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TITLE: Innovative In-Vivo Kinetic System to Facilitate Rehabilitation and Maintenance Residuum Health After Limb Loss

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14. ABSTRACT This is the first yearly report for the project. In summary, we have progressed a total of 680 tasks including 648 (95%) that have been completed during this year leading the creation of over 3,900 files. The main milestones achieved include hiring staff, obtain ethic certificate from Griffith University's HREC, develop collaborations with key experts, establish roadmap for experiments for up to 100 short experiments, analyze a series of experiments to cross-validate physical and digital phantoms of the residuum, start to build prototypes (Deliverable 1), plan for human experiments for the proof of safety and efficacy (Deliverable 2) and utility (Deliverable 3), publish 4 abstracts, submit 2 manuscripts, obtain 2 grants, and submit 6 grants. Altogether, we will argue that the project is within the budget, on the scope and on time with key all milestones achieved for this first year.					
15. SUBJECT TERMS Diagnostic tool; Loading; Prosthesis; Quantitative Ultrasound; Residuum health; Skin; Socket; Tissue breakdown; Limb amputation; Modelling; Digital twin					
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Table of Contents

	<u>Page</u>
1. Introduction.....	2
2. Keywords	3
3. Accomplishments.....	3
3.1. Major goals of the project	3
3.2. Accomplishment under these goals.....	4
Phase 1: Kick-off tasks	5
Phase 2: Key developments and deliverables	7
Phase 3: Share outcomes.....	33
Phase 4: Exit strategy.....	39
Phase 5: Post-funding tasks	42
3.3. Opportunities for training and professional development.....	43
3.4. Dissemination of the results to communities of interest	43
3.5. Plan to do during the next reporting period to accomplish the goals	43
4. Impact	44
4.1. Impact on the development of the principal discipline(s) of the project.....	44
4.2. Impact on other disciplines	45
4.3. Impact on technology transfer.....	45
4.4. Impact on society beyond science and technology	45
5. Changes/Problems.....	46
5.1. Changes in approach and reasons for change.....	46
5.2. Changes that had a significant impact on expenditures	46
5.3. Significant variations.....	46
5.4. Significant changes in use or care of human subjects.....	47
5.5. Significant changes in use or care of vertebrate animals	47
5.6. Significant changes in use or care of biohazards, and/or of select agents	48
6. Products.....	48
6.1. Publications, conference papers, and presentations	48
7. Participants & Other Collaborating Organizations	49
7.1. Individual contributions on the project	49
7.2. Change in the active other support of the PD/PI(s)	56
7.3. Other organizations involved as partners	56
8. Special Reporting Requirements.....	56
8.1. Collaborative awards.....	56
8.2. QUAD charts	56
9. Appendices.....	56
9.1. Appendix A: Detailed SOW.....	56
9.2. Appendix B: Overview of Y1 activity	56
9.3. Appendix C: QUAD chart.....	56
9.4. Appendix D: PDFs of all publications	56

1. Introduction

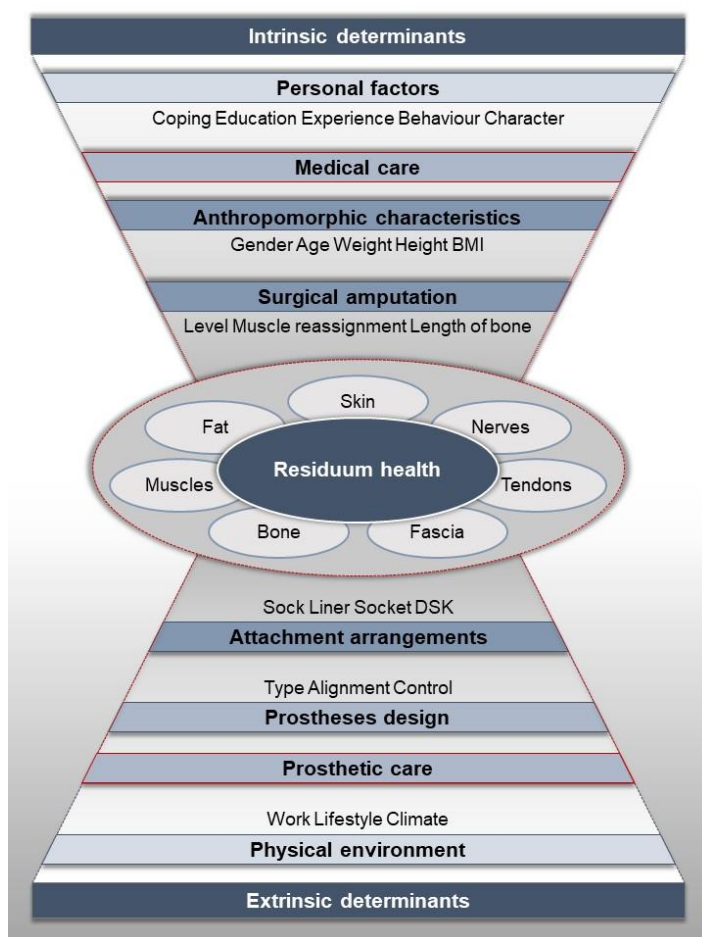
The scope of this project of research is to equip rehabilitation specialists with the In-vivo Kinetic system 2.0 capable to diagnose common neuromusculoskeletal disfunctions compromising residuum health of Service Members and Veterans suffering from limb loss.

The objectives will be to collect all required information to demonstrate the safety of In-vivo Kinetic system 2.0 for the end-users, as well as its medical efficacy and utility for care providers. These validations are required by the regulatory legislators, requiring a rigorous and validated research protocol involving researchers and physicians, as well as cohorts of end-users.

In the short term, we anticipate that this innovative In-vivo Kinetic system 2.0 will provide the entire clinical management team with an improved non-invasive diagnostic tool. In return, their ability to perform personalized and real-time assessments of the residuum of Service Members and Veterans will help not only to prevent, but more importantly, to treat the most common medical and prosthetic neuromusculoskeletal issues. For example, the In-vivo Kinetic system 2.0 could play an essential role in early detection of osteoporosis, heterotopic bone formation and soft tissues at risk of deep tissue injury and ulceration. This new tool could also guide personalized prescription for prosthetic fitting including design of costly sockets and selection of expensive components.

Altogether, this project will significantly contribute to an increase in functional outcome and quality of life of Service Members and Veterans with lower limb loss suffering from typical and regular issues compromising residuum health. This means that the In-vivo Kinetic system 2.0 will contribute to the return of Service Members to pre-injury function that could, subsequently, provide an avenue for return to active duty. Finally, this diagnostic tool could increase cost-effectiveness of prosthetic prescription, thereby reducing the lifetime financial burden associated with prosthetic use.

Figure 1. Overview of intrinsic and extrinsic determinants of residuum health influenced by neurological phantom pain as well as acute and chronic issues affecting skin (e.g., oedema, contact dermatitis, eczematization, keratosis, epidermoid cysts, bacterial and fungal infections, intertrigo, tumors, ulcers, verrucose hyperplasia, allergy to liners), fat (e.g., excessive superficial and intramuscular adipose tissues), muscles (e.g., disuse atrophy, fat infiltration, tendinitis, contractures, weakness), bones (e.g., stress fractures, osteopenia, heterotopic ossification), and nerves (e.g., neuroma). (Credit: PI-Frossard, extracted from ART07).



2. Keywords

Activity of daily living; Diagnostic tool; Health related quality of life, Kinetic; Loading; Neuromusculoskeletal disfunctions; Modelling; Prosthesis; Prosthetic use; Quantitative Ultrasound; Residuum; Skin; Socket; Socket–limb interface; Tissue breakdown; Tissue degeneration; Transfemoral amputation; Transtibial amputation; Mechanical properties.

3. Accomplishments

3.1. Major goals of the project

The mains goals are:

- Create a prototype of In-vivo Kinetic system 2.0 including loading and ultrasound measurements as well as neuromusculoskeletal modelling
- Establish the proof of safety and efficacy (TRL-6) to determine ability to safely and accurately estimate the loading and tissue deformation
- Establish the Proof of utility (TRL-7) to determine the ability to measure differences in tissue deformation in response to loading constraints
- Design of clinical trial including complete written description of scientific rationale and research activities for the clinical trial.

The Statement of Work (SOW) detailed in Figure 2 indicated that these goals will be achieved during the course of five main including phases of kick-off (e.g., Create project management structure, Hire staff, Develop collaborations, Purchase equipment, Obtain ethics approval), key developments and deliverables (e.g., Plan experiments, Create phantom of residuum, Build prototypes (Deliverable 1), Proof of safety and efficacy (Deliverable 2), Proof of utility (Deliverable 3), Design clinical trial (Deliverable 4)), share outcomes (e.g., Report to stakeholders, Publish outcomes), exit strategy (e.g., Develop strategic collaborations, Seek funding, End appointments, Closing project) as well as post-funding tasks (e.g., Publish outcomes, Investigate commercialization). The extended SOW is provided in Appendix A: Detailed SOW.

The percentage of completion of the goals and intermediate task is included in the GANTT chart for Y1 is provided in Sections 9.2, Appendix B: Overview of Y1 activity.

