

Development of Analysis Techniques for dynamic magnetic resonance imaging

– Master Thesis –

to be awarded

Master of Science in Medical Photonics

submitted by

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Abstract

Acknowledgements

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List of Acronyms

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1 Introduction

1.1 The Knee Joint

The knee joint, a pivotal structure in the human body, plays an essential role in locomotion. Additionally, it functions to control the center of body mass and posture in the activities of daily living by facilitating a wide range of movements. As such, the knee's health and integrity are vital for overall quality of life, influencing everything from basic mobility to participation in complex sports. A comprehensive survey across 15 European countries and Israel found that knee pain was the third most commonly reported type of chronic pain. This underscores the significant public health concern it represents (Breivik et al. 2006). Furthermore, arthritis/osteoarthritis (OA) was identified as the most common cause of this pain.

This situation has not improved over time. In Germany for instance, a recent retrospective study has found that the number of patients with OA is steadily rising (Obermüller et al. 2024). Knee-related issues are prevalent and impactful due to the inherent complexity of the knee joint itself. As a hub of various anatomical structures working in unison, the knee supports a range of movements and bears significant loads, making it susceptible to a variety of injuries and conditions. Understanding the anatomy of the knee is the first step in tackling this problem.

Anatomy and Function

The knee joint is the largest and the most superficial synovial joint in the body. (Daley, Agur, and Moore 2023). It comprises three primary articulations: two femorotibial articulations (see Figure 1) and one femoropatellar articulation. These articulations, illustrated in figures 1 and 2, are defined by their complexity and incongruence, features that are crucial for the joint's biomechanical performance.

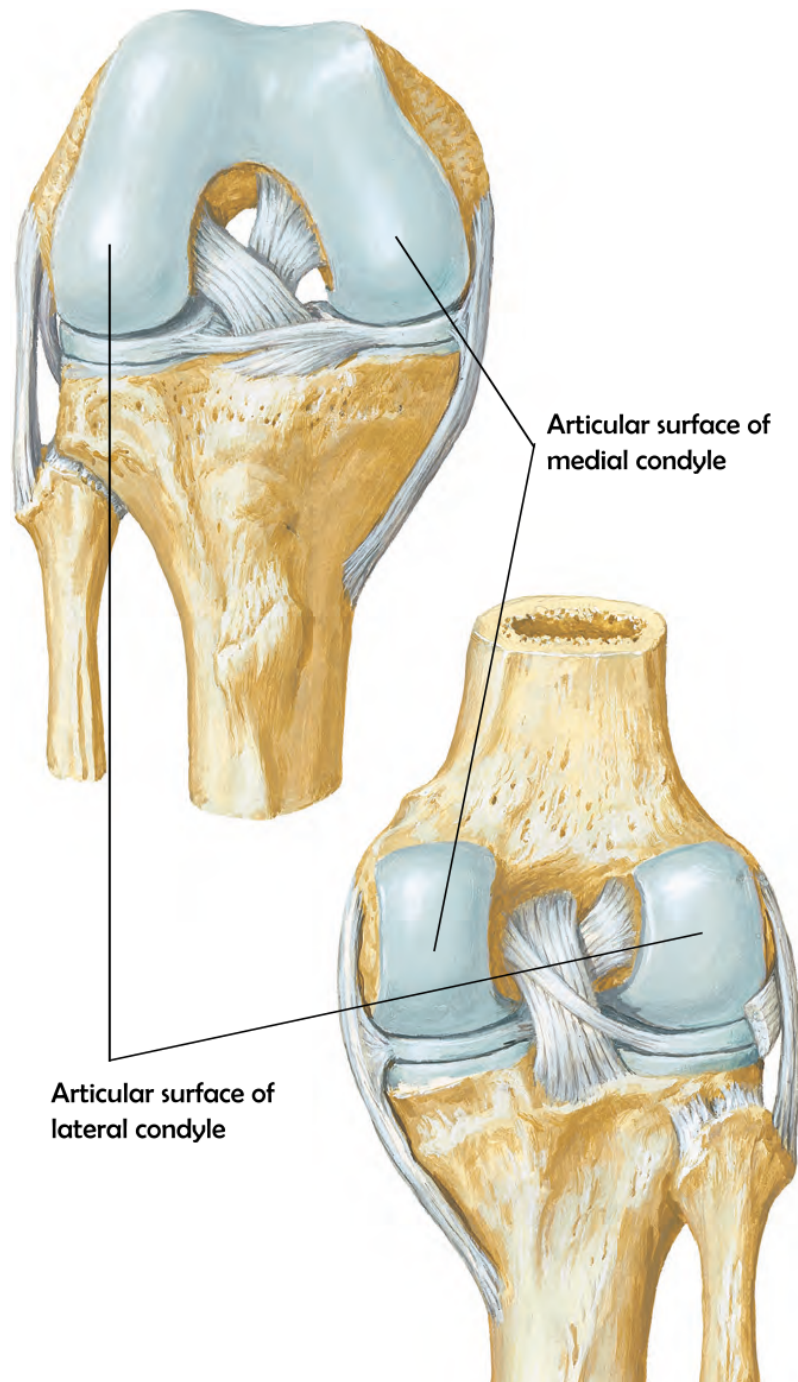


Figure 1: Anterior (flexed,top) and posterior (extended, bottom) view of the right knee with their articular surfaces labeled. (Netter 2023, p.519)

