Safety of an Intentionally Displaced Reza Band® Upper Esophageal Sphincter (UES) Assist Device

Protocol Number: RB-002-01

Clinical Study Report

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1. EXECUTIVE SUMMARY

The safety of the *Reza Band*™ UES Assist Device (*Reza Band*) when placed as intended, and intentionally displaced laterally, was evaluated based on changes in heart rate, blood pressure, cardiac rhythm and intraocular pressure (IOP), as compared to baseline. Measurements of heart rate, blood pressure, cardiac rhythm and IOP were initially taken at baseline (i.e., without the *Reza Band* in place). The measurements were repeated at specified time points after the *Reza Band* was placed as intended at the cricoid, and with the *Reza Band* intentionally displaced laterally, both right and left sides of the neck, over the carotid and jugular vasculature.

Twenty (20) subjects were enrolled into the study who met the inclusion and exclusion criteria, and who were representative of the intended *Reza Band* patient population, i.e., subjects were clinically diagnosed with esophagopharyngeal reflux with extra-esophageal symptoms (chronic cough, choking, aspiration, chronic post nasal drip, sore throat and throat clearing).

No adverse events were reported during this study. There was no effect on heart rate, blood pressure, cardiac rhythm or IOP, when the *Reza Band* was initially placed compared to baseline, or when the *Reza Band* was intentionally displaced laterally. These results demonstrate that the device is unlikely to result in adverse impact if the device is displaced over the vascular structures of the neck.

This study also demonstrated that significantly less pressure is applied when the *Reza Band* is displaced laterally as compared to when placed as intended at the cricoid cartilage. Also, more than 5lbs. of force is required to intentionally laterally displace the *Reza Band* from its cricoid location. These findings demonstrate that the *Reza Band* is unlikely to be laterally displaced when properly fit, and that should lateral displacement occur, the applied pressure is significantly less than the prescribed pressure when being fit.

This study supplements the results of the previously conducted *Reza Band* pivotal clinical study, and demonstrates that the device is unlikely to result in adverse impact, if the device is laterally displaced.

2. INTRODUCTION

The *Reza Band* is fit by a physician to apply external pressure to the cricoid to treat the symptoms of esophagopharyngeal reflux. The *Reza Band* was developed to provide a non-invasive and non-pharmacologic treatment option for patients with esophagopharyngeal reflux. A pivotal safety and effectiveness clinical study (RB-001-02) of the *Reza Band* was previously conducted in 95 subjects at 5 investigational sites. The study evaluated the performance of the *Reza Band* in this patient population and the *Reza Band* was found to be significantly effective with no serious or unexpected adverse events reported.

A question was subsequently raised about whether there is the potential for an increased risk, associated with unintentional displacement of the *Reza Band* over the major vascular structures of the neck. Although these types of adverse events were not reported in the 95-subject pivotal study of the *Reza Band*, it was suggested that pressure on the carotid artery during displacement of the *Reza Band* could theoretically result in direct compressive occlusion of the vessel, reflex bradycardia, or dislodgement of an atheromatous plaque causing stroke and that these risks could be increased in patients with thin necks or in elderly users with comorbid

cardiovascular disease. It was also suggested that pressure on the jugular vein potentially could lead to an increase in IOP that, if prolonged and/or frequent, may lead to the risk of development of glaucomatous vision loss.

This study was designed to evaluate the impact of *Reza Band* placement as intended and with intentional lateral displacement, over the carotid and jugular vasculature on heart rate, blood pressure, cardiac rhythm, and IOP. This was an acute study where subjects wore the device under medical supervision while the various assessments were being conducted.

3. STUDY DESIGN

The study design, which was reviewed by FDA, was a prospective, non-randomized, open label, clinical study conducted at a single site. Twenty (20) subjects representative of the intended *Reza Band* patient population were enrolled into the study.

Measurements of heart rate, blood pressure, cardiac rhythm and IOP were initially taken at baseline (i.e., without the *Reza Band* in place). The measurements were repeated at specified time points after the *Reza Band* was placed as intended at the cricoid and with the *Reza Band* intentionally displaced laterally, over both the right and left sides of the neck, over the carotid and jugular vasculature. The *Reza Band* was initially fit to apply a pressure of at least 20mmHg as recommended in the device labeling, and then the Comfort Dial was maximally actuated in order to represent a more challenging situation than expected clinically.

Measurements of heart rate, blood pressure, cardiac rhythm and IOP were taken immediately after the *Reza Band* was placed on the neck in each of the specified scenarios (cricoid, right displacement and left displacement), 5 minutes after placement (except for IOP) and again 15 minutes after placement. The *Reza Band* was removed and 3 minutes later, IOP was again measured in each placement scenario[1]. After these assessments were conducted, the force needed to move the *Reza Band* from its intended position to completely off the cricoid, was measured.

