18 MONTH USE OF MEDTRONIC ENLITE - COMPARISON WITH DEXCOM G4

CGM sensor evaluation

Abstract

This document presents the conclusions drawn from an 18 month use of the Medtronic Enlite sensor, combined with Medtronic Paradigm insulin pump, and makes a comparison with results obtained with the Dexcom G4 sensor. Based upon my personal experience, I can conclude that for my body, the Enlite mainly focuses on hypoglycemia detection, hereby using a machine gun strategy, and less on accuracy of returned glycemic values. The Dexcom G4 on the other hand shows higher stability, better accuracy and offers a better hypoglycemia detection.

This report is to be considered as an FYI, and should not be generalized to be fact for a general patient base.

VANSTRAELEN, Guy, PhD
cgminfo@gmail.com
Contents

1. GLOSSARY .......................................................................................................................... 3
2. INTRODUCTION ................................................................................................................ 3
3. IMPORTANT PARAMETERS ................................................................................................. 3
4. CALIBRATION TECHNIQUES ............................................................................................... 5
   4.1 INTRODUCTION ............................................................................................................. 5
   4.2 CALIBRATION ALGORITHMS ..................................................................................... 5
5. DEFINITION OF ALGORITHM ACCURACY ......................................................................... 6
6. SENSOR PLACEMENT .......................................................................................................... 7
   6.1 IM SENSOR PLACEMENT ............................................................................................ 7
   6.2 IS SENSOR PLACEMENT ........................................................................................... 8

DISCUSSION OF RESULTS ...................................................................................................... 8

6.3 DESCRIPTION OF MEASUREMENT CONDITIONS ............................................................. 8
6.4 SENSOR ACCURACY .......................................................................................................... 9
   6.4.1 EEE score ............................................................................................................... 9
   6.4.2 MARD score ......................................................................................................... 9
6.5 HYPOGLYCEMIA DETECTION .......................................................................................... 9

7. MEDTRONICS SENSOR ISSUES ......................................................................................... 12
   7.1 LOCKED-DOWN ISIG VALUE ....................................................................................... 12
   7.2 ENLITE SERTER PROBLEM ...................................................................................... 13

8. COMPARISON MEDTRONIC ENLITE VS DEXCOM G4 ..................................................... 14
   8.1 INTRODUCTION .......................................................................................................... 14
   8.2 DEXCOM G4 ACCURACY ........................................................................................ 14
   8.2.1 EEE score ............................................................................................................ 14
   8.2.2 MARD score comparison .................................................................................... 15
   8.2.3 Linear correlation MGL vs BG .......................................................................... 16
8.3 DEXCOM G4 DETECTION OF HYPOGLYCEMIA ............................................................... 16

9. MEDTRONIC PARADIGM VS ANIMAS VIBE INSULIN PUMP ........................................... 18
10. CONCLUSION ..................................................................................................................... 19

FIGURES IN THIS DOCUMENT

FIGURE 1: DEMONSTRATION OF THE VARIABILITY OF THE GI VALUE .................................. 4
FIGURE 2: DEFINITION OF ACCURACY ................................................................................ 6
FIGURE 3: IM SENSOR PLACEMENT ..................................................................................... 8
FIGURE 4: ACCURACY ACCORDING TO CALIBRATION METHOD USED, IM + IS, IM AND IS, AND STANDARD DEVIATION ............................................................. 9
FIGURE 5: PERCENTAGE OF DETECTED HYPOS ................................................................ 10
FIGURE 6: PERCENTAGE OF UNDETECTED HYPOS ............................................................ 10
FIGURE 7: PERCENTAGE OF FALSE ALERTS ...................................................................... 11
FIGURE 8: ILLUSTRATION OF ISIG LOCKDOWN ................................................................. 12
FIGURE 9: ACCURACY OF THE Dexcom G4 SENSOR .......................................................... 14
FIGURE 10: COMPARISON ENLITE VS G4, EACH CHARACTERIZED BY THE SENSOR’S AVERAGE ACCURACY .... 15
FIGURE 11: PERCENTAGE OF HYPOS DETECTED BY THE DEXCOM G4 ................................ 16
FIGURE 12: PERCENTAGE OF HYPOS MISSED BY THE DEXCOM G4 ................................... 17
FIGURE 13: PERCENTAGE OF FALSE ALARMS FOR THE DEXCOM G4 ................................ 17

