asymmetry, and how ptosis surgery on the eyelids affects brow height asymmetry. Our initial hypothesis is that there is no relationship between Post-op eyebrow asymmetry and any of the predictors in the model including *Age*, *Gender*, *Laterality*, *Pre-op MRD symmetry*, *Pre-op PTB symmetry* and *Post-op MRD symmetry*.

To determine symmetry and asymmetry and in order to maintain consistency in our definitions, the following measurements and criteria were used:

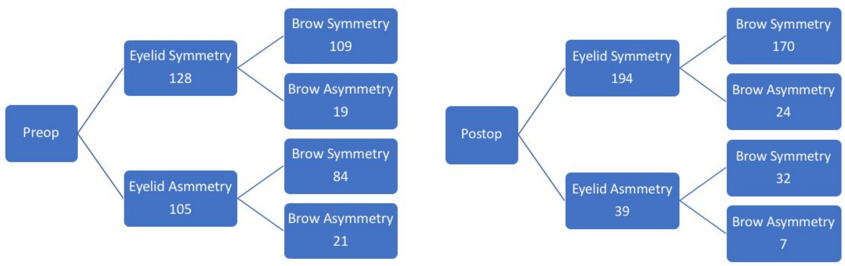
The Pupil-to-brow variable (`*PTB*`) is a measure from the center of the pupil to the lower border of the eyebrow; the margin reflex distance variable (`*MRD1*`) is measured as the distance from the center of the pupil to the upper eyelid margin. In our study, `*PTB*` and `*MRD1*` were measured for both eyes both before and after the ptosis surgery operation; we will refer to these measurements as pre-operational and post-operational respectively. According to recent studies[1], asymmetric eyebrows were noticed by lay observers if a patient's left and right eye `*PTB*` difference exceeded 3.5 mm; asymmetric eyelids were noticed when the patient's left and right eye `*MRD1*` difference exceeded 1mm. These thresholds are the functional basis of our analysis and invariably define asymmetry and symmetry quantitatively.

2. Description of dataset

The dataset we received was culled from a surgical log database and had separate recorded observations for a patient's left eye and right eye. After excluding 70 lines of missing data, the dataset had 602 lines of data, leaving us with data for 301 total patients. However, since the data recorded all surgical incidences, only 236 patients were eligible to be included for the analysis. These patients were filtered by the variable `*Include (1=yes, 2=no, 3=maybe)*`; only observations which had the value 1 were used in the final analysis. Additionally, we removed 3 patients who had omitted data. We ended up with 233 patients' data to be included in our analysis.