4. TEST ARTICLES AND TEST EQUIPMENT

The Somna External Manometer connected to the Somna Pressure Sensor was used at the time of the fitting of the *Reza Band*. The External Manometer visually displays the pressure (in mmHg) being applied to the cricoid by the *Reza Band* to ensure the intended pressure was applied. See Appendix 1 of the study protocol for illustrations of the *Reza Band* and the External Manometer connected to the Pressure Sensor. The following test articles were used in this study:

- Somna *Reza Band* UES Assist Device (Part Number 101-1160-00)
- Somna External Manometer (Part Number 101-1240-00)
- Somna Pressure Sensor (Part Number 101-1230-00)

1 It has been reported that intraocular pressure (IOP) initially rises when a necktie is tightened, but returns to baseline. As reported by Talty, et al., the rise is first seen in 3 minutes, but by the end of 15 minutes it returns to the original pressure. Based on this information, IOP was obtained 3 minutes after removal of the Reza Band (Talty P, O'Brien PD. Does extended wear of a necktie cause raised intraocular pressure? J Glaucoma 2005;14:508-510).

The following test equipment was used in this study:

- IOP was measured by the Goldmann applanation tonometry method, using the Topcon SL-2ED Slit Lamp.
- Heart rate, cardiac rhythm and blood pressure were obtained with the Datascope Passport® 2 Patient Monitor.
- Mechanical force gauge with 0.1 lbs. resolution (Chatillon DFE-200)

5. STUDY CONDUCT

5.1 IRB Approval and Study Dates

The study was approved by the New England IRB, as a non-significant risk device study, on August 6, 2014. The first subject was screened and evaluated on August 7, 2014 and the study concluded on August 15, 2014. Each subject completed the study and his or her participation was within a single day.

5.2 Study Investigator and Location

The study investigator was a certified by the American Board of Otolaryngology and is a fellow in the American Academy of Otolaryngology–Head and Neck Surgery and the American College of Surgeons.

A practicing optometrist, obtained intraocular pressure, using a Goldmann applanation tonometer.

A cardiovascular surgeon, reviewed the cardiovascular results (heart rate, blood pressure and cardiac rhythm) and provided his analysis of those parameters. Those analyses are contained within the body of the report.

5.3 Investigational Subjects

Twenty (20) subjects were enrolled into the study. Subjects were representative of the intended *Reza Band* patient population. All subjects provided written informed consent prior to participation.

All enrolled subjects met the following inclusion and exclusion criteria specified in the protocol:

5.3.1 Inclusion Criteria

- 18 years of age or older
- Willing and able to provide informed consent
- Understood the clinical study requirements
- Clinically diagnosed with esophagopharyngeal reflux with extra-esophageal symptoms (i.e., chronic cough, choking, aspiration, chronic post nasal drip, globus, sore throat, throat clearing)
- Reflux Symptom Index (RSI) >13

5.3.2 Exclusion Criteria

- Treated with another investigational medical device and/or drug during the study
- Receiving treatment for sleep apnea with continuous positive airway pressure (CPAP)
- Female subjects who were pregnant or breast feeding
- Previous head or neck surgery or radiation
- History of carotid artery disease, thyroid disease, or cerebral vascular disease
- Suspected esophageal cancer
- Nasopharyngeal cancer
- Had either a pacemaker or implanted cardioverter-defibrillator (ICD)
- History of glaucoma

5.4 Study Procedures

5.4.1 The evaluations performed in this study included:
- Pressure being applied by the *Reza Band*
- Blood Pressure
- Heart Rate
- Cardiac Rhythm (Electrocardiogram)
- Intraocular Pressure (both eyes)
- Force to displace *Reza Band*

5.4.2 Evaluations were performed with the *Reza Band* worn in three anatomical locations:
- Worn as intended at the cricoid;
- Intentionally displaced laterally to the left side of the neck; and,
- Intentionally displaced laterally to the right side of the neck.

5.4.3 Parameters under investigation were assessed at the following times, as shown in Appendix 3 of the study protocol:
- Baseline
- Immediately after *Reza Band* placement and each lateral displacement
- 5 minutes after placement and each displacement (except for IOP)
- 15 minutes after placement and each displacement
- 3 minutes after removal (IOP only).

5.4.4 All evaluations were to be performed with the subject in the supine position, except for when evaluating IOP and the force required to displace the *Reza Band*, for which the subject was to be seated.

5.4.5 The protocol required that the subjects were not to be wearing any closed collars, neckties or other restrictive clothing. If a subject presented with this type of clothing, it was to be loosened and/or removed, if possible. The subject was to wait a minimum of 15 minutes after the clothing had been loosened or removed before participating in the study. However, none of the subjects presented with any restrictive clothing.

5.4.6 The *Reza Band* was fit per the Instructions for Use (see Appendix 4 of study protocol) using the Pressure Sensor connected to the External Manometer. Once the *Reza Band* had been fit to achieve a minimum pressure of 20 mmHg, the Comfort Dial was to be turned clockwise (fully actuated) for the maximum pressure, until it came to the stop. The subject was to remain still and look forward without moving as the pressure setting was being completed. The pressure being displayed by the External Manometer was recorded on the Case Report Form (see Appendix 5 of the study protocol).

