The IST Programme
Project No. 10378

SimBio

SimBio - A Generic Environment for Bio-numerical Simulation

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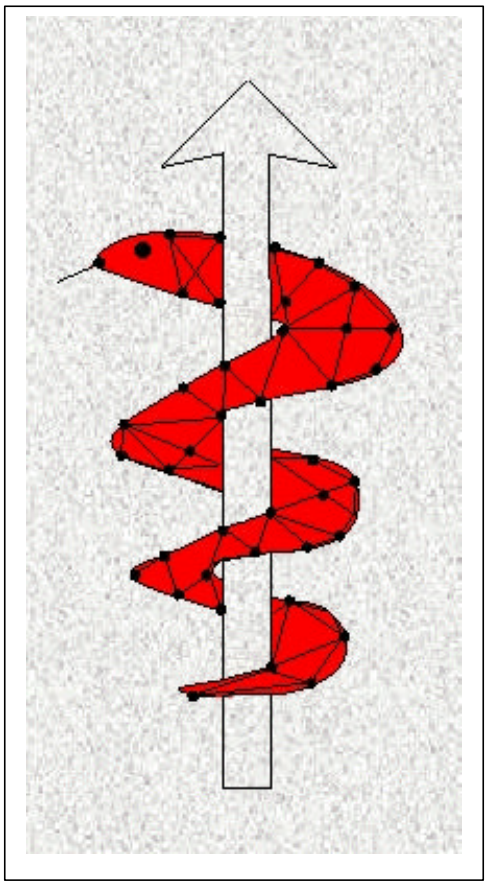

Deliverable D7.3a
Design Report for Test Application 7.3
Knee Prosthesis

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1 Introduction

The central objective of Workpackage 7 is to evaluate and validate the SimBio environment. It consists of three subtasks that will assess the utility of SimBio simulations for three medical applications, namely, Electromagnetic Source Localisation in the Brain, Bio-mechanical Head Modelling and Knee Loading Models with Prosthesis Design Problems.

This document is the first deliverable (a) of Subtask 7.3. It provides the requirements specification for the third test application in the validation and evaluation of the SimBio environment with respect to the knee joint. The purpose of Deliverable 7.3a is to specify how the validation and evaluation tasks will be achieved through the remaining 30 months of the project.

1.1 The SIMBIO Project

The central objective of the SimBio project is the improvement of clinical and medical practices by the use of numerical simulation for bio-medical problems. The project will construct a generic environment, running on parallel and distributed computing systems, capable of handling a range of important problems relevant to the target community of clinical and medical service providers. The creation of the SimBio environment should enable improvements in: non-invasive prognosis and diagnosis, pre-operative planning, design and implantation of prostheses and postoperative verification and evaluation of treatment success. The application evaluations in the project will demonstrate the effectiveness of the SimBio environment and thus accelerate the take-up of this IT technology within the medical area.

1.2 Why the knee joint?

The knee joint is the largest joint in the body. Its healthy functioning is essential for an individual's capacity to walk and perform activities of daily living. A review of Hospital Episode Statistics (HES) 1994-1995 revealed that 40,704 finished consultant episodes (FCEs) related to knee derangement in England (Beard, *et al*., 1999). These injuries resulted in 28,530 primary knee arthroscopies, not including the private sector or follow-up procedures (OECD, 1994). Knee arthroscopy is the commonest orthopaedic procedure performed in the U.K and North America (Olgivie-Harris *et al*., 1994).

A search of the Trent Region of England's Patient Information System (PIS) revealed 4,041 FCEs relating to internal knee derangement of which 2,320 (62%) were diagnosed as meniscal injuries (Beard *et al*., 1999).

1.2.1 Function of the menisci

The menisci perform important roles in force transmission across the knee joint carrying between 40-70% of load (Walker and Erkman, 1975), shock absorption, stability (improving joint congruence) and lubrication. To perform these functions efficiently, the menisci are dynamic structures. Performing a total meniscectomy to treat a knee injury has been implicated in degenerative changes in the knee later in life, such as osteo-arthritis (Fairbank, 1948) that may ultimately result in the patient requiring a Total Knee Replacement (TKR). To delay or prevent needing this major procedure, now where possible, attempts are made to salvage the meniscal tissue either by performing a partial meniscectomy or by repairing meniscal tears with sutures (van Arkel and de Boer, 1995).

1.2.2 Meniscal implants

However, in some cases the meniscus is too badly damaged and attempts have been made to design alternative treatments, such as transplanting human meniscal tissue (van Arkel and de Boer, 1995) or encouraging meniscal regeneration using a collagen scaffold (Stone *et al*., 1997). Gaining ethical

approval for these procedures is difficult and the techniques are not proven. Where they have been tested failures associated with poor alignments have occurred (van Arkel and de Boer, 1995). SimBio will enable virtual prototyping of test designs for a meniscal implant to improve the potential for a successful implant post-project.

1.3 Evaluation and Validation of the SIMBIO Environment

As described above, the purpose of Workpackage 7 is to evaluate and validate the tools provided by the SIMBIO environment. Subtask 7.3 specifically focuses on one area, the application of the SIMBIO tools to the human knee joint.

The SimBio environment will be used to create finite element (FE) models of normal and pathological knees from medical scan data provided from Magnetic Resonance (MR) Imaging. The image processing and mesh generation tools required to achieve the models are described in Design Reports 1.1a and 1.2a, respectively. The FE models will then be used to predict dynamic loading within the knee, which will be compared with actual loading measures (simulating a gait cycle) taken dynamically during the MR imaging process. This process will assess the functionality and utility of the SimBio environment for a specific orthopaedic application.

Once the validity of the environment has been determined, it will be used to evaluate two surgical scenarios. The first will simulate the effects of *damage* to meniscal tissue on the kinematics and strains within the knee. The second will simulate the effects of meniscal *repair* (partial meniscectomy) on the kinematics and strains within the knee. A final simulation study will create designs for a prototype prosthetic meniscus and evaluate the influence that their characteristics have on the kinematics and strains within the joint. The scope of the evaluation is to use the environment to create and test the designs. Subtask 7.3 does not aim to build or implant physical prostheses. This is beyond the remit of the project.

2 Design Requirements

To achieve subtask 7.3, the design of the task and its subtasks must be considered carefully. The following section details the design requirements necessary for successful task completion.

2.1 Acquisition of Magnetic Resonance (MR) Images of the knee joint

To create the FE models of the knee, suitable medical scan data must be collected from which the FE meshes can be generated. The knee joint consists of hard tissues such as bone, and soft tissues, such as articular cartilage, menisci and ligaments. Imaging these tissues during one scan session requires an imaging modality that is capable of detecting all of the tissues. The modality bested suited to this task is Magnetic Resonance Imaging (MRI), which has the advantage of being non-invasive and having no known risks to patients, and has an overall accuracy approaching 94% (Kaplan, 1993). It will be used to acquire a series of cross sectional images from which the main structures will be segmented and the geometry of the knee joint will be reconstructed. Using these segmented data will enable a finite element mesh of a knee to be built as in a prior ESPRIT project (Holt *et al*., 1999).

Ethical approval for using MR imaging for normal volunteers and patients has been sought from the North Sheffield Research Ethics Committee and approval was received on the 7th March 2000.

2.1.1 Choice of MR Scan protocols

Although MR imaging is capable of detecting all the tissues within the knee joint, certain scan parameters can enhance the contrast-resolution of different types of tissue. The primary structures of

interest for SimBio are the menisci. However, in addition, the articular cartilage, cruciate ligaments and bone must be discriminated clearly.

Several scanning sessions using differing scan parameters have been carried out using two normal volunteers to optimise the scan protocol that will be used. A range of scanning protocols has been investigated and is summarised in Appendix A. The comments in the table give an indication of the usefulness of the protocol in this study.

2.1.1.1 Static

To create a high-quality mesh, a high-quality static MR scan of the knee is required that differentiates the key structures. Issues to be considered are the spatial resolution and the contrast resolution of the MR image. To produce a detailed geometry, the scan slice should have as many data points as close together as possible, that is, it should have high spatial resolution. This infers a minimal scan slice thickness for each slice and a greater number of slices. However, a counter requirement for optimal MR imaging is that the selected pulse sequence should return significantly different signals for the different tissues, that is, it should demonstrate high contrast. Optimal MR sequence must balance the needs of spatial resolution and tissue contrast. In addition, the time required for each sequence has be considered, generally the higher the resolution the greater the acquisition more time will be required for each scan sequence.

A T2* gradient echo sequence (as shown in Figures 2.1 and 2.2.) appears to be a well-suited sequence for the static imaging of the knee. The scan parameters associated with Figure 2.2 appear to offer a good compromise between scan time and both spatial resolution and tissue contrast. The scan time used for the pilot tests was approximately 9 minutes. It is anticipated that this may need to be increased up to 12 minutes to ensure that the full volume of large knee joints can be imaged.

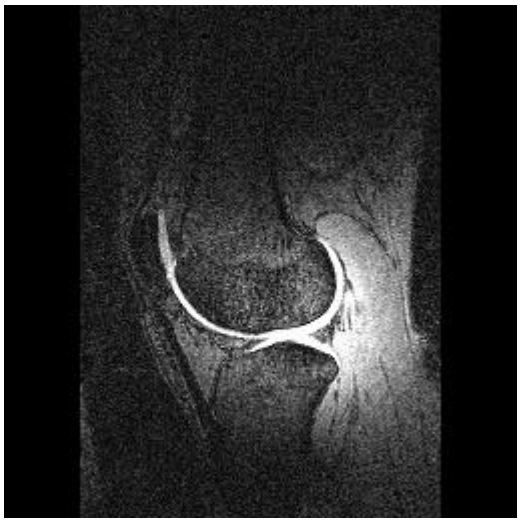

Figure 2-1: Sagittal slice through knee
RF-FAST sequence with effective pixel size 0.7mm

TR 39.0ms, TE=13.0ms, flip angle = 60, TMJ coil

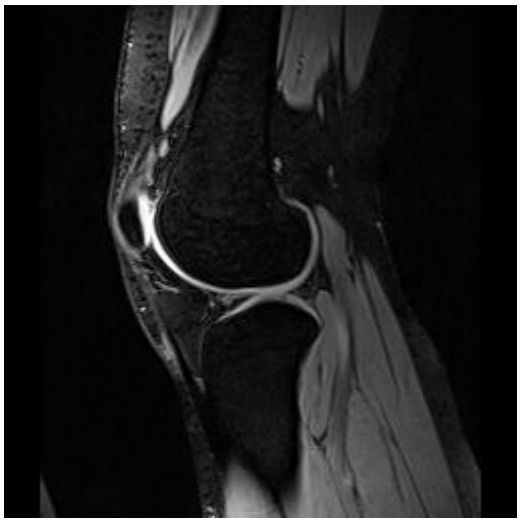

Figure 2-2: Sagittal slice through knee
T2* sequence with effective pixel size 0.7mm

TR=47.0ms, TE=15ms, flip angle = 30, shoulder joint coil

Dynamic

The purpose of the dynamic scanning is to visualise the behaviour of the menisci while the knee undergoes light loading under controlled exercise using a traditional MR scanner. Although studies have been performed to image the dynamic motion of the knee and the menisci previously, these have used Open (0.5 Tesla) MR scanners, which are not available generally in hospitals. A non weight-bearing study of meniscal motion from 0-90 degrees of knee flexion has been carried out (Kawahara, *et al.*, 1999), together with weight-bearing studies of the patello-femoral joint (Pearle *et al.*, 1999) from 0-

40 degrees of knee flexion and the menisci between 0 and 90 degrees of knee flexion (Vedi *et al.*, 1999). None of the studies applied known loads through one knee joint or used a typical 1.5T closed MR scanner. Thus, in addition to validating the SimBio tools, developing such a method would have benefits for the majority of hospitals that use closed MR scanners.