TABLES IN THIS DOCUMENT

TABLE 1: ALTERNATIVE CALIBRATION ALGORITHMS ......................................................... 5
TABLE 2: MEASUREMENT CONDITIONS ................................................................................ 8
1. GLOSSARY

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG</td>
<td>Blood Glucose level measured using a glucometer</td>
</tr>
<tr>
<td>CF</td>
<td>Calibration Factor, Conversion Factor, expressed in mg/dl/nA or mmol/dl/nA; equal to GI</td>
</tr>
<tr>
<td>CGM</td>
<td>Continuous Glucose Monitoring</td>
</tr>
<tr>
<td>EEE</td>
<td>Equivalence Error in %</td>
</tr>
<tr>
<td>GI</td>
<td>Glucose Insensitivity in mg/dl/nA or mmol/dl/nA; equal to CF</td>
</tr>
<tr>
<td>IM</td>
<td>Intra-Muscular</td>
</tr>
<tr>
<td>IS</td>
<td>Interstitial</td>
</tr>
<tr>
<td>ISIG</td>
<td>Current signal generated by the CGM sensor; expressed in nA</td>
</tr>
<tr>
<td>MARD</td>
<td>Mean Absolute Relative Difference in %</td>
</tr>
<tr>
<td>MGL</td>
<td>Measured Glucose Level</td>
</tr>
<tr>
<td>RE</td>
<td>Relative Error in %</td>
</tr>
<tr>
<td>RTGI</td>
<td>Real Time Glucose Insensitivity, calculated as $\frac{BG^{mg/dl}}{ISIG^{nA}}$</td>
</tr>
<tr>
<td>WGI</td>
<td>GI calculated using a walking average</td>
</tr>
</tbody>
</table>

2. INTRODUCTION

This document reflects the results and conclusions drawn from an 18 month use of the Medtronic Paradigm insulin pump, combined with the Enlite CGM sensor. In reading and evaluating this document it should be kept in mind that the report is written, based upon personal results, and that no guarantee can be given for the general validity. Please consult with your medical professional before adapting my findings.

The CGM sensors are only approved for interstitial use, and their functioning is only guaranteed for this particular case. In this report, the use will be extended to IM (intramuscular) application, and results show a higher accuracy and better hypoglycemia prediction for the latter case. The exact location of sensor placement, being a critical factor, will be discussed in more detail under paragraph 6.

As the goal of this document is the supporting of diabetic's patients in maintaining their health, helped by a CGM sensor, a short comparison will be made with the Dexcom G4 sensor, which shows a far superior quality, both in reliability and in cost.

3. IMPORTANT PARAMETERS

The Paradigm insulin pump/CGM sensor combo returns two main values, one measured and one calculated. The measured value is the ISIG or Electrical Current Signal (in nA), corresponding to the electrical current generated by the enzymes contained in the CGM sensor in response to the glucose level. As will be demonstrated using practical results, the electrical current vs glucose relationship is very irregular, time dependent, very different for every sensor, and with a pretty low correlation.

A second value being returned is the calculated glucose level (MGL in mg/dl or mmol/dl). This number is derived directly from the ISIG value using a conversion or calibration factor CF, which is a value which is in principle set or modified during sensor calibration, and which indicates the glucose concentration required for generating 1 nA of signal current (expressed in mg/dl/nA or mmol/dl/nA). An alternative name used in literature is the sensor sensitivity, although more correct is to consider it as a Glucose Insensitivity value GI, and this is also the term which will be used throughout the remainder of this document. Acceptable GI values for the Medtronic Enlite range from approximately 3 mg/dl/nA for a new sensor up to 6-7 mg/dl/nA at the end of life. Once the value of 7 mg/dl/nA passed, the sensor is considered to ready for replacement, as ISIG values become too small to allow for an accurate measurement.