5.4.7 With the *Reza Band* fit as intended, at the cricoid position, the evaluations as provided in the Study Procedure Schedule were conducted, and the results were recorded on the Case Report Form, and an electrocardiogram generated.

5.4.8 Once those evaluations had been completed, using the randomization scheme provided in the clinical protocol, the *Reza Band* was moved laterally to the side of neck. The *Reza Band* setting was not changed from when fit at the cricoid position and with the Comfort Dial fully actuated (maximal pressure) as described in 5.4.6. The evaluations were again conducted, as specified in the Study Procedure Schedule.

5.4.9 The *Reza Band* was then moved laterally to the other side of the neck, and the evaluations were again conducted, as specified in the Study Procedure Schedule.

5.4.10 After the assessments had been completed, the amount of force needed to move the *Reza Band* completely off the intended position at the cricoid, was measured and then the subject's participation was concluded.

6. STUDY ENDPOINTS

Safety of an intentionally displaced *Reza Band* was evaluated based on changes in heart rate, blood pressure, cardiac rhythm and IOP, as compared to baseline. Please refer to Section 8, Study Results for study findings.

7. ADVERSE EVENTS

Study subjects were monitored for potential risks, including arrhythmia, vascular occlusion, hypertension, hypotension, IOP changes, and discomfort wearing the *Reza Band*.

No adverse events were reported during this study.

8. STUDY RESULTS

Study results are summarized in this section.

8.1 Subject Demographics and Other Characteristics

Table 1 and Table 2 below show the subject demographics and other characteristics. The study population included 12 males (60%) and 8 females (40%). Nineteen (19) subjects were Caucasian and 1 subject was African American. The mean age of the study subjects was 46.3

years (range 19.5 to 71.6). The mean BMI was 28.7 (range 20.3 to 40.3). The mean neck size was 15.6" (range 13.5 to 19.0). The mean RSI was 29.7 (range 16 to 41), thus all subjects had symptoms of esophagopharyngeal reflux. All subjects met the inclusion and exclusion criteria and the study population was representative of the intended user population. Of note, one subject had a neck size of 13.5", representative of the lower end of the 5th percentile neck size for an adult female, and one subject had a neck size of 19.0", representative of higher end of the 5th percentile, for an adult male.

Table 1
Subject Age, BMI, Neck Size and RSI

Variable	Age (years)	BMI	Neck Size (Inches)	RSI
Mean	46.3	28.7	15.6	29.7
Standard Deviation	17.3	5.2	1.4	7.8
Median	50.0	28.4	16.0	29.5
Range	19.5 – 71.6	20.3 – 40.3	13.5 – 19.0	16 - 41

Table 2
Subject Gender and Race

Variable	Gender (Male) N (%)	Gender (Female) N (%)	Race (Caucasian) N (%)	Race (African American) N (%)
Gender and Race	12 (60%)	8 (40%)	19 (95%)	1 (5%)

8.2 Pressure Applied by the *Reza Band* at Cricoid and When Laterally Displaced

In accordance with the study protocol, after baseline measurements of heart rate, blood pressure, cardiac rhythm and IOP were taken, and the *Reza Band* was fit per the Instructions for Use (see Appendix 4 of the study protocol) using the External Manometer and Pressure Sensor. Once the *Reza Band* had been fit to achieve a minimum pressure of 20 mmHg, the Comfort Dial was fully actuated, until the Comfort Dial came to the stop, to achieve the maximum pressure, and the resulting maximum pressure was recorded.

These pressure measurements are summarized in Table 3 below. The mean initial pressure, with the Comfort Dial not actuated, was 20.9 mmHg (range 20-24 mmHg). All pressures were set to at least 20 mmHg as required by the protocol.

With the Comfort Dial fully actuated, to achieve the maximum pressure, the mean pressure attained was 32.6mmHg (range 26-39mmHg). This pressure was below the maximum pressure of 50mmHg, as described in the study protocol, but nevertheless represents the maximum pressure that would be expected, with the Comfort Dial fully actuated, when the *Reza Band* is fit in accordance with the Instructions for Use.

The maximum pressure with the Comfort Dial fully actuated was also measured with the *Reza Band* displaced laterally over the vascular structures of the neck. As expected, based on the design of the *Reza Band*, when the *Reza Band* was displaced laterally, the pressures were lower, when the *Reza Band* was fit as intended at the cricoid cartilage. The mean pressure when displaced laterally to the left was 13.3 mmHg (range 7-22 mmHg), and 14.6 mmHg (range 6-22 mmHg), when displaced laterally to the left. These pressure data demonstrate that the

highest pressure is achieved when the *Reza Band* is fit as intended over the cricoid. The potential for high pressures being applied by the *Reza Band*, adversely impacting the sensitive structures of the neck, should the *Reza Band* be displaced, is low.