Unlike the needs of the static scans, primarily the dynamic scan sequences must have a minimal acquisition time. Ideally imaging the knee through a range of motion requires sequences that can be completed in 1 to 2 seconds to result in scanning frequencies of between 0.5 and 1Hz. However, such fast scans are at the expense of tissue resolution and it has to be accepted that the image resolution acquired will be much poorer than for the static sequences. A compromise must be made between tissue resolution and acquisition time. For SimBio, the dynamic scans must be able to discern the bone contours and the menisci to enable the kinematics of the knee and the menisci to be reconstructed. Examples of preliminary dynamic scan sequences are shown in Appendix B. The images from sequence 4442 took approximately 1 second each to acquire and are generally adequate for discerning the bone contours; however, the tissue resolution is poor for the menisci. The images from the second sequence (4826) used a pseudo-dynamic protocol and took approximately 5 seconds per image to capture. Although not the quickest acquisition time, this MR sequence yields significantly higher tissue contrast than 4442. Thus, the selected sequence for dynamic imaging is likely to have an acquisition of between 1 to 5 seconds per image. The Open MR studies described in the previous paragraph also used similar acquisition times. Vedi *et al.*, (1999) used “near real-time” and Pearle *et al.*, (1999) used approximately 2 second image acquisition times.

2.1.2 Selection of optimal radio-frequency (RF) coils for imaging the knee

Achieving a MR signal from the magnetised tissues of interest requires the application of a short radio frequency (RF) pulse (equal to the Larmor frequency of the hydrogen proton nuclei) to cause the net longitudinal magnetisation to rotate away from its alignment by an angle, termed the excitation flip angle. Receiving the MR signal emitted requires the use of a radio-frequency receive coil. To maximise the signal to noise ratio the RF receive coil is usually placed close to body part under investigation, in this case close to the knee.

Two requirements must be achieved for the optimal choice of coil. Firstly the coil must give good coverage throughout the joint and secondly it must allow the patient to carry out an exercise protocol unhindered. Three coils were identified for their potential suitability in scanning the knee joint. These were the bilateral tempero-mandibular joint (TMJ) coil, the large joint coil and the shoulder coil. Identical scan sequences have made on the knees of two volunteers using the three coils and the optimal coil has been identified as the shoulder coil as shown in Figure 2.5.

Figure 2-3 The bilateral TMJ coil

Figure 2-4 The large joint coil

Figure 2-5 The shoulder joint coil

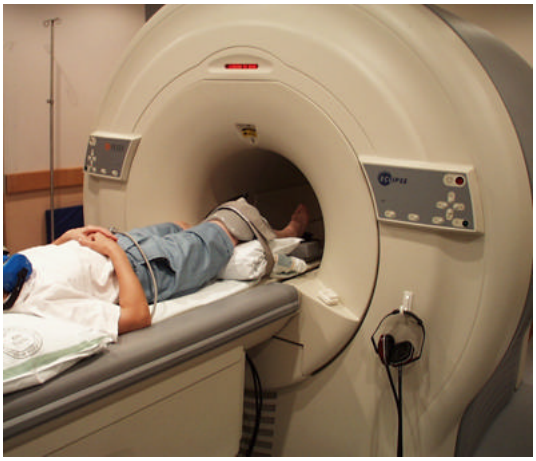

Figure 2-6: A volunteer about to enter the MR scanner (Eclipse 1.5T, Marconi Medical Systems) with the shoulder coil in situ on the right knee.

2.1.3 Dynamic loading of the knee during exercise

A key aspect to validating and evaluating the SimBio environment for the orthopaedic simulations will be the ability to image *in vivo* the kinematics of the joint and to measure the forces exerted during a dynamic exercise protocol. To achieve this a MR-compliant test rig is required.

2.1.3.1 Design of a MR Compliant Test Rig

The purpose of the task is to validate the quality of the FE models created using the SimBio environment. To achieve this, it is necessary to know the actual behaviour of the structure that is being modelled and the forces that it undergoes before it can be determined whether the behaviour of the model is valid.

A mechanism to allow a patient to undertake a controlled exercise protocol while exerting known light forces is necessary. However, this mechanism or rig must be capable of fitting within the bore of the MR scanner. In addition, the rig must be fabricated from materials that are MR compliant, essentially limiting them to wood or plastic. Ideally, the rig should capable of maintaining the centre of the knee centre in a stationary position within the bore (to maintain it within the optimal scanning volume) while the patient flexes and extends the knee. As can be seen in Figure 2.7 below, the space within the MR bore is limited, with a bore height of 46 cm from the top of the bed to the top of the bore.

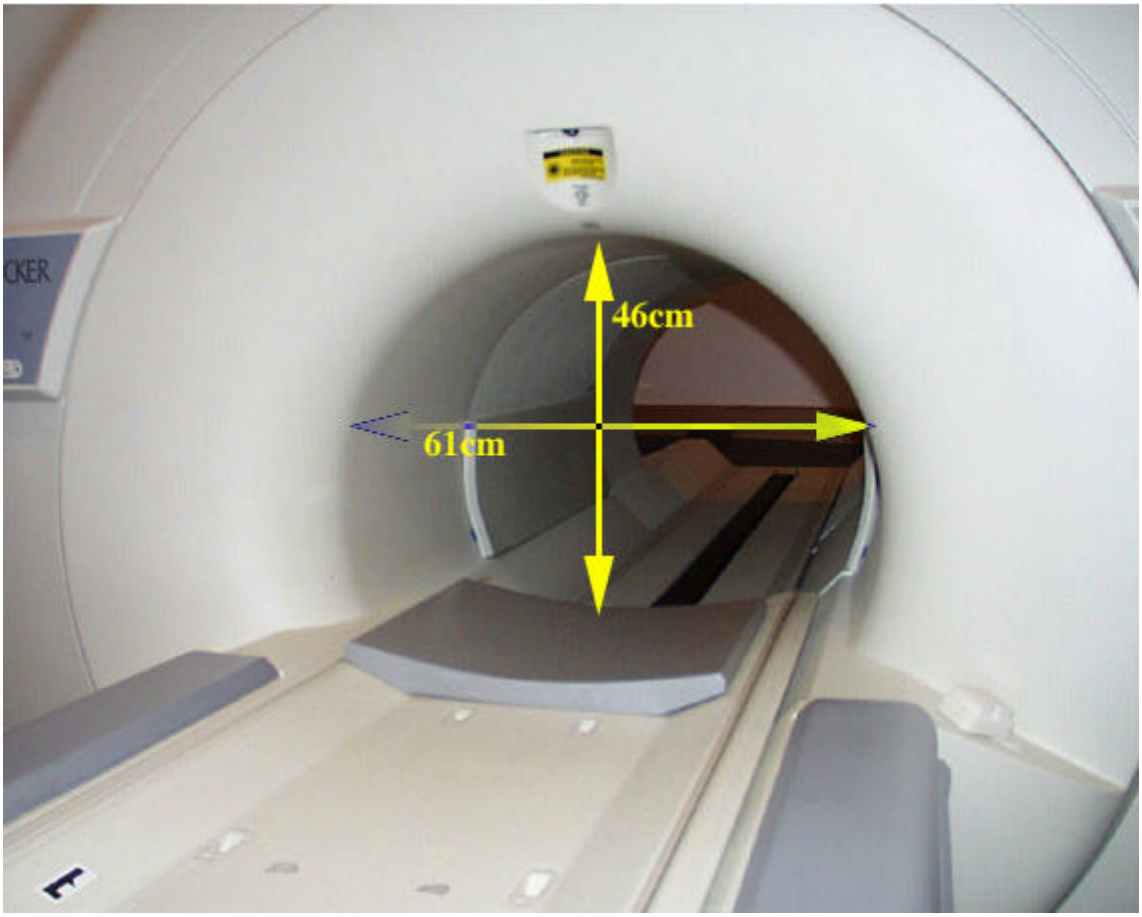

Figure 2-7: The Eclipse 1.5 T scanner (Marconi Medical Systems) showing the dimensions of the MR bore.

To allow the exercise protocol to be carried out, it is more likely that the design of the rig will aim to minimise the excursions of the joint centre from the optimal scanning volume.

