Imperial College London

Investigating Brown Adipose Tissue Activation in Humans

Study Protocol

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Version 3

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Imperial College London

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BACKGROUND

Obesity is a leading cause of premature morbidity and mortality in the UK and worldwide. Recent UK Government figures state that 65% of men, 58% of women and 28% of children in the England are overweight or obese[1]. Calorie restriction and increased exercise are effective but difficult to sustain. The only therapeutic options currently available are anti-lipid absorption medication (which is largely ineffective) and bariatric surgery (known as the "gastric bypass" andassociated with significant risks). There is therefore an urgent need for other anti-obesity therapies to be investigated and developed.

Gut hormones hold great promise as potential agents to treat obesity. Studies of gut hormones infused into human volunteers have demonstrated that they reduce appetite, induce early satiety (the sensation of feeling full) and increase energy expenditure (the quantity of energy used by the body)[2,3]. We have also shown that the sustained weight loss achieved following bariatric surgery is mediated in part through an elevation in the patients' own gut hormones [4]. There is emerging evidence that the appetite-altering effects of gut hormones are mediated in the brain[5]. However, whilst the elevation in energy expenditure induced by gut hormones can be reliably and safely measured in humans using indirect calorimetry[3], the mechanism by which they actually exert this effect in humans remains unclear.

Depots of functioning brown adipose tissue (BAT) have recently been identified in adult humans[6-8]. BAT is likely to be an importanteffector by which circulating hormones increase energy expenditure, due to its unique ability to dissipate metabolic energy (from ingested food and fat stores) as heat (BAT thermogenesis). Studies in rodents indicate that gut hormone administration increases BAT mass and thermogenesis[9,10]. However, the effect of gut hormones on BAT activity in humans is unknown.

Combined positron emission tomography (PET) and computed tomography (CT) scanning is currently the standard technique for assessing BAT activity in humans. Using 18-flurodeoxyglucose (^{18}F-FDG, a radioactive glucose analogue which is avidly taken up by thermogenically active brown adipocytes), PET-CT has identified BAT activation in response to both cold temperature and insulin infusion [7].There are two weaknesses with PET-CT for BAT imaging. The first is that it is unable to visualise BAT unless it is

stimulated. This is because on a CT scan, brown and white fat stores look identical. Only when brown fat is stimulated (usually by exposing the volunteer to cold temperatures) does brown fat take up more radioactive tracer and become identifiable on a PET-CT scan. Secondly, these scans involve exposre to ionising radiation.

For these reasons other imaging modalities are being investigated. The first is magnetic resonance imaging. By taking advantage of small differences in water content between the two types of fat, MRI is being developed to detect BAT deposits within WAT, even in the unstimulated state [13,14]. Secondly, infrared thermal imaging cameras can be used to safely and non-invasively measure the difference in temperature of BAT compared with surrounding tissues. Activated BAT releases energy (in the form of heat) and thus activated BAT will be at a higher temperature than surrounding non-activated BAT tissue. Recent data suggests that thermal imaging can be used to assess BAT activation in humans aged between 3-58 years[12] in response to cold temperature stimulation. However there are no studies validating the technique of thermal imaging or Magnetic Resonance Imaging (MRI)for measurement of BAT with the gold standard technique of PET-CT.

OBJECTIVES

This project aims to investigatebrown adipose tissue activation in humans. To do this we will:

1. **assess BAT activation in response to glucagon infusion in healthy volunteers using PET-CT, thermal imagingand MRI;**
2. **utilise thermal imaging to assess BAT activation in clinical scenarios and conditions where increased BAT activation is anticipated.**

GENERAL METHODOLOGY STATEMENT

Intravenous infusions by the Section of Investigative Medicine follow protocols established after extensive experience investigating the physiological role of numerous peptide hormones in humans. Single and combinationinfusion of gut hormones have been performed on large cohorts of human volunteers within this department without adverse event (ethics refs: 2002/6261 and 09/H0707/76).

