Aim of the Study

The overall aim of this project is to develop high resolution MR imaging sequences and anatomical measurement methods to enhance the understanding of soft tissue behaviour of fat and muscle around the ischial tuberosities and coccyx in the loaded and unloaded erect seated body position in regard to wheel chair users. This will require measuring the effect of loading and unloading using the subject's own weight on soft tissue around the ischial tuberosities on fat and muscle, and assessing their movement and change of 3D shape. In the unloaded situation, imaging will be carried out with the subject supported by a customised wooden ring, whilst in the loaded situation the subject will be seated normally. Specifically, this study will involve:

1) MR imaging of normal volunteers in unloaded and loaded seated positions in a 0.6T FONAR imaging system
2) Image quality assessment
3) Analysis of images and development of a measurement system for describing the amount and direction of soft tissue deformation in the seated position.

Primary research question

What is the optimum MR scanning technique for the visualisation of soft tissue deformation in the seated position?

Secondary research question

How do soft tissues around the ischial tuberosities distort and move when in the loaded and unloaded seated position?

Outcomes

1.   Novel MR imaging protocols for subjects seated in an upright MR scanner to allow accurate analysis of the soft tissue anatomy around the ischial tuberosities and coccyx.
2.   Identification of anatomical locations/features to aid quantitative understanding of the normal soft tissue anatomy around the ischial tuberosities and coccyx in an unloaded and loaded seated position.
3.   Measurement of tissue distortion around the ischial tuberosities in the seated position

Background:

Reduced muscular activity and paralysis after a SCI lead to disuse muscle atrophy and reduce soft tissue coverage over the bony prominences of the pelvic region (Linder-Ganz et al 2008, Castro et al 1999). As muscle bulk decreases, regional vascularity diminishes and the proportion of avascular fatty tissue increases. Loss of normal muscle tone leads to abnormal responses to environmental stimuli.

The development of pressure ulcers (PU) is multi factorial. These range from intrinsic issues such as mobility, age, nutrition and hydration, illness, sensory impairment and moisture to extrinsic factors such as interface pressures, friction and shear forces (Vanderwee et al. 2007). Historically, research into the impact of loading damage focused on externally applied pressure and the movement of the skin surface (Sprigle and Sonenblum, 2011). Despite years of research, studies have been unable to determine a threshold of acceptable pressure. This is most likely because external pressure itself is not solely responsible for the damage. Instead, damage likely results from internal strains caused by the external pressure. Therefore, researchers are beginning to focus on how the tissue deforms (Bouten et al 2003, Gawlitta et al 2007). Currently there is no satisfactory method of measuring shear, however, its contribution to pressure ulcer development is well documented (Linder-Ganz et al 2008). Imaging modalities such as MR offer an innovative way to view and assess tissue deformation, shear and viability (Makhsous et al 2011, Stekelenburg et al 2006). MR is currently the best imaging modality for identification of the boundaries between muscle and fat tissues (Shabshin et al 2010). The open

stand-up MR 0.6 Tesla system from FONAR is ideally suited to perform loaded and unloaded MR scans of the buttocks focused around the ischial tuberosities where pressure ulcers are most likely to occur.

Soft tissue deformation can be variable depending on what type of interface (cushion) the subjects are sitting on. One goal of this study is to develop a method that can be used to look at how the soft tissue deforms whilst the subject is seated on different surfaces. Although this future testing is outside the scope of the current study, it has an impact on the scan protocol, as multiple imaging would then be required. Therefore, an aim must be to reduce the scan time so as to reduce the amount of time a subject must maintain the same position. While the immediate outcome of this study will be a method to investigate 3D tissue deformation in the seated human buttocks, this methodology will be deployed within studies to improve our understanding of PU development and individual risk factors.