Knowing that the correctness of the GI value is critical in returning an accurate glucose level, and combined with knowledge of the behavior of a real time CGM sensor's transfer curve (examples shown in Figure 1), it can be understood that the choice of an optimum calibration algorithm is the determining factor to assure the reliability of the sensor. There are however two aspects to be considered. On the one hand there is the correctness of the by the insulin pump returned glucose concentration, and on the other hand there is the prediction and prevention of hypoglycemia. Although
both are closely related or one is an expression of the other, we will see that the simultaneous fulfillment of both aspects is extremely difficult under the constraint of only 2 - 3 calibrations or blood glucose measurements a day. For a CGM sensor evaluating body fluids, the key for an acceptable balance between both, is the calibration method that is being used. It will be illustrated, based upon practical results, that the Medtronic calibration algorithm is mainly focused on the prevention of hypoglycemia, hereby slightly neglecting the accuracy of returned glucose levels. Other calibration algorithms can be used, and a few simple examples will be demonstrated.

The following figures give a few examples of the BG versus ISIG dependence for a particular sensor (transfer curve). A sensor’s “run away” behavior, caused by a degradation of the sensor’s sensitivity as a function of time, and upon my experience being one of the major reasons for sensor malfunction, is demonstrated in these figures by using a different color for each of the 6 days of operation. The first figure, top left, shows the almost “ideal” sensor behavior, which is a linear relationship between BG and ISIG, with a minor sensitivity loss over time. The second figure, on the right, corresponds to an extremely irregular sensor behavior, with large degradation over time and with a poor correlation between ISIG value and BG. All of the last 3 images show a phenomenon that occurs regularly, and which is, as I would call it, a “current lock-down”, an ISIG value which gets stuck around or below 10 nA, independent of the glucose level. For sensor 2 this occurs on day 2, for both sensors 3 and 4, it occurs at day 3, with a partial recovery, which is still unaccounted for, and for which no explanation is available.

---

Figure 1: Demonstration of the variability of the GI value

---

1 All BG measurements done using a verified Roche Accuchek Performa Nano
4. CALIBRATION TECHNIQUES

4.1 Introduction
Taking into account the variability of the real-time GI (equal to BG/ISIG) indicates that ideally a real-time algorithm should be used for updates to the GI (CF) value being used. This would however implicate the use of a large quantity of BG measurements, hereby making the use of a CGM sensor impractical and making it partially loose its benefit. The patented technique used by Medtronic is a mathematical technique, based upon a linear regression of the weighted last 3 calibrations done, but besides this a heuristic and continuous adaptation is applied based upon the sensed changes in glucose concentration. In developing a GI update algorithm the following facts should be taken into account:

a. The majority of diabetics limit the number of glucometer tests to 2 … 4, which is a major constraint as we will see.
b. Using the instantaneous BG to determine the GI value will lead to large errors in glycemic readings, mainly caused by the variability of the real-time GI (RTGI), and for this reason a smoothing of the GI value has to be used, resulting in an acceptable error over a range of glycemic values.
c. Priority has to be given to accuracy and/or hypoglycemia prediction. Accomplishing both is difficult (valid for the Medtronic Enlite, not for the Dexcom G4) because of a steep drop in GI values during rapid changes in glycemic value.

The main reason for point b. is the slowness of reaction of the enzymes contained in the CGM sensor, in addition to the delay between blood glucose values and interstitial fluid glucose levels. What is typically seen is a strong drop in GI when glucose levels drop (BG drops and ISIG stays initially unchanged) and an increase in GI values, for example after having a carbohydrate rich meal (BG rises but ISIG stays initially unchanged). To examine this effect closer, about 50% of the sensors were placed intra-muscular (partly elimination of delay interstitial versus inter-capillary), while the other 50% was placed interstitially.

For the calibration algorithm, 3 options are being examined:

1) GI factor obtained through a progressive linear regression, in this case the Medtronic calibration
2) Use of the RTGI at time of calibration
3) Use of a weighted GI (WGI walking average) calculated from the RTGI and previous GI.