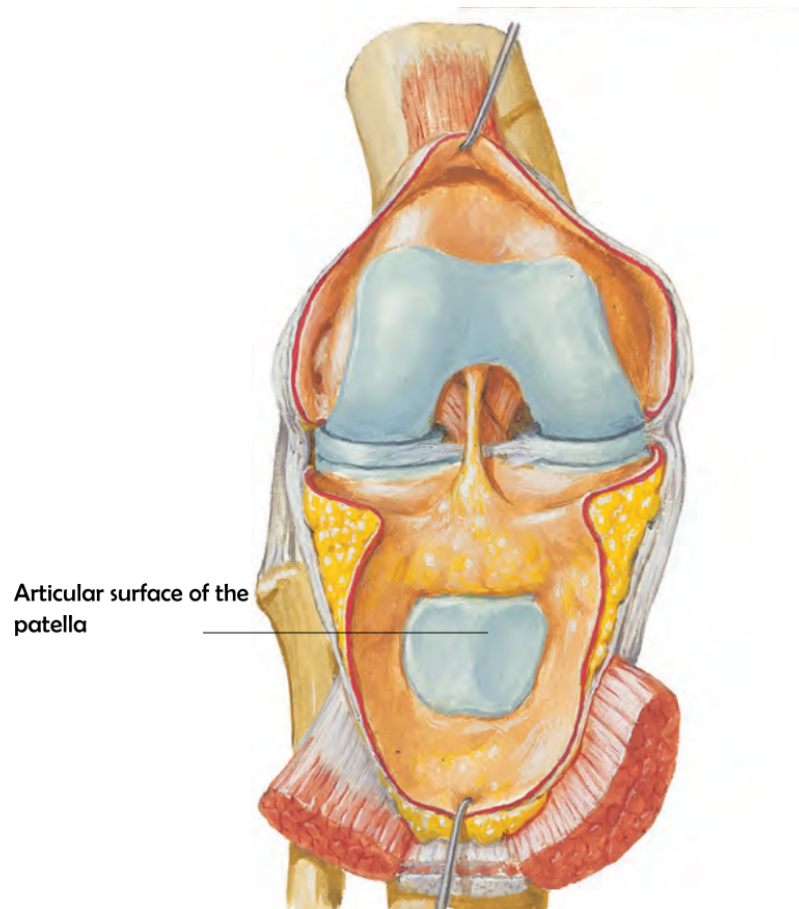


Figure 2: Right joint opened, knee slightly in flexion, with the patellar articulation labelled. (Netter 2023, p.517)

This design allows the knee to manage a wide array of movements and bear significant loads. Figure 3 illustrates the knee's capacity for multidimensional movement, highlighting the joint's sophisticated structural design that enables this versatility. However, this inherent design also renders the knee vulnerable to a range of forces (Standring and Gray 2021).

Such mechanical forces, influenced by activities and body mass index (BMI), are significant causes of OA and represent one of the most modifiable risk factors (Heidari 2011). Furthermore, abnormal joint loading is considered a key mechanical driver of osteochondral changes thought to contribute to the initiation and progression of knee OA (Coburn et al. 2023).

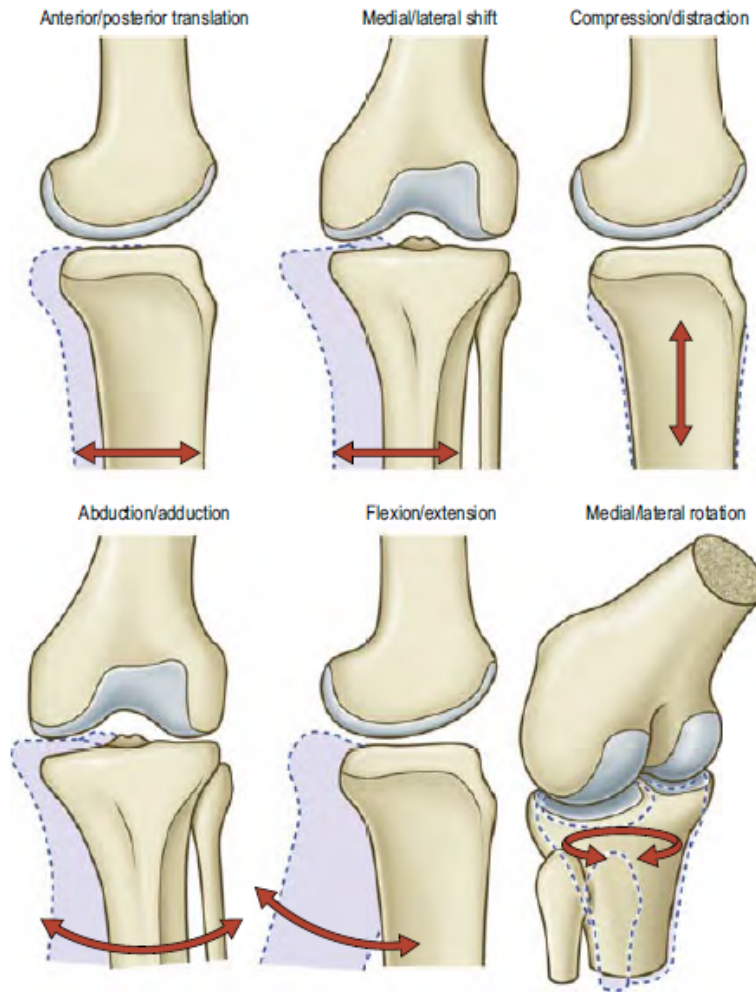


Figure 3: The knee joint motion in three dimensions, described using six independent variables (degrees of freedom) (Standring and Gray 2021, p. 1412).

The relationship between biomechanical stresses and knee health highlights the need for diagnostic tools that fulfill two key criteria: they must capture the knee's dynamic behavior during motion and assess the joint under varying loads. Dynamic magnetic resonance imaging (MRI) excels in meeting these requirements as one of the most advanced imaging modalities.

1.2 Dynamic MRI

In a broad sense, dynamic MRI is an umbrella term encompassing various MRI techniques designed to capture and visualize physiological processes and motion over time. The dynamic aspect of MRI is crucial for studying systems or structures

involving inherent motion, such as blood flow, tissue perfusion, or cardiac activity. For the purposes of this project, the focus of "dynamic MRI" narrows down to capturing the bulk movement of the knee joint undergoing active flexion extension cycles inside the scanner. Compared to traditional static MRI scans, which are highly susceptible to motion artifacts compared to other imaging modalities (Zaitsev, Maclaren, and Herbst 2015), dynamic MRI techniques not only accommodates motion, but can even leverage it to offer comprehensive insights into the functional and biomechanical properties of the concerned structures. Among these techniques, CINE imaging, particularly renowned in cardiac MRI, is considered the gold standard for evaluating cardiac function (Menchón-Lara et al. 2019). Its high regard in cardiac MRI demonstrates the method's precision and adaptability—traits that are leveraged in knee imaging.

