Technical Report on

Stā Active Device to Treat Elbow Pain

Minneapolis, December 3, 2020

ABSTRACT

Stā Active provided raw data set of a phase 1 clinical trial on the effectiveness of their device to treat elbow pain for N=24 patients undergoing a 10-week therapy with the device. The study design was a single intervention group pre-posttest design with no control group. Researchers at the University of Minnesota performed the relevant statistical analysis. Analysis showed that a 10-week treatment resulted in a median increase of 65% of grip strength, a mean increase of 76% in arm function as measured by the upper extremity functional index, and a median decrease of 56% in the level of pain experienced.

INTRODUCTION

Stā Active provided a raw data set of a phase 1 clinical trial to Dr. Jürgen Konczak at the University of Minnesota for further statistical analysis. Researchers of the University of Minnesota were not involved in any phases of patient recruitment and data collection. This report focuses solely on the statistical analysis and refrains from interpreting the impact of the data.

The study design was a single intervention group pre-posttest design with no control group. Participants presented with pain associated with lateral epicondylitis or tennis elbow. The participants were assessed at Baseline and after the completion of the intervention (Week 10). For this analysis, data from N=24 participants with complete data sets were included. Stā Active provided data on three continuous dependent variables: *Grip Strength* of the affected arm, the *Upper Extremity Functional Index* (*UEFI Score*), and a *Pain Score* derived from a visual analog scale. Time was the one independent variable (*Baseline* and *Week 10*). For the statistical analysis, variables were derived to represent the difference between these scores for each participant by subtracting the Baseline from the Week 10 scores. This method was utilized for all three dependent variables and then used to assess normality and for outliers.

Determining if data followed a normal distribution. In order to meet the assumptions necessary for analysis using a paired t-test, there must be one continuous dependent variable (i.e. *scores*) and one independent variable of dichotomous pairs (*Baseline* and *Week 10*). The data must approximate normality, meaning that the differences between the dependent variables (*scores* at *Baseline* and *Week 10*) are roughly normally distributed within a bell curve shape. This assumption was tested via the Kolmogorov-Smirnov test of normality.

Outlier analysis. Boxplots were used to visualize data and to separate them into quartiles. The box represents the middle 50% of the data. The bottom of the box reflects the boundary of the first quartile (Q1 = 25%), the top of the box denotes the upper boundary of the third quartile (Q3 = 75%). The respective range between Q1 and Q3 refers to the interquartile range (IQR). The dark line in the middle of the box is the median value of the data. For those data sets deemed to be normally distributed, data points 2 times outside the length of the IQR were considered as outliers. For the data that were not normally distributed, outliers were determined to be 1.5 times outside the IQR (Schwertman et al., 2004).

Statistical analysis. Primary analyses compared the mean (paired-samples t-test) or median (Wilcoxon signed-rank test) differences. A secondary analysis also was performed to determine the correlation between variables at Baseline and at Week 10. Significance was accepted at p = 0.05 level. Appropriate corrections to this p-value for repeated testing were made using the Holms-Bonferroni method (Holm, 1979). Data were analyzed using SPSS Statistics 26.0.

RESULTS

Grip Strength

A first question to answer was if the intervention led to any significant gains in grip strength as exerting high grip strength is associated with pain in people with a tennis elbow injury. The distribution of the *Grip Strength* data and the individual change for each participant are shown in Figure 1**.** Subsequent statistics indicated that the difference scores between Baseline and were not normally distributed as assessed by Kolmogorov-Smirnov's test (p = 0.001; see Figure 2A). As the data were not normally distributed, outliers were determined as > 1.5 IQR. There were three outliers within the data set, one that was more than 1.5 IQR and two were more than 3 IQR box-lengths from the edge of the box (Figure 2B). The data were analyzed with and without the outliers to determine whether they would cause a significant change to the results.

