

STATISTICAL SUMMARY

OXITONE LTD. – QD04.5.1-4

STUDY TO EVALUATE THE PRECISION AND
ACCURACY OF THE OXITONE 1000 WHEN USED IN
A CONTINUOUS AND SPOT PROSPECTIVE MODE
FOR NON-INVASIVE OXYGEN SATURATION
MEASUREMENTS

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1. INTRODUCTION

This report presents the statistical analyses performed on the data from the QD04 study – Trial to Evaluate the Precision and Accuracy of the Oxitone 1000 when used in a continuous and spot prospective mode for non-invasive oxygen saturation measurements. The objective of the study was to assess and validate the Oxitone 1000 performance in continuous or spot oximetry monitoring and its capabilities (functionality, usability and performance) relative to reference readings. The end goal was to assess the accuracy and precision of the Oxitone 1000 measurement of pulse rate and oxygen saturation.

1.1. Summary of Study Design

This was a prospective, single-arm, single-center, open-label clinical study, performed on patients as well healthy subjects.

1.2. Study Endpoints

1.2.1. Efficacy Endpoints

1.2.1.1. Primary Endpoints

- Oxygen saturation as measured from the Oxitone 1000 and the reference device.
- Pulse rate as measured from the Oxitone 1000 and the reference device.

1.2.1.2. Secondary Endpoint

- Usability questionnaire.

1.2.2. Safety Endpoints

- All adverse events (AE).
- All serious adverse events (SAE).

1.2.3. Data Analysis Sets

1.2.3.1. Full Analysis Set (FA)

The full analysis set consists of all subjects who passed screening successfully.

1.2.3.2. Per-Protocol (PP)

The per-protocol analysis set consists of all subjects who finished the study without major protocol violations.

1.2.3.3. Statistical Analysis of Analysis Sets

The FA set served as the main set for efficacy and safety assessments. Efficacy analyses were planned to be performed on the PP set as well.

1.3. Statistical Considerations

1.3.1. General Analysis Considerations

Statistical analyses were performed using SAS® v9.4 (SAS®, SAS Institute Cary, NC USA) software. The required significance level of findings is equal to or lower than 5%. All statistical tests were two-sided, if not defined otherwise. Where confidence limits are appropriate, the confidence level was 95%.

Baseline demographic and other baseline characteristics, together with safety analyses, are performed on all enrolled subjects. Baseline values are defined as the last valid value prior to treatment.

Measurements for pulse rate and oxygen saturation, collected in the automatically generated files, were averaged every twelve seconds, excluding the first three minutes in every position (sit, stand, after walk and rest), data collected during motion and all missing or non-reliable data.

Continuous variables were summarized by a mean, standard deviation, minimum, median and maximum and categorical variables by a count and percentage.

Accuracy calculations were based on the healthy subjects as well as the patients.

Precision was measured on healthy subjects only.

1.3.2. Disposition of Subjects

The number of subjects screened, the screen failures, the FA set, the number of major protocol violations, the PP set and the number of patients with invalid data for analysis of primary endpoint are tabulated, per subject population and overall.

1.3.3. Demographic and Background Variables

Demographic and background variables are tabulated per subject population and overall. Continuous variables are summarized by a mean, standard deviation, minimum, median and maximum and categorical variables by a count and percentage.

1.3.4. Efficacy Analysis

1.3.4.1. Primary Endpoints

1.3.4.1.1. Oxygen Saturation

Accuracy

The root-mean-square (rms) difference between measured values (SpO_{2i}) and reference values (S_{Ri}), is stated:

$$A_{rms} = \sqrt{\frac{\sum_{i=1}^n (SpO_{2i} - S_{Ri})^2}{n}}$$

Furthermore, a comparison between the Oxitone 1000 measurement and the reference measurement is made using methods described by Bland and Altman. The correlation (Pearson's correlation coefficient) and mean difference between the reference and Oxitone 1000 measures are presented together with a 95% confidence interval. A high correlation and a mean difference value near zero are expected if the two devices (Reference vs. Oxitone 1000) output the same values. In addition, a Bland-Altman plot of the mean versus the difference is presented, and the 95% limits of agreement calculated together with their respective confidence intervals. As a measure of accuracy, the mean bias and its standard deviation (with their 95% confidence intervals) are estimated from random effects analysis of variance models programmed in SAS® using the MIXED procedure.

Linear regression models (Deming or Passing-Bablok regression as appropriate) were fitted to the values obtained from both samples; the slope and intercept together with their respective 95% CI are presented.

All these calculations were done per subject population and overall.

Precision

The precision of a measurement expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at two levels: repeatability and reproducibility. Repeatability expresses the precision under the same operating conditions over a short interval

of time. Reproducibility expresses the precision between different operating conditions. These measures reported are in accordance with ICH guidance Q2 (R1) and CLSI guidelines EP15-A2.

The above-mentioned statistics and their 95% two-sided confidence intervals (CI) were calculated using a random effects analysis of variance model programmed in SAS® using the MIXED procedure. The confidence interval of the reproducibility was calculated with bootstrap methodology using 10,000 simulated samples.

It is recommended that the precision be less than $\pm 1\%$.

1.3.4.1.2. Pulse Rate

This was analyzed in a similar manner as oxygen saturation.

1.3.4.2. Secondary Endpoint

1.3.4.2.1. Usability

The results from the usability questionnaire were tabulated, using descriptive statistics, per subject population and overall.

1.3.5. Success Criterion

The study success criterion, per the guidance document (ISO 80601-2-61 (2011) Particular Requirements for Pulse Oximeter Equipment), is $A_{rms} < 4.0\%$ in the range of SpO₂ between 70% and 100%.

1.3.6. Safety Analysis

All adverse events (AE) and all serious adverse events (SAE) are presented by seriousness, severity and relation to treatment.

1.3.7. Handling of Missing Data

When the Oxitone pulse oximeter or the reference pulse oximeter showed low quality of measurement, the Oxygen saturation and/or Pulse rate for the respective oximeter was not included in the analysis.

2. RESULTS

2.1. Disposition of Subjects

Table 1 presents the disposition of subjects per subject population and overall.

Among the patients, 27 subjects were screened, of whom 4 were screen failures and 23 were included in the FA set. 2 subjects had invalid data for the analysis of the primary endpoint because of instability of the reference measurement and a low perfusion index.

Among the healthy subjects, 16 subjects were screened, of whom 1 was a screen failure and 15 were included in the FA set. All subjects had valid data for the analysis of the primary endpoint.

Table 1: Disposition of Subjects

Patients	Screened	27
	Screen Failure	4
	Full Analysis Set (FA)	23
	Patients with Invalid Data for Analysis of Primary Endpoint	2
Healthy Subjects	Screened	16
	Screen Failure	1
	Full Analysis Set (FA)	15
	Patients with Invalid Data for Analysis of Primary Endpoint	0
All	Screened	43
	Screen Failure	5
	Full Analysis Set (FA)	38
	Patients with Invalid Data for Analysis of Primary Endpoint	2

Since there were no major protocol violations, the FA set and the PP set are equal. Therefore, analyses of efficacy and safety are presented for the FA set only.

2.2. Demographic and Background Variables

Table 2 presents general demographic variables per subject population and overall.

Table 2: General Demographic Variables

				FA
Patients	Age (years)		N	23
			Mean (SD)	60.4 (9.83)
			Median [Range]	62.0 [37.0;78.0]
	Gender	Male	% (n/N)	47.8% (11/23)
		Female	% (n/N)	52.2% (12/23)

				FA
	Weight (kg)		N	22
			Mean (SD)	76.1 (17.48)
			Median [Range]	74.5 [49.0;106.0]
	Height (cm)		N	22
			Mean (SD)	164.9 (10.74)
			Median [Range]	167.0 [148.0;183.0]
	BMI (kg / cm2)		N	22
			Mean (SD)	27.9 (5.64)
			Median [Range]	27.8 [18.1;38.8]
Healthy Subjects	Age (years)		N	15
			Mean (SD)	51.5 (15.52)
			Median [Range]	54.0 [26.0;74.0]
	Gender	Male	% (n/N)	66.7% (10/15)
		Female	% (n/N)	33.3% (5/15)
	Weight (kg)		N	15
			Mean (SD)	79.6 (10.76)
			Median [Range]	77.0 [61.0;100.0]
	Height (cm)		N	15
			Mean (SD)	175.3 (10.81)
			Median [Range]	175.0 [161.0;192.0]
	BMI (kg / cm2)		N	15
Mean (SD)			26.0 (3.48)	
Median [Range]			24.6 [21.4;31.6]	
All	Age (years)		N	38
			Mean (SD)	56.9 (12.97)
			Median [Range]	60.5 [26.0;78.0]
	Gender	Male	% (n/N)	55.3% (21/38)
		Female	% (n/N)	44.7% (17/38)
	Weight (kg)		N	37
			Mean (SD)	77.5 (15.05)
			Median [Range]	77.0 [49.0;106.0]
	Height (cm)		N	37
			Mean (SD)	169.1 (11.82)
			Median [Range]	169.0 [148.0;192.0]
	BMI (kg / cm2)		N	37
Mean (SD)			27.1 (4.92)	
Median [Range]			25.4 [18.1;38.8]	

Table 3 presents blood pressure and EKG per subject population and overall.

Table 3: Blood Pressure and EKG

				FA
Patients	Systolic Blood Pressure (mmHg)		N	14
			Mean (SD)	132.5 (20.14)
			Median [Range]	128.0 [99.0;161.0]
	Diastolic Blood Pressure (mmHg)		N	14
			Mean (SD)	73.1 (12.64)
			Median [Range]	73.5 [47.0;89.0]

				FA
	Position	Sitting	% (n/N)	100% (14/14)
	EKG	Rhythm-Normal sinus	% (n/N)	4.3% (1/23)
		Atrial Fibrillation	% (n/N)	4.3% (1/23)
		NA/Not Done	% (n/N)	91.3% (21/23)
Healthy Subjects	Systolic Blood Pressure (mmHg)		N	13
			Mean (SD)	130.5 (18.85)
			Median [Range]	128.0 [96.0;154.0]
	Diastolic Blood Pressure (mmHg)		N	13
			Mean (SD)	76.1 (8.55)
			Median [Range]	74.0 [58.0;87.0]
	Position	Sitting	% (n/N)	100% (13/13)
	EKG	NA/Not Done	% (n/N)	100% (15/15)
	All	Systolic Blood Pressure (mmHg)		N
			Mean (SD)	131.5 (19.18)
			Median [Range]	128.0 [96.0;161.0]
Diastolic Blood Pressure (mmHg)			N	27
			Mean (SD)	74.5 (10.77)
			Median [Range]	74.0 [47.0;89.0]
Position		Sitting	% (n/N)	100% (27/27)
EKG		Rhythm-Normal sinus	% (n/N)	2.6% (1/38)
		Atrial Fibrillation	% (n/N)	2.6% (1/38)
		NA/Not Done	% (n/N)	94.7% (36/38)

Table 4 presents smoking history per subject population and overall.

Table 4: Smoking History

				FA
Patients	Smoking History	Never Smoked	% (n/N)	39.1% (9/23)
		Smoked	% (n/N)	34.8% (8/23)
		Still Smoking	% (n/N)	26.1% (6/23)
	Number or Packs per Year	4	% (n/N)	16.7% (1/6)
		5	% (n/N)	16.7% (1/6)
		10	% (n/N)	16.7% (1/6)
		15	% (n/N)	16.7% (1/6)
		20	% (n/N)	16.7% (1/6)
		50	% (n/N)	16.7% (1/6)
		Number of Years Since Quitting Smoking	8	% (n/N)
	10		% (n/N)	12.5% (1/8)
	15		% (n/N)	12.5% (1/8)
	20		% (n/N)	12.5% (1/8)
	Less than 1		% (n/N)	12.5% (1/8)
	2		% (n/N)	12.5% (1/8)
	6		% (n/N)	12.5% (1/8)
	30		% (n/N)	12.5% (1/8)
	Time Since Last Cigarette	0:30	% (n/N)	16.7% (1/6)
		1:00	% (n/N)	50.0% (3/6)
		1:10	% (n/N)	16.7% (1/6)
		10:00	% (n/N)	16.7% (1/6)

			FA	
Healthy Subjects	Smoking History	Never Smoked	% (n/N)	66.7% (10/15)
		Smoked	% (n/N)	33.3% (5/15)
	Number or Packs per Year	0.5	% (n/N)	20.0% (1/5)
		3	% (n/N)	20.0% (1/5)
		8	% (n/N)	20.0% (1/5)
		20	% (n/N)	20.0% (1/5)
		24	% (n/N)	20.0% (1/5)
	Number of Years Since Quitting Smoking	5	% (n/N)	20.0% (1/5)
		10	% (n/N)	40.0% (2/5)
		12	% (n/N)	20.0% (1/5)
		26	% (n/N)	20.0% (1/5)
	All	Smoking History	Never Smoked	% (n/N)
Smoked			% (n/N)	34.2% (13/38)
Still Smoking			% (n/N)	15.8% (6/38)
Number or Packs per Year		0.5	% (n/N)	9.1% (1/11)
		3	% (n/N)	9.1% (1/11)
		4	% (n/N)	9.1% (1/11)
		5	% (n/N)	9.1% (1/11)
		8	% (n/N)	9.1% (1/11)
		10	% (n/N)	9.1% (1/11)
		15	% (n/N)	9.1% (1/11)
		20	% (n/N)	18.2% (2/11)
		24	% (n/N)	9.1% (1/11)
Number of Years Since Quitting Smoking		5	% (n/N)	7.7% (1/13)
		8	% (n/N)	7.7% (1/13)
		10	% (n/N)	23.1% (3/13)
		15	% (n/N)	7.7% (1/13)
		20	% (n/N)	7.7% (1/13)
		Less than 1	% (n/N)	7.7% (1/13)
		2	% (n/N)	7.7% (1/13)
		6	% (n/N)	7.7% (1/13)
		12	% (n/N)	7.7% (1/13)
		26	% (n/N)	7.7% (1/13)
Time Since Last Cigarette		0:30	% (n/N)	16.7% (1/6)
		1:00	% (n/N)	50.0% (3/6)
		1:10	% (n/N)	16.7% (1/6)
		10:00	% (n/N)	16.7% (1/6)

Table 5 presents the diagnoses for the patients.

Table 5: Diagnoses for the Patients

			FA
Patients	Asthma	% (n/N)	26.1% (6/23)
	Bronchiectasis	% (n/N)	4.3% (1/23)
	Bronchitis (RADS)	% (n/N)	4.3% (1/23)
	COPD	% (n/N)	34.8% (8/23)

			FA
	Dyspnea	% (n/N)	8.7% (2/23)
	OSA	% (n/N)	8.7% (2/23)
	Post-inflammatory Pulmonary Fibrosis	% (n/N)	4.3% (1/23)
	Pulmonary Fibrosis	% (n/N)	4.3% (1/23)
	Pulmonary Nodules, Cough	% (n/N)	4.3% (1/23)
	Respiratory abnormality	% (n/N)	4.3% (1/23)
	Sarcoidosis	% (n/N)	21.7% (5/23)

Table 6 presents skin types per subject population and overall.

