University at Buffalo
The State University of New York
University at Buffalo Institutional Review Board (UBIRB)
Office of Research Compliance | Clinical and Translational Research Center Room 5018
875 Ellicott St. | Buffalo, NY 14203
UB Federalwide Assurance ID#: FWA00008824

Complete Research Protocol (HRP-503)

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Template Instructions

Sections that do not apply:

- *In several sections, the addition of checkboxes for **Not Applicable** have been added to the template as responses.*
    - *If an N/A checkbox is present, select the appropriate justification from the list.*
    - *If an N/A checkbox is not present, or if none of the existing checkboxes apply to your study, you must write in your own justification.*
- *In addition:*
    - *For research where the only study procedures are records/chart review: Sections 6, 21, 22, 24, 25, 26 and 27 do not apply.*
    - *For exempt research: Section 6 may not apply. Section 6.1 will still apply if there is a study intervention.*

Studies with multiple participant groups:

- *If this study involves multiple participant groups (e.g. parents and children), provide information in applicable sections for each participant group. Clearly label responses when they differ. For example:*

Response Example
Intervention Group:
Control Group:

Formatting:

- *Do not remove template instructions or section headings when they do not apply to your study.*

If you are pasting information from other documents using the "Merge Formatting" Paste option will maintain the formatting of the response boxes.

Amendments:

- *When making modifications or revisions to this and other documents, use the **Track Changes** function in Microsoft Word.*
- *Update the version date or number **on Page 3.***

PROTOCOL TITLE:

Include the full protocol title.

Response:

A cross sectional study of insulin resistance and cognitive function scores in patients with prostate cancer on androgen deprivation therapy (ADT).

PRINCIPAL INVESTIGATOR:

Name
Department
Telephone Number
Email Address

Response: Paresh Dandona, MD, PhD

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Robert Pili, MD

VERSION NUMBER/DATE:

Include the version number and date of this protocol.

Response: 10.05.2020

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?

FUNDING:

Indicate any funding for this proposal. This should match the Funding Sources page in Click IRB.

Response: Sponsored with Investigator Initiated Funds (IIF)

GRANT APPLICABILITY:

Indicate whether this protocol is funded by a grant (e.g. NIH, foundation grant). For a grant with multiple aims, indicate which aims are covered by this research proposal.

NOTE: This question does not apply to studies funded by a sponsor contract.

Include a copy of the grant proposal with your submission.

Response: NA

RESEARCH REPOSITORY:

Indicate where the research files will be kept, including when the study has been closed. The repository should include, at minimum, copies of IRB correspondence (approval, determination letters) as well as signed consent documents. This documentation should be maintained for 3 years after the study has been closed.

Response:

Location: Diabetes Endocrinology Research Center of WNY

Address: 1000 Youngs Road, Suite 105 Williamsville NY 14221

Department: Diabetes and Endocrinology

1.0 Study Summary

Study Title	A cross sectional study of insulin resistance and cognitive function scores in patients with prostate cancer with or without androgen deprivation therapy (ADT)
Study Design	Cross sectional study
Primary Objective	To investigate the possible cellular and molecular mechanisms underlying insulin resistance in patients undergoing androgen deprivation therapy for prostatic carcinoma including determining the expression of insulin signaling genes and proinflammatory genes associated with insulin resistance.
Secondary Objective(s)	1. Determine level of insulin resistance at different stages of ADT treatment compared to those not on ADT 2. Correlate level of insulin resistance to the expression of insulin signaling genes and inflammatory mediators associated with insulin resistance 3. Determine the effect of insulin resistance on body composition of men undergoing ADT 4. Determine cognitive function scores in patients receiving ADT at various stages.
Research Intervention(s)/ Investigational Agent(s)	None
IND/IDE #	NA
Study Population	Patients with Prostate cancer from Roswell Park Comprehensive Cancer Center
Sample Size	40
Study Duration for individual participants	Up to 7 days

Study Specific Abbreviations/ Definitions	

2.0 Objectives*

2.1 Describe the purpose, specific aims, or objectives of this research.

Response:

PRIMARY OBJECTIVE

To investigate the possible cellular and molecular mechanisms underlying or associated with insulin resistance in patients undergoing androgen deprivation therapy for prostatic carcinoma including determining the expression of insulin signaling genes and proinflammatory genes associated with insulin resistance.

SECONDARY OBJECTIVES

1. Determine level of insulin resistance at different stages of ADT treatment compared to those not on ADT

2. Correlate level of insulin resistance to the expression of insulin signaling genes and inflammatory mediators associated with insulin resistance

3. Determine the effect of insulin resistance on body composition of men undergoing ADT.

4. Determine cognitive function scores in patients receiving ADT at various stages.

2.2 State the hypotheses to be tested, if applicable.

NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.

Response:

We hypothesize that ADT results in increase in insulin resistance and in inflammatory mediators which may interfere with insulin signal transduction. We hypothesize that ADT results in greater adiposity and an increase in plasma insulin and glucose concentrations with a concomitant increase in HOMA-IR, plasma TNFα and IL-1β with a decrease in the expression of IRβ, IRS-1, AKT and GLUT-4 in adipose tissue

3.0 Scientific Endpoints*

3.1 Describe the scientific endpoint(s), the main result or occurrence under study.

NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should ***not*** *be a date.*

Response:

PRIMARY ENDPOINTS

- Determine levels of IRS-1 serine phosphorylation in adipose tissue and MNC as marker of inflammation induced insulin resistance
- Changes in expression of insulin signaling genes; IRβ, IRS-1 and AKT-2 in both adipose tissue and mononuclear cells and expression of GLUT-4 in adipose tissue in subjects with prostate cancer on ADT compared to those not on ADT
- Changes in expression of proinflammatory genes that interfere with insulin signaling transduction (TNF-α, IL-1β, IKK-β, SOCS-3, PTB-1B, JNK-1, TLR-4) in adipose tissue and mononuclear cells will be assessed

SECONDARY ENDPOINTS

- Comparison in expression of insulin signaling genes and of proinflammatory genes associated with insulin resistance in adipose tissue and mononuclear cells among subjects with prostate cancer at various stages of ADT
- Measurement of insulin resistance by HOMA-IR method in subjects with prostate cancer on ADT compared to those not on ADT
- Correlation of insulin resistance as measured by HOMA-IR to the expression of insulin signaling genes and proinflammatory genes associated with insulin resistance in adipose tissue and mononuclear cells
- Changes in plasma levels of glucose, insulin and lipid concentrations in subjects with prostate cancer on ADT compared to those not on ADT
- Changes in plasma concentrations of inflammatory markers like free fatty acids (FFA), CRP (C-reactive protein), leptin, adiponectin, TNF-α and IL-1β will be assessed
- Changes in lean body mass and fat mass; total and regional as measured by DEXA scan
- Changes in cognitive function scores in subjects with prostate cancer on ADT compared to those not on ADT

4.0 Background*

4.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute to existing knowledge. Describe any gaps in current knowledge. Include relevant preliminary findings or prior research by the investigator.