A Wilcoxon signed-rank test was conducted to determine the effect of the intervention on grip strength. Of the 23 participants, *Grip Strength* increased in 22 participants (96%) by Week 10. One participant revealed a lower *Grip Strength* after the intervention. With the outliers included in the dataset, there was a statistically significant increase in grip strength after the 10-week intervention (*Md* = 90.0 lbs) compared to grip strength at Baseline (*Md* = 60.0 lbs), z = 4.168, $p < 0.001$. Analysis of the difference scores remained statistically significant even after removal of the outliers, z = 3.884, $p < 0.001$. Median relative improvement in grip strength due to the intervention was 62% (range: -0.8% – 430%). This result indicates that <u>median grip strength was significantly higher after intervention</u> using the device.

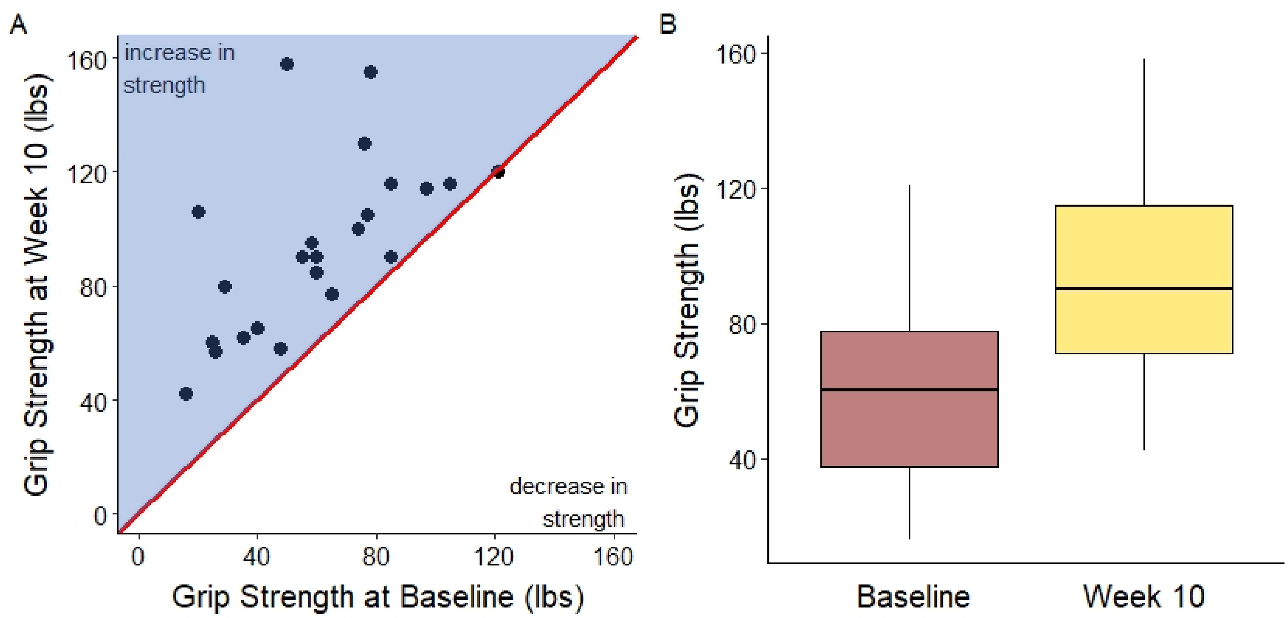

Figure 1. *Change in grip strength scores due to intervention.* ***A****. Scatterplot of Baseline versus post-test scores at Week 10. The red line represents the line of equality. Each data point corresponds to the Baseline/post-test coordinates of a single participant. Data points on or near this line indicate no or only minimal intervention-induced change. Note that most data points fall into the upper blue triangle indicating that the intervention was associated with gains in grip strength for the majority of participants.* ***B.*** *Boxplot of both the Baseline and Week 10 grip strength data. Line within a box indicates the median. Length of whiskers indicate the 1st and 99th percentiles of the distribution, respectively.*