1.2.1 CINE imaging

CINE, derived from 'cinematography,' refers to creating a movie-like sequence of images. In the context of dynamic knee MRI, this technique can be used to reconstruct a "movie" of a single flexion-extension cycle. This visualization is achieved by aggregating multiple partial datasets acquired over various cycles. The knee's movement cycle is segmented into distinct stages, each corresponding to a specific angle of flexion or extension. For each stage, k-space — the Fourier transform space from which MR images are reconstructed — is incrementally sampled. This data is gathered across multiple repetitions of the movement cycle, ensuring comprehensive coverage of k-space and thus, high-resolution imaging of each movement phase. This technique works robustly only if the cycles are sufficiently similar (Curtis and Cheng 2022). Achieving this consistency in dynamic MRI of the knee, which naturally involves significant movement variations, requires precise synchronization of the imaging process.

1.2.2 Gating

This synchronization, known as gating, aligns image acquisition with specific, repeatable points in the knee's movement cycle. By ensuring each captured image corresponds accurately to a consistent phase of motion, it minimizes the discrepancies that can arise from cycle-to-cycle variations, enhancing the reliability of biomechanical analyses. Although there are two types of gating, namely prospective

and retrospective, it is the latter that is the standard for CINE imaging as it provides a more consistent image quality (Edelman 2005, p. 102). In retrospective gating, the data is acquired continuously throughout the motion cycle. The data is then reordered post-acquisition into a coherent sequence that shows the knee at different positions along the motion cycle. This necessitates external information that captures the precise moment and position of the knee throughout its range of movement beyond just the raw data acquired during the MRI scan. A previously reported novel knee loading device is employed to address this, which comes with an optical sensor attachment that provides this vital information (Brisson et al. 2022).

1.2.3 Knee loading device

The MR-compatible knee loading device employed in this study is illustrated in Figure 5. This device allowed for a range of motion of approximately 25 to 45 degrees (subject-dependent), enabling subjects to perform knee flexion and extension cycles under both loaded and unloaded conditions. For loading, the device was equipped with compartments for weight plates and sandbags, providing a physiological load of 10 to 12 kilograms. These weights are positioned at the distal end of the device, directly influencing the mechanics of knee extension. As the subject extends the knee, they must overcome not only the natural resistance of their body weight but also the additional external load imposed by these weights. Central to this device’s functionality is an optical fiber position sensor (MR338-Y10C10, Micronor, 155 Camarillo, CA, USA), which precisely measures the absolute angle from 0° to 360° with a resolution of 0.025° (Rickenbach 2013). This measurement capability is critical for synchronizing the knee’s movement with MRI data reconstruction.

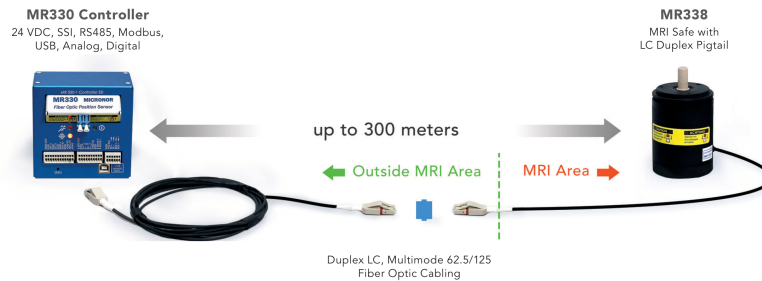


Figure 4: The MR330 controller (left) and MR338 optical fiber position sensor system (right), showcasing the connection from the controller to the sensor via duplex LC multimode fiber optic cabling.

As shown in Figure 4 , the MR330 controller interfaces with the MRI-safe MR338 position sensor to facilitate precise measurement within the MRI environment, accommodating up to 300 meters of fiber optic cabling. The controller is connected to a laptop placed outside the scanner while the sensor is attached to the device within. To enhance signal acquisition and the clarity of imaging, two flexible coils (cite the coils here, perhaps also show a picture) were positioned at key anatomical locations: one at the distal femur and another at the proximal tibia, as specified in the MRI protocol.

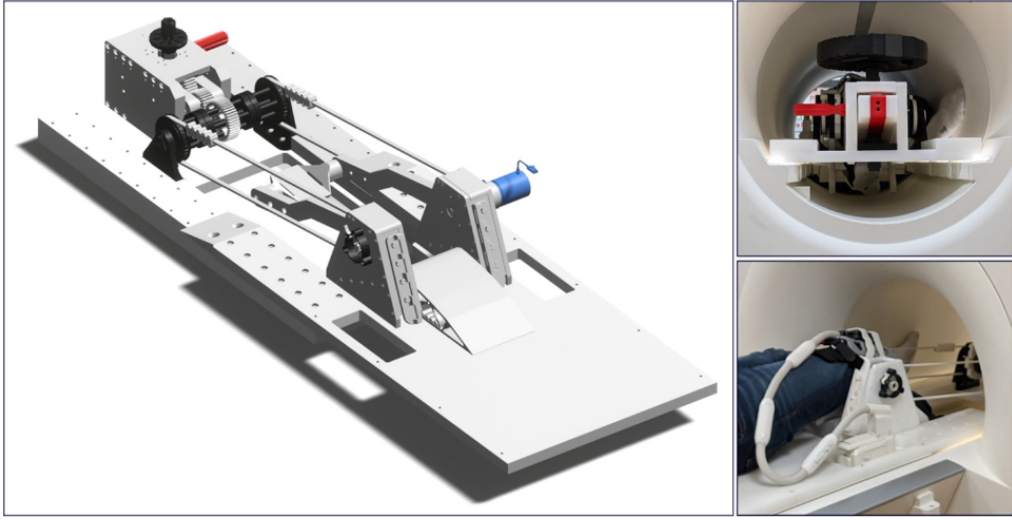


Figure 5: A 3D rendering of the knee motion/loading device (left) and two photographs of the device in a Siemens Magnetom Prisma Fit MRI scanner (right). The top right image (rear view) demonstrates how the distal part of the device sits atop the rails within the scanner bore, which are normally used to guide and support the patient table. The bottom right image (front, oblique view) demonstrates an individual positioned in the device with a flexible coil around the index knee, the thigh secured between the proximal pillow blocks and the ankle fastened to the leg support, as well as the coil plug setup.