Response:

Prostate cancer (PrCa) is the most common non-cutaneous malignancy amongst men in the United States. Early stage, organ-confined PrCa can be cured by surgery or radiotherapy. While the majority of men are diagnosed with early stage disease, many present with more advanced disease or are otherwise not good candidates for curative therapies. In addition, one third of patients with localized disease will eventually develop metastatic PrCa. The mainstay treatment of locally advanced, as well as recurrent or metastatic PrCa is androgen deprivation therapy (ADT) [1], which blocks the production of male hormones and induces tumor cell apoptosis [2].

ADT either via castration or more frequently, gonadotropin-releasing hormone (GnRH) agonists (such as leuprolide), reduces serum testosterone (T) to castrate levels [3]. Despite initial responses, almost all patients will eventually develop disease progression, which in the presence of continuous ADT is defined as castration resistant PrCa (CRPC). Some CRPC patients may respond for a number of years to sequential administration of more potent anti-androgens combined with ongoing continuous ADT [4]. Thus, it is not unusual for men with advanced PrCa to be on continuous ADT for many years.

ADT resulting in drastically low testosterone levels can have multitude of adverse effects on the metabolic, cardiovascular and bone health in men with prostate cancer. Prostate cancer patients receiving ADT experience bone loss, muscle loss and increased fat mass (sarcopenic obesity), and increased insulin resistance; thus leading to increased risk of development of Type 2 Diabetes Mellitus (T2DM). These changes can be seen as early as within 3 months of therapy and continue to occur even after 2 years on ADT therapy (5). One of the earliest metabolic changes seen with ADT is hyperinsulinemia which is associated with fat mass increase. Sarcopenic obesity is a new term used for combination of excess weight and reduced muscle mass (6). The earliest prospective study on body composition and insulin resistance following ADT in men with non-metastatic prostate cancer was conducted by Smith et al in 2001 (7). The study showed ADT in newly diagnosed men with PCa resulted in increase in fat mass from 20.2±9.4 kg at baseline to 21.9±9.6 kg at 3 months (P=0.008), while lean body mass decreased from 63.2±6.8 kg at baseline to 61.5±6.0 kg (P=0.016). Another prospective study confirmed these changes by showing that there was a 9.4% increase (p value < 0.001) in subcutaneous fat and 2.7% decrease (p value < 0.001) in lean mass after 12 months of ADT in 40 men (8). Visceral fat did not change in this study. Similar findings were also observed in a recent study of 34 men receiving ADT and 29 men with prostate cancer but not receiving ADT (9). Subcutaneous fat mass increased by 3.4 kg and lean mass decreased by 1.5 kg after 12 months of ADT.

Several retrospective and prospective studies have shown increased risk development of insulin resistance and T2DM in PCa patients receiving ADT. In the same study done by Smith et al[7], they also showed increase in serum fasting serum insulin levels from 11.8 mU/L at baseline to 19.3 mU/L at 3 months. A short term study showed statistically significant increase in fasting serum glucose levels in PCa patients on ADT for 6 months suggesting compensatory hyperinsulinemia[10]. A cross sectional study by Basaria et al, which recruited men on ADT for at least 12 months and age matched men with PCa not on ADT, showed hyperinsulinemia and fasting hyperglycemia more prevalent in ADT group than the control group[11,12] and the severity of these metabolic complications was directly related to the duration of ADT [12]. Subsequent population based study looked into the health data of 73,196 men > 66 years old and showed that men undergoing ADT experienced a 44% increase in development of diabetes than men not undergoing ADT [13]. Similar analysis of a Canadian Database with an age matched cohort study including about 20,000 men > 66 years of age treated for prostate cancer found increased risk of diabetes (by 16%) in men treated with ADT compared to ADT naïve men [14]. These men were followed for an average of 6.47 years. Thus, long term ADT has been shown to cause increased incidence of sarcopenic obesity, insulin resistance and T2DM, all leading to increased adverse metabolic and cardiovascular outcomes.

Studies have shown an increase in insulin resistance as measured by HOMA of insulin resistance (HOMA-IR) in subjects with low Testosterone levels irrespective of diabetes [15,16]. And this is mediated through an increase in inflammatory mediators that interfere with insulin signaling. Our previous study on hypogonadal men in T2DM have shown that patients with hypogonadotropic hypogonadism (HH) have an increase in insulin resistance and increase in inflammatory mediators, which may interfere with insulin signal transduction[17]. Our results clearly showed that type 2 diabetes patients with HH had significant increase in insulin resistance (as measured by hyperinsulinemic-euglycemic clamps, decreased GIR by 36%) compared to the type 2 diabetes patients without HH. There was a marked reduction in expression of IR-β, IRS-1, AKT-2 and GLUT-4 in adipose tissue, the major genes mediating insulin signaling in the adipose tissue in HH men compared to eugonadal men. We also showed in the same study, that replacement of testosterone for 6 months lead to an increase in insulin sensitivity (measured through HE clamps), significant increase in the expression of above genes in adipose tissue and suppression of inflammatory mediators which interfere with insulin signaling. This explains the mechanism of increased insulin resistance in hypogonadal men reversed by testosterone supplementation.

Several reports have also linked the use of ADT to cognitive decline in men with prostate cancer[18]. Gonzales et al. reported in patients on ADT for prostate cancer had a statistically significant impairment in cognitive function compared to an education and age matched cohort of patient not on ADT as early as 6 months[19]. A recently published large retrospective analysis of more than 150,000 patients with prostate cancer who were followed for a period of at-least 10 years showed an increase in the diagnosis of Alzheimer's disease (AD) and dementia in patients treated with ADT compared to patient

who did not receive ADT. The HR for AD and dementia was proportional to the doses of ADT with higher HR seen in patients who received >4 doses of ADT[20].

4.2 Include complete citations or references.

Response:

*1. Gilbert SM, Kuo YF, Shahinian VB. Prevalent and incident use of androgen deprivation therapy among men with prostate cancer in the United States. Urol Oncol 2011;**29**(6):647-53.*

2. Sharifi N, Gulley JL, Dahut WL. Androgen deprivation therapy for prostate cancer. JAMA: the jour/jama.294.2.238.

*3. Grossmann M, Zajac JD. Management of side effects of androgen deprivation therapy. Endocrinology and metabolism clinics of Nor nal of the American Medical Association 2005;**294**(2):238-44.*

*4. Sartor O, de Bono JS. Metastatic Prostate Cancer. N Engl J Med 2018;**378**(17):1653-54.*

5. Collins L, Basaria S. Adverse effects of androgen deprivation therapy in men with prostate cancer; a focus on metabolic and cardiovascular complications. Asian Journal of Andrology 2012; 14: 222-225.

6. Zamboni M, Mazzali G, Fantin F, Rossi A, Di Francesco V. Sarcopenic obesity: a new category of obesity in the elderly. Nutr Metab Cardiovasc Dis 2008;18:388.

7. Smith JC, Bennett S, Evans M, Kynaston HG, Parmar M et al. The effects of induced hypogonadism on arterial stiffness, body composition, and metabolic parameters in males with prostate cancer. J Clin Endocrinol Metab 2001; 86: 4261–7.