We are working with partners in Georgia Institute of Technology, Atlanta (Professor Stephen Sprigle and Dr Sharon Sonenblum), and FONAR Corporation (Dr John Greenhalgh, MR applications specialist), Melville, New York who have developed some initial scanning experience the Open 0.6T FONAR system (Sonenblum et al 2012). We have been asked to provide specialist MR scanning techniques for the visualisation of tissues around the ischial tuberosities. Dr Winder and Dr Sonenblum have collaborated with FONAR at their Research Centre in New York to do some initial MR testing. From this pilot work we have identified the appropriate RF coil and appropriate 2D spin echo sequences to provide high quality anatomical visualisation. However, we now need to explore these sequences, along with 3D techniques to optimise our scanning protocol (that is to ensure maximum signal to noise ratio in a reasonable scan time). Figure 1 shows a sagittal T1 of the IT from initial techniques. Figure 2 shows rendered MR images of unloaded and loaded gluteus maximus muscle and the deformation it endures under loading.
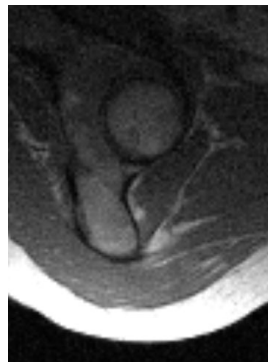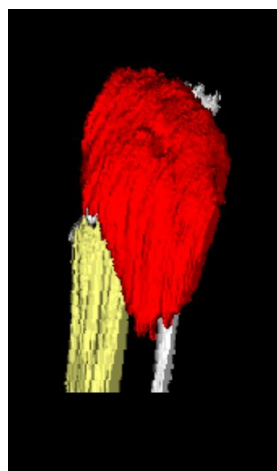

Figure 1 showing sagittal T1 MR of the muscle and fat configuration under the ischial tuberosity in the seated position whilst being unloaded.

a)

b)

Figure 2 showing a) loaded gluteus maximus (red) and b) unloaded gluteus maximus (hamstring in yellow and bone in white in both images)

Methods

Study 1. Optimize the MR scanning technique for imaging soft tissue deformation for sitting.

MR imaging will be carried out at Medica Stand UP MR in Atlanta, using a 0.6 T FONAR MR system.

MR imaging will be carried out on 8 normal volunteers seated in an unloaded position (a special

seat has been developed in Atlanta to support the body during scanning without compressing the buttocks) and loaded with the subject's own body weight. To accomplish consistent seated posture, we will measure pelvic tilt, hip and knee angles, and foot positioning relative to the lower limb using goniometers and inclinometers. A series of 3D gradient echo and thin slice 2D fast spin echo sequences will be tested to develop optimum imaging of localised areas of the pelvic region (left/right IT and coccyx). Sagittal, coronal and transverse planes, with slice thicknesses from 0.5 mm – 3.0 mm, phase encoding steps from 128 to 256 will be acquired. Subjects will be given a unique code identifier and no names used to maintain anonymity. Image pre-processing and analysis will be carried out using Analyze AVW v11.0 and Geomagics Qualify 2012. Technical advice will be given by FONAR MR specialist on bandwidth selection and partial Fourier imaging.

Subject recruitment

Subject's will be recruited through Georgia Tech, Atlanta via university email system. Subject's must be over 18 years, able to satisfy MR safety checklist, able to give written informed consent. Subject's will be excluded for the following reasons, if they are MR contraindicated, have had previous surgery of the buttocks area, previously had a pressure ulcer of the buttocks and physically do not fit into the FONAR system aperture. Maximum size and weight based on FONAR recommendations will be included in the exclusion criteria. We will apply purposive sampling to ensure we get a range of subject sizes that are representative of the typical population. To optimize scan time we require agile healthy volunteers so that scan positioning on and off cushions can be carried out efficiently.

Subject's consent will be obtained by Dr Sharon Sonenblum who is trained in human subject ethics and consenting in the US.

Ethical permission will be obtained from both the Ethics Committees of the University of Ulster and Georgia Institute of Technology. Peer review has been carried out by health care researchers at the University of Ulster.

US ethics   At Georgia Tech faculty, Dr. Sonenblum is required to pursue Institutional Review Board (IRB) approval for taking MRI scans on research participants (approval has been applied for and approved). This includes obtaining informed consent from all participants, and training in the protections of human subjects for all participating researchers. The mission of the Georgia Tech IRB reads: "Georgia Institute of Technology's Institutional Review Board is charged with the responsibility of safeguarding the rights and welfare of human participants in research. The university's program of human research participant protection is based on the three primary ethics principles set forth in the Belmont Report, issued in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research: • Respect for persons, • Beneficence, and • Justice." Drs. Cathcart and Winder will be added to the Georgia Tech IRB application.

