

FINAL REPORT FOR MENG PROJECT

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A novel device for personalised graft tensioning in anterior cruciate ligament reconstruction surgery

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Abstract

The initial tension applied to an anterior cruciate ligament (ACL) replacement graft upon fixation is of paramount importance for functional outcome of the knee [1, 2, 3, 4]. Current initial tension protocols are either force-based or laxity-based and have amounted to no consensus on the ideal initial tension needed for recovery of normal knee mechanics and optimal biologic incorporation of the graft [5, 6]. Graft and fixation method stiffness have been shown to affect the load-displacement behaviour of the knee as well as final graft tension [7, 8], but no method exists to take these factors into account in clinical trial investigations of optimal initial graft tension.

Having identified the need to establish a novel stiffness-based graft-tensioning method for ACL reconstruction surgery (ACLRS), half of the work necessary to do so was completed within the 10-month scope of this project. A graft stiffness measuring device was devised and designed, as well as a clinical trial to evaluate the impact of this new stiffness-based protocol on ACLRS outcomes. Due to the ongoing pandemic, testing was not performed but merely outlined.

Future work to finalise the novel tensioning method involves designing and validating a button fixation method of suitable stiffness for this new protocol and developing a dynamic model of the knee to compute initial tension recommendations from graft stiffness and fixation method stiffness.

Acknowledgements

I would like to thank my supervisor, Dr Warren Macdonald, whose guidance and expertise were invaluable in formulating this novel research topic, and whose support throughout has encouraged me to pursue ambitious results.

I would also like to acknowledge Mr Rajarshi Bhattacharya, our partner consultant orthopaedic and trauma surgeon in this project, for his feedback and collaboration throughout.

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Chapter 1

Background

1.1 ACL reconstruction: epidemiology and principles

The ACL is instrumental to knee stability, angulation and rotation. ACL rupture, caused by excessive torsion or extension of the joint, is one of the most common forms of knee injuries worldwide, estimated at 300 000 and 16 000 cases a year in the US and UK respectively [9, 10]. Further, with an increasing number of children and young adults taking part in sports activities and an increasing proportion of seniors staying active longer, the rate of ACL ruptures around the world is on the rise [10, 11, 12].

ACL ruptures are most often treated surgically, with ACLRS consisting of an arthroscopic intervention; the surgeon removes the torn ACL from the inter-condylar notch of the knee, drills tunnels from the original ACL footprints in the inter-condylar notch through the tibia and femur and passes a ligament graft through both. Once fixed in position, it replaces the ACL. Autogenous hamstring tendon (HT) and patellar tendon (PT) grafts are most commonly used for this purpose worldwide, at 63% and 26% respectively [13]. Our partner in this project, consultant orthopaedic and trauma surgeon at Charing Cross and St Mary's Hospitals Mr Bhattacharya, specifically uses 4-stranded gracilis semitendinosus HT autografts fixed in place with a femoral EndoButton and tibial screw.

1.2 The importance of graft tensioning in ACLRS

Overall, PT and HT techniques are thought to be equivalent in outcome, each having their own specific benefits and downsides [14, 15, 16]. However, Freedman et al [15] performed a meta-analysis of both methods and identified a 2.9% graft failure rate and 3.5% incidence of grade 2 or higher pivot shift results, indicating un-natural knee laxity, post-ACLRS. Improper graft tensioning may explain these results in up to 77% of cases [1]. Specifically, under-tensioning the graft can render it unsolicited throughout the knee's range of motion causing the knee to be lax and unstable [17]. Over-tensioning the graft can over-constrain the knee leading to a restricted range of motion (ROM), potential graft or graft fixation failure, and an unfavourable environment for biologic incorporation [18, 19, 20, 21]. Either way, improper graft tensioning will cause reconstructed knee mechanics to diverge from those of a normal knee and affect the patient's return to full physical capacity.

Using the data above, improper graft tensioning can be estimated to be the cause of up to 4.9% of poor ACLRS outcomes. According to numbers from the NHS's ACL SNNAP trial [22], in the UK, this represents around 790 unsatisfactory surgeries a year at the price of £3.3 million, as well as around 465 revision surgeries a year, costing the NHS an extra £2 million. These figures are based on the 1999 paper by Getelman et al [1] and may need adjusting, but nonetheless are expected to increase with the rate of incidence of ACL ruptures.

The ramifications of improper graft tensioning go further than the financial aspect of repeat-surgeries and functional outcome for the patient though. Its long-term implications on patient wellbeing are considerable: it was estimated that around 11% of ACLRS patients go on to develop osteoarthritis (OA) as a result of altered joint mechanics incurred by inappropriately tensioned

ACL grafts [23, 24, 25, 26]. At the time of writing, OA has been found to be promoted equally under high and low initial tension regimes up to 7 years post operatively [24, 25]. Other studies have investigated the histopathological signs of early osteoarthritis and concluded that knee cartilage may be particularly at risk of damage during the first months after surgery. Whilst these processes aren't yet fully understood, two cartilage biomarkers found in synovial fluid have provided particular insight into cartilage degeneration processes after traumatic joint injuries. Firstly, an increase in synovial fluid degradative enzyme concentrations, when combined with high joint contact forces and shear stresses under inappropriately tensioned ACL grafts, could exacerbate OA development [27, 28]. Secondly, an increase in synovial fluid inflammatory cytokine concentrations has been associated with important collagen loss in the first month post-operatively, potentially increasing the onset probability of post-traumatic OA development [29].

Investigating the ideal initial tension needed to restore individual patients' natural knee mechanics therefore also seems of paramount importance to mitigate cartilage degeneration and diminish the rate of post-ACLRS OA development.

1.3 The limitations of current tensioning protocols

Despite the importance of initial graft tension for ACLRS outcome being widely recognised for reasons cited above, and despite the existence of graft tensioning devices on the market,¹ few surgeons control the amount of tension they apply at fixation since literature shows no consensus regarding optimal initial graft tension for recovery of normal knee mechanics. Clinical trials investigating the impact of initial tension in ACLRS on functional outcome and OA development use one of two gold standard protocols:

- Laxity-based, matching or over-constraining laxity in the reconstructed knee compared to the contralateral knee
- Force-based, applying set amounts of tension to the graft in different patient groups

Several initial graft-tension randomized controlled trials using these methods have been reported for the most common graft types – PT and 2-stranded HT (Table 1.1). Altogether, no significant differences in outcome have been seen between tension groups.

Table 1.1: Example initial tension study outcomes for PT and 2-stranded HT grafts

Author, year	Graft used	Initial tension protocol	Outcome
Yasuda et al 1997 [3]	2-stranded HT grafts connected in series with polyester tape	Force-based	Less AP laxity in high-tension group after 2 years
Kim et al 2006 [30]	2-stranded HT autografts	Force-based	No significant differences between tension groups after 2.8 years
Van Kampen et al 1998 [31]	PT autografts	Force-based	No significant differences between tension groups after 2 years
Yoshiya et al 2002 [32]	PT autografts	Force-based	No significant differences in AP laxity between tension groups after 2 years
Nicholas et al 2004 [33]	PT autografts	Force-based	Less AP laxity in high-tension group after 20 months

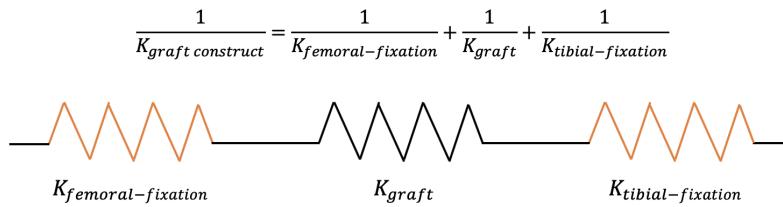
The 4-stranded HT autograft method utilised by Mr Bhattacharya has been particularly understudied compared to those mentioned above: no randomized controlled trial evaluated it prior to 2009 [6]. In 2002 [34], an ex-vivo force-based porcine model study recommended a relatively high initial tension between 80N and 140N for an EndoButton-fixed 4-stranded HT graft to withstand normal ACL loads. Having evaluated only 3 such graft constructs, it is likely an underpowered experiment and these results should be considered with caution. In 2013, Fleming et al [35] performed the first randomized human controlled trial comparing two laxity-based initial-tension protocols in 4-stranded HT autografts fixed at the femur with an EndoButton. The trial was appropriately powered and no significant difference in outcome after 36 months was observed between tension groups.

¹Intrafix (Mitek, Norwood, MA); Graft Tensioner (Arthrotek, Warsaw, IN); Tension Isometer (MEDmetric, San Diego, CA)

Overall, studies obtain similar results across force and laxity groups. No consensus has been reached regarding the optimal amount of initial tension needed for recovery of normal knee mechanics. The only generally accepted fact is that a large amount of initial tension restricts ROM, causes a large posterior subluxation of the tibia, dangerously loading the PCL in the resting state, and incurs high joint contact forces thought to promote greater rates of OA [21, 24, 26].

1.4 Graft and fixation-method stiffness as confounding factors

It has been shown that graft construct stiffness affects the anterior-posterior load-displacement behaviour of the knee and final graft tension [7, 8]. Graft construct stiffness is defined in this report using a springs-in-series model (figure 1.1)(equation 1) as the combined femoral fixation, graft, and tibial fixation stiffness.



Using To et al's³⁶ experimentally-derived fixation stiffness values (which pair up different femoral- and tibial-fixation methods), we can re-write:

$$\frac{1}{K_{\text{graft construct}}} = \frac{1}{K_{\text{fixation}}} + \frac{1}{K_{\text{graft}}} \quad \therefore \quad K_{\text{graft construct}} = \frac{K_{\text{graft}} \times K_{\text{fixation}}}{K_{\text{graft}} + K_{\text{fixation}}} \quad (\text{eq. 1})$$

Figure 1.1: **Springs-in-series model of the ligament graft construct.** Denoting stiffness as K , then knowing the stiffness of the fixation method and that of each patient's graft would allow computation of the ligament graft construct's stiffness.