8. Smith MR, Finkelstein JS, McGovern FJ, Zietman AL, Fallon MA, Schoenfeld DA, and Kantoff PW. Changes in body composition during androgen deprivation therapy for prostate cancer. The Journal of clinical endocrinology and metabolism. 2002;87(2):599-603

9. Cheung AS, Hoermann R, Dupuis P, Joon DL, Zajac JD, and Grossmann M. Relationships between insulin resistance and frailty with body composition and testosterone in men undergoing androgen deprivation therapy for prostate cancer. European journal of endocrinology. 2016;175(3):229-37.

10. Nishiyama T, Ishizaki F, Tsutomu A, Shimura H, Takahashi K. The influence of androgen deprivation therapy on metabolism in patients with prostate cancer. J Clin Endocrinol Metab 2005; 90: 657–60.

11. Basaria S, Muller DC, Carducci MA, Egan J, Dobs AS. Hyperglycemia and insulin resistance in men with prostate carcinoma who receive androgen deprivation therapy. Cancer 2006; 106: 581–8.

12. Basaria S, Muller DC, Carducci MA, Egan J, Dobs AS. Relation between duration of androgen deprivation therapy and degree of insulin resistance in men with prostate cancer. Arch Intern Med 2007; 167: 612–3.

13. Keating NL, O'Malley AJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer. J Clin Oncol 2006; 24: 4448–56.

14. Alibhai SM, Duong-Hua M, Sutradhar R, Fleshner NE, Warde P et al. Impact of androgen deprivation therapy on cardiovascular disease and diabetes. J Clin Oncol 2009; 27: 3452–8.

15. Hamilton EJ, Gianatti E, Strauss BJ, et al. Increase in visceral and subcutaneous abdominal fat in men with prostate cancer treated with androgen deprivation therapy. Clin Endocrinol (Oxf) 2011;74:377–383

16. Tsai EC, Matsumoto AM, Fujimoto WY, Boyko EJ. Association of bioavailable, free, and total testosterone with insulin resistance: influence of sex hormone-binding globulin and body fat. Diabetes Care 2004;27:861–868

17. Dhindsa S, Ghanim H, Batra M, Kuhadiya ND, Abuaysheh S, Sandhu S, Green K, Makdissi A, Hejna J, Chaudhuri A, Punyanitya M, Dandona P. Insulin resistance and inflammation in hypogonadotropic hypogonadism and their reduction after testosterone replacement in men with type 2 diabetes. Diabetes Care. 2016 Jan 1;39(1):82

18. *Treanor, C.J., J. Li, and M. Donnelly, Cognitive impairment among prostate cancer patients: An overview of reviews. Eur J Cancer Care (Engl), 2017.* ***26****(6)*

19. *Gonzalez, B.D., H.S. Jim, M. Booth-Jones, B.J. Small, S.K. Sutton, H.Y. Lin, J.Y. Park, P.E. Spiess, M.N. Fishman, and P.B. Jacobsen, Course and Predictors of Cognitive Function in Patients With Prostate Cancer Receiving Androgen-Deprivation Therapy: A Controlled Comparison. J Clin Oncol, 2015.* ***33****(18): p. 2021-7.*

20. *Jayadevappa, R., S. Chhatre, S.B. Malkowicz, R.B. Parikh, T. Guzzo, and A.J. Wein, Association Between Androgen Deprivation Therapy Use and Diagnosis of Dementia in Men With Prostate Cancer. JAMA Netw Open, 2019.* ***2****(7): p. e196562.*

5.0 Study Design*

5.1 Describe and explain the study design (e.g. case-control, cross-sectional, ethnographic, experimental, interventional, longitudinal, observational).

Response:

It will be a cross sectional study with 2 groups of patients.

One group will be men with prostate cancer in various stages of ADT and the control group will be men with prostate cancer not on ADT.

6.0 Study Intervention/Investigational Agent

6.1 Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.

Response:

NA

6.2 Drug/Device Handling: If the research involves drugs or device, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

- *If the control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference that SOP in this section.*

Response:

NA

6.3 If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

- *Identify the holder of the IND/IDE/Abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:*

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

Response:

7.0 Local Number of Subjects

7.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed locally.

Response:

40

7.2 If applicable, indicate how many subjects you expect to screen to reach your target sample (i.e. your screen failure rate).

Response:

We expect to screen 130 to 150 patients

7.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

Response:

Preliminary assessment suggests up to 20 patients per month begin treatment with ADT in the GU oncology clinic. We anticipate that a majority (10) will be eligible and 30% (3) will agree to participate in the trial.

8.0 Inclusion and Exclusion Criteria*

*8.1 Describe the criteria that define who will be **included** in your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

1. Male, age ≥ 18 years of age.

2. Body Mass Index of > 25 kg/m^2

3. Biopsy-confirmed prostate adenocarcinoma of any stage/grade currently on androgen deprivation therapy (ADT) for minimum of 3 months

4. Biopsy-confirmed prostate adenocarcinoma of any stage/grade not on ADT for control group

5. Hemoglobin > 11 g/dL, Creatinine < 1.5x ULN and liver function tests < 2x ULN

6. Participant must be able to read, write, and understand the English language and be able to provide written consent

7. Participant must understand the investigational nature of this study and sign an Independent Ethics Committee/Institutional Review Board approved written informed consent form prior to receiving any study related procedure

*8.2 Describe the criteria that define who will be **excluded** from your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

1. Known clinically significant severe COPD, ischemic heart disease, congestive heart failure, and/or significant cardiac arrhythmias
2. Any patient with known diabetes (A1c > 6.4%) or an anti-diabetic drug
3. Any condition contraindicating additional blood collection beyond standard of care
4. Subjects with known allergy to lidocaine (this is used to anesthetize area for fat biopsy)
5. Unwilling or unable to follow protocol requirements
6. Any condition which in the Investigator's opinion deems the participant an unsuitable candidate to undergo study procedures.
7. Subjects on chronic use of androgens, or opiates in the last 6 months or with panhypopituitarism, congenital HH (hypogonadotropic hypogonadism), prolactinoma, head trauma

8.3 Indicate specifically whether you will include any of the following special populations in your study using the checkboxes below.

NOTE: Members of special populations may not be targeted for enrollment in your study unless you indicate this in your inclusion criteria.

Response: NA

☐ Adults unable to consent

☐ Individuals who are not yet adults (infants, children, teenagers)

☐ Pregnant women

☐ Prisoners

8.4 Indicate whether you will include non-English speaking individuals in your study. ***Provide justification if you will exclude non-English speaking individuals.***

*In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may **not** be routinely excluded from research as a matter of convenience.*

In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English. Some examples include pilot studies, small unfunded studies with validated instruments not available in other languages, studies with numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.

Response:

We will not have non-English speaking individuals in this study. We have patients that English is a second language, but they are able to read, write and understand it. This population is less than 10% of the total population

We are excluding non-English speaking individuals as this is a small study and no benefits will be withheld.

9.0 Vulnerable Populations*

*If the research involves special populations that are considered vulnerable, **describe the safeguards included to protect their rights and welfare.***

NOTE: You should refer to the appropriate checklists, referenced below, to ensure you have provided adequate detail regarding safeguards and protections. You do not, however, need to provide these checklists to the IRB.