This healthy human volunteer investigation will comply in full with the standard procedures that were developed at the behest of the RPMS ethics committee. This followed extensive discussion with a number of experts and their purpose is to ensure safety and efficacy in peptide preparation and administration. The procedures used in this study will be the same as those used in previous studies carried out by our group (ethics refs: 2002/6261 and 09/H0707/76).

Indirect calorimetry is a well-established technique in our laboratory. The calorimeter captures expired air from a large, transparent canopy, worn over the head and thorax, and is typically very well tolerated. Thermal imaging remotely measures the emission of infrared radiation from the surface of the skin using a small camera, does not involve ionizing radiation, and therefore does not expose the subjects to any additional risks.

^{18}F-FDG PET-CT imaging is a well-established methodology and theImanovagroup has conducted a number of similar studies over the last 6 years. While PET studies involve additional ionizing radiation exposure for the participants, the levels of exposure from this study are in line with other experimental protocols conducted in healthy volunteers. We are proposing a T2* (echo planar) MR scanning protocol in a 3T scanner to perform fat extraction and MRI thermography. Magnetic resonance imaging is safe and widely used in clinical practice. It does not involve ionizing radiation.

METHODFOR OBJECTIVE 1

To assess BAT activation in response to glucagon infusion in healthy volunteers using PET-CT, thermal imagingand MRI.

We have chosen one gut hormone, glucagon, to investigate using both thermal imaging, PET-CTand MRI. We have previously shown that glucagon induces a large rise in energy expenditure (EE) in healthy volunteers without any side effects[3]. To minimise radiation exposure, only volunteers who have a demonstrable rise in energy expenditure (EE) in response to glucagon infusion will undergo PET-CT scans.

Recruitment

Healthy male volunteers will be recruited via posters, newspaper advertisements and/or e-mail distribution lists. Initially, the volunteer will be asked to contact the investigators. After a brief telephone call to assess that the volunteer broadly fits the inclusion criteria (age, weight, current illnesses), they will be invited to attend a full screening visit. Based on data from previous studies of gut hormone infusions carried out by our group, and the existing literature on ^{18}F-FDG PET-CT imaging of BAT, we estimate that we will need to recruit n=20 volunteers (with n=16 needed to complete this arm of the study).

Screening Visit

All volunteers will undergo medical history taking and examination. Inclusion and exclusion criteria are detailed below. Basic investigations performed prior to inclusion will comprise height and weight measurement, blood tests (full blood count, urea and electrolytes, liver function tests, thyroid function tests and plasma glucose) and an electrocardiogram.

Informed consent is a crucial part of the study. All of the research doctors undertaking this process are MRCP qualified and experienced in taking informed consent for human research studies according to GCP guidelines. They will also have undertaken radiation protection courses, and will have sufficient expertise to discuss the ionising radiation aspects of the study with volunteers.

Inclusion criteria for healthy volunteers for Objective 1

- Age 18-40 years*
- Male
- Healthy as determined by screening history and investigations detailed above.
- Body mass index 18-25 kg/m^2 and a stable weight for 3 months.

Exclusion criteria for healthy volunteers for Objective 1

- History of alcoholism or substance abuse within the last 5 years.
- History of major medical or psychiatric disease.
- Any other condition, including social circumstances, deemed likely to interfere with the ability to participate reliably in the trial.
- History of hypersensitivity to any of the components of the infusions.
- Treatment with an investigational drug within the preceding 2 months.
- Treatment with any drug that is known to stimulate or inhibit BAT activation.
- Volunteers who have donated, or intend to donate, blood within three months before or following study completion.
- Claustrophobia.

- Pacemaker, metal implant, clips, implanted device, shrapnel or bullet, metal in eyes that precludes magnetic resonance imaging.
- Significant structural abnormality on brain scan.
- Cumulative radiation exposure in the preceding 12 months totalling 10mSv or more.