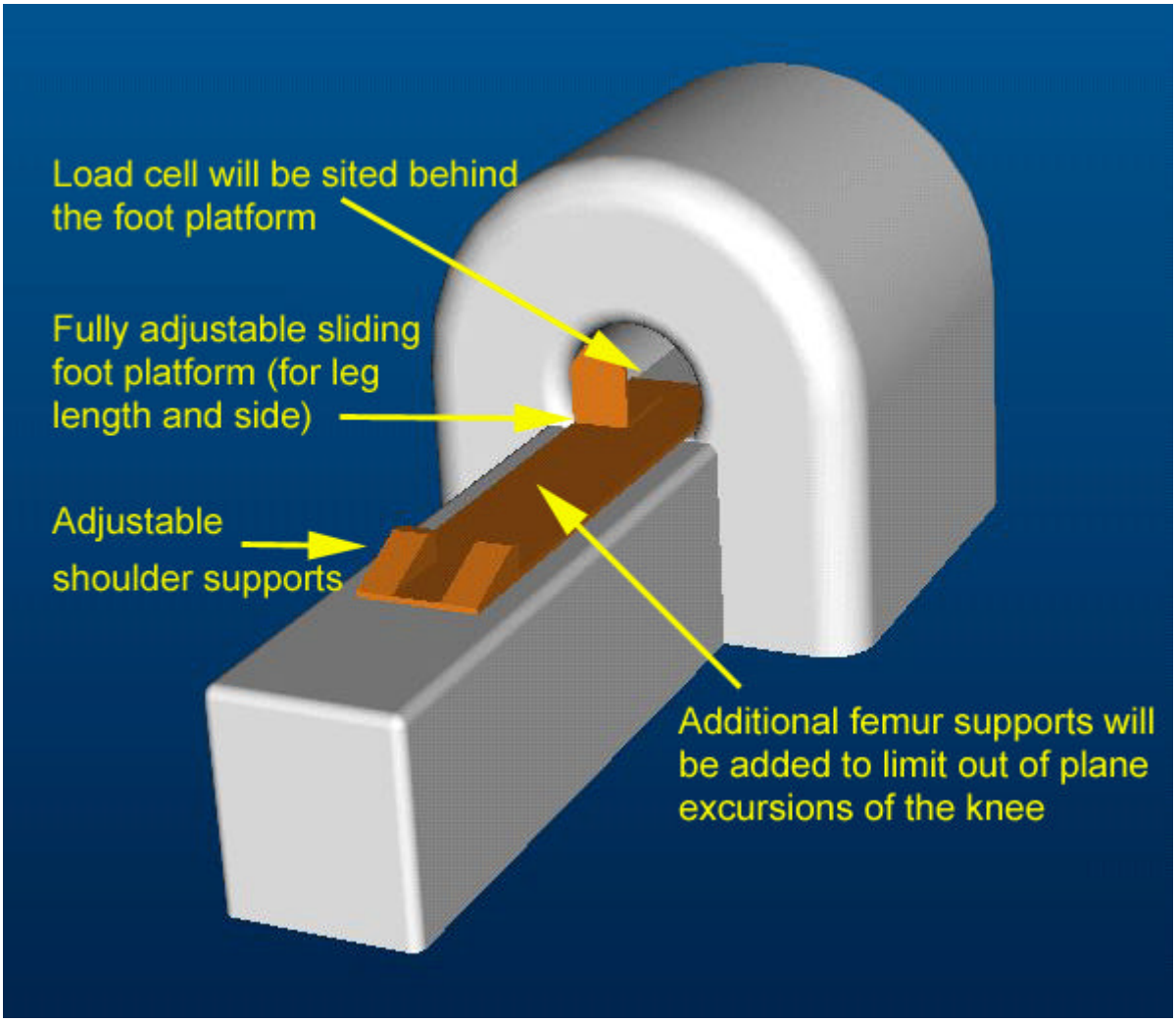

Figure 2-8. A preliminary design for the USFD MR-compliant test rig

The rig will be attached to the bed of the scanner on which the patient will lie, thus allowing the patient and rig to be slid in and out of the MR scanner together. Additional adjustable supports will be added to prevent sideways excursions of the femur and tibia. The patient will press against the foot platform from a flexed position to an extended position while being imaged.

2.2 Creating finite element meshes from MR Images

As stated earlier in section 2.1 of this report, the creation of segmented structures from the MR scans of the knee is necessary for building high-fidelity FE meshes. Thus subtask 7.3 is dependent on the success of workpackage 1. This is to be expected, as the purpose of ST7.3 is to evaluate the tools developed within the SimBio environment.

2.2.1 Interaction with Workpackage 1: Subtasks 1.1 and 1.2.

Subtasks 1.1 and 1.2 are responsible for creating image processing tools and mesh generation tools respectively. Image processing tools will be required to segment the structures from the MR scans while mesh generation tools will be used to create valid meshes that can be imported into commercial finite element solvers such as PAM-SAFE™ from ESI. The time in which these patient-specific meshes can be created is likely to be a key requirement for the eventual exploitation of these tools within the medical field. The goal will be to complete the process within hours rather than weeks.

To segment the components of each knee (normal and patient) individually and then build the FE meshes is likely to take considerable time. Thus, an alternative approach is being pursued that will combine the segmentation and mesh generation processes. Firstly, a “standard” knee will be segmented

to form a template and then meshed to form a mesh template. Patient knee images will then be segmented and these segments will be registered to the template. The registration mapping will enable the standard mesh to be transferred to the patient segments.

Figure 2.7 shows a parameterised medial meniscus created with Matlab™ using a quadratic with a total of 13 parameters that can serve as a standard template to aid the segmentation process. Once the template has been meshed (Figure 2.8), it will permit meshes from patient MRI data to be formed by mapping patient data to the template using the non-linear registration algorithm within WP1.1.

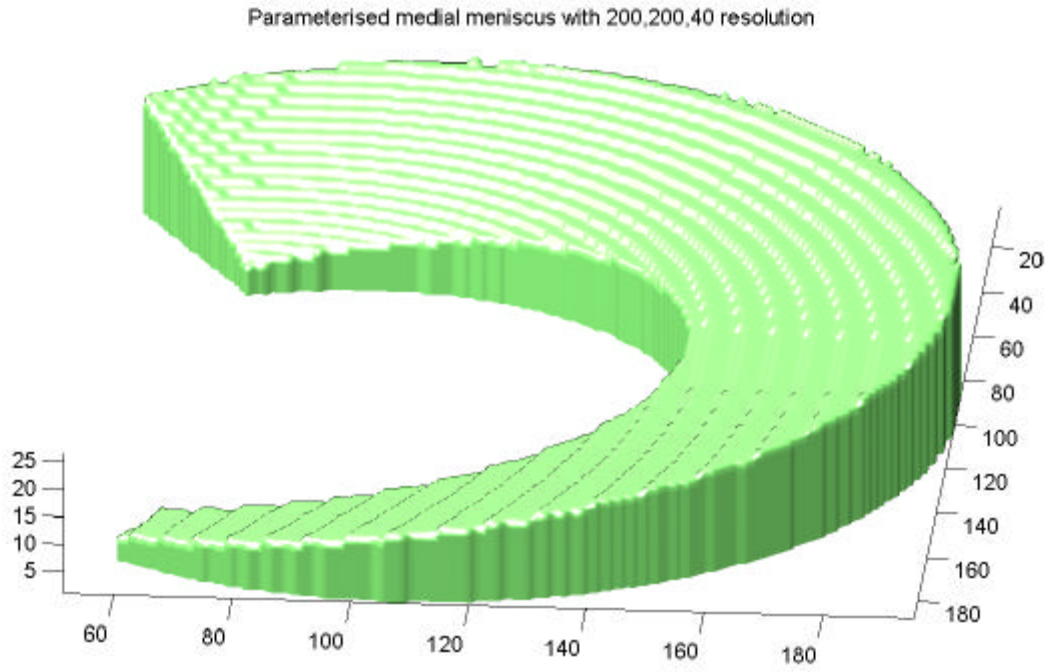

Figure 2-9: A parameterised medial meniscus created using MatlabÔ

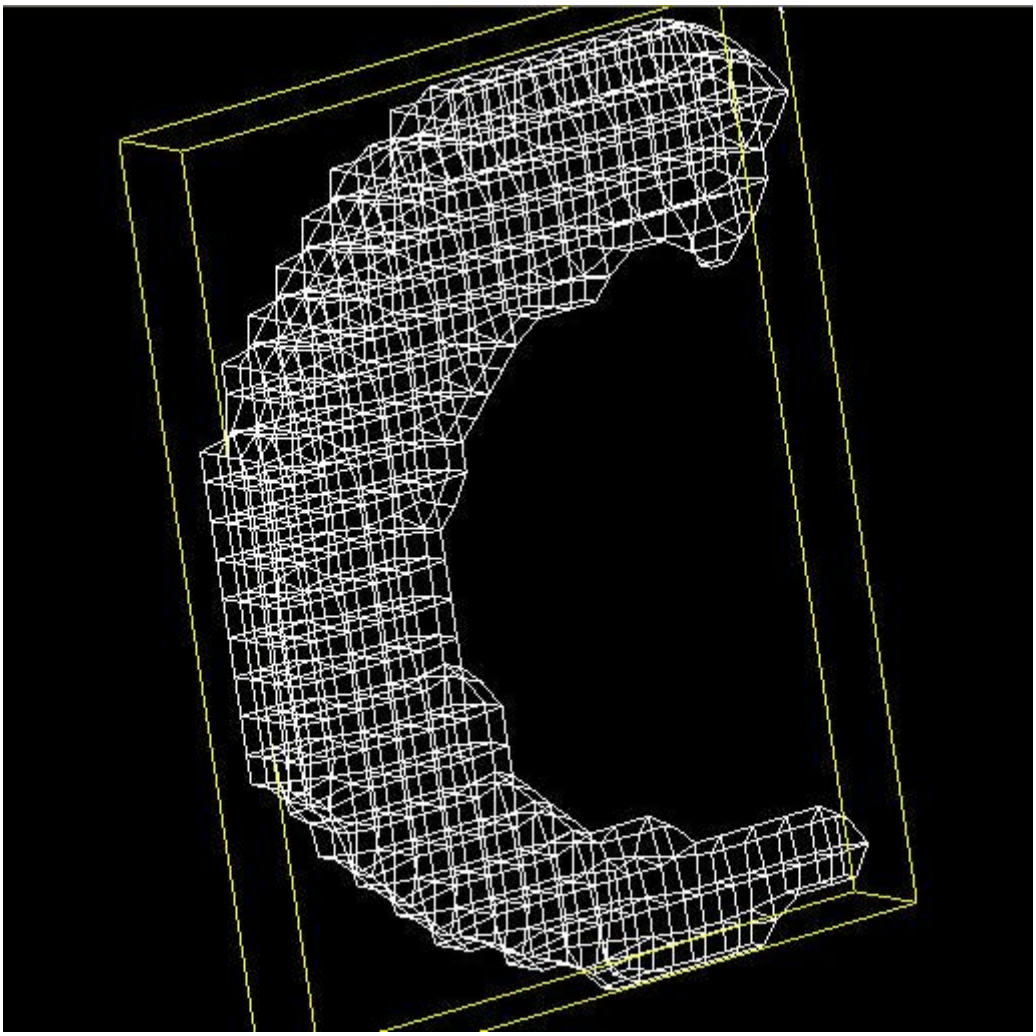

Figure 2-10 A smoothed hexahedral mesh of the parameterised medial meniscus created using the SimBio VGrid tool.

2.2.2 Types of finite element meshes

The quality of the simulation results will be governed in part by the quality of the finite element mesh used. Thus, it will be important to validate that the type of element used is appropriate and that the resulting mesh of the knee can provide valid approximations of the actual kinematics and strains within the knee.

The results from a previous EU project (Kneesup, involving ESI and USFD) indicated areas of its knee mesh that would require improvement. The finite element models of the cruciate ligaments were too stiff in compression resulting in altered kinematics of the joint from normal. Thus, in the SimBio knee model, the cruciate ligaments will be simplified initially to ensure that the kinematics of the joint are valid. The kinematics of the joint will also be affected by the smoothness of the articulating surfaces, such as the contours of the femoral condyles and their articular cartilages and the menisci and tibial articular cartilage.
It will be important to ascertain the degree of smoothness required for meshing the articular structures. This will be determined by assessing the kinematics of the joint using the preliminary meshing tools and modifying the meshes if required. Techniques to ensure adequate smoothness (as described in D1.2a) include, creating hybrid meshes to ensure localised smoothing at the articular boundaries and if necessary, ultimately specifying C1 surface continuity, where the tangent vectors to each curve segment match at the joint point. However, this may have an adverse effect on the complexity of the solutions and the time taken for their convergence.

For the first phase of the simulations, subtask 7.3 will model the bones as rigid structures and focus on the quality of the articular cartilage and meniscal meshes, using simplified cruciate ligaments validated against the kinematic and strain data collected from normal individuals.