Particularly, in 2004, Eagar et al [8] performed a cadaveric study on 4-stranded HT grafts to investigate the impact of fixation method stiffness and initial tension post-ACLRs on:

1. The unloaded posterior subluxation of the tibia,
2. The anterior laxity of the reconstructed knee,
3. Graft tension under application of a 225N anterior load.

Their findings are of great interest to this project.

Firstly, both fixation stiffness and initial tension were shown to affect the graft's final tension. As such, fixation stiffness is just as important a consideration as initial tension is in preventing dangerous post-operative loading of the graft.

Secondly, it was estimated that a high initial tension of 200N would best restore anterior laxity of the knee when using the femoral-EndoButton/tibial screw fixation method, as used by Mr Bhattacharya. This high tension was found to effectively counterbalance the low stiffness of the fixation method. However, this amount of initial tension also caused a 4mm subluxation of the tibia and an unnaturally high final graft tension. This may suggest the femoral EndoButton/tibial screw fixation method is not best suited for recovery of natural knee mechanics.

Finally, the ideal initial tension/fixation stiffness combination to provide near-natural posterior subluxation, anterior laxity, and final graft tension all together was found to be around 25N with

a $94N/mm$ stiff fixation. It is suggested this may be achieved with a bone mulch at the femur and 5 sutures tied to a post or double staples at the tibia.

This study was the first to consider both fixation stiffness and initial tension as variables affecting graft performance post-operatively. It did not consider the effects of graft stiffness on construct stiffness because fixation method stiffness ($18\text{--}269N/mm$) is much less than the average 4-stranded HT graft's stiffness ($460\text{--}1450N/mm$) [36], meaning that prior to bone regeneration in the tunnels, the fixation method is the determining factor of construct stiffness. However, it remains unclear whether this biomechanical disadvantage of the fixation method remains key after bone regeneration: it may be that once the tunnels are filled in, graft stiffness alone defines construct stiffness. The bone-to-graft healing process post-ACLRs is not yet well understood, as demonstrated by a recent systematic review [37], hence the importance of graft stiffness for construct stiffness and in turn for recovery of normal knee mechanics in the long-term cannot be ruled out. Graft stiffness would therefore be a useful research measure to consider in parallel of fixation stiffness to evaluate long-term outcomes of ACLRs.

In conclusion, there is strong evidence suggesting that graft construct stiffness as a whole may be a confounding factor in the determination of an ideal initial tension for ACLRs. The current laxity-and force-based strategies of searching for a one-fits-all initial tension value to restore optimal knee mechanics, consequently, seem unsuited.

Chapter 2

Aims & Objectives

The above in-depth ACLRS literature review allowed us to establish a niche in the procedure which we could address. It would be of great surgical interest to develop a new kind of initial tension protocol which would be stiffness-based – a protocol based on individual patients' graft construct stiffnesses for recovery of normal knee mechanics on a case-to-case basis.

The aim of this research is to develop the above-mentioned protocol and associated surgical tools to eventually lead to a clinical trial of the technique, with an interest in investigating (1) graft construct mechanics pre- and post-bone-regeneration in the tunnels and (2) the protocol's impact on functional outcome of the reconstructed knee, rate of repeat surgeries, and long-term progression of OA.

With this goal in mind, the research topic was split into four aims. Two will be addressed in future MSc/PhD projects, described in the discussion section of this report, and two were addressed within this project's 10-month scope, as follows:

AIM 1: Design a graft stiffness measuring device

- Design
 - Its use should be straightforward so as not to increase surgical time
 - Its assembly must be unambiguous
 - Its design should have few to no potentially germ-harbouring nooks and crannies
- Testing
 - Accuracy of the stiffness result
 - Impact of graft creep on results
 - Surgeon feedback

AIM 2: Plan a clinical trial

- Define clear research objectives for evaluating the stiffness-based protocol's impact on ACLRS outcomes
- Outline key logistics and measurements
- Calculate necessary sample size for an appropriately powered trial

Chapter 3

Final Design

3.1 Design overview

The graft stiffness measuring device designed was made to fit with DePuy Synthes' existing Mitek Sports Medicine Graft Preparation System [38]. The whole set-up is shown in figure 3.1 (mechanical drawings in appendix A) and works as follows:

- Attach the loop-end of the graft to the stiffness measuring device's hook and secure its other end at the Mitek graft clamp.
- Lock both towers into position on the Mitek board such that the graft be held horizontally between the two; neither slack nor in tension.
- Pull the handle of the stiffness measuring device straight outwards and turn it 90 degrees in either direction to lock the system into position.
- Check the indicator on the side of the device to read off the graft's stiffness.

This process is expected to last 10 to 45 seconds and be performed by the surgical assistant whilst the surgeon prepares the tibial and femoral tunnels for the graft. This device will therefore add little to no time to the procedure.

In the following sections, we will delve into the design of specific mechanisms within the device to understand its function. All parts were created with ease of surgical-grade cleaning in mind; keeping the overall device open and visible, and avoiding nooks and crannies which may harbour bacteria.

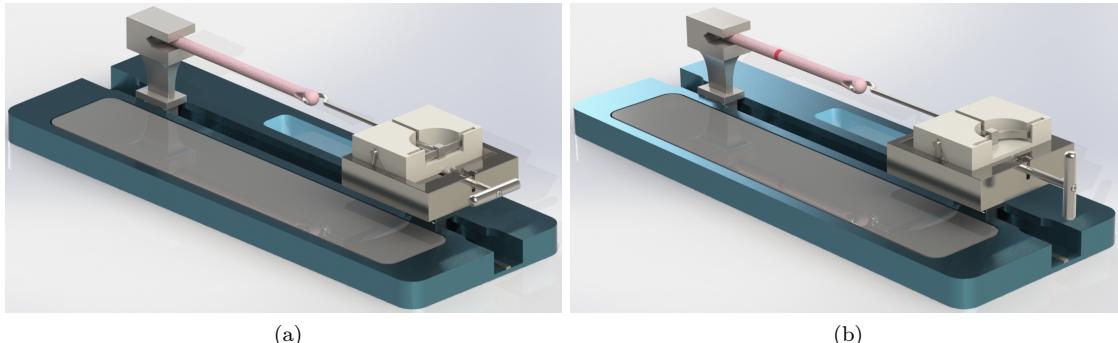


Figure 3.1: **Image of Solidworks device design.** (a) initial device position. (b) final device position. In both images the right tower is the stiffness measuring device, the left tower and base are simplified representations of the Mitek graft preparation board and graft clamp.

3.2 Spring displacement mechanism

The design of this graft stiffness measuring device was based on the assumption that an ACL graft behaves like a linear spring under a step load F , that is, that its displacement x follows the characteristic equation $F = K_g x$, K_g being the grafts' stiffness. Then, applying a displacement to the graft connected in series with a spring as shown in figure 3.2, we have:

$$x_g = \frac{F}{K_g} \quad (3.1)$$

$$x_s = \frac{F}{K_s} \quad (3.2)$$

$$x_g + x_s = d \quad (3.3)$$

From here, we can compute the following equations:

$$K_g = \frac{F}{d - x_s} \quad (3.4)$$

$$x_s = d - \frac{F}{K_g} \quad (3.5)$$

$$F = \frac{d K_g K_s}{K_g + K_s} \quad (3.6)$$

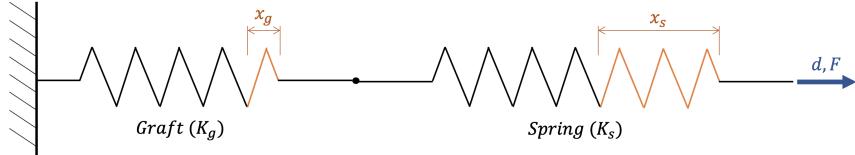


Figure 3.2: **Springs-in-series model of a graft and spring with important parameters.** K_s spring stiffness, K_g graft stiffness, x_s spring displacement, x_g graft displacement, d total displacement applied to the system, F load applied due to d .

Detecting the spring's displacement in such a system therefore allows to determine the graft's stiffness (equation 3.4). In order to design this system to the specific requirements of 4-stranded HT grafts, we first had to select the best values of d and K_s to use, abiding by the following two constraints;

- The load F felt by the graft should be physiologically safe. 4-stranded HT grafts were reported to have an ultimate tensile strength of $2831 +/- 583\text{N}$.^[4] Taking a safety factor (SF) of 2 on the lower end of this range constituted our first design constraint: the maximum allowable load would be $UTS_{SF2} = 1174\text{N}$.
- We should aim to use a combination of variables which results in the largest possible d in order to obtain the largest possible x_s (equation 3.5) since this would provide a greater sensitivity to K_g .

For individual displacement values in the range of $d = [4; 16]\text{mm}$, load was computed from equation 3.6 for combinations of $K_s = [10; 175]\text{N/mm}$ and $K_g = [460; 1450]\text{N/mm}$ in MATLAB (appendix B). The latter was expanded relative to To et al's reported range of $[662; 1246]\text{N/mm}$ for 4-stranded HT grafts ^[36] in order to ensure the device would perform despite the high variability of tendon mechanical properties between patients ^[39, 40]. Based on the above-mentioned constraints, a spring stiffness of 85N/mm and displacement of 14mm were selected for the device (Figure 3.3).