*The lifetime risk for a healthy adult of developing a fatal malignancy following exposure to ionising radiation similar to that expected in our study is approximately 1:1800. This is low compared with the average UK cancer mortality rate of about 1 in 4, leading to a marginal added risk due to the study participation. However, higher BAT activation is expected in young adults[11]. We have therefore decided to enrol young adults in our study, in order to be able to demonstrate the principle of glucagon induced BAT activation in a small pilot study. Thus, while the risk e risk remains very small but is slightly greater in younger subjects. Given that only those subjects who have demonstrated significant rises in EE in response to glucagon would be put forward for PET-CT scanning, we expect to be able to achieve the aims of our study with a minimal number of subjects exposed to additional ionising radiation.

Study Visitsfor Objective 1

After the screening visit, volunteers will be invited to attend 7 study visits. There will be a time interval of at least two days between visits.

During Visit 1, 2 and 3, volunteers will receive an intravenous infusion of (A) saline under thermoneutral conditions, (B) saline with cold stimulationor(C) glucagon, allocated in a randomised single-blinded fashion. Resting and stimulated energy expenditure will be measured with a standard indirect calorimeter (as previously used successfully in this laboratory[3]). Supraclavicular deposits of BAT will be imaged using infrared thermography (i.e. thermal imaging).

If the volunteers have demonstrated a measurable rise in EE or BAT activation during these first 3 study visits, they will be asked to complete Visits4to 7. During Visit 4 and Visit 5, volunteers will receive an intravenous infusion of (A) saline or(B) glucagon, allocated in a randomised single-blinded fashion, and undergo a 60-minute dynamic FDG PET-CT scan.During Visit 6 and Visit 7, volunteers will receive an intravenous infusion of (A) saline (with cold stimulation) or (B) glucagon, allocated in a randomised single-blinded fashion, and undergo a 60-minute MRI scan.

Details of Study Visit Preparation, Blood Sampling, GlucagonInfusion, and Cold Stimulation.

To minimise the usual hepatic glycogen depletion that occurs during an overnight fast, participants will be asked to avoid alcohol and strenuous exercise for 24 hours prior to each study visit, and to consume a high energy snack as late as possible on the evening before each visit, in addition to their normal dietary intake. When they arrive on the ward in the morning, two pink (20G) intravenous cannulaewill be inserted – one in each arm.

The infusion rate will be calculated according to body surface area, with the dose of glucagon based on our previous published experience of administering the hormone [3]. The expected maximum glucagon dose will be up to an equivalent of 100 ng/kg/min. To minimise peptide adsorption to syringes and infusion lines, the vehicle for intravenous infusions will be Haemaccel, or an equivalent safe colloid,diluted with 0.9% saline. The infusion will last 90 minutes. During the course of each study visit the volunteer will undergo serial venous blood samples. There will be a maximum of ten 8 ml samples taken per visit. These will be tested for circulating hormones, glucose and other metabolites. Over the course of the seven studyvolunteers will donate no more than a total of 560ml of blood. At regular time points, the volunteers will also be asked about their general wellbeing. Heart rate and blood pressure will be measured periodically using conventional ward equipment.

BAT in humans has been reliably demonstrated to be activatedby exposure to cold temperatures. Thus, cold exposure can be used as a positive control method. We will do this by placing the volunteers' hands in a bowl of cool water or using a cooling vestfor the duration of the infusion. We will ensure that the volunteer does not become uncomfortably cold, since we specifically want to avoid shivering.The cooling vest will be a commercially available unit that can be comfortably worn on the torso (as pictured below). The vest has integrated tubing through which cold water can be pumped to cool the volunteer. Temperatures can be accurately controlled using a thermostat on the water pump, and we are aiming to cool the volunteer comfortably. If the volunteer starts to shiver or is uncomfortable will will raise the temperature or remove the vest immediately.

