**Protocol Title:**

Accuracy of Dexcom G6 after Radiation Exposure—A Cross Sectional and Longitudinal Analysis

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**REVISION HISTORY**

| Revision # | Version Date | Summary of Changes | Consent Change? |
|---|---|---|---|
| 2 | 15April2022 | Removal of SOC care arm, control data will be Dexcom accuracy data that is publicly available. Moving forward all enrolled participants will not have the transmitter covered with a lead apron during SOC radiological procures. | Yes, removal of SOC arm language |
| 3 | 23May2022 | Clarifications throughout, addition of glucometer blood sugar checks 10 days prior to data export requests | Yes, clarification though out and home glucometer use request |
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**Study Summary:**

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| **Study Title** | Accuracy of Dexcom G6 after Radiation Exposure—A Cross Sectional and Longitudinal Analysis |
| **Study Design** | A single-center prospective trial on the effects of standard of care radiation exposure on the Dexcom G6 continuous glucose monitoring (CGM) device. |
| **Primary Objective** | To determine if standard of care radiation exposure longitudinally effects the accuracy and precision of the G6 transmitter in the post TPIAT inpatient population |
| **Secondary Objective(s)** | Reduce burden for patients to remove and waste a functional and expensive Dexcom G6 CGM for radiologic procedures. |
| **Research Intervention** | Participants will have their study provided Dexcom G6 CGM uncovered for standard of care procedures that involve radiation exposure while inpatient at CCHMC |
| **IND/IDE #** | NA |
| **Study Population** | Post total pancreatectomy with islet autotransplantation (TPIAT) patients |
| **Sample Size** | N = 40 |
| **Study Duration for individual participants** | 3 months of active study participation |

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|---|---|
| **Abbreviations** | total pancreatectomy with islet autotransplantation (TPIAT)<br>Identification, ID<br>Principal Investigator, PI<br>Good Clinical Practice, GCP<br>Adverse Reactions, AE<br>Severe Adverse Reactions, SAEs<br>continuous glucose monitoring (CGM)<br>point of care (POC)<br>Data and Safety Monitoring Board (DSMB)<br>Standard of Care (SOC) |

**Study Objective**

We will establish accuracy and precision data for the lifespan (up to about 3 months) of the Dexcom G6 transmitter exposed to inpatient radiation (x-ray and/or CT scan) that is not covered with lead apron.

**Background**

There are limited data published regarding the accuracy and precision of continuous glucose monitoring (CGM) devices after radiation exposure. While manufacturers, specifically Dexcom, recommend to remove CGM systems with MRI and CT scan there is some ambiguity surrounding radiation exposure from a diagnostic x-ray as only a few cross-sectional studies have been conducted [1]. Spanakis et al assessed the accuracy and precision of Dexcom two hours pre- and post-imaging. They reported that ongoing CGM use during multiple radiology procedures was safe and reliable based on 98.1% of glucoses falling into Zone A and B of Clark Error Grid analysis which represents values that result in no difference in clinical decision making. However, this analysis did not assess the transmitter longitudinally to ensure accuracy over its 3-month lifespan. A second report, based on simulation of a radiotherapeutic procedure (80 GY) found that the components of G6 retained basic functionality and data integrity after exposure and again did not include assessment of the transmitters 3-month lifespan.

At CCHMC, we are in the unique position to work with a hospitalized population who utilize Dexcom G6 CGMs while inpatient. The patients are children and adolescents who have had a total pancreatectomy with islet autotransplantation (TPIAT) and receive, on average, 6 radiology procedures (defined as CT scans or x-rays) over a 2-week period following TPIAT. This population has a target glucose range of 80-120 mg/dL and Dexcom is used to monitor trends under careful oversight by the pediatric endocrinology service. Because these patients represent a complex surgical population, they often have post-operative events that include abdominal pain, vomiting, and fever. Radiology procedures are frequently obtained for

assessment of obstruction, abscesses and/or thrombi. At our institution if the sensor and transmitter is not in the field of interest, current practice is to cover the Dexcom (sensor and transmitter) during all radiology procedures with a lead apron and have careful assessment of sensor values compared to glucometer glucose readings while in-hospital and the 3 months post-operatively. The repeated radiation exposure over a short timeframe (2-3 weeks) in the context of established monitoring of device performance by providers who specialize in pediatric diabetes management makes this population ideal for studying CGM performance. A transmitter is changed every 3 months and a sensor is changed every 7-10 days.