2.2.3 Elements used in Mesh Generation and Mesh Quality

As part of ST7.3, ESI will use its expertise to investigate the development of 10 node tetrahedral elements and will compare these to existing 4 node tetrahedra and 8 node hexahedra used in PAM-SAFE™. ESI will contribute to assessing the quality of the meshes imported into PAM-SAFE™.

2.2.4 Boundary conditions

Having formed the meshes, suitable boundary conditions must be applied to the FE model to ensure that it behaves appropriately. One of the first scenarios will be to simulate the behaviour of a normal knee during the gait cycle, which will require the muscle and tendon system around the joint to be modelled. Simulated tendons will be inserted into the bones of the FE model to simulate the insertion points of the muscles around the joint and appropriate forces will be applied to the knee through the tendons to "drive" the gait cycle.

The gait cycle has been studied extensively (for example (Winter, 1990) thus actual data is available to aid the validation of the simulated gait cycle. Once it has been validated, a modified gait cycle, stair climbing and descending, will be simulated. This scenario has particular relevance to those patients with meniscal injuries. Hoshino and Wallace (1987) investigated load bearing across the knee joint in impact studies of cadaveric knees and these results will aid the validation process

2.2.5 Material Properties

Material properties for the components of the knee joint will be collected from existing literature as part of WP2 and provided by the materials database created in WP2. It is not within the remit of the project for USFD to perform actual materials testing. However, if the literature fails to provide adequate information, then it may be possible to carry out limited testing at USFD after month 20. However, it must be noted that separate ethical approval for such testing would need to be sought, and provided, before this could occur.

2.2.6 Participants

It is anticipated that 12 normal participants and 12 patients (scanned twice) will be scanned for SimBio. However, if repeat scans are needed this number may be reduced. As stated in section 2.1, ethical approval has been received for their participation.

3 Timetable

Deliverable Number	Deliverable Name	WP Number	Lead Participant	Delivery: Project Month
D1.1b	Preliminary IP-Tool Release	1	8 (USFD)	12
D1.2b	Preliminary MG-Tool Release	1	1 (NEC)	12
D7.3b	First Evaluation Report	7	8 (USFD)	18
D1.1c	Final IP-Tool Release	1	8 (USFD)	30
D1.2c	Final MG-Tool Release	1	1 (NEC)	30
D7.3c	Final Evaluation Report	7	8 (USFD)	36

Table 3-1: Deliverable dates affecting ST7.3

3.1 Months 6-12

As shown in Table 3.1, the first releases of the image processing (IP) and mesh generation (MG) tools are not due until month 12. During the six months prior to the official IP tool release, work will be undertaken to segment a normal knee from the MRI data collected. It is likely that this will be achieved using existing Matlab™ code written for Kneesup (Holt *et al.*, 1998) by USFD together with pre-release versions of the SimBio IP tool.

Once a segmented dataset of the knee has been created, the individual components will be meshed. A pre-release version of the VGrid MG tool has already been used to mesh an existing segmented cadaveric knee. However, this pre-release tool does not include the 2-D elements that will be required initially for the simplified (as described in 2.2.2.) cruciate and collateral ligaments. One approach to this problem is to create 3-D meshes from the segmented MRI images (as described in D1.1a and D1.2a) of the ligaments and to extract the 2D or 1D mesh automatically from the 3-D mesh. For example, the middle surface of the 3-D mesh can be used to represent the cruciate ligament in 2-D.

As discussed in D1.2a, there are two approaches that will be investigated for the meshing the knee:

1. Using the SimBio VGrid Tool
2. Using a *mesh template* approach that combines meshing and segmentation

ESI will provide an import filter to allow the vista meshes created by VGrid to be used in PAM-SAFE™. USFD will provide to ESI, meshes in the form of a list of the internal nodes and their connectivity's (plus node numbering if necessary). In addition, USFD will provide ESI with MRI images of the knee so that ESI may assess its preliminary automatic "MRI to mesh" generation software. N.B. This is **not** part of the Technical Annex.

Initially, a part-meshed version of the knee (minus collateral and cruciate ligaments) will be imported into PAM-SAFE™ and its 2-d elements will be used to represent the ligaments and meniscal fibres. Later in the project (after 24 months) it is anticipated the majority of the knee will be meshed using SimBio tools and imported into PAM-SAFE™.

The alternative *mesh template* approach (described in D1.2a) for mesh generation will be pursued and tested during this period in parallel with using the VGrid MG tool. Parameterised "standard" versions of the knee components, starting with menisci, will be constructed and meshed to form a *mesh template*. The mesh template will used to steer the segmentation (described in D1.1a) and meshing of individual knee components by registering to it using existing registration algorithms developed at USFD. The mapping function produced will be used to "distort" the template mesh to form a new individual mesh.

The test rig will be built and tested during this period to enable MRI data (static and dynamic) to be collected for the normal participants. It will be constructed and tested in two phases:

1. The first prototype rig will aim to ensure that the kinematics of the knee can be imaged pseudo-dynamically with minimal out-of-plane movement and minimal excursion of the joint from the iso-centre of the scanner. Thus ensuring that Analysis Task 1 (described in 3.2) can be conducted without delay.
2. Once the prototype rig can ensure adequate control of the knee kinematics, a mechanism (such as a load cell) will be integrated into the design to measure the force exerted (against a foot platform) by a participant while he or she is being scanned. The force measurement device is anticipated to be the most problematic aspect of the rig design due to the constraint on metal materials permitted within the MR scanning environment. The load analysis task (Task 2 described in 3.2) that relies on this device will thus be conducted after the kinematic analysis (Analysis Task 1), thus allowing a time buffer if modifications are required.

By **Month 12**, the following should have been achieved:

- A prototype rig will have been built and tested. At a minimum, it will provide for the pseudo-dynamic imaging of the knee to be conducted and ideally, it will also permit force measurements to be collected at the same time
- Static and pseudo-dynamic MR imaging of a normal knee will have been carried out
- The components of a normal knee will have been segmented and meshed

3.2 Months 12-18

During this six month period validation of the finite element model of the knee will be undertaken. Its purpose is to validate the Preliminary IP and MG tools due for release at Month 12 and the behaviour of the Finite Element (FE) knee model produced using the SimBio tools. The validation analysis will utilise PAM-SAFE™ (provided by ESI) as the simulation environment. The first analysis task for validation is to simulate the behaviour of a knee during a gait cycle. The simulation task can be broken down into two parts:

1. Analysing the kinematics of the knee joint during the gait
2. Analysing the strains developed in the menisci during the gait cycle

3.2.1 Analysis Tasks

To achieve the *validation* tasks the following assumptions will be made for modelling the components of the knee:

- Bones: Rigid
- Articular cartilages: Solid, linear isotropic nearly incompressible
- Collateral ligaments and tendons: Linear bars and seatbelts
- Cruciate ligaments: Modelled using membrane elements (considering a tension stiffness but no compression stiffness in the fibre direction).
- Patella tendon: Modelled using membrane elements with one fibre direction
- Menisci: Linear anisotropic.
- Muscles: Cable elements

Validation task, V1 can be split into two further parts, A and B

a. The first part of analysis task 1 will simulate a simple flexion and extension of the knee, constraining the distal femur to zero displacement in all degrees of freedom and applying a rotational constraint to the tibia as a function of time. This will be undertaken by USFD in months 12-14.

b. The second part will use applied muscle forces to drive motion of the knee to simulate gait. Forces will be applied to nodes representing the insertion points of the quadriceps and hamstring muscles at their proximal ends in a constant given direction to simulate the action of the muscles on these tendon elements. Variation in and difference between the 'quadriceps' and 'hamstring' forces will be used to provide joint compression and flexion of the joint through given positions. Data from Winter, (1990) will be used to provide the tibial rigid body with an accurate mass, centre of mass and moment of inertia. The applied forces will be adjusted to ensure an adequate approximation of the stress concentrations in the joint. This task will be undertaken by USFD in months 14-16.

Validation task, V2:

a. The final task will apply force up through the long axis of the tibia at incremented knee flexion angles (0-60 degrees) to simulate stepping onto a flat surface as in stepping up and down when using stairs. The forces applied will be comparable to those applied by the participants in the test rig while being MR imaging. The data measured from the test rig and the MR images of the meniscal behaviour will be used to validate the simulated behaviour of the menisci under load in the joint. This simulation task will be undertaken by ESI in months 15-18, with USFD providing the measured data.
b. As an additional analysis to the Technical Annex, ESI wishes to run an additional simulation relevant to activities of daily living. An appropriate task will be decided with our surgical colleagues in USFD.

Subtasks 1A and 1B are likely to be the easier of the two tasks to complete so will be undertaken first. In addition, the kinematics of the simulated joint will have to be validated before Task 2A, the strain analysis, can be validated. USFD and ESI will cooperate in achieving these two tasks. USFD will provide training to Smith and Nephew (S&N) as required during months 12-15 in the use of the SimBio tools so that S&N may contribute fully to the development of the exploitation plan.

ESI will provide their expertise in the use of PAM-SAFE™ and their knowledge gained from the production and analysis of the KneesUp FE model produced as part of a prior ESPRIT Project. Their input will be invaluable in the appropriate selection of PAM-SAFE™ elements, and assessment of the quality of meshes generated.

The FE model created will be tuned as required to ensure realistic behaviour during the simulated gait cycle. The analysis tasks will concentrate on validating the behaviour for one normal knee before progressing onto the individual normal knees.

If not already complete, the rig force measurement system will be completed. MR Imaging of, and data collection from, additional normal knees will continue during this period.

By **Month 15**, the participating surgeon will begin to screen suitable patients (since a three month lead time is required to allow for waiting lists and processing) for the evaluation phase of the project. Two scanning sessions will be required per patient; one to image the knee pre-operatively while the meniscus is damaged, and a further session post-operatively once the meniscus has been repaired surgically.

At **Month 16**, the First Evaluation Report (D7.3b) will be started to ensure its prompt delivery at Month 18.

Depending on the image processing and mesh generation approach taken (either separate or combined as described in 2.2.1), individual FE models from the normal datasets will be created. This is in preparation for creating the patient FE models later in the project.

At **Month 18**, the second deliverable (D7.3b) will be complete.

3.3 Months 18-24

It is planned that MR imaging (static and dynamic) of the knees of patients prior to meniscal surgery will commence at Month 18. Image processing to segment the components of the patients' knees will be undertaken. It is likely that tuning of the image processing algorithms will be required to cope with

the expected pathological conditions, such as meniscal tears. Depending on the meshing approach used, meshing of the segmented patient knees will be undertaken. The meshing algorithm for the menisci and articular cartilages may need modifications to cope with lesions of the cartilages plus tears and tissue loss in the menisci. The quality of the resultant meshes will be assessed prior to their use in the evaluation analyses. ESI will test the resultant meshes for their utility in PAM-SAFE™.

Re-imaging of those patients who have undergone partial meniscectomy will be carried out during this period when deemed appropriate by the participating surgeon.