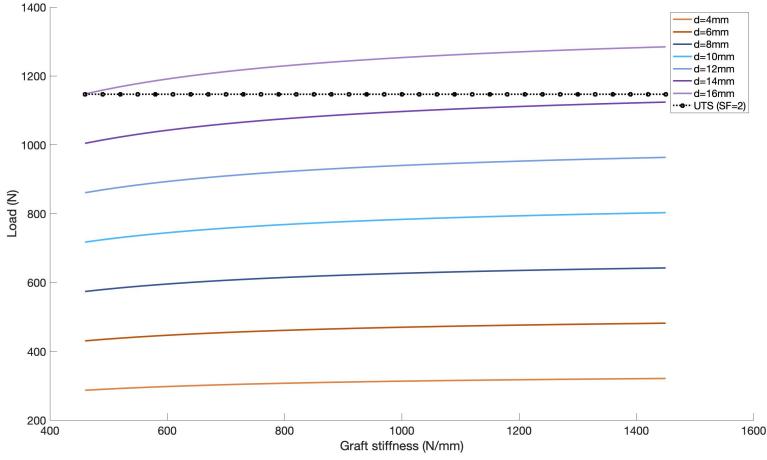


Figure 3.3: **F as a function of K_g for different displacement values d and our chosen spring stiffness $K_s = 85\text{N/mm}$.** $d = 14\text{mm}$ selected for this device since it allows application of the highest possible load below UTS_{SF2} . MATLAB script in appendix B (figure B.2).

Obtaining an 85 N/mm spring

A leaf spring was favoured for the purpose of this device. As can be seen in figure 3.4, the spring slots into the slider and, when pulled on by the connector, can be assumed to behave like a simply supported beam in bending. Its dimensions were determined using appropriate characteristic equations such that it both have our desired stiffness of 85N/mm , and under no circumstance falls out of its slotted position when deformed (see appendix C).

Obtaining a 14mm displacement

The displacement mechanism was designed as a pull-and-lock handle. The handle itself was designed using anthropometric data of the hand [41]: with a length of 4.5cm , it can be securely gripped between an operator's two fingers. As seen in figure 3.4, the handlebar sports a thick disk at its end which slots perfectly between the slider and the base, meaning it can be freely rotated in this position. The bar also bears two opposing fins. When pulling the handle outwards, these come into action: holding the handle horizontally orients the fins vertically, allowing them to pass through the opening at the front edge of the base; performing one 90-degree rotation in either direction positions the fins orthogonally to this opening, locking the system into place. This happens at a displacement of exactly 14mm , as required from above.

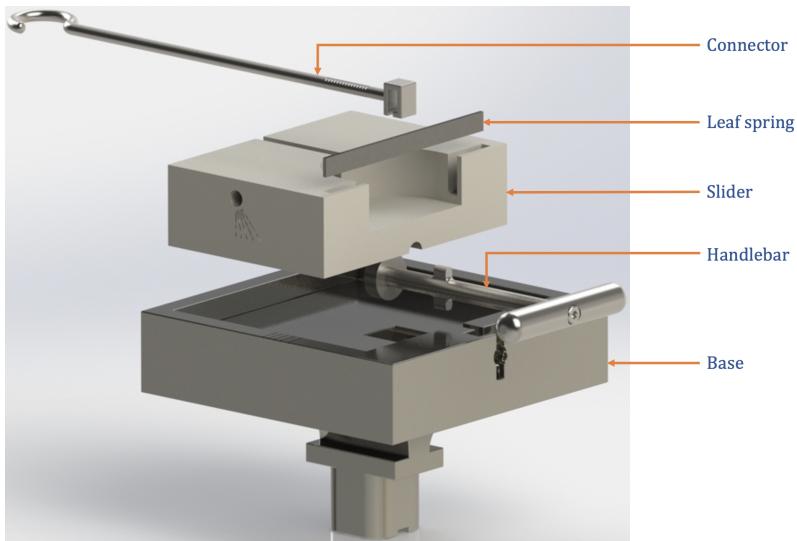


Figure 3.4: **Annotated Solidworks image of the device's spring and displacement mechanisms.**

3.3 Graft stiffness indicator mechanism

The slider's displacement under action of the handle causes the spring to bend and graft to extend simultaneously, linked by the connector (figure 3.5). Since the graft's and the spring's displacements must sum up to 14mm, then depending on how stiff the graft is, the spring will extend more or less. We can therefore extrapolate graft stiffness from spring displacement. In our device, this was done via a rack and pinion mechanism which transfers the linear spring displacement into rotational motion, from which graft stiffness displayed.

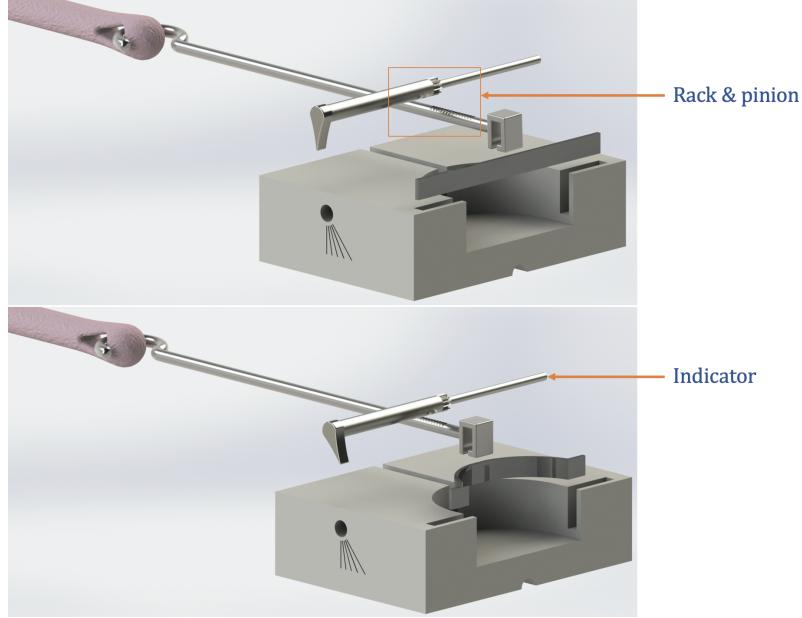


Figure 3.5: **Annotated Solidworks image of the device's stiffness indicating mechanism.** Top: initial position. Bottom: example final position.

Mechanism

From equation 3.5 and using load values computed via the MATLAB script in appendix B (figure B.1), we can compute minimum and maximum spring displacements to be:

$$x_{s,min}|_{K_g,min=460N/mm} = 11.82mm \quad \text{and} \quad x_{s,max}|_{K_g,max=1450N/mm} = 13.30mm \quad (3.7)$$

For one full pinion rotation to correspond to maximal spring displacement, and considering rack displacement is equal to the arc length the pinion is rotated by, then the pinion radius r was computed as:

$$2\pi r = x_{s,max}|_{K_g,max=1450N/mm} \Leftrightarrow r = \frac{13.30}{2\pi} \Leftrightarrow r = 2.12mm \quad (3.8)$$

From here, the pinion was designed with 12 small teeth (module $m = 0.3$), allowing more precise displacement considering they need not withstand large forces but only translate motion. Further, considering rack displacement can be related to pinion angular displacement as $\theta = \frac{x_s}{r}$, then:

$$\theta|_{x_{s,min}} = 320^\circ \quad \text{and} \quad \theta|_{x_{s,max}} = 360^\circ \quad (3.9)$$

This gave us a 40° critical range within which graft stiffness values could be displayed. For this application, precise stiffness values are not needed. It was therefore reasonable to split graft stiffness results into four 10° sectors providing ballpark values of graft stiffness. These sector lines can be

seen in figures 3.1 and 3.4 on the slider and projected onto the base for easy read-off. They could be injection-moulded into the parts at manufacture.

Design considerations

The connector was designed to be unambiguous in its use: it could be brought onto the spring from above or from below and has a rack on either side for interaction with the pinion to accommodate both possibilities. It would therefore perform identically in either orientation providing ease of set-up for the surgical assistant. Its hook end was also designed to fit all grafts, which are typically 8 to 8.5mm in diameter and no larger than 10mm [42, 43] (appendix D).

It was further hypothesised that fibres within the graft, in its bundled and sutured state, may be led to realign under the axial load, potentially causing it to shift in all directions. Since the rack and pinion have very small teeth, any vertical motion could disengage the mechanism and in turn falsify results. To mitigate this possibility, the system was designed with the indicator rod sat on top of the connector, forcing it in place.

3.4 Material selection

Surgical grade metals and plastics should be used in this device, ensuring they are fit for sterilisation. Since the device contains rotating parts, and since metal-on-metal contacts are known to manifest friction and wear behaviour which can lead to unwanted adhesion and bonding, a mix of stainless steel and polycarbonate parts were chosen to prevent such effects, as can be seen in figure 3.6.

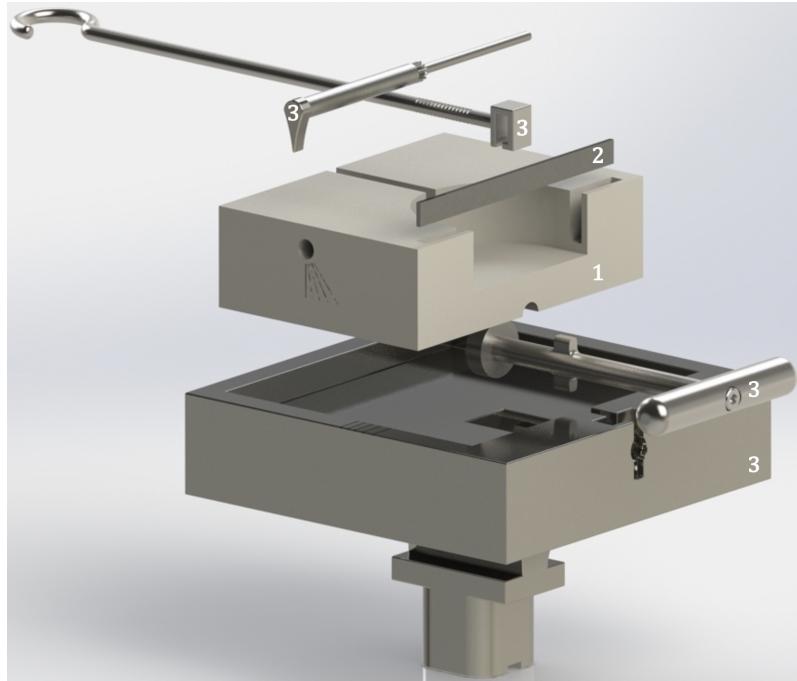


Figure 3.6: Solidworks image of the stiffness measuring device. Material 1: polycarbonate. Material 2: AISI 316 stainless steel sheet. Material 3: AISI 316L stainless steel.

