DATA REVIEW PROTOCOL

PROTOCOL TITLE:
Optimizing Collection Time for Islet Cell Isolation

PRINCIPAL INVESTIGATOR:

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REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?

Table of Contents

1.0 Study Summary

Study Title	Optimizing collection time for islet cell isolation
Study Design	Retrospective chart review
Primary Objective	Determine the optimal timing to maximize islet cell yield during islet cell collection
Secondary Objective(s)	None
Study Population	Patients who have undergone islet cell isolation during pancreatectomy at DHMC from 2015-2020
Data Size	~40 patients
Date Range of Data	2015-2020
Study Duration	NA – complete after initial data analysis
Study Specific Abbreviations/ Definitions	IAT – islet autotransplant

2.0 Objectives

2.1 The purpose of the study is to determine the optimal time to begin collection during islet cell isolation to maximize islet cell yield

2.2 We hypothesize that minimizing islet cell fragmentation during collection will provide the maximum yield of islet cells

3.0 Background

3.1 We are fortunate at DHMC to be one of the few centers in the world that provides islet cell isolation. This is a process by which a patient has either a part or their complete pancreas removed and the islet cells – those that make insulin – are harvested and transfused back into the liver. By performing this procedure, patients are able to have their pancreas removed but often do not develop the major consequence of this intervention which is the development of uncontrolled diabetes.

Since 2015, DHMC has offered this procedure and thus far approximately 40 patients have undergone this intervention. In the spirit of quality improvement, we are looking at our processes to determine if there is a way we can optimize our isolation techniques to maximize the islet cell yield.

One of the critical steps in the isolation process is deciding when to stop breaking down the pancreas and start collecting the islet cells. When the cells are first starting to be broken down, they are embedded in acinar tissue. These "embedded" cells are then separated from the acinar tissue to become "free" islets. If the "free" islets continue to be broken down they turn into islet cell "fragments". So in essence one has to have fragments present in order to have all of the "embedded" islets become "free".

While it is generally believed that "free" islets give the maximum amount of insulin, it is not known whether having "embedded" islets and/or "fragments" is beneficial or detrimental. As such we are not clear whether we should err on the side of having more "embedded" islets or more" fragments" in order to maximize yield.

3.2 We do not have any preliminary data evaluating this question specifically in our islet cell isolation process.

3.3 The importance of this project is that it will have a direct impact on how we isolate our cells. Currently there is no literature to our knowledge that details the pertinent question – i.e. is it better go longer on the process to have more "fragments" in the pursuit of

"free" islets or is it better to stop the isolation sooner and you will not hurt the "free" yield by having more "embedded" islets.

4.0 Study Endpoints

4.1 The primary endpoint/outcome is the percent change in three month c-peptide level from pre-operative baseline in patients who have undergone pancreatomy with islet cell isolation

4.2 There are no primary or secondary safety endpoints

5.0 Date Range of Data

01/01/2015-10/22/20

6.0 Study Methods

6.1 The department of surgery maintains a quality control database of all patients who have undergone islet cell transplant at DHMC. We will obtain de-identified data from this registry with clinical information about the patients and the islet cell process. These data will then be used to perform a retrospective review.

6.2 See above. The data will be obtained from the surgical database at DHMC. All data will be de-identified and will be transferred to the enclosed case report form by the primary investigator Dr. Gardner.

6.3 Dr. Timothy Gardner will be the reviewer of the database. Research assistant Stephen Hadley will have access to the de-identified data.

6.4 We will evaluate all patients who have undergone islet isolation since 2015 (the year in which we started performing the procedure). This is approximately 40 patients.

7.0 Genetic Research

There is no genetic research being performed

8.0 Selection of Participants

8.1 Patients who have undergone islet isolation at DHMC will be included. We will only include them if they have the baseline and three month c-peptide levels so that the primary outcome can be

evaluated. The exposure variable will also be necessary which will be the percent of free vs embedded cells, as well as the number of islet cell fragments.

8.2 The ages of patients who have undergone islet isolation procedures at DHMC range from 16-76

8.3 We will plan on including patients who were 16 at the time of their isolation – there are two patients who underwent isolation at age 16.

9.0 Vulnerable Populations

We do not plan to include any vulnerable patient populations.

10.0 Risks to Subjects

10.1 The only risk would be a breach of data. However, we are using de-identified data – see case report form. All of the patients in the study are patients of Dr. Timothy Gardner.

11.0 Potential Benefits to Subjects

11.1 The patients in the study will not have any direct benefit from the study

12.0 Data Management and Confidentiality

12.1 Our primary exposure will be the percent of embedded, free and fragmented islets. The primary outcome measure ods the change from baseline in the three month-c-peptide levels. We will use scatterplots and linear regression to evaluate any trends in data.

12.2 Data will be completely de-identified. The EXCEL spreadsheet will only be shared by the investigators and will be password protected. The spreadsheet will be delated upon completion of the data analysis and publication of results.

12.3 The data are collected from the islet cell surgery database.

12.4 The data will be stored on a password protected EXCEL spreadsheet that only Dr. Gardner and Mr. Hadley will have access to. These will be stored on a thumb drive. The data will be destroyed once data collection has been completed and the results published.

12.5 There are no data bank procedures planned.

13.0 Consent Process

13.1 We do not plan on obtaining consent

13.2 We are requesting a waiver of consent due to minimal risk, the fact that this waiver will not affect the patient's welfare, and the fact that some patients have been lost to follow-up or are deceased and consent cannot be obtained.

14.0 Process to Document Consent in Writing

14.1 NA

14.2 If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent.

This type of consent is not usually requested for a data review. Under a waiver of documentation of consent, an investigator must still obtain consent from the participant. However, the investigator does not need to obtain a signed consent form from participants if the IRB agrees that the following criteria are met:

- The only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether she or he wants documentation linking her or him with the research, and the participant's wishes will govern; or
- The research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.

15.0 Appendices

Appendix A and B must be completed and included in the protocol.

Instructions:
Appendix A: *See attached*

Appendix B: *Coded Identifier List: NA – there is no identifier list*

APPENDIX A: DATA COLLECTION DOCUMENT

Instructions: List all elements to be collected during the review.

APPENDIX B: CODED IDENTIFIER LIST

Instructions: NA