3.4 Months 24-30

Completion of the patient MR imaging is planned for Month 27. Further tuning of the FE knee models (meshes and boundary conditions) will be undertaken to ensure the appropriate behaviour (validity) of the analyses. The simplified models of the ligaments used initially may be improved if required.

The final version of the simulated knee is expected to use the following elements (initial versions specified in 3.2.1):

- Bones: Rigid
- Articular cartilages: Solid, strain energy isotropic nearly incompressible
- Collateral ligaments and tendons: Non-linear bars and seatbelts
- Cruciate ligaments: Modelled using membrane elements (considering a tension stiffness but no compression stiffness in the fibre direction).
- Menisci: Non-linear anisotropic using a composite approach.
- Patella tendon: Modelled using membrane elements with one fibre direction
- Muscles: Cable elements

Preliminary evaluation analyses of patient data will be performed using the Preliminary Release IP and MG tools together with PAM-SAFE™. ESI will give input to USFD in generating meshes of menisci with pathologies. USFD will run preliminary analyses of simulated meniscal damage for effects on the motion of the joint.

3.5 Months 30-36

At month 30, the final release versions of the SimBio tools will be available. The final 6 months will be used to undertake the final evaluation simulations, namely determining the behaviour of the simulated pathological (that is, with loss of tissue) menisci, before and after repair. Each evaluation analysis can be broken down into two phases.

3.5.1 Evaluation analyses:

The first evaluation analysis, E1 can be split as follows:

a. The effect of a damaged meniscus upon the kinematics of the knee joint
b. The effect of a damaged meniscus upon the load distribution of the knee joint

and the second evaluation analysis, E2:

a. The effect of partial meniscectomy (<30% tissue loss) upon the kinematics of the knee joint
b. The effect of a partial meniscectomy (<30% tissue loss) upon the load distribution of the knee joint.

The evaluation analyses will re-run the tasks 1a (kinematic) and 2b (loading) described in 3.2.1 used in the validation analyses but using the different meniscal models. USFD will generate the individual knee meshes and meniscal models and run the kinematic evaluation tasks E1a and E2a. USFD will provide the meshes to ESI, who will run the load distribution tasks, E1b and E2b.

Once these analyses have been performed, the pre- and post-operative simulation results of the removal of meniscal tissue can be compared for its effects upon the kinematics of the joint (i.e. E1a and E2a) and the strain distribution within the joint (i.e. E1b and E1b).

At **Month 34**
Formulation of the final deliverable, the final evaluation report will commence.

3.5.2 Meniscal implant design simulation

In addition, this last six-month period will be used for the final simulation task of testing a prototype design for a meniscal implant. Factors that are likely to affect the design of such an implant include the geometry of the structure, its material properties, and the manner of attaching the implant to the tibia.

This task will be carried out by USFD and S&N working together in collaboration. Smith and Nephew will provide 2 person months to the task and will contribute by running a patient specific simulation of an implanted meniscus. In addition, Smith and Nephew's experience in the field of orthopaedic implants will be of great value during this phase particularly in the type and properties of material suitable for implantation and the materials suitable for the attaching the implant.

At **Month 36**

The final deliverable will be complete.

4 Exploitation

Smith & Nephew considers that there are two main exploitation routes for the results of the SimBio project:

- The software can be used to form the basis of a product that can assist surgeons in the diagnostic and pre-operative planning stages of knee surgery, and also predict the biomechanical behaviour of the patients' knees after surgical intervention.

- Alternatively, the SimBio software can be used a research tool within the company and used to understand knee biomechanics in more detail, and to design better implants (knees, ligaments or menisci). Each of these routes will now be described in more detail.

The primary output from a software product will be a better stress distribution in the different regions of a knee after surgery. For example, the maximum stresses in either the cartilage or menisci might be lower. It is assumed that a more even stress distribution will lead to a clinical advantage. However, this assumption has yet to be proven, and would require a clinical trial. In addition, any final optimised version of the software will have to undergo further clinical trials if clinicians are to use the output from the software in deciding between various treatment regimes. The clinicians themselves must also see a benefit in using the software, i.e. it must show "better judgment" than that of the clinicians. This may be particularly difficult to show. Smith & Nephew cannot see a surgical product originating from the SimBio project, especially after taking into account the time and costs required to complete a clinical trial.

However, SimBio software could be used to visualise patients' knees better and in more detail. One of the key outputs from the project is that patient specific data can be analysed and later visualised. Clinicians could benefit from the better images, and then use their own experience before deciding upon what intervention, if any, should be made. The advantages of this approach are that the software would not require any formal clinical trials, merely validation. This validation already forms a key part of the SimBio programme.

Smith & Nephew can envisage several uses of the SimBio software within its research environment. Implants could be better designed, and better matched to patient anatomy. Outer surgical procedures could also benefit. For example, menisectomies are carried out, often with little understanding of the underlying biomechanics of the knee. Different cutting positions and different volumes of meniscus

being removed could be modelled. Better tools could be developed, and ultimately, artificial menisci with material properties and geometries optimised for typical patients could be designed. Operations of the anterior cruciate ligament would also benefit from a more detailed understanding. Smith & Nephew is interested both in ACL prostheses or autograft positioning, and in the surgical tools used in these operations.

The planning of individual surgical procedures in orthopaedics is based upon the application of the expertise and experience of the surgeon. S&N believe that, in this context, the use of the software will be limited, at least in the medium term, to the provision of supplementary diagnostic information. Substantial and long-term validation of the software will be required before any surgeon would base a clinical decision on the software output. The first steps in this validation process, based on outcome prediction, are integral to workpackage 7.3. The more immediate interest for S&N is in the development of a better understanding of knee biomechanics, and in application to the design of a new range of implants and associated tools.
As an academic partner, the University of Sheffield sees its exploitation of SimBio primarily as research-based. However, we would wish to continue to collaborate with our industrial partners, such as Smith and Nephew. We expect to use the tools developed beyond the end of the project in two main areas, Academic Research and Consultancy. Extending the use of the SimBio Environment to other areas of our clinical expertise, such as heart valve design, orthopaedic prosthesis design, and plastic surgery applications will be highly advantageous. In addition, our surgical colleagues in the newly formed Sheffield Institute for Sports Medicine (affiliated to USFD) consider that the SimBio tools are likely to have utility in two main areas of orthopaedic surgery:

- SimBio is likely to offer advantages in the shorter term in certain areas of pre-operative planning. For example, sizing meniscal allographs is currently inaccurate and is performed in the operating theatre. SimBio could allow more accurate assessment of defect size prior to surgery and improve the selection of allograph dimensions. This approach could also be applied to the sizing of grafts used to treat chondral defects.
- In the longer term, it is believed that SimBio will have major implications for new orthopaedic development.

ESI considers that the SimBio environment will help to make its biomechanical analysis software more user-friendly for clinical and medical end-users. For this type of activity, typically a surgeon needs tools to assist in making pre and post-operative decisions for a specific case, the patient. With the SimBio environment, the end-user will be able to mesh almost automatically the MRI data of their patient's biological segment (for example, the knee). A material database will be available to define the model and a mechanical analysis of a specific case (for example, the gait cycle) can be performed with the PAM-SAFE™ package. The SimBio environment proposes only one interface for the different software and databases necessary to conduct a numerical biomechanical analysis. These are interconnected in the background, which will make the work more convenient for the end-user.

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6 Appendix A

6.1 Documentation for the MRI Scan Sequences

All MR imaging performed using a Marconi Medical Systems Eclipse 1.5T at the Northern General Hospital, Sheffield, UK.

Volunteer "A" LEFT Knee. Slice Thickness 1.4mm for all series except 3&10
DOV:17.9cm x 17.9 cm. 256x 256, Effective pixel size: 0.7mm

Sequence Number	MRI Code	Renamed Number	Sequence Type	**Receive Coil**	Number of slices
4476	A	1	FAST LOCALISER TR=15, TE=4, Flip angle 25	Bilateral TMJ	2
	B	2	TE 15 FAST COR/AX PILOT TR=35, TE=15, Flip angle 30		2
	C	**3**	RF-FAST/VOL/FATSAT TR=39, TE=13, Flip angle=60		116 Thickness 0.7mm
	D	4	FAST LOCALISER TR=10, TE=3, Flip angle=20		2
	E	5	TE 15 FAST COR/AX PILOT TR=35, TE=15, Flip angle 30		2
	F	**6**	RF-FAST/VOL/FATSAT/ TR 39.0, TE 13.0, Flip angle=60		58
	G	**7**	T2*/S/RF FST/VOL/FSAT/MAST TR 43.0, TE 15.0, Flip angle =30		58
	H	**8**	T2*/S/RF FST VOL TR 27.0, TE 13.0, Flip angle=60		58
	I	**9**	T2*/S/RF FST VOL TR 27.0, TE 13.0, Flip angle=60		58
	J	**10**	TE 4.4/RFFVOL TR=15, TE=4, Flip angle=25		90 Thickness 1.5mm
4477	A	1	FAST LOCALISER TR=10, TE=3, Flip angle=20	**Single large joint**	2
	B	2	TE 15 FAST COR/AX PILOT TR=35, TE=15, Flip angle 30		2
	C	**3**	T2*/S/RF FST/VOL/FSAT/MAST TR 43.0, TE 15.0, Flip angle=30		60

Volunteer "R" RIGHT Knee. Slice thickness 2.0mm for all series
DOV: 17.9cm x 17.9cm, 256x 256, Effective pixel size: 0.7mm

Sequence Number	MRI Code	Renamed Number	Sequence Type	Receive Coil	Number of slices
4708	A	1	FAST LOCALISER TR=10, TE=3, Flip angle =20	**Bilateral TMJ**	2
	B	2	FAST LOCALISER TR=10, TE=3, Flip angle=20		2
	C	3	TE 15 FAST 3 PLANE PILOT TR=35, TE=15, Flip angle=30		3
	D	**4**	T2*/S/RF FST/VOL/FSAT/MAST TR 47.0, TE 15.0, Flip angle=30		60
4709	A	1	FAST LOCALISER TR=10, TE=3, Flip angle=20	**Single large Joint**	2
	B	2	TE 15 FAST 3 PLANE PILOT TR=35, TE=15, Flip angle=30		3
	C	**3**	T2*/S/RF FST/VOL/FSAT/MAST TR 47.0, TE 15.0, Flip angle=30		60
4711	A	1	FAST LOCALISER TR=10, TE=3, Flip angle =20	**Single shoulder Joint**	2
	B	2	TE 15 FAST 3 PLANE PILOT TR=35, TE=15, Flip angle=30		3
	C	**3**	T2*/S/RF FST/VOL/FSAT/MAST TR 47.0, TE 15.0, Flip angle =30		60

SEQUENCE NUMBER 4826 (DYNAMIC)
Volunteer "A" Right Knee, Sequence 10 slice thickness 3mm (with 2mm interval)
FOV = 16.0 x 16.0cm, 256x256, Effective pixel size = 0.62mm
Receive coil: = Single shoulder joint