Details of Indirect Calorimetry

On Visits 1, 2 and 3, volunteers will undergo indirect calorimetry to measure energy expenditure in response to glucagon or saline infusion. After arrival and insertion of the intravenous cannulae (but prior to the start of the intravenous infusion), participants will be placed inside the comfortable canopy of thecalorimeter, whilst reclining on a bed.

The calorimeter captures expired air from a large, transparent canopy, worn over the head and thorax, and is typically very well tolerated. Each participant will be asked to lie in a semi-recumbent position under the canopy. Once the carbon dioxide content of the air entering the chamber has stabilised, measurements will be taken for 20 minutes in order to assess the participants' basal metabolic rate (BMR) and respiratory quotient (RQ).A second set of measurements will be taken 60 minutes after the start of the intravenous infusion (for a period of 20 minutes) to assess the effect of the infusion on the participants' metabolic rate.

Details of Thermal Imaging

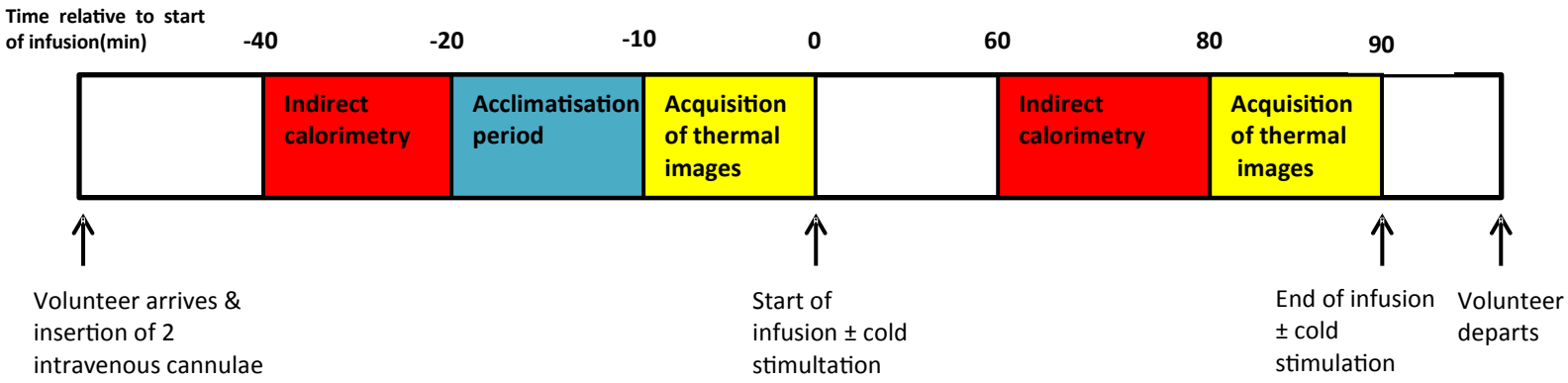
Thermal images will be obtained during Visits 1, 2 and 3 after the periods of indirect calorimetryhave been completed. The area of the body that will be imaged (in a single frame) will include the lower head, neck and upper thorax. Volunteers will be asked to wear a vest style T-shirt on the day of the study in order to facilitate this, and an additional wrap will be provided for modesty. The volunteer will sit facing the thermal imaging camera (FLIR T440bx) mounted on a tripod. Participants will sit still in an upright position with arms adducted, shoulders relaxed and horizontal for the duration of the imaging to ensure image quality. They will be seated away from direct heat sources and open windows. Room temperature will be maintained between 19-23^{o}C.

The thermal imaging camera will be positioned 1.0 – 1.6 m from the chair on which the volunteer is seated. The optimal distance for image acquisition will be the distance at which the volunteer's shoulders fill the camera-viewing screen. The distance from the chair to the camera will be recorded. Three consecutive images will be taken of a temperature controlled block in order to calibrate the images (i.e. these will be control images).

