The attached document is the study protocol included for the following protocol:

Title: Patterns and Prevalence of FDG Extravasation in PET/CT Scans (Lucerno device)

ClinicalTrials.gov NCT03041090

Document Date: February 14, 2017

Protocol Title: Patterns and Prevalence of FDG extravasation in PET/CT scans

---

X 7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

The participant completes a questionnaire for research purposes.

8. [FOR IRB use only]. Continuing review of research previously approved by a convened IRB only when condition (a), (b), or (c) is met.

a) Previously approved research where
   (i) The research is permanently closed to the enrollment of new subjects;
   (ii) All subjects have completed all research-related interventions; and
   (iii) The research remains active only for the long term follow-up of subjects.

b) Previously approved research where no subjects have been enrolled and no additional risks have been identified.

c) Previously approved research where the remaining research activities are limited to data analysis.

9. [FOR IRB use only]. Continuing review or research not conducted under an investigational new drug application or investigational drug exemption where expedited categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

---

* * * Background, Purpose, Study Procedures * * *

Title

Patterns and Prevalence of FDG extravasation in PET/CT scans

Complete Sections 1 - 16. In sections that allow reference to sponsor protocol or grant, clearly state section and page numbers. Any information that is different or specific to the local site should be in the SLU application. Specify N/A as appropriate. Do not leave any required sections blank.

1. Background

Page numbers from a sponsor's protocol/grant may be referenced in 1a and 1b.

a) **Provide an introduction and background information. Describe past experimental and/or clinical findings leading to the formulation of the study, if applicable. Investigator Initiated studies must cite references in the response provided or attach a bibliography. *<a href="javascript:showPopUpdata('HELP','Application Consideration:**

In this question the IRB requires a brief introduction with supporting background information to describe your study. Do not include overly lengthy descriptions.

Investigator Initiated studies (i.e., the Principal Investigator has conceived, designed, and is conducting the research) are required to cite references in the response or should upload a referenced bibliography in the Attachments section.')">?HELP?*

With the commercialization of the first PET/CT scanner in 2001, this technology has played an ever increasing role in oncology, neurology, cardiology, and other applications. PET with 18F-FDG is used to diagnose, stage, and restage many cases of cancer; the accuracy ranges from 80% to 90% and is often better than that of anatomic imaging (1). Since the introduction of PET/CT, numerous studies have shown that this whole-body dual- technique imaging is better than PET or CT alone for staging and restaging most cases of cancer. The improvement in accuracy coupled with the convenience of presenting anatomic and functional information to physicians has rendered PET/CT the most important cancer imaging technique at present (2). Furthermore, the use of PET/CT has been advocated as a first-line imaging technique for whole-body tumor staging, restaging, and assessing response to therapy for different types of neoplasms (3). Since changes in FDG accumulation have been shown to be useful as an imaging biomarker for assessing response to therapy (4), PET/CT scanning through this combination of molecular and anatomical imaging is playing an ever increasing role as a way to quantitatively measure individual response to therapy and to even evaluate new drug therapies. (5) The standardized uptake value (SUV) is commonly used as a relative measure of the labeled tracer uptake. The SUV is a ratio of the radioactivity concentration in an area of interest to the decay corrected amount of radiolabeled tracer divided by the patients weight in grams. It is believed that the two largest factors that influence SUV are: injected dose and patient size. (5)

Primary factors that impact the delivered dose of FDG include: the uptake duration between injection and scan, residual syringe activity measurement, dose extravasation (also referred to as infiltration) near the injection site, patient weight measurement, clock synchronization for measuring dose assays and scanning, and data entry.

An extravasation or infiltration is a common problem that can occur when the radio-labeled tracer infuses the tissue near the venipuncture site, and can result from the tip of the catheter slipping out of the vein or passing through the vein. Additionally, the blood vessel wall can allow part of the tracer to infuse the surrounding tissue. As a result, the radio-labeled dose being delivered is inaccurate and as Kinahan has pointed out the accuracy of the calculated dose is critically important to the SUV calculations; errors in an SUV calculation in one assessment scan can severely impact patient treatment and research conclusions.