Table 6: Skin Types

				FA
Patients	Skin Type	Type II (scores 7-13) Fair	% (n/N)	21.7% (5/23)
		Type III (scores 14-20) Medium	% (n/N)	26.1% (6/23)
		Type IV (scores 21-27) Olive	% (n/N)	34.8% (8/23)
		Type V (scores 28-34) Brown	% (n/N)	13.0% (3/23)
		Type VI (scores 35-36) Black	% (n/N)	4.3% (1/23)
Healthy Subjects	Skin Type	Type II (scores 7-13) Fair	% (n/N)	46.7% (7/15)
		Type III (scores 14-20) Medium	% (n/N)	46.7% (7/15)
		Type IV (scores 21-27) Olive	% (n/N)	6.7% (1/15)
All	Skin Type	Type II (scores 7-13) Fair	% (n/N)	31.6% (12/38)
		Type III (scores 14-20) Medium	% (n/N)	34.2% (13/38)
		Type IV (scores 21-27) Olive	% (n/N)	23.7% (9/38)
		Type V (scores 28-34) Brown	% (n/N)	7.9% (3/38)
		Type VI (scores 35-36) Black	% (n/N)	2.6% (1/38)

Table 7 presents spirometry data for the patients.

Table 7: Spirometry Data for the Patients

			FA
Patients	FVC (%)	N	23
		Mean (SD)	90.7 (19.72)
		Median [Range]	84.4 [61.0;134.0]
	FEV1 (%)	N	23
		Mean (SD)	80.1 (23.77)
		Median [Range]	76.0 [42.0;127.0]
	FEV1/FVC (%)	N	23
		Mean (SD)	72.5 (12.52)
		Median [Range]	76.0 [42.1;90.0]
	DLCO (%)	N	8
		Mean (SD)	83.0 (23.82)
		Median [Range]	82.7 [48.0;124.0]

Table 8 presents medical history per subject population and overall.

Table 8: Medical History

				FA
Patients	Central Nervous System	No History	% (n/N)	100% (23/23)
		Present	% (n/N)	0% (0/23)
	Eyes, Ears, Nose & Throat	No History	% (n/N)	95.7% (22/23)
		Present	% (n/N)	4.3% (1/23)
	Cardiovascular	No History	% (n/N)	78.3% (18/23)
		Past History	% (n/N)	17.4% (4/23)
		Present	% (n/N)	4.3% (1/23)
	Respiratory	No History	% (n/N)	17.4% (4/23)
		Past History	% (n/N)	4.3% (1/23)
		Present	% (n/N)	78.3% (18/23)
	Gastrointestinal	No History	% (n/N)	95.7% (22/23)
		Present	% (n/N)	4.3% (1/23)
	Genitourinary	No History	% (n/N)	100% (23/23)
	Hematologic	No History	% (n/N)	100% (23/23)
	Endocrine	No History	% (n/N)	78.3% (18/23)
		Past History	% (n/N)	4.3% (1/23)
		Present	% (n/N)	17.4% (4/23)
	Lymphatic	No History	% (n/N)	100% (23/23)
	Dermatologic	No History	% (n/N)	95.7% (22/23)
		Present	% (n/N)	4.3% (1/23)
	Musculoskeletal	No History	% (n/N)	91.3% (21/23)
		Present	% (n/N)	8.7% (2/23)
	Surgical History	No History	% (n/N)	95.7% (22/23)
Present		% (n/N)	4.3% (1/23)	
Other	No History	% (n/N)	69.6% (16/23)	
	Past History	% (n/N)	4.3% (1/23)	
	Present	% (n/N)	26.1% (6/23)	
Allergies	No	% (n/N)	59.1% (13/22)	
	UNK	% (n/N)	40.9% (9/22)	
Healthy Subjects	Central Nervous System	No History	% (n/N)	100% (15/15)
		Present	% (n/N)	0% (0/15)
	Eyes, Ears, Nose & Throat	No History	% (n/N)	93.3% (14/15)
		Past History	% (n/N)	6.7% (1/15)
	Cardiovascular	No History	% (n/N)	93.3% (14/15)
		Past History	% (n/N)	6.7% (1/15)
	Respiratory	No History	% (n/N)	93.3% (14/15)
		Past History	% (n/N)	6.7% (1/15)
	Gastrointestinal	No History	% (n/N)	86.7% (13/15)
		Past History	% (n/N)	6.7% (1/15)
		Present	% (n/N)	6.7% (1/15)
	Genitourinary	No History	% (n/N)	100% (15/15)
	Hematologic	No History	% (n/N)	93.3% (14/15)
		Present	% (n/N)	6.7% (1/15)
	Endocrine	No History	% (n/N)	80.0% (12/15)
		Present	% (n/N)	20.0% (3/15)
	Lymphatic	No History	% (n/N)	100% (15/15)
	Dermatologic	No History	% (n/N)	93.3% (14/15)
		Past History	% (n/N)	6.7% (1/15)
	Musculoskeletal	No History	% (n/N)	100% (15/15)

				FA
	Surgical History	No History	% (n/N)	100% (15/15)
	Other	No History	% (n/N)	100% (14/14)
	Allergies	No	% (n/N)	100% (15/15)
All	Central Nervous System	No History	% (n/N)	100% (38/38)
		No History	% (n/N)	94.7% (36/38)
		Past History	% (n/N)	2.6% (1/38)
	Eyes, Ears, Nose & Throat	Present	% (n/N)	2.6% (1/38)
		No History	% (n/N)	84.2% (32/38)
		Past History	% (n/N)	13.2% (5/38)
	Cardiovascular	Present	% (n/N)	2.6% (1/38)
		No History	% (n/N)	47.4% (18/38)
		Past History	% (n/N)	5.3% (2/38)
	Respiratory	Present	% (n/N)	47.4% (18/38)
		No History	% (n/N)	92.1% (35/38)
		Past History	% (n/N)	2.6% (1/38)
	Gastrointestinal	Present	% (n/N)	5.3% (2/38)
		No History	% (n/N)	100% (38/38)
		Present	% (n/N)	97.4% (37/38)
	Genitourinary	Present	% (n/N)	2.6% (1/38)
		No History	% (n/N)	78.9% (30/38)
		Past History	% (n/N)	2.6% (1/38)
	Hematologic	Present	% (n/N)	18.4% (7/38)
		No History	% (n/N)	100% (38/38)
		Past History	% (n/N)	94.7% (36/38)
	Endocrine	Present	% (n/N)	2.6% (1/38)
		No History	% (n/N)	94.7% (36/38)
		Past History	% (n/N)	2.6% (1/38)
	Lymphatic	Present	% (n/N)	2.6% (1/38)
		No History	% (n/N)	94.7% (36/38)
		Past History	% (n/N)	2.6% (1/38)
	Dermatologic	Present	% (n/N)	2.6% (1/38)
		No History	% (n/N)	94.7% (36/38)
		Past History	% (n/N)	5.3% (2/38)
	Musculoskeletal	Present	% (n/N)	97.4% (37/38)
		No History	% (n/N)	2.6% (1/38)
		Present	% (n/N)	2.6% (1/38)
	Surgical History	Present	% (n/N)	2.6% (1/38)
		No History	% (n/N)	81.1% (30/37)
		Past History	% (n/N)	2.7% (1/37)
	Other	Present	% (n/N)	16.2% (6/37)
		No	% (n/N)	75.7% (28/37)
UNK		% (n/N)	24.3% (9/37)	

Table 9 presents COPD data for the patients.

Table 9: COPD Data for the Patients

				FA	
Patients	COPD Severity Grading	Stage I: Mild COPD	% (n/N)	25.0% (2/8)	
		Stage II: Moderate COPD	% (n/N)	50.0% (4/8)	
		Stage III: Severe COPD	% (n/N)	25.0% (2/8)	
	Total COPD Assessment Score			N	9
				Mean (SD)	17.9 (7.77)
				Median [Range]	19.0 [6.0;32.0]

Table 52 in the appendix presents the concomitant medication.

Table 10 presents pre-test vital signs per subject population and overall.

Table 10: Pre-test Vital Signs

			FA
Patients	Heart Rate	N	23
		Mean (SD)	70.5 (10.44)
		Median [Range]	68.0 [52.0;91.0]
	Oxygen Saturation (%)	N	23
		Mean (SD)	97.5 (1.59)
		Median [Range]	98.0 [94.0;100.0]
	Perfusion Index	<3 % (n/N)	26.1% (6/23)
		3-5 % (n/N)	8.7% (2/23)
		>5 % (n/N)	65.2% (15/23)
	Systolic Blood Pressure (mmHg)	N	23
		Mean (SD)	131.1 (19.18)
		Median [Range]	129.0 [99.0;162.0]
	Diastolic Blood Pressure (mmHg)	N	23
		Mean (SD)	71.7 (12.89)
		Median [Range]	70.0 [46.0;91.0]
Healthy Subjects	Heart Rate	N	15
		Mean (SD)	72.5 (9.65)
		Median [Range]	71.0 [53.0;89.0]
	Oxygen Saturation (%)	N	15
		Mean (SD)	98.2 (1.15)
		Median [Range]	98.0 [97.0;100.0]
	Perfusion Index	<3 % (n/N)	20.0% (3/15)
		3-5 % (n/N)	40.0% (6/15)
		>5 % (n/N)	40.0% (6/15)
	Systolic Blood Pressure (mmHg)	N	14
		Mean (SD)	128.1 (19.43)
		Median [Range]	123.5 [96.0;154.0]
	Diastolic Blood Pressure (mmHg)	N	14
		Mean (SD)	75.2 (7.87)
		Median [Range]	73.5 [58.0;87.0]
All	Heart Rate	N	38
		Mean (SD)	71.3 (10.05)
		Median [Range]	71.0 [52.0;91.0]
	Oxygen Saturation (%)	N	38
		Mean (SD)	97.8 (1.45)
		Median [Range]	98.0 [94.0;100.0]
	Perfusion Index	<3 % (n/N)	23.7% (9/38)
		3-5 % (n/N)	21.1% (8/38)
		>5 % (n/N)	55.3% (21/38)
	Systolic Blood Pressure (mmHg)	N	37
		Mean (SD)	129.9 (19.06)
		Median [Range]	128.0 [96.0;162.0]
	Diastolic Blood Pressure (mmHg)	N	37
		Mean (SD)	73.0 (11.27)
		Median [Range]	71.0 [46.0;91.0]

2.3. Efficacy Endpoints

2.3.1. Primary Endpoints

2.3.1.1. Accuracy

2.3.1.1.1. Oxygen Saturation

Patients and Healthy Subjects

A_{rms}

The main claim of accuracy is based on the root-mean-square difference between measured values and reference values, A_{rms}. The study success criterion, per the guidance document (ISO 80601-2-61 (2011) Particular Requirements for Pulse Oximeter Equipment), is A_{rms} < 4.0% in the range of SpO₂ between 70% and 100%.

A_{rms} = 2.12762% < 4.0%. Thus, the success criterion was met for patients and healthy subjects.

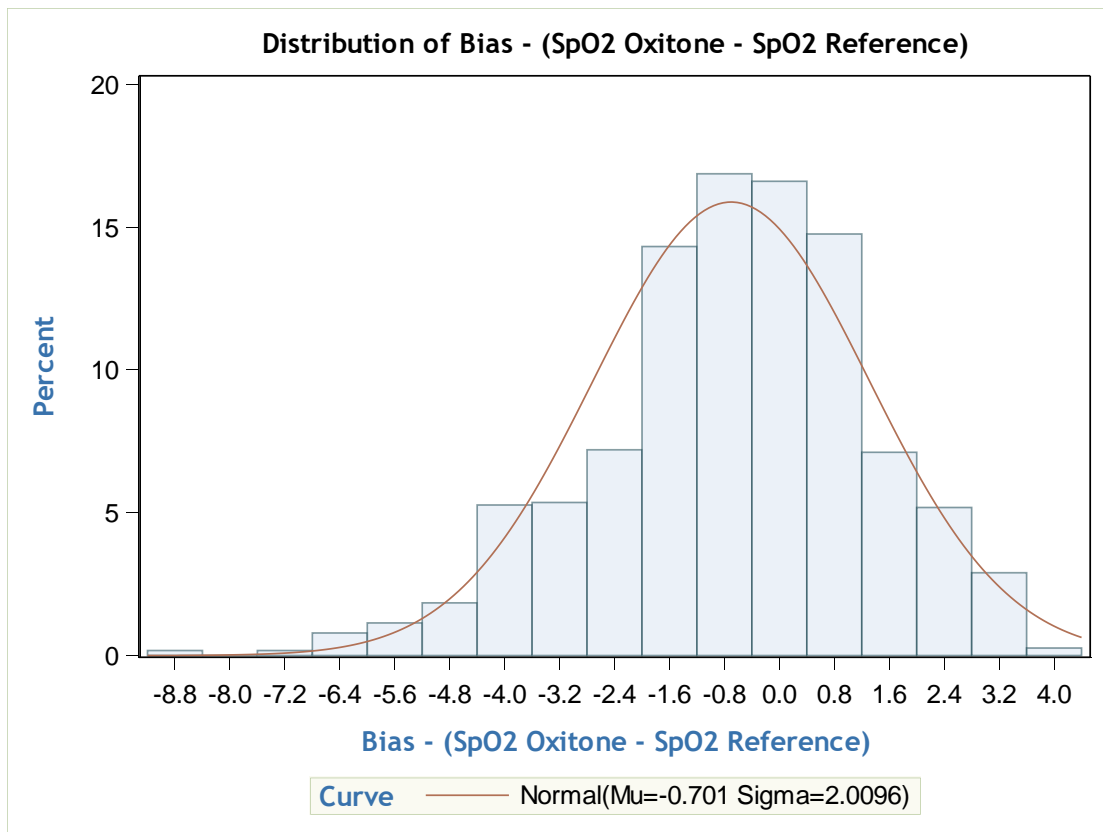
Descriptive Statistics

Table 11 presents the descriptive statistics of Oxygen saturation as measured by Oxitone 1000 and the reference, as well as the difference between them. Figure 1 presents the distribution of this difference. In this population, we see from the figure that the differences follow a rather symmetric pattern and appear to follow a normal distribution. The mean SpO₂ as measured by Oxitone was 96.45% (range 83.8-99.0) and for the reference 97.18% (range 91.3-100.0).