Figure 2. SOW and associated GANTT chart indicating the quarterly and yearly periods of activity for the five main phases of the development of the project before (Y0), during (Y1, Y2) and post (Y3, Y4).

Phase	Task	Pre		During								Post	
		Y0	Y0	Y1	Y1	Y1	Y1	Y2	Y2	Y2	Y2	Y3	Y3
		Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
1	Phase 1: Kick-off tasks												
1.1	Create project management structure												
1.2	Hire staff												
1.3	Develop collaboration												
1.4	Purchase equipment												
1.5	Obtain ethics approval												
2	Phase 2: Key developments and deliverables												
2.1	Plan experiments												
2.2	Create phantom of residuum												
2.3	Build prototypes (Deliverable 1)												
2.4	Proof of safety and efficacy (Deliverable 2)												

Phase 1: Kick-off tasks

- **Phase 1.1: Create project management structure**

- **Phase 1.1.1: Manage project**

- Manage the research contract with DoD including to provision of additional information about the PI and CIs (e.g., list of supports), budget (e.g., quotes, adjustment of salaries, adjustment of on-costs), and clarify requirements for ethics application as well as organizing signature of the contract and formal starting date of the project.
 - Organize kick-off meetings to present overview and processes in place to organize, monitor and report projects activities (Figure 3).
 - Create and update management plans and registries to organize, monitor and report projects activities related to charter, dashboard, team, stakeholders, risks, finances, data collection, data analysis, publications, IP and communication (Figure 4).

- **Phase 1.2: Hire staff**

- Hire staff including

- PI-Frossard was hired as Professor equivalent to Principal Research Fellow starting on 01/07/2021 (0.8 FTE, 2-year contract).
 - PI-Langton was hired as Senior Research Fellow 1 starting on 01/07/2021 (1 FTE, 2-year contract).
 - Dr Nataliya Perevoshchikova was hired as Senior Research Fellow 2 starting on 01/07/2021 (0.75 FTE, 2-year contract).

- **Phase 1.3: Develop collaboration**

- Phase 1.3.1: Attract key experts

- Derek Smith and Antonio Grimm (Griffith ADaPT), specialists Computer Assisted Design and in 3D printing and design for additive manufacturing.
 - Amy Gould (Griffith Centre for Biomedical and Rehabilitation Engineering), specialist in digital media communication (Figure 3).
 - Dr Kevin Moerman (National University of Ireland Galway), specialist in modelling of lower limb residuum.
 - Prof Stefanie Feih (Griffith university), specialist in modelling, 3D printing, design for additive manufacturing and polymer composite material performance.
 - Prof Mark Pitkin (Tuft University), specialist in developments if osseointegrated implants for bone-anchored prosthesis.
 - Ass/Pro Joshua Byrne (Griffith university), specialist of health economic evaluations of medical device.
 - Prof Adam Findlay retired Major General, AM (Griffith University), specialist in strategic collaboration with the Australian Defence (Figure 5).

- **Phase 1.5: Obtain ethics approval**

- Phase 1.5.1: Obtain ethics approval from GUG

- Receive approval for ethic application from Griffith University Human Research Ethics Review (GU Ref No: 2021/931) for Workflow for Dynamic Anatomical Ultrasonography (DAU) of an adult able-bodied healthy thigh.
 - Receive approval for low/negligible risk ethic application from Griffith University Human Research Ethics Review (GU2022/351) for biomechanical analyses of residual limb of individuals living.

- Phase 1.5.2: Obtain ethics approval from DoD

- Submit documents for US-HRPO ethic approval.

Figure 3. First team meeting to present overview and processes in place to organise, monitor and report projects activities. From left to right: Dr Nataliya Perevoshchikova, Ass / Prod David Saxby, Prof Rob Barrett, Dr Claudio Pizzolato, Prof Laurent Frossard, Prof David Lloyd, Prof Christian Langton, Amy Gould, Derek Smith.



Figure 4. Registries used to organize, monitor and report projects activities related to charter, dashboard, team, stakeholders, risks, finances, data collection, data analysis, publications, IP and communication (Credit: PI-Frossard).

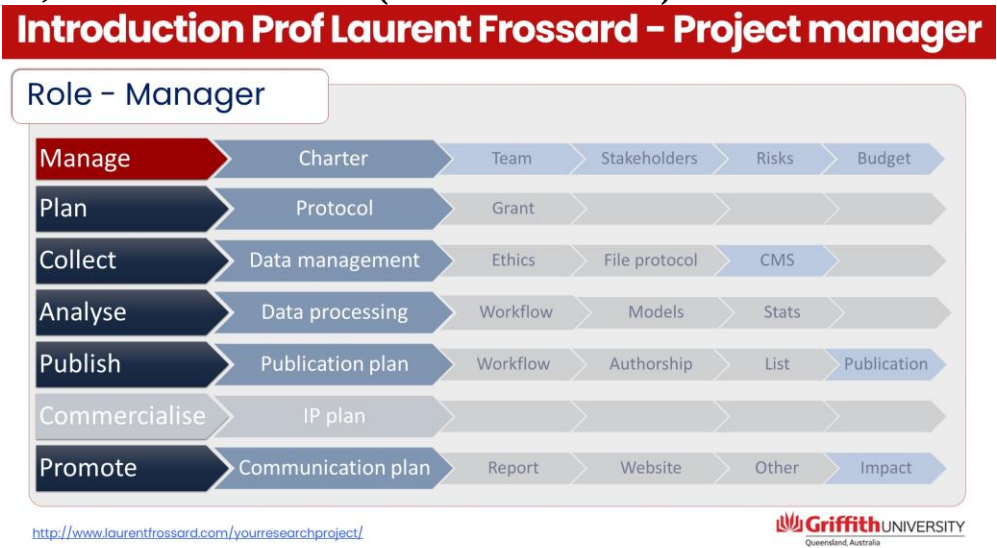


Figure 5. Brainstorming session with Prof Adam Findlay (retired Major General, AM) about to discuss relevance of the outcomes of this project to current and former Service Members suffering from limb loss and potential collaboration with the Australia Department of Defence (Credit: PI-Frossard).



Phase 2: Key developments and deliverables

• Phase 2.1: Plan experiments

- Phase 2.1.1: Establish roadmap for experiments
 - Create and update roadmap for the development of In-Vivo Kinetic system 2.0 including up to 100 short experiments lasting between 10 min and 30 min each (Figure 6, Table 2).

Figure 6. Initial mind map of roadmap for development of In-Vivo Kinetic system 2.0 (Credit: CI-Langton).

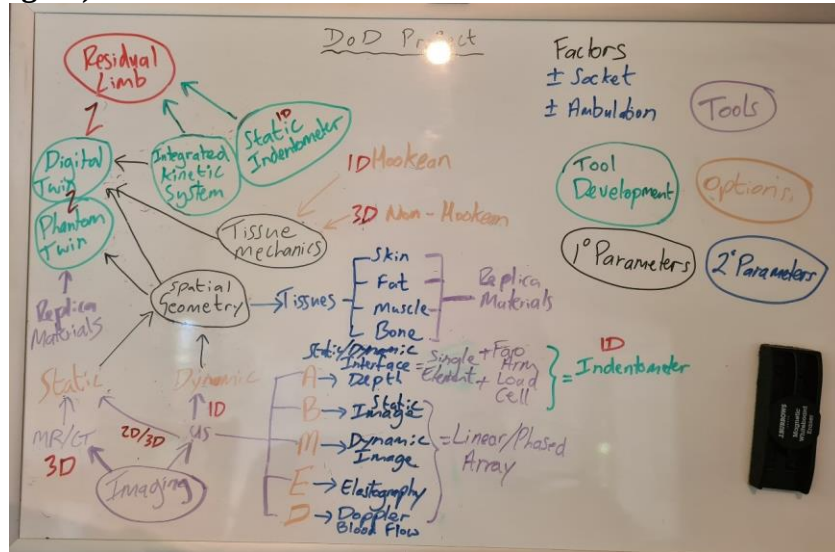


Table 2. Roadmap for the development of the In-Vivo Kinetic system 2.0 including 100 short experiments (version 23).