To further enhance the quality and precision of our imaging, and to maximize the potential for precise image reconstruction, a previously reported radial golden-angle gradient-echo FLASH sequence was used, which is more robust against motion artifacts than Cartesian sequences (Aleksiev et al. 2022). The following sections will detail the key components of this technique — radial golden-angle acquisition and the gradient-echo FLASH sequence.

1.2.4 Radial golden-angle acquisition

As the name suggests, radial golden-angle acquisition specifically modifies how k-space is sampled. Unlike traditional static MRI, which typically employs Cartesian sampling, this method utilizes radial sampling. Here, the data points are collected along radial lines spreading out from the center of k-space, resembling spokes on a wheel. Figure 6 depicts a generic radial sampling scheme. The separation between any two adjacent circles defines the separation Δk_r in the radial sampling direction, whereas, the angular separation between any two successive angular lines in k-space (such as between the two example lines shown in the figure) defines $\Delta\theta$. The two quantities Δk_r and $\Delta\theta$ are constrained by the Nyquist sampling criterion. (Brown et al. 2014)

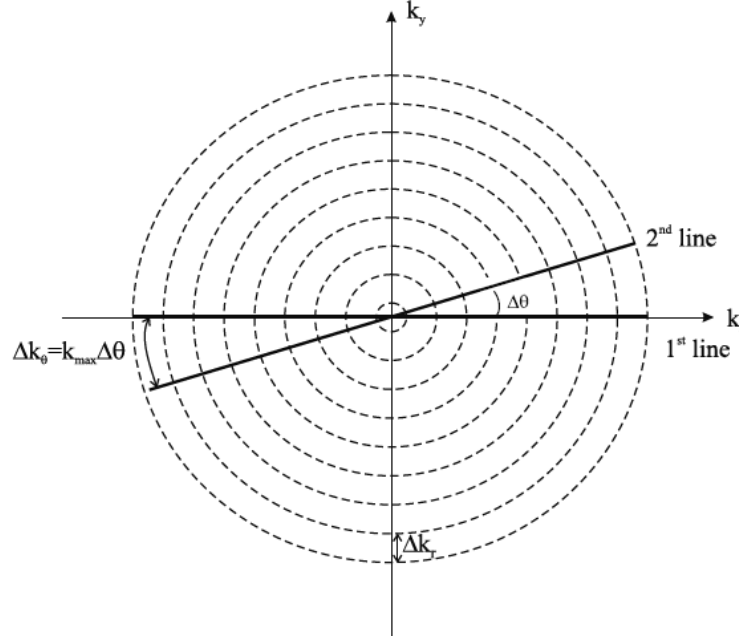


Figure 6: Generic radial k-space sampling (Brown et al. 2014, p.306)

The 'golden-angle' strategy, which we employ, optimizes this approach by spacing the radial lines at an angle of approximately 111.25 degrees. This specific angle helps in evenly covering the k-space without overlapping, ensuring that each new image frame provides unique information, thus enhancing image quality and temporal resolution.

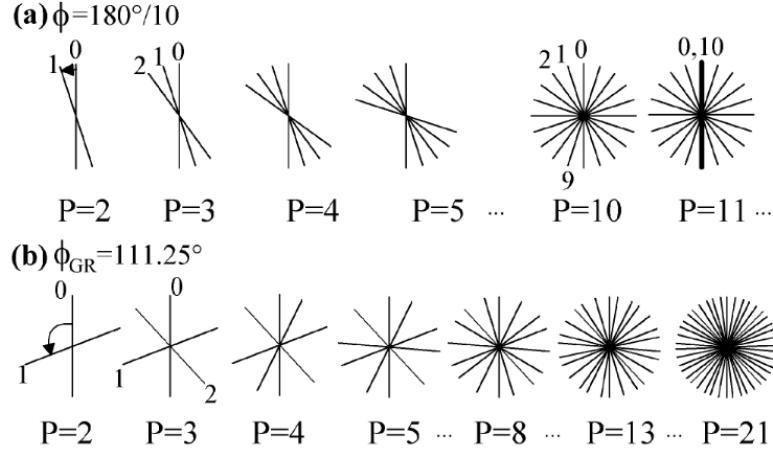


Figure 7: Radial k-space sampling strategies. (a) Fixed angular increment, showing potential for uneven k-space coverage. (b) Golden-angle sampling, ensuring uniform distribution across k-space (Winkelmann et al. 2007).

Figure 7 provides a visual comparison between traditional fixed increment and the golden-angle methods in k-space sampling. It highlights how each approach affects the distribution of sampling lines across k-space. In the figure, part (a) shows radial sampling using a fixed angular increment. This traditional method can lead to gaps or overlaps in data collection, depending on the number of radial profiles used. Part (b) demonstrates the golden-angle method, where each new radial line is placed at an increment of approximately 111.25 degrees. This approach allows for a more uniform distribution of sampling lines across the k-space, enhancing image quality by preventing gaps and reducing redundancy in data collection. Figure blank shows the k-space of a specific frame during the knee flexion cycle and the corresponding reconstructed MRI image.