For comparing the accuracy of calibration techniques, an error value has to be defined, and preferably one that takes the sensor’s lifetime into account. This will be discussed under 5.

4.2 Calibration algorithms
4 alternative and basic calibration algorithms were examined with the purpose of comparing their precision and hypoglycemia prediction with the Medtronic calibration algorithm. Looked at were, with code name given:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAL0</td>
<td>For CAL0 the RTGI at the time of calibration is used, without any further smoothing and without taking the GI history into account. Three calibrations a day are used.</td>
</tr>
<tr>
<td>CAL3</td>
<td>Presents a walking average of the last 2 GI values used, corresponding to the 3 calibrations that are done daily. As the effect of the use of a weighing factor is found to be minimum, this factor was taken as 1.</td>
</tr>
<tr>
<td>CAL5</td>
<td>Similar, but the number of daily calibrations is increased to 5.</td>
</tr>
<tr>
<td>LF</td>
<td>Similar, but with the number of daily calibrations is raised to 15-20</td>
</tr>
</tbody>
</table>

Table 1: Alternative calibration algorithms
5. **DEFINITION OF ALGORITHM ACCURACY**

Important in comparing the different calibration algorithms is a definition of a quantity, indicative of the accuracy over a sensor’s lifetime. In saying this, we already give the two factors of importance, first of all the actual accuracy or error at the time of BG measurement, and secondly the time span over which this error was present.

We can best illustrate this with an example. Figure 2 shows at the top both the BG and CGM values, as a function of time, and at the bottom is shown in blue, the Relative Error RE at the time of every BG measurement, as a function of time. As measure for the accuracy could be taken the RE multiplied by the time that this error is present, or in other words, the area under the blue curve. To express this in a more meaningful quantity, we can calculate an equivalent and time independant error, the Equivalent Equalized Error EEE, giving rise to the same quantity (EEE x Time).

![Measure for accuracy](image)

**Figure 2: Definition of Accuracy**

The practical meaning of the EEE is that every value returned by the CGM will have this error, as a plus or as a minus. This accuracy will further in this document be indicated as the EEE score.

Besides the EEE also a also more standard way of judging the performance of continuous monitoring sensors is used, and this is done by calculating the MARD value or Mean Absolute Relative Difference value.
The WARD is obtained through a pure statistical calculation and is given by:

\[ \text{WARD} = \frac{1}{N} \times \sum_{i=1}^{N} \frac{BG(i) - CGM(i)}{BG(i)} \]

With

- \( N \): number of samples
- \( BG(i) \): measured BG at sampling time \( i \)
- \( CGM(i) \): reflected CGM value at sampling time \( i \)

Remarks

1. The Medtronic calibration can be considered as being very conservative, and not reacting fast enough to changes in BG/ISIG, hereby increasing the inaccuracy of the reflected glycemic value.
2. It is recommended to calibrate when returned glucose levels are stable. However, indicated glycemic values can be stable while the ISIG value fluctuates. My recommendation would be to provide an indicator on the insulin pump, reflecting when the ISIG value is stable instead, providing at the same time indication of sensor malfunctioning or instability, and I’m thinking here for example about the current lock-down.
3. A great difficulty in calibrating is the difference between individual sensor behavior. Each sensor has its own glucose response, and an improvement could be made by having the calibration method to be selectable in order to accommodate a change in behavioral response. A matching can be done during calibration. Even simpler and down a few levels, is an automatic selection of a calibration technique, based upon sensor response and for example during day time, the calibration could go for accuracy, and go at night for hypo prevention.
4. The availability of an up to date calibration factor is important, and for this reason I think that every BG measurement should be used as an implicit calibration.

6. SENSOR PLACEMENT
About 50% of the sensors was placed IS, and the other half was placed IM. The reason for this trial was the, for me excessive error in reflected glycemic values. The idea behind the approach is that muscles have an excellent support system providing them with oxygen and fuel, and as such I expected to have much shorter delays for IM with regards to changing blood glucose levels, and an according higher accuracy with respect to IS. Placing the sensor is however tricky, and it has taken quite a bit of experimenting to find an acceptable location.