Experiment	Code
→ 1 Phantoms	
→ 1.1 Samples	
→ 1.1.1 Single set layer	
→ 1.1.1.1 Single set layer for gels samples	E1
→ 1.1.1.2 Single set layer for silicones and polymers samples	E2
→ 1.1.1.3 Single set layer for 3D-printed materials	E3
→ 1.1.2 Single proportioned layer	
→ 1.1.2.1 Single set layer for gels samples	E4
→ 1.1.2.2 Single set layer for silicones and polymers samples	E5
→ 1.1.2.3 Single set layer for 3D-printed materials	E6
→ 1.1.3 Multi-layered with set dimension	
→ 1.1.3.1 Multi-layered with set dimension (Si, Fi, Mi)	E7
→ 1.1.4 Multi-layered with proportioned dimensions	
→ 1.1.4.1 Multi-layered with proportioned dimensions (Si, Fi, Mi)	E8
→ 1.2 Replica residuum	
→ 1.2.1 Static multiple proportioned layers	

————→ 1.2.1.1 Sample Si, Sample Fi, Sample Mi, Sawbone	E9
————→ 1.2.2 Dynamic multiple proportioned layers	
————→ 1.2.2.1 Compression / Decompression of sawbone	E10
————→ 1.2.2.2 Flexion / Extension of sawbone	E11
————→ 1.2.2.3 Adduction / Abduction of sawbone	E12
————→ 1.2.2.4 Internal / External rotation of sawbone	E13
→ 2 Animal specimen	
————→ 2.1 Porcine leg	
————→ 2.1.1 Half porcine leg (Skin, Fat, Muscle, bone)	E14
————→ 2.1.2 Full porcine leg (Skin, Fat, Muscle, Bone, Muscle, Fat, Skin)	E15
————→ 2.2 Lamb shank	
————→ 2.2.1 Full lamb shank (Skin, Fat, Muscle, Bone, Muscle, Fat, Skin)	E16
→ 3 Able-bodied (ABD)	
————→ 3.1 Lying	
————→ 3.1.1 Thigh in supine position	E17
————→ 3.1.2 Thigh in prone position	E18
————→ 3.1.3 Thigh in lateral recumbent position	E19
————→ 3.2 Standing static	
————→ 3.2.1 Thigh standing on two legs	E20
————→ 3.2.2 Thigh standing on mock up	E21
————→ 3.3 Walking	
————→ 3.3.1 Thigh walking on mock up	E22
→ 4 Transfemoral amputation with socket-suspended prosthesis (SSP-TFA)	
————→ 4.1 Lying	
————→ 4.1.1 Sound limb	
————→ 4.1.1.1 Supine position	E23
————→ 4.1.1.2 Prone position	E24
————→ 4.1.1.3 Lateral recumbent position	E25
————→ 4.1.2 Residuum without socket	
————→ 4.1.2.1 Supine position	E26
————→ 4.1.2.2 Prone position	E27
————→ 4.1.2.3 Lateral recumbent position	E28
————→ 4.1.3 Residuum with socket	
————→ 4.1.3.1 Supine position	E29
————→ 4.1.3.2 Prone position	E30
————→ 4.1.3.3 Lateral recumbent position	E31
————→ 4.2 Standing static	
————→ 4.2.1 Sound limb	
————→ 4.2.1.1 Standing on two legs	E32
————→ 4.2.2 Residuum without socket	
————→ 4.2.2.1 Residuum relaxed for baseline	E33
————→ 4.2.2.2 Residuum relaxed with indentation	E34
————→ 4.2.2.3 Compression / Decompression of the residuum	E35
————→ 4.2.2.4 Flexion / Extension of the residuum	E36
————→ 4.2.2.5 Adduction / Abduction of the residuum	E37

—→ 4.2.3 Residuum with socket and prosthesis	
—→ 4.2.3.1 Standing on two legs	E38
—→ 4.2.3.2 Compression / Decompression of the residuum	E39
—→ 4.2.3.3 Flexion / Extension of the residuum	E40
—→ 4.2.3.4 Adduction / Abduction of the residuum	E41
—→ 4.3 Walking	
—→ 4.3.1 Walking at self-selected speed	E42
—→ 4.3.2 Walking at fast speed	E43
—→ 4.3 Activities of daily living	
—→ 4.3.1 Ascending and descending ramp	E44
—→ 4.3.2 Ascending and descending slope	E45
—→ 5 Transtibial amputation with socket-suspended prosthesis (SSP-TTA)	
—→ 5.1 Lying	
—→ 5.1.1 Sound limb	
—→ 5.1.1.1 Supine position	E46
—→ 5.1.1.2 Prone position	E47
—→ 5.1.1.3 Lateral recumbent position	E48
—→ 5.1.2 Residuum without socket	
—→ 5.1.2.1 Supine position	E49
—→ 5.1.2.2 Prone position	E50
—→ 5.1.2.3 Lateral recumbent position	E51
—→ 5.1.3 Residuum with socket	
—→ 5.1.3.1 Supine position	E52
—→ 5.1.3.2 Prone position	E53
—→ 5.1.3.3 Lateral recumbent position	E54
—→ 5.2 Standing static	
—→ 5.2.1 Sound limb	
—→ 5.2.1.1 Standing on two legs	E55
—→ 5.2.2 Residuum without socket	
—→ 5.2.2.1 Residuum relaxed for baseline	E56
—→ 5.2.2.2 Residuum relaxed with indentation	E57
—→ 5.2.2.3 Compression / Decompression of the residuum	E58
—→ 5.2.2.4 Flexion / Extension of the residuum	E59
—→ 5.2.2.5 Adduction / Abduction of the residuum	E60
—→ 5.2.3 Residuum with socket and prosthesis	
—→ 5.2.3.1 Standing on two legs	E61
—→ 5.2.3.2 Compression / Decompression of the residuum	E62
—→ 5.2.3.3 Flexion / Extension of the residuum	E63
—→ 5.2.3.4 Adduction / Abduction of the residuum	E64
—→ 5.3 Walking	
—→ 5.3.1 Walking at self-selected speed	E65
—→ 5.3.2 Walking at fast speed	E66
—→ 5.3 Activities of daily living	
—→ 5.3.1 Ascending and descending ramp	E67
—→ 5.3.2 Ascending and descending slope	E68

→ 6 Transfemoral amputation with bone-anchored prosthesis (BAP-TFA)	
→ 6.1 Lying	
→ 6.1.1 Sound limb	
→ 6.1.1.1 Supine position	E69
→ 6.1.1.2 Prone position	E70
→ 6.1.1.3 Lateral recumbent position	E71
→ 6.1.2 Residuum with implant	
→ 6.1.2.1 Supine position	E72
→ 6.1.2.2 Prone position	E73
→ 6.1.2.3 Lateral recumbent position	E74
→ 6.2 Standing static	
→ 6.2.1 Sound limb	
→ 6.2.1.1 Standing on two legs	E75
→ 6.2.2 Residuum with implant	
→ 6.2.2.1 Residuum relaxed for baseline	E76
→ 6.2.2.2 Residuum relaxed with indentation	E77
→ 6.2.2.3 Compression / Decompression of the residuum	E78
→ 6.2.2.4 Flexion / Extension of the residuum	E79
→ 6.2.2.5 Adduction / Abduction of the residuum	E80
→ 6.3 Walking	
→ 6.3.1 Walking at self-selected speed	E81
→ 6.3.2 Walking at fast speed	E82
→ 6.3 Activities of daily living	
→ 6.3.1 Ascending and descending ramp	E83
→ 6.3.2 Ascending and descending slope	E84
→ 7 Transfemoral amputation with bone-anchored prosthesis (BAP-TTA)	
→ 7.1 Lying	
→ 7.1.1 Sound limb	
→ 7.1.1.1 Supine position	E85
→ 7.1.1.2 Prone position	E86
→ 7.1.1.3 Lateral recumbent position	E87
→ 7.1.2 Residuum with implant	
→ 7.1.2.1 Supine position	E88
→ 7.1.2.2 Prone position	E89
→ 7.1.2.3 Lateral recumbent position	E90
→ 7.2 Standing static	
→ 7.2.1 Sound limb	
→ 7.2.1.1 Thigh standing on two legs	E91
→ 7.2.2 Residuum with implant	
→ 7.2.2.1 Residuum relaxed for baseline	E92
→ 7.2.2.2 Residuum relaxed with indentation	E93
→ 7.2.2.3 Compression / Decompression of the residuum	E94
→ 7.2.2.4 Flexion / Extension of the residuum	E95
→ 7.2.2.5 Adduction / Abduction of the residuum	E96
→ 7.3 Walking	

—→ 7.3.1 Walking at self-selected speed	E97
—→ 7.3.2 Walking at fast speed	E98
—→ 7.3 Activities of daily living	
—→ 7.3.1 Ascending and descending ramp	E99
—→ 7.3.2 Ascending and descending slope	E100

- **Phase 2.2: Create phantom of residuum**

- Prepare, collect and analyze series of:
 - E1 to E3 Experiments to test single set layer of samples with candidate materials such as gel, silicon, polymers that could potentially mimic material proprieties of a particular replica tissue such as skin, fat, muscle, fascia (Figure 7, Figure 8, Figure 9, Figure 10, Figure 11, Figure 12, Figure 13, Figure 14).
 - E4 to E6 Experiments to test proportioned simple layers of samples with candidate materials such as gel, silicon, polymers that could potentially mimic material proprieties of a particular replica tissue such as skin, fat, muscle, fascia (Figure 15).
 - E8 Experiments to test proportioned triple layers of samples with candidate materials such as gel, silicon, polymers that could potentially mimic material proprieties of residuum replica tissues such as skin, fat, muscle, fascia (Figure 16, Figure 17, Figure 18, Figure 19, Figure 20, Figure 21, Figure 22, Figure 23, Figure 24, Figure 25, Figure 26).
 - E9 Experiments to test multi-layered phantoms with proportioned dimensions proportioned layers of selected materials mimicking material proprieties of whole residuum replica tissues including skin, fat, muscle, bone (Figure 27, Figure 28, Figure 29, Figure 30, Figure 31, Figure 32).
 - E14 Experiments to test a DAU and modeling process on half porcine leg (Figure 33, Figure 34).
 - E17 to E19 Experiments to test DAU and modeling process on the thigh of an able-bodied (Figure 35, Figure 36, Figure 37, Figure 38).