Extravasations/infiltrations may in fact contribute to the wide variability in researcher's efforts to characterize SUV thresholds for clinical decision making. Velasquez found that the "thresholds for metabolic response in the multicenter multiobserver non-QA settings were -34% and 52% and in the range of -26% to 39% with centralized QA". (6) In local practices and even in practices and research centers employing Quality Assurance checks, these issues with SUV calculations have left oncologists and researchers needing to see significant changes in SUV values to be somewhat assured they are making sound treatment decisions or reaching proper research conclusions.
While there is very little published information on FDG extravasation rates, they are not insignificant and the impact on SUV is not fully characterized. Thus, this study hopes to look at the frequency and patterns of extravasation episodes to better characterize their effect on SUV values.

AuthorJournalYearNInf RateComments
Hall, et al (7)
Ohio State UJ Nuc Med200619021% (39)Prospective
Krumrey, et al (8)
St Louis UJ Nuc Med200998
983% (3)
9% (9)Using automated injector

Manual injection Osman, et al (9) St Louis UFrontiers in Oncology201140010.5% (42)Retrospective Silva-Rodriguez, et al (10) U Santiago, SpainMed Physics20141,36718%Retrospective

Please save frequently

b) Describe any animal experimentation and findings leading to the formulation of the study, if there is no supporting human data.

In oncology, whole-body PET/CT is typically performed from the head to the pelvic floor [7](eyes to thighs). The use of the term whole-body is misleading because the most commonly used field of view (FOV) for arms-up whole-body PET/CT protocols includes only the base of skull to the upper thighs and does not include the brain, skull, and large portions of both upper and lower extremities. In such FOV, the most commonly used site of injection, namely the antecubital fossa (inside of the elbow), is frequently not included in the imaging field. In the Frontiers in Oncology article, Osman also determined that based on the commonly used FOV at most PET/CT centers, that when infiltration is present, it may be unnoticed by clinicians in approximately 31% of the cases. (7) [See sources for citations on previous question] Lucerno Dynamics, a privately held company in North Carolina, has also discovered that the static image may be incapable of reporting on the quality of FDG administration during the ~60 minute uptake period. Lucerno's system has been used in two investigational studies at two centers. At one center, the system was used with 8 patients for a total of 15 scans. At the other center, the system was used with 40 patients for a total of 85 scans. Similar rates of infiltrations were found to those described in the published articles. Based on this experience, Lucerno has found that infiltrations can partially resolve during the uptake period, so that even if they are visible in the PET image, the image may not reveal the extent of the infiltration. This could severely and negatively impact research and therapy decisions and thus patient outcomes. The Lucerno devices (Lucerno ID) are nonsignificant risk devices that add only 2-3 minutes to the current standard of care PET/CT scanning process. Lucerno ID sensors are applied to the patient's skin before the injection of the radiotracer and are removed after the FDG uptake period and prior to the PET/CT imaging process. The Lucerno ID has the ability to identify infiltrations, whether they are within or outside the FOV of reviewing clinicians, and can alert clinicians before their patient undergoes a compromised PET/CT scan due to the infiltration. This technology can prevent patients from receiving the additional CT radiation exposure of a compromised scan, can save cost, and can improve patient outcomes by ensuring more accurate PET scan interpretation.

2. Purpose of the study

a) Provide a brief lay summary of the project in <200 words. The lay summary should be readily understandable to the general public.

PET (Positron Emission Tomography) images are used to help make patient management decisions in staging and treatment assessment, often after a cancer diagnosis. Improper injections of PET tracers (dye) may occur approximately 15% of the time. This is known as extravasation or infiltration, and it compromises the doctor's ability to read the PET image. Often, the site where the tracer is injected into the vein (usually in the inside of the elbow) are not in the images taken, so reading physicians are unaware that an extravasation has occurred.

Protocol Title: Patterns and Prevalence of FDG extravasation in PET/CT scans

---

Technology exists to capture time activity curves (amount of tracer in a location over a period of time) during the PET tracer uptake period (usually once the tracer is injected, the tracer circulates for 60 minutes prior to images), which can enable physicians to accurately detect extravasations. This information is currently unavailable to physicians reading routine PET/CT scans.

Time activity curves information gathered from these sensors during the circulation period appear to match the brief pictures taken approximately 70 minutes after the tracer injection.

This study will determine if these time activity curves correspond to PET images of the injection site taken during the tracer uptake period. If time activity curves correspond to PET images, they can be used to determine if the tracer was properly injected. If there was an improper injection, clinicians can be alerted to this fact and interpret the image with this additional information.