After the acclimatisation period and acquisition of control images, study images will be acquired continuously for 10 minutes prior to the start of the infusion. End-infusion study images will be acquired continuously during the last 10 minutes of the infusion. The visit protocol for Visits 1, 2 and 3 is outlined in Figure 1.

From each thermal image stream, using existing methodology[12], the maximal temperature over defined regions of interest in the neck region will be recorded. Data will be analysed using Prism.

Figure 1 – Visit Protocol for Study Visits 1, 2 and 3 for Healthy Volunteers



Details of PET-CT

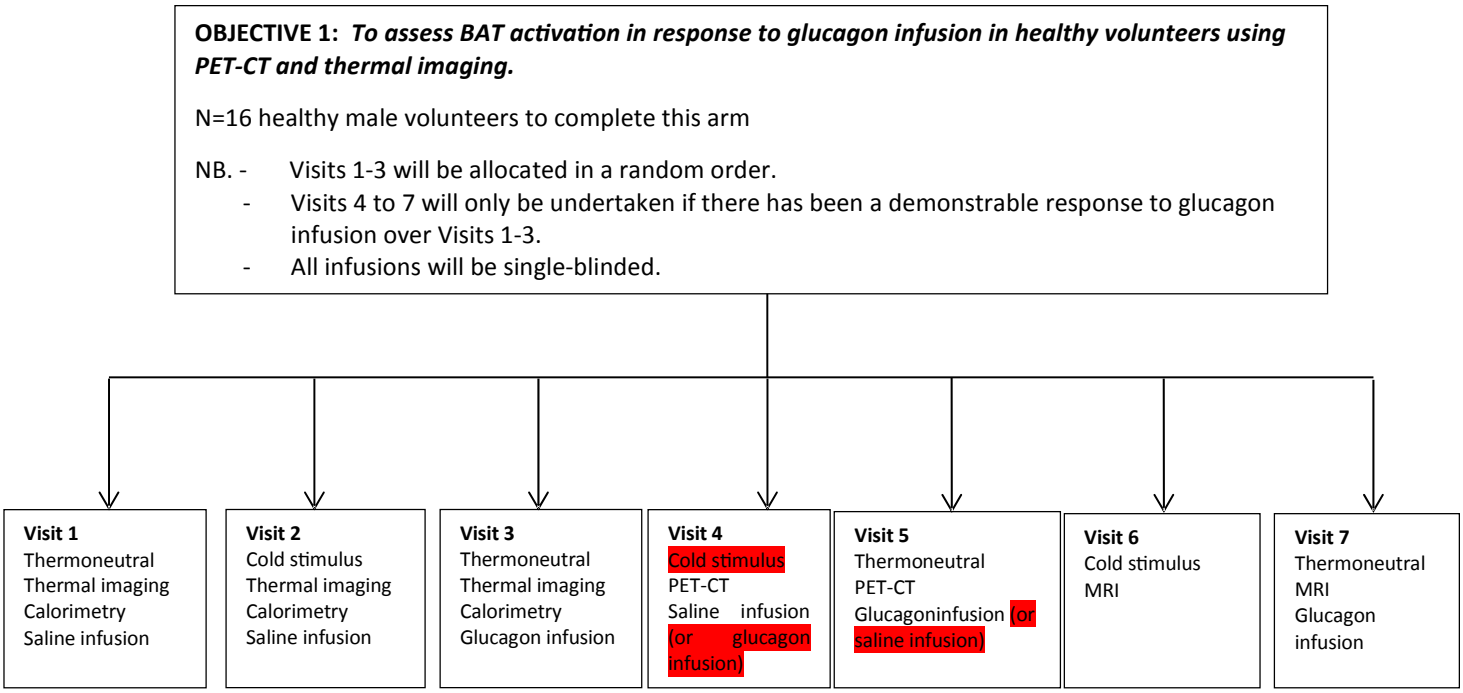
Volunteers who have demonstrated rises in EE or BAT activation in response to glucagon infusion over Visits 1-3 will be invited to attend Visits 4 and 5, to measure BAT activation using PET-CT at the Imanova Imaging Unit in Hammersmith Hospital. The study timetable for Objective 1 is shown in Figure 2.