*9.1 For research that involves **pregnant women,** safeguards include:*
NOTE CHECKLIST: Pregnant Women (HRP-412)

Response:

We will not be using subjects from vulnerable populations

☒ **N/A**: This research does not involve pregnant women.

*9.2 For research that involves **neonates of uncertain viability or non-viable neonates,** safeguards include:*
NOTE CHECKLISTS: Non-Viable Neonates (HRP-413), or Neonates of Uncertain Viability (HRP-414)

Response:

☒ **N/A:** This research does not involve non-viable neonates or neonates of uncertain viability.

*9.3 For research that involves **prisoners**, safeguards include:*
NOTE CHECKLIST: Prisoners (HRP-415)

Response:

☒ **N/A:** This research does not involve prisoners.

*9.4 For research that involves **persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children")**, safeguards include:*
NOTE CHECKLIST: Children (HRP-416)

Response:

☒ **N/A:** This research does not involve persons who have not attained the legal age for consent to treatments or procedures ("children").

*9.5 For research that involves **cognitively impaired adults**, safeguards include:*
NOTE CHECKLIST: Cognitively Impaired Adults (HRP-417)

Response:

☒ **N/A:** This research does not involve cognitively impaired adults.

*9.6 Consider if other specifically targeted populations such as students, employees of a specific firm, or educationally or economically disadvantaged persons are vulnerable. **Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.***

Response:

No specific populations or vulnerable groups will be targeted. All subjects enrolled in this study will be of legal adult consenting age with the ability to speak, read and interrupt the English language. Subjects will have the ability to speak with the research team regarding any questions or concern they have before signing the consent. Subjects will be made aware that this study is voluntary, and they are able to stop participating at any time they feel uncomfortable. Subjects will not be pressured into participating and their clinic standard of care will remain the same if they participate or choose not to participate.

10.0 Eligibility Screening*

*10.1 Describe **screening procedures** for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria.*

📎 *Include all relevant screening documents with your submission (e.g. screening protocol, script, questionnaire).*

Response:

Prospective participants referred to the research center from Roswell Park Comprehensive Cancer Center (RPCCC) and Great Lakes Cancer Care GU clinics will be asked about their interest in participating in the research study. If the subject wants to participate in the study, they will be referred to the research coordinator at the Diabetes and Endocrinology Center of WNY to screen for the study, and sign the informed consent form. The subject's medical history and current medications will be obtained as well as their blood pressure and vitals. A physical examination will also be done. Blood samples will be taken in order to evaluate CBC, HbA1c, and CMP. Patients meeting all the inclusion and exclusion criteria based on all screening tests will be enrolled in the study

☐ **N/A:** There is no screening as part of this protocol.

11.0 Recruitment Methods

☐ **N/A:** This is a record review only, and subjects will not be recruited.
NOTE: If you select this option, please make sure that all records review procedures and inclusion/exclusion screening are adequately described in other sections.

11.1 Describe when, where, and how potential subjects will be recruited.

NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study. Include specific methods you will use (e.g. searching charts for specific ICD code numbers, Research Participant Groups, posted advertisements, etc.).

Response:

Study participants will be recruited from the RPCCC (Roswell Park Comprehensive Cancer Center) GU Oncology clinical program (Hematology and Oncology, Urology, and Radiation Oncology), Prostate Cancer Survivorship group and Biodata Repository (BDR) and Great Lakes Cancer Care GU clinics by the attending physicians. Patient records will be reviewed at the time of clinical encounter as well as from the BDR to identify potentially eligible individuals. If a participant is identified during clinical encounter, physicians will speak to them about their interests in participating in research. If a participant is identified from the BDR, they will be contacted through phone by the GU team (members listed in the study) about their interests in participating in research. The GU team will refer the interested participants to the Diabetes and Endocrinology Research Center of Western New York where they will be screened and consented

11.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.

NOTE: Privacy refers to an individual's right to control access to him or herself.

Response:

Patient charts will be screened at the time of clinical encounter as well as from the BDR according to the study inclusion and exclusion criteria by the clinical staff and physicians of GU oncology group at RPCCC and Great Lakes Cancer Care GU clinics. If the patient qualifies and is of consenting age, the physicians will speak to them about their interests in participating in research. If a participant is identified from the BDR, they will be contacted through phone by the GU team (members listed in the study). If the patient agrees, attending physician will give their information to the research coordinator at Diabetes and Endocrinology Center of WNY to be contacted for further evaluation. All personal information will be kept confidential and locked in the coordinator office.

11.3 Identify any materials that will be used to recruit subjects.

NOTE: Examples include scripts for telephone calls, in person announcements / presentations, email invitations.

For advertisements, include the final copy of printed advertisements with your submission. When advertisements are taped for broadcast, attach the final audio/video tape. NOTE: You may submit the wording of the advertisement prior to taping to ensure there will be no IRB-required revisions, provided the IRB also reviews and approves the final version.

Response:

Patients will be identified through screening of clinical charts from RPCCC GU oncology clinic program, Prostate Cancer Survivorship group, Biodata Repository (BDR) and Great Lakes Cancer Care GU clinics.

12.0 Procedures Involved*

*12.1 Provide a description of **all research procedures or activities** being performed and when they are performed once a subject is screened and determined to be eligible. Provide as much detail as possible.*

NOTE: This should serve as a blueprint for your study and include enough detail so that another investigator could pick up your protocol and replicate the research. For studies that have multiple or complex visits or procedures, consider the addition of a schedule of events table in in your response.

Response:

This is a cross sectional study designed to establish the cellular and molecular mechanisms underlying insulin resistance and the interference in insulin signal transduction in patients undergoing Androgen Deprivation Therapy for prostatic carcinoma.

Patients interested in participating who meet the inclusion/exclusion criteria and who agree to undergo blood draws, fat biopsy and DEXA imaging will be identified by the

GU team at RPCCC and Great Lakes Cancer Care GU clinics. These patients will be referred to the Diabetes and Endocrinology Research Center of WNY where they will undergo blood draws in fasting state.

Screening Visit:

Participants will be asked to complete the following procedures prior to participating in the study (screening visit): 1) Informed consent; 2) Medical History 3) Physical Exam; 4) Blood draws for fasting labs before 10:00 am including; CBC, CMP, and HbA1c. 30 ml of blood will be drawn at this visit. Participants will be given a urine container for 24-hr urine collection to be brought on the study visit day.

Visit Day:

If they meet the criterion for the study, they will be called in for the study visit where they will undergo blood draws in fasting state. HOMA-IR method will be used to determine insulin resistance. 40 ml of blood will be drawn at this visit.

Subcutaneous fat biopsies will be performed. Participants will be referred to get a DEXA scan within 7 days of getting fat biopsies.

Fat Aspiration Procedure:

Subcutaneous fat tissue aspiration will be performed on abdomen at a 10 cm distance from the umbilicus under sterile conditions and local anesthesia. 0.5-3 gm tissue will be aspirated and cleared from blood and fluids contaminants by centrifugation. The upper adipose tissue will be collected into a separate sterile tube, washed twice with cold sterile PBS and centrifuged to remove the PBS. Total RNA, nuclear extracts and total cell lysates will be prepared from the adipose tissue.