Table 11: Descriptive Statistics of Oxygen Saturation

	N	Mean	SD	Min	Median	Max
SpO ₂ Oxitone	1153	96.45	1.88	83.8	96.86	99.0
SpO ₂ Reference	1198	97.18	1.27	91.3	97.20	100.0
Difference - (SpO ₂ Oxitone - SpO ₂ Reference)	1138	-0.70	2.01	-9.0	-0.58	4.1

Figure 1: Distribution of Difference - (SpO2 Oxitone - SpO2 Reference)



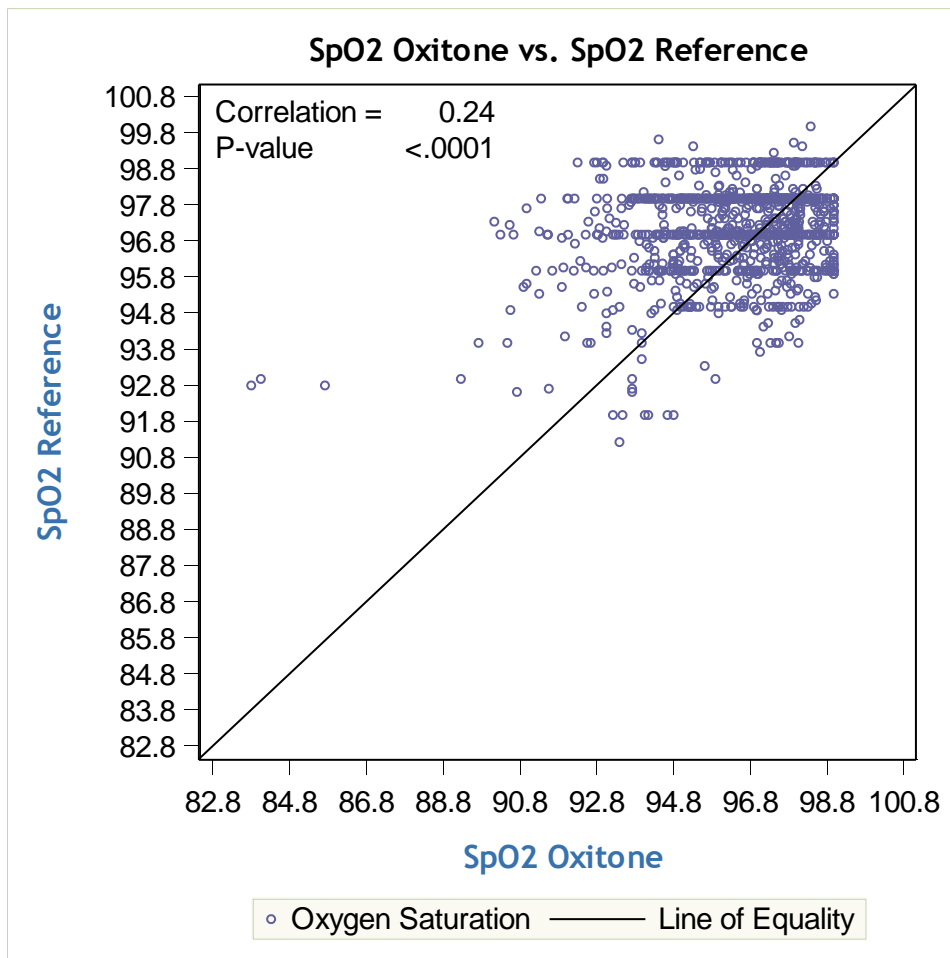
Correlation

Table 12 presents the correlation and its 95% confidence interval. Figure 2 shows a scatter plot of the Oxygen saturation measured by Oxitone 1000 and by the reference respectively. There are 1138 pairs of oxygen saturation measurements. We find a statistically significant correlation (Pearson’s correlation coefficient) between Oxitone and reference, $r=0.23635$ (95% CI: [0.180618, 0.290374], $p<0.0001$).

Table 12: Correlation with 95% Confidence Interval

Pearson Correlation Statistics (Fisher's z Transformation)									
Variable	With Variable	N	Sample Correlation	Fisher's z	Bias Adjustment	Correlation Estimate	95% Confidence Limits		p Value for H0:Rho=0
SpO2_Oxitone	SpO2_Reference	1138	0.23635	0.24090	0.0001039	0.23625	0.180618	0.290374	<.0001

Figure 2: Correlation Between SpO2 Oxitone and SpO2 Reference



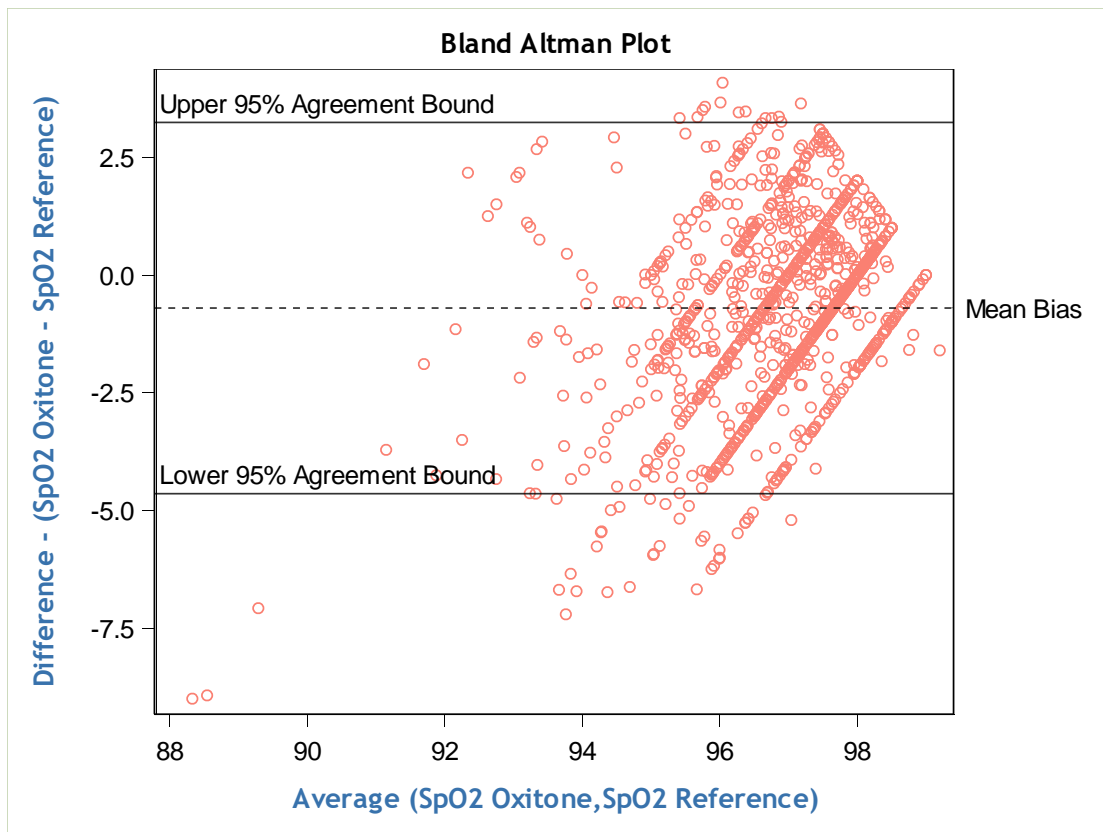
Agreement

Table 13 presents the 95% limits of agreement with the respective 95% confidence interval for each limit. Figure 3 presents the Bland-Altman plot. Most differences between the two measurements will lie between the 95% agreement limits of [-4.64, 3.24] %.

Table 13: Limits of Agreement

Lower 95% Agreement Bound	95% CI Lower Agreement Bound	Upper 95% Agreement Bound	95% CI Upper Agreement Bound
-4.64	[-5.80 - -3.48]	3.24	[2.08 - 4.40]

Figure 3: Bland-Altman Plot



Bias

Table 14 presents the mean bias and its 95% confidence interval and Table 15 presents the SD bias and its 95% confidence interval. The model estimated mean difference between Oxitone and the reference oxygen saturation, i.e. the bias, is -0.7014% (95% CI: [-0.8223, -0.5804]%). The standard deviation of this difference, i.e. the precision, is 2.00958% [95% CI:[1.930, 2.096]%).

Table 14: Mean Bias with 95% Confidence Interval

Mean Bias	95% CI
-0.7014	-.7014 with 95%CI:[-.8223 --.5804]

Table 15: SD Bias with 95% Confidence Interval

SD of Bias	95% CI
2.00958	2.010 with 95%CI:[1.930 - 2.096]

Deming Regression

Table 16 presents the results from the Deming Regression. The slope is 0.28 (95% CI: [0.199, 0.36]) and the intercept is 70.23 (95% CI: [62.457, 77.995]).

Table 16: Deming Regression Slope and Intercept with Confidence Limits

Deming Slope [95% CI]	Deming Intercept [95% CI]
0.28 [0.199, 0.36]	70.23 [62.457, 77.995]

Patients

A_{rms}

The main claim of accuracy is based on the root-mean-square difference between measured values and reference values, A_{rms}. The study success criterion, per the guidance document (ISO 80601-2-61 (2011) Particular Requirements for Pulse Oximeter Equipment), is A_{rms} < 4.0% in the range of SpO₂ between 70% and 100%.

A_{rms} = 2.41095% < 4.0%. Thus, the success criterion was met for patients.

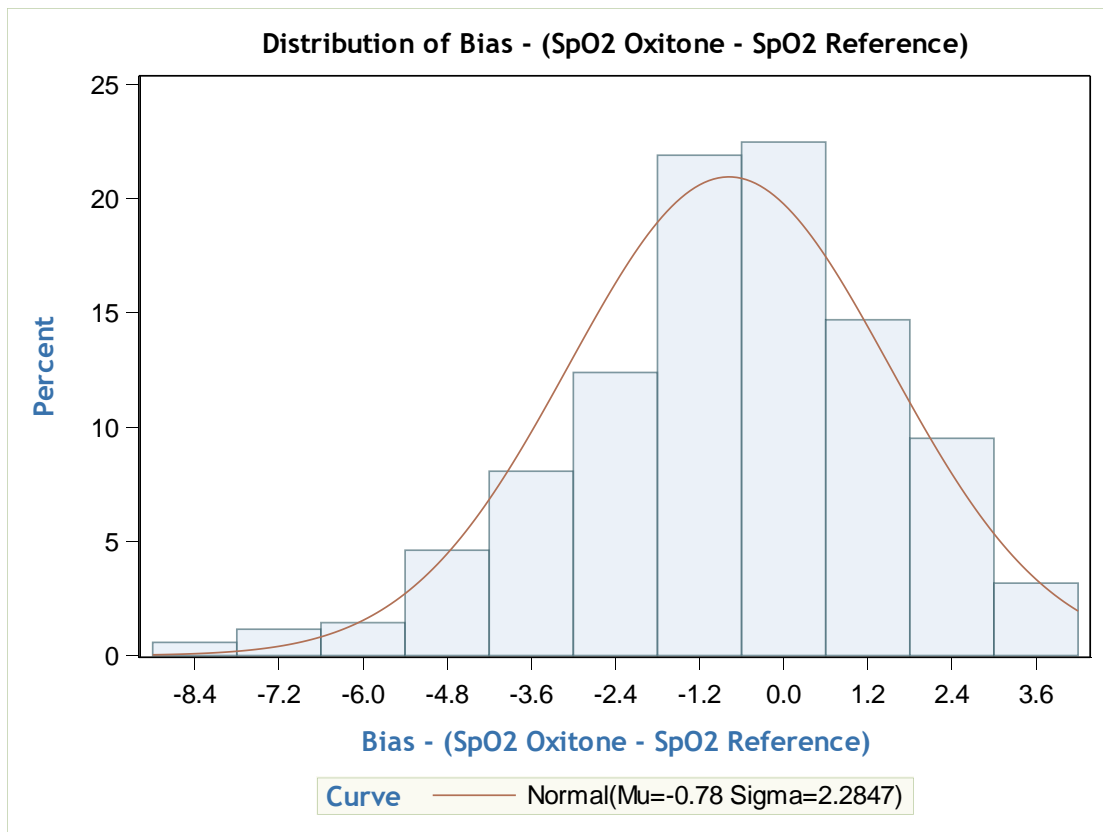
Descriptive Statistics

Table 17 presents the descriptive statistics of Oxygen saturation as measured by Oxitone 1000 and the reference, as well as the difference between them. Figure 4 presents the distribution of this difference. In this population, we see from the figure that the differences follow a rather symmetric pattern and appear to follow a normal distribution. The mean SpO₂ as measured by Oxitone was 95.94% (range 83.8-99.0) and for the reference 97.18% (range 91.3-99.3).

Table 17: Descriptive Statistics of Oxygen Saturation

	N	Mean	SD	Min	Median	Max
SpO ₂ Oxitone	348	95.94	2.28	83.8	96.33	99.0
SpO ₂ Reference	367	96.75	1.65	91.3	97.00	99.3
Difference - (SpO ₂ Oxitone - SpO ₂ Reference)	347	-0.78	2.28	-9.0	-0.61	4.1

Figure 4: Distribution of Difference - (SpO2 Oxitone - SpO2 Reference)



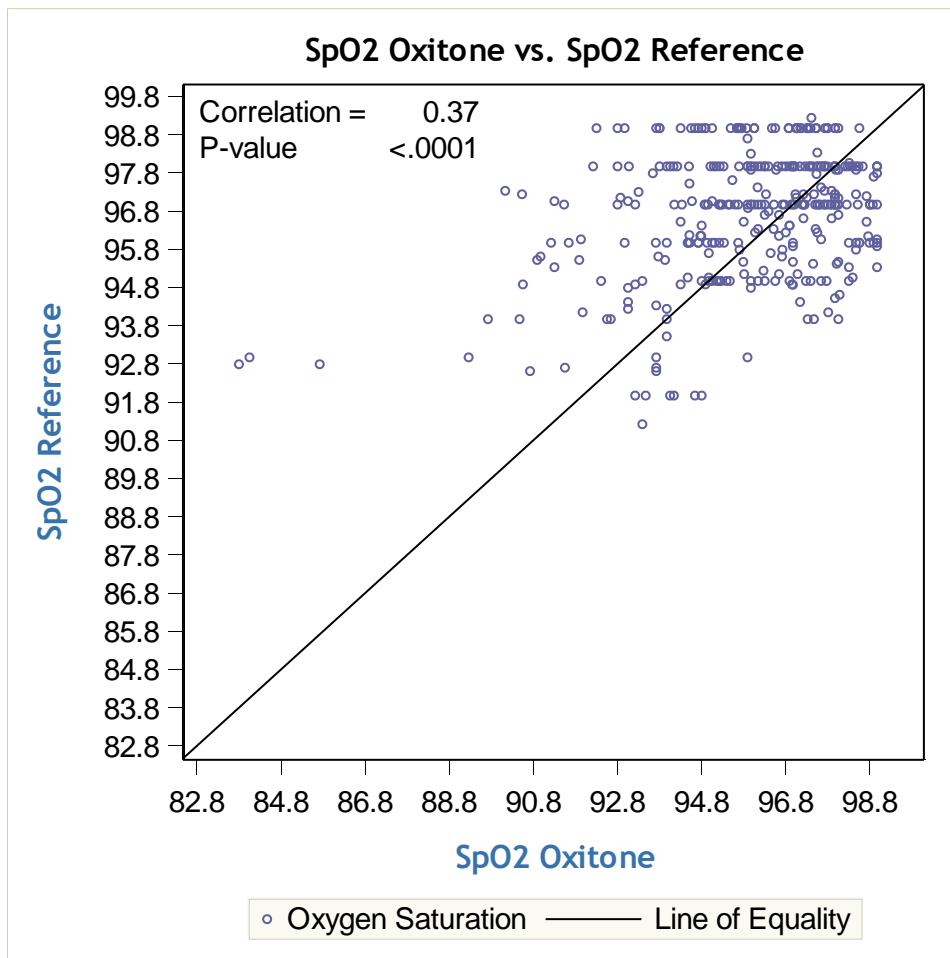
Correlation

Table 18 presents the correlation and its 95% confidence interval. Figure 5 shows a scatter plot of the Oxygen saturation measured by Oxitone 1000 and by the reference respectively. There are 347 pairs of oxygen saturation measurements. We find a statistically significant correlation (Pearson’s correlation coefficient) between Oxitone and reference, $r=0.36758$ (95% CI: [0.272365, 0.454823], $p<0.0001$).