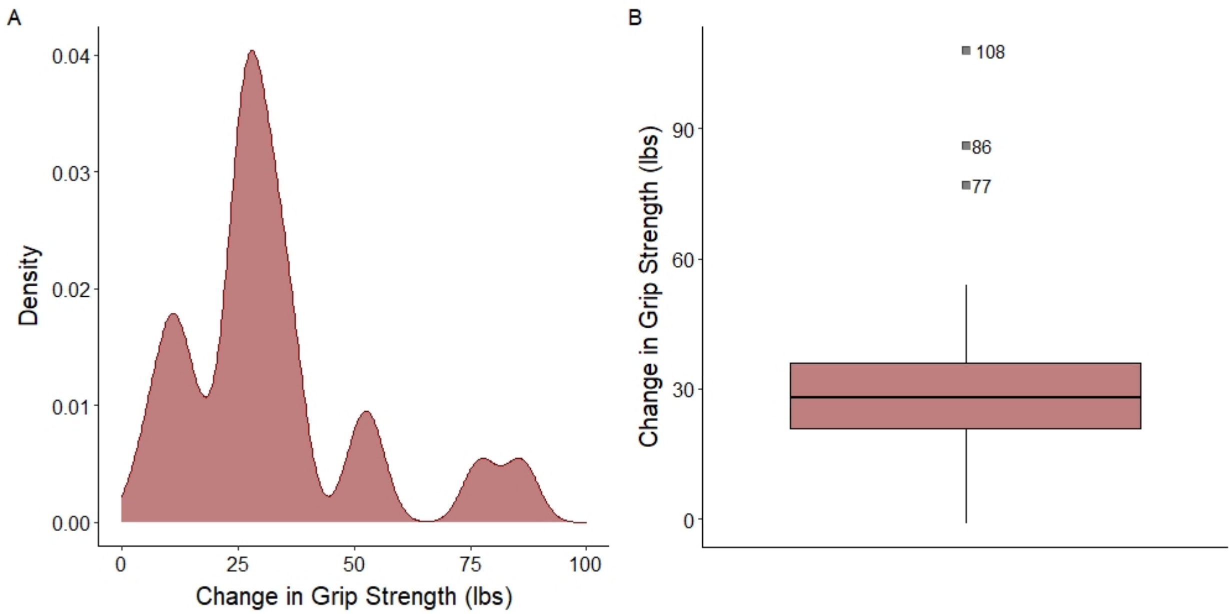

Figure 2. A. *Density of the predicted distribution of grip strength change between Baseline and Week 10. Note that the data distribution is skewed to the left indicating that most of the strength gains were between 5 and 45 lbs.* ***B.*** *Boxplot of the change in grip strength between Baseline and Week 10. The shaded box represents the values between the 25th and 75th percentile. Line within a box indicates the median. Length of whiskers indicate the 1st and 99th percentiles of the distribution, respectively. Outliers include subject 19 (score difference = 77 lbs), subject 24 (score difference = 86 lbs), and subject 20 (score difference = 108 lbs).*

UPPER EXTREMITY FUNCTIONAL INDEX

The Upper Extremity Functional Index (UEFI) is a patient reported outcome measure used to assess the functional impairment in individuals with musculoskeletal upper limb dysfunction. Higher scores indicate greater function and lower scores indicate greater impairment. The distribution of the UEFI scores and the individual change for each participant are shown in Figure 3. The data were normally distributed, as assessed by Kolmogorov-Smirnov's test (p = 0.200) (Figure 4A) and there were no outliers (Figure 4B). In absolute terms, the mean change in UEFI was 26 (SD = 17.3), which corresponded to a mean relative improvement of 75.6% for the group. A paired-samples t-test was used to determine whether there was a statistically significant mean change in UEFI scores pre- and post-intervention. UEFI scores were statistically significantly higher at Week 10 (M = 73.04, SD = 7.799) than at Baseline (M = 47.00, SD = 15.183), $t_{(23)}$ = 7.501, $p < 0.001$. The results indicate that the intervention significantly raised mean UEFI scores from Baseline to Week 10.