Imaging:

Lean body mass and fat mass, total and regional (appendicular and trunk) will be measured by DEXA scan within 7 days of fat biopsy.

Cognitive score questionnaire:

The subjects will be asked to complete questionnaire to assess their cognitive function on the day of the study visit after they undergo fat biopsy and blood draw.

MMSE (Mini-mental State Examination) test and MoCA (Montreal Cognitive Assessment) questionnaires will be given to be completed.

12.2 Describe what data will be collected.

NOTE: For studies with multiple data collection points or long-term follow up, consider the addition of a schedule or table in your response.

Response:

Clinical Laboratory Assay:

All measurements will be carried out by Quest Diagnostics. Total testosterone and estradiol concentrations will be measured by liquid chromatography-tandem mass spectrometry. Tracer equilibrium dialysis is considered the gold standard for measuring free steroid hormone concentrations and this methodology will be used to measure the free testosterone and free estradiol. SHBG, LH and FSH concentrations will be measured by a solid phase, chemiluminescent immunometric assay. Free testosterone concentrations will also be measured from the concentrations of total testosterone, SHBG and albumin by the formulas of Sodergard et al.

Mononuclear cell Isolation:

Blood samples will be collected in Na-EDTA and carefully layered on lymphocyte medium. Samples will be centrifuged, and two bands separate out at the top of the red blood cell pellet. The mononuclear cell (MNC) band will be harvested and washed twice with Hanks' balanced salt solution. This method yields > 95% MNC preparation.

Quantifications of mRNA Expression by RT-PCR:

Expression of inflammatory mediators involved in insulin resistance and those that mediate insulin signaling will be tested by RT-PCR in mRNA isolated from MNC and adipose tissue. Total RNA will be isolated from MNC and adipose tissue using a commercially available RNAqueous-4PCR kit and adipose tissue RNA Isolation kit (Ambion, Austin, TX). Real-time RT-PCR will be performed using the Stratagene Mx3000P qPCR system (La Jolla, CA), SYBR Green Master Mix (Qiagen, CA), and gene-specific primers for IKK-b, SOCS-3, PTEN, PTP-1B, JNK-1, TLR-4, IL-1b, IR, IRS-1, AKT-2, and GLUT4 (Life Technologies, Frederick, MD). All values will be normalized to the expression of a group of housekeeping genes including actin, ubiquitin C, and cyclophilin A. The normalization factor used is calculated by Gene Norm software and is based on the values of all housekeeping genes used.

Western Blotting:

MNCs and adipose tissue total cell lysates will be prepared, and electrophoresis and immunoblotting will be carried out as described before. Polyclonal antibodies against IR (Abcam, Cambridge, MA), AKT-2, SOCS-3, IKK-b, and actin (Santa Cruz Biotechnology, Santa Cruz, CA) will be used, and all values will be corrected for loading to actin.

Plasma measurements:

Free fatty acid (FFA) levels will be measured by a colorimetric assay (Wako Chemicals, Richmond, VA). ELISA will be used to measure plasma concentrations of glucose (Cayman Chemical), insulin (EMD Millipore, Billerica, MA), CRP (American Diagnostica, Inc.), leptin, adiponectin, tumor necrosis factor (TNF)-a, and interleukin (IL)-1b (R&D Systems, Minneapolis, MN

12.3 List any instruments or measurement tools used to collect data (e.g. questionnaire, interview guide, validated instrument, data collection form).

Include copies of these documents with your submission.

Response:

Please see forms for screening visit and for regular visits

12.4 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).

Response:

Electronic medical records, clinical charts and research files

*12.5 Indicate whether or not **individual** subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings will be shared with subjects or others (e.g., the subject's primary care physician) and if so, describe how these will be shared.*

Response:

Individual participant lab results will be disclosed to the participant upon their request. If the participant requests documentation be shared with another physician, physician office or hospital the participant must come to the research center to collect said documentation and/or the documentation can be mailed to their given home address.

*12.6 Indicate whether or not **study** results will be shared with subjects or others, and if so, describe how these will be shared.*

Response:

Not Applicable. Study results will not be shared with the subjects. However, unidentifiable study results could be published in the form of a manuscript or abstract and will be reported to clinicaltrilas.gov.

13.0 Study Timelines*

13.1 Describe the anticipated duration needed to enroll all study subjects.

Response:

6 months

13.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.

Response:

Up to 7 days

13.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected, and all analyses have been completed).

Response:

12 months

14.0 Setting

14.1 Describe all facilities/sites where you will be conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility, department, and type of room are relevant. Do not abbreviate facility names.

NOTE: Examples of acceptable response may be: "A classroom setting in the Department of Psychology equipped with a computer with relevant survey administration software," "The angiogram suite at Buffalo General Medical Center, a fully accredited tertiary care institution within New York State with badge access," or, "Community Center meeting hall."

Response:

The study will be conducted at the following centers:

Roswell Park Comprehensive Cancer Center – GU oncology clinic and Great Lakes Cancer Care GU clinics; where recruitment of patients will occur

Diabetes and Endocrinology Center of WNY – Where procedures as outlined above will occur.

The Diabetes Research Center has facilities and exam rooms available for infusion studies and presence of study coordinator and registered nurse for data collection and blood work at all times. Equipment include ultra-low freezers for sample storage, centrifuges, microscopes for sample preparation, infusion pumps, ELISA, PCR and immunoblotting instrumentation. CTRC location is a fully equipped laboratory

14.2 For research conducted outside of UB and its affiliates, describe:

- *Site-specific regulations or customs affecting the research*
- *Local scientific and ethical review structure*

NOTE: This question is referring to UB affiliated research taking place outside UB, i.e. research conducted in the community, school-based research,

international research, etc. It is not referring to multi-site research. UB affiliated institutions include Kaleida Health, ECMC, and Roswell Park Cancer Institute.

Response:

☒ **N/A:** This study is not conducted outside of UB or its affiliates.

15.0 Community-Based Participatory Research

15.1 Describe involvement of the community in the design and conduct of the research.

NOTE: Community-Based Participatory Research (CBPR) is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Response:

☒ **N/A:** This study does not utilize CBPR.

15.2 Describe the composition and involvement of a community advisory board.

Response:

☒ **N/A:** This study does not have a community advisory board.

16.0 Resources and Qualifications

*16.1 Describe the qualifications (e.g., education, training, experience, expertise, or certifications) of the Principal Investigator **and** staff to perform the research. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.*

NOTE: If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify a person by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that the person meets the qualifications described to fulfill their roles.

Response:

All study personnel are educated, trained, and licensed as required for their delegated role in this study. All study personnel have also received the required university training and will be trained by the PI before the study starts

The GU team at Roswell Park Comprehensive Cancer Center and Great Lakes Cancer Care GU clinics who will be reviewing the patients' records for recruitment include the attending physicians (Dr. Chatta and Dr. Pili) and the fellows (Dr. Pandey and Dr. Goyal) all of whom are listed on the study.