Table 18: Correlation with 95% Confidence Interval

Pearson Correlation Statistics (Fisher's z Transformation)									
Variable	With Variable	N	Sample Correlation	Fisher's z	Bias Adjustment	Correlation Estimate	95% Confidence Limits		p Value for H0:Rho=0
SpO2_Oxitone	SpO2_Reference	347	0.36758	0.38562	0.0005312	0.36712	0.272365	0.454823	<.0001

Figure 5: Correlation Between SpO2 Oxitone and SpO2 Reference



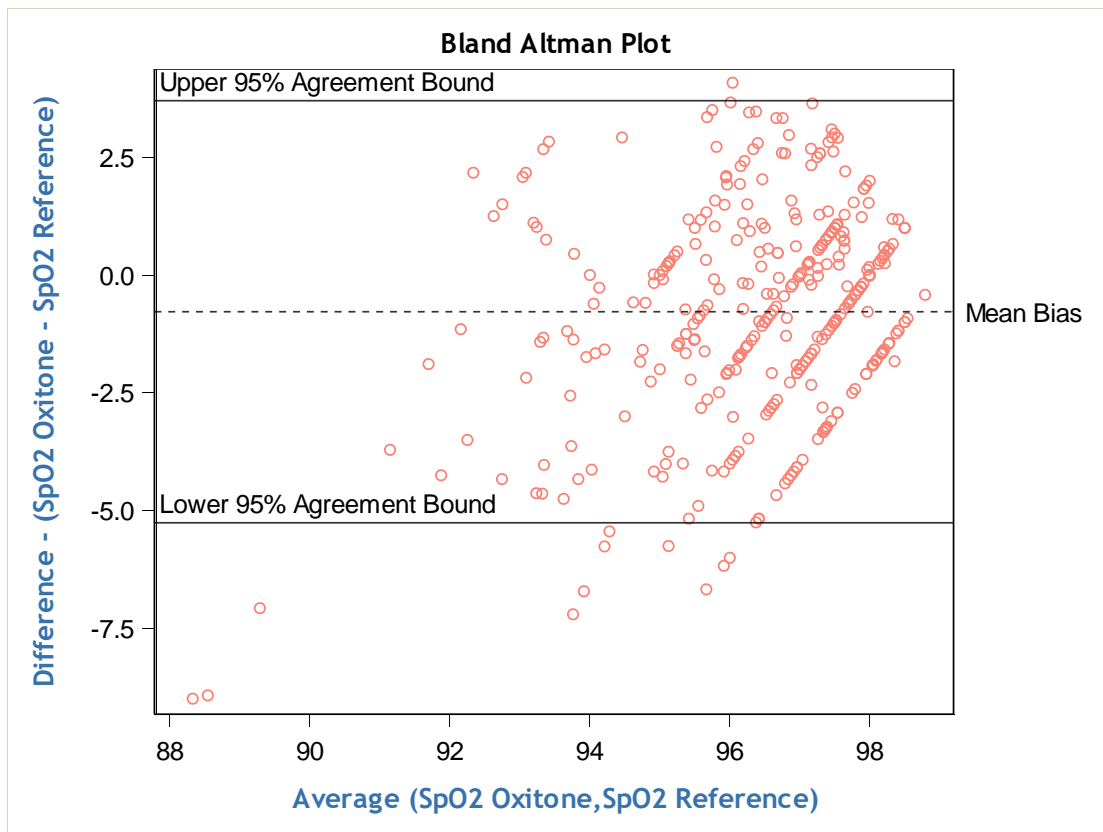
Agreement

Table 19 presents the 95% limits of agreement with the respective 95% confidence interval for each limit. Figure 6 presents the Bland-Altman plot. Most differences between the two measurements will lie between the 95% agreement limits of [-5.26, 3.70] %.

Table 19: Limits of Agreement

Lower 95% Agreement Bound	95% CI Lower Agreement Bound	Upper 95% Agreement Bound	95% CI Upper Agreement Bound
-5.26	[-7.03 - -3.48]	3.70	[1.92 - 5.48]

Figure 6: Bland-Altman Plot



Bias

Table 20 presents the mean bias and its 95% confidence interval and Table 21 presents the SD bias and its 95% confidence interval. The model estimated mean difference between Oxitone and the reference oxygen saturation, i.e. the bias, is -0.7796% (95% CI: [-1.035, -0.5238]%). The standard deviation of this difference, i.e. the precision, is 2.28472% [95% CI:[2.126, 2.469]%).

Table 20: Mean Bias with 95% Confidence Interval

Mean Bias	95% CI
-0.7796	-.7796 with 95%CI:[-1.035 --.5238]

Table 21: SD Bias with 95% Confidence Interval

SD of Bias	95% CI
2.28472	2.285 with 95%CI:[2.126 - 2.469]

Deming Regression

Table 22 presents the results from the Deming Regression. The slope is 0.47 (95% CI: [0.334, 0.606]) and the intercept is 51.65 (95% CI: [38.522, 64.774]).

Table 22: Deming Regression Slope and Intercept with Confidence Limits

Deming Slope [95% CI]	Deming Intercept [95% CI]
0.47 [0.334, 0.606]	51.65 [38.522, 64.774]

Healthy Subjects

A_{rms}

The main claim of accuracy is based on the root-mean-square difference between measured values and reference values, A_{rms} . The study success criterion, per the guidance document (ISO 80601-2-61 (2011) Particular Requirements for Pulse Oximeter Equipment), is $A_{rms} < 4.0\%$ in the range of SpO₂ between 70% and 100%. $A_{rms} = 1.99065\% < 4.0\%$. Thus, the success criterion was met for healthy subjects.

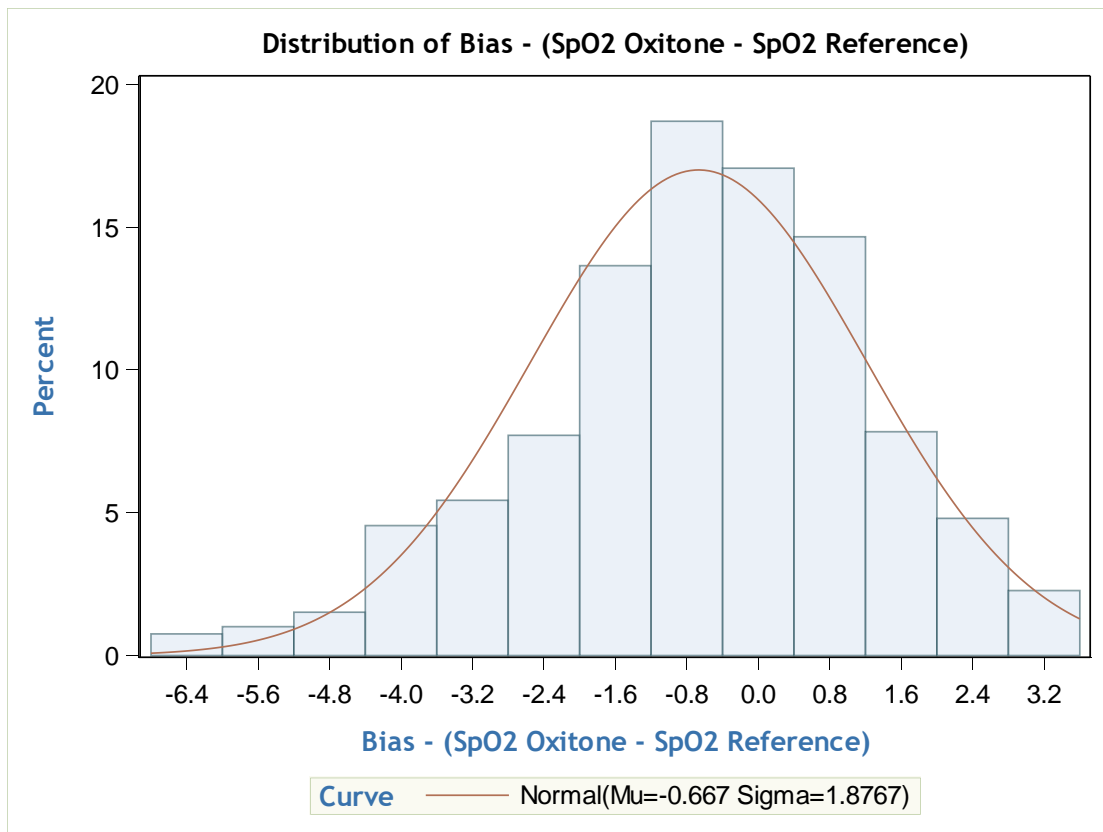
Descriptive Statistics

Table 23 presents the descriptive statistics of Oxygen saturation as measured by Oxitone 1000 and the reference, as well as the difference between them. Figure 7 presents the distribution of this difference. In this population, we see from the figure that the differences follow a rather symmetric pattern and appear to follow a normal distribution. The mean SpO₂ as measured by Oxitone was 96.67% (range 90.3-99.0) and for the reference 97.37% (range 93.4-100.0).

Table 23: Descriptive Statistics of Oxygen Saturation

	N	Mean	SD	Min	Median	Max
SpO ₂ Oxitone	805	96.67	1.63	90.3	97.00	99.0
SpO ₂ Reference	831	97.37	1.00	93.4	97.45	100.0
Difference - (SpO ₂ Oxitone - SpO ₂ Reference)	791	-0.67	1.88	-6.7	-0.56	3.6

Figure 7: Distribution of Difference - (SpO2 Oxitone - SpO2 Reference)



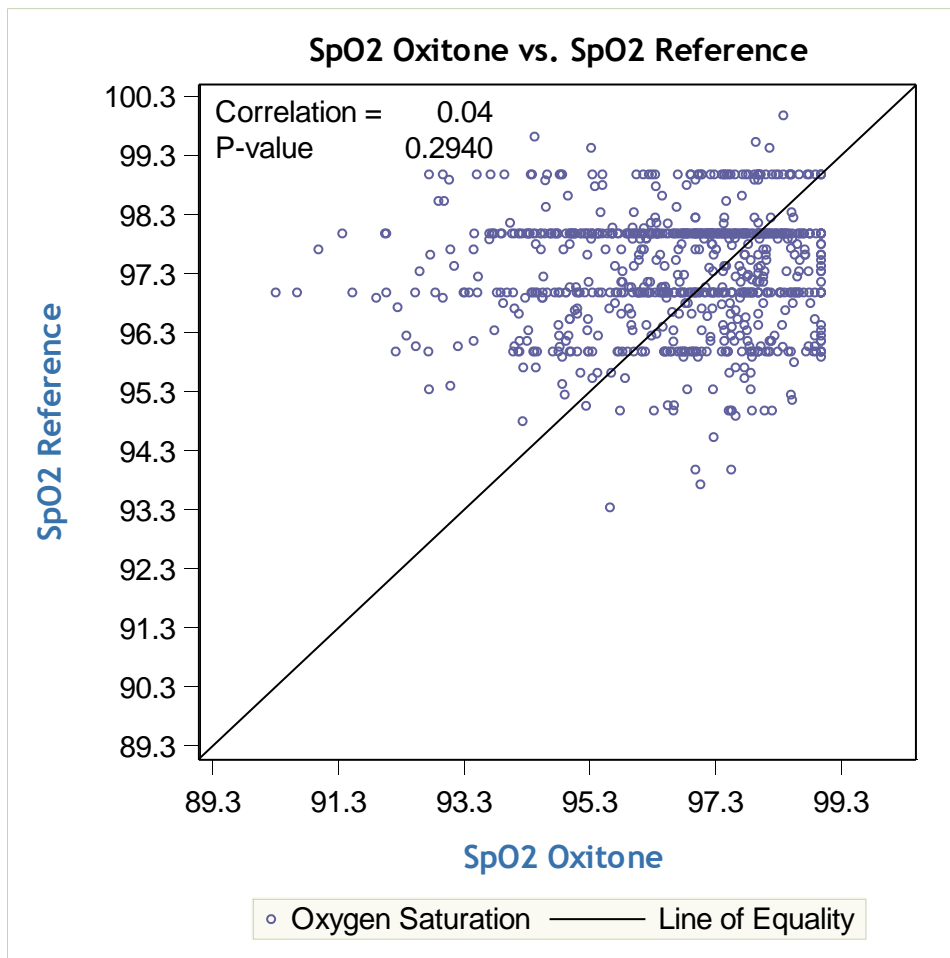
Correlation

Table 24 presents the correlation and its 95% confidence interval. Figure 8 shows a scatter plot of the Oxygen saturation measured by Oxitone 1000 and by the reference respectively. There are 791 pairs of oxygen saturation measurements. We find a statistically non-significant correlation (Pearson’s correlation coefficient) between Oxitone and reference, $r=0.03736$ (95% CI: [-0.032452, 0.106769], $p=0.2940$).

Table 24: Correlation with 95% Confidence Interval

Pearson Correlation Statistics (Fisher's z Transformation)									
Variable	With Variable	N	Sample Correlation	Fisher's z	Bias Adjustment	Correlation Estimate	95% Confidence Limits		p Value for H0:Rho=0
SpO2_Oxitone	SpO2_Reference	791	0.03736	0.03738	0.0000236	0.03734	-0.032452	0.106769	0.2940

Figure 8: Correlation Between SpO2 Oxitone and SpO2 Reference



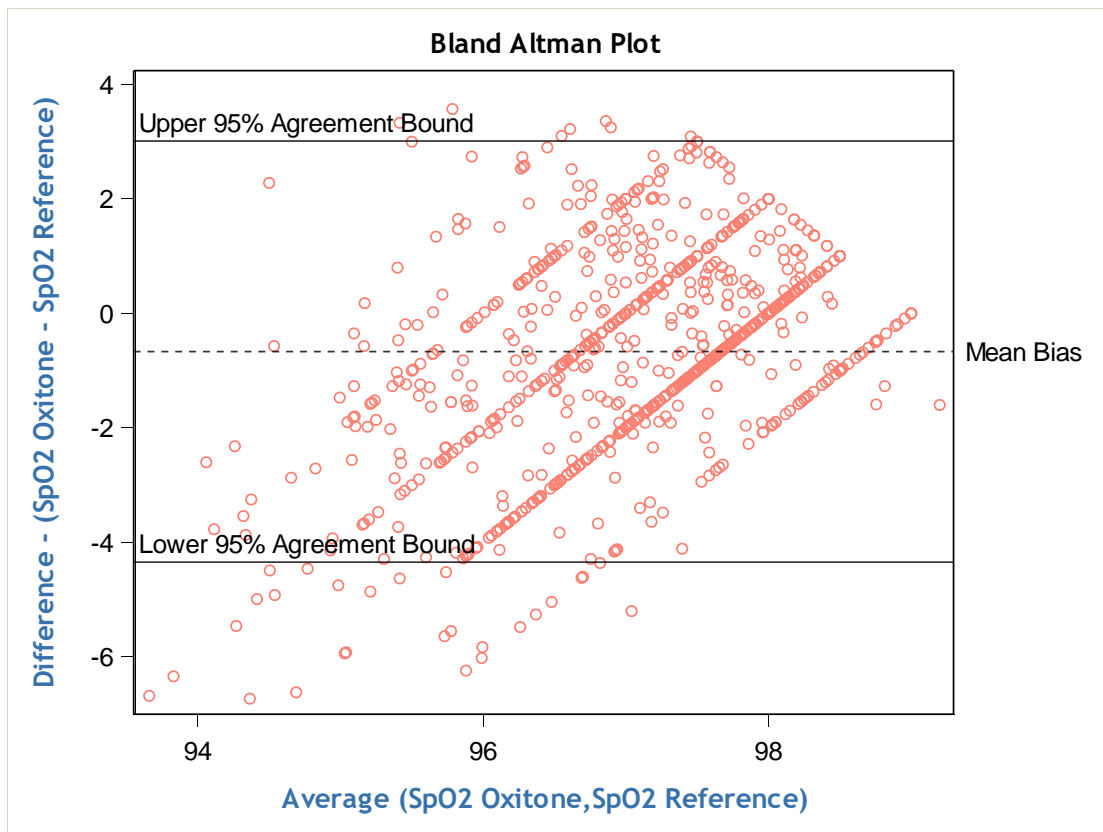
Agreement

Table 25 presents the 95% limits of agreement with the respective 95% confidence interval for each limit. Figure 9 presents the Bland-Altman plot. Most differences between the two measurements will lie between the 95% agreement limits of [-4.35, 3.01] %.