Comments	MRI Code	Renamed Number	Sequence Type	Size	Number of slices	Slice thickness (mm)
Good contrast but noisy. Menisci and bone clearly defined.	10	10	T2* Cine/Sag TR=29.0, TE 13.0 Flip angle=20	**256 x 256**	30	3

SEQUENCE NUMBER 4442 (STATIC & DYNAMIC)

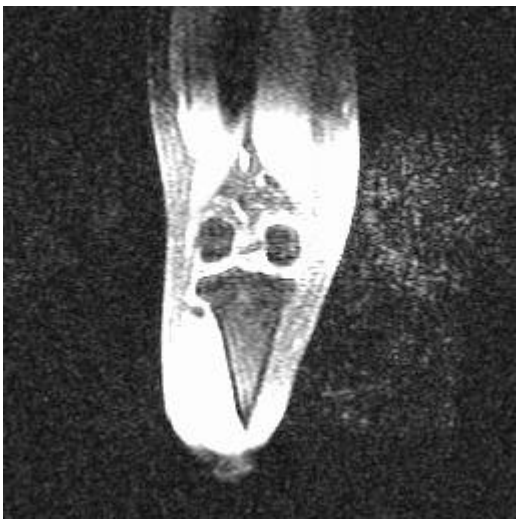
Volunteer "A" Right Knee, Sequence 3, slice thickness 2mm

N^{o}. 3 FOV = 17.9x17.9cm, 256x256, Effective pixel size =0.7mm
N^{o} 4 & 5 FOV = 34.9x34.9cm, 256x256, Effective pixel size =1.36mm
Remainder (not 15) = 27.9x27.9cm, 256x256, Effective pixel size =1.08mm
N^{o} 15 = 43.6x43.6cm, 128x128, Effective pixel size= 3.4mm
* Sagittal view, C = coronal view, a = axial view, Receive coil: Single shoulder joint

Comments	MRI Code	Renamed Number	Sequence Type (Single shoulder joint coil)	Size	Number of slices	Slice thickness (mm)
c = poor	A	1	2 PLANE FAST LOCALISER TR=16, TE=3, Flip angle = 20	256 x 256	2 1= t 2 = c	10
c = good t & s = Poor resolution	B	2	TE 3.7 FAST 3 PLANE PILOT TR=10, TE=4, Flip angle=20	512 x 512	3 1= c 2 = a 3 =s	10
Excellent resolution	C *	3	T2*/S/RF FST/VOL/FSAT/MAST TR=47, TE=15, Flip angle=30	256 x 256	60	2
Dark & grainy	D c	4	TE 3.7 TR 23.0, TE 3.0, Flip angle=20	256 x 256	10	5
Dark & grainy	E c	5	TE 3.7 TR=23, TE=3.0, Flip angle=20	256 x 256	2	5
1=blurred 2=good res	F c	6	TE 1.5 TR=10, TE=1.0, Flip angle=30	256 x 256	2	9.8
1=blurred 2=not good	G c	7	TE 1.5 TR 6.0, TE 1.0, Flip angle=90	256 x 256	2	9.8
1=blurred 2=sim to F	H c	8	TE 1.5 TR=6.0, TE=1.0, Flip angle =20	256 x 256	2	9.8
1=blurred 2=dark bone	I c	9	TE 3.7 TR=22, TE=3.0, Flip angle=20	256 x 256	2	9.8
1=fuzzy 2=good cart	J *	10	TE 3.7 TR=22.0, TE=3.0, Flip angle =20	256 x 256	2	9.8
1:light bone 2=bright bone	K*	11	TE 1.5 TR=6.0, TE=1.0, Flip angle =20	256 x 256	2	9.8
1= blurred 2=grey bone	L c	12	TE 3.7 TR=22.0, TE= 3.0, Flip angle =20	256 x 256	2	9.8
1=blurred 2= grey bone	M c	13	TE 3.7 TR=22.0, TE=3.0, Flip angle =20	256 x 256	2	9.8
1= blurred 2= sim to 13	N c	14	TE 3.7 TR=8.0, TE=3.0, Flip angle =20	256 x 256	2	9.8
Both U/S	O c	15	TE 2.7 TE=6.0, TE=2.0, Flip angle =90	128 x128	2	9.8
1=blurred 2= dark cart	P c	16	TE 7.5 TR=1,500, TE=75.0, Flip angle=90	256 x256	2	9.8
Both v. poor	Q c	17	TE 7.5 TR=8,000, TE=75.0, Flip angle=90	256 x 256	2	9.8
1=fuzzy 2=bright bone	R *	18	TE 7.5 TR=1,500, TE=75.0, Flip angle=90	256 x 256	2	9.8

7 Appendix B

7.1 Dynamic MRI Scan Images



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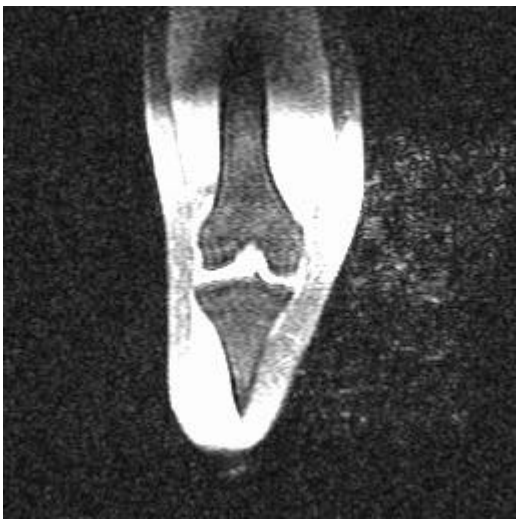

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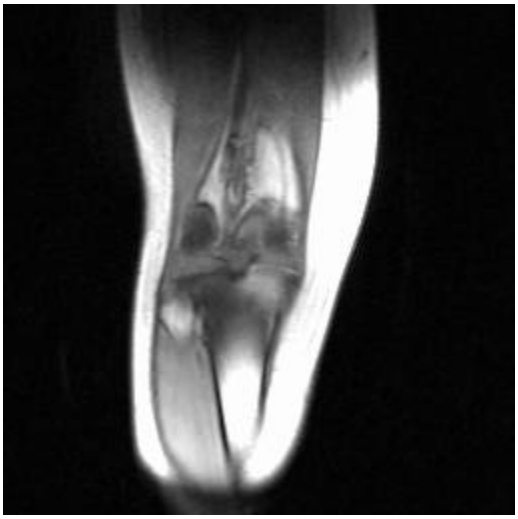

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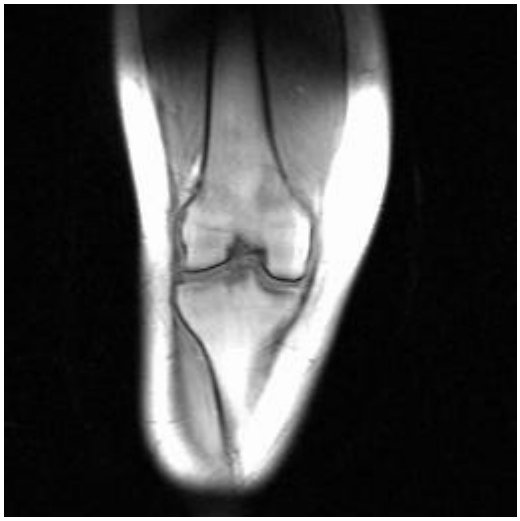

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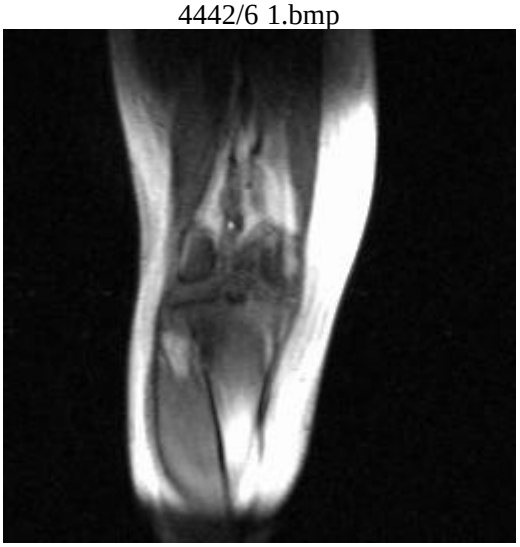

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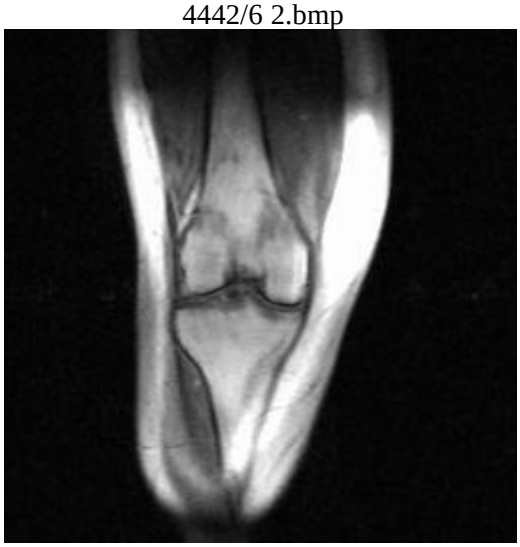

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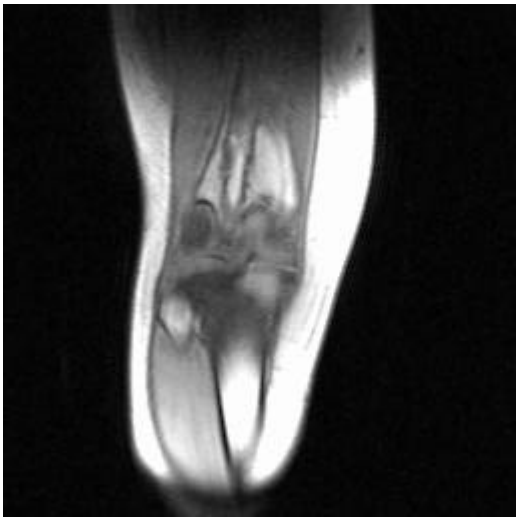

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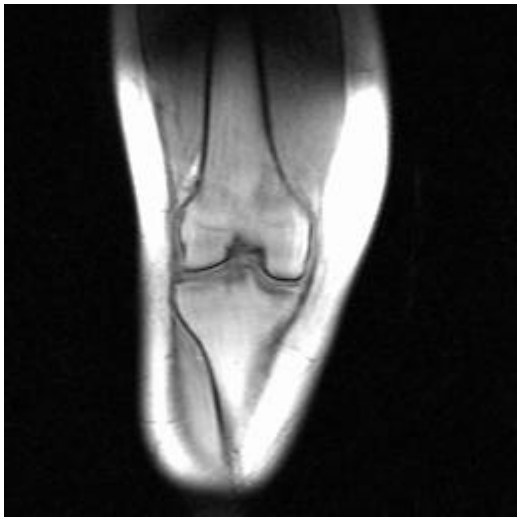