**Rationale**

It is of great burden for patients to remove and waste functional and expensive medical equipment for radiologic procedures, especially if there are repeated procedures planned over a short period. There is minimal data to suggest, at least in the short term, that accuracy and precision is not affected by radiation in commonly ordered radiology procedures. Our aim is to contribute to this knowledge base and assess *longitudinally* the accuracy and precision of the G6 transmitter during and after exposure to radiation in an inpatient post-TPIAT population.

**Study End Points**:

CGM readings will be assessed for accuracy and precision. Publicly available accuracy data will be compared to study glucometer readings over the 3 months expected lifespan of the Dexcom G6 CGM transmitter used post TPIAT.

Time to Dexcom G6 CGM transmitter replacement needed over the 3 months post TPIAT will be compared to the standard device life expectancy.

We will take the following into consideration with our analysis:

Hydroxyurea a known substance to interfere with CGM sensor values is started approximately day 7 post-TPIAT and can result in erroneously elevated glucose sensor value 6-9 hours post-administration [2]. For this reason, data from 10 hours post Hydroxyurea dosing will not be used in the initial data analysis.

**Study Intervention**:

Enrolled participants will NOT have a lead apron used to cover their Dexcom G6 transmitter during radiation exposure procedures performed while participant is inpatient post TPIAT.

Transmitter accuracy and precision will be monitored for 3 months post TPIAT or until the transmitter is changed.

**Study Procedures:**

Our main goal is to assess the accuracy and precision of the Dexcom G6 transmitter readings after radiation exposing SOC procedures for which the transmitter is uncovered compared to publicly available accuracy data. Transmitter function will be assessed by comparing the device readings to glucometer readings.

Patients undergoing a TPIAT and planned to receive a Dexcom G6 CGM will be approached for participation in this study prior to post surgery CGM placement.

An anticipated 40 participants will be enrolled and will NOT have a lead apron used to cover their Dexcom G6 device during radiation exposure procedures performed while participant is inpatient post TPIAT.

Dexcom G6 CGM data and point of care (POC) testing with a glucometer (such as the ACCU-CHEK® Inform II Meter) will be utilized for this study while inpatient and a standard issue meter when outpatient. While participants are inpatient POC monitoring will occur every 1 hour when insulin administration is administered intravenous and every 3 hours with the transition to subcutaneous insulin administration. Inpatient POC glucose values and Dexcom reports will be collected. Once discharged, CGM and glucometer readings will be collected by downloading readings using software at the 1 (+/-3 days) week post discharge clinic visit,1 month (+/- 7 days) post TPIAT, 2 months (+/- 7 days) post TPIAT and before the transmitter is due to be changed (expected 3 months (+/- 7 days) post TPIAT).

The Dexcom CGM has an online platform called Clarity that can generate reports or raw data files of continuous glucose readings. The home glucometer used for the study has a mobile app that can generate reports or raw data files of glucometer readings. Reports will be reviewed at the time of set data download time points by delegated study staff.

Downloaded data will be stored on a secure server utilizing the participants study ID.

Participants will be requested to check their glucose values with the Contour glucometer 4 times a day for the ten days leading up to study data requests at study time points, but we will accept a minimum of 2 times per day the 7 days prior to a scheduled download to compare the functionality of the Dexcom G6 CGM. Participants (or parents) will be contacted and reminded to check blood sugars at the beginning of this 10-day period at each time point.

While participant is inpatient post TPIAT and outpatient for the life of the CGM transmitter, the number of and type of radiation procedure will be collected from their EMR.

After discharge participants will be contacted at the 1 (+/-3 days) week post discharge clinic visit, 1 month (+/- 7 days) post TPIAT, 2 months (+/- 7 days) post TPIAT and before the transmitter is due to be changed (expected 3 months post TPIAT). Participants will be asked to provide information on any radiation procedures that may have occurred outside of CCHMC, and study staff will confirm the transmitter has not yet been changed. If at any point the transmitter is changed for any reason, the participant will no longer be actively enrolled in the study but data for the transmitter will be collected. If the transmitter is changed due to clinical recommendations such as due to technical issues with readings or calibrations or due to radiologic procedures in which it is in the field of interest, they will be considered completed in the study. If the transmitter is changed due to participant preference with no reason to believe the transmitter was not working properly or needed to be removed for clinical procedures then the participant will be withdrawn. Any termination of participation prior to the anticipated approximately 3-month post TPIAT time point will be noted with reason for early completion/withdraw recorded.