Table 25: Limits of Agreement

Lower 95% Agreement Bound	95% CI Lower Agreement Bound	Upper 95% Agreement Bound	95% CI Upper Agreement Bound
-4.35	[-6.12 - -2.57]	3.01	[1.24 - 4.79]

Figure 9: Bland-Altman Plot



Bias

Table 26 presents the mean bias and its 95% confidence interval and Table 27 presents the SD bias and its 95% confidence interval. The model estimated mean difference between Oxitone and the reference oxygen saturation, i.e. the bias, is -0.6670% (95% CI: [-0.8102, -0.5239]%). The standard deviation of this difference, i.e. the precision, is 1.87675% [95% CI:[1.789, 1.974]%).

Table 26: Mean Bias with 95% Confidence Interval

Mean Bias	95% CI
-0.6670	-.6670 with 95%CI:[-.8102 --.5239]

Table 27: SD Bias with 95% Confidence Interval

SD of Bias	95% CI
1.87675	1.877 with 95%CI:[1.789 - 1.974]

Deming Regression

Table 28 presents the results from the Deming Regression. The slope is 0.04 (95% CI: [-0.03, 0.104]) and the intercept is 93.79 (95% CI: [87.357, 100.231]).

Table 28: Deming Regression Slope and Intercept with Confidence Limits

Deming Slope [95% CI]	Deming Intercept [95% CI]
0.04 [-0.03, 0.104]	93.79 [87.357, 100.231]

2.3.1.1.2. Pulse Rate

Patients and Healthy Subjects

A_{rms}

The main claim of accuracy is based on the root-mean-square difference between measured values and reference values, A_{rms}.

A_{rms} = 1.72946 bpm for patients and healthy subjects.

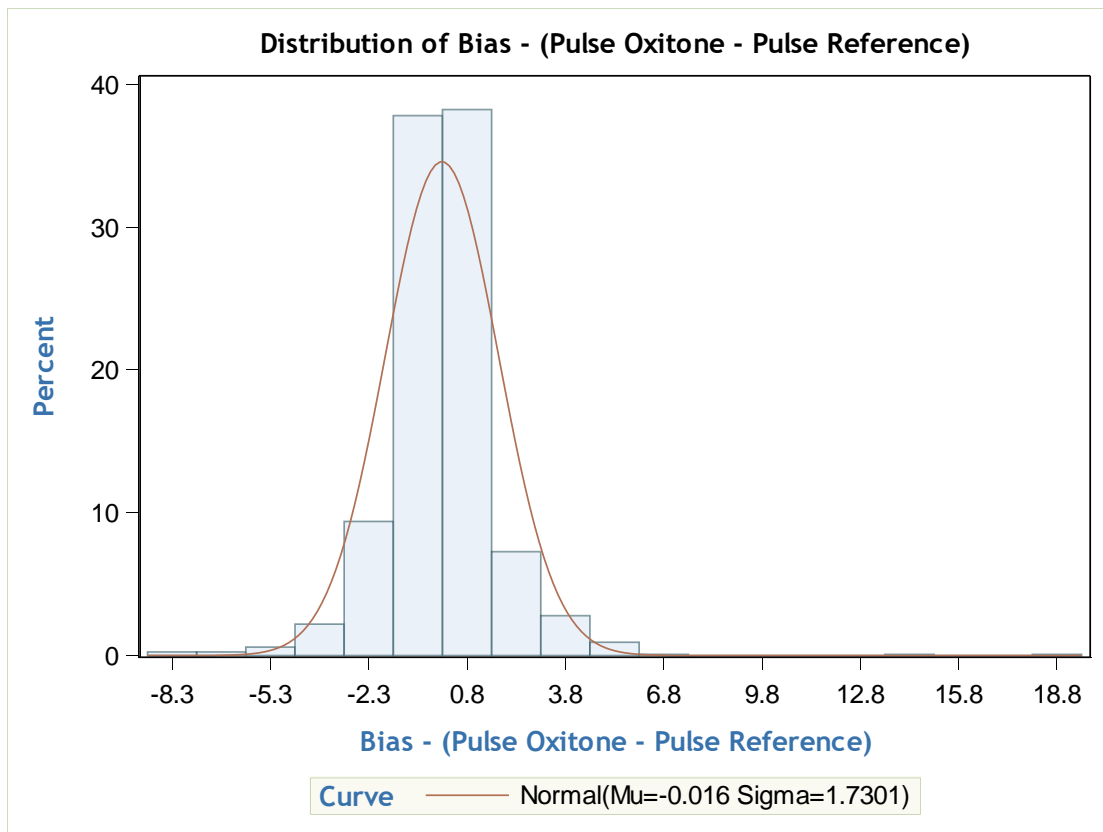
Descriptive Statistics

Table 29 presents the descriptive statistics of Pulse rate as measured by Oxitone 1000 and the reference, as well as the difference between them. Figure 10 presents the distribution of this difference. In this population, we see from the figure that the differences follow a rather symmetric pattern and appear to follow a normal distribution. The mean pulse as measured by Oxitone was 74.64 bpm (range 50.9-119.6) and for the reference 74.60 bpm (range 51.8-118.6).

Table 29: Descriptive Statistics of Pulse Rate

	N	Mean	SD	Min	Median	Max
Pulse Oxitone	1197	74.64	11.57	50.9	73.30	119.6
Pulse Reference	1198	74.60	11.73	51.8	73.45	118.6
Difference - (Pulse Oxitone - Pulse Reference)	1182	-0.02	1.73	-8.6	-0.02	18.6

Figure 10: Distribution of Difference - (Pulse Oxitone - Pulse Reference)



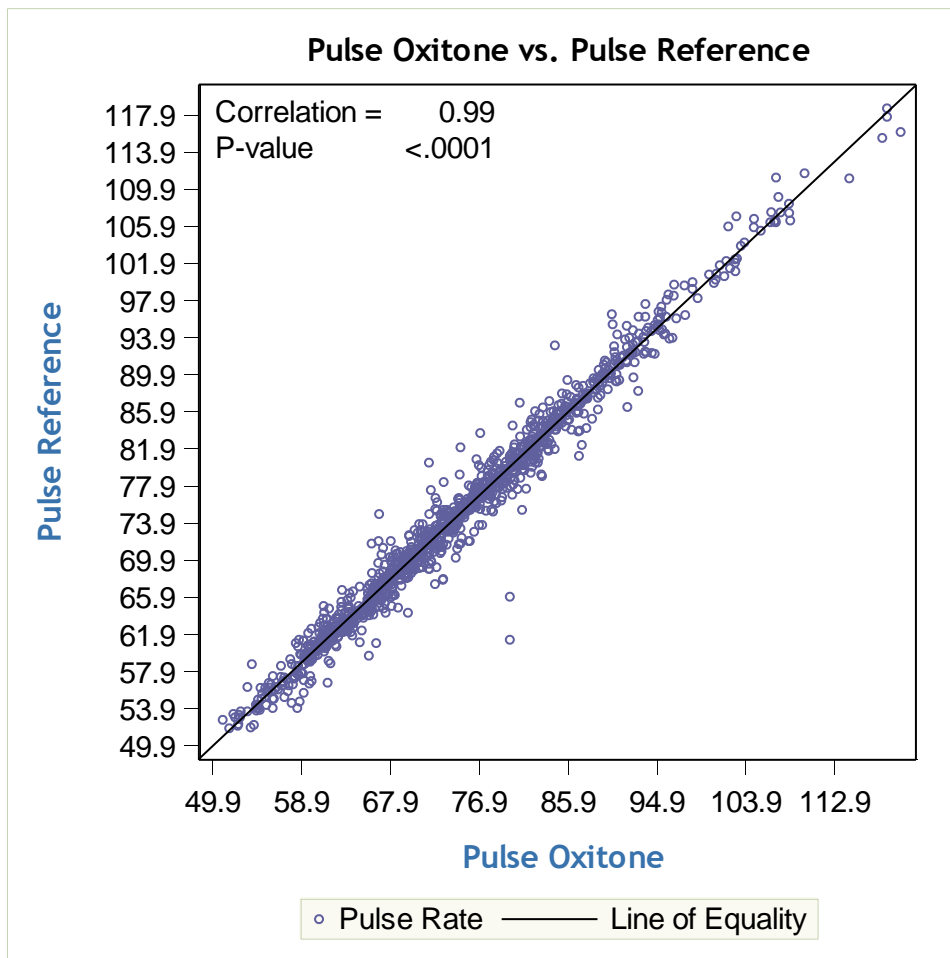
Correlation

Table 30 presents the correlation and its 95% confidence interval. Figure 11 shows a scatter plot of the Pulse rate measured by Oxitone 1000 and by the reference respectively. There are 1182 pairs of pulse measurements. We find a statistically significant correlation (Pearson's correlation coefficient) between Oxitone and reference, $r=0.98908$ (95% CI: [0.987762, 0.990248], $p<0.0001$).

Table 30: Correlation with 95% Confidence Interval

Pearson Correlation Statistics (Fisher's z Transformation)									
Variable	With Variable	N	Sample Correlation	Fisher's z	Bias Adjustment	Correlation Estimate	95% Confidence Limits		p Value for H0:Rho=0
Pulse_Oxitone	Pulse_Reference	1182	0.98908	2.60261	0.0004187	0.98908	0.987762	0.990248	<.0001

Figure 11: Correlation Between Pulse Oxitone and Pulse Reference



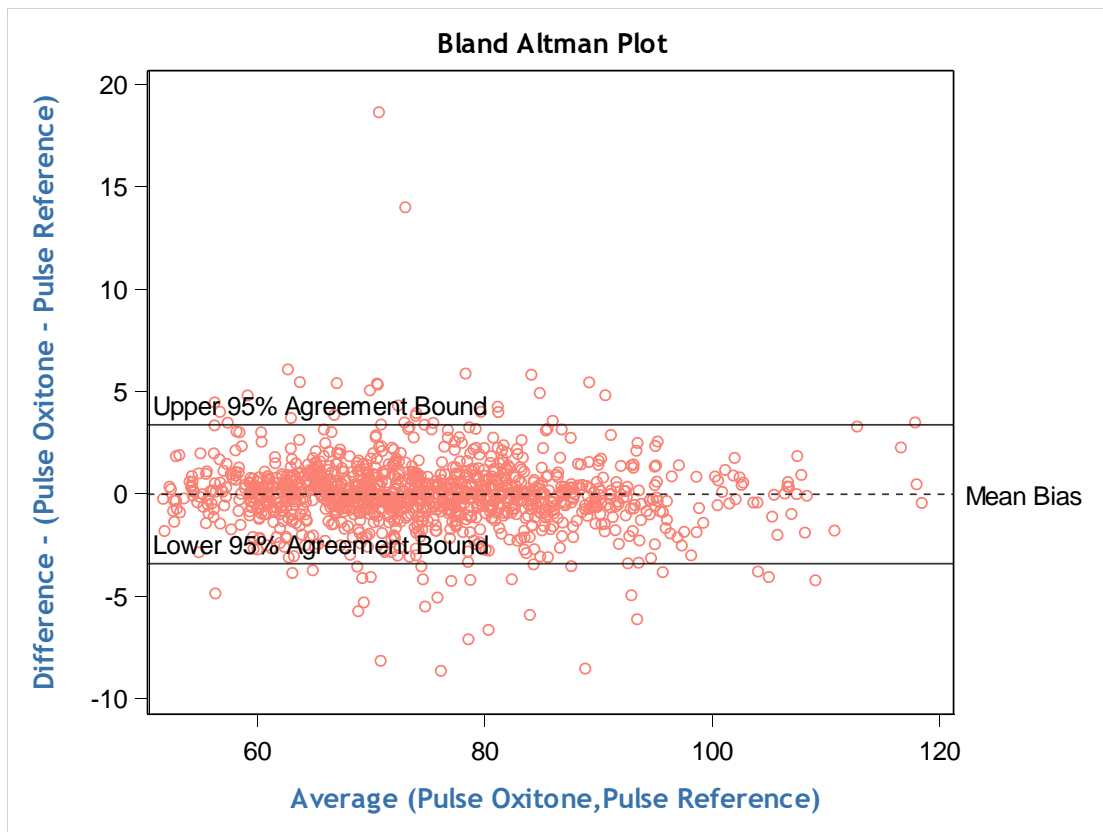
Agreement

Table 31 presents the 95% limits of agreement with the respective 95% confidence interval for each limit. Figure 12 presents the Bland-Altman plot. Most differences between the two measurements will lie between the 95% agreement limits of [-3.41, 3.38] bpm.

Table 31: Limits of Agreement

Lower 95% Agreement Bound	95% CI Lower Agreement Bound	Upper 95% Agreement Bound	95% CI Upper Agreement Bound
-3.41	[-4.41 - -2.41]	3.38	[2.37 - 4.38]

Figure 12: Bland-Altman Plot



Bias

Table 32 presents the mean bias and its 95% confidence interval and Table 33 presents the SD bias and its 95% confidence interval. The model estimated mean difference between Oxitone and the reference pulse, i.e. the bias, is -0.01574 bpm (95% CI: [-0.1179, 0.0864] bpm). The standard deviation of this difference, i.e. the precision, is 1.73012 bpm [95% CI:[1.663, 1.803] bpm).

Table 32: Mean Bias with 95% Confidence Interval

Mean Bias	95% CI
-0.01574	-.0157 with 95%CI:[-.1179 -0.0864]

Table 33: SD Bias with 95% Confidence Interval

SD of Bias	95% CI
1.73012	1.730 with 95%CI:[1.663 - 1.803]

Deming Regression

Table 34 presents the results from the Deming Regression. The slope is 1.01 (95% CI: [1.006, 1.024]) and the intercept is -1.14 (95% CI: [-1.848, -0.424]).

Table 34: Deming Regression Slope and Intercept with Confidence Limits

Deming Slope [95% CI]	Deming Intercept [95% CI]
1.01 [1.006, 1.024]	-1.14 [-1.848, -0.424]

Patients

A_{rms}

The main claim of accuracy is based on the root-mean-square difference between measured values and reference values, A_{rms} .

A_{rms} = 1.89009 bpm for patients.