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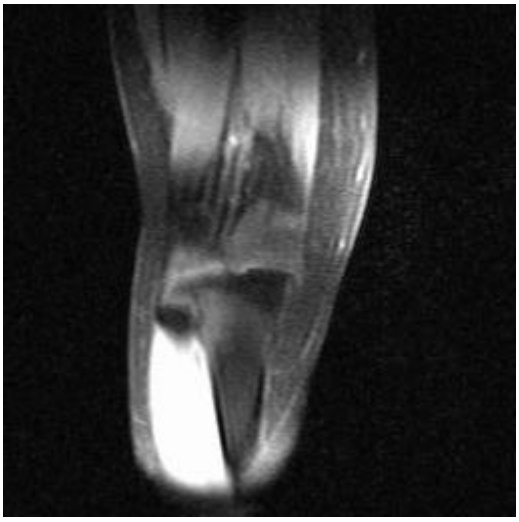

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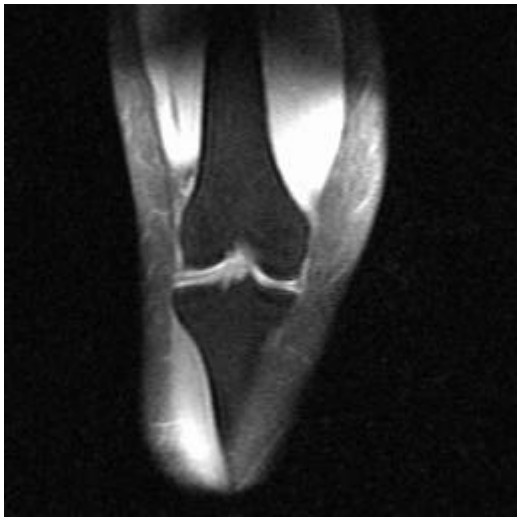

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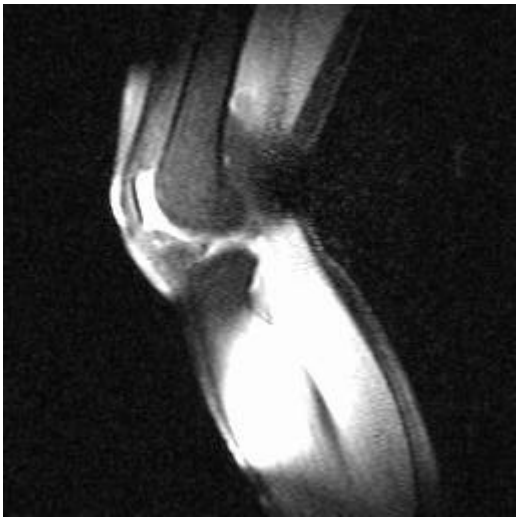

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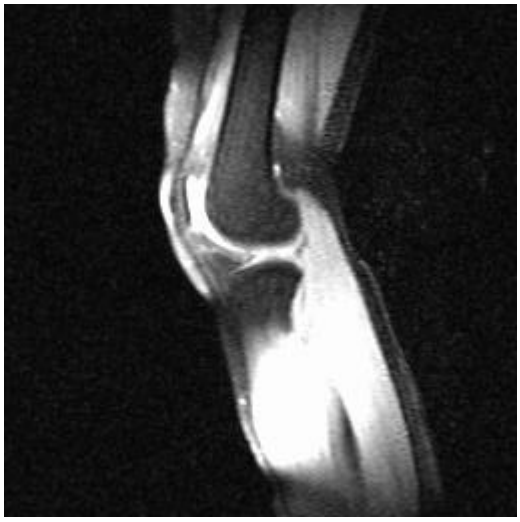

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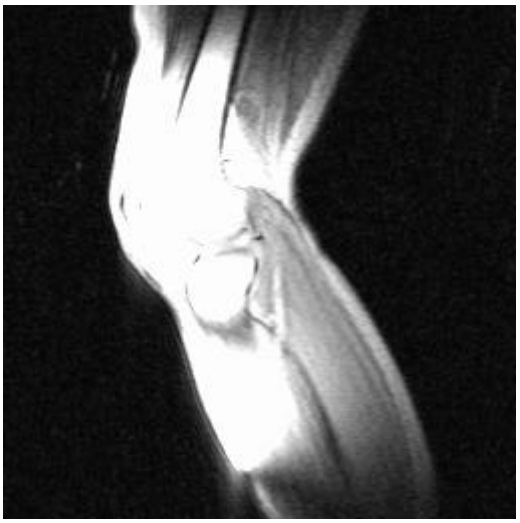

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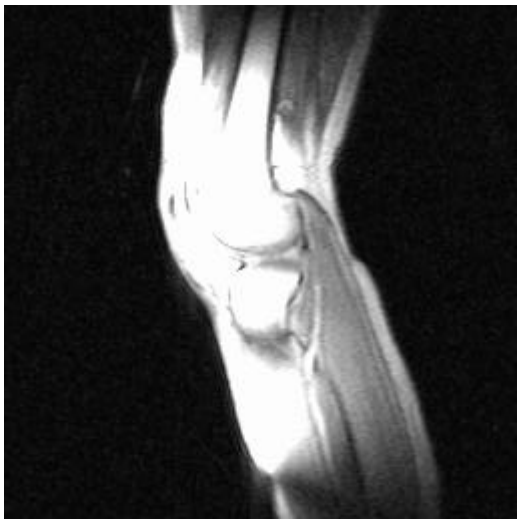

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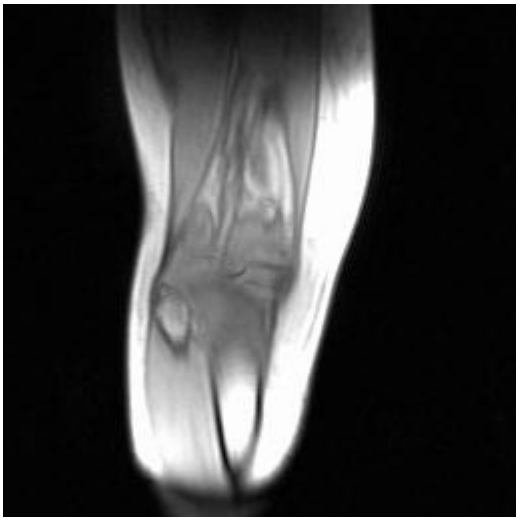

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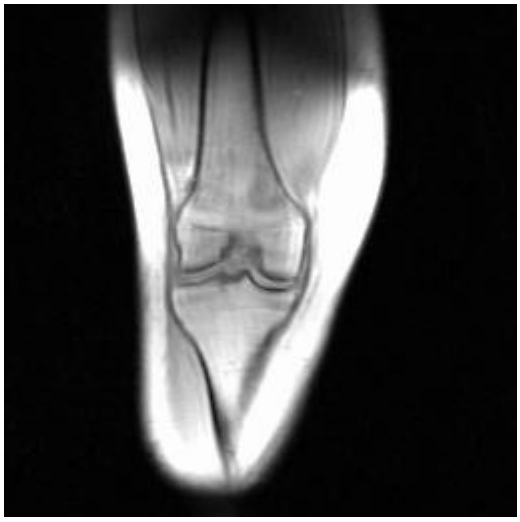

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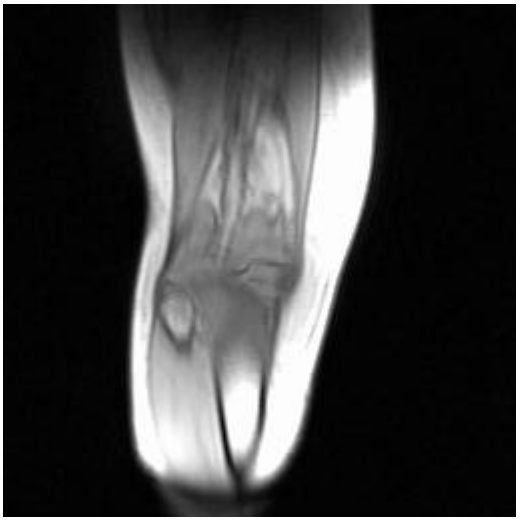

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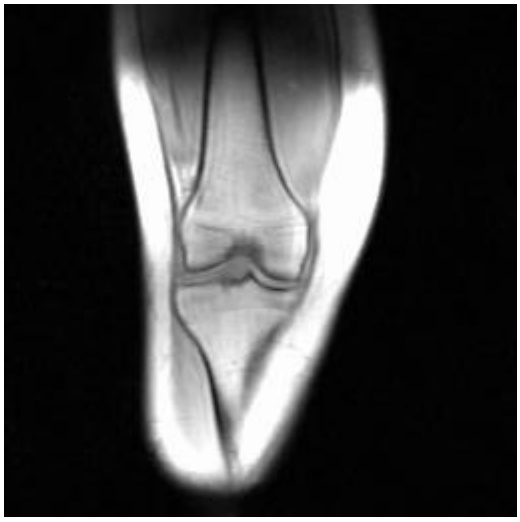
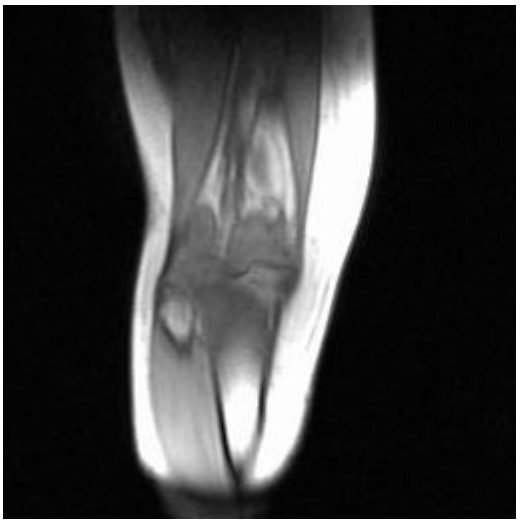
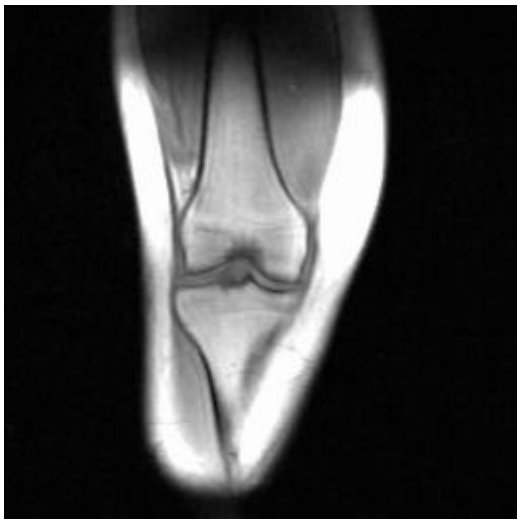