Figure 7. E1 to E3 Experiments: Example of early solid partially-hydrated gelatine blocks with variable further hydration (e.g., 0% and 50% water concentration) (Credit: CI-Langton).

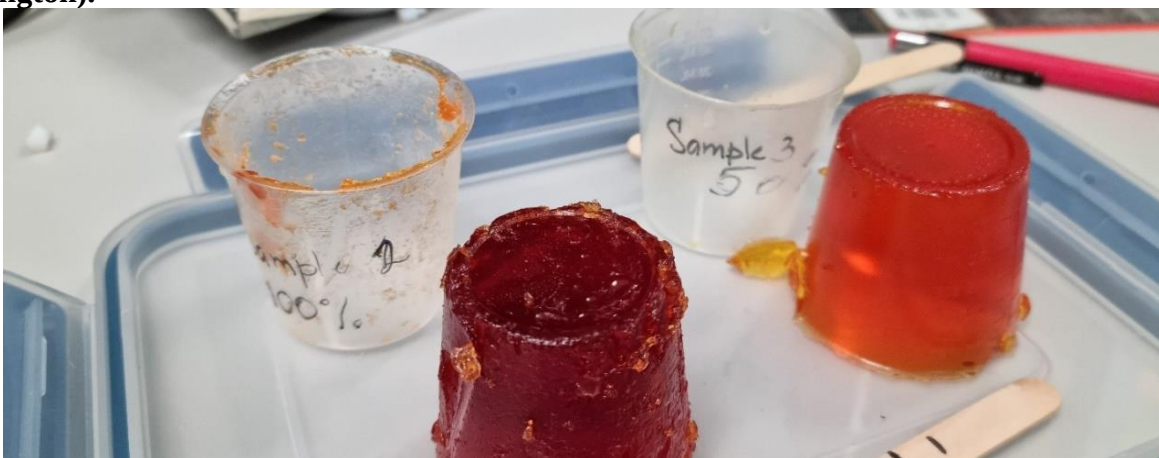


Figure 8. E1 to E3 Experiments: Preparation of samples with gelatine powder between 2.5 and 15 g/60ml susceptible to have the same mechanical and ultrasound proprieties of skin, fat and muscles to be tested during E1 experiments (Credit: CI-Langton).

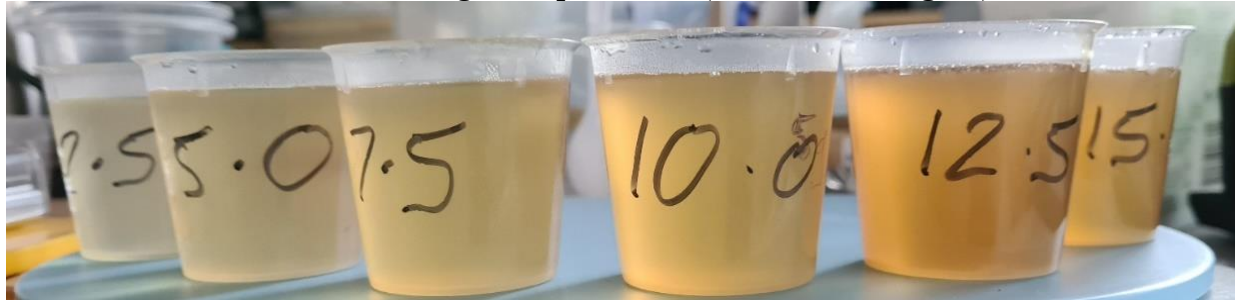


Figure 9. E1 to E3 Experiments: Bench test of ultrasound measurements of mechanical proprieties of materials considered to represent the skin, fat, muscle or bone for physical phantom. (A) reference signal obtained solely with the plastic container, (B) signal obtained with sample (Credit: CI-Langton).

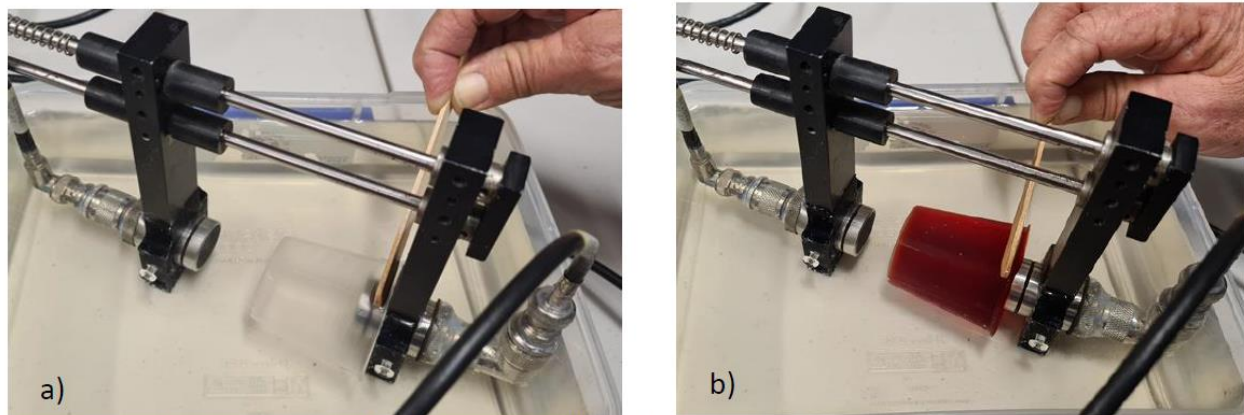


Figure 10. E1-E3 Experiments: Testing protocol including Phase A-Design of sample, Phase B-Setup of test-rig, Phase C-Mechanical testing, Phase D-Design of model (Credit: PI-Frossard, SRF2-Perevoshchikova)).

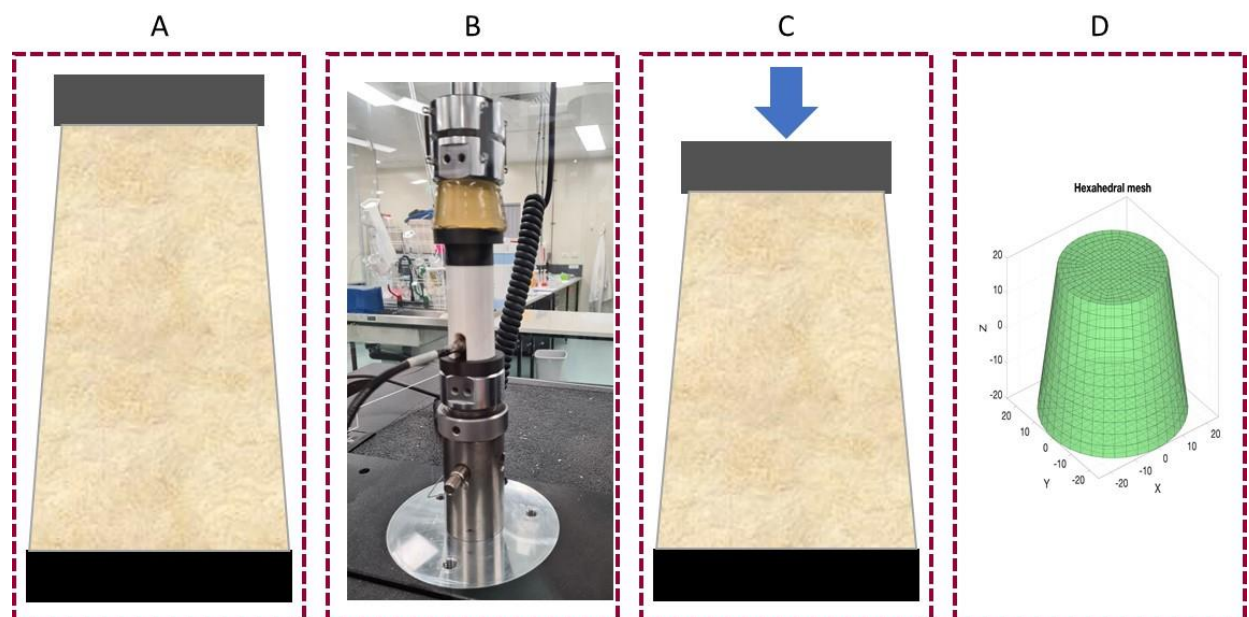


Figure 11. E1-E3 Experiments: Overview of the test-rig including the Instron machine applying the vertical load on ultrasound indenter on sample during where ultrasound transducer goes through the dark grey sample platen, hence in direct contact with the sample (Credit: PI-Frossard).