Page numbers from a sponsor's protocol/grant may be referenced in 2b and 2c.

b) List your research objectives (specific aims & hypotheses of the study).

The study will try to answer the following questions:
•How often do infiltrations of FDG occur in routine PET/CT imaging?
•Can the Lucerno ID (sensor device) accurately determine the presence or absence of an extravasation as confirmed by PET imaging?
•Can patterns be identified in the conditions that tend to lead to extravasation?
•Is there a way to quantify the impact of an extravasation on the injected dose, and thus the SUV calculation?

Our hypothesis is that the Lucerno ID device accurately captures dose extravasations. Data extracted from Lucerno ID may help quantify extravasation and, in so doing, may allow for developing correction factors for measured SUV.

Please save frequently

c) Describe the study design (e.g., single/double blind, parallel, crossover, control, experimental, observational, etc.). If the study is investigator-initiated, a timeline for individual subject recruitment, follow-up, and analysis for the study is required. Also, indicate if the subjects will be randomized.

Investigator initiated, non blinded, experimental, non-randomized study

d) If subjects will be given placebo, please justify placebo use. *?HELP?*

N/A

3. Study Procedures

a) N Is this project a multicenter study (i.e., same project is conducted elsewhere by a different investigator) OR does this study involve conduct of research at multiple sites?

Is SLU acting as a coordinating center for other sites OR is the SLU PI a direct recipient of a federal grant for this research? If yes, complete and attach the Supplemental

Application for Coordinating Center Activities.

Will the SLU site be participating in all parts/procedures/arms of the study?

If No, explain what SLU will NOT participate in:

Please save frequently

Page numbers from a sponsor's protocol/grant may be referenced in 3b, 3c, and 3d.

b) **Describe all the procedures, from screening through end-of-study, that the human subject must undergo in the research project, including study visits, drug treatments, randomization and the procedures that are part of standard of care. Specify which procedures are for research and which are standard of care. Please note: The box below is for text only. If you would like to add tables, charts, etc., attach those files in the Attachment section (#16).**

Patients will be identified once they arrive for their standard of care PET/CT exam. If it is determined there is time and a sensor device is available, a subject will be asked about interest in participation. If they are interested, an informed consent dialogue will occur between patient and engaged team member such as a PET technologist, physician, or research coordinator. The informed consent document will be signed and retained (behind two locks) by engaged members of the research team. This includes the PI, other investigators (MDs), engaged PET technologists and/or the research coordinator.

Once consent is obtained the patient will continue on with the standard of care screening process (name, DOB, height, weight, eating status, etc. will be obtained for the standard of care PET/CT exam). Lara Systems is planned for use once we get this system which is planned for the week of 10/17/2016. Our plan would be to still use the LD1 ID until we get the Lara device or as a back up if the Lara device is not working properly. Just before the radioactive FDG is injected, the four sensors (injection site, contralateral arm - similar position to injection site, liver, and over the subclavian area) on the Lucerno ID device will be placed on the subject by the PET/CT technologist. The device sensors will remain in place for the FDG uptake period (typically 60-90minutes). The patient will be lying on the scanning table or in a reclined chair for this uptake period, depending on the availability of the imaging table. During the uptake period, if the scanner and imaging table are available, the subject will have dynamic PET only images taken to correlate sensor data with imaging. This is not a necessary part of the protocol and will only be performed if the scanner is available. If the PET/CT scanner is not available, the sensors will be placed in the same locations and at the end of the uptake period, sensor only data will be retained After the uptake time is complete, the sensors will be removed by the technologist and the patient will proceed on with their standard of care PET/CT imaging. The patient will not receive any extra radiation due to the study and should only add 5 minutes to the time of their PET/CT scan.

The study team will then upload the sensor data to a PC in the PET/CT department where it will be coded and sent to Lucerno Dynamics via a software for analysis. If requested, the coded PET data obtained during the uptake phase (no additional radiation involved with this imaging) will be complied and shared with Lucerno Dynamics. The patient will also be asked to complete a quick survey on the comfort of use for the Lucerno ID device. This coded paper survey will be shared with Lucerno Dynamics for further development of this device.

c) **If the proposed study is a clinical trial where a drug, vaccine, device or other treatment is compared to a placebo group or comparison treatment group, what are the guidelines or endpoints by which early decisions regarding efficacy or lack of efficacy can be made? For example, it may be reasonable to stop enrollment on a study when efficacy has already been**

clearly demonstrated, to avoid unnecessary enrollments of additional subjects. Alternatively, it may be reasonable to stop enrollment when it is clear that efficacy will never be demonstrated, given the statistical power of the study as designed. Describe the guidelines that are in place to assist in making these determinations, if relevant to the proposed study.