6.1 IM sensor placement
What was needed is a muscle, easy reachable and located close to the skin. Appropriate to me seemed to be the deltoid muscle, and this was then also applied. The deltoid reaches from about halfway the upper arm, to the shoulder joint, and then the question is raised, what is the best location in this muscle? Sensors were tried from bottom to top of the deltoid, and the best location was found to be close to the bottom muscle attachment. The explanation is simple. Near the muscle-bone attachment (scapula and clavicle at the top and humerus at the bottom) muscle movement is restricted, whereas in between the 2 attachment points, the muscle is allowed to move considerable, and as a matter of fact, the movement was with me sufficient to rip off the little catheter that sits under the sensor body and absorbs body fluids. The most comfortable and also the most reliable location turned out to be the bottom of the deltoid. The deltoid and preferred location are depicted in Figure 3.
6.2 IS sensor placement
The sensor was placed on the inside of the hip joint joining the belly, which seemed to be like a comfortable place.

DISCUSSION OF RESULTS
Automated software routines were written to provide a reflection of sensor accuracy combined with a specific calibration procedure, and the hypo prediction quality. Also returned is a histogram showing the number of hypos in 30 minute intervals throughout the day, allowing to draw conclusions regarding the reason for hypo concentration at a specific time, and the glycemic tendency as a function of time in the day, allowing to extract conclusions regarding the basal amount of insulin, and the reaction to food with addition of a bolus. Although the theoretical borderline value for hypoglycemia is taken as 70 mg/dl, the analysis was extended to glycemic values of 60, 50 and 41 mg/dl. The value of 41 mg/dl was taken, taking into account that 40 is the lowest value which can be returned by the Medtronic sensor/insulin pump combination.

6.3 Description of measurement conditions
As already mentioned, about half of the sensors are placed IS and the other half are placed IM. This experiment returns the same percentage of good and bad sensors, independent of placement, which is a pretty good confirmation that if problems occur, they are due to the sensor, and not due to the placement. And, with bad is meant sensors not holding up their 6 day lifespan, sensors with a current lock-down or other irregular behavior.

All sensors included in this study were examined after removal, and only not visibly damaged sensors were included in the results.

<table>
<thead>
<tr>
<th>Total number of sensors</th>
<th>62</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number placed IS</td>
<td>30</td>
</tr>
<tr>
<td>Number placed IM</td>
<td>32</td>
</tr>
<tr>
<td>% of good sensors</td>
<td>68%</td>
</tr>
<tr>
<td>Total number of good sensors</td>
<td>41</td>
</tr>
<tr>
<td>Number placed IS</td>
<td>20</td>
</tr>
<tr>
<td>Number placed IM</td>
<td>21</td>
</tr>
</tbody>
</table>

Table 2: Measurement conditions

2 By Courtesy of Real Bodywork ref. www.realbodywork.com
6.4 Sensor accuracy

6.4.1 EEE score
Figure 4 displays the average sensor accuracy corresponding to the calibration algorithm used, combined with its standard deviation, and based upon 15-20 BG measurements a day. It can be clearly seen that the Medtronic calibration algorithm lays behind in accuracy. The standard deviation, being the spread of accuracy, decreases, and the accuracy, increases with the number of calibration points taken, 3, 5 or 15-20. It can also be concluded that IM use of the sensor offers a higher accuracy for Medtronic, whereas for a walking average, the advantage is seen only if the number of BG measurements is limited to 3. When more, then no apparent difference is seen. It is interesting to notice that use of the raw 3-calibration RTGI data (CAL0) gives a higher accuracy than when using the smoothed 3-point GI (CAL3), and that it approaches in accuracy the 5-calibration smoothed GI.

In evaluating the accuracy, it is important to remember the time lag between changing interstitial glucose level and blood glucose level, which is a main error contributing factor.

![Figure 4: Accuracy according to calibration method used, IM + IS, IM and IS, and standard deviation](image)

6.4.2 MARD score
The WARD is given, taking only reference values or calibration times into account, and taking all BG measurements into account. No significant difference is seen between IM and IS use.