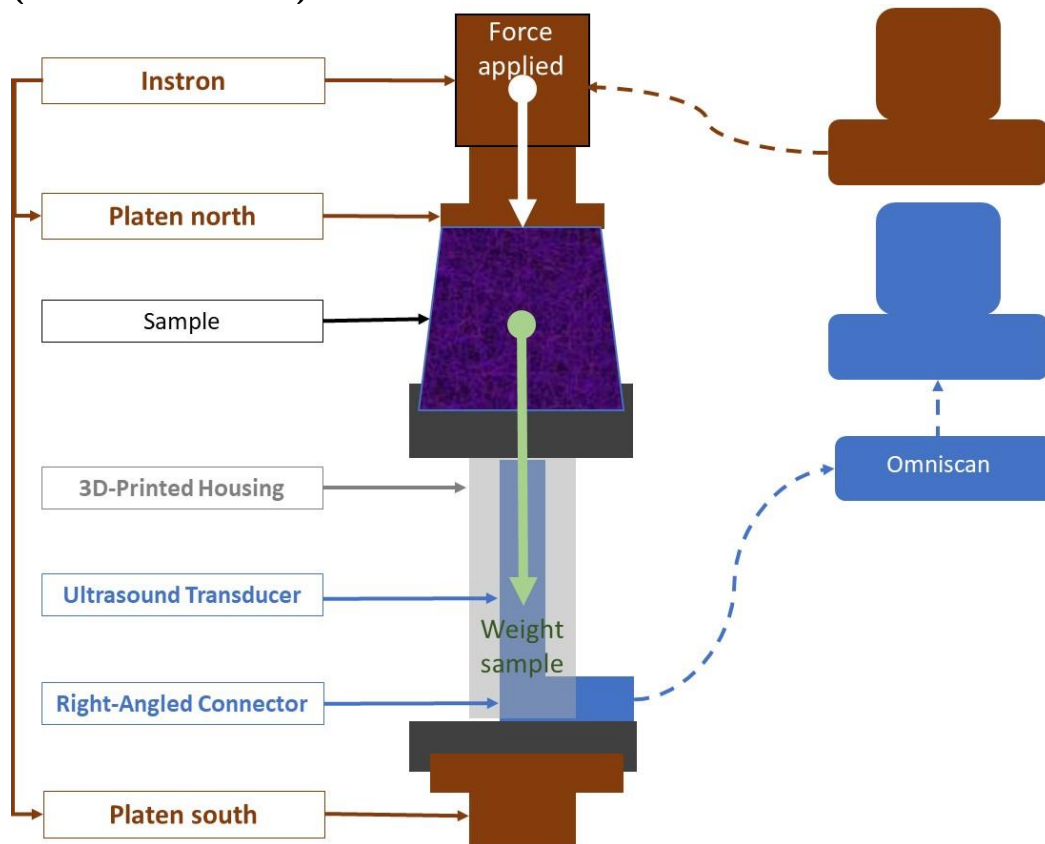


Figure 12. E1-E3 Experiments: Team effort during experiments with SFR2-Perevoshchikova (left) and PI-Langton (right) (Credit: PI-Frossard)



Figure 13. E1-E7 Experiments: Overview of the test rig used to perform with samples and physical phantom of the replica tissues (skin, fat, muscle) of the residuum (Credit: PI-Frossard).

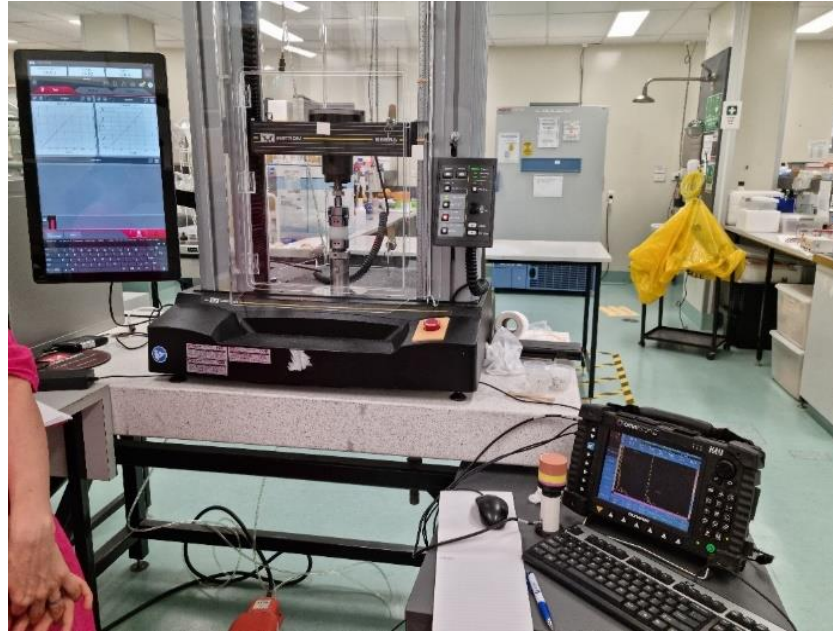


Figure 14. E1 to E3 Experiments: Example of digital phantom considering effect of indentation depending on the size of the physical phantom (Credit: SRF2-Perevoshchikova).

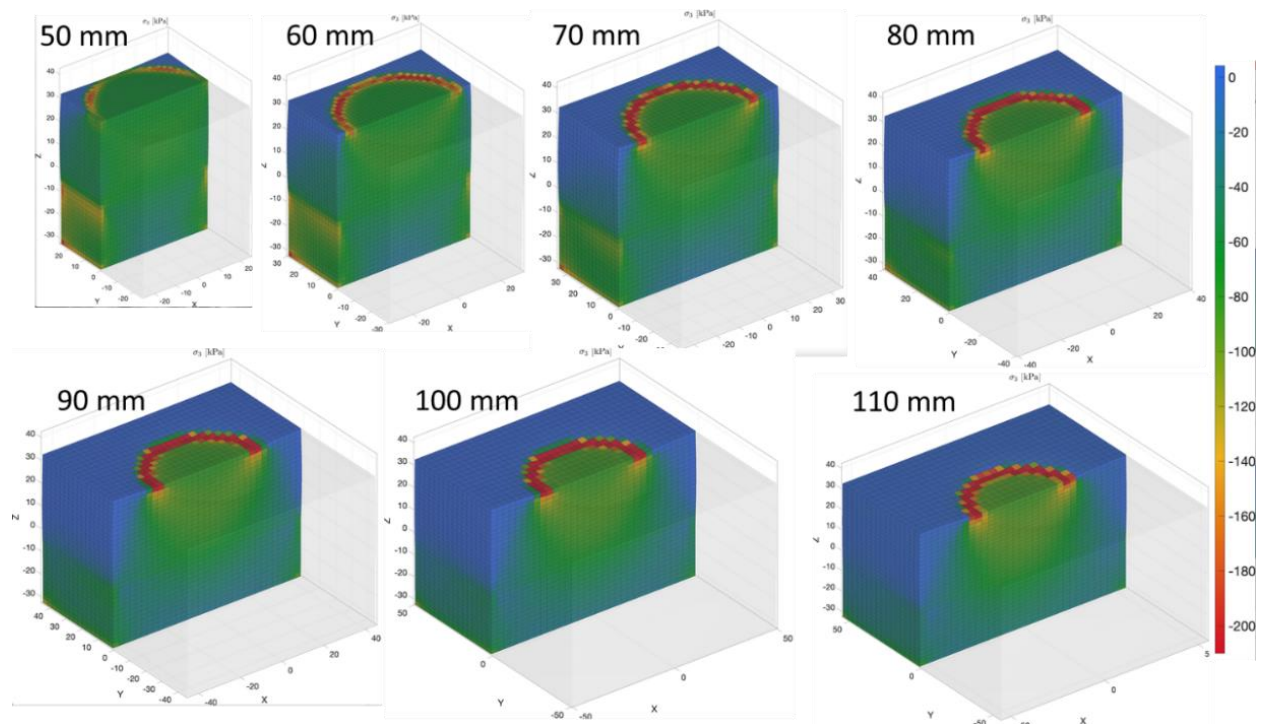


Figure 15. E7 experiments: Team discussion between SRF2-Perevoshchikova and CI-Langton (Credit: PI-Frossard).



Figure 16. E8 Experiments Proposed testing protocol including Phase A-Design of sample, Phase B-Setup of test-rig, Phase C-Mechanical testing, Phase D-Design of model (Credit: PI-Frossard).

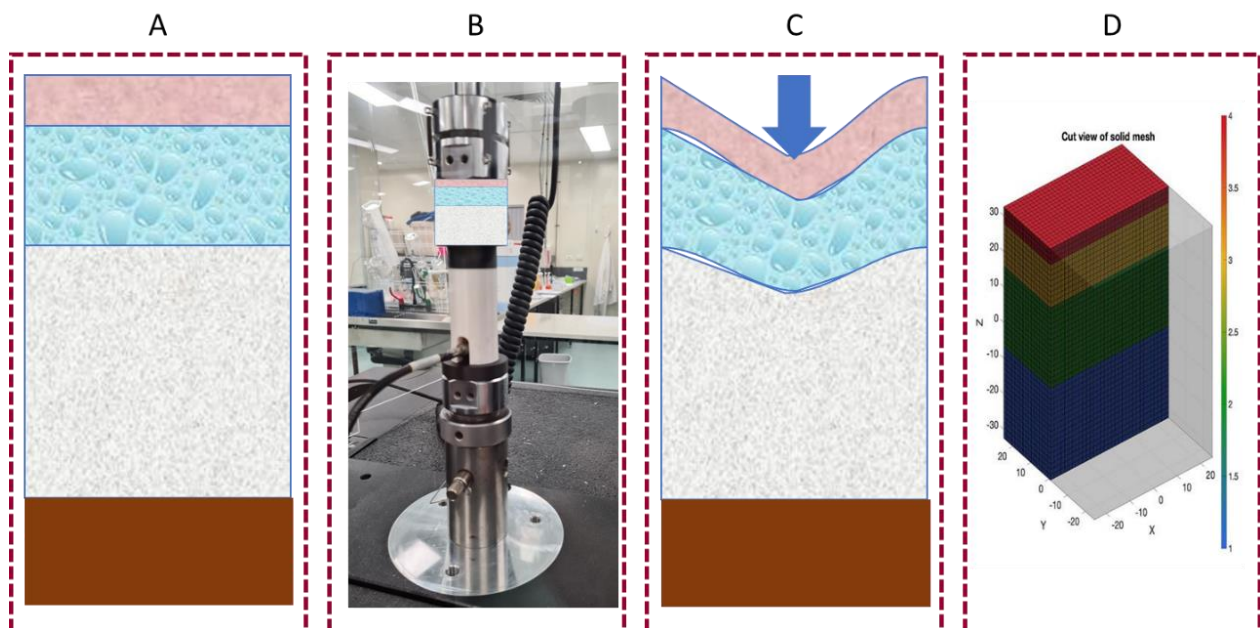


Figure 17. E8 Experiments: Preparation of the test-rig including the Instron machine applying the vertical load on ultrasound indenter on multi-layered with proportioned dimensions where ultrasound transducer goes through the dark grey sample platen, hence in direct contact with the sample (Credit: PI-Frossard).