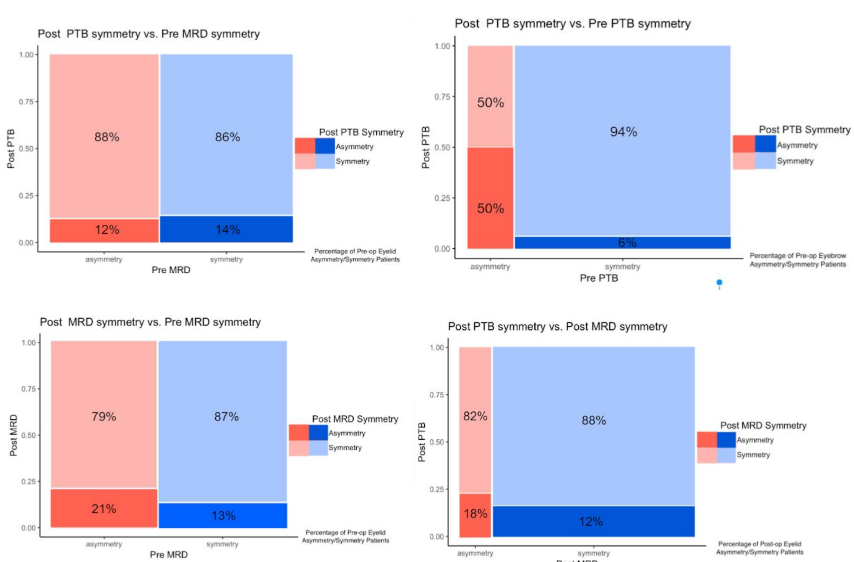
3. Exploratory data analysis

The initial part of our study was primarily composed of exploration of the data. In order to explore the data, we found it fit to first look at the patients' data separated by their post-operational and pre-operational variables. It seems, before modeling, that we can make some sort of descriptive inference about the patient data with regards to asymmetry. We see that pre-operationally, there are 128 patients that had eyelid symmetry and 105 with eyelid asymmetry. Of those with eyelid symmetry, 109 had brow symmetry and 19 had brow asymmetry. Graphic 1** helps display the categorized data.



***Graphic 1: Exploratoration of Data*

We also explored 4 variable relationships as displayed in Graphic 2**: *post-operational PTB symmetry* versus *pre-operational MRD symmetry* (top left), *post-operational PTB symmetry* versus *pre-operational PTB symmetry* (top right), *post-operational MRD symmetry* versus *pre-operational MRD symmetry* (bottom left), and *post-operational PTB symmetry* versus *post-operational MRD symmetry* (bottom right). We can determine the percent of patients that retained or changed their asymmetry based on the variables being compared.



***Graphic 2: Exploratory Plots*

4. Variables and Definitions

To determine asymmetry, numerical variables `*PreMRDdiff*`, `*PostMRDdiff*`, `*PrePTBdiff*`, and `*PostPTBdiff*` were used. `*PreMRDdiff*` and `*PostMRDdiff*` measure the pre-operative and post-operative difference between *MRD1* of one eye and the other. `*PrePTBdiff*` and `*PostPTBdiff*` measure the pre-operative and post-operative difference between *PTB* of one eye and the other. For clearer interpretation, `*PreMRDdiff*`, `*PostMRDdiff*`, `*PrePTBdiff*`, and `*PostPTBdiff*` were transformed into categorical variable according to the eyebrow/eyelid symmetry definition; this transformation is visualized in Graphic 3**. For `*PreMRDdiff*` and `*PostMRDdiff*`, any values that exceed 1 mm were coded to have value 1, indicating asymmetry; values that were below 1 mm were coded to have value 0, indicating symmetry. For `*PrePTBdiff*` and `*PostPTBdiff*`, any values that exceed 3.5 mm were coded to have value 1, indicating asymmetry; values that were below 3.5 mm were coded to have value 0, indicating symmetry. We had three additional variables: the binary variable `*Lateral*` was included to differentiate patients who had unilateral or bilateral surgery; the numerical variable `*Age*` which shows patients age ín years; and the categorical variable `*Gender*` which indicates whether the patient was male or female.

***Graphic 3: Categorize MRD and PTB variables*

5. Methods and approaches

To see the relationship between eyelid symmetry and eyebrow symmetry and the effects of ptosis surgery, we sought to build a model that would help us determine which variables were significant in predicting postoperative measures. To do this, we used logistic regression and multiple linear regression in our analysis.