Table 3
Comparison of *Reza Band* Applied Pressure
At Cricoid and Laterally Displaced

Variable	Cricoid Pressure (Comfort Dial OFF) (mmHg)	Cricoid Pressure (Comfort Dial MAXIMUM) (mmHg)	Displaced to Left (Comfort Dial MAXIMUM) (mmHg)	Displaced to Right (Comfort Dial MAXIMUM) (mmHg)
Mean	20.9	32.6	13.3	14.6
Standard Deviation	1.4	3.3	4.9	4.0
Median	20	34	12	15
Range	20-24	26-39	7-22	6-22

8.3 Effect of *Reza Band* Placement and Displacement on Heart Rate

Heart rate was assessed at the following time points during this study:

- Baseline (B)
- Immediately after placement of the *Reza Band* at the cricoid (C-0)
- 5 minutes after placement at the cricoid (C-5)
- 15 minutes after placement at the cricoid (C-15)
- Immediately after lateral displacement of the *Reza Band* to the left (L-0)
- 5 minutes after lateral displacement to the left (L-5)
- 15 minutes after lateral displacement to the left (L-15)
- Immediately after lateral displacement of the *Reza Band* to the right (R-0)
- 5 minutes after lateral displacement to the right (R-5)
- 15 minutes after lateral displacement to the right (R-15)

Heart rate data for the study subjects are summarized in Table 4 below. As the data indicate, heart rate was stable throughout the study and there was no impact of *Reza Band* when placed as intended or laterally displaced, on heart rate.

Table 4
Effect of *Reza Band* Placement and Displacement
Heart Rate
Beats per Minute (bpm)

Time Point	B	C-0	C-5	C-15	L-0	L-5	L-15	R-0	R-5	R-15
Mean	63.5	65.5	63	64.5	64.3	60.8	61.9	65.9	62.9	62.8
Standard Deviation	8.2	11.0	7.8	9.5	9.0	7.7	8.4	10.0	8.3	8.2
Median	63.5	63.5	62	62	63.5	58.5	62	64.5	61	60
Minimum	50	50	50	50	52	50	46	52	48	50
Maximum	81	93	77	87	80	77	74	82	79	77

An Analysis of Variance (One Way) was conducted to determine whether there was any effect of *Reza Band* placement or displacement on heart rate. As shown in Table 5 below, the p-value was 0.71301, demonstrating that in this study there was no significant effect, due to either the intended placement or intentional lateral displacement, of the *Reza Band*, on heart rate.

Table 5
Analysis of Variance (One-Way)
Heart Rate

Groups	Sample Size	Sum	Mean	Variance
56	19	1,213.	63.84211	68.25146
53	19	1,257.	66.15789	119.14035
52	19	1,208.	63.57895	57.1462
56	19	1,234.	64.94737	90.49708
55	19	1,231.	64.78947	80.28655
55	19	1,160.	61.05263	60.83041
54	19	1,183.	62.26316	71.64912
53	19	1,265.	66.57895	94.92398
53	19	1,206.	63.47368	66.26316
53	19	1,203.	63.31579	65.11696

ANOVA						
Source of Variation	SS	df	MS	F	p-level	F crit
Between Groups	484.10526	9	53.78947	0.69486	0.71301	2.26472
Within Groups	13,933.89474	180	77.41053			
Total	14,418.	189				

In addition to the Analysis of Variance, student t-tests were conducted to determine the potential impact of *Reza Band* intended placement and lateral displacement, on heart rate, at various time intervals, as compared to baseline. The data, which are summarized in Table 6 below, demonstrate that there was no significant impact on heart rate during *Reza Band* placement or displacement.

Table 6
Student's t-test
Heart Rate
Baseline vs. All Others

Time Point	B	C-I	C-5	C-15	L-I	L-5	L-15	R-I	R-5	R-15
p-Value	N/A	0.5092	0.5092	0.8601	0.8601	0.2911	0.5476	0.4017	0.8490	0.8036