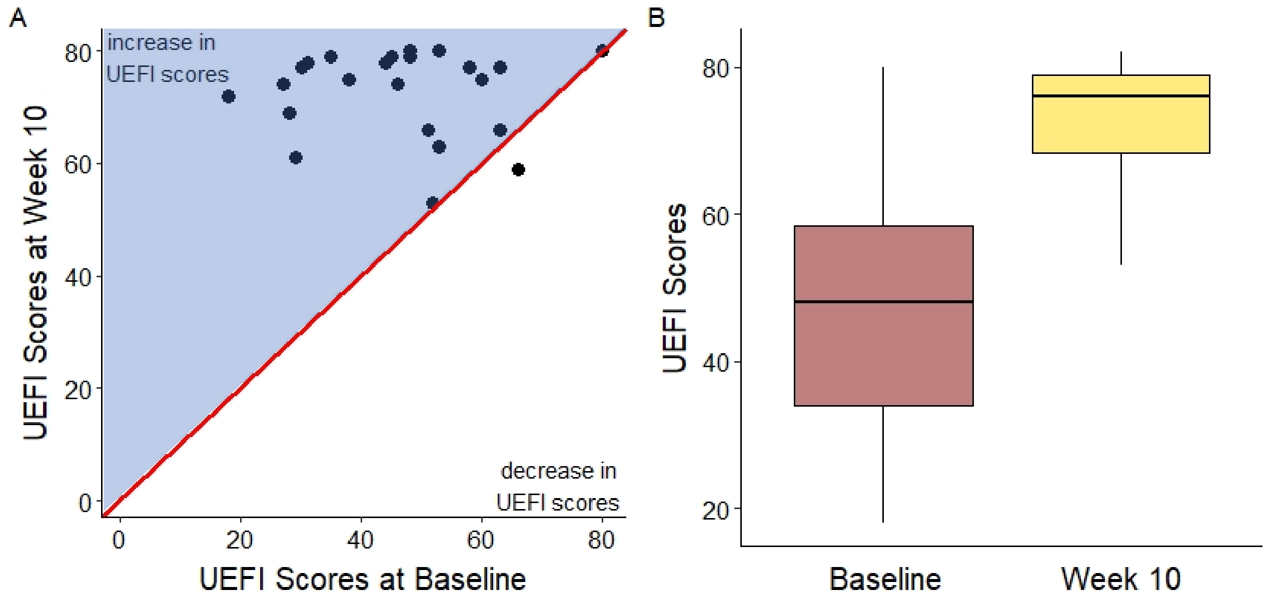

Figure 3. *UEFI scores before and after the intervention.* ***A.*** *Scatterplot of Baseline versus post-test scores at Week 10. The red line represents the line of equality. Each data point corresponds to the Baseline/post-test coordinates of a single participant. Data points on or near this line indicate no or only minimal intervention-induced change. Note that most data points fall into the upper blue triangle indicating that the intervention was associated with an increase in UEFI for the majority of participants.* ***B.*** *Boxplot of the UEFI scores at Baseline and Week. Line within a box indicates the median. Length of whiskers indicate the 1st and 99th percentiles of the distribution, respectively. There were no outliers at Baseline or Week 10.*

PAIN SCORE

The study used a visual analog scale to indicate the level of pain prior and post intervention (0 = no pain, 10 = max. pain). The difference between pain scores at Baseline and Week 10 failed the assumption of normality as assessed by the Kolmogorov-Smirnov's test ($p = 0.019$) (Figure 4A). However, there were no outliers (Figure 4B). A Wilcoxon signed-rank test was conducted to determine the effect the intervention on pain scores. Of the 24 participants, 23 reported lower pain scores at Week 10 compared to Baseline and only 1 participant reported a greater pain score after the intervention. There was a statistically significant decrease in reported pain scores after the intervention (Week 10: $Md = 3.50$) compared to the initial pain level before the intervention (Baseline: $Md = 8.50$), $z = -4.245$, $p < 0.001$ (Figure 5). The results indicate that the median pain scores were reduced across the 10-week intervention. The median relative reduction in pain during the 10-week intervention was 56.3%.