<table>
<thead>
<tr>
<th></th>
<th>EEE score</th>
</tr>
</thead>
<tbody>
<tr>
<td>MARD calibration only</td>
<td>18.9%</td>
</tr>
<tr>
<td>MARD all samples</td>
<td>21.3%</td>
</tr>
</tbody>
</table>

Table 3: MARD values for Medtronic Enlite

6.5 Hypoglycemia detection
As both CAL0 and CAL3 lack a good detection of hypoglycemia, they are omitted in the following figures.

It can be concluded that the Medtronic 3-point calibration IM offers the same hypoglycemia detection efficiency as the 5-point walking average calibration. A small improvement is seen for IS use. Important is again that the hypoglycemia detection capability increases with the number of calibrations done.
Figure 7 gives the number of false alarms that are being generated. For Medtronic we can see that about half of the alarms are false alarms, when considering a hypo limit of 70 mg/dl.

Figure 5: Percentage of detected hypos

Figure 6: Percentage of undetected hypos
Figure 7: Percentage of false alerts

Table 4 resumes all results for the theoretical hypoglycemia alert limit set at 70 mg/dl. It is clear that the Medtronic calibration algorithm is mainly focused upon hypoglycemia detection, but using their technique implies simultaneously, a high number of false alerts, which excludes the sensor from being a hypo detector (per definition <10% missed and <10% false alarms).

<table>
<thead>
<tr>
<th></th>
<th>IM</th>
<th>CAL5</th>
<th>LF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detected</td>
<td>72.5%</td>
<td>63.5%</td>
<td>82.4%</td>
</tr>
<tr>
<td>Undetected</td>
<td>39.2%</td>
<td>48.2%</td>
<td>23.4%</td>
</tr>
<tr>
<td>False alert</td>
<td>34.6%</td>
<td>29.1%</td>
<td>13.7%</td>
</tr>
<tr>
<td></td>
<td>IS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detected</td>
<td>71.7%</td>
<td>68.7%</td>
<td>84.0%</td>
</tr>
<tr>
<td>Undetected</td>
<td>47.7%</td>
<td>46.0%</td>
<td>29.3%</td>
</tr>
<tr>
<td>False alert</td>
<td>43.0%</td>
<td>35.5%</td>
<td>19.7%</td>
</tr>
</tbody>
</table>

Table 4: Analysis of hypoglycemia detection capability
7. MEDTRONICS SENSOR ISSUES

7.1 Locked-down ISIG value

The most common expression of sensor malfunction for me, was a locked-down ISIG value, meaning that the sensor loses its sensitivity to glucose levels (RTGI > 10 mg/dl/nA), and generates only currents in the 7-10 nA range. The occurrence of this phenomenon is often the reason for calibration errors initiating the end-of-life. Little can be done to assure a sensor recovery, and as was seen, reflected glucose levels are extremely erroneous, requiring sensor replacement. It was however found out that “sometimes”, and the word “sometimes” is essential, recovery can be established by providing the sensor with a glucose boost, meaning letting glucose levels rise to well over 200 mg/dl. The reason is not understood, and this fact is only mentioned as an FYI. No support to resolve the issue, or explanation to the cause, was given by the Medtronic sensor development division. After during a 5 month period the majority of Enlite sensors showed this problem, I decided to switch to the Dexcom G4 sensor, combined with the Animas Vibe insulin pump. Preliminary results covering a 4 month period are presented in 8.

It is appropriate to add a remark regarding the CAL ERROR which is easily obtained for this situation. A common reason for a calibration error is a too large difference between BG and value calculated by the insulin pump. In order to avoid this error, there are 3 options:

(i) Activating the “NEW SENSOR” function, which will reinitialize the whole calibration procedure,
(ii) If the 12 hrs counting from the last calibration are not past yet, simply waiting with the calibration till a crossing in BG curve and curve for the by the insulin pump returned glucose concentration is eminent and doing a calibration as soon as their difference is less than 10-15%,
(iii) In case a calibration has to be done immediately, the use of a fake BG value, less than 10-15% different from the value given by the insulin pump, but going towards the true BG.