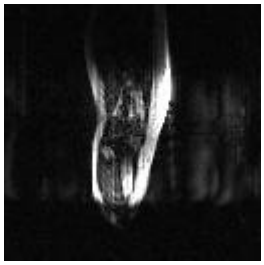
4442/13 2.bmp



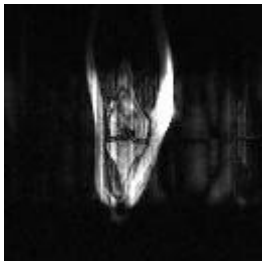
4442/14 1.bmp



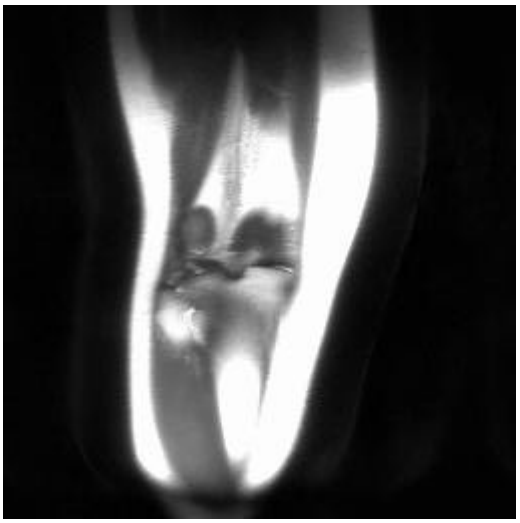
4442/14 2.bmp



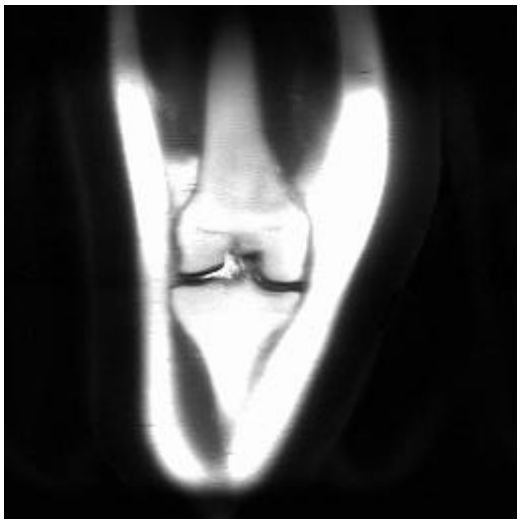
4442/15 1.bmp



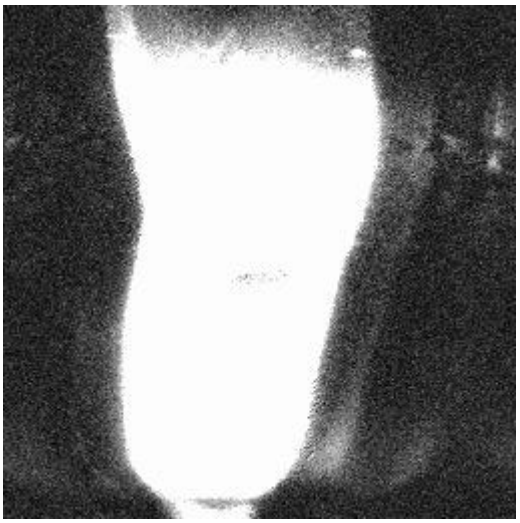
4442/15 2.bmp



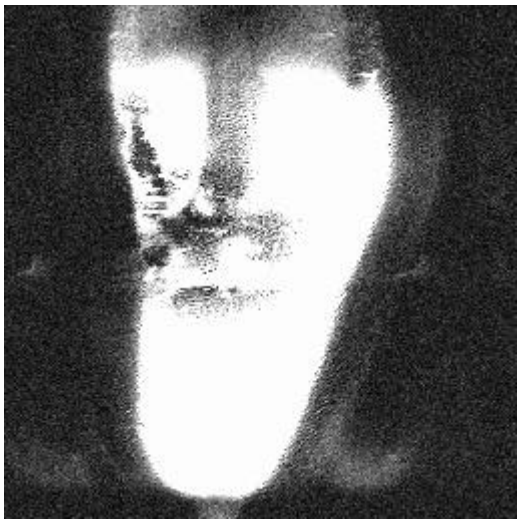
4442/16 1.bmp



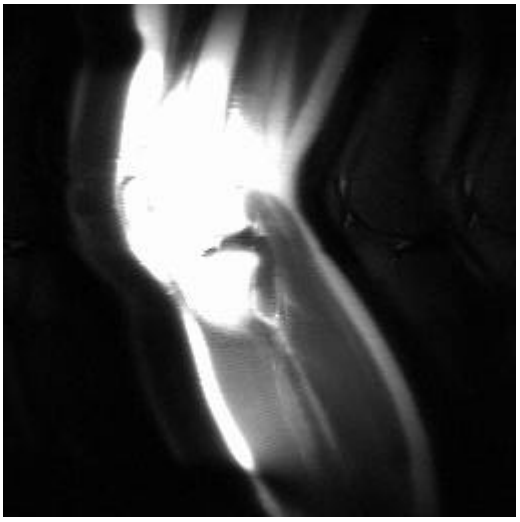
4442/16 2.bmp



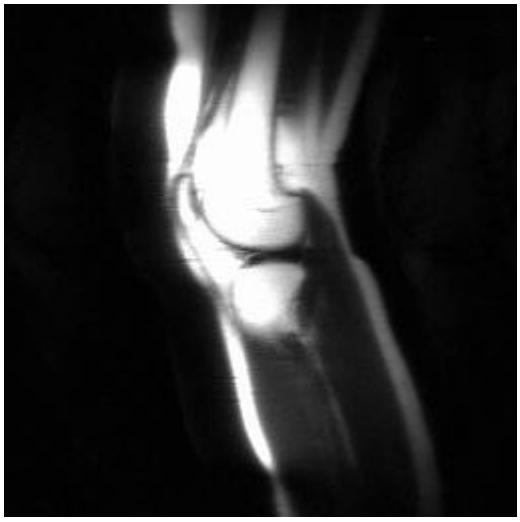
4442/17 1.bmp



4442/17 2.bmp



4442/18 1.bmp

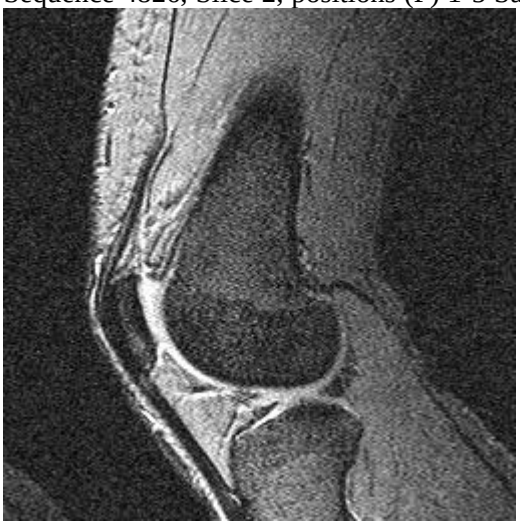


4442/18 2.bmp

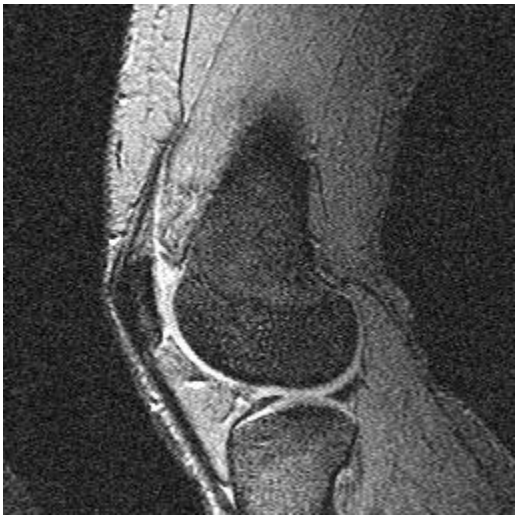
Pseudo-dynamic scan protocol

Position knee, take 6 sagittal MR slices (five second acquisition time per slice) through knee, extend knee and reposition, repeat MR scans for 5 positions.

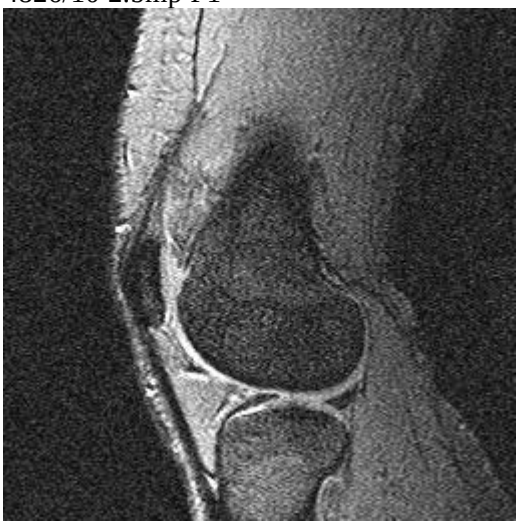
Sequence 4826, Slice 2, positions (P) 1-5 Sagittal slice



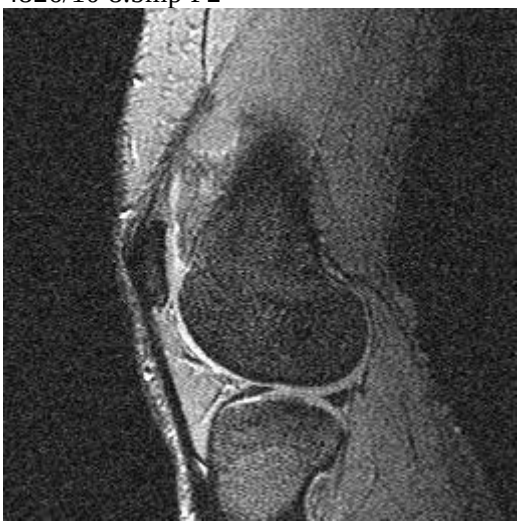
4826/10 2.bmp P1



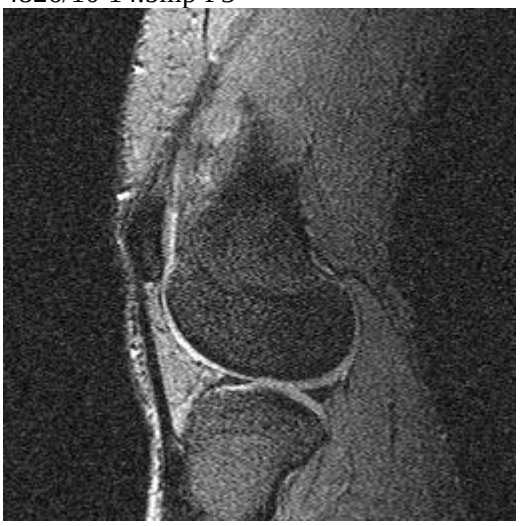
4826/10 8.bmp P2



4826/10 14.bmp P3



4826/10 20.bmp P4



4826/10 26.bmp P5