Method 1: Logistic Regression

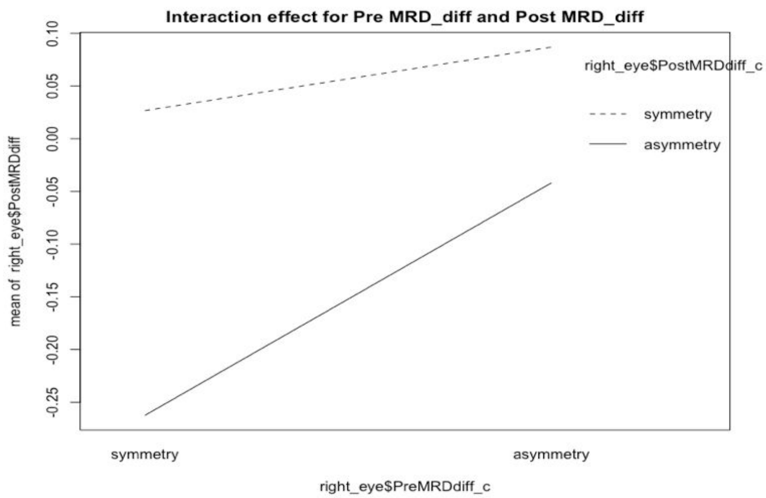
Logistic regression is a commonly used statistical method for biomedical data analysis where there is one or more independent variables that determine an outcome. The analysis results are interpretable by a logistic model. In order to fit our data into a logistic model, we categorized the differences into two factors: symmetry (value = 1) and asymmetry (value = 0) by filtering variables `*PreMRDdiff*`, `*PostMRDdiff*`, `*PrePTBdiff*`, and `*PostPTBdiff*` according to their symmetry definition. Since the data was recorded separately for each eye, we took the set of observations from `*PreMRDdiff*`, `*PostMRDdiff*`, `*PrePTBdiff*`, and `*PostPTBdiff*` calculated by right eye - left eye (The odd observations). An interaction term between pre-operative and post-operative MRD difference was also included, along with variables

`Gender`, `Age`, and `Lateral`. We fit these variables into our model with the `P*ostPTBdiff*` variable, or post-operation PTB asymmetry, as our response variable. Table 1* contains the model output summary.

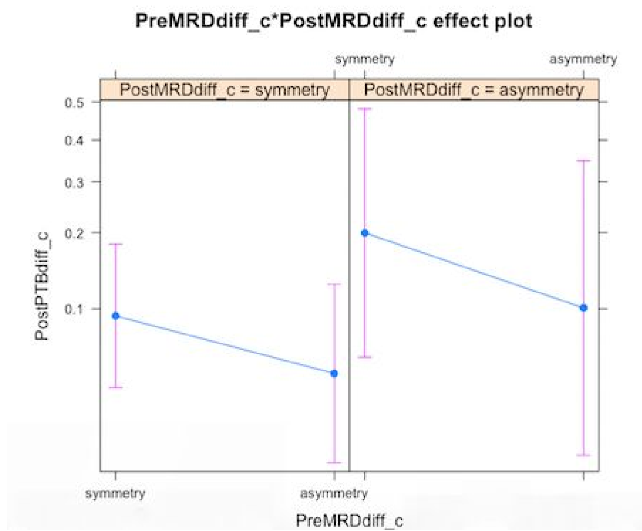
	Estimate	P-value	Odds Ratio
Age	0.02511	0.2238	1.03
Lateral	-0.42972	0.4455	0.65
Gender	0.26727	0.5816	1.31
PrePTBdiff_c asymmetry	2.84435	1.47e-09 ***	17.19
PreMRDdiff_c asymmetry	-0.61069	0.3136	0.54
PostMRDdiff_c asymmetry	0.88076	0.2388	2.41
PreMRDdiff_c asymmetry *PostMRDdiff_c asymmetry	-0.18499	0.8697	0.83

**Table 1: Full Logistic Regression Model Output*

We view the model output summary to determine how to improve and reduce the model. The variables *`Lateral`* and *`Gender`* were excluded since they are not significant factors in predicting post-operative PTB asymmetry as seen in Table 1*. We examine the relationship between pre-operative MRD difference and post-operative MRD difference. The interaction effect plot shows the two lines are not parallel, we also calculated the correlation between these two variables with cor=0.066 and p-value=0,.1547, we conclude there is no significant relationship was found between pre-operative MRD difference and post-operative MRD difference, interaction term was excluded from the final model. From the effects plot, we learned that given the patient had eyelid symmetry after surgery, there is a higher probability for them to have post eyebrow symmetry for those with eyelid symmetry before surgery than those who had eyelid asymmetry. Given the patient had eyelid asymmetry after surgery, there is a higher probability for them to have post eyebrow symmetry for those who had eyelid asymmetry before surgery.