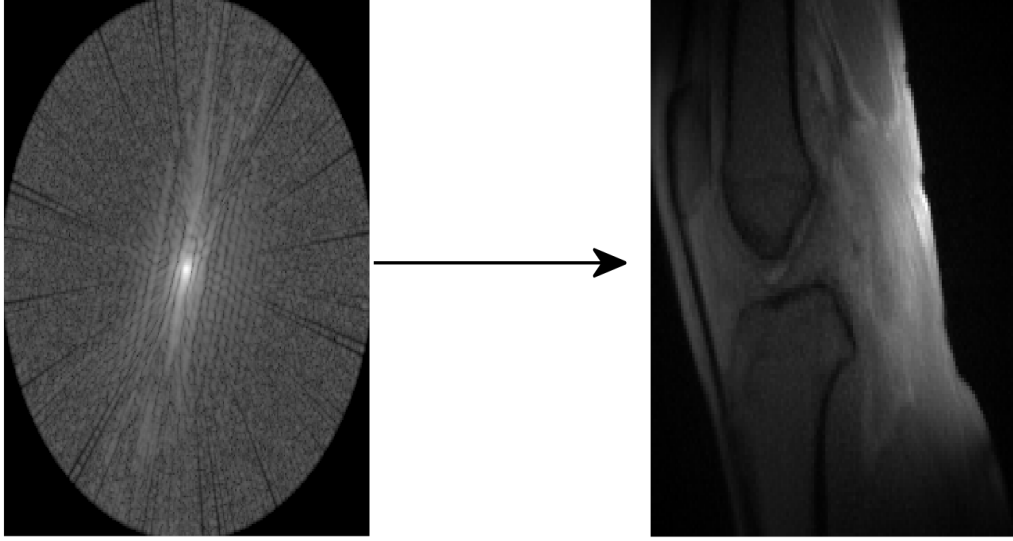


Figure 8: **Example of k-space and reconstructed image.** Left: K-space data from a specific angle during the knee flexion cycle. Right: Corresponding reconstructed MRI image, illustrating the detailed visualization achievable through golden-angle sampling.

1.2.5 Gradient Echo FLASH sequence

Gradient echo (GRE) is a prime candidate for dynamic MRI because it is a fast scanning process. There are two major factors that contribute to its speed. First, unlike the spin echo, we do not need to wait for a long time for the longitudinal magnetization component M_z to sufficiently recover for another repetition. This is because in a GRE sequence, a smaller flip angle is used. Secondly, we do not need to wait for the spins to refocus after the application of a 180° rf pulse, because there is no such pulse applied. Instead, the refocusing is done here by using magnetic field gradients of opposite polarity. The scheme of GRE sequence is depicted in Figure 9. The notation is as follows: α° : flip angle (less than 90°), RF: radio frequency pulse, SS: slice selecting gradient, PE: phase encoding, FE: frequency encoding, TE: echo time and TR: repetition time. Note that in the frequency encoding direction, a negative dephasing lobe is followed by a positive gradient that brings the spins back into phase to generate the signal.

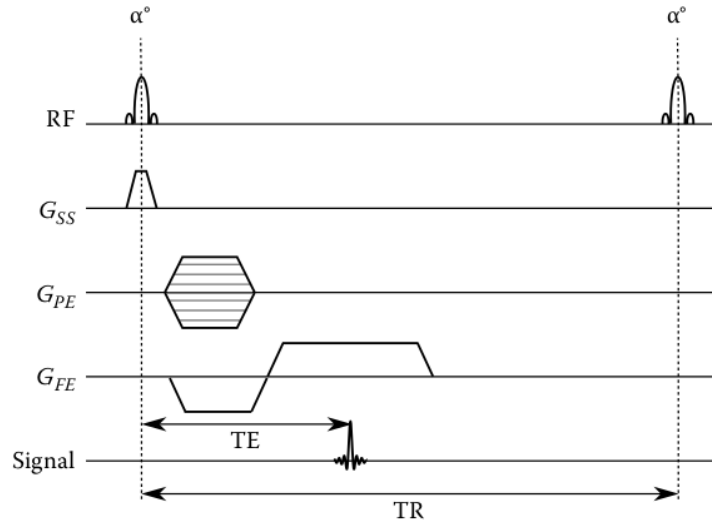


Figure 9: Simplified diagram of the GRE sequence that depicts the refocusing gradient applied in the frequency encoding direction (Berry and Bulpitt 2009, p.233).

After a series of rf pulses are delivered, we reach a condition in gradient echo sequences called the **steady state**. In this state, the magnitude of the longitudinal magnetization component M_z is the same at the end of every TR. Similarly, we can also have a residual transverse magnetization M_{xy} at the start of every repetition cycle. If we deliberately dephase this residual transverse magnetization, the sequence is described as incoherent or spoiled gradient echo sequences.

FLASH is a type of spoiled GRE. It is a naming scheme adopted by Siemens that spells Fast Low-Angle Shot. Other vendors have their own naming schemes for such a sequence. General Electric calls it Spoiled Gradient Echo (SPGR) and Philips calls it by the name T_1 fast field echo (T1-FFE). (Bernstein, King, and Zhou 2004, p.583). The introduction of the FLASH technique in the 1980s, known for its rapid acquisition capabilities, marked a significant advancement in MRI technology. It allowed for clearer imaging of dynamic processes and reduced artifacts associated with movement. The original paper on FLASH highlights the technique’s potential for ‘recording NMR movies’ to visualize physiological changes, a capability now fully integrated into contemporary MRI practices.” (Haase et al. 1986)

1.3 Research Necessity

With the advanced capabilities to capture high-resolution CINE MRI images of the knee during flexion-extension cycles under both loaded and unloaded conditions, we are now faced with the challenge of extracting meaningful biomechanical insights from this data. The first critical step in any such analysis typically involves segmenting the key anatomical structures within the images—namely, the femur and tibia. This process is crucial because accurate segmentation directly influences the reliability of subsequent biomechanical measurements.

Manual segmentation, while simple, is exceedingly time-consuming and susceptible to human error, highlighting the need for more efficient methodologies. In response, this thesis proposes the development of a semi-automated segmentation pipeline. This approach aims to reduce the manual effort required while maintaining high accuracy, thereby accelerating the analysis process and reducing potential biases introduced by manual methods.

Once segmentation is achieved, the next step involves measuring a biomechanical parameter—specifically, the distance between chosen anatomical landmarks on the femur and tibia. This measurement serves as an indirect indicator of joint space, which is crucial for assessing knee health. Derived from 2D images captured in the sagittal plane throughout the knee’s flexion-extension cycle, this parameter allows for an analysis of how relative positions between the femur and tibia vary under different conditions of movement and load.

