

BiliCare™ Clinical Data – White Paper  
**Comparative Clinical Study**  
**Summary**

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**BiliCare**

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## 1. ABSTRACT

**Objectives:** The objective of the study was to evaluate the transcutaneous bilirubin (TcB) measurements obtained using the BiliCare device by comparing them to the TSB (Total Serum Bilirubin) obtained using the invasive method and to those obtained using the JM-103 device, a non-invasive device used in hospitals for performing bilirubin measurements

**Methods:** The research population included 75 neonates at gestational age  $\geq 35$  weeks, prior to discharge. The neonate's skin tone was classified to be either Caucasian or dark brown. The enrolled neonates were tested with the two BiliCare devices (property of Gerium Medical), consecutively, and additionally with the JM-103 device

**Results:** Pearson correlation was applied for testing the correlation of bilirubin results between the different methods. High Pearson correlations coefficients with high statistical significance were found between the BiliCare devices to the TSB ( $r=0.902$ ,  $p<0.0001$ ), and between the JM-103 device to TSB value ( $r =0.896$ ,  $p<0.0001$ ). The variation as measured by standard deviation and by RMSE (Root Mean Square Error) were found to be lower in the BiliCare devices than in the JM-103 device: 1.54 mg/dl and 1.89 mg/dl (respectively) for standard deviation and 1.6 mg/dl and 1.9 mg/dl (respectively) for RMSE.

**Conclusion:** A statistically and clinically significant correlation between the BiliCare device and total serum bilirubin levels was found ( $N=148$ ,  $r=90.23\%$ ,  $STD= 1.54$  mg/dl,  $p<0.0001$ ). These test results demonstrate higher accuracy when compared with the JM-103 device and conclude that the BiliCare can safely be used to predict TSB levels in neonates.

## 2. Introduction and Background

The aim of this document is to compare the results of the BiliCare device with the results obtained with the use of the JM-103 device, a non-invasive device used at the hospital for performing bilirubin measurements. The study took place at Soroka University Medical Center, Be'er Sheva, Israel during the period of October 2012 - January 2013.

Transcutaneous bilirubin (TcB) is a measurement of the yellow color of the blanched skin and subcutaneous tissue, not of the serum, and is used as a screening tool to help determine at risk infants and whether the TSB should be measured. TcB measurements are being used with increasing frequency in hospital nurseries and in some outpatient settings. They have the advantage of providing instantaneous information and probably reduce the likelihood of missing the diagnosis of significant hyperbilirubinemia or kernicterus.<sup>1,2,3,4</sup> The shortening of newborn hospital stays after birth and the observation that kernicterus is still occurring<sup>6,7,8</sup> has drawn attention to the importance of identifying and monitoring the jaundiced newborn infant. The use of TcB screening is deemed to be more accurate than visual assessment and reduces the number of blood tests for bilirubin determination, without compromising detection of infants with elevated TSB values.

### BiliCare device

The BiliCare Noninvasive Bilirubin Meter is a transcutaneous bilirubin screening device that uses transmission rather than reflection technology. BiliCare uses the ear of the neonate as the measuring site. It emits light in two visible wavelengths to the ear tissue and measures the light transmitted through the

ear tissue. On its way through the ear's tissue, the light path is obstructed by bilirubin molecules which absorb some of the light.



The light sources used are two semiconductor LEDs, one blue and one green. A high precision circuit measures the absorbance of the light and the thickness of the tissue and accordingly calculates the bilirubin level, which is immediately presented on the device's display.

### **JM-103 device**

Minolta JM-103 Jaundice Meter (Draeger Medical Systems Inc, Telford, US) is a non-invasive transcutaneous bilirubinometer. This device uses reflection method. JM-103 uses the forehead or the sternum as the measuring site.



## **3. Study Design Methods**

This study was designed as a prospective, non-randomized inclusive study in order to compare the BiliCare device to the JM-103.