Formal statistical analysis will assess accuracy of the Dexcom transmitter between the publicly available accuracy data and the enrolled participant data. Performance evaluation will include the proportion of CGM values within +/-20% of the reference (POC) glucose values > 100 mg/dL or within +/-20 mg/dL of reference glucose values < 100 mg/dL (%20/20), the analogous %15/15, and the mean absolute relative difference (MARD, expressed as a percentage)

between temporally matched CGM and reference values (Wadwa et al. Diabetes technology & Therapeutics. 20:6 2018).

**Data and Specimen Banking**

De-identified data will be retained for future potential research or FDA submission. No specimens will be collected for this study.

**Sharing of Results with Participants**

Study participants will be informed immediately if the Dexcom G6 CGM that they are utilizing is malfunctioning. Additionally, after final analysis participants will be informed of the result of the study by a study team member. This information will be communicated to the participants verbally or by written communication based on participant's preference.

**Study Timelines**

The study will commence after Dexcom Company and local IRB approval. In addition, support of a study coordinator will be required to assist with IRB submission, obtaining consent and insuring protocol procedures both inpatient and outpatient. Proposed start winter 2021. CCHMC performs 1-2 TPIATs per month thus patient recruitment would occur over a 15-19 month period.

**Inclusion and exclusion criteria:**

Inclusion Criteria: planned TPIAT at CCHMC, staying inpatient at CCHMC post TPIAT, planned to receive a Dexcom G6 CGM.

Exclusion criteria: hemo- or peritoneal dialysis.

**Vulnerable populations:**

Individuals who are not yet adults will be permitted to participate in the study following written informed consent and assent (if aged 11-17) with said individual and their parent/guardian.

Legal guardians unable to provide consent for their child to participate in the study will not be enrolled.

This study will involve participants that are children and potentially participants that are mentally impaired. To ensure that their rights and welfare are protected we will:

- Make adequate provisions for soliciting assent from children 11-17 years of age
- Make adequate provisions for soliciting parental permission for children and mentally impaired adults.

The risk to participate in the intervention portion of this study holds the prospect of direct benefit for the subject.

**Analysis and Methods**

This is a prospective assessment of accuracy and precision of the Dexcom G6 after radiation exposure.

All post-TPIAT patients at Cincinnati Children's Hospital Medical Center wear the Dexcom G6 as standard of care and are under the careful surveillance of pediatric endocrinology.

Participants will be enrolled and assigned into the exposure group.

CONTROL GROUP: Publicly available accuracy data from Dexcom

EXPOSURE GROUP: patients who will NOT have the CGM covered during radiologic procedures involving x-rays.

Standard of care at CCHMC is that sensor values do not replace point of care (POC) testing with a glucometer (such as the ACCU-CHEK® Inform II Meter) while inpatient. POC monitoring will occur every 1 hour when insulin administration is administered intravenous and every 3 hours with the transition to subcutaneous insulin administration. After discharge a provider and family may choose to space out these glucometer readings and eventually transition to relying only on CGM values for SOC, but for this study we are asking families to conduct regular glucometer checks to have comparison data at our study time points.

The following data will be collected during the life of the transmitter (approximately 3 months after placement):

- POC glucose values (from inpatient and outpatient glucometers)
- Dexcom CGM Clarity reports (inpatient and outpatient)
- Timing of interfering substances (hydroxyurea)
- Dates of clinically indicated x-rays and CT scans and radiation exposures (RADS) to radiation field of interest
- Indication for radiologic testing (nausea, vomiting, fever, pain, etc)
- Documentation of apron use during radiologic assessment

The G6 transmitter will  be issued while inpatient and be sent home with the families at discharge. Assessment of Dexcom reports compared to POC and home monitoring will be collected at 1 (+/-3 days) week post discharge clinic visit, 1 month (+/- 7 days) post TPIAT, 2 months (+/- 7 days) post TPIAT and before the transmitter is due to be changed (expected 3 months post TPIAT).