1.4 Thesis Structure

Structure of the thesis is as follows:

2 Methodology

2.1 Data Collection Methods

2.1.1 Procedure Details

Dynamic MRI scans were conducted on four healthy individuals, ranging in age from 28 to 37 years and weighing between 55 to 90 kilograms, utilizing a 3 T Siemens Prisma fit scanner. These volunteers were free from any known musculoskeletal

disorders and provided their written consent, adhering to the ethical standards approved by the institutional review board. For all of these subjects, the left leg was scanned.

Once the subject was placed supine in the scanner, the thigh was secured on a wedge positioner, and the lower leg was attached to an ankle rest, just above the malleoli, using Velcro straps to minimize lateral movement. The knee to be examined is aligned with the device's axis of rotation, while the other leg rests alongside the MRI scanner's bore. Knee motion is guided by a belt and sprocket assembly running alongside the lower leg, connected to a gearbox activated by the leg support as the participant flexes and extends the knee. Once the subject was positioned at the scanner's isocenter, their leg naturally assumed a flexed posture due to the design of the device. In this configuration, the leg is cradled by the device arm which is positioned below the level of the knee, ensuring that the leg remains flexed without the volunteer exerting any force.

The volunteer engaged in a controlled exercise, following a metronome set at 60 beats per minute. This pace dictates a four-beat flexion to extension cycle, with the leg being flexed at the first beat and fully extended by the fourth. This equals to 8 beats per cycle, or 7.5 cycles every minute. Initially conducted under a loaded condition with weights added to the distal end of the device, the process is repeated without the added resistance to compare both states. The scan duration is around two and a half minutes, amounting to 20 full flexion-extension-flexion cycles.

2.1.2 Sequence Parameters and Reconstruction (incomplete)

Table 2.1.2, lists the MRI sequence parameters along with their respective units.

Table 1: MRI Sequence Parameters

Sequence Parameters	Values
Shape	(352, 276, 16, 100)
Acquisition Duration	160 [s]
Acquisition Type	2D
Dwell Time	0.0024 [s]
Echo Time	2.51 [ms]
Field Strength	2.89362 [T]
Flip Angle	8.0 [degrees]
Field of View (FOV)	192.0 x 192.0 x 3.0 [mm]
Frequency	123.25 [MHz]
Inversion Time	150000 [ms]
Matrix Size	176 x 176 x 1
Repetition Time	5.8 [ms]
Scanner Name	MAGNETOM Prisma

In this study, 276 spokes are utilized to sample one complete k-space dataset. Given the repetition time (TR) of 5.8 milliseconds, it takes approximately 1.6 seconds to acquire a full k-space dataset consisting of these spokes. Over the course of the experiment, 100 such k-space datasets are acquired, aligning with the 100 repetitions noted. The total scan duration extends just over two and a half minutes, a timeframe reported by the subjects as being manageable, regardless of whether the scan was conducted under loaded or unloaded conditions.

To illustrate the principle of radial k-space sampling, Figure X presents a simplified model, which includes only 25 spokes and demonstrates 10 sampling points on one spoke. In practice, as given in table 2.1.2, we have 352 points per spoke, and 276 spokes in total per k-space.

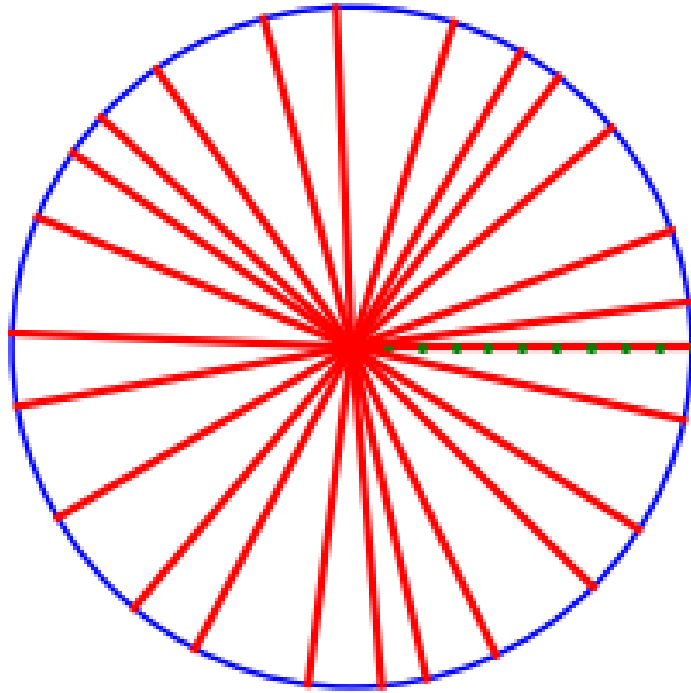


Figure 10: This illustration depicts a radial sampling pattern with 25 red spokes, using the golden angle for spacing. Only one spoke is detailed, showing 10 green points to represent sampling positions.

2.2 Data Analysis

All the analysis and data visualization were done using the python programming language (v3.11.5). To begin, the data in nifti (Neuroimaging Informatics Technology Initiative) format is loaded using nibabel (v5.1.0) library. It is then visualized using napari(v0.4.18), a multi-dimensional interactive image viewer in Python. Figure 11 shows the initially loaded data along with the viewer user interface.

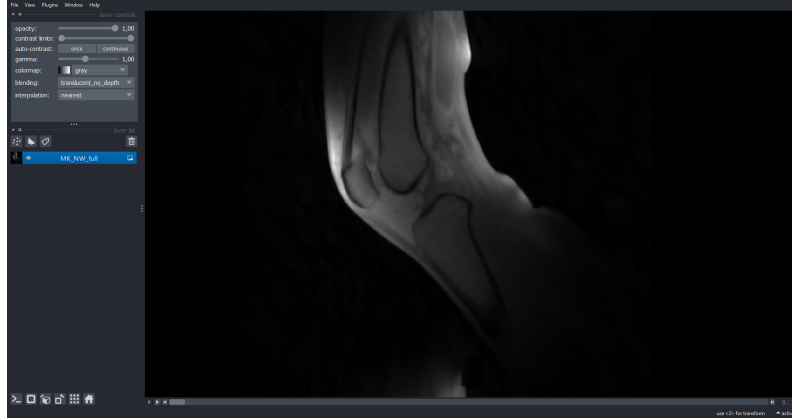


Figure 11: An example of the layout of the Napari viewer application showing one of the frames of CINE data.