This study does not include a control group, so there will be no comparison or efficacy measured.

d) Describe how data analysis will be performed (statistical tests, methods of evaluating data) and indicate the smallest group/unit for which separate reporting will occur. For studies involving a questionnaire, if data and reliability information are available, please describe or provide references. For full board, unfunded studies describe sample size determination and power analysis. If none, please justify.

The coded data (information will have study number only) will be reviewed by Lucerno Dynamics individually after each patient to look for quality. The quality will be reviewed to assess the injection site data visually and with time activity curves. Interval analysis will be done once significant recruitment has been achieved and reported if seen fit by SLU and Lucerno Dynamics. The data will be reviewed to look at group data and injeciton quality.

Please save frequently

e) State if deception (including incomplete disclosure of study purpose/procedures) will be used. If so, describe the nature of the deception and provide a rationale for its use. Also, describe debriefing procedures or justify a waiver of the requirement to debrief. NOTE: for studies using deception, an alteration of consent must be justified in the Informed Consent section of the protocol (#13) and the debriefing script/statement must be uploaded in the Attachments section (#16). <a href=http://www.slu.edu/Documents/research/irb/Deception_Incomplete.doc target=_blank > See IRB Deception Guidelines.

f) Is there an accepted standard of care and/or standard practice at SLU for the condition/disease/situation being studied? This information will assist in comparing the risk/benefit ratio of study procedures relevant to usual care that would be received outside of the research context. *?HELP?* N

If yes, please describe the standard of care and standard practice at SLU for the condition/disease/situation being studied.

g) Does this study involve any diagnostic imaging, labwork or genetic testing that could result in clinical discovery (diagnoses, genetic mutations, etc.)? Note that this could include discovery that is expected (related to the research) or incidental (not related to research aims, but possible, like a mass/shadow found in imaging despite not looking for it). Y

If yes, please describe and include whether there are plans to share findings with study participants.

This would be rare as these are additional images in the same location as the standard of care images; however, this is always a possibility with additional imaging. If something unexpected or unknown is discovered on the images, the reading physician will review with the Primary Investigator and inform the referring physician.

Protocol Title: Patterns and Prevalence of FDG extravasation in PET/CT scans

---

h) **Is this study subject to the NIH Genomic Data Sharing Policy?** **N**

The NIH GDS policy applies to all NIH-funded research that generates large-scale human genomic data as well as the use of these data for subsequent research and includes: genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, metagenomics, epigenomic and gene expression data, irrespective of NIH funding mechanism. Click here for more specific examples.

---

* * * Radioisotopes or Radiation Machines * * *

You have not selected the Radioisotopes option in the General Checklist. If you would like to add Radioisotopes information, please select the option to enable this section.

4. Radioisotopes or Radiation Machines

In this section, investigators must enter all radiation usage associated with the protocol.

Important: Protocols that involve non-standard of care radioactive materials (which includes the terms "radioisotopes", "radionuclides", "radiopharmaceuticals", and "nuclear medicine studies", e.g., "PET", "MUGA", "Zevalin", and/or specific radionuclides such as "F-18", "Tc-99m", "Th-201", "I-131", "Ra-233", "Y-90", etc.) will receive review by the Radiation Safety Officer (RSO) and/or Radiation Safety Committee (RSC). In these cases, submission to the RSO/RSC should occur first, even before submission to IRB. For more information on how to submit for radiation safety review, see RSC instructions or contact the Radiation Safety Officer at 977-6895.

(1) It is the responsibility of the PI to assure the accuracy and completeness of the data submitted in this section, consistent with guidelines provided below. (2) For projects requiring radiation procedures, please refer to this guidance.

a) **If applicable, list and quantify the radiographic diagnostic and therapeutic procedures associated with this protocol by clicking "Add" and adding to Table 1 below. (Includes X-ray, fluoroscopy, CT, radioactive materials, nuclear medicine, PET-CT, radiation oncology, accelerator, Cyber Knife procedures, etc.)**

1. **Radiation Procedure:**	PET/CT
2. **Total number of exams:**	1
3. **Are the procedures being performed as a normal part of the clinical management for the medical condition that is under study SOC (Standard of Care)?**	Y
If yes, specify the number of exams for each listed procedure that are SOC.	1

NOTE: If all procedures are SOC (i.e., #2 and #3 are the same), you are finished with this procedure box. If there are procedures that are NOT SOC, proceed with this section.