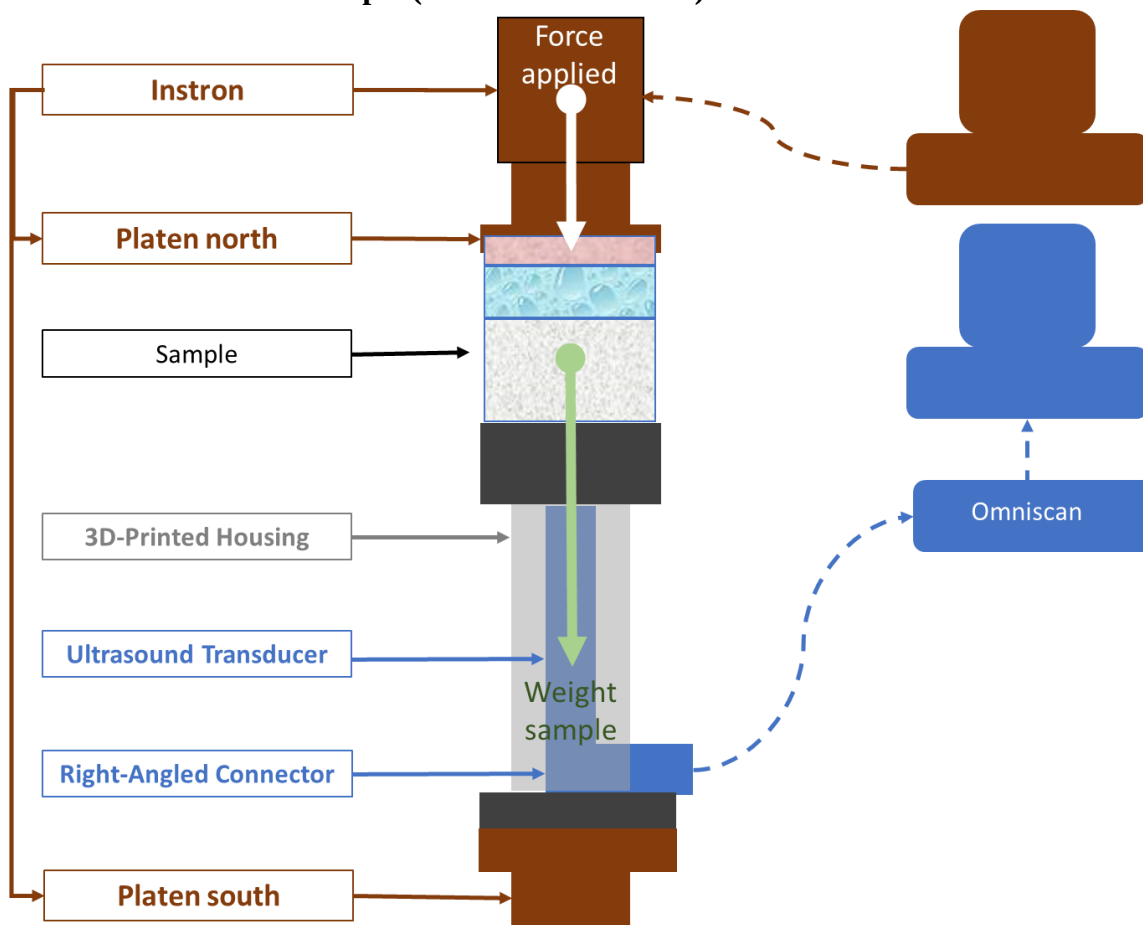


Figure 18. E8-114a experiments: Overview of the test rig including Instron machine used to perform with physical phantom of the replica tissues (skin, fat, muscle) of the residuum without (top) and with (bottom) Omniscan measurments (Credit: PI-Frossard).





Figure 19. E8-1141a Experiments: Example of the before (left) and during ramp test deformation (right) of physical phantom performed with Instron machine during of (Credit: PI-Frossard).

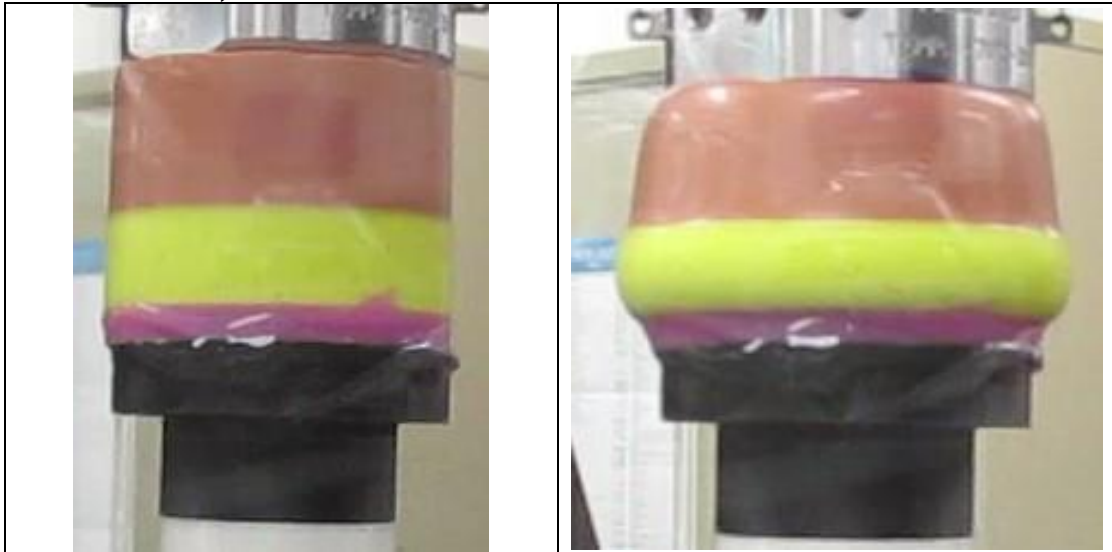


Figure 20. E8-1141a Experiments: Example of deformation rendered by the model of the digital phantom (Credit: SRF2-Perevoshchikova).



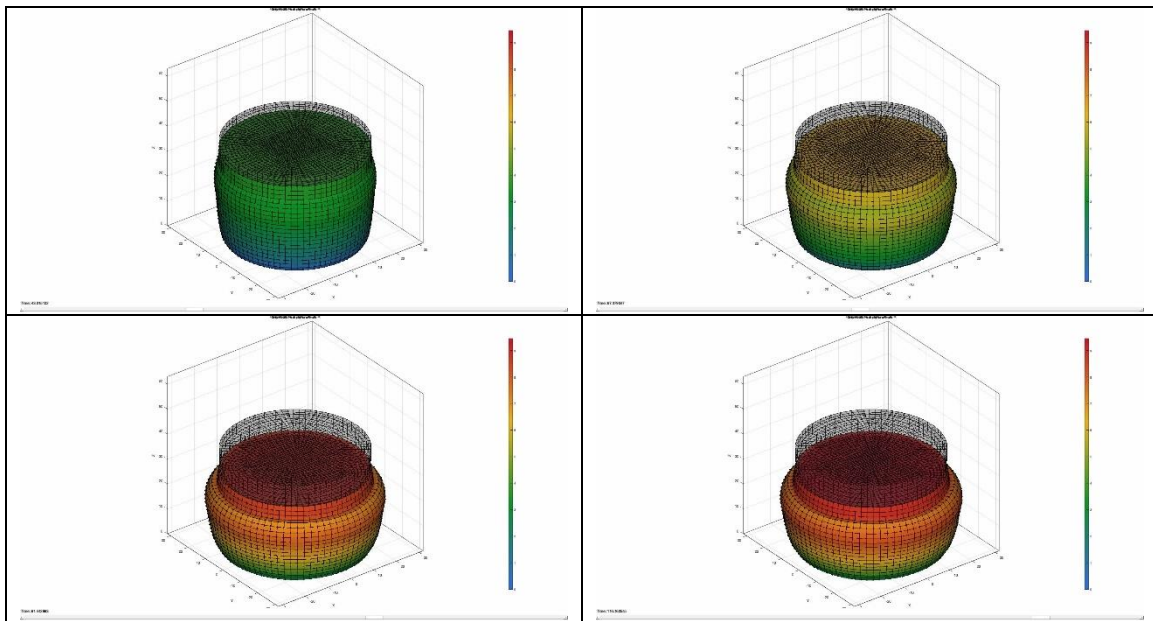


Figure 21. E8-1141b Experiments: Team discussion about setting up of experiments including Prof Feih, SRF2-Perevoshchikova and CI-Langton, from left to right respectively (Credit: PI-Frossard).