Chapter 4

Clinical Trial Design

Sub-standard quality of randomised control trials (RCT) have been shown to be prevalent in orthopaedic literature [44, 45]. In this light and thinking ahead to running an appropriately designed clinical trial for this device, the purpose of this section was to lay out some groundwork for it in advance. Having such insight this far in advance will also serve as proof of concept and may aid in securing partnerships with interested surgeons.

4.1 Study objectives

Primary aim

To compare mean AP laxity and pivot shift test results in ACL reconstruction patients randomized to receive a stiffness-based initial graft tension (group 1) versus a random, manually applied graft tension (group 2), over 36 months post-operatively.

Secondary aim

There are two secondary aims of this prospective study and more may be added at a later date:

- To compare the incidence of OA post-operatively between the two groups using Knee injury and Osteoarthritis Outcome Scores (KOOS)[46] and Whole Organ Magnetic Resonance (WORM) scores [47, 48].
- To closely monitor immediate post-operative recovery over 6 months in order to investigate the evolution of knee mechanics during graft remodelling and bone infilling of the tunnels.

Rationale for the selection of outcome measures

The proposed RCT investigating the impact of a stiffness-based initial tension protocol on functional outcome of ACLRS is innovative. To the best of the author's knowledge, there is no previous record of the existence of a graft stiffness measuring device and no study has examined graft stiffness as a key variable affecting ACLRS. The primary and secondary aims of this study are expected to add greatly to the field, improving understanding of knee kinematics, ideal initial tension guidelines, and the mechanical implications of biologic incorporation of ACL grafts.

4.2 Study design

Conduct

This study could be conducted as a single- or multi-centre trial. The surgical method for these procedures should be standardised and followed identically by all participating surgeons.

Selection criteria

The following inclusion criteria will apply to this RCT:

- Reconstruction to be performed within 3 months after injury to mitigate effects of pre-surgical rehabilitation on results
- Patient wishes to receive a 4-stranded HT graft

- Patient lives within 60 miles of treating hospital for greater compliance to the follow-up plan (as described below)
- Patient meets requirement for undergoing an MRI scan

The following exclusion criteria will also apply:

- No concomitant injuries
- No chronic knee injuries
- No previous knee injuries sustained in either the affected or collateral knee
- No evidence of OA on current radiographs

Ethical considerations

Inclusion of children: individuals under 18 years old will not be included in this study due to the uncertainty associated with ACL injury management in skeletally immature patients [49] which may confound results.

Inclusion of minorities: the patient sample for this study is not limited to any specific group. Any individual, regardless of sex, sexual orientation, race, religion or belief is to be accepted on the trial should they conform to the above selection criteria and give their full consent.

Randomisation and blinding

These processes will include:

- Allocation concealment, ensuring the person enrolling the subject into the study has no knowledge of group allocations.
- Allocation randomisation, ensuring the person enrolling the subjects cannot predict the next assignment.
- A double-blinded structure: aiming to reduce information bias as much as possible, both the surgeons (up until the procedure) and the investigators will be blinded to the identity of either group. Investigators include those performing the post-replacement assessments and the statisticians.

Risks and benefits

Reported usual tensions applied to ACL grafts range from 20N to 145N [1, 3, 30]. It is reasonable to assume in advance that the graft tensions which will be recommended by the new stiffness-based protocol will fall into this range. As such, whether a patient receives treatment within the first or second group of this study, the risk and benefits of this trial would be equivalent to those of regular ACL reconstruction procedures.

4.3 Measurement schedule

At each follow-up appointment, all patients will complete a pivot shift test, KOOS questionnaire, and evaluate AP laxity using a KT-1000 arthrometer (MEDmetric Corp, San Diego, CA), reported in many studies to perform reliably [7, 14, 15, 25, 30, 32, 33, 50]. These will be scheduled at 1, 2, 3, 4, 5, 6, 8, 12, 24, and 36 months after surgery. Patients will additionally undertake periodic MRI scans to compute WORM scores, as often as deemed necessary by the team taking this research forward.

4.4 Study power: estimation of sample size

Sample size was estimated based on assumptions from the study's primary aim. Fleming et al [35] and Kim et al [30] have previously reported AP laxity differences (injured versus contralateral knee). Due to the range of their values, an average was taken to arrive at an estimate that group 2 in this study might see a mean AP laxity of $4.1mm$ with standard deviation $\sigma = 1.6mm$. Assuming

the data in both groups to be normally distributed, we can estimate the number of patients n needed in order to detect a minimum difference d between the two groups at a confidence level of $(1 - \alpha)$ and power of $(1 - \beta)$ from equation 4.1 [51] using critical Z values. Results in table 4.1.

$$n = \frac{2\sigma^2(Z_{\frac{\alpha}{2}} + Z_{\beta})^2}{d^2} \quad (4.1)$$

Table 4.1: Number of patients required in each group to obtain a confidence level defined by α ; power defined by β ; and minimum detectable difference defined by d .

$d(mm)$	α	$\beta = 0.2$		$\beta = 0.25$	
		0.05	0.1	0.05	0.1
0.2		1004	787	888	685
0.3		446	350	395	305
0.4		251	197	222	171
0.5		161	126	142	110
0.6		112	87	99	76
0.7		82	64	72	56
0.8		63	49	56	43

Chapter 5

Testing & Evaluation

Had the pandemic not happened, a device prototype would have been manufactured and the following tests would have been performed.

5.1 Stiffness reading accuracy

In order to test for stiffness reading accuracy, four helical tension springs of following stiffnesses would have been purchased:

- Within $[460; 550] N/mm$ expected to lead the indicator into the first stiffness sector of the device
- Within $[580; 730] N/mm$ expected to lead it into the second sector
- Within $[760; 1000] N/mm$ expected to lead it into the third
- And within $[1060; 1450] N/mm$ expected to lead it into the fourth

To suspend the springs horizontally with the stiffness measuring device, a wooden plank of a couple of centimetres in thickness would have been cut down to about an 8cm tall piece with a hook screw fixed securely at a height of 6.4cm, making it level with the connector on the device as currently designed. The plank would have been fastened tightly to a table-top using a clamp; a spring hooked onto it; hooked at its other end to the stiffness measuring device; and the device would have in turn been secured to the table-top using a clamp.

In this secured position, the device could be used as outlined in part 3.1 of this report. Each spring would have been trialled and its stiffness as displayed on the device recorded. Since the device does not aim to provide a precise stiffness value, it would have been enough to simply record the stiffness sector which the indicator pointed at.

In the case where all results were as expected, this would have been sufficient to show stiffness reading accuracy. In the case where one result was inconclusive, one would expect all other results to also be. In this case, a protractor would have been used to measure the indicator's angular offset from the desired position, and this result would have been taken into account to redesign the device's rack and pinion mechanism and/or sector display. This test would then have been repeated until conclusive results were obtained.

5.2 Impact of ligament creep

In order to determine whether a graft experiences creep which might render its stiffness reading time-dependent, a study on cadaver grafts would have been performed:

- Firstly, assuming that semitendinosus and gracilis tendons could be procured from one or more cadavers, either provided by the Department of Medicine at Imperial, or by the Department of Bioengineering's Blast Injury Studies Laboratory, who regularly store cadaver limbs for their experiments.

- And secondly, assuming Mr Bhattacharya would have assisted in sampling the tendons and preparing the 4-stranded graft(s) following his usual operating technique.

If both were possible, then the grafts would be placed on the same test rig as created for the stiffness accuracy test described above. Two features would be added; a small fluorescent tag placed on the tip of the device's indicator, and a camera, fixed in position opposite the indicator. The camera would record a 10-minute video for each graft test from the time the handle is pulled on the stiffness measuring device. The system is not to be disturbed during this time. The videos would then be digitised through software such as DLTdv8, a MATLAB application, in order to precisely track the fluorescent tag on the indicator and output a graph of indicator angle θ (in degrees) as a function of time. The mean time taken for θ to reduce by 2 degrees would be identified as the maximum time within which reliable graft stiffness readings can be made. After that, should one wish to view the result again, the measurement should simply be repeated.

Whilst the device is only expected to be used for 45 seconds at a time at most, tracking graft creep over 10 minutes accounts for any extra time the graft may spend under tension on the device whilst the surgeon finishes preparing the patient's knee to receive the graft.

5.3 Surgeon feedback

The device would have been presented to Mr Bhattacharya to collect design feedback in terms of ambiguity of set-up, ease of use, ease of cleaning, and overall look and function. This feedback would have then been integrated into the design process.

Chapter 6

Discussion & Conclusion

A graft stiffness measuring device was designed for the specific application of 4-stranded HT grafts, taking into account safe loading of the specimens and designing to surgical-grade material, functional and hygiene requirements. A clinical trial was also outlined, defining clear research objectives to investigate the impact of this device and its associated protocol on ACLRS outcomes, and serving as groundwork for establishing an ethically and statistically sound study. It is clear that undertaking a clinical trial involves establishing a complete protocol abiding by official guidelines such as 'The Revised CONSORT Statement for Reporting Randomized Trials' [52], as recommended by the UK government, as well as future clearance by an independent ethics committee.