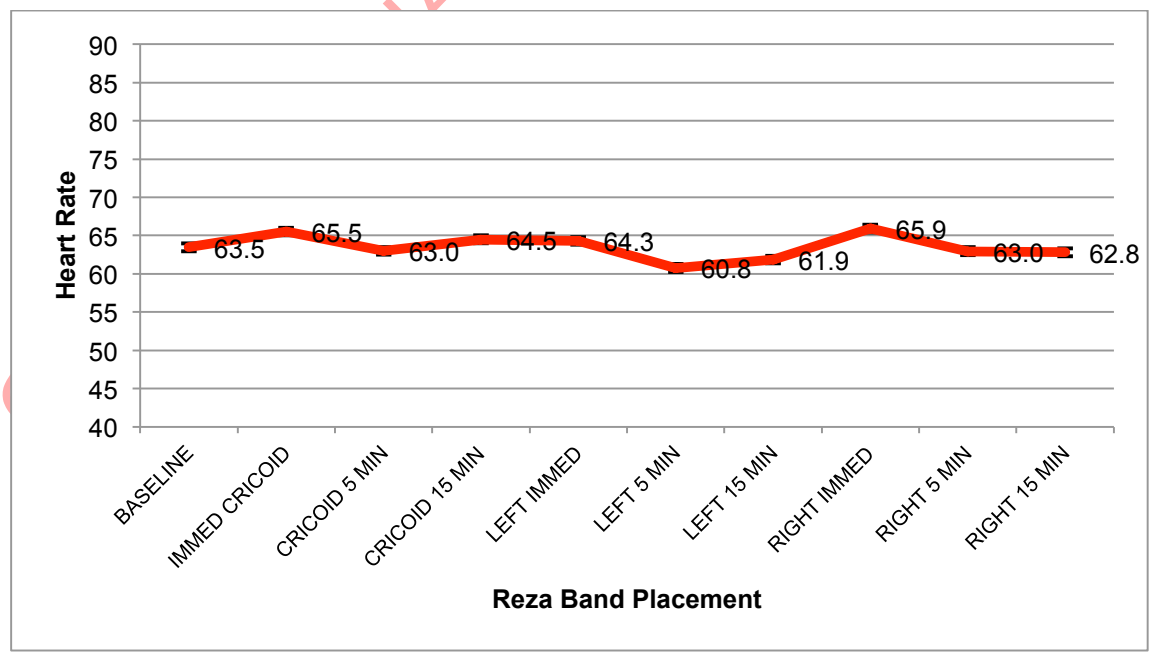
Heart rate data are graphically presented in Figure 1 below. Error bars illustrate the consistency in heart rate during *Reza Band* intended placement and lateral displacement.

In addition to the aggregate heart rate data for the study population described above, heart rate variability was also reviewed at the individual subject level. As expected, there was some variability, but no trends were apparent as a function of *Reza Band* intended placement or lateral displacement. Please refer to Attachment 2 for the raw data for individual subject data.

The maximal heart rate difference, at any assessment compared to baseline, was also evaluated at the subject level. The mean maximal difference in heart rate for all time points compared to baseline was 6.1 +/- 7.8bpm. The median maximal heart rate difference was 5 bpm and the range was -9 bpm to 23bpm.

The maximal heart rate difference at any time point compared to baseline for all but 3 subjects was at or below 10bpm. The three subjects with greater heart rate variability (RB-002-08, RB-002-13 and RB-002-18), had a maximum heart rate difference compared to baseline of 16, 23 and 23bpm, respectively. Analysis of the data reveals no trends in the heart rate for these 3 subjects.

Figure 1
Heart Rate as a Function of *Reza Band* Placement



8.4 Effect of *Reza Band* Placement and Displacement on Blood Pressure

Blood pressure was assessed at the same time points as heart rate, specifically:

- Baseline (B)
- Immediately after placement of the *Reza Band* at the cricoid (C-0)
- 5 minutes after placement at the cricoid (C-5)
- 15 minutes after placement at the cricoid (C-15)
- Immediately after intentional displacement of the *Reza Band* to the left (L-0)
- 5 minutes after displacement to the left (L-5)
- 15 minutes after displacement to the left (L-15)
- Immediately after intentional displacement of the *Reza Band* to the right (R-0)
- 5 minutes after displacement to the right (R-5)
- 15 minutes after displacement to the right (R-15)

8.4.1 Systolic Blood Pressure

Systolic blood pressure data are summarized in Table 7 and Table 8 below. It can be seen that the systolic blood pressure was stable throughout the study and there was no impact of the *Reza Band* placement at the cricoid, or the lateral displacement.

Table 7
Effect of *Reza Band*
Systolic Blood Pressure (mmHg)

Time Point	B	C-0	C-5	C-15	L-0	L-5	L-15	R-0	R-5	R-15
Mean	122.8	124.5	123.0	123.6	125.3	121.9	122.3	123.5	121.6	120
Standard Deviation	13.87	10.98	13.27	13.24	12.69	12.94	12.01	11.78	11.08	10.4
Median	121.5	126	122.5	126	126	121.5	122	123.5	123	119
Minimum	106	104	104	104	105	100	104	104	104	106
Maximum	145	145	149	148	149	153	147	147	144	137

An Analysis of Variance (One Way) was conducted to determine whether there was any effect of *Reza Band* intended placement or lateral displacement on systolic blood pressure. As shown in Table 8 below, the p-level was 0.96912, demonstrating that there was no significant effect by the *Reza Band* intended placement or lateral displacement, in relation to systolic blood pressure.

Table 8
Analysis of Variance (One-Way)
Systolic Blood Pressure

Groups	Sample Size	Sum	Mean	Variance
118	19	2,338.	123.05263	201.7193
112	19	2,378.	125.15789	118.14035
114	19	2,346.	123.47368	181.04094
115	19	2,357.	124.05263	180.60819
112	19	2,393.	125.94737	159.83041
116	19	2,322.	122.21053	174.84211
114	19	2,331.	122.68421	148.22807
110	19	2,360.	124.21053	135.84211
108	19	2,323.	122.26316	118.76023
111	19	2,288.	120.42105	109.59064

ANOVA						
Source of Variation	SS	df	MS	F	p-level	F crit
Between Groups	434.23158	9	48.24795	0.31563	0.96912	2.26472
Within Groups	27,514.84211	180	152.86023			
Total	27,949.07368	189				

The maximal systolic blood pressure difference, as compared to baseline, was also assessed at the individual subject level. The mean maximal difference in systolic blood pressure, at any time point, as compared to baseline, was 8.25 +/-9.7mmHg. The median maximal systolic blood pressure difference at any time point was 7mmHg and the range was -14 to 27mmHg.