Positron emission tomography (PET),has become a routine research tool over the past 25 years. We will use 18-flurodeoxyglucose (^{18}F-FDG), an analogue of glucose to measure the metabolic rate of BAT. Metabolically active brown adipocytes avidly take up glucose, and are expected to increase their metabolic rate, and therefore the uptake of both glucose and 18F-FDG following stimulation with cold or glucagon. ^{18}F-FDG has been previously used to study BAT activation with PET[6-8]. Dynamic PET data will be collected from the upper torso and neck will be acquired, areas known to contain significant amounts of BAT. In order to quantify the PET data adequately, a low-dose CT scan of the upper torso and chest will be conducted prior to each PET scan, in order to estimate tissue attenuation of the PET signal. The ionizing radiation exposure from the two ^{18}F-FDG PET scans (maximal administration of 185MBq per scan) and two low-dose CT scans of the upper torso, is expected to be approximately 9.5mSv.

At each PET-CT visit two intravenous cannulae will be inserted into the forearm or cubital veins in order to administer the ^{18}F-FDG and glucagon or saline infusion (via one cannula), and collect blood samples during the course of the PET-CT scans (via the second cannula). The glucagon or saline infusion will be initiated and then the volunteers will be then be led into the scanner room where the 18F-FDG bolus will be is administered immediately prior to the scan. Subjects will undergo a brief low dose CT followed by a 60-minute dynamic PET scan. Volunteers will be lying on a bed throughout the scan and can communicate with (and will be reassured by) the radiographer and researchersas necessary.

Images will be quantified by deriving standard outcome parameters for the defined regions of interest, using established methodology. All of the PET-CT scans will also be formally reported by a consultant radiologist. Although the PET-CT scans are not performed with the aim of clinical diagnosis, and this may not be considered of diagnostic quality, they may reveal an incidental finding relevant to the subjects health status. In this situation the report would be communicated to the volunteer and the volunteer's GP, who would arrange the appropriate specialist referral. A significant abnormality would exclude that volunteer from further participation in the study.

Figure 2 – Study Timetable for Objective 1



Details of MRI

Volunteers who have successfully completed visits 1-5 will also be invited to attend Visits 6 and 7. The objective of these visits is to measure BAT activation using MRI at the Imanova Imaging Unit, Hammersmith Hospital.

Magnetic Resonance Imaging (MRI), has become a routine clinical and research tool[13,14]. Our 60 minute scanning protocol is designed to firstly differentiate BAT from WAT in the resting (baseline) state (utilizing differences in their relative water contents) and then to measure BAT temperature change following stimulation with either cold or glucagon infusion. MRI data will be collected from the upper torso and neck, areas known to contain significant amounts of BAT. MRI does not involve the use of ionizing radiation.

At each MRI visit two intravenous cannulae will be inserted into the forearm or cubital veins. One will be used to administer the glucagon or saline infusion and the other for blood sampling (as in all previous study visits). Volunteers will be lying on a bed throughout the scan and can communicate with (and will be reassured by) the radiographer and researchers as necessary.

All of the MRI scans will also be formally reported by a consultant radiologist. Although the MRI scans are not performed with the aim of clinical diagnosis, and thus may not be considered of diagnostic quality, they may reveal an incidental finding (not previously picked up on the CT scan) relevant to the subjects health status. In this situation the report would be communicated to the volunteer and the volunteer's GP, who would arrange the appropriate specialist referral. A significant abnormality would exclude that volunteer from further participation in the study.