** Graphic 4: Interaction Plot for pre-operative MRD difference and post-operative MRD difference*



**Graphic 5: Effects plot for pre-operative MRD difference and post-operative MRD difference*

	Estimate	P-value	Odds Ratio
Age	0.02381	0.24723	1.02
PrePTBdiff_c asymmetry	2.87917	5.71e-10 ***	17.80
PreMRDdiff_c asymmetry	-0.42450	0.36322	0.65
PostMRDdiff_c asymmetry	0.77569	0.17028	2.17

**Table 1: Reduced Logistic Regression Model Output*

In our final model, we found that `*PrePTBdiff* , the pre-operational PTB difference, was the most statistically significant predictor for our response. Keeping all other variables constant, a patient who has eye brow asymmetry before operation is 17.80 times more likely to have eye brow asymmetry after the operation. This difference is statistically significant (p=0.000). A confusion matrix was also produced to test the performance of our final logistic model. Overall, the model correctly classified the post-operational eyebrow symmetry (10+193)/233= 87.12% of the time which speaks to the model's predictive power.

	Actual Values		Predicted Values
	Symmetry	Asymmetry	
Symmetry	193 TRUE NEGATIVE	21 FALSE POSITIVE TYPE I ERROR	214
Asymmetry	9 FALSE NEGATIVE TYPE II ERROR	10 TRUE POSITIVE	19
Row totals	202	31	233

**Table 2: Confusion matrix for reduced logistic regression model*

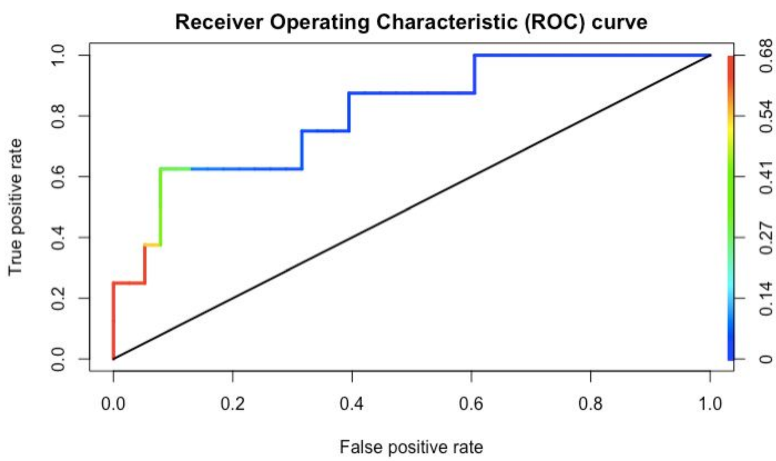
Cross Validation

We performed cross validation to to evaluate our model by partitioning the original sample into a training set (80%) to train the model, and a test set (20%) to evaluate it. Table 3 presents the summary result of logistic regression ran on 80% of the data. We obtained a higher odds ratiod, meaning that keeping all other variables constant, the patient who has eye brow asymmetry before operation is 21.71 times more likely to have eye brow asymmetry after the operation. The purpose of cross validation is to test the predictability model. The aaccuracy rate was (3+33)/46=84.78%, which was close to the accuracy rate of 87.12% we obtained previously.

	Estimate	P-value	Odds Ratio
Age	0.03667	0.16344	1.04
PrePTBdiff_c asymmetry	3.07800	1.35e-10 ***	21.71
PreMRDdiff_c asymmetry	-0.68758	0.20874	0.50
PostMRDdiff_c asymmetry	0.09410	0.902945	1.10

**Table 3: Summary Results for Cross Validation*

The Receiver Operating Characteristic (ROC) curve performed relatively well. The ROC curve is a plot of the true positive rate against the false positive rate. The closer the curve follows the left-hand border and then the top border of the ROC space, the more accurate the test. The area under the curve is a measure of sensivitiy, the true positive in confusion matrix.