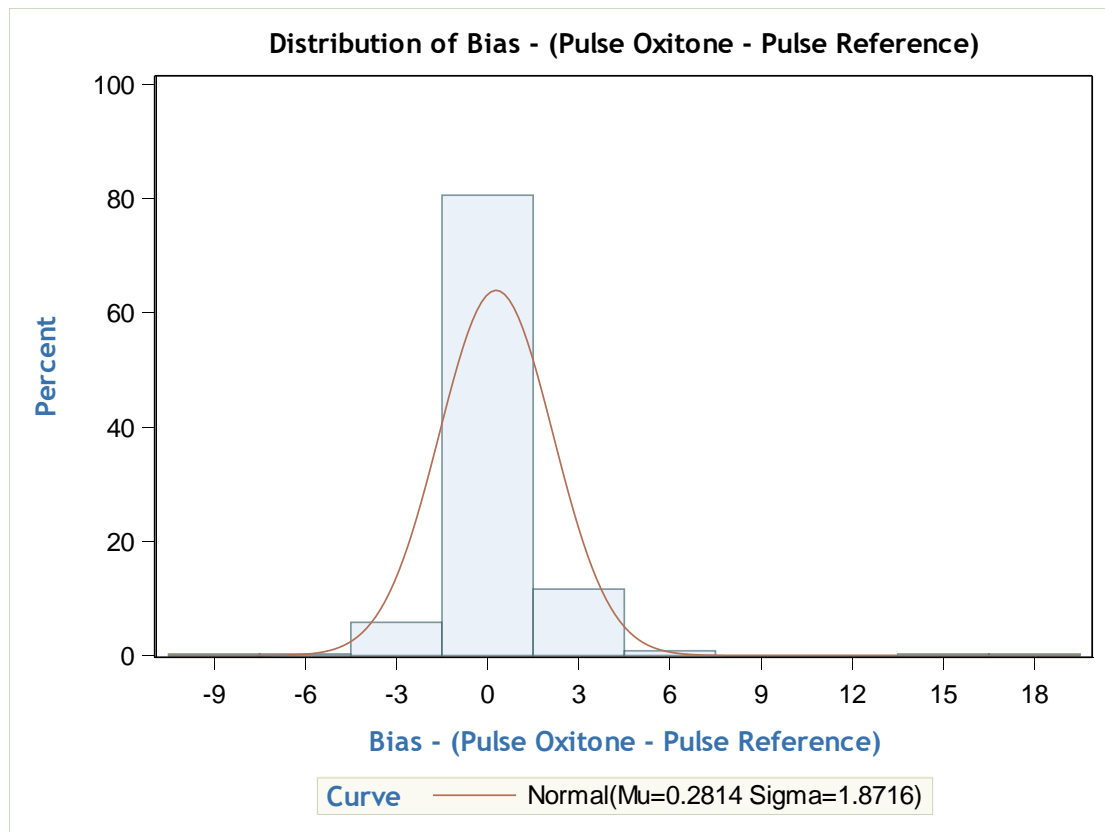
Descriptive Statistics

Table 35 presents the descriptive statistics of Pulse rate as measured by Oxitone 1000 and the reference, as well as the difference between them. Figure 13 presents the distribution of this difference. In this population, we see from the figure that the differences follow a rather symmetric pattern and appear to follow a normal distribution. The mean pulse as measured by Oxitone was 72.10 bpm (range 50.9-95.8) and for the reference 71.81 bpm (range 51.8-96.5).

Table 35: Descriptive Statistics of Pulse Rate

	N	Mean	SD	Min	Median	Max
Pulse Oxitone	362	72.10	10.43	50.9	71.59	95.8
Pulse Reference	367	71.81	10.45	51.8	71.09	96.5
Difference - (Pulse Oxitone - Pulse Reference)	361	0.28	1.87	-8.5	0.09	18.6

Figure 13: Distribution of Difference - (Pulse Oxitone - Pulse Reference)



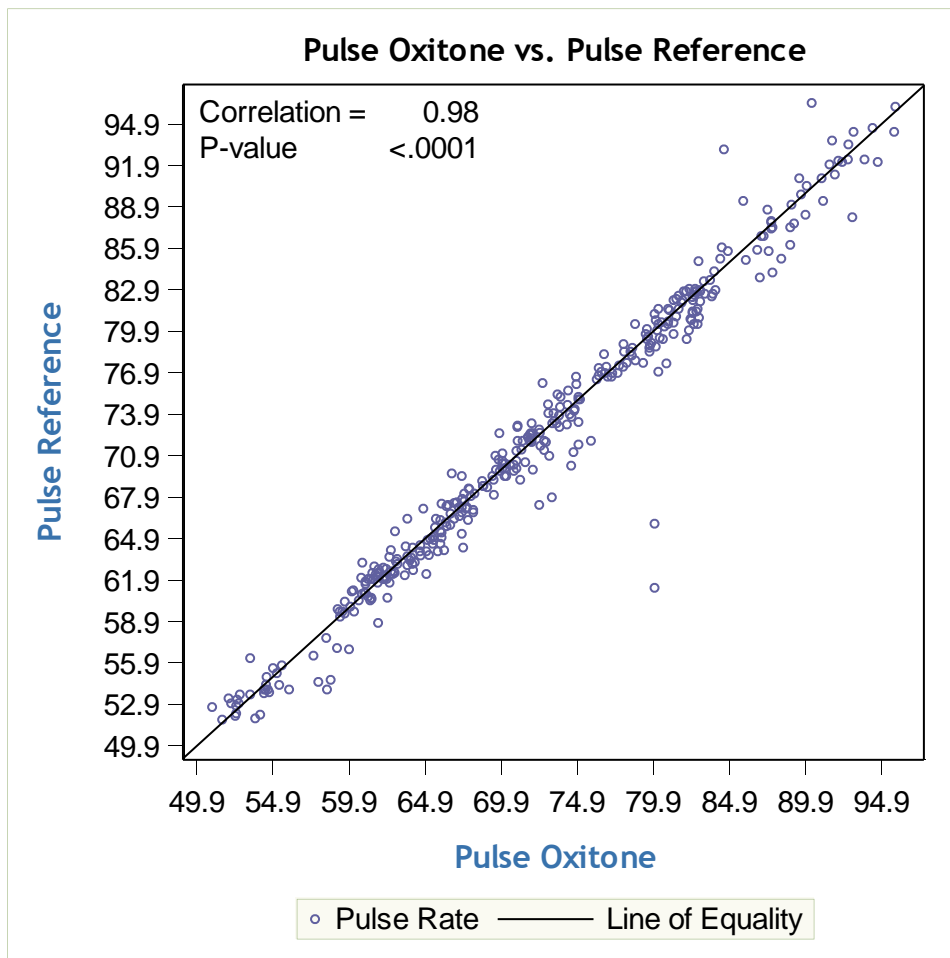
Correlation

Table 36 presents the correlation and its 95% confidence interval. Figure 14 shows a scatter plot of the Pulse rate measured by Oxitone 1000 and by the reference respectively. There are 361 pairs of pulse measurements. We find a statistically significant correlation (Pearson's correlation coefficient) between Oxitone and reference, $r=0.98400$ (95% CI: [0.980294, 0.986935], $p<0.0001$).

Table 36: Correlation with 95% Confidence Interval

Pearson Correlation Statistics (Fisher's z Transformation)									
Variable	With Variable	N	Sample Correlation	Fisher's z	Bias Adjustment	Correlation Estimate	95% Confidence Limits		p Value for H0:Rho=0
Pulse_Oxitone	Pulse_Reference	361	0.98400	2.40998	0.00137	0.98395	0.980294	0.986935	<.0001

Figure 14: Correlation Between Pulse Oxitone and Pulse Reference



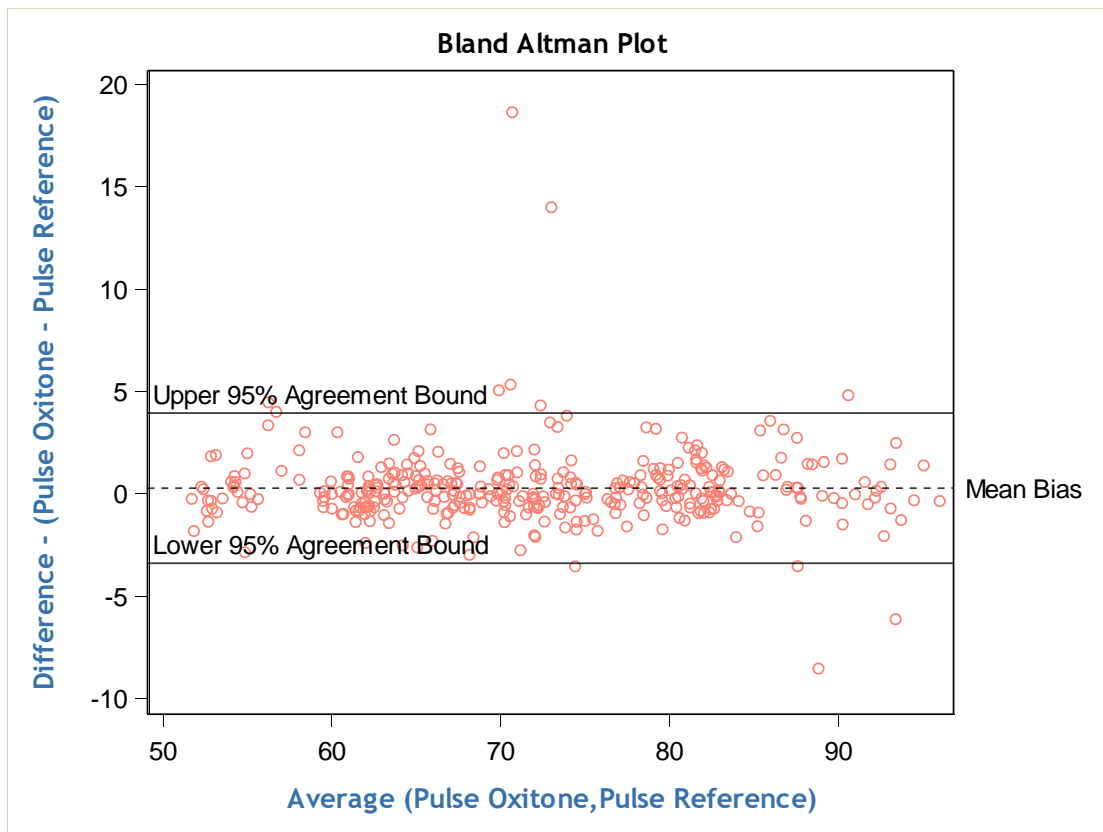
Agreement

Table 37 presents the 95% limits of agreement with the respective 95% confidence interval for each limit. Figure 15 presents the Bland-Altman plot. Most differences between the two measurements will lie between the 95% agreement limits of [-3.39, 3.95] bpm.

Table 37: Limits of Agreement

Lower 95% Agreement Bound	95% CI Lower Agreement Bound	Upper 95% Agreement Bound	95% CI Upper Agreement Bound
-3.39	[-4.84 - -1.93]	3.95	[2.49 - 5.41]

Figure 15: Bland-Altman Plot



Bias

Table 38 presents the mean bias and its 95% confidence interval and Table 39 presents the SD bias and its 95% confidence interval. The model estimated mean difference between Oxitone and the reference pulse, i.e. the bias, is 0.2814 bpm (95% CI: [0.0759, 0.4869] bpm). The standard deviation of this difference, i.e. the precision, is 1.87162 bpm [95% CI:[1.744, 2.019] bpm).

Table 38: Mean Bias with 95% Confidence Interval

Mean Bias	95% CI
0.2814	0.2814 with 95%CI:[0.0759 -0.4869]

Table 39: SD Bias with 95% Confidence Interval

SD of Bias	95% CI
1.87162	1.872 with 95%CI:[1.744 - 2.019]

Deming Regression

Table 40 presents the results from the Deming Regression. The slope is 1.01 (95% CI: [0.99, 1.028]) and the intercept is -0.92 (95% CI: [-2.293, 0.451]).

Table 40: Deming Regression Slope and Intercept with Confidence Limits

Deming Slope [95% CI]	Deming Intercept [95% CI]
1.01 [0.99, 1.028]	-0.92 [-2.293, 0.451]

Healthy Subjects

A_{rms}

The main claim of accuracy is based on the root-mean-square difference between measured values and reference values, A_{rms} .

A_{rms} = 1.65391 bpm for healthy subjects.

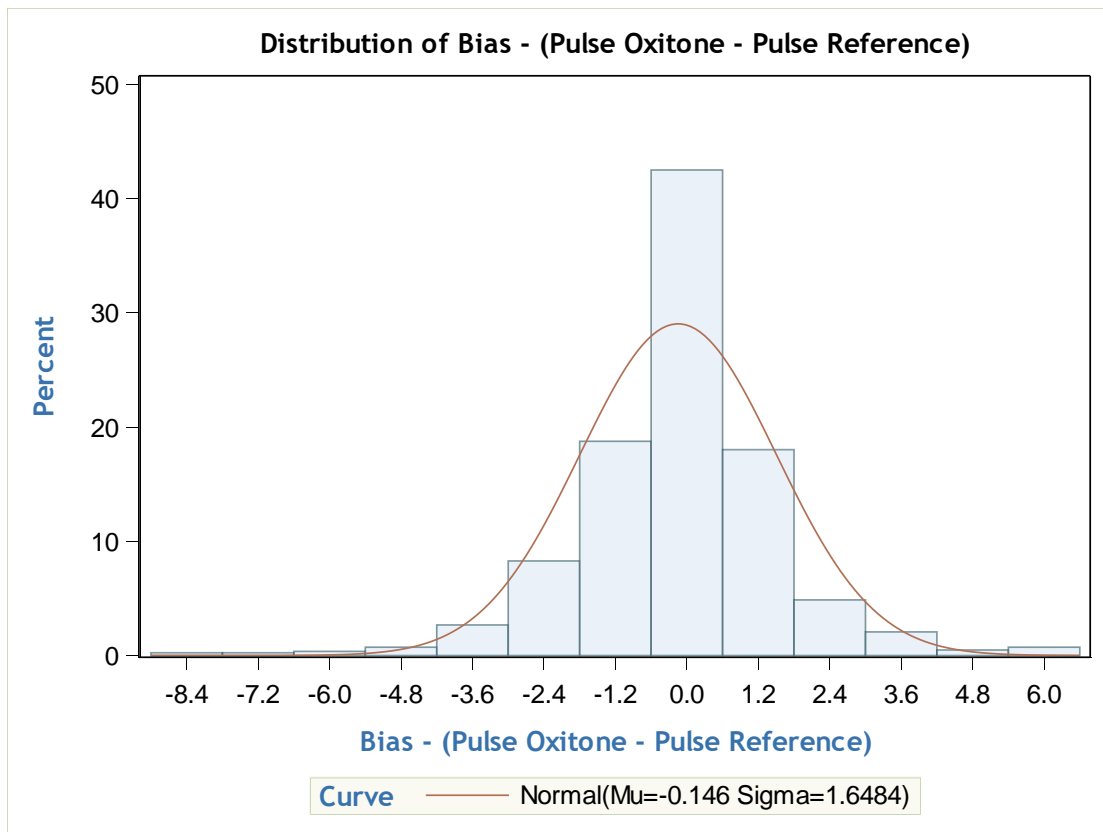
Descriptive Statistics

Table 41 presents the descriptive statistics of Pulse rate as measured by Oxitone 1000 and the reference, as well as the difference between them. Figure 16 presents the distribution of this difference. In this population, we see from the figure that the differences follow a rather symmetric pattern and appear to follow a normal distribution. The mean pulse as measured by Oxitone was 75.74 bpm (range 53.9-119.6) and for the reference 75.83 bpm (range 54.3-118.6).