Two endocrine providers will perform the clinical assessment of the outpatient reports of glucometer and CGM. Formal analysis will be completed after 3 months of transmitter data is collected.

**Statistical Consideration**

Several accuracy methods will be ascertained. The %20/20 and%15/15 will be assessed from the participant's medical record for both inpatient and outpatient settings will be reviewed. In addition, use of Clark Error Grid Analysis will be performed on data points collected after 10 hours of hydroxyurea dosing.

**Recruitment**

Recruitment will occur at Cincinnati Children's Hospital Medical Center (CCHMC) or by phone after the patient has been verified to meet inclusion criteria for the study by delegated study staff. The recruitment goal is to recruit 40 individuals that are planning to utilize Dexcom G6 CGM system post TPIAT. Potential participants will be approached about the study after TPIAT has been scheduled.  CCHMC is projected to perform 1-2 TPIATs per month (12-24 patient per

year). The primary recruitment strategy would consist of in-person invitation by delegated study staff. Secondary recruitment strategies may include introduction letters sent by mail or email and phone calls. Recruitment phone calls may result in performing eConsent following proper CCHMC eConsent process.

**Withdrawal of Subjects**

Participants will be withdrawn from the study if any of the following become true:

Participant no longer wishes to remain in the study,

Participant has moderate to severe skin inflammation from adhesive,

Participants that cannot provide 3 months of Dexcom G6 readings data from the original transmitter and glucometer readings due to noncompliance with study requests,

PI no longer feels it is safe for the participant to continue in the study.

**Risk Assessment**

The use of Dexcom 6 CGM is standard of care in the TPIAT population at CCHMC. The device is used to monitor trends and does not replace POC glucose monitoring while inpatient, but it may be used exclusively at a point post-discharge if the provider and family agree. If the sensor and transmitter is in the field of radiologic interest it will be removed. If the sensor and transmitter is not in the field of interest, standard of care at our institution is to cover with a lead apron. After discussion with our local radiologist, radiation exposure is thought to be minimal/scatter and we have not documented any inaccuracy in transmitter readings (clinical experience, unpublished). This proposal will request that participants leave their CGM and transmitter uncovered during radiologic procedures. The families are instructed to monitor POC glucoses values every 3-4 hours and to not use a sensor value in this immediate post-operative period to dose insulin. The families are asked to have all insulin dose calculations from glucometer POC reading, although over time the provider and family may choose to rely more on the CGM as SOC.

Immediate risk-LOW

Long-range risk-LOW

**Potential Benefits to Subjects**

Participants will be provided a study Dexcom G6 transmitter and initial sensor, and any additional needed sensors during the 3-month participation period per participant. The information gained from this study outweighs any perceived risk as it may provide documentation that after minimal radiation exposure the accuracy of the sensor and transmitter is unaffected. Subsequently, it would no longer be necessary to remove device and waste expensive supplies with radiologic studies. These benefits would apply to all Dexcom G6 wearers.

To aid study data consistency, participants who are not using a glucometer approved by the study will also be provided this device and needed supplies for the 3-month study window.

**Data Management and Confidentiality**

Participants will be assigned a participant ID, which will be used to associate participants to participant data and CGM results. Participant identification will be kept in the form of an enrollment log. The enrollment log will be destroyed at the earliest opportunity.

Dexcom CGM and POC glucometer data will be saved on a secure server in the form of study participant ID labeled Excel files. The study will also collect demographic information (such as age, gender, BMI), radiologic studies performed (type and procedure data) and date of operation and date of discharge. Study data will be stored on a secure sever.

Collected data will be kept confidential and will only be shared with authorized study staff.

**Provisions to Monitor the Data to Ensure the Safety of Subjects**.

Adverse event monitoring: No surgery related complications will be tracked for this study, only events relating to the function of the study CGM will be collected.

Monitoring and auditing procedures will be followed to ensure that the study is conducted, documented, and reported in accordance with the IRB approved protocol, the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines, and applicable regulatory requirements of Cincinnati Children's Hospital Medical Center.

An independent medical monitor will assess the progress of this clinical study, the safety data, critical efficacy endpoints and provide recommendations to study personnel annually.