The advantage of using (ii) and (iii) is the fact that the insulin pump keeps returning values, and that one does not have to wait for the 3 hours to a first calibration to pass.

From all Enlite sensors used, the percentage of good ones was only 68%. It should however be taken into account that many factors affect the sensor operation, and it would be wrong to blame Medronic. Numbers mentioned in medical publications talk about 78%.

Figure 8: Illustration of ISIG lockdown
7.2 Enlite serter problem

A last point that has to be mentioned is a regularly occurring Enlite serter problem, where the needle stays stuck in the serter, after pushing for release. This issue was also mentioned to me by my Medtronic provider. In some cases it is possible to get the needle back out, but in other cases, only serter replacement is appropriate. If Medtronic will take action for improvement is at this point unclear.
8. COMPARISON MEDTRONIC ENLITE VS DEXCOM G4

8.1 Introduction
The step from the Medtronic Enlite to the Dexcom G4 was refreshing in many ways. Not only as a matter of stability, accuracy and detection of hypos, but as important, from a financial point of view. These points will be briefly discussed in the following paragraphs. As remarked before, these results are derived from my personal experience, limited to only 19 weeks of Dexcom use, and covering 8 sensors. No guarantee is given for the applicability of my results to other patients.

8.2 Dexcom G4 accuracy

8.2.1 EEE score
The guaranteed lifetime of the sensor is 7 days, but from my limited use, I can already say that a 2nd week can be added without loss in accuracy, and even a 3rd week can be added, however under condition of increasing the number of daily calibrations, in order to maintain an acceptable accuracy. It is interesting to notice that the accuracy is found to be best during its 2nd week of operation, which may mean that the sensor needs time to settle. The difference with the Medtronic Enlite is enormous.

It may be easier to understand the accuracy numbers, when comparing the results returned by a Medtronic Enlite sensor and a Dexcom G4 sensor, both placed IS, and having an accuracy corresponding to the average value of resp. 24% and 17.3%. This is done in Figure 10 and the efficiency of the G4 compared to the Enlite can be clearly seen. Please note that the 17.3% is the average over 3 weeks of using the same Dexcom G4 sensor, and as mentioned before, the delay in glycemic values, body fluid compared to blood glucose, strongly affects the error value.
Figure 10: Comparison Enlite vs G4, each characterized by the sensor’s average accuracy

### 8.2.2 MARD score comparison

Table 5 clearly shows again the better performance of the Dexcom G4 sensor, and as already concluded, an accuracy improvement is found in week 2 of sensor operation. Taking all glucose measurements into account, the Dexcom G4 is still winner over the Medtronic Enlite in its 3rd week of operation, but the sensor is ready for replacement. The lower WARD score in week 3, when taking all samples into account, compared the value when only taking calibration values into account, is caused by the fact that a calibration is done as soon as there is a for me too large deviation between BG and MGL. As such, the calibration points will show the largest error.

<table>
<thead>
<tr>
<th></th>
<th>WARD calibration only</th>
<th>WARD all measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medtronic Enlite</td>
<td>18.9%</td>
<td>21.3%</td>
</tr>
<tr>
<td>Dexcom G4</td>
<td>14.9%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Dexcom G4 week 1</td>
<td>12.7%</td>
<td>13.5%</td>
</tr>
<tr>
<td>Dexcom G4 week 2</td>
<td>11.4%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Dexcom G4 week 3</td>
<td>24.4%</td>
<td>17.6%</td>
</tr>
</tbody>
</table>

Table 5: Comparison of MARD score for Medtronic Enlite vs Dexcom G4
8.2.3 Linear correlation MGL vs BG

Another important aspect to examine is the linear correlation \((MGL = m \times BG + b)\) of the measured glucose concentration and the true BG, and here again an immense difference is seen between the 2 sensors. In the ideal case, both glucose concentrations should be equal, resulting in a scatter plot in a straight line with slope equal to 1. \(R^2\) is the coefficient of determination and denotes the strength of the linear association between MGL and BG. For a perfect correlation its value is 1. Values > 0.8 are indicative for a strong correlation, whereas values < 0.5 indicate a weak correlation. A comparison displaying the average values for all good sensors used is given in Table 6 and doesn't need clarification.