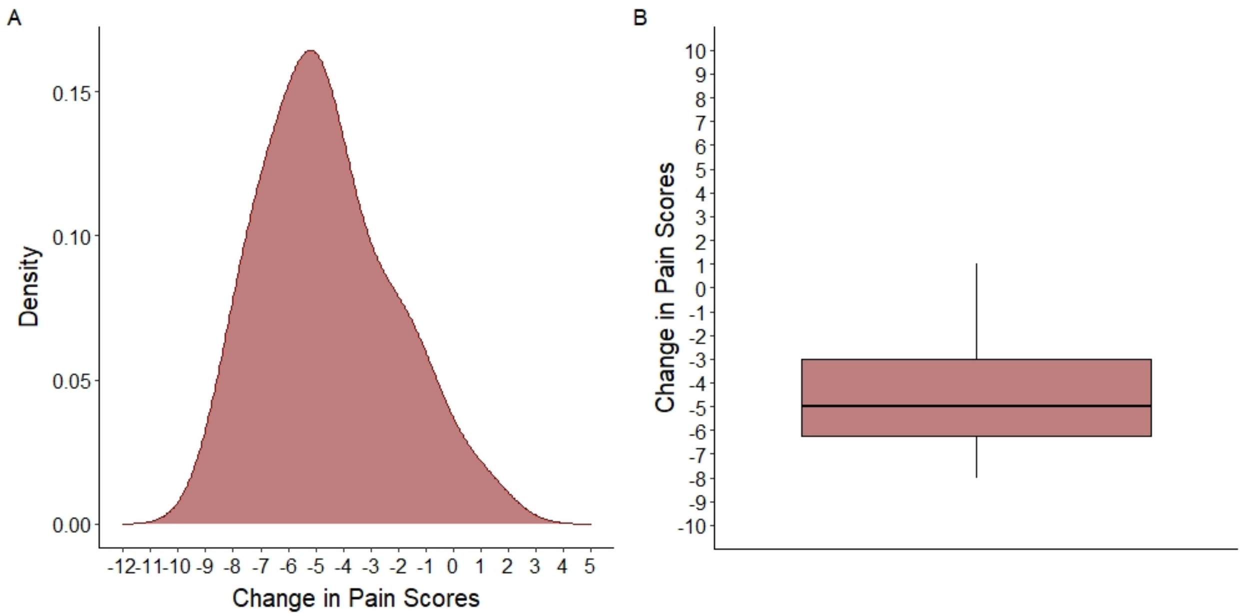

Figure 4. A. *The predicted distribution of the difference between pain scores at Week 10 and Baseline. Data did not approximate a normal distribution (see Kolmogorov-Smirnov's test of normality).* ***B.*** *Boxplot of the difference in pain scores before and after the intervention. Line within the box indicates the median. Length of whiskers indicate the 1st and 99th percentiles of the distribution, respectively. There were no outliers.*