Once the data is loaded, several distinct steps were performed to semi-automate the segmentation of tibia and femur. This involves first finding one boundary edge each for the bones, and then tracking them across the full flexion-extension cycle by computing their respective transformation matrices.

2.2.1 Segmentation

Step 1: Edge Detection

The Canny filter (Canny 1986), as implemented in the scikit-image’s feature library (v0.21.0), was employed to apply an edge filter to the images. The Canny edge detection algorithm operates in several key steps to identify edges with high accuracy in images. Initially, the image is smoothed using a Gaussian filter to reduce noise and potential false edge detections. Following this, the algorithm calculates the gradient intensity and direction at each pixel, which helps in identifying the edges’ boundaries.

Subsequently, the algorithm applies double thresholding, which involves two thresholds: a low and a high. Pixels with intensities above the high threshold are marked as strong edge pixels, while those below the low threshold are discarded. Pixels between these two thresholds are marked as weak edge pixels but can only be accepted as true edge pixels if they are connected to strong edge pixels. This step helps in discriminating between real edges and noise. Finally, edge tracking by hysteresis completes the process by converting weak edge pixels that are connected to strong edge pixels into strong edges, ensuring the continuity and completeness of detected

edges in the image. Various parameters of the Canny algorithm were adjusted, including edge thresholds and Gaussian blur, to optimize edge detection. Figure 12 shows the output of this step.

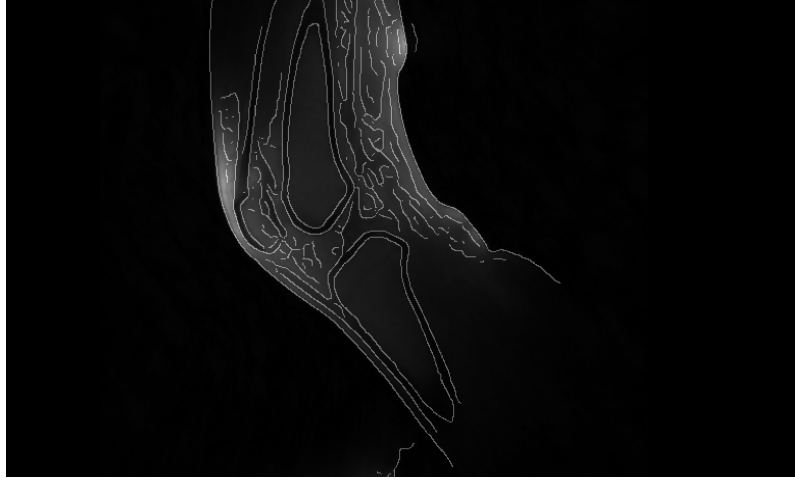


Figure 12: Output of canny edge detection algorithm overlaid on top of the image.

Subsequently, the scikit-image's morphology library was utilized to remove small elements from the binary image. The image was then skeletonized to a one-pixel width, retaining only long and consistent edges.

Step 2: Labelling

For the final selection of the desired edge, a labeling algorithm from SciPy, an open-source Python library designed for scientific computing(v1.11.3) was used. The goal was to isolate an edge that accurately represents the overall shape of the bone slice. Labelling was useful in this regard as it allowed for easy separation of distinct edges. Figure 13 shows the output from the labelling algorithm, where each color represents a separate label.

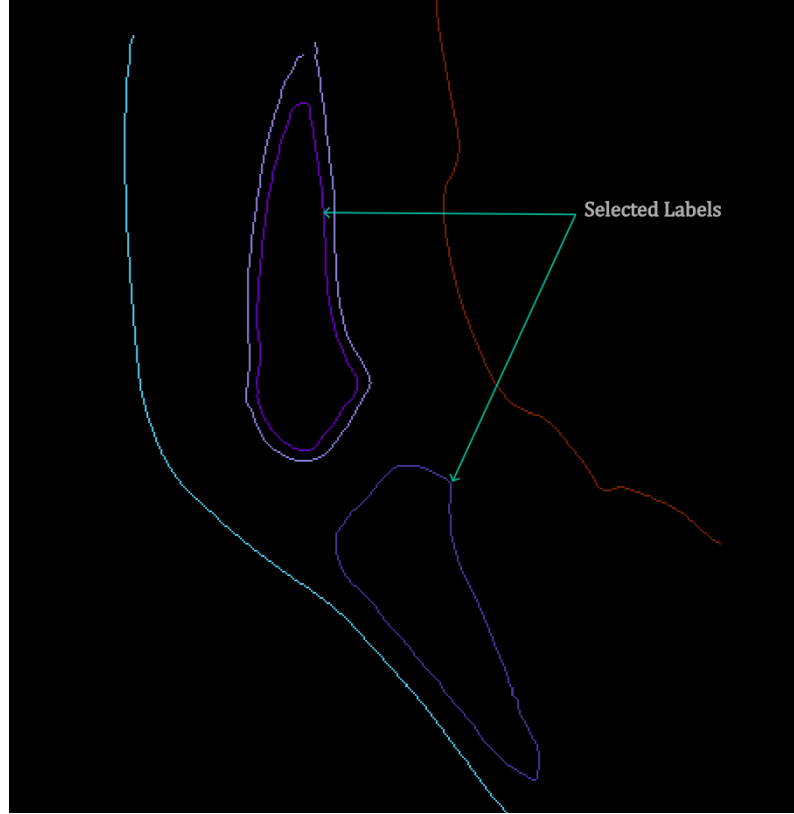


Figure 13: Output from the labeling algorithm with the representative edges for femur (top) and tibia(bottom) pointed out.

After choosing the appropriate labels, a binary image for each frame is obtained, where the foreground has the boundary for the interior edge of tibia and femur, and the background is null.