Table 41: Descriptive Statistics of Pulse Rate

	N	Mean	SD	Min	Median	Max
Pulse Oxitone	835	75.74	11.86	53.9	74.33	119.6
Pulse Reference	831	75.83	12.05	54.3	74.64	118.6
Difference - (Pulse Oxitone - Pulse Reference)	821	-0.15	1.65	-8.6	-0.08	6.1

Figure 16: Distribution of Difference - (Pulse Oxitone - Pulse Reference)



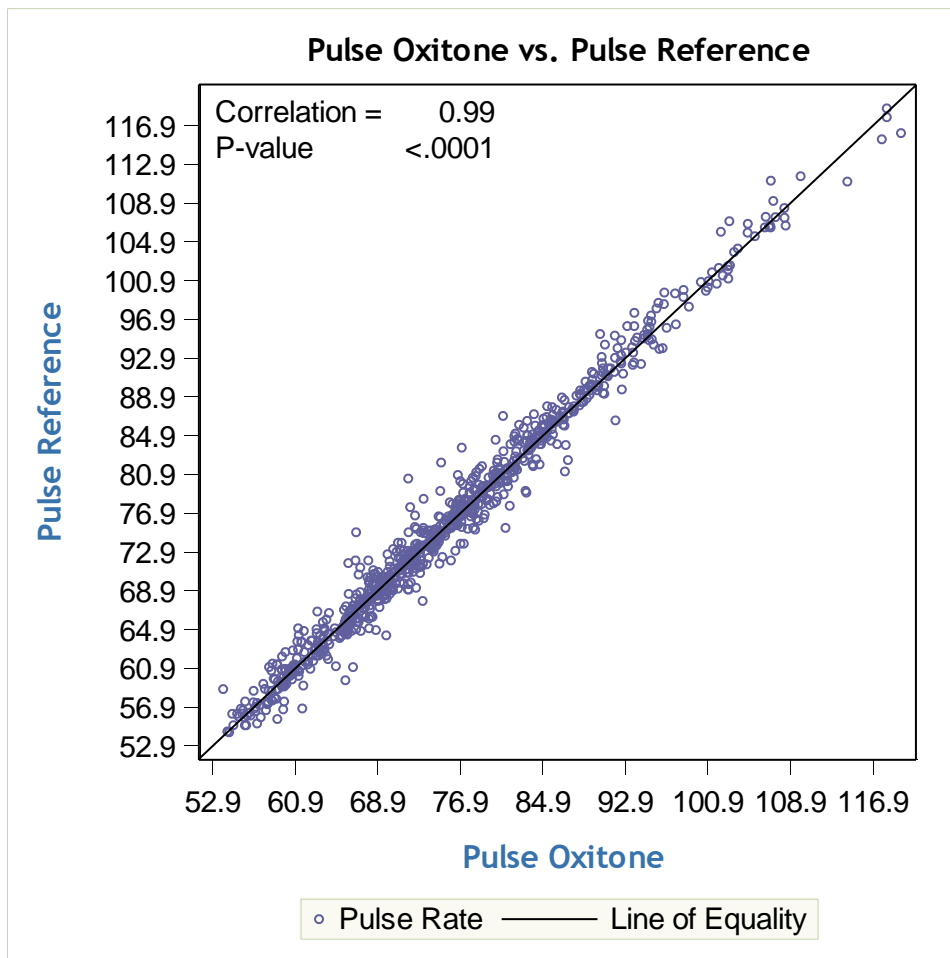
Correlation

Table 42 presents the correlation and its 95% confidence interval. Figure 17 shows a scatter plot of the Pulse rate measured by Oxitone 1000 and by the reference respectively. There are 821 pairs of pulse measurements. We find a statistically significant correlation (Pearson’s correlation coefficient) between Oxitone and reference, $r=0.99060$ (95% CI: [0.989210, 0.991786], $p<0.0001$).

Table 42: Correlation with 95% Confidence Interval

Pearson Correlation Statistics (Fisher's z Transformation)									
Variable	With Variable	N	Sample Correlation	Fisher's z	Bias Adjustment	Correlation Estimate	95% Confidence Limits		p Value for H0:Rho=0
Pulse_Oxitone	Pulse_Reference	821	0.99060	2.67756	0.0006040	0.99059	0.989210	0.991786	<.0001

Figure 17: Correlation Between Pulse Oxitone and Pulse Reference



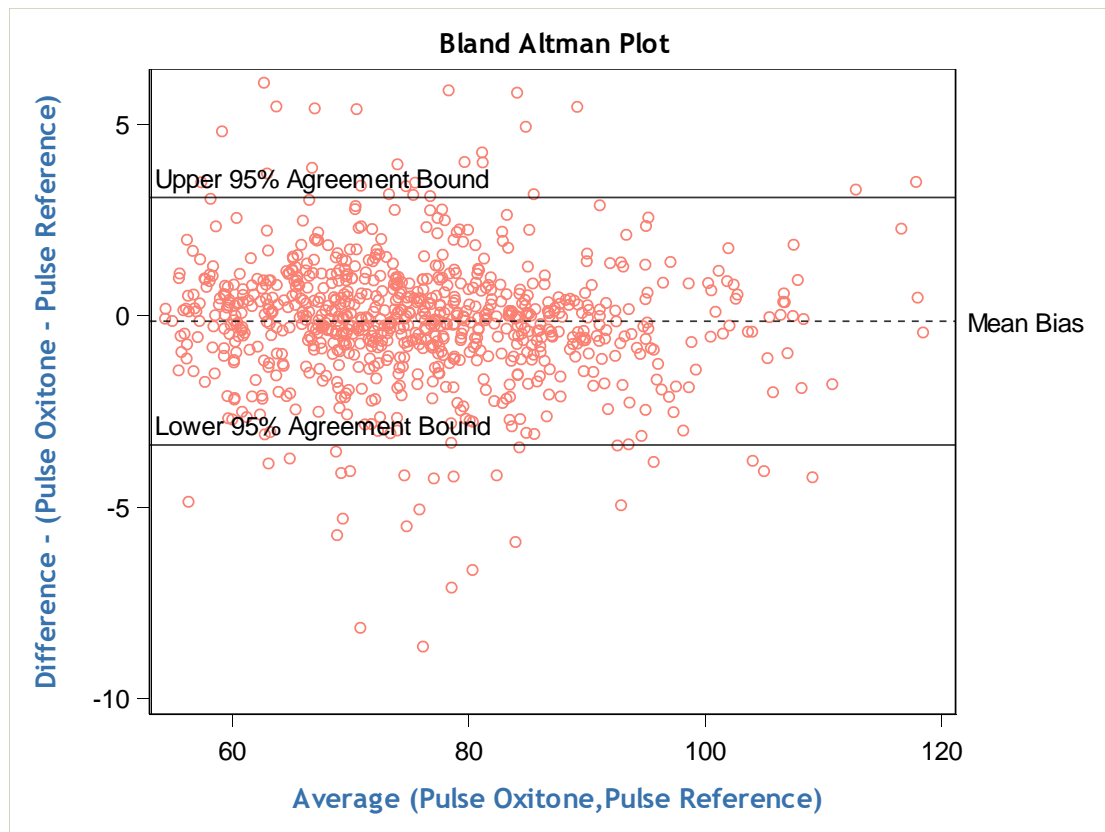
Agreement

Table 43 presents the 95% limits of agreement with the respective 95% confidence interval for each limit. Figure 18 presents the Bland-Altman plot. Most differences between the two measurements will lie between the 95% agreement limits of [-3.38, 3.08] bpm.

Table 43: Limits of Agreement

Lower 95% Agreement Bound	95% CI Lower Agreement Bound	Upper 95% Agreement Bound	95% CI Upper Agreement Bound
-3.38	[-4.94 - -1.82]	3.08	[1.52 - 4.64]

Figure 18: Bland-Altman Plot



Bias

Table 44 presents the mean bias and its 95% confidence interval and Table 45 presents the SD bias and its 95% confidence interval. The model estimated mean difference between Oxitone and the reference pulse, i.e. the bias, is -0.1464 bpm (95% CI: [-0.2698, -0.0230] bpm). The standard deviation of this difference, i.e. the precision, is 1.64842 bpm [95% CI:[1.572, 1.732] bpm).

Table 44: Mean Bias with 95% Confidence Interval

Mean Bias	95% CI
-0.1464	-.1464 with 95%CI:[-.2698 --.0230]

Table 45: SD Bias with 95% Confidence Interval

SD of Bias	95% CI
1.64842	1.648 with 95%CI:[1.572 - 1.732]

Deming Regression

Table 46 presents the results from the Deming Regression. The slope is 1.01 (95% CI: [1.003, 1.025]) and the intercept is -0.95 (95% CI: [-1.816, -0.085]).

Table 46: Deming Regression Slope and Intercept with Confidence Limits

Deming Slope [95% CI]	Deming Intercept [95% CI]
1.01 [1.003, 1.025]	-0.95 [-1.816, -0.085]

2.3.1.2. Precision

2.3.1.2.1. Oxygen Saturation

Healthy Subjects

Repeatability

Table 47 presents accuracy and repeatability statistics of the Oxitone 1000 measurement, where the repeatability is represented by the standard deviation of repeated measurements, as well as respective 95% confidence intervals and CV. Repeatability is 1.367% (95% CI: [1.303, 1.438]%), with a CV of 1.4%.

Table 47: Repeatability Statistics with Confidence Limits

Accuracy (mean)	95% CI	Repeatability (SD)	95% CI	CV
96.6970	[95.637 - 97.757]	1.367	[1.303 - 1.438]	1.4%

Reproducibility

Table 48 presents reproducibility statistics of the Oxitone 1000 measurement, where the reproducibility is represented by the standard deviation of repeated measurements between devices, as well as its 95% confidence interval and CV. Reproducibility is 1.355% (95% CI: [1.287, 1.426]%), with a CV of 1.4%.

Table 48: Reproducibility Statistics with Confidence Limits

Reproducibility (SD)	95% CI	CV
1.355	[1.287 - 1.426]	1.4%

2.3.1.2.2. Pulse Rate

Healthy Subjects

Repeatability

Table 49 presents accuracy and repeatability statistics of the Oxitone 1000 measurement, where the repeatability is represented by the standard deviation of repeated measurements, as well as respective 95% confidence intervals and CV. Repeatability is 4.606 bpm (95% CI: [4.393, 4.841] bpm), with a CV of 6.1%.

Table 49: Repeatability Statistics with Confidence Limits

Accuracy (mean)	95% CI	Repeatability (SD)	95% CI	CV
75.2382	[59.871 - 90.606]	4.606	[4.393 - 4.841]	6.1%

Reproducibility

Table 50 presents reproducibility statistics of the Oxitone 1000 measurement, where the reproducibility is represented by the standard deviation of repeated measurements between devices, as well as its 95% confidence interval and CV. Reproducibility is 4.564 bpm (95% CI: [4.235, 4.896] bpm), with a CV of 6.1%.

Table 50: Reproducibility Statistics with Confidence Limits

Reproducibility (SD)	95% CI	CV
4.564	[4.235 - 4.896]	6.1%

2.3.2. Secondary Endpoint

2.3.2.1. Usability

Table 51 presents usability data for the Oxitone device and for the reference device, per subject population and overall. Figure 19 and Figure 20 present the level of comfort using the devices and data for device display readable and clear for all subjects in the FA set. Among all subjects in the FA set, 83.8% (31/37) reported that the level of comfort using Oxitone device was good or very good. 38.9% (14/36) reported that the level of comfort using reference device was good or very good. Regarding if the device display was readable and clear, 97.3%

(36/37) said good or very good about the Oxitone device and 100% (36/36) said so about the reference device.

Table 51: Usability

			FA	
Patients	Level of Comfort Using Reference Device	Not at All	% (n/N)	23.8% (5/21)
		Poor	% (n/N)	4.8% (1/21)
		Neutral	% (n/N)	28.6% (6/21)
		Good	% (n/N)	9.5% (2/21)
		Very Good	% (n/N)	33.3% (7/21)
	Level of Comfort Using Oxitone Device	Not at All	% (n/N)	4.5% (1/22)
		Neutral	% (n/N)	9.1% (2/22)
		Good	% (n/N)	18.2% (4/22)
		Very Good	% (n/N)	68.2% (15/22)
	Reference Device Display Readable and Clear	Very Good	% (n/N)	100% (21/21)
Oxitone Device Display Readable and Clear	Good	% (n/N)	4.5% (1/22)	
	Very Good	% (n/N)	95.5% (21/22)	
Healthy Subjects	Level of Comfort Using Reference Device	Not at All	% (n/N)	6.7% (1/15)
		Poor	% (n/N)	33.3% (5/15)
		Neutral	% (n/N)	26.7% (4/15)
		Good	% (n/N)	33.3% (5/15)
	Level of Comfort Using Oxitone Device	Neutral	% (n/N)	20.0% (3/15)
		Good	% (n/N)	40.0% (6/15)
		Very Good	% (n/N)	40.0% (6/15)
	Reference Device Display Readable and Clear	Good	% (n/N)	13.3% (2/15)
		Very Good	% (n/N)	86.7% (13/15)
	Oxitone Device Display Readable and Clear	Neutral	% (n/N)	6.7% (1/15)
Good		% (n/N)	20.0% (3/15)	
Very Good		% (n/N)	73.3% (11/15)	
All	Level of Comfort Using Reference Device	Not at All	% (n/N)	16.7% (6/36)
		Poor	% (n/N)	16.7% (6/36)
		Neutral	% (n/N)	27.8% (10/36)
		Good	% (n/N)	19.4% (7/36)
		Very Good	% (n/N)	19.4% (7/36)
	Level of Comfort Using Oxitone Device	Not at All	% (n/N)	2.7% (1/37)
		Neutral	% (n/N)	13.5% (5/37)
		Good	% (n/N)	27.0% (10/37)
		Very Good	% (n/N)	56.8% (21/37)
	Reference Device Display Readable and Clear	Good	% (n/N)	5.6% (2/36)
		Very Good	% (n/N)	94.4% (34/36)
	Oxitone Device Display Readable and Clear	Neutral	% (n/N)	2.7% (1/37)
		Good	% (n/N)	10.8% (4/37)
Very Good		% (n/N)	86.5% (32/37)	