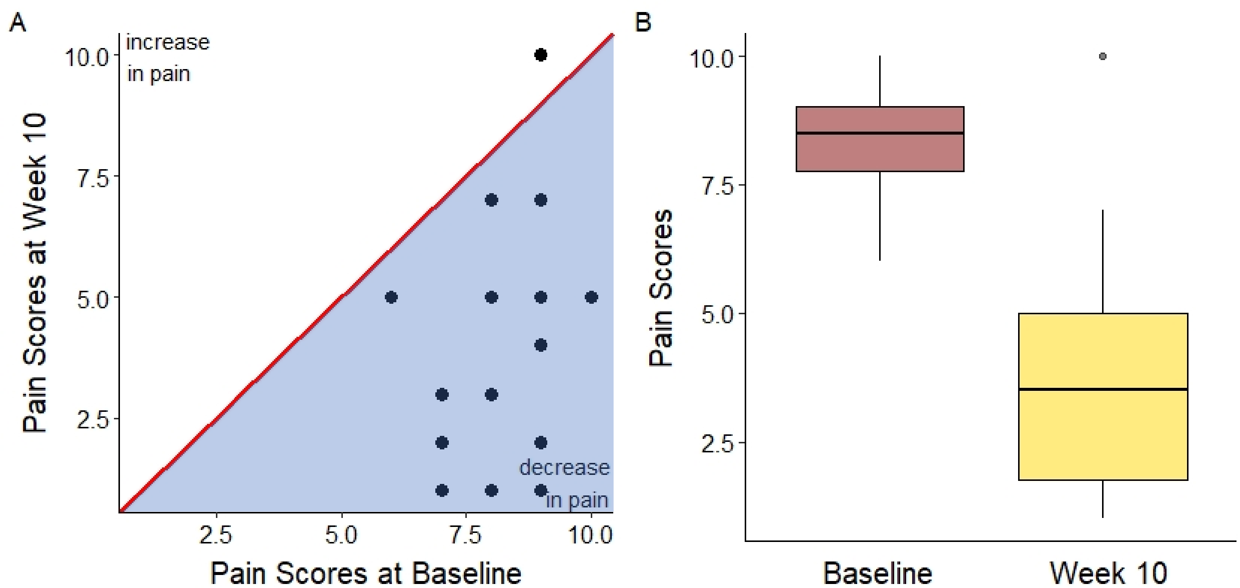

Figure 5. *Data visualization of the data points at Baseline and after the intervention show a trend towards lower pain scores after the intervention than before.* ***A.*** *The scatterplot data indicate that there is a difference in pain scores from Baseline to Week 10. If there were no difference, then the data points would align along the superimposed line of equality. As the data points are primarily below the line of equality, then the data show higher Baseline scores than at Week 10.* ***B.*** *The figure on the right is a boxplot of the pain score data at Baseline and at Week 10. The leftmost boxplot represent the Baseline scores and the rightmost boxplot represent Week 10 scores. Although there is one outlier at Week 10, there is a clear reduction of reported pain scores from Baseline to Week 10.*

Correlation Analysis

In a second analysis step, we performed a set of correlational analyses to understand the relationship and dependency between pain level, UEFI score and gains in grip strength on the variables separately at Baseline and at Week 10 (Figure 6). A Pearson product correlation revealed a statistically significant, large positive correlation between grip strength and UEFI score at Baseline ($r = 0.541$, $p = 0.008$, Figure 6A), with grip strength accounting for 29.3% of the variance in UEFI. In addition, the relationship between pain scores and UEFI scores at Week 10 yielded a statistically significant, large negative correlation ($r = -0.686$, $p < 0.001$, Figure 6F). Pain scores explained 47.1% of the variance in the UEFI scores. All other correlations for the pairs did not reach the level of significance.