Image quality will be assessed quantitatively using signal to noise ratio and spatial resolution measures. Also, a 5 point Likert scale will be used to qualitatively assess subjective image contrast (differentiation between bone, muscle and fat) and visibility and delineation of the following anatomy: fat/muscle interface (gluteus maximus, hamstrings, piriformis, obturator internus, adductor magnus, gracilis and fat), blood vessel bifurcation (within the ischial rectal fat), peak of the ischial tuberosity, fovea of head of femur, intermuscle fascial lines and common ligament insertion of the hamstring muscle. The Likert scale will consist of the following; 1 invisible/absent, 2 poorly visualised, 3 acceptable, 4 good and 5 excellent (Ba-Ssalamah et al 2002). Images will also be assessed for presence of movement, chemical shift, phase wrap and any other artefacts.

Each image will be assessed for quality (signal to noise, contrast between fat and muscle, image resolution) by 2 researchers experienced in Diagnostic image assessment. The results will be crossed checked by a 3rd Researcher in Atlanta and an Anova analysis will be used to measure variability.

Study 2: Analyse images and develop a measurement system for reporting on deformation in response to loading.

MR images from Study 1 (unloaded and loaded) will be used for analysis

Image Analysis

The goal of the MRI analysis is to describe the deformation of individuals' buttocks. Preliminary analyses have illustrated that we can describe global deformations (i.e., change in tissue

thickness or volume underneath the ischial tuberosities). Global deformation has the advantage that it is relatively easy to measure.

Localized strain is likely to have a more direct relationship to tissue damage, but is much more complex in measurement and will be the work of phase 2 of measurement analysis once image optimisation has been achieved.

Data processing will be performed collaboratively with image processing experts at Georgia Tech, as well as medical imaging professionals at the University of Ulster. Both sets of expertise are needed for valid results. The radiographer's expertise will be important for identifying anatomical features and artefacts in the images. Image processing expertise is needed to facilitate faster segmentation of the images, and to implement non-rigid segmentation techniques for the calculation of localized strain. Anatomical landmarks like fascia planes and blood vessel bifurcations will be potential features identified as references points for measurements as well as the peak of the Ischial tuberosity and fovea of the head of femur. 3D visualisation of muscle groups and fat around the IT (Gluteus maximus, semimembranosus/semitendinosus [hamstrings], piriformis, obturator internus, adductor magnus and gracilis) to demonstrate deformation will also be initially visualised.

Image Segmentation
Achieving the measurements of both global and local deformation requires segmenting the bone and soft tissue of the buttocks (specifically, the gluteus, hamstrings, and obturator internus muscles, and fat). We will implement a user-assisted, semi-automated method developed and in use at Georgia Tech (Karesev 2011) to segment the MRI scans. The result will be object maps of the pelvis, the gluteus, hamstrings, and obturator internus muscles, and fat for each scan of each individual participant.

Global Measures
Our preliminary work studying model and human buttocks indicated that 1D measurements were inadequate. So while our emphasis will be on volumetric (3D) measurements of deformation, we will also evaluate 1D and 2D measurements for comparison with existing work (Table 1). Because individuals vary in size and shape, a consistent region of interest (ROI) must be defined for each metric. This analysis will utilize a ROI that is anchored using the ischial tuberosity, which is easily identifiable in the MRI scan and will not change in size or shape when load is added. An elliptical prism with 1.5 cm x 2.5 cm diameters (coronal and sagittal planes, respectively) about the apex of the ischial tuberosity will be used (**ROI**, Figure 3). This is based on the typical geometry of the ischial tuberosity and should include predominantly tissue beneath the bone.