Figure 22. E8-Exp 1141b experiments: Overview of the test rig including Instron machine used to perform experiments with physical phantom of the replica tissues (skin, fat, muscle) of the residuum without (top) and with (bottom) Omniscan measurments (Credit: PI-Frossard).

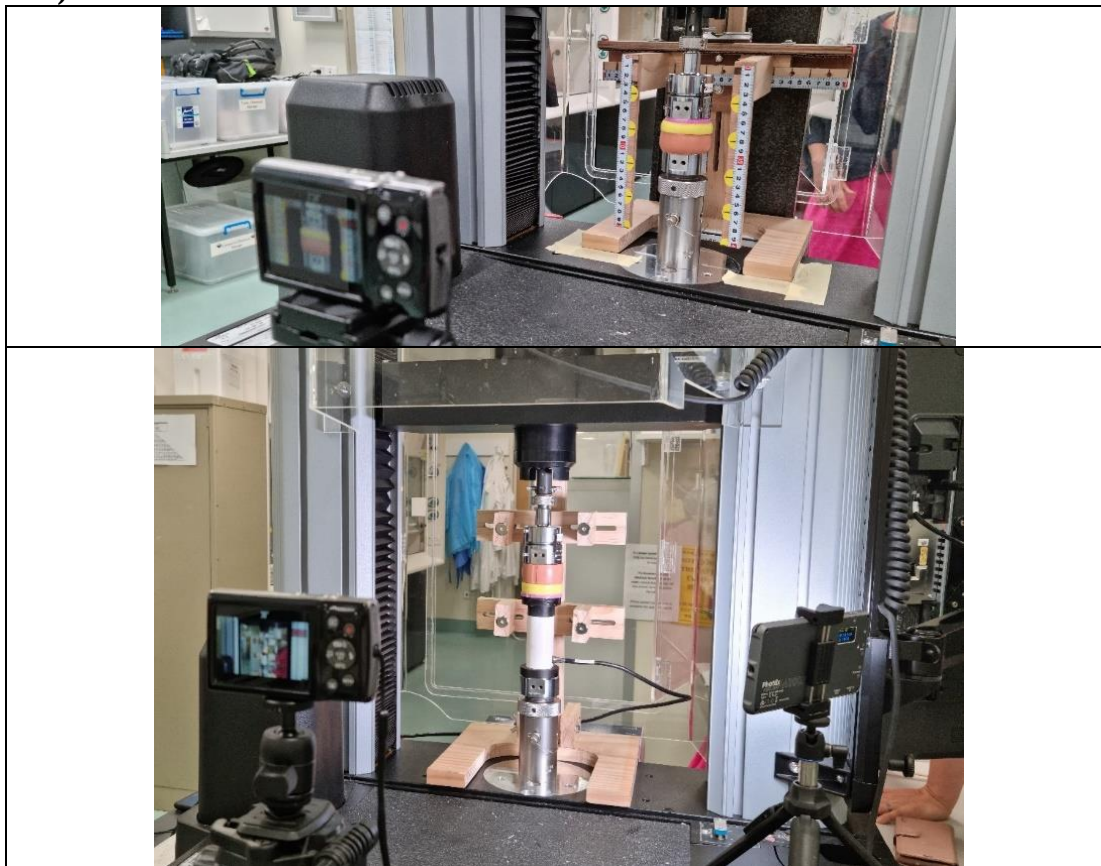
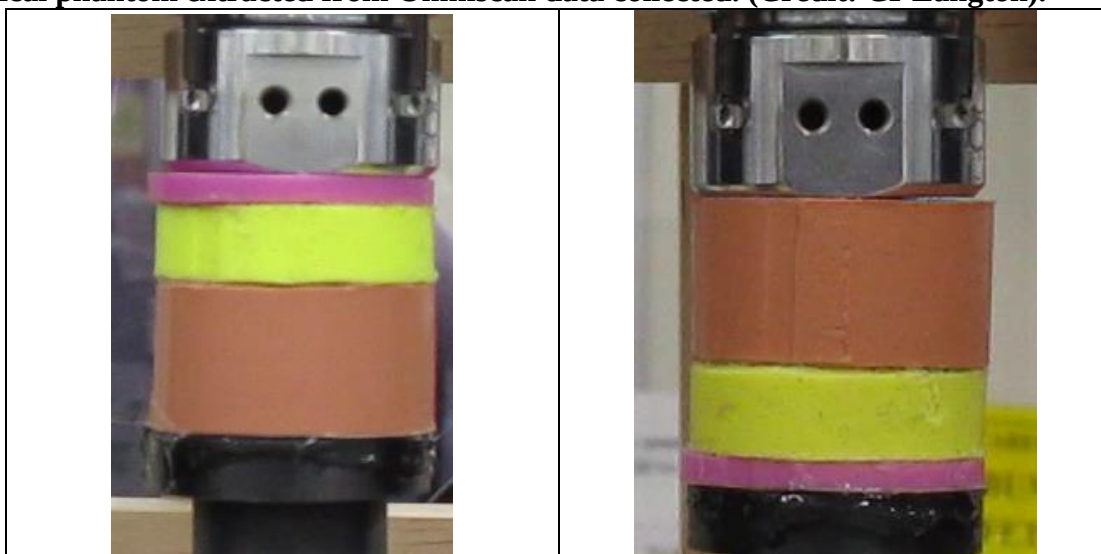


Figure 23. E8-1141b Experiments: Example A-Scan (top) 2D-Mmode (middle) and 3D-Mmode (bottom) when the sample mimicking the muscle (left) and the skin (right) of physical phantom extracted from Omniscan data collected. (Credit: CI-Langton).



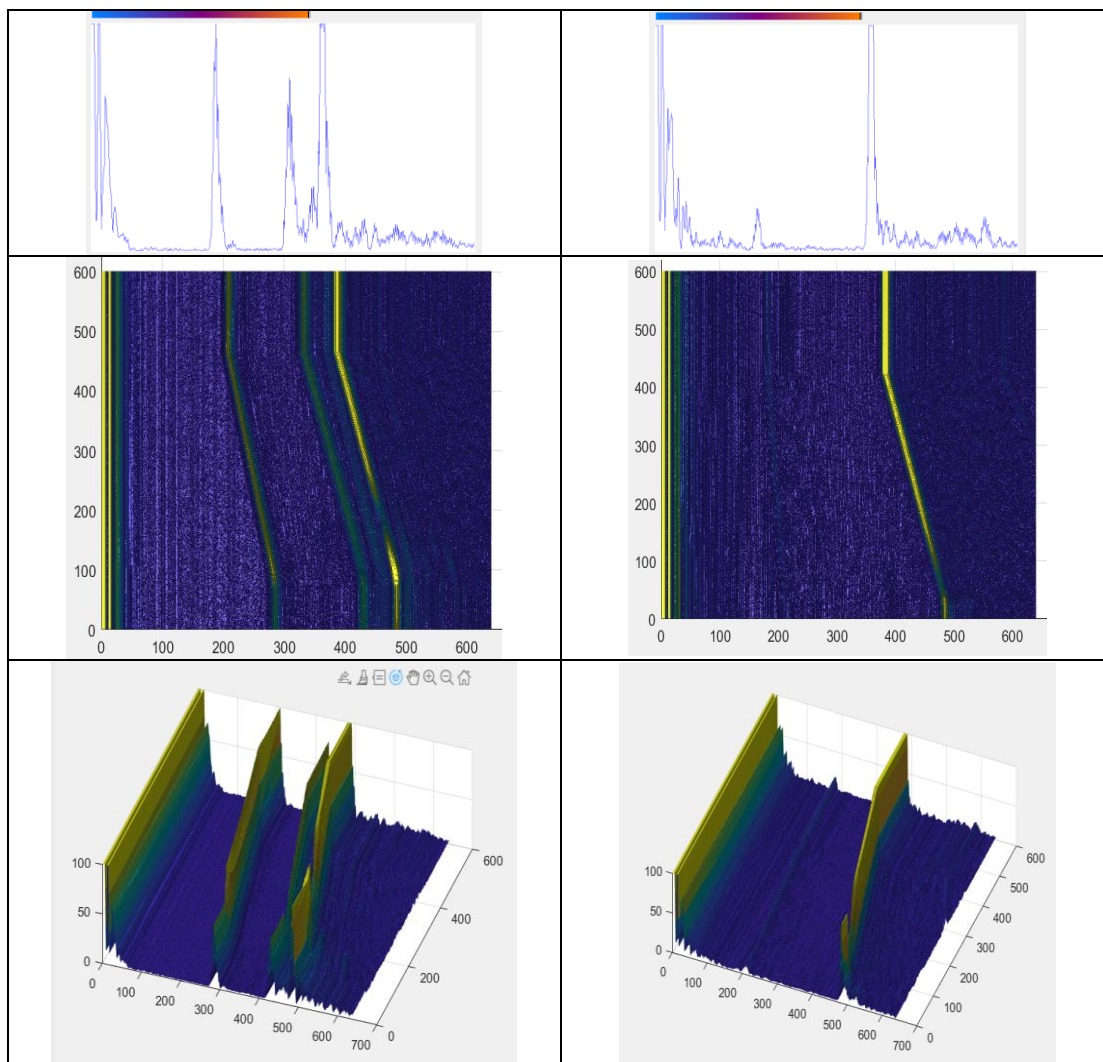


Figure 24. E8-1141b Experiments: Automated detection of depth of skin/fat, fat/muscle, muscle/bone interfaces (Credit: PI-Frossard, CI-Langton).