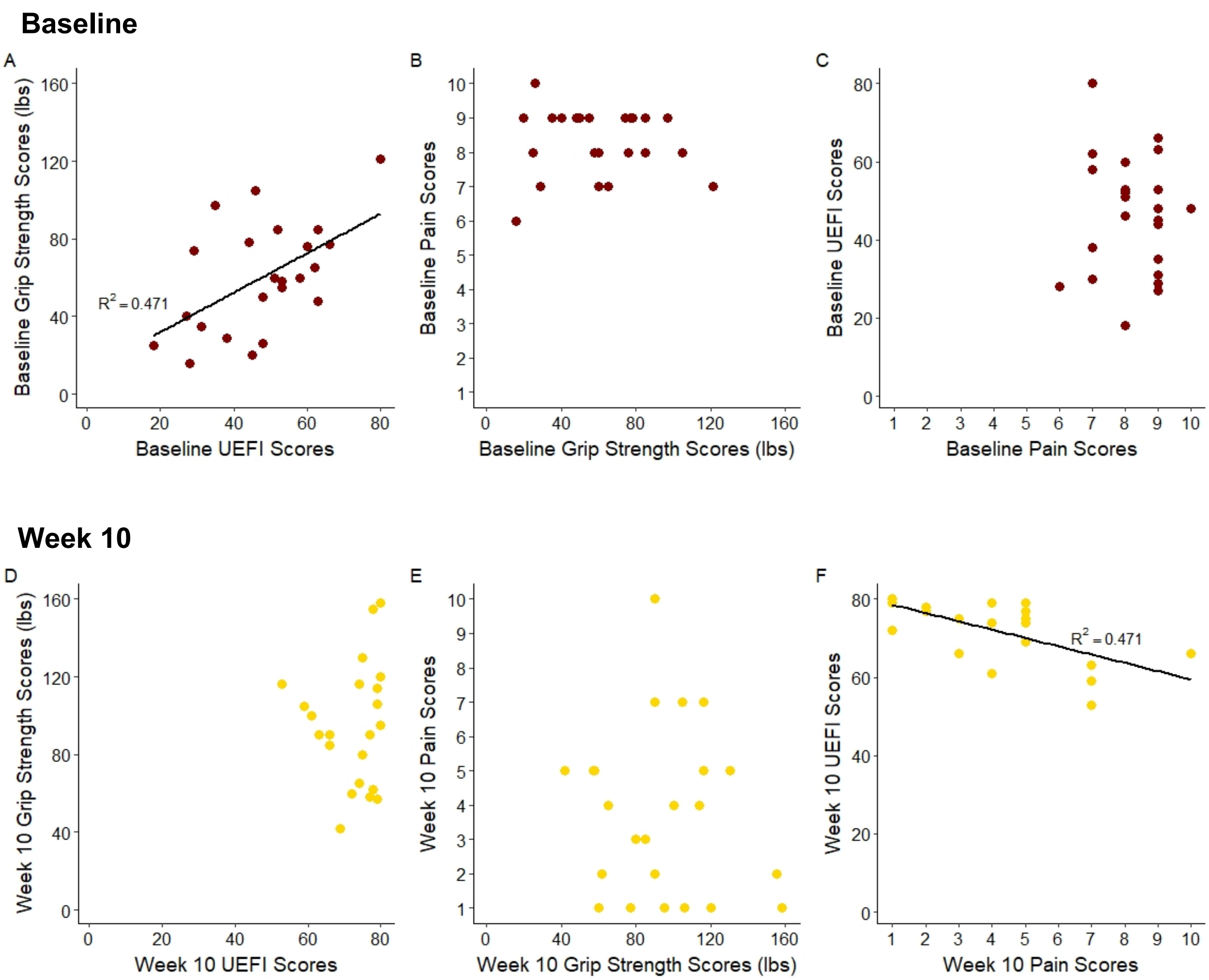

Figure 6. *Relationship between grip strength, UEFI and pain scores at Baseline (top row) and Week 10 (bottom row). Note that only grip strength and UEFI at Baseline and Uefi and pain scores at Week 10 are significantly linearly related.*

Supplementary Materials

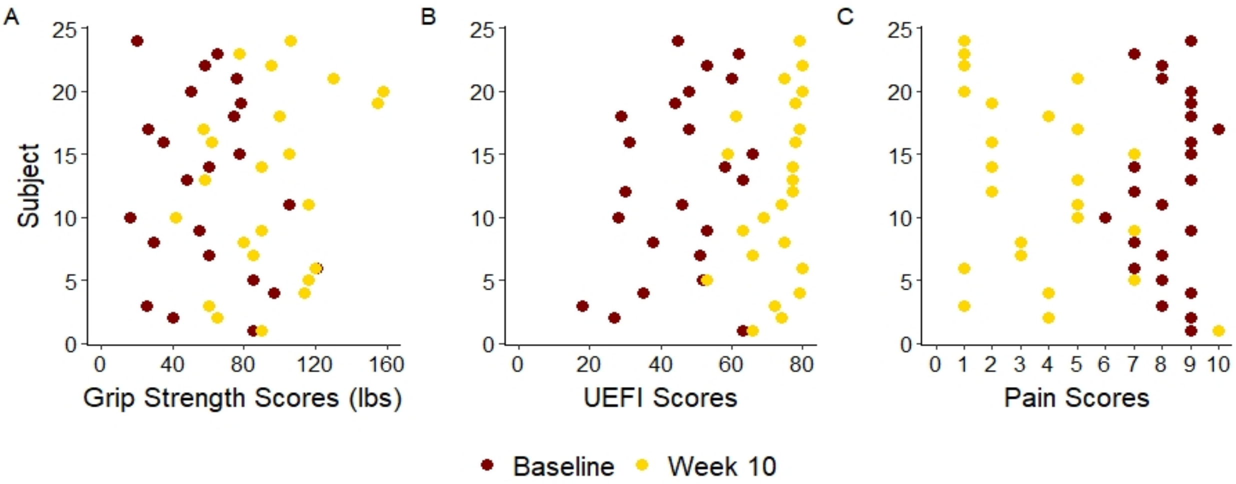

Figure 7. *Absolute change in each of the three measurements for each individual. Mapped are the individual values at Baseline and Week 10. Note the rightward shift at Week 10 for grip strength and UEFI score, indicating increased strength and upper extremity function. point of (**A**) grip strength, (**B**) UEFI scores, and (**C**) Pain scores. Note the leftward shift Week 10, indicating a reduction in pain.*