METHOD FOR OBJECTIVE 2

To utilise thermal imaging to assess BAT activation in clinical scenarios

Utilising indirect calorimetryand thermal imaging, we will investigate energy expenditure and BAT activation in patients with conditions which are rationally associated with a potential rise in energy expenditure and/or BAT activation for example bariatric surgery, phaeochromocytoma and thyrotoxocosis.

Recruitment

Patients will be recruited from Outpatient Clinics in Imperial College NHS Healthcare Trust by the researchers. We aim to recruit n=30 patientsfor each one of the following conditions of interest: bariatric surgery, phaemochromocytoma, thyrotoxicosis and neuroendocrine tumours. Participation in the study will not delay or influence the clinical management of the patient and their conditions.

Screening Visit

All volunteers will undergo medical history taking and examination. Inclusion and exclusion criteria are detailed below. Basic investigations performed prior to inclusion will comprise height and weight measurement, blood tests (full blood count, urea and electrolytes, liver function tests, thyroid function tests and plasma glucose) and an electrocardiogram. Where other blood tests have been performed as part of routine clinical care, these results may be accessed by the clinical research team.

Informed consent is considered a crucial part of the study. All of the research doctors undertaking this process are medicallyqualified and experienced in taking informed consent for human research studies according to GCP guidelines.

Inclusion criteria for patients with conditions of interest

- Age >18 years
- Diagnosed with a condition known to be associated with prolonged exposure to endogenously elevated gut hormones or likely to be associated with increased energy expenditure and/or BAT activation.

Exclusion criteria for patients with conditions of interest

- As for Objective 1, but allowing for the primary condition of interest.
- Pregnancy.

Patients with conditions of interests visits

Each patient will attend their first study visit on the same day they are recruited from an Outpatient Clinic. Up to 5 subsequent follow-up visits will then be scheduled to investigate the effect of treatment of the underlying condition over time on EE and/or BAT activation. Therefore each patient will be invited to attend a maximum of 6 study visits.

Each study visit will consist of a single 20 ml blood sample, thermal imaging (with or without cold stimulation, as described above) for up to 30 minutes and indirect calorimetry (as described above) for

up to 60 minutes. Premenopausal females will be asked to take a urine pregnancy test at each study visit to exclude pregnancy. The participants with medical conditions of interest will not have intravenous cannulae inserted. They will not be subjected to any gut hormoneor saline infusions, and they will not have any PET-CT scans as part of this study.However if the patient has one or more PET-CT scans as part of their routine clinical care, then analysis of the scan(s) will be included in the study providing the region of interest (supraclavicular area and neck) is included in the scan(s).

The venous blood sample taken at each study visit will be tested for gut hormones, pituitary hormones, thyroid hormones, glucose and other metabolites. Over the course of their participation in this study, each patient will donate no more than a total of 150ml of blood.

OUTCOME MEASURES

1. Change in BAT signal between the baseline and stimulated state in response to glucagon infusion, as detected by PET-CT, thermal imagingand MRI.
2. BAT activation in different pathological states pre- and post-treatment.

SAFETY AND WELLBEING OF THE VOLUNTEERS

Over the last 25 years, the Department of Metabolic Medicine has infused or injected synthetic human gut hormone peptides (singly or in combination) to a large number of volunteers with no untoward side effects at the doses that will be used in this study.

Every effort will be made to ensure the volunteer's comfort throughout each study visit. At all times, the volunteers will be in direct communication with the investigators. They may press an alarm bell to request immediate cessation of the procedure and withdrawal from the PET-CT scanner. If the volunteer is unable to cope with the scan, from the point of view of lying still for the required time or because of claustrophobia, they will be excluded from further participation. Subjects will be free to discontinue their participation at any time.

The maximum number of PET-CT scans a volunteer will have in this study is 2 PET-CT scans, and only those volunteers with significant response to glucagon infusion in Visits 1-3 for Objective 1 (i.e. up to 16 volunteers) will have PET-CT scans. Since the total radiation exposure will not exceed 9.5mSv, the estimated risk of developing a fatal cancer as a result of having 2 PET-CT scans in this study is 1 in 1800 for a healthy adult. This is much lower than the UK cancer mortality rate of approximately 1 in 4.