Three subjects (RB-002-03, RB-002-15 and RB-002-16) had maximal systolic blood pressure differences greater than 20mmHg, when compared to baseline (24, 26 and 27mmHg, respectively), at some point during the study. The absolute maximum systolic blood pressure for these subjects was 131, 132, and 135mmHg, respectively. Even with the differences being greater than 20mmHg, as compared to baseline, the absolute systolic blood pressure values were considered within normal limits.

The increases in the systolic blood pressure were not due to the presence of the Reza Band, at any of the three anatomical locations, for any of the subjects. The known variability of the systolic blood pressure for all subjects, including the three subjects, was considered normal and typical. If there were going to be an effect of the *Reza Band* on the compression of the carotid, heart rate and blood pressure would be expected to decrease, due to the parasympathetic response of the vagus nerve. If compression at the carotid were to occur, the carotid sinus would elicit the parasympathetic response, and would cause the heart to slow, and potentially cause the blood pressure to drop. There was no blood pressure drop with any of the subjects.

Therefore, it was concluded that systolic blood pressure for all subjects was within normal limits. Additionally, review of the heart rate data reveals no trends for these 3 subjects.

The Case Report Forms for all subjects are provided under Attachment 2.

8.4.2 Diastolic Blood Pressure

Diastolic blood pressure data are summarized in Table 9 and Table 10 below. As the data in Table 9 demonstrate, diastolic blood pressure was stable throughout the study and there was no apparent impact of *Reza Band* placement or displacement for the study population.

Table 9
Effect of *Reza Band*
Diastolic Blood Pressure (mmHg)

Time Point	B	C-0	C-5	C-15	L-0	L-5	L-15	R-0	R-5	R-15
Mean	68.25	72.15	72	73.25	72.85	71.25	73.5	73.3	71.6	71.8
Standard Deviation	10.65	8.96	9.44	10.83	8.85	11.72	10.21	8.41	8.78	6.58
Median	67.5	71.5	71.5	73.5	71	70.5	75	75	70.5	70
Minimum	43	56	53	51	55	42	50	56	55	58
Maximum	85	90	93	98	88	98	91	87	87	85

An Analysis of Variance was conducted to determine whether there was any effect of *Reza Band* placement or displacement on diastolic blood pressure. As shown in Table 10 below, the p-value was 0.85084, indicating there was no significant effect on *Reza Band* placement or displacement on diastolic blood pressure.

Table 10
Analysis of Variance (One-Way)
Diastolic Blood Pressure

Groups	Sample Size	Sum	Mean	Variance
43	19	1,322.	69.57895	82.47953
61	19	1,382.	72.73684	77.53801
62	19	1,378.	72.52632	88.26316
51	19	1,414.	74.42105	94.92398
62	19	1,395.	73.42105	75.81287
42	19	1,383.	72.78947	94.95322
50	19	1,420.	74.73684	77.64912
61	19	1,405.	73.94737	65.83041
60	19	1,372.	72.21053	73.50877
68	19	1,368.	72.	44.88889

ANOVA						
Source of Variation	SS	df	MS	F	p-level	F crit
Between Groups	370.67895	9	41.18655	0.53086	0.85084	2.26472
Within Groups	13,965.26316	180	77.5848			
Total	14,335.94211	189				

The maximal diastolic blood pressure difference compared to baseline was also assessed at the individual subject level. The mean maximal difference in diastolic blood

pressure at any time point compared to baseline was 11.85 +/- 7.9mmHg. The median maximal diastolic blood pressure difference at any time point was 12.5mmHg and the range was -2 to 25mmHg.

Four subjects (RB-002-01, RB-002-03 and RB-002-13 and RB-002-16) each had single diastolic blood pressure differences greater than 20mmHg, when compared to baseline (25, 23, 22 and 21mmHg, respectively). The maximum diastolic blood pressure for these subjects was 68, 87 98 and 87mmHg, which is considered normal.

These transient increases in the diastolic blood pressure are considered normal, due to the known variability of blood pressure, and not due to the presence of the *Reza Band*. As discussed above, if a compression of the carotid did occur, the effect would be a decrease of the blood pressure, due to the parasympathetic response of the vagus nerve.

8.5 Effect of *Reza Band* Placement and Displacement on Cardiac Rhythm

The electrocardiograms (ECGs) were reviewed by the cardiologist, to determine whether there was any impact on cardiac rhythm, when the *Reza Band* was placed as intended, or intentionally displaced, over the jugular and carotid vasculature. It was determined that there was no change in the ECGs for any of the subjects at any time during the study, when comparing the baseline ECG, to any other ECG, at any point in the study, for all subjects. Therefore, it was concluded that there was no effect of cardiac rhythm by the presence of the *Reza Band*, either at the cricoid, displaced to the left or displaced to the right. See Attachment 2 for the ECG strips.