<table>
<thead>
<tr>
<th>Sensor</th>
<th>m</th>
<th>b</th>
<th>(R^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medtronic Enlite</td>
<td>0.91</td>
<td>17.97</td>
<td>0.54</td>
</tr>
<tr>
<td>Dexcom G4</td>
<td>0.98</td>
<td>-0.42</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Table 6: Comparison of the correlation MGL vs BG

8.3 Dexcom G4 detection of hypoglycemia

Also the detection of hypos is a step ahead of Medtronic. The experienced results are shown in the figures below.

![Figure 11: Percentage of Hypos detected by the Dexcom G4](image-url)
Figure 12: Percentage of Hypos missed by the Dexcom G4

Figure 13: Percentage of false alarms for the Dexcom G4
Table 7 resumes the results for the Dexcom G4, hypo limit 70 mg/dl, as compared to the Medtronic Enlite.

<table>
<thead>
<tr>
<th></th>
<th>Medtronic Enlite</th>
<th>Dexcom G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>24.7%</td>
<td>17.3%</td>
</tr>
<tr>
<td>Detected hypos</td>
<td>71.7%</td>
<td>74.2%</td>
</tr>
<tr>
<td>Missed hypos</td>
<td>47.7%</td>
<td>48.1%</td>
</tr>
<tr>
<td>False alerts</td>
<td>43%</td>
<td>30.2%</td>
</tr>
</tbody>
</table>

Table 7: Comparison of hypo detection Medtronic Enlite vs Dexcom G4

It is clear that for the Dexcom G4, accuracy and hypo detection go hand-in-hand, and that as the Dexcom G4 accuracy is much better, more hypos are being detected. Important to notice is the difference in the number of false alerts, which is indicative for the Medtronic hypo catching strategy. The algorithm used is clearly too aggressive.

9. **MEDTRONIC PARADIGM VS ANIMAS VIBE INSULIN PUMP**

As final topic in this report, I want to address the companion to the CGM sensor, namely the insulin pump. Medtronic is here definitely on the winning hand with the Paradigm, and only positive things can be mentioned. A few examples:

- User friendliness, with the availability of an ESC button for returning to the main screen, whereas the Animas requires the patient to struggle through menus before arriving home.
- Volume of the reservoir, 3 ml for the Paradigm, and only 2 ml for the Vibe, obligating most users to switch reservoirs before the 3 day replacement time mark has been reached.
- Issueless battery replacement for the Paradigm, whereas for the Animas, the pump and infusion set has to be re-primed.

A tip for Animas users being at the 2 ml edge, is to prime by hand, and next to replace the insulin dose dispended, by a new dose till the reservoir is filled. This will guarantee an additional ~ 20U.
10. CONCLUSION

This report resumed the conclusions drawn from an 18 month use and study of the Medtronic Enlite CGM sensor, and a comparison with results from a shorter use of the Dexcom G4 sensor is made.

The main points considered are accuracy and the hypoglycemia predictability. From practical results, valid for my person, it is clear that the Medtronic Enlite lacks in accuracy, evaluated using the traditional MARD score and a newly defined EEE score, and mainly focusses on hypoglycemia prevention, whereas the Dexcom G4 offers both superior accuracy and excellent hypoglycemia detection, with a reduced number of false alarms. It is also found that the Medtronic Enlite has a large variability between sensors, and that only about 70% of the sensors survive the theoretical 6 day life span, whereas all Dexcom G4 sensors used showed a very similar behavior, and a defect rate close to zero.

The Dexcom G4 does not only offer advantages in terms of accuracy and hypoglycemia prevention, but also offers an important cost saving, as the sensor’s efficiency does not change when adding a second week to the theoretical life span.

With regards to the accompanying insulin pump, the Medtronic Paradigm vs Animas Vibe, the Medtronic Paradigm is the clear winner given its high user-friendliness and issueless operation. This might however change with the release of a new Roche insulin pump combined with Dexcom sensor, which is supposed to be on the market in 2014, and I’m highly looking forward to using this combination.