Describe other resources available to conduct the research.

16.2 Describe the time and effort that the Principal Investigator and research staff will devote to conducting and completing the research.

NOTE: Examples include the percentage of Full Time Equivalents (FTE), hours per week. The question will elicit whether there are appropriate resources to conduct the research.

Response:

The principal investigator supervises the research project and weekly research meetings are conducted to discuss the recruitment rate, resolve and discuss issues related to the conduct, safety, analysis of the study and related publications. PI is expected to spend 5% of his academic time on this research. The co-investigators and study coordinator provide coverage to the research related activity during regular hours..

16.3 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research, if applicable.

NOTE: One example includes: on-call availability of a counselor or psychologist for a study that screens subjects for depression.

Response:

Available medical literature will be provided as deemed appropriate or requested by patient through UB libraries, Pubmed, Google scholar as all the investigators have access to medical literature through listed resources above

The patient will also have access to physician (Investigators and Co-Investigators) who will be available to address any adverse effects or other questions during the course of the study

16.4 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Response:

Education through meetings, conferences and discussions

17.0 Other Approvals

17.1 Describe any approvals that will be obtained prior to commencing the research (e.g., school, external site, funding agency, laboratory, radiation safety, or biosafety).

Response:

As the subjects will be recruited from RPCCC GU oncology clinics and Great Lakes Cancer Care GU clinics. There is a global reliance agreement between Roswell Park CCC and UB IRBs, thus RPCCC will rely on the UB IRB review of this study.

☐ **N/A:** This study does not require any other approvals.

18.0 Provisions to Protect the Privacy Interests of Subjects

18.1 Describe how you will protect subjects' privacy interests during the course of this research.

NOTE: Privacy refers to an individual's right to control access to him or herself. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.

Examples of appropriate responses include: "participant only meets with a study coordinator in a classroom setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."

Response:

Patient charts will be screened at the time of clinical encounter as well as from the BDR according to the study inclusion and exclusion criteria by the clinical staff and physicians of GU oncology group at RPCCC and Great Lakes Cancer Care GU clinics. If the patient qualifies and is of consenting age, the physicians will speak to them about their interests in participating in research. If the patient agrees, they will be asked to make an appointment at the Diabetes and Endocrinology Center of WNY to review and sign the consent. They will do this in a private, screen off area of the research department and will be allowed to discuss the consent in detail with the research coordinator and or study doctor.

Patient will be no notified that it is completely voluntary to participate in the research study and can withdraw at any time.

We will not be accessing any medical information of the patients for whom the services are not provided by our clinic providers

18.2 Indicate how the research team is permitted to access any sources of information about the subjects.

*NOTE: Examples of appropriate responses include: school permission for review of records, consent of the subject, HIPAA waiver. This question **does apply** to records reviews.*

Response:

Consent of the subject and partial HIPAA waiver

19.0 Data Management and Analysis*

19.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.

Response:

The demographic features of the population and screening lab results will be displayed in tables. Statistical analysis will be carried out using SPSS and SigmaStat software (SPSS, IL). All data will be expressed as mean ± S.E of arbitrary units and percent change is calculated from the means. To evaluate similarity between the study groups, baseline values for subject's demographics will be compared using appropriate parametric and non-parametric tests based upon the nature of the data

19.2 If applicable, provide a power analysis.

NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.

Response:

Based on our previous study, HH men have greater insulin resistance by 30% compared to eugonadal men. Therefore, a sample size of 20 patients in each group is sufficient to provide adequate power (80%) to detect a significant difference ($p<0.05$) in insulin resistance of ≥30% between patients with ADT (negligible testosterone) and non-ATD patients (low to normal testosterone) assuming the standard deviation of the diffidence is ≤30%. and a drop-out rate of about 15%.

19.3 Describe any procedures that will be used for quality control of collected data.

Response:

Three investigators and research nurse will double check the accuracy of collected data. All laboratory testing will be standardized using references and standards.

20.0 Confidentiality*

A. Confidentiality of Study Data

*Describe the local procedures for maintenance of confidentiality of **study data and any records that will be reviewed for data collection**.*

*20.1 A. Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, and separation of identifiers and data, as applicable. Include physical (e.g. paper) **and** electronic files.*

Response:

All data records will be stored on password protected computers and or in locked cabinets within the research department. All subject data will be stored on a deidentified coded collection form. Collected data will also be stored on a password protected computer in the research department and all subject files will only be accessible by authorized study personnel. This includes Red cap (research electronic data captures) software.

20.2 A. How long will the data be stored?

Response:

Data storage have no expiration date and will be stored for a minimum of 7 years. The researchers may continue to rely on this for future use in research study.

20.3 A. Who will have access to the data?

Response:

Those physicians, nurses, and laboratory staff that are on all documentation for the study will have access to the data.

20.4 A. Who is responsible for receipt or transmission of the data?

Response:

Those physicians, nurses, and laboratory staff that are on all documentation for the study will have access to the data and can handle transfer of data.

20.5 A. How will the data be transported?

Response:

All data are stored at one location and is not transported unless it is being archived. At that point files will be transferred to Iron Mountain for storage and archiving.

B. Confidentiality of Study Specimens

*Describe the local procedures for maintenance of confidentiality of **study specimens**.*

☐ **N/A:** No specimens will be collected or analyzed in this research. *(Skip to Section 21.0)*

20.6 B. Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.

Response:

The specimens will be stored in the laboratory located at the CTRC located in 875 Ellicott St. Buffalo NY14203. Samples will be stored in a locked -80^{o} C freezer.

20.7 B. How long will the specimens be stored?

Response:

Specimens storage has no expiration date and will be stored for a minimum of 7 years. The researchers may continue to rely on this for future use in research study

20.8 B. Who will have access to the specimens?

Response:

Those physicians, nurses, and laboratory staff that are on all documentation for the study will have access to the specimens

20.9 B. Who is responsible for receipt or transmission of the specimens?

Response:

Those physicians, nurses, and laboratory staff that are on all documentation for the study will have access to specimens and can handle transfer of samples

20.10 B. How will the specimens be transported?

Response:

Samples will be transported by the laboratory technician which will be hand delivered using dry ice in a properly labeled Styrofoam container.

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

☐ **N/A:** This study is not enrolling subjects or is limited to records review procedures only. This section does not apply.

NOTE: Minimal risk studies may be required to monitor subject safety if the research procedures include procedures that present unique risks to subjects that require monitoring. Some examples include: exercising to exertion, or instruments that elicit suicidality or substance abuse behavior. In such cases, N/A is not an acceptable response.

21.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Response:

We do not expect subjects to experience adverse reaction from fat biopsy procedures. However, patients will be under close monitoring by our staff during the entire process of the biopsy procedure. The investigators will assess other risks including the physical, psychological, social, legal and economic harm to these patients. The investigators listed above will carefully watch for any invasion of privacy and breach of confidentiality.