**Provisions to Protect the Privacy Interests of Subjects**

Participant data are password protected with restricted access to only qualified personnel involved in this research study. Documents and records are kept under lock and key in the Division of Endocrinology. Only the Principal Investigator (PI) and designees will have access to the participant information.

Participants will be encouraged to ask questions about the research and will be well informed about the procedures that are happening. Participants will also be reminded that they have the right to withdraw from the study at any time.

**Compensation for Research-Related Injury**
No compensation will be provided; no research related injuries are anticipated.

**Economic Burden to Subjects**
Subjects will be responsible for all standard of care treatments and pharmaceutical costs. Study will provide a Dexcom G6 sensor and transmitter. If the study transmitter fails prior to the end of the 3-month (90 day) sensor life expectancy, a replacement transmitter will be provided. Patients who are not using a Glucometer approved by the study will be provided the device and needed supplies for study data consistency.

Participants will be compensated $50.00 for their time and effort through ClinCard if minimum requested study procedures are followed. If participants remove their CGM early due to preference (not transmitter failure or for clinical reasons) or fail to provide the minimum requested glucometer readings, they will receive a prorated amount.

All participants who participate to some extent will receive $15 at 1 week post discharge timepoint or study withdrawal (if prior to discharge), participants will get an additional $10 at the 1-month and 2-month time points for completing the minimum requirements, and a final $15 at

the 3-month timepoint for completing the minimum requirements. If participation is ended early for clinical reasons (such as transmitter failure or a procedure requires the removal of the device) then participants will receive the full $50 if they were meeting minimum requirements at time of completion. In rare and unusual circumstances, the PI may use discretion to pay participants allotted timepoint amount if minimum requirements are not fully met.

**Consent and Consent Documentation Process**

Prior to an anticipated in-person clinic visit, patients may be contacted to let them know we have a new research study to test the effect of clinical x-ray exposure on the Dexcom G6 CGM. Consent may take place by several methods: in-person paper consent, in-person electronic consent (using REDCap for the eConsent) or over the phone (via paper or REDCap for eConsent). The eConsent form has been developed in CCHMC's REDCap, a secure, web-based, HIPAA-compliant, data collection platform with a user management system allowing project owners to grant and control varying levels of access to data collection instruments and data (e.g. read only, de-identified-only data views) for other users. Participants and/or Parents/LAR of potential participants will participate in the consent/assent process (based on age and CCHMC guidelines) by being approached either in-person at a participating institution or remotely via telephone/video call/telehealth application and accessing the REDCap survey electronically on personal portable electronic devices. During the consent/assent process, participants and/or parents/LAR will be consented by a member of the key study personnel, either in-person or remotely through telephone/video call/telehealth application. Participant and/or parent/LAR signatures will be obtained using a written signature, either on the paper form or directly through REDCap. Upon completion of the consenting process, a copy of the consent form will either be given to the participant and/or parents/LAR in paper form or emailed to them via REDCap, depending on the method used to complete the consenting process. In all cases, the consent process will be documented in an informed consent process note and a copy of the signed consent(s) will be kept in the patient's electronic medical record. Signed eConsent documents will be housed electronically in REDCap's File Repository.

No study procedures will be performed until consent/assent has been obtained.

**Available Resources**

Potential patients will be recruited through established databases. CCHMC performs approximately 36-48 TPIAT per year. Past studies have had consent rates near 100%. Thus, we anticipate being able to recruit 40 TPIAT patients in 15-19 months of recruitment.

All participating research staff will have dedicated time allocated to conducting and completing the research.

Participants will be seen as part of this study in the clinical setting at CCHMC, as well as by remote means, such as phone calls.

Participants will have access to medical and psychological resources that might be needed as a result of this study.

Prior to initiating study procedures all staff will be trained by the lead PI, or delegated study staff, on study specific procedures. No persons will be added to the study or have tasks delegated to them without receiving the necessary training to complete delegated tasks.

Participants will be monitored by medically trained study staff such as an endocrinologist or a certified nurse practitioner.

A statistician is available to assists with the final data analysis.

**References**


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3. Wadwa P, Laffel l, Shah V, Garg S. Accuracy of factory-calibrated, real-time continuous glucose monitoring system during 10 days of use in youth and adults with diabetes. Diabetes Technol Ther, 2018 20:6. DOI: 10.1089/dia.2018.0150