At least one experienced physician will be present at all times during the study visits and subjects will be encouraged to report any unusual or unpleasant sensations immediately. During the entire course of the study, a physician will be available 24 hours on a direct line, which will be given to all volunteers. A second physician will be on back-up call.

The most common minor side effect (although still rare) of glucagon infusion is mild nausea. This effect is even less likely to occur in this study, which proposes to use doses that produce physiological post-prandial plasma levels in fasted subjects. If nausea does occur, it wears off very quickly when the infusion is discontinued, because this peptide hormone is significantly metabolised within minutes. If a volunteer experiences this side effect then no further infusions of glucagon will be administered to that volunteer.

ADVERSE EVENTS

An adverse event is any untoward medical occurrence in a patient or clinical study subject. A serious adverse event is an adverse event that results in death, is life-threatening, requires hospitalization or prolongs an existing inpatient's hospitalization, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect. All non-serious adverse events will be recorded in the Trial Master File. If a serious adverse event occurs, a serious adverse event form will be completed and sent to the Chief Investigator and the Sponsor within 24 hours. All serious adverse events that are unexpected and related to the study will be reported to the Local Research Ethics Committee. Serious adverse events will be reported as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

Although no serious adverse effects are anticipated, any such effect will terminate the arm of the study during which the serious adverse effect occurred.

DATA HANDLING

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.Personal contact details are required for communication with the subjects participating in the study. This information is held solely for communication between the researchers and participants. Details stored on university computers will be password protected and will only be accessed by the researchers involved in the study. Personal identifiers will be deleted 6 months after the participant has completed their involvement in the study.

Information held on NHS computers is solely for the purpose of hospital booking and routine sample collection and analysis (e.g. for medical screening). This information is password protected in a similar manner to that of other hospital patients.

Subjects will be given a personal study code number which will be used throughout the study and in the analysis of data. Coded samples or images will also be treated with confidentiality when undergoing analysis. Analysis will take place in the Imanova Clinical Imaging Centre and the Department of Investigative Medicine at Hammersmith Hospital and be carried out by the researchers themselves. The data will be kept in a secure environment in these departments, under the authority of Professor Bloom. Data will be stored for 15 years after completion of the study. Only the researchers will have access to this data.

REGULATORY COMPLIANCE

The Chief Investigator has obtained approval from the xxx Research Ethics Committee. The study has been submitted for Site Specific Assessment (SSA) at each participating NHS Trust. The Chief Investigator will obtain a copy of the Trust R&D approval letter before accepting participants into the study. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Consent to enter the study will be sought from each participant only after a full explanation has been given, an information leaflet offered and time allowed for consideration. Signed participant consent will be obtained. The right of the participant to refuse to participate without giving reasons will be respected. After the participant has entered the study the clinician remains free to give alternative treatment to that specified in the protocol at any stage if he/she feels it is in the participant's best interest, but the reasons for doing so should be recorded. In these cases the participants remain within

the study for the purposes of follow-up and data analysis. All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

FUNDING AND INDEMNITY

The study will be funded internally by the Imanova PET Pilot Study Grant (awarded in November 2012) and the Section of Investigative Medicine, Division of Diabetes, Endocrinology and Metabolism. Healthy volunteers will be paid expenses of up to £100 per study visit and patients with conditions of interest will be paid expenses of up to £75 per study visit.

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trust taking part in this study.Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study, and Imperial College Healthcare NHS Trust holds standard NHS Hospital Indemnity and insurance cover with NHS Litigation Authority for NHS Trusts in England, which apply to this study (as both the healthy volunteers and the patients with conditions of interest will be registered as patients of Imperial College Healthcare NHS Trust).

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