Measurements of tissue deformation will use the intersection of the segmented muscle and fat regions with the ROI to measure *tissue thickness* measured below the apex of the ischial tuberosity (1D measurement), *tissue area* below the ischial tuberosity within the ROI measured at the coronal and sagittal planes (2D measurement), and *volume of tissue* below the ischial tuberosity within the ROI (3D measurement) (Table 1). Although much of the tissue is incompressible and will not change under load, the tissue will be displaced outside of the ROI, resulting in a change in our volume measurement.
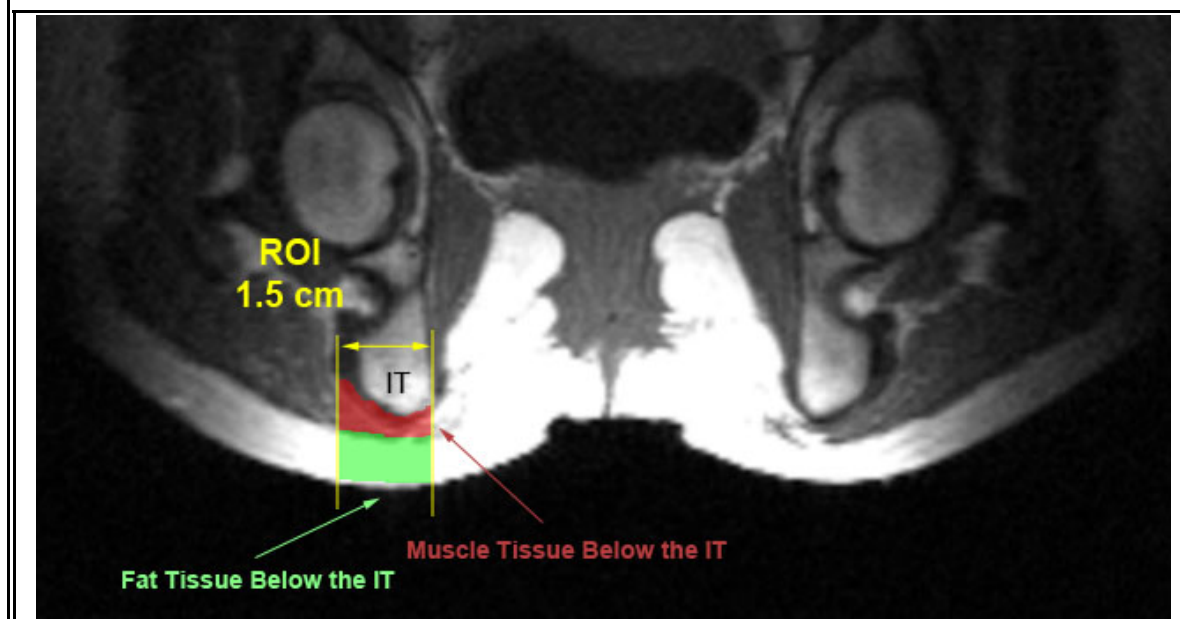

Figure 3. Illustration of buttock region of interest (ROI) from the coronal perspective, highlighting tissue below the IT.

Table 1. Measurements of Tissue Dimensions Below the ischial tuberosity (IT).

	Muscle	Fat
1-D	Apex of IT to muscle-fat boundary layer	Muscle-fat boundary layer to skin border
2-D	Area below apex of IT to muscle-fat boundary in coronal plane	Area below muscle-fat boundary plane to skin in coronal
2-D	Area below apex of IT to muscle-fat boundary in sagittal plane	Area below muscle-fat boundary to skin in sagittal plane
3-D	3D volume of muscle	3D volume of fat

Local Strain Measurement (phase 2 of measurement analysis)

Once the segmentations have been achieved and dimensions in the ROI measured, we plan to calculate a deformation vector field (a complete deformation description that includes shear strains) using non-rigid registration techniques (Klein 2009, Zitova and Flusser 2003) of the loaded and unloaded volumes. The resulting deformation vector field will permit thorough analysis of the complex deformations, represented by the shear, curl, and divergence over the volume (Romano and Price 2012). Volumetric changes will be found through the divergence. Tissue movement due to incompressibility can be identified through the remaining vector components (i.e., shear and curl). Rigid motion of the tissue can be found through the residual vector after projecting the vector field onto the gradient operator-defined coordinate vector subspace.

We plan to utilize a low cardinality radial basis function approximation of non-rigid transformations with completely adjustable function parameters (to identify as part of the registration procedure). Further, we will investigate both stochastic optimization and user-guidance as pre-conditioners to gradient-based approaches.

Service User

The REAR lab at Georgia Tech work with War Veterans Associations and those military personal with SCI. They provide input into their work and test the cushions that are being tested in the study when required.

How will reliability and validity be determined?