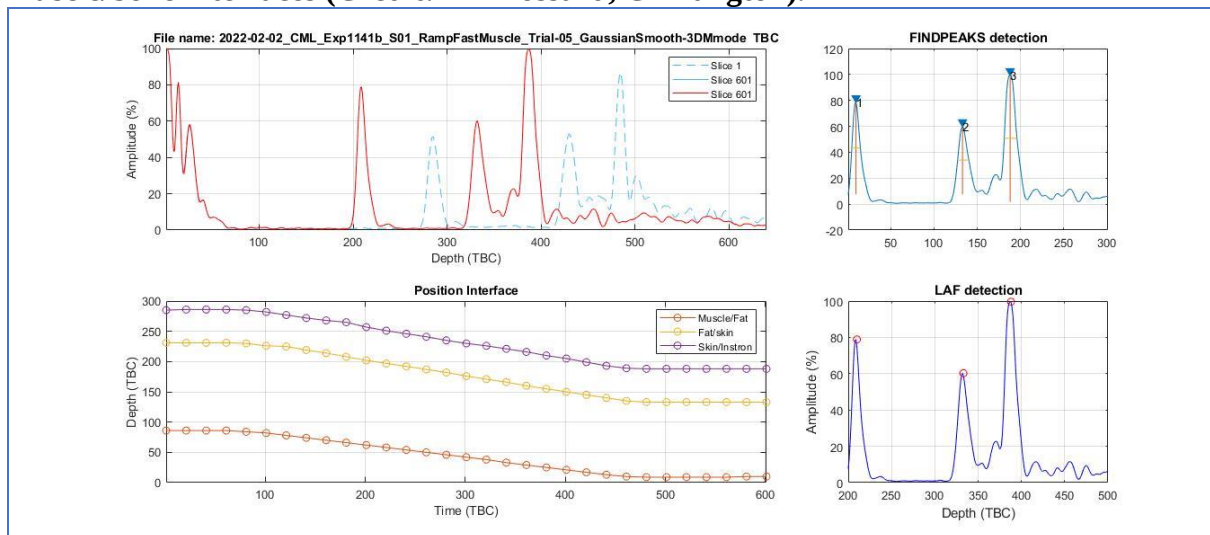


Figure 25. E8-1141b Experiments: Deformation of sample including skin/fat, fat/muscle, muscle/bone interfaces (Credit: PI-Frossard, SRF2-Perevoshchikova).

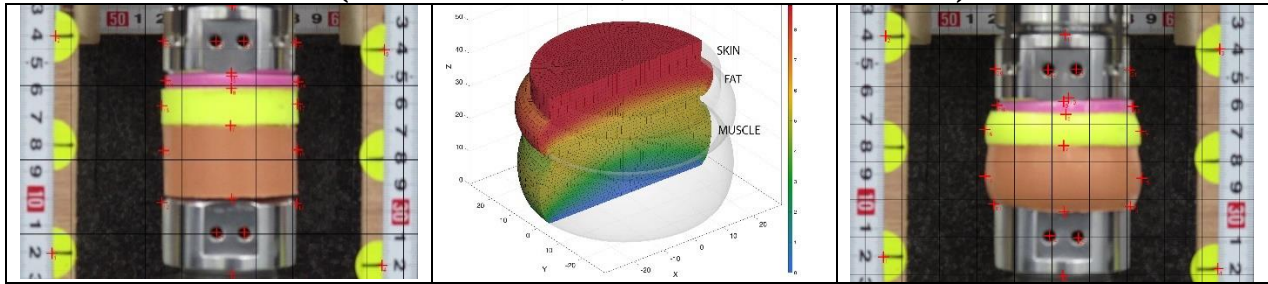


Figure 26. E8-1141b Experiments: Depth of skin/fat, fat/muscle, muscle/bone interfaces (Credit: PI-Frossard, CI-Langton, SRF2-Perevoshchikova)).

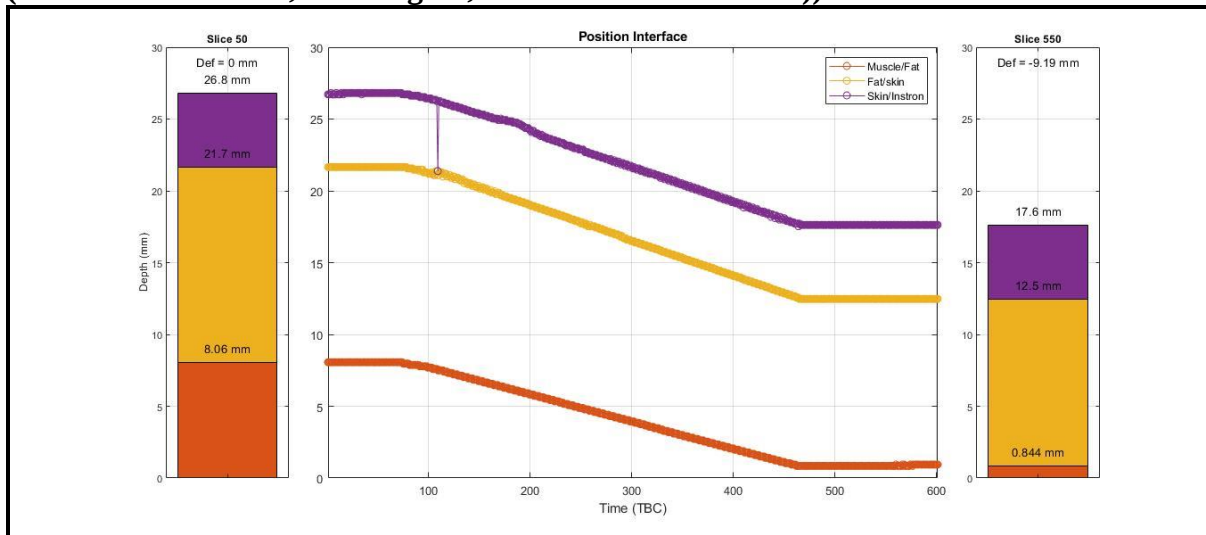
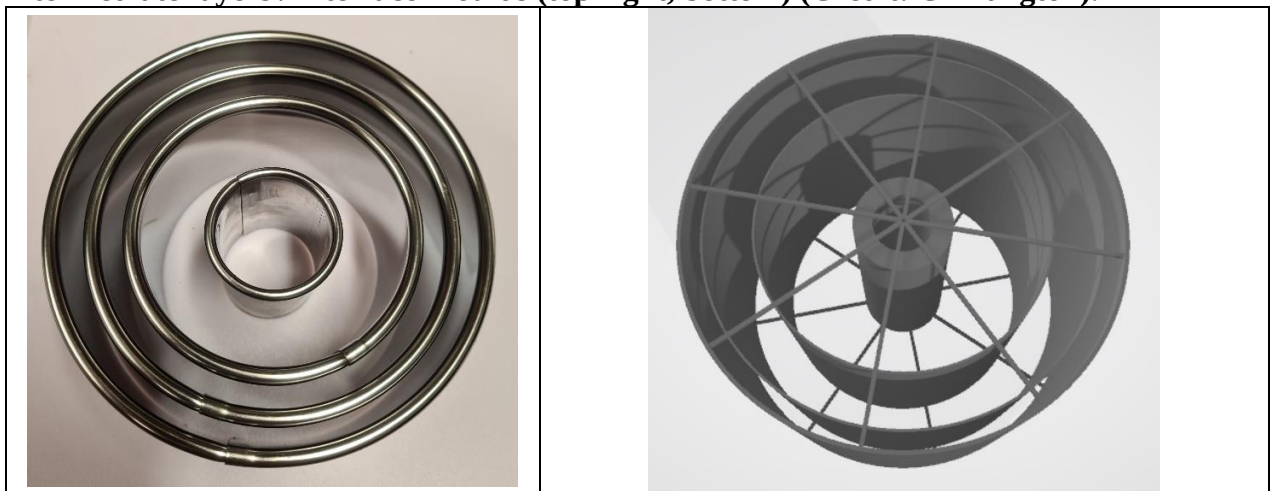


Figure 27. E9-E13 Experiments: Evolution of design of moulds used to create skin/fat, fat/muscle, muscle/bone interfaces from 'cookie-cutter' (top left), STL to 3D-printed intermediate-layers / interface-moulds (top right, bottom) (Credit: CI-Langton).