This device is a first prototype serving as a proof of concept. There are many ways in which it could be improved;

- Material can be cut out in places where it serves no functional purpose, hence refining the device's look and reducing its weight and cost.
- Electrical features could be implemented to improve the device's precision, such as using a laser or an electronic dial indicator to display graft stiffness results. Care would have to be taken, however, to ensure that these features are able to endure surgical-grade sterilization.
- The design would benefit from being walked through with a manufacturer who may recommend changes to facilitate the manufacturing process.
- Performing the three tests mentioned above would enable us to validate the device's function and ensure user satisfaction.

As introduced in this report's Aims & Objectives section, two further tasks will be undertaken as future MSc/PhD projects to complete the design of our novel stiffness-based graft tensioning protocol, due to lack of time and resources within this project's scope.

This includes, firstly, the design of a stiffer EndoButton to reach the $94N/mm$ mark defined by Eagar et al [8] as ideal for recovery of normal knee mechanics when paired with an initial tension of $25N$. The button's use should be similar to that of the EndoButton currently used by Mr Bhattacharya to bring minimal change to his surgical technique.

Secondly, the development of a dynamic model of the knee to compute initial tension recommendations from graft stiffness and fixation method stiffness. Briefly, this model would simulate flexion/extension of the knee (fixed femur, dynamic tibia) to evaluate ROM under varying initial tension and graft stiffness values, with fixation stiffness equal to that of the button we design. What is desired is a system which, when fed a graft stiffness value, will output the allowable range of initial tension values for that construct to obtain near-natural ROM, considering both pre- and post-bone-regeneration environments in the tunnels. It is foreseen that results from this model could be validated using Eagar et al's findings: a fixation stiffness value of $94N/mm$ should recommend around $25N$ of initial tension. This value will vary for different graft stiffness values considering Eagar et al assumed infinite graft stiffness in their study, but the model should nonetheless approach it. The range of ideal initial tensions recommended for the pre- and post-bone-regeneration models can then be overlapped to hopefully obtain an ideal range of initial tension for long-term functional recovery of the reconstructed knee. The indicator mechanism on

the device could then be modified such that it display these ideal initial tension ranges, rather than graft stiffness values, upon loading of a graft. The surgical protocol for our stiffness-based tensioning method would look like the following:

1. Start surgery as usual preparing the 4-stranded graft
2. Place graft on the stiffness measuring device designed and action the handle
3. Check the indicator on the side of the device to read off the initial tension recommended for that patient
4. Secure graft in femoral tunnel using the button fixation designed
5. Tension graft according to recommendation in step (3) using one of 3 existing devices on the market¹
6. Secure graft at the tibial tunnel using a screw and close

The graft stiffness measuring device designed also has applications beyond ACLRS, as it could be easily adapted to determine the stiffness of any ligament or tendon in the body. This would be done by designing leaf springs of suitable stiffness for each tissue type to ensure the range of loads applied are always physiologically safe, and by adjusting the stiffness indicator mechanism to accommodate for a greater range of results. This device could therefore open the door to a range of surgical trials in the field of biomechanics which up until now, had to settle for cadaveric studies due to their reliance upon large lab-based instruments such as Instron machines for results.

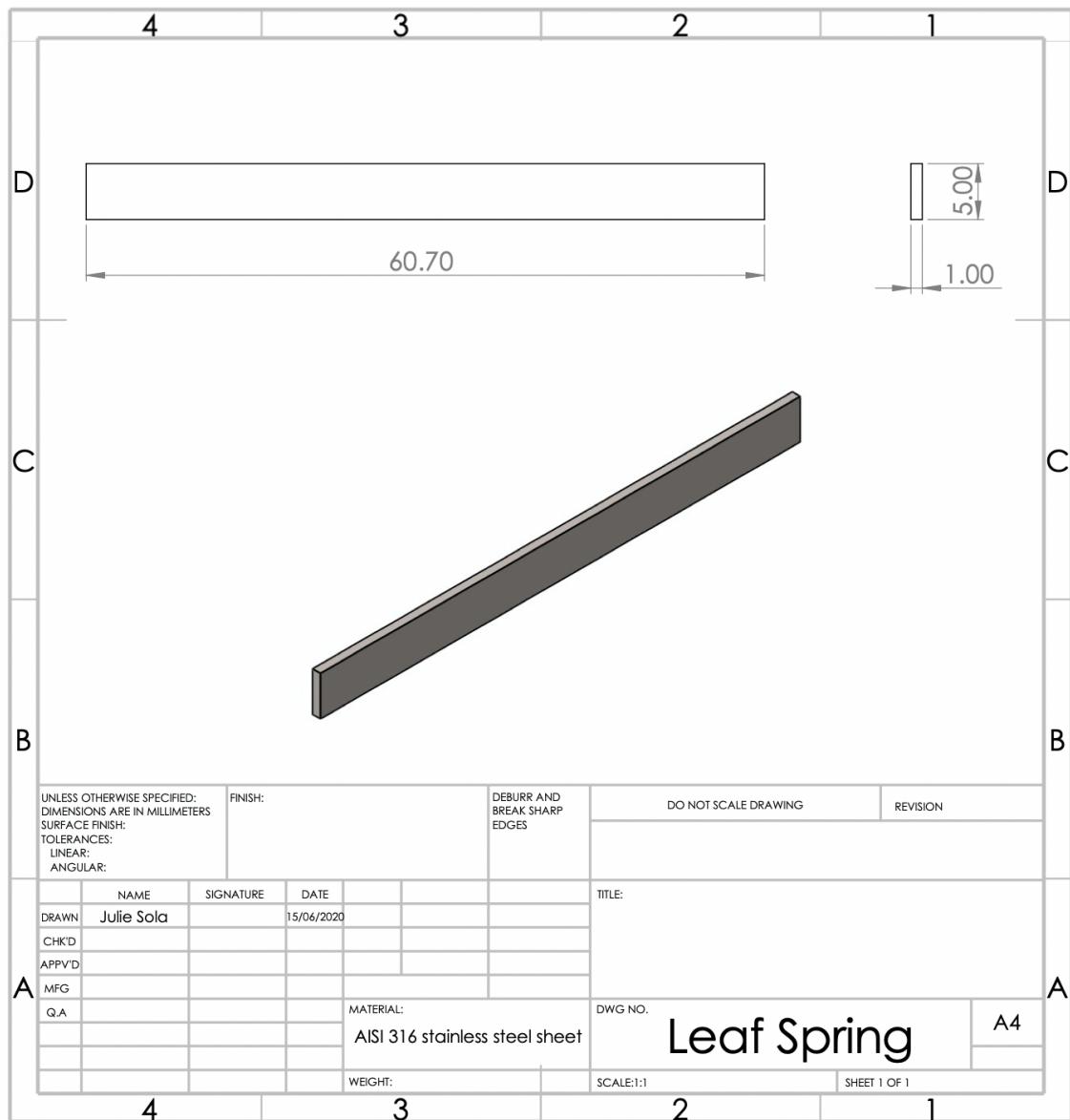
The long-term vision of this work was to break the trend of trying to find an ideal ‘one-fits-all’ initial tension value for ACLRS, as done by studies up until now, and rather establish a protocol for personalised graft tensioning based on individual patient’s graft stiffnesses. In light of the probable 790 unsatisfactory surgeries a year in the UK, if we can pinpoint the effect of pre-tension and graft stiffness, then we can make recommendations that will help surgeons tailor their technique to each patient for optimal recovery. The graft stiffness measuring device designed shows promise for applications within and beyond the scope of ACL repairs, and the clinical trial outlined gives an initial idea of how many patients would need to be recruited for a study of this novel stiffness-based initial tension protocol to provide statistically significant results.

¹Intrafix (Mitek, Norwood, MA); Graft Tensioner (Arthrotek, Warsaw, IN); Tension Isometer (MEDmetric, San Diego, CA)