8.6 Effect of *Reza Band* Intended Placement and Lateral Displacement on Intraocular Pressure (IOP)

IOP was assessed in each eye at the following time points during this study:

- Baseline (B)
- Immediately after placement of the *Reza Band* at the cricoid (C-0)
- 15 minutes after placement at the cricoid (C-15)
- 3 minutes after removal of the *Reza Band* (C-R)
- Immediately after intentional displacement of the *Reza Band* to the left (L-0)
- 15 minutes after displacement to the left (L-15)
- 3 minutes after removal of the *Reza Band* following left displacement (L-R)
- Immediately after intentional displacement of the *Reza Band* to the right (R-0)
- 15 minutes after displacement to the right (R-15)
- 3 minutes after removal of the *Reza Band* following right displacement (R-R)

8.6.1 Left Eye Intraocular Pressure

Left eye IOP data are summarized in Table 11 and Table 12 below. The left eye IOP was stable throughout the study and there was no impact of *Reza Band* intended placement or lateral displacement.

Table 11
Effect of *Reza Band*
Left Eye IOP (mmHg)

Time Point	B	C-0	C-15	C-R	L-0	L-15	L-R	R-0	R-15	R-R
Mean	16.15	15.90	16.20	15.90	15.65	15.80	15.85	15.55	15.85	15.80
Standard Deviation	3.13	3.13	2.84	2.97	3.07	2.98	2.98	2.84	2.89	2.86
Median	16.5	16	17	16	16.5	16	17	16	16	16
Minimum	10	11	10	9	9	10	10	10	10	10
Maximum	20	21	20	20	20	20	20	19	20	20

An Analysis of Variance was conducted to determine whether there was any effect of *Reza Band* intended placement or lateral displacement on left eye intraocular pressure. As shown in Table 12 below, the p-level was 0.9981, demonstrating that there was no significant effect of *Reza Band* placement or displacement on left eye intraocular pressure.

Table 12
Analysis of Variance (One-Way)
Intraocular Pressure
Left Eye

Groups	Sample Size	Sum	Mean	Variance
12	19	311.	16.36842	9.35673
11	19	307.	16.15789	8.91813
17	19	307.	16.15789	8.47368
16	19	302.	15.89474	9.32164
17	19	296.	15.57895	9.81287
16	19	300.	15.78947	9.39766
17	19	300.	15.78947	9.28655
16	19	295.	15.52632	8.48538
16	19	301.	15.84211	8.80702
16	19	300.	15.78947	8.61988

ANOVA						
Source of Variation	SS	df	MS	F	p-level	F crit
Between Groups	12.04737	9	1.3386	0.14794	0.9981	2.26472
Within Groups	1,628.63158	180	9.04795			
Total	1,640.67895	189				

The maximal left eye IOP difference at any time point compared to baseline was also assessed at the individual subject level. The mean maximal difference in left eye IOP at any time point compared to baseline was 0.40 +/- 1.23mmHg. The median maximal left eye IOP difference, at any time point, as compared to baseline, was 0 mmHg, and the range was -1 to 5mmHg.

All subjects had a maximal difference, as compared to baseline, ranging from -1 to +1 mmHg, except for subject RB-002-01. The Optometrist reported that the subject with a maximal IOP difference of 5 mmHg had squeezed his eyes due to stinging of the eye drops used prior to baseline IOP being measured, which was considered to be the cause of his low initial IOP measurements (12mmHg at baseline and 11mmHg immediately after placement of the *Reza Band* at the cricoid). The subject's subsequent IOPs in the left eye, ranged between 16 and 17mmHg.

Excluding the anomaly with subject RB-002-001, there was no significant difference in IOP in the right eye in any subject, when compared to the baseline IOP.

8.6.2 Right Eye Intraocular Pressure

Right eye IOP data are summarized in Table 13 and Table 14 below. The right eye IOP was stable throughout the study and there was no impact of *Reza Band* placement or displacement.

Table 13
Effect of *Reza Band*
Right Eye IOP (mmHg)

Time Point	B	C-0	C-15	C-R	L-0	L-15	L-R	R-0	R-15	R-R
Mean	15.85	15.65	15.70	15.60	15.50	15.85	15.50	15.70	15.85	15.60
Standard Deviation	3.30	3.25	2.96	3.20	3.12	3.20	3.05	2.79	2.89	2.84
Median	16	16	16	16	16	16.5	16.5	16	16	16
Minimum	8	9	9	8	8	9	9	9	9	9
Maximum	20	20	20	20	19	20	19	19	20	19

An Analysis of Variance was conducted to determine whether there was any effect of *Reza Band* placement or displacement on right eye IOP. As shown in Table 14 below, the p-level was 0.9999, demonstrating there was no significant effect of *Reza Band* placement or displacement on right eye intraocular pressure.