The reliability of the MR scanning has already been assessed in repetitive scanning of silicone based buttock models and the variability of repetitive distance, area and volume measurements have been calculated. (Manuscript in preparation). Our data showed that variation in measurements across multiple scans was less than 10% for thickness and less than 5% for area and volume measures. Intraclass correlation coefficients (ICC) also showed excellent agreement between the same 2 independent assessors. ICC for thickness was 0.986 (95% CI 0.977-0.992) and was 0.998 (CI 0.997-0.999) for volume. We are currently developing semi-automated tissue segmentation and measurement routines for use with the human data, in collaboration with the Intelligent Vision and Automation Laboratory at Georgia Tech. We plan to repeat the testing done with the models on our human subjects. That is, we will take repeated scans of an individual and have multiple assessors perform analysis of individual scans in order to calculate reliability and validity.

Healthy Volunteers

Healthy volunteers will be used to develop a clear understanding of normal tissue and anatomy (the overall purpose of this proposal is to image "normal" subjects, which we believe is the first step needed) and its movement before examining SCI patients and the changes they will have in their muscle shape.

Imaging individuals with SCI introduces many new challenges, including challenges transferring in and out of the MRI space and maintaining a stable posture for extended durations. While we are confident that all of these challenges can be overcome, initial protocol development will benefit from easy transfers between surfaces and the ability of participants to sit for extended durations while we manipulate protocol parameters. Furthermore, there is a benefit to understanding normative anatomy and tissue responses before tackling the complexity of individuals with SCI. Our recent case study (Sonenblum et al, 2012) represents the first time anyone has tried to understand 3D deformations of the seated buttocks. We recognise that MR imaging may need to be adapted for SCI subjects. This will form part of the other research programme currently under development. In fact, we are applying for research funding through the National Institute of

Disability and Rehabilitation Research to carry out MR imaging of subjects with SCI (this will not occur if funded until later in 2014)

Incidental Findings

The Participant Information Sheet given out during the consenting process indicates that all MR imaging will be reviewed by practitioners experienced in viewing medical images. If an abnormality is visualised the images will be referred to a Consultant radiologist to review and issue a report which will be sent to the patient's medical practitioner.

Magnetism Transfer (MT)

The FONAR 0.6 T system does not have the gradient power or software to currently perform Magnetisation Transfer and therefore will not form part of the imaging protocol development. While such options might be available in traditional MRI scanners, we believe it is necessary to study the buttocks in a true seated posture, an option only available on the FONAR scanners.

Potential Impact of the study

People with SCI are at risk from pressure ulcer development throughout their lifetime. The proposed research will produce a methodology for investigating 3D tissue deformation in the seated human buttocks which will be applied in further research to assess subjects with SCI and to assess the impact of new seating cushions for wheelchairs. By developing a methodology to measure and characterize 3D buttock deformation studies can be designed to evaluate cushion performance and inform the design of improved wheelchair cushions that accommodate the loaded buttocks with minimal tissue deformation. This will have an impact on people with SCI by ultimately improving their quality of life and reduce the costs of the treatment of pressure ulcers.

Finally, development of a methodology to measure 3D buttock deformation can be applied to other areas of seating. Many people who are not at risk of pressure ulcer development are required to sit for extended durations of time. For example, pilots, flight officers and truck drivers are often unable to get out of their seats. Better designs of aircraft and vehicle seats, facilitated by the new methodology to measure 3D buttocks deformation, can minimize discomfort and seating fatigue that can adversely impact performance.

There will also be significant impact on Radiographic research expertise in Ulster and in the potential for developing further radiographic research.

Dissemination

Results will be disseminated at both Radiographic and Clinical Engineering high quality peer reviewed journals and conferences. For example, we aim to submit to European Journal of Radiology, Journal of Tissue Viability and target conferences such as UK Radiology Congress European Congress of Radiology and the British Association of Magnetic Resonance Radiographers Annual Conference. Also, results will be configured for presentation to the European Seating Symposium and Medical Engineering and Physics Conferences. A final report will be provided to the Society of Radiographers for web based dissemination.

Gannt Chart Timeline

Project start date 1st July 2013 and end date 30th June 2014.

Activity	Quarter 1	Quarter 2	Quarter 3	Quarter 4
Research governance	▓			
Subject recruitment and imaging		▓	▓	
Data analysis		▓	▓	▓
Dissemination			▓	▓