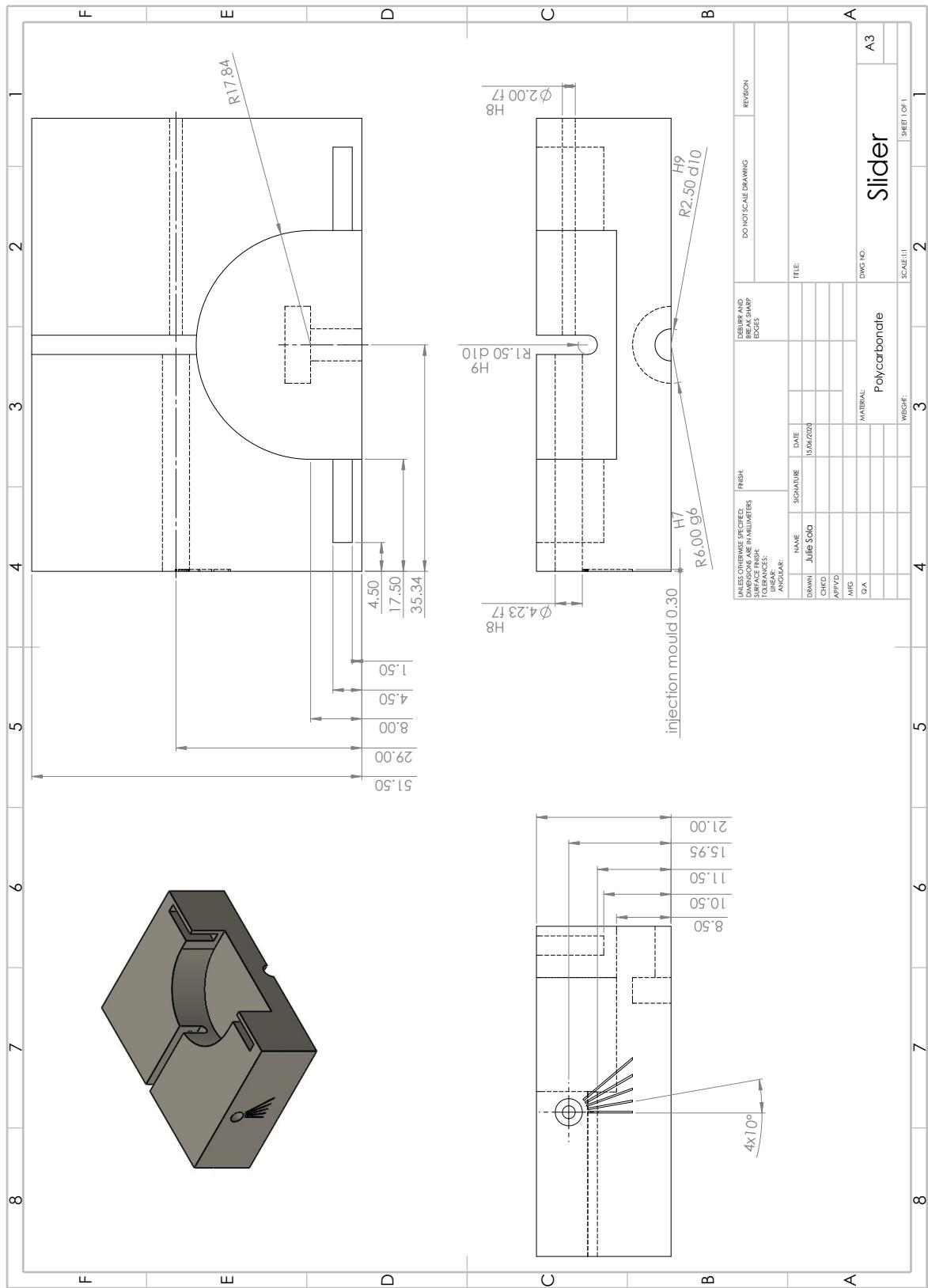
Appendix A

Mechanical drawings of device parts

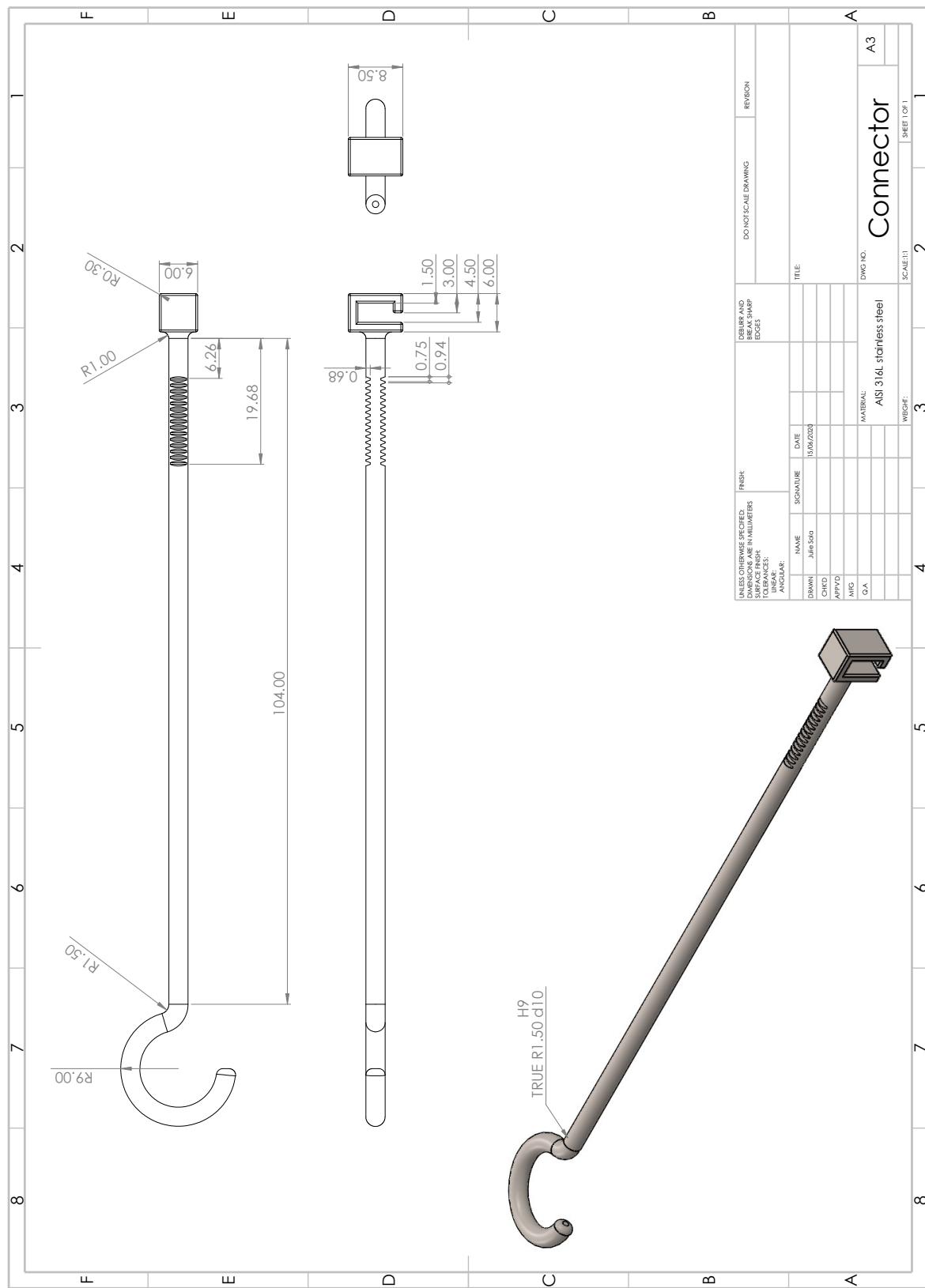
A.1 Leaf Spring



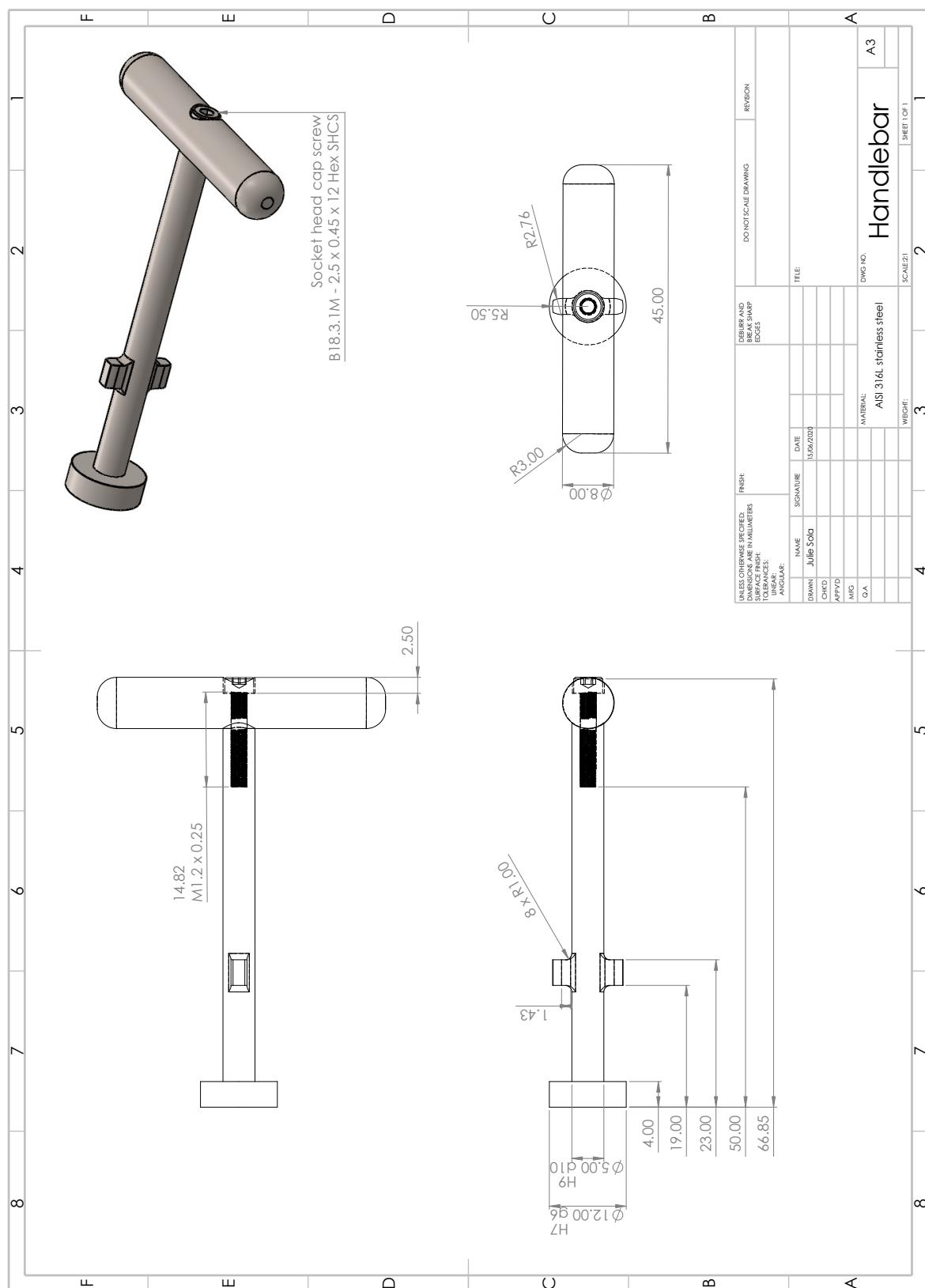
A.2 Slider



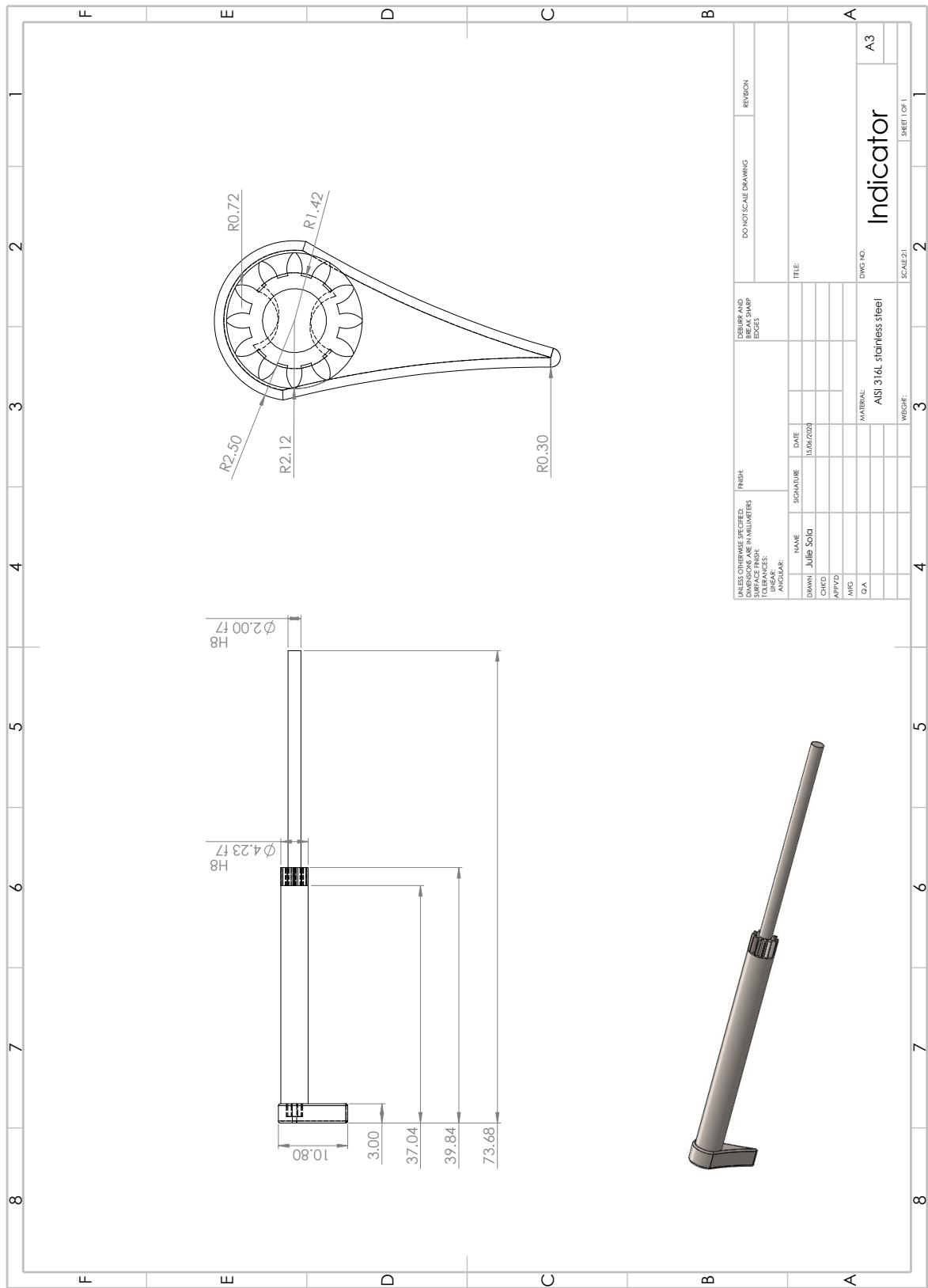
A.3 Connector



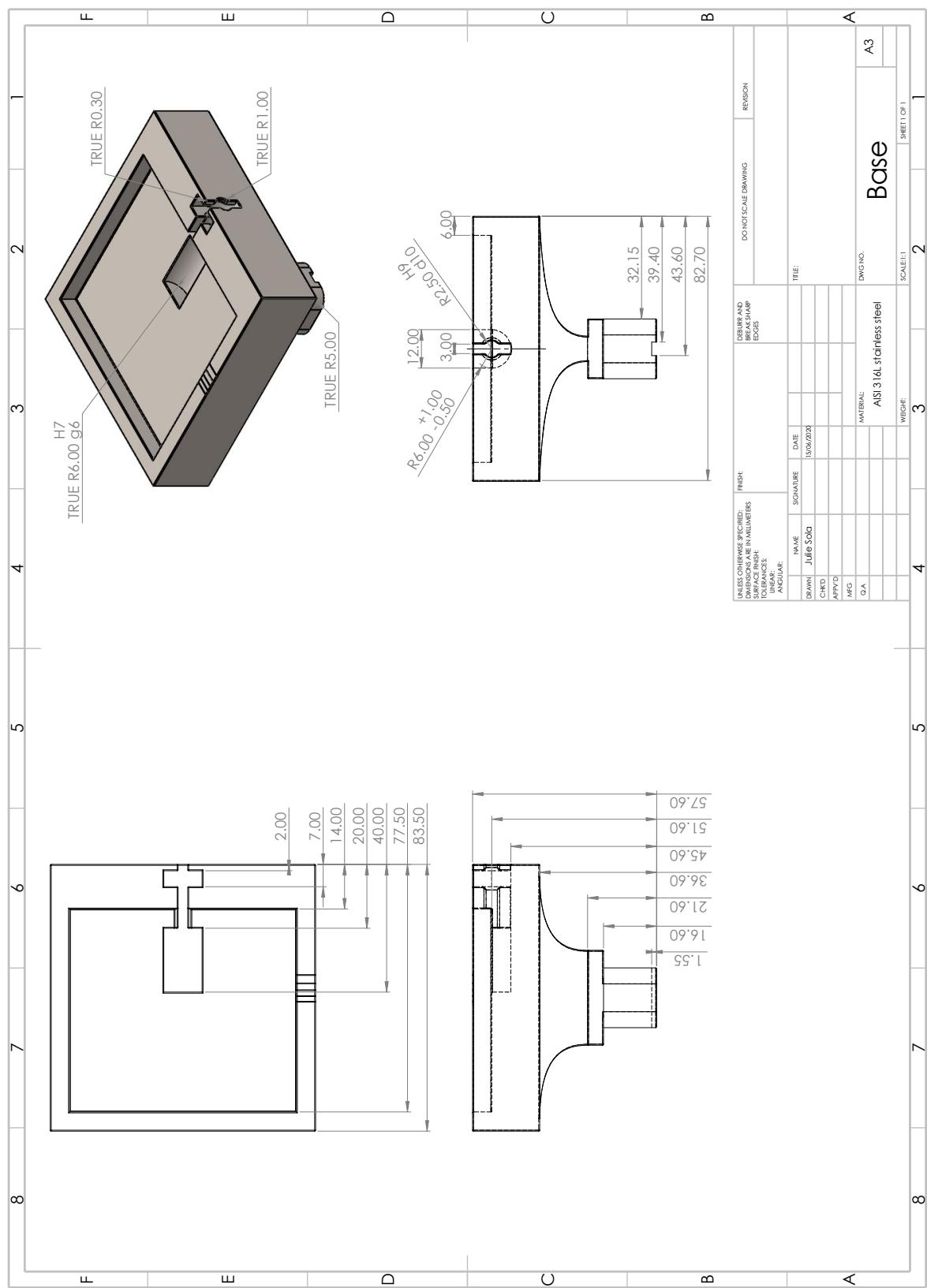
A.4 Handlebar



A.5 Indicator



A.6 Base



Appendix B

MATLAB script: force-displacement calculations

```
clear all;
% IMPORT SPRING STIFFNESS AND GRAFT STIFFNESS RANGES
Kg_data = xlsread('KsKgtest.xlsx', 'A2:A35');
Ks_data = xlsread('KsKgtest.xlsx', 'B2:B35');

% initialise load and spring displacement matrices
F = zeros(34);

% populate force matrix
for i = 1:34
    for j = 1:34
        F(i,j) = (14 * Ks_data(i) * Kg_data(j))/(Ks_data(i) + Kg_data(j));
    end
end

% plot load as a function of spring and graft stiffness
figure
surf(Kg_data, Ks_data, F);
set(gca, 'fontsize', 18)
title('Load applied as a function of graft & spring stiffness for total
displacement 14mm', 'fontsize', 20)
xlabel('Graft stiffness (N/mm)', 'fontsize', 20)
ylabel('Leaf Stiffness (N/mm)', 'fontsize', 20)
zlabel('Resulting Force Applied (N)', 'fontsize', 20)
```