Step 3: Obtaining the set of reference points

Upon successfully isolating the binary edge images of the tibia and femur in Step 2, the subsequent step deals with establishing a set of reference points along each bone's edge in the first frame. This frame, captured when the knee is in a fully flexed position, serves as the reference frame for the study. The purpose of establishing these reference points is twofold: to simplify the complex data set for efficient processing and to ensure a consistent basis for accurately calculating transformations between subsequent frames. This is essential, as direct use of the densely packed binary edge data would be computationally cumbersome and less precise for such transformations.

To begin, the points along the boundary were organised and sorted. This was done by first, defining a starting point, and then iteratively using a greedy nearest

neighbor algorithm for sorting. The most distal point of the bone was taken as the initial seed. Various functions from the numeric python library 'Numpy' (v. 1.26.4) were employed for this task.

Once the points are sorted, the next step involves downsampling these points to a set of uniform equidistant reference points along the boundary of the binary edge. The necessity for this step arises from the inherent irregularity and density of the binary edge data. Directly sampling every n th point from the sorted list would not suffice, as it could result in uneven spacing due to the variable distances between consecutive points in the original data.

This process begins by calculating the cumulative distances between each consecutive pair of points in the sorted list. Using these distances, a total path length is established. The desired interval between the new points is then determined by dividing this total path length by the number of intervals (number of desired points minus one). Between 50 to 80 points were found to be sufficient to accurately reflect the edge contours.

To achieve precise positioning of these points, cubic spline interpolation from SciPy's interpolate library is used. This interpolation method is particularly effective for ensuring that the new points adhere closely to the original curve while maintaining equidistant. Figure 14 depicts this result.

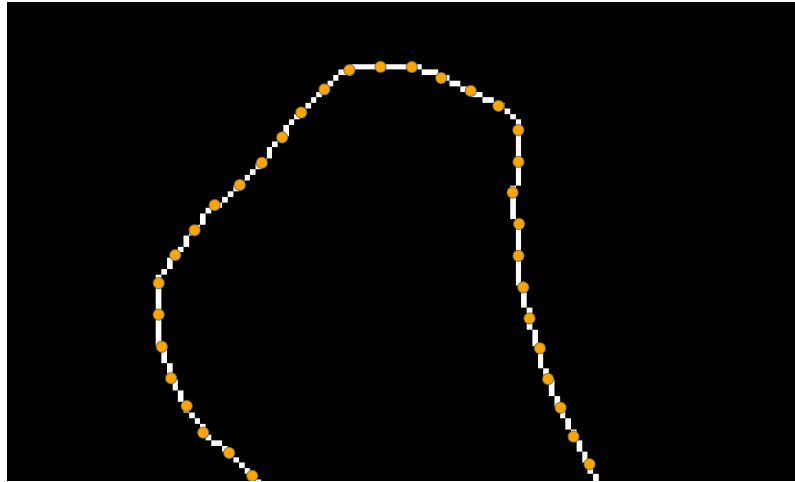


Figure 14: A zoomed in look at the equidistant sampled points (orange) along the boundary of the tibia edge (white).

Step 4: Transformation matrices computation

In this step, a set of transformation matrices are obtained, each matrix containing the parameters that align the segment of the bone in one frame to the next. Given that the subject movement is restricted to only a single plane, it is reasonable to assume that the edges of the bone undergo motions that can be described by rigid transformations. These transformations include solely the translation in the sagittal plane, and rotation about transverse axis. In this approach, it is assumed that the bone does not undergo any deformation, and that through plane motion is negligible throughout the motion cycle.

Mathematically, the transformation of each point from one frame to the next can be expressed as

$$p' = R(\phi)p + t \quad (1)$$

where:

- p is the coordinate of the point in its current frame
- p' is the coordinate of the point in the next frame
- ϕ is the angle of rotation
- $R(\phi)$ is the rotation matrix, given by

$$R(\phi) = \begin{bmatrix} \cos \phi & \sin \phi \\ -\sin \phi & \cos \phi \end{bmatrix}$$

– t is the translation vector,

$$t = \begin{bmatrix} x \\ y \end{bmatrix}$$

- x and y are the translations in the cartesian coordinate system.

As such, only three parameters, x , y , and ϕ need to be computed. To compute these, a cost function is defined that measures the sum of squared distances between each point in the reference frame and its corresponding point in the transformed frame. The optimization of this cost function is performed using a nonlinear least squares approach, where the initial guessThe optimization process uses the `fmin` function from SciPy's optimization module, which is configured to stop when the change in the cost function is below a small tolerance, ensuring precise alignment of the frames. This method ensures that the computed transformations accurately represent the actual movements of the bone throughout its movement cycle. Figure 15 provides

a visual representation of the overlap of the reference points from the fully flexed initial position to the frame where the lower leg has been rotated by an angle of 12 degrees as reported by the rotary angle encoder.

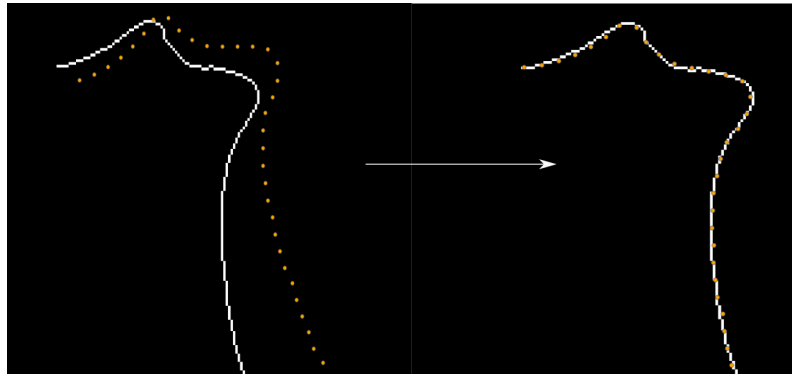


Figure 15: Left: The reference points in the first frame (orange) overlayed with the binary edge image of the target frame (white). Right: The reference points have been transformed by using the results from the optimization showing almost perfect overlap, illustrating the effective alignment achieved through the minimization of the cost function.

3 Results

4 Discussion

5 Conclusion

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A Appendix

If needed for supplementary material, such as detailed description of data collection, tables, or figures.

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