4. **Are the procedures being performed because the research subject is participating in this project (e.g., extra CT scans, more fluoroscopy time, additional Nuclear Medicine Studies, etc.), i.e., Not Standard of Care?**	N

Protocol Title: Patterns and Prevalence of FDG extravasation in PET/CT scans

---

If yes, specify the number of exams for each listed procedure that are NOT SOC.

5. **Estimated Effective Dose per Procedure (mrems):** 0

   Specify the estimated effective dose for each procedure that is NOT SOC. You may use data from the DUKE Radiation Safety Committee Website:
   Adult Patients: CLICK HERE.
   Pediatric Patients: CLICK HERE.
   Use of additional references that may provide a higher degree of accuracy of radiation dose estimates for procedures at Saint Louis University Hospital are encouraged. All references, including use of the Duke website, must be specified below.

6. Effective Dose Subtotal (mrems): 0
   Calculated by multiplying the Number of procedures that are NOT SOC (question #4) by Estimated Effective Dose per Procedure (question #5).

7. **References. Specify the resource/reference used for estimating the dose for this procedure.**

b) Total estimated research radiation dose * : N/A

* Calculate from the table above by adding the Effective Dose Subtotals for all procedures.

NOTE: Informed Consent Radiation Exposure Risk Statement- The applicant must insert the appropriate Informed Consent Radiation Exposure Risk Statement template language into the SLU IRB Informed Consent, inclusive of applying the total estimated research radiation dose specified in item b) from the table above, as instructed in the SLU IRB Informed Consent Template. Contact the IRB Office at 977-7744 or irb@slu.edu with any questions.

---

* * * Devices * * *

5. Devices

a) Please list in the space below all investigational devices to be used on subjects during this study.

b) Please list in the space below all FDA approved devices to be used on subjects during this study.

FDA Approved Devices

Protocol Title: Patterns and Prevalence of FDG extravasation in PET/CT scans

---

Device Name	Manufacturer	Provide IDE #. Documentation of IDE # required unless imprinted on sponsor protocol (attach in section #16).
Lucerno ID	Lucerno Dynamics	

1. **Device Name** — Lucerno ID
2. **Manufacturer** — Lucerno Dynamics
3. **Describe the device to be used and attach the device manual in section #16.**

   Lucerno ID device is made by Lucerno Dynamics and is a lightweight sensor that can adhere to skin and obtain radioactive counts. Lara is also a device made by Lucerno Dynamics and is a lightweight sensor that can adhere to skin and obtain radioactive counts. The LD1 and Lara Lucerno devices (Lurcerno ID) are both attached to the subject in the same manner and are considered non-significant risk.
4. **Provide the PMA approval or 510(k) clearance number or attach letters in section #16.** — document titled 2015-02-17 NSR Determination_signed.pdf
5. **Does the research involve use of a commercially available device for an unapproved purpose?** — N
6. **This device research is:Note: Attach documentation/justification in section #16.**

   Exempt from IDE regulations, (submit required attachments)

   Non-Significant risk, (submit required attachments)

   Significant risk, (submit required attachments)

The risk determination should be based on the proposed use of a device in an investigation and not on the device alone.

7. **Provide IDE #. Documentation of IDE # required unless imprinted on sponsor protocol (attach in section #16). See Guidance.**
8. **Who holds the IDE? (Could be manufacturer, study sponsor, or an individual investigator acting as the 'sponsor').**
9. **If a SLU Investigator is serving as sponsor-investigator of the IDE, click Yes to assure that the additional FDA requirements will be followed.** — Yes, the additional FDA requirements will be followed.

---

* * * Drugs, Reagents, Chemicals, or Biologic Products * * *

6. Drugs, Reagents, Chemicals, Biologic Products, or Dietary Supplements, Vitamins, and Other Food Agents

Pilot	Phase I	Phase II
Phase III	Phase IV	Not Phased

List placebo if it is considered a drug (contains more than inactive ingredients). For example, normal saline is considered a drug that should be listed, whereas placebo tablets are usually inert ingredients that do not need to be listed.