Figure B.1: Compute load F from graft and spring stiffness K_g and K_s from equation 3.6

```

clear all;

% IMPORT GRAFT STIFFNESS RANGE
Kg_data = xlsread('KsKgtest.xlsx', 'A2:A35');

Ks = 85; % set spring stiffness (units N/mm)
F = zeros(34,7); % initialise load matrix, each column containing force data
for a disp value
    for d = 1:7
        for i = 1:34
            F(i,d) = ((2*d+2) * Ks * Kg_data(i))/(Ks + Kg_data(i));
        end
    end

% populate displacement matrix
for d = 1:7
    for i = 1:34
        F(i,d) = ((2*d+2) * Ks * Kg_data(i))/(Ks + Kg_data(i));
    end
end

% plot figure
figure
hold on
plot(Kg_data, F(:,1), '-','color',[.871,.513,.267], 'LineWidth', 2.5)
plot(Kg_data, F(:,2), '-','color',[.737,.333,.063], 'LineWidth', 2.5)
plot(Kg_data, F(:,3), '-','color',[.22,.328,.573], 'LineWidth', 2.5)
plot(Kg_data, F(:,4), '-','color',[.286,.714,1], 'LineWidth', 2.5)
plot(Kg_data, F(:,5), '-','color',[.467,.608,.906], 'LineWidth', 2.5)
plot(Kg_data, F(:,6), '-','color',[.459,.263,.694], 'LineWidth', 2.5)
plot(Kg_data, F(:,7), '-','color',[.643,.502,.812], 'LineWidth', 2.5)
plot(Kg_data, UTS, ':ks', 'LineWidth', 2.5)
set(gca, 'fontsize', 18)
grid off
xlabel('Graft stiffness (N/mm)', 'fontsize', 20)
ylabel('Load (N)', 'fontsize', 20)
legend('d=4mm', 'd=6mm', 'd=8mm', 'd=10mm', 'd=12mm', 'd=14mm', 'd=16mm', 'UTS (SF=2)')

```

Figure B.2: Plot load F as a function of graft stiffness K_g for different displacement values d and our chosen spring stiffness $K_s = 85\text{N/mm}$ as plotted in figure 3.3

Appendix C

Leaf spring design

Leaf spring dimensions to reach the $85N/mm$ mark

For a simply supported beam of rectangular cross-section, as depicted in figure C.1, we can write:

$$K = \frac{48EI}{L^3}, \quad I = \frac{hb^3}{12} \quad (\text{C.1})$$

$$\Rightarrow K = \frac{4Eb^3}{L^3} \quad (\text{C.2})$$

$$\Rightarrow L = \left(\frac{4Eb^3}{K}\right)^{\frac{1}{3}} \quad (\text{C.3})$$

Where K is beam stiffness in N/mm ; E is Young's modulus ($192999N/mm^2$ for AISI 316 stainless steel sheet metal); I is second moment of area in mm^4 ; L is the distance between the beam supports in mm ; and h and b are beam height and thickness respectively in mm . Since $1mm$ thick AISI 316 sheets are widely available for purchase, we set $b = 1mm$, and choosing $h = 5mm$ then necessitated $L = 35.68mm$ in order to achieve $K = 85N/mm$.

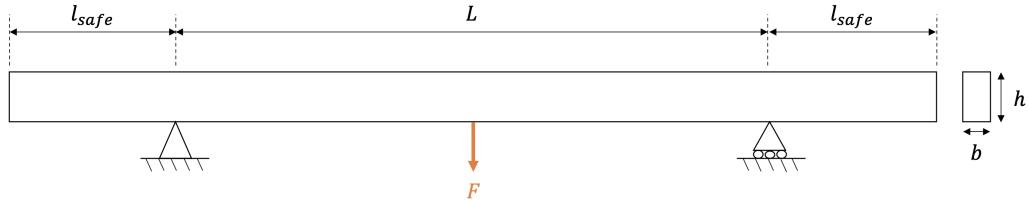


Figure C.1: Diagram of simply supported beam in bending.

Additional spring length l_{safe} such that it always stays in position

Since the beam is placed into slots within the slider, when the spring undergoes bending we must ensure it does not slide out of its slotted position. To this end, the following calculations were performed following variables identified in figure C.2.

$$\begin{cases} s = \alpha R \\ L = 2R\sin\left(\frac{\alpha}{2}\right) \\ d_{max} = R(1 - \cos(\frac{\alpha}{2})) \end{cases} \quad (\text{C.4})$$

Let's solve for α and R from the second and third equations of C.4, looking to substitute these values into the first equation and solve for s later.

$$\begin{cases} 35.68 = 2R\sin\left(\frac{\alpha}{2}\right) \\ 13.22 = R(1 - \cos(\frac{\alpha}{2})) \end{cases} \quad (\text{C.5})$$

From equation 2 of C.5,

$$R = \frac{13.22}{1 - \cos\left(\frac{\alpha}{2}\right)} \quad (\text{C.6})$$

Subbing into equation 1 of C.5,

$$35.68 = 2\sin\left(\frac{\alpha}{2}\right) \frac{13.22}{1 - \cos\left(\frac{\alpha}{2}\right)} \quad (\text{C.7})$$

$$\Rightarrow \frac{36.68}{26.44} = \frac{\sin\left(\frac{\alpha}{2}\right)}{1 - \cos\left(\frac{\alpha}{2}\right)} \quad (\text{C.8})$$

Substituting $\frac{\alpha}{2}$ as θ and $A = \frac{35.68}{26.44}$ for simplicity;

$$A\left(1 - \cos\left(\frac{\alpha}{2}\right)\right) = \sin(\theta) \quad (\text{C.9})$$

$$\sin^2(\theta) = (A - A\cos(\theta))^2 \quad (\text{C.10})$$

$$1 - \cos^2(\theta) - (A - A\cos(\theta))^2 = 0 \quad (\text{C.11})$$

$$1 - \cos^2(\theta) - A^2 + 2A\cos(\theta) - A^2\cos^2(\theta) = 0 \quad (\text{C.12})$$

Letting $\cos(\theta) = u$ and subbing in for the value of A;

$$(-1 - A^2)u^2 + 2Au + (1 - A^2) = 0 \quad (\text{C.13})$$

$$-2.821u^2 + 3.642u - 0.821 = 0 \quad (\text{C.14})$$

$$\Rightarrow u = \frac{1.64213}{5.64213} \text{ or } u = 1 \quad (\text{C.15})$$

$$(\text{C.16})$$

$$\Rightarrow \begin{cases} \theta = \arccos\left(\frac{1.64213}{5.64213}\right) + 2\pi n \\ \theta = 2\pi - \arccos\left(\frac{1.64213}{5.64213}\right) \\ \theta = 2\pi n \end{cases} \quad (\text{C.17})$$

Where $n \in N$. Plugging these values back into equation C.9 to verify them yields:

$$\Rightarrow \begin{cases} \arccos\left(\frac{1.64213}{5.64213}\right) + 2\pi n & \text{TRUE - non-trivial} \\ 2\pi - \arccos\left(\frac{1.64213}{5.64213}\right) & \text{FALSE} \\ 2\pi n & \text{TRUE - trivial} \end{cases} \quad (\text{C.18})$$

Following the non-trivial result, then $\frac{\alpha}{2} = 73.0791^\circ$. Subbing this value back into C.6 gives us:

$$\Rightarrow R = \frac{13.22}{1 - \cos(73.0791^\circ)} \quad (\text{C.19})$$

$$\Rightarrow R = 18.6473 \text{ mm} \quad (\text{C.20})$$

We can now compute beam length when maximally deflected following equation 1 of C.4:

$$\Rightarrow s = 48 \text{ mm} \quad (\text{C.21})$$

Since $s - L = 48 \text{ mm} - 35.68 \text{ mm} = 12.32 \text{ mm}$, then $l_{safe} = (12.5 \pm 0.1) \text{ mm}$ (as annotated in figure C.1) is needed on either side of the beam to avoid it slipping out of position. Therefore, the leaf

spring must have a total length of $60.68 \pm 0.2\text{mm}$, and both slots in the slider should be around 13mm in length to accommodate for l_{safe} .

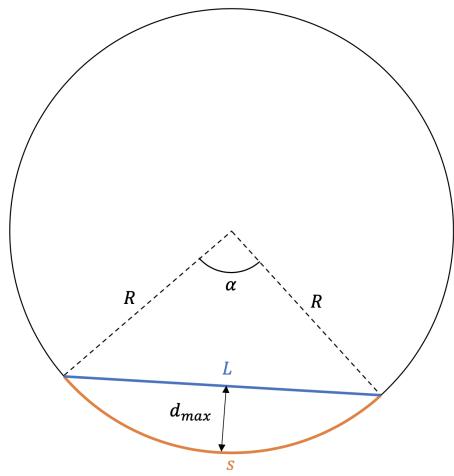


Figure C.2: Simplified diagram relating the beam in its initial state (length $L = 35.68\text{mm}$) to the beam in its deformed state (length s). R the radius of curvature of the beam. α the angle of curvature of the beam. d_{max} the maximal deflection of the beam under force F , as shown in figure C.1.

Appendix D

Connector hook design

As cited in the main body of text, surgeons aim to create ACL grafts of around 8mm in diameter from the hamstring and semitendinosus tendons, but in some cases these can go up to 10mm in diameter. The connector's hook in this device must accommodate for such grafts. This means that a hook radius had to be chosen such that $c \geq 10\text{mm}$, as referred to in figure D.1. This leads to:

$$c \geq 10 \Leftrightarrow \sqrt{2R^2} \geq 10 \quad (\text{D.1})$$

$$\Leftrightarrow \sqrt{2}R \geq 10 \quad (\text{D.2})$$

$$\Leftrightarrow R \geq 7.07 \quad (\text{D.3})$$

$$\Leftrightarrow R = 7.5\text{mm} \text{ so } c = 10.6\text{mm} \quad (\text{D.4})$$

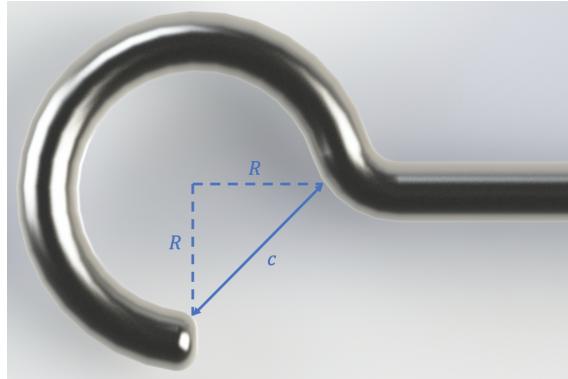


Figure D.1: Solidworks zoom-in on the connector's hook.

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