**Graphics 6: ROC curve*

Method 2: Multiple Linear Regression

Multiple linear regression is a statistical method that attempts to model the relationship between two or more explanatory variables and a response variable by fitting a linear equation to the data. We checked necessary conditions for linear regression and concluded that the conditions had been appropriately met. Since our logistic model included categorical variables, we conducted multiple linear regression analysis by keeping all variables PreMRDdiff, PostMRDdiff, PrePTBdiff, and PostPTBdiff numerical. PostPTBdiff, Post-operative PTB asymmetry remain as our response variable. Again, we found that “PrePTBdiff is the most statistically significant predictor for our response. Table 4* contains our full model output summary.

	Estimate	P-value
Age	-0.0119662	0.122
PrePTBdiff	0.6425896	<2e-16 ***
PreMRDdiff	0.0086867	0.913
PostMRDdiff	-0.0016640	0.991
Length_follow_up	0.0007406	0.975

**Table 4: Multiple Linear Regression Output*

6. Conclusions

Looking at the results of both our logistic regression and multiple linear regression models, we find that both models are fit to predict post-operational asymmetry in patient based on their pre-operational state. Based on the performance of our logistic regression model and multiple linear regression model, we conclude that the `*PrePTBDiff*` variable is the most significant predictor with `*PostPTBDiff*` as the response variable. Both models point to the predictive power of this variable specifically and allow us to reject the null hypothesis that there is no relationship between `*PostPTBDiff*` and the other variables found in the patient data.

7. Challenges

One of the main challenges to our project was formulating the right question. Initially, the focus of the study was unclear which made formulating the right approaches to our question difficult as well. Being able to define the purpose of the whole study was something that slowed early development of our study. The open-ended exploratory nature of much of the study allowed for various questions to be developed all the while one primary focus was hard to attain. Once we were able to reduce our study to have one specific question and goal, then we were able to move forward in our modeling and analysis.

8. Recommendations/Improvements

A simple improvement to our study would be to include more steps in our regression to show the nature of the variable importance and the degree to which each variable helped predict our response variable. Variable importance plots and model approximation can be used to do this. An additional analysis that we sought to incorporate was a random forest model. We ran a few random forest models and obtained results but found that our logistic and multiple linear regression still remained the most interpretable. A look into additional machine learning methods and their usefulness in predictive power would be a future endeavor for this study.

9. Auxiliary Method Comparison: Random forest vs Multiple Linear Regression

It has been noted in Ulrike Grömping's paper[1] that machine learning techniques such as random forest are particularly successful compared to linear regression models when dealing with smaller sample sizes and large numbers of predictor variables or features. Grömping writes that "variable importance in regression is an important topic in applied statistics" and we remark that the comparison of methods is indeed necessary to have when implementing both parametric and non-parametric methods. Non-parametric methods such as random forests allow for high accuracy in small n (sample size), high p (number of predictors) datasets while parametric methods, such as single or multiple linear regression cannot produce similar success. We take into account that our dataset has a large number of samples with a low amount of predictors and compare then, the interpretability of the two methods; we conclude that, though machine learning, successfully predicts our response variable with large sample size n and low number p predictors, its interpretability is of little to no use in our analysis on brow asymmetry.

References

1. Grömping, U. (2009). Variable Importance Assessment in Regression: Linear Regression versus Random Forest. *The American Statistician,63*(4), 308-319. doi:10.1198/tast.2009.08199
2. Huijing MA, van der Palen J, van der Lei B. The effect of upper eyelid blepharoplasty on eyebrow position. J Plast Reconstr Aesthetic Surg. 2014;67(9):1242-1247.