The research population included 75 neonates at gestational age  $\geq 35$  weeks, prior to discharge. The neonate's skin tone was classified to be either Caucasian or dark brown. The enrolled neonates were tested with the two BiliCare devices (property of Gerium Medical) and consecutively by the JM-103 device, within 30 minutes of the sampling of serum bilirubin.

Statistical analysis was performed to evaluate the results. The primary analysis was based on the comparison of the noninvasive and invasive methods. The noninvasive method was carried out by using the BiliCare device (Transcutaneous Bilirubin - TcB), and the invasive blood test total serum bilirubin method (TSB) was performed by heel stick. All TSB samples were tested in the institutional main laboratory. Further analysis was performed to compare the TcB results between the two devices – BiliCare and JM-103.

## 4. Summary of Results

75 subjects participated in the study.

Table 1 describes the baseline characteristics of the cohort:

Characteristic		Value
Gestational age (weeks, mean±SD)		38.69±1.47
Weight (grams, mean±SD)		3195.16±510.75
Gender	Male	44 (58.6%)
	Female	31 (41.4%)
Skin type	Caucasian	44 (58.6%)
	Dark brown	31 (41.3%)
Blood transfusion		0 (0%)
Phototherapy prior to or during test		0 (0%)
TSB bilirubin <8 (mg/dl)		29 (38.7%)
TSB bilirubin 8-12 (mg/dl)		31 (41.3%)
TSB bilirubin >12 (mg/dl)		15 (20%)

All 75 subjects were tested with the BiliCare device I, and 73 of them were tested also with additional BiliCare device, either II or III; 62 subjects were tested with BiliCare device II and 11 subjects were tested with BiliCare device III. All 75 subjects were tested with the JM-103.

Pearson correlation was applied for testing the correlation of bilirubin results between the different methods. High Pearson correlations coefficients with high statistical significance were found between the BiliCare devices to the TSB ( $r=0.902$ ,  $p<0.0001$ ), and between the JM-103 device to TSB value ( $r=0.896$ ,  $p<0.0001$ ). The variation as measured by standard deviation and by RMSE (Root Mean Square Error) were found to be lower in the BiliCare devices than in the JM-103 device: 1.54 mg/dl and 1.89 mg/dl (respectively) for standard deviation and 1.6 mg/dl and 1.9 mg/dl (respectively) for RMSE.

*Figure 1: Scatter plot of BiliCare measurements and TSB values*

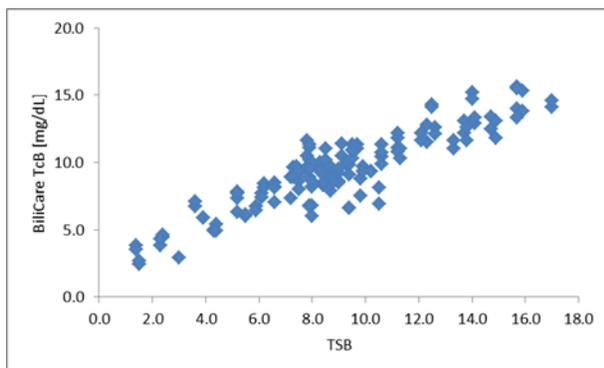
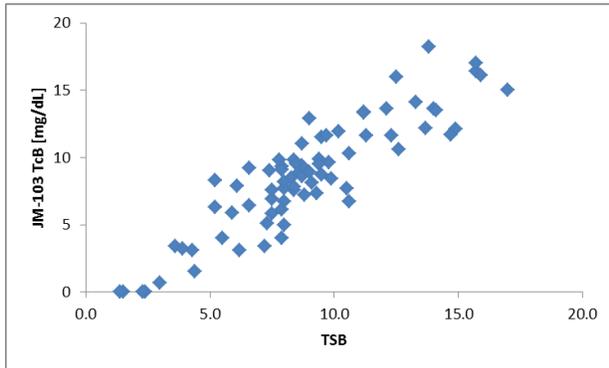


Figure 2: Scatter plot of JM-103 measurements and TSB values



Two cut-off points were analyzed: 11mg/dl and 12 mg/dl

At a cut-off point of 11 mg/dl with BiliCare, the sensitivity was 94.44%, and the specificity was 91.96%, the negative predictive value was 98.1%, indicating that given a BiliCare value below 11 mg/dl, there was a 2% chance that the TSB is greater than or equal to 11 mg/dl.