21.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

Response:

Blood Pressure, Height, Weight, and adverse reaction reported by subjects are monitored at the visit

21.3 Describe any safety endpoints.

Response:

NA

21.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

Response:

On site during the visit. We also encourage participants to call us if they develop any adverse reaction

21.5 Describe the frequency of safety data collection.

Response:

The data collection will be done after all study visits

21.6 Describe who will review the safety data.

Response:

The safety data will be reviewed by the principle and sub investigators as well as the research coordinator

21.7 Describe the frequency or periodicity of review of cumulative safety data.

Response:

Safety data will be reviewed every three months during the duration of the study. Study endpoint data will be reviewed once after half of the recruited patients have completed the study and then at the end of the study

21.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

Response: N/A (since you are not listing any safety endpoints)

21.9 Describe any conditions that trigger an immediate suspension of the research.

Response:

Serious adverse reaction/ side effects from blood draws or fat biopsy procedure

- Significant high incidence of SAE and events leading to withdrawal of subjects determined based on the continuous review by the investigators.
-

22.0 Withdrawal of Subjects*

☐ **N/A:** This study is not enrolling subjects. This section does not apply.

*22.1 Describe **anticipated** circumstances under which subjects may be withdrawn from the research without their consent.*

Response:

Serious adverse reactions during fat biopsy procedure (done on the day of study visit only) or DEXA scan or from blood draws (done at both screening visit and study visit).

22.2 Describe any procedures for orderly termination.

NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.

Response:

The principal investigator of the study can remove a participant from the research study without their approval if for any reason he/she feels is appropriate, including: severe side effect, injury or medical condition which may place subjects at risk of further complications if they continue to participate, failure to keep the scheduled appointments, or other administrative reasons

22.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.

Response:

If a subject withdraws from the research, the data collected to that point will be used toward the research finding.

If necessary, they will be asked to complete an end of study visit for their safety.

23.0 Risks to Subjects*

23.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.

NOTE: Breach of confidentiality is always a risk for identifiable subject data.

Response:

The risks associated with the study blood draw are generally considered to be minimal. All subjects will be informed of the complication of administration of intravenous (IV) line, which includes mild bruising at the site of IV line, which should resolve in few days. They will also be informed about the possibility of infiltration of the IV line at the time of performing blood draws in which case another IV line at different site will be secured and this may lead to bruising at more than one sites. Serious risks associated with IV puncture may also include infections and thrombosis. If any of these serious side effects is observed, the patients will be asked to call us immediately or seek immediate medical help.

The risks involved with fat biopsy procedure are also very minimal. This procedure is performed under local anesthesia and therefore study subjects might experience momentary discomfort at the time of giving local anesthesia. There is a small risk of bleeding at the site of incision, but this will be controlled with cotton gauzes and pressure. The risk of infection is very rare as the procedure is done under sterile conditions.

The risks associated with the DEXA scan are generally considered to be minimal. However, subjects may experience some discomfort when placed in the proper positioning for optimal scanning. DEXA scans involve exposure to radiation. This radiation dose is not standard of care and will occur only as a result of participation in the study. At doses much higher than received from a DEXA scan, radiation is known to increase the risk of developing cancer after many years. At the dose subjects will receive, it is very likely that there will be no effects at all.

Patients always run a risk of breach of confidentiality when doing a research trial. However, procedures are in place to minimize this risk as described in the protocol and consent.

23.2 Describe procedures performed to lessen the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.

Response:

We will collect no more than 40 ml of blood on each visit (screening visit and study visit). We will follow standard sterilization procedures. Snacks will be provided at end of study. Safety data will be collected at screening and during the study.

*23.3 If applicable, indicate **which procedures** may have risks to the subjects that are currently unforeseeable.*

Response: N/A

23.4 If applicable, indicate which research procedures may have risks to an embryo or fetus should the subject be or become pregnant.

Response:

NA, this study is limited to male patients only

23.5 If applicable, describe risks to others who are not subjects.

Response:

NA

24.0 Potential Benefits to Subjects*

24.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit.

*NOTE: Compensation **cannot** be stated as a benefit.*

Response:

There will be no direct benefit to the participants from this research study or from the biomarker assessment, and results will not be reported in the clinical record.

25.0 Compensation for Research-Related Injury

☐ **N/A:** The research procedures for this study do not present risk of research related injury (e.g. survey studies, records review studies). This section does not apply.

*25.1 **If the research procedures carry a risk of research related injury,** describe the available compensation to subjects in the event that such injury should occur.*

Response:

Routinely, Buffalo General Hospital, Erie County Medical Center, and/or the University at Buffalo, State University of New York, its agents, or its employees do not compensate for or provide free medical care for human subjects/participants in the event that any injury results from participation in a human research project. In the unlikely event that they become ill or injured as a direct result of participating in this study, they may receive medical care, that will be billed to their insurance, paid by patient or 3rd paying party.

25.2 Provide a copy of contract language, if any, relevant to compensation for research related injury.

*NOTE: If the contract is not yet approved at the time of this submission, submit the current version here. If the contract is later approved with **different language regarding research related injury**, you must modify your response here and submit an amendment to the IRB for review and approval.*

Response:

NA

26.0 Economic Burden to Subjects

26.1 Describe any costs that subjects may be responsible for because of participation in the research.

NOTE: Some examples include transportation or parking.

Response:

All research expenses will be covered. Participants will not be subjected to any out of pocket cost

☐ **N/A:** This study is not enrolling subjects or is limited to records review procedures only. This section does not apply.

27.0 Compensation for Participation

27.1 Describe the amount and timing of any compensation to subjects, including monetary, course credit, or gift card compensation.

Response:

- Screen: $0
- Visit 1: blood draw ($25), fat biopsy ($50), and DEXA ($25)

*Total compensation for all completed visits: $100.00

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

☐ **N/A:** There is no compensation for participation. This section does not apply.

28.0 Consent Process

28.1 Indicate whether you will be obtaining consent.

NOTE: This does not refer to consent documentation, but rather whether you will be obtaining permission from subjects to participate in a research study. Consent documentation is addressed in Section 29.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*
☐ ***No*** *(If no, Skip to Section 29.0)*

28.2 Describe where the consent process will take place. Include steps to maximize subjects' privacy.

Response:

All participants will come to the research department at Diabetes and Endocrinology research to be consented. Participants will be placed in a private room where they can review the consent. Participant questions and or concerns will be address with a member of the study team or research doctor if applicable. The research coordinator will discuss in length the participant's requests for privacy of their PHI

28.3 Describe how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study.

NOTE: It is always a requirement that a prospective subject is given sufficient time to have their questions answered and consider their participation. See "SOP: Informed Consent Process for Research (HRP-090)" Sections 5.5 and 5.6.

Response:

Participants will be made aware that participating in research is completely voluntary, and they may withdraw at any time with no consequence to their routine clinic care. If the patients require time to decide and or discuss partaking in a research study, the subject will be given said time

28.4 Describe any process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.

Response:

The research coordinator and study team are available to answer any question or concerns with the patient during the duration of the research trial. At each study visit, the patient is asked a series of questions to ensure they are on task with the study visits and feel comfortable. Upon departing from their study visit, the patients are told of their next visit and given detail instruction for their next visit. If study is revised or amendment or new information becomes that may affect patients' participation, the patient may be re-consented to ensure patient ongoing consent.