Figure 19: Level of Comfort Using Device

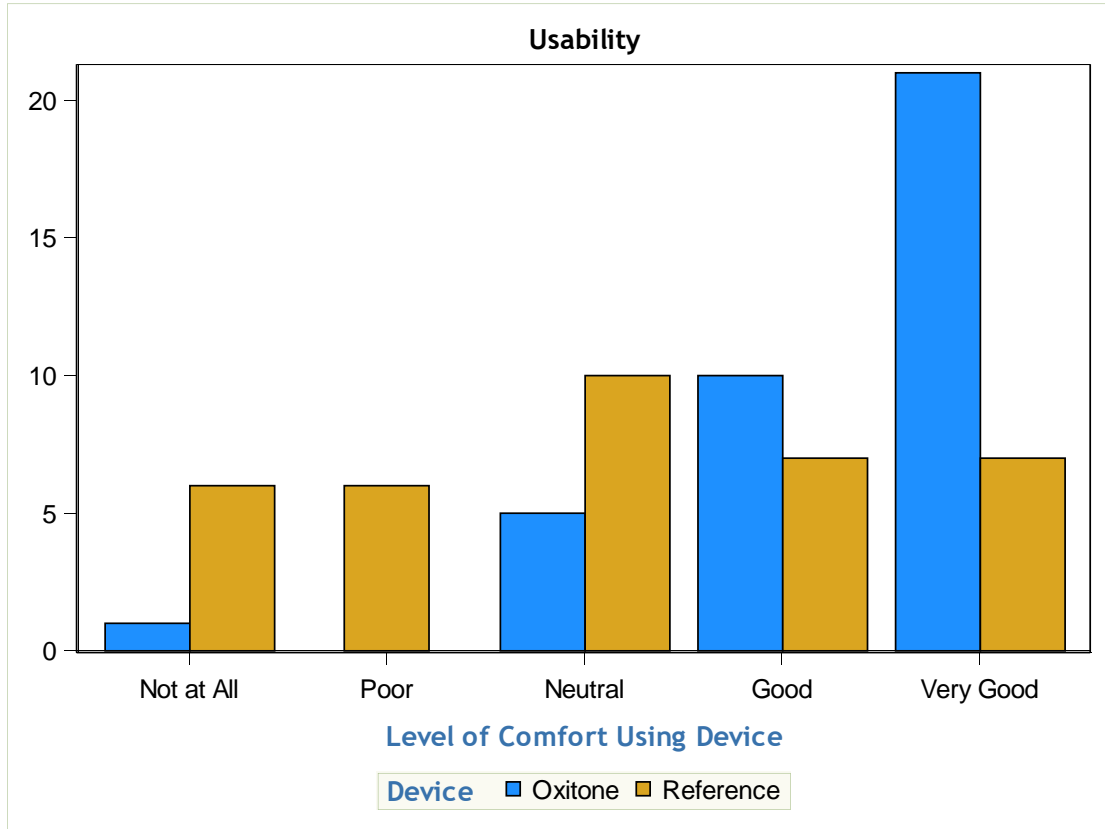
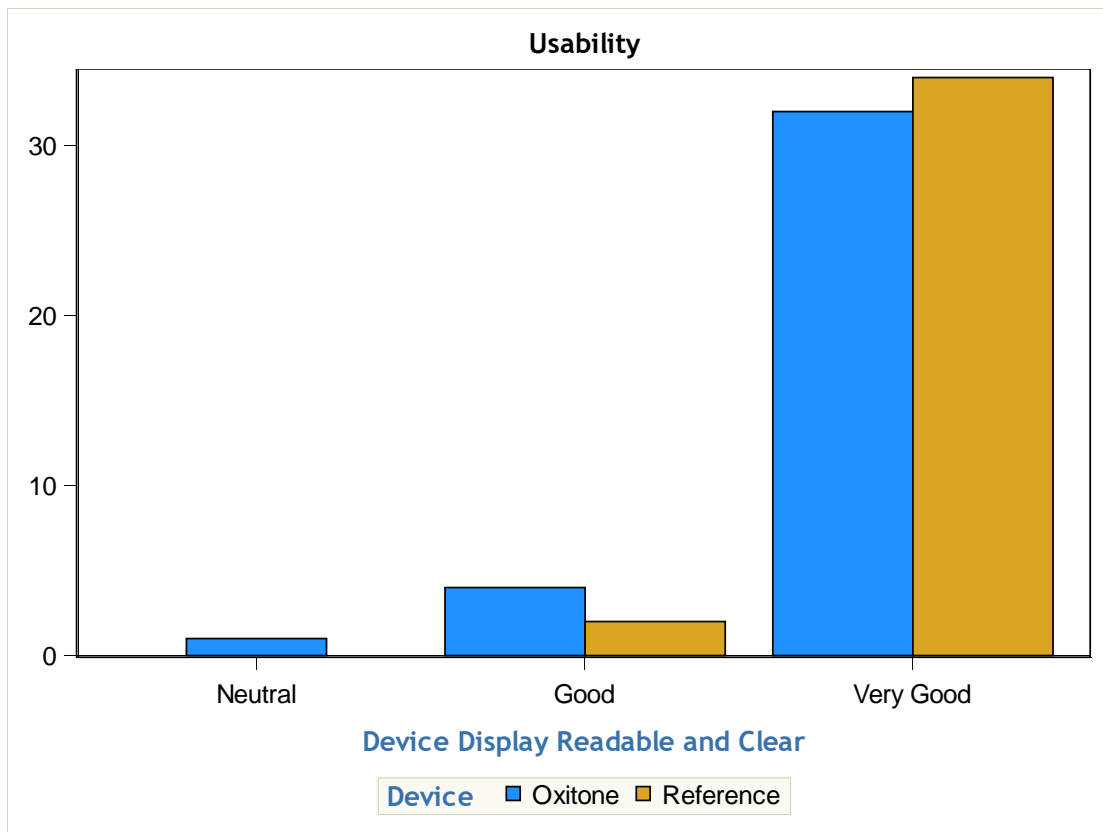


Figure 20: Device Display Readable and Clear



2.4. Safety Endpoints

There were no (0) adverse events or Serious adverse events reported throughout the study, among 38 subjects (healthy and patients) in the FA set. The exact binomial 95% confidence interval for the AE rate is [0.00%, 9.25%].

3. SUMMARY AND CONCLUSIONS

In summary in the study we have shown that:

Accuracy

- For all subjects (healthy and patients), the root-mean-square difference between measured values and reference values of oxygen saturation, $A_{rms} = 2.12762\%$ and that of pulse, $A_{rms} = 1.72946$ bpm.

Precision

- The repeatability of Oxitone is 1.367% (95% CI: [1.303, 1.438]%) for oxygen saturation and 4.606 bpm (95% CI: [4.393, 4.841] bpm) for pulse.
- The reproducibility of Oxitone is 1.355% (95% CI: [1.287, 1.426]%) for oxygen saturation and 4.564 bpm (95% CI: [4.235, 4.896] bpm) for pulse.

Usability

- 83.8% (31/37) of the subjects reported that the level of comfort using Oxitone device was good or very good, whereas 38.9% (14/36) using reference device.

Safety

- There were no (0) adverse events throughout the study, among 38 subjects (healthy and patients) in the FA set. The exact binomial 95% confidence interval for the AE rate is [0.00%, 9.25%].

We conclude that the Oxitone measurement of oxygen saturation and pulse fulfills the success criterion for A_{rms} (accuracy), shows high repeatability and reproducibility (i.e. small standard deviation) (precision), has a high level of comfort (usability) and is safe (safety).

4. APPENDIX

Table 52 presents the concomitant medication.

Table 52: Concomitant Medication

Subject Id	Name of Medication	Route	Total Daily Dose	Units	Indication for Use	Start Date	Ongoing
M-030	Cardiloc	Unk	Unk	Unk	Unk	Unk	Yes
M-030	Bedodeka	Unk	Unk	Unk	Unk	Unk	Yes
M-030	Vasodip	Unk	Unk	Unk	Unk	Unk	Yes
M-033	Incruse	Unk	Unk	Unk	Unk	Unk	Yes
M-033	Relvar	Unk	Unk	Unk	Unk	Unk	Yes
M-035	Qvar Autohaler Inh 100mcg	Puff	2	2	Unk	Unk	Yes
M-035	Travatan Bak Free 0.004% Col	Drops	1	1	Unk	Unk	Yes
M-035	Calcium Carbonate 1500mg 600m	Cap	1	2	Unk	Unk	Yes
M-035	Azarga Col 1/5ml 1cf/5ml	Drops	1	2	Unk	Unk	Yes
M-035	Prolia Prefil Sc 60mg 60	Unk	1	1	Unk	Unk	Yes
M-035	D Tabs 400iu	Cap	1	3	Unk	Unk	Yes
M-035	Anoro Ellipta 55mcg/22	Puff	1	1	Unk	Unk	Yes
M-036	Relvar	Inh	1+1	Unk	Copd	Unk	Yes
M-036	Incruse	Inh	1+1	Unk	Copd	Unk	Yes
M-037	Micropirin 100mg	Oral	1	1	Unk	Unk	Yes
M-037	Normiten 25mg	Oral	1	1	Unk	Unk	Yes
M-037	Norvasc 5mg	Oral	1	1	Unk	Unk	Yes
M-037	Zinnat 500mg	Oral	2	1	Unk	Unk	Yes
M-037	Rulid 150mg	Oral	2	1	Unk	Unk	Yes
M-037	Aerovent 0.25mg	Inh	4	1	Unk	Unk	Yes
M-037	Flixotide Nebules 0.Gmg	Inh	2	1	Unk	Unk	Yes
M-037	Prednitone 40mg	Oral	1	1	Unk	Unk	Yes
M-038	Relvar	Inh	1+1	Unk	Copd	Unk	Yes
M-039	Loratadin	Po	1+1		Unk	Unk	Yes
M-039	Azenil	Po	1+1		Bronchiectasis	Unk	Yes
M-039	Mucolyt	Po	1+3		Brochiectasis	Unk	Yes
M-039	Seretide	Inh	1+2		Copd	Unk	Yes
M-040	Seretide	Inh	Unk	Unk	Bronchitis	Unk	Yes
M-041	Symbicort	Inh	1+2	Unk	Copd	Unk	Yes
M-043	Enaladex	Po	5	Mcg	Unk	Unk	Yes
M-043	Normalol	Po	25	Unk	Unk	Unk	Yes
M-043	Rosuvastatin	Unk	Unk	Unk	Unk	Unk	Yes
M-044	Symbicort	Inh	2+2	Unk	Asthma/Copd	Unk	Yes
M-045	Cardiloc 2.5mg	Tab	Unk	Unk	Unk	Unk	No
M-045	Terbutaline Sulphate	Unk	Unk	Unk	Unk	Unk	No
M-045	Nasocort Aqua	Nasal Spr	Unk	Unk	Unk	Unk	No
M-045	Micropirin 100mg	Oral	Unk	Unk	Unk	Unk	No
M-045	Ipratropium Bromide 0.25mg	Inh	Unk	Unk	Unk	Unk	No
M-045	Diskus Seretide	Inh	2	1	Unk	Unk	No
M-045	Enalapri	Tab	Unk	Unk	Unk	Unk	No
M-045	Elatrol	Tab	Unk	Unk	Unk	Unk	No
M-045	Citalopram Hydrobromide 20mg	Tab	Unk	Unk	Unk	Unk	No
M-045	Carbocysteine 375mg	Cap	Unk	Unk	Unk	Unk	No
M-045	Bisacodyl 5mg	Tab	Unk	Unk	Unk	Unk	No
M-045	Atorvastatin 40mg	Tab	Unk	Unk	Unk	Unk	No
M-045	Aerius 5mg	Tab	1	1	Unk	Unk	No
M-045	Disothiazide	Tab	Unk	Unk	Unk	Unk	No
M-046	Avamys Aq. Nasal 120 Inh	Spr	1	1	Unk	Unk	Yes
M-046	Relvar Ellipta 184mcg/22mcg	Puff	1	1	Unk	Unk	Yes

Subject Id	Name of Medication	Route	Total Daily Dose	Units	Indication for Use	Start Date	Ongoing
M-047	Simovil 20mg	Oral	1	1	Unk	Unk	Yes
M-047	Micropirin 100mg	Oral	1	1	Unk	Unk	Yes
M-049	Alendronate 10mg	Oral	1	1	Unk	Unk	No
M-049	Bezafibrate 400mg	Oral	1	1	Unk	Unk	No
M-049	Calcium Carbonate	Unk	1	1	Unk	Unk	No
M-049	Colecalciferol	Oral	1	1	Unk	Unk	No
M-049	Euthyrox 100mg	Oral	1	1	Unk	Unk	No
M-049	Lanton 30mg	Oral	1	1	Unk	Unk	No
M-049	Loratadine 10mg	Oral	1	1	Unk	Unk	No
M-049	Seretide Diskus	Inh	1	2	Unk	Unk	No
M-049	Simvastatin 40mg	Oral	1	1	Unk	Unk	No
M-049	Spiriva Pwd 18mcg	Inh	1	1	Unk	Unk	No
M-049	Avamys 27.5mcg	Inh	1	1	Unk	Unk	No
M-050	Doxazosin Mesylate Cpl 2mg	Oral	2	1	Unk	Unk	No
M-050	Metformin	Oral	2	1	Unk	Unk	No
M-050	Candesartan	Oral	1	1	Unk	Unk	No
M-050	Amlodipine	Oral	1	1	Unk	Unk	No
M-050	Atorvastatin	Oral	1	1	Unk	Unk	No
M-050	Cartia Box Of 28 Tab 100 Mg	Oral	1	1	Unk	Unk	No
M-050	Bisoprolol	Oral	2	1	Unk	Unk	No
M-051	Relvar 184/22	Inh	1	1	Unk	Unk	Yes
M-052	Symbicort 160/4.5	Inh	1	1	Unk	Unk	Yes
M-052	Avamys	Inh	1	1	Unk	Unk	Yes
M-054	Relvar 92/22	Unk	1	1	Unk	Unk	Yes
M-055	Symbicort 160/4.5mcg	Inh	1	1	Puff	Unk	No
M-055	Tritace 5mg	Oral	1	1	Unk	Unk	No
M-055	Micropirin 100mg	Oral	1	1	Unk	Unk	No
M-055	Aerovent 0.25mg	Inh	2	Cc	Unk	Unk	No
M-055	Ventolin 5mg	Inh	0.5	Cc	Unk	Unk	No
M-055	Mucolit 375mg	Oral	1	1	Unk	Unk	No
M-056	Eliquis	Po	5	Mg	Atrial Fibrillation	Unk	Yes
M-056	Procor	Po	200	Mg	Atrial Fibrillation	Unk	Yes
M-103	Eucreas 50m/850mg	Oral	1	1	Unk	2013	Yes
M-104	Glucofast	Unk	2	1	Unk	Unk	Yes
M-105	Aspirin	Unk	50mg	1	Blood Clotting	Unk	Yes
M-105	Glucomin	Unk	100mg	2	Diabetes	Unk	Yes
M-109	Aspirin	Oral	1	1	Unk	1996	Yes
M-109	Pravalipe 20mg	Oral	1	1	Unk	2000	Yes
M-109	Glucomin	Oral	1	1	Unk	2005	Yes
M-109	Provigil	Oral	2	1	Unk	2006	Yes
M-109	Rafasal	Oral	1	1	Unk	1976	Yes
M-109	Disodiazid 10mg	Oral	1	1	Unk	1975	Yes
M-109	Vazodipe Combo 10mg	Oral	1	1	Unk	2000	Yes
M-110	Lantus	Subcutaneous	1x14	14 Units	Unk	2008	Yes
M-110	Victoza	Subcutaneous	1x1.8	1.8mg	Unk	2014	Yes
M-110	Glucophage 850mg	Oral	3	1	Unk	2004	Yes
M-110	Repaglinide 1mg	Oral	3	1	Unk	2006	Yes
M-110	Dapagliflozin 10mg	Oral	1	1	Unk	Jan-2016	Yes
M-110	Bezafibrate 400	Oral	1	1	Unk	2006	Yes
M-110	Atorvastatin 40mg	Oral	1	1	Unk	2006	Yes
M-110	Ramipril 2.5mg	Oral	1	1	Unk	2004	Yes
M-114	Glucomin	Oral	2	1	Unk	2015	Yes
M-116	Litorva	Oral	1	1	Unk	Unk	Yes
M-116	Cardiobloc 0.25mg	Oral	1	1	Unk	Unk	Yes