When analyzing a cut-off point of 11 mg/dl with the JM-103, the sensitivity was 77.78%, and the specificity was 98.25%. The negative predictive value was 93.33%, indicating that given a JM-103 value below 11 mg/dl, there was a 7% chance that the TSB is greater than or equal to 11 mg/dl.

When analyzing a cut-off point of 12 mg/dl with BiliCare, the sensitivity was 80%, and the specificity was 99%. The negative predictive value was 95%, indicating that given a BiliCare value below 12 mg/dl, there was 5% chance that the TSB is greater than or equal to 12 mg/dl.

When analyzing a cut-off point of 12 mg/dl with the JM-103, the sensitivity was 80%, and the specificity was 95%. The negative predictive value was 95%, indicating that given a JM-103 value below 12 mg/dl, there was a 5% chance that the TSB is greater than or equal to 12 mg/dl.

No adverse events were reported during the study execution.

Table 2: Summary Statistics of the Differences in Bilirubin Levels Between Methods using BiliCare and JM-103 devices

This table includes the following statistics: N, Mean, Standard deviation (STD), Root Mean Square Error (RMSE), and Median.

Differences in Bilirubin levels	N	Mean	STD	RMSE	Median
Differences between BiliCare devices and TSB	148*	0.44	1.54	1.6	0.55
Differences between JM 103 device and TSB	75	-0.27	1.89	1.9	-0.20

\*Analysis per device (all measurements)

## 5. Discussion

Neonatal hyperbilirubinemia is the most common condition that requires medical attention in newborns. The shortening of a hospital stay to less than 48 hours makes monitoring of jaundice challenging as peak bilirubin levels occur after 48 hours.<sup>1</sup> A safe and effective non-invasive method to estimate serum bilirubin in babies is of enormous benefit.

Transcutaneous bilirubin (TcB) measurements are being used with increasing frequency in hospital nurseries and in some outpatient settings. They have the advantage of providing instantaneous information and probably reducing the likelihood of missing the diagnosis of significant hyperbilirubinemia or kernicterus. They could be used in clinical practice to reduce blood sampling.<sup>1</sup> Both the American Academy of Pediatrics (AAP)<sup>2</sup> and NICE<sup>3</sup> have published guidelines regarding the management of neonatal hyperbilirubinemia in term infants. Both groups have endorsed the use of the total serum bilirubin (TSB) or a transcutaneous bilirubin (TcB) measurement to identify infants with significant hyperbilirubinemia requiring repeat testing or phototherapy.

The BiliCare device is a novel device designed to predict the TcB levels in newborns. A high precision circuit checks the absorbance of the light and accordingly calculates the bilirubin level, which is immediately presented on the device's display. The main advantage of BiliCare over other TcB measurement devices currently available is that while these devices use reflection technology, BiliCare is based on transmission technology. Transmission allows use of simpler modeling assumptions, is less dependent upon geometrical variations, less sensitive to motion artifacts, and it reduces the number of unknowns by measuring the thickness of the tissue. In addition, blood depletion in the measurement site is done automatically by the device using a set of springs that apply a fixed amount of pressure that is user independent. Therefore, transmission is expected to provide results that are more stable and more robust than those obtained using reflection. This is reflected in the comparative study results detailed above.

## 6. Conclusion

TcB measurements using the BiliCare correlate closely with TSB measurements in the sample population. A statistically and clinically significant correlation between the BiliCare device and total serum bilirubin levels was found (N=148, r=90.23%, STD= 1.54 mg/dL, p<0.0001). These test results demonstrate higher accuracy when compared with the JM-103 device. The correlation between JM-103 device and total serum bilirubin levels was found (N =75, r =0.896%, STD = 1.89 mg/dl, p<0.0001). These test results demonstrate the ability of the BiliCare device to accurately and non-invasively measure bilirubin.

## 7. References

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