28.5 *Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." Pay particular attention to Sections 5.4-5.9. If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:*

- *The role of the individuals listed in the application who are involved in the consent process*
- *The time that will be devoted to the consent discussion*
- *Steps that will be taken to minimize the possibility of coercion or undue influence*
- *Steps that will be taken to ensure the subjects' understanding*

Response:

☒ We have reviewed and will be following "SOP: Informed Consent Process for Research (HRP-090)."

Non-English Speaking Subjects

☒ **N/A:** This study will not enroll Non-English-speaking subjects. *(Skip to Section 28.8)*

28.6 *Indicate which language(s) other than English are likely to be spoken/understood by your prospective study population or their legally authorized representatives.*

NOTE: The response to this Section should correspond with your response to Section 8.4 of this protocol.

Response:

NA

28.7 If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language, how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study, and any process to ensure ongoing consent. Indicate the language that will be used by those obtaining consent.

NOTE: Guidance is provided on "SOP: Informed Consent Process for Research (HRP-090)."

Response:

NA

Cognitively Impaired Adults

☒ **N/A**: This study will not enroll cognitively impaired adults.
(Skip to Section 28.9)

28.8 Describe the process to determine whether an individual is capable of consent.

Response:

Adults Unable to Consent

☒ **N/A**: This study will not enroll adults unable to consent.
(*Skip to Section 28.13)*

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 28.9 and 28.10) ***and, where possible, assent of the individual should also be solicited*** *(Sections 28.11 and 28.12).*

28.9 Describe how you will identify a Legally Authorized Representative (LAR). Indicate that you have reviewed the "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" for research in New York State.

NOTE: Examples of acceptable response includes: verifying the electronic medical record to determine if an LAR is recorded.

Response:

☐ We have reviewed and will be following "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

28.10 ***For research conducted outside of New York State****, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

This research will not be conducted outside the state of NY

28.11 Describe the process for ***assent of the adults****:*

- *Indicate whether assent will be obtained from all, some, or none of the subjects.* ***If some, indicate which adults will be required to assent and which will not.***

Response:

- ***If assent will not be obtained from some or all subjects, provide an explanation of why not.***

Response:

28.12 Describe whether ***assent of the adult*** *subjects will be documented and the process to document assent.*

NOTE: The IRB allows the person obtaining assent to document assent on the consent document using the "Template Consent Document (HRP-502)" Signature Block for Assent of Adults who are Legally Unable to Consent.

Response:

Subjects who are not yet Adults (Infants, Children, and Teenagers)

☒ **N/A**: This study will not enroll subjects who are not yet adults. *(Skip to Section 29.0)*

*28.13 Describe the criteria that will be used to determine **whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research** under the applicable law of the jurisdiction in which the research will be conducted **(e.g., individuals under the age of 18 years)**. For research conducted in NYS, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."*

NOTE: Examples of acceptable responses include: verification via electronic medical record, driver's license or state-issued ID, screening questionnaire.

Response:

*28.14 **For research conducted outside of New York State**, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

NA

28.15 Describe whether parental permission will be obtained from:

Response:

NA

☐ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☐ Parent permission will not be obtained. A waiver of parent permission is being requested.

NOTE: The requirement for parent permission is a protocol-specific determination made by the IRB based on the risk level of the research. For guidance, review the "CHECKLIST: Children (HRP-416)."

*28.16 Describe whether permission will be obtained from individuals **other than parents**, and if so, who will be allowed to provide permission. Describe your procedure for determining an individual's authority to consent to the child's general medical care.*

Response:

NA

*28.17 Indicate whether assent will be obtained from all, some, or none of the **children**. If assent will be obtained from some children, indicate which children will be required to assent.*

Response:

NA

28.18 When assent of children is obtained, describe how it will be documented.

Response:

NA

29.0 Waiver or Alteration of Consent Process

Consent will not be obtained, required information will not be disclosed, or the research involves deception.

☒ **N/A:** A waiver or alteration of consent is not being requested.

29.1 If the research involves a waiver or alteration of the consent process, please review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure that you have provided sufficient information for the IRB to make the determination that a waiver or alteration can be granted.

NOTE: For records review studies, the first set of criteria on the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" applies.

Response:

29.2 If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response:

30.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 31.0)

30.1 Indicate whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not or if there are any exceptions, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.

NOTE: 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 is sometimes referred to as 'verbal consent.' Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information.

If you will document consent in writing, attach a consent document with your submission. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)". If you will obtain consent, but not document consent in writing, attach the script of the information to be provided orally or in writing (i.e. consent script or Information Sheet).

Response:

☒ We will be following "SOP: Written Documentation of Consent" (HRP-091).

31.0 Multi-Site Research (Multisite/Multicenter Only)*

☒ **N/A:** This study is not an investigator-initiated multi-site study. This section does not apply.

31.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed across all sites.

Response:

*31.2 If this is a multi-site study **where you are the lead investigator**, describe the processes to ensure communication among sites, such as the following. See "WORKSHEET: Communication and Responsibilities (HRP-830).":*

- *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*

- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately in accordance with applicable federal regulations and local laws.*
- *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

Response:

31.3 Describe the method for communicating to engaged participating sites (see "WORKSHEET: Communication and Responsibilities (HRP-830)"):

- *Problems (inclusive of reportable events)*
- *Interim results*
- *Study closure*

Response:

*31.4 If this is a multicenter study **where you are a participating site/investigator**, describe the local procedures for maintenance of confidentiality. (See "WORKSHEET: Communication and Responsibilities (HRP-830).")*

- *Where and how data or specimens will be stored locally?*
- *How long the data or specimens will be stored locally?*
- *Who will have access to the data or specimens locally?*
- *Who is responsible for receipt or transmission of the data or specimens locally?*
- *How data and specimens will be transported locally?*

Response:

31.5 If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Local recruitment methods are described elsewhere in the protocol.

- *Describe when, where, and how potential subjects will be recruited.*

- *Describe the methods that will be used to identify potential subjects.*
- *Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)*

Response:

32.0 Banking Data or Specimens for Future Use*

☐ **N/A:** This study is not banking data or specimens for future use or research outside the scope of the present protocol. This section does not apply.

*32.1 If data or specimens will be banked (stored) for **future use, that is, use or research outside of the scope of the present protocol**, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.*

NOTE: Your response here must be consistent with your response at the "What happens if I say yes, I want to be in this research?" Section of the Template Consent Document (HRP-502).

Response:

The study data/specimens will be stored in a locked closet or -80 freezer at the research facility of the Diabetes and Endocrinology Center of WNY and at research laboratory (875 Ellicott St, CTRC) for at least 7 years

The research staff (study personnel including coordinator) only will be authorized to access data and or specimens

32.2 List the data to be stored or associated with each specimen.

Response:

Patient ID number, study visit information and date of collection will be stored with specimen. Other data stored will include record files of all patients participating in the study, including data collection sheets and lab result..

32.3 Describe the procedures to release banked data or specimens for future uses, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

Response:

No data or specimens will be released to any party outside research team.