Table 14
Analysis of Variance (One-Way)
Intraocular Pressure
Right Eye

Groups	Sample Size	Sum	Mean	Variance
12	19	305.	16.05263	10.60819
10	19	303.	15.94737	9.27485
16	19	298.	15.68421	9.22807
16	19	296.	15.57895	10.81287
15	19	295.	15.52632	10.26316
18	19	299.	15.73684	10.53801
16	19	294.	15.47368	9.81871
16	19	298.	15.68421	8.22807
16	19	301.	15.84211	8.80702
17	19	295.	15.52632	8.37427

ANOVA						
Source of Variation	SS	df	MS	F	p-level	F crit
Between Groups	6.33684	9	0.70409	0.07338	0.9999	2.26472
Within Groups	1,727.15789	180	9.59532			
Total	1,733.49474	189				

The maximal IOP difference, as compared to baseline, was also assessed at the individual subject level. The mean maximal difference, in right eye IOP, at any time point, as compared to baseline, was 0.45 +/- 1.39mmHg. The median maximal right eye IOP difference, at any time point, as compared to baseline, was 0 mmHg, and the range was -1 to 6mmHg.

All subjects had a maximal difference, as compared to baseline, ranging from -1 to +1mmHg (except for subject RB-002-01). The Optometrist reported that the subject with a maximal IOP difference of 6mmHg had squeezed his eyes due to stinging of the eye drops used prior to baseline IOP being measured, which was considered to be the cause of his low initial IOP measurements (12mmHg at baseline and 10mmHg immediately after placement of the *Reza Band* at the cricoid). The subject's remaining IOPs, in the right eye, ranged between 15 and 18mmHg.

Excluding the anomaly with subject RB-002-001, there was no significant difference in IOP in the right eye, in any subject, when compared to the baseline IOP.

8.7 Force Required to Displace *Reza Band* from Cricoid Cartilage

After all the study assessments had been completed, the force required to completely displace the *Reza Band*, as initially fit, with the Comfort Dial fully actuated, from its intended location at the cricoid, was measured. These data are summarized in Table 15 below.

The mean force required to intentionally displace the *Reza Band* from its intended placement at the cricoid, was 5.6lbs. (with a range 5.1 – 6.5lbs.), which is in excess of the >2lbs. specification in place for the engineering testing, using Plexiglas neck rings. This result was not unexpected,

as the skin and anatomy of the neck provide greater resistance to unintentional displacement than the smooth Plexiglas rings used for bench testing.

These results furthermore demonstrate that when fit in accordance with the Instructions for Use, the *Reza Band* resists intentional (and therefore also unintentional) lateral displacement from its intended placement, at the cricoid.

Table 15
Force Required to Displace *Reza Band* from Cricoid (lbs.)

Variable	Displacement Force (lbs.)
Mean	5.6
Standard Deviation	0.47
Median	5.55
Range	5.1 – 6.5

9. DISCUSSION AND CONCLUSIONS

This study was designed to evaluate whether there is a potential risk, associated with unintentional lateral displacement of the *Reza Band* over the major vascular structures of the neck. The *Reza Band* was placed as intended over the cricoid, and intentionally laterally displaced, over the vasculature, on both the right and left sides of the neck. Under each placement/displacement scenario, heart rate, blood pressure, cardiac rhythm and IOP were measured at specific time points, in subjects representative of the intended user population.

No adverse events were reported in this study, which was conducted under medical supervision. Furthermore, there was no effect of *Reza Band* placement over the cricoid, as intended, or intentional lateral displacement, over the jugular and carotid structures of the neck, on heart rate, systolic or diastolic blood pressure, intraocular pressure, or cardiac rhythm.

This study demonstrated that the skin and neck anatomy resist *Reza Band* displacement, with more than 5lbs. of force required to intentionally displace the *Reza Band* laterally completely off the cricoid. Therefore, when the *Reza Band* is fit as described in proposed labeling, the potential for displacement is low.

In addition, study results demonstrate that when the *Reza Band* is set to apply its maximal pressure with the Comfort Dial fully actuated, and then displaced laterally, the pressure being applied is significantly reduced (mean of 59.2%, when displaced laterally to the left and a mean of 55.2%, when displaced laterally to the right), as compared to the applied baseline pressure.

Therefore, in the event the *Reza Band* is displaced laterally, the likelihood of impacting sensitive structures of the neck is also low. This finding is corroborated by the study data showing no effect on heart rate, blood pressure, cardiac rhythm, or intraocular pressure, either when the *Reza Band* is placed as intended over the cricoid cartilage, or when it is laterally displaced, over the jugular and carotid vasculature.

In summary, this study in which subjects were monitored for any potential impact of *Reza Band* intended placement or lateral displacement, on heart rate, blood pressure, cardiac rhythm and IOP, further demonstrates the safety of the *Reza Band*, and supplements the safety and effectiveness data generated in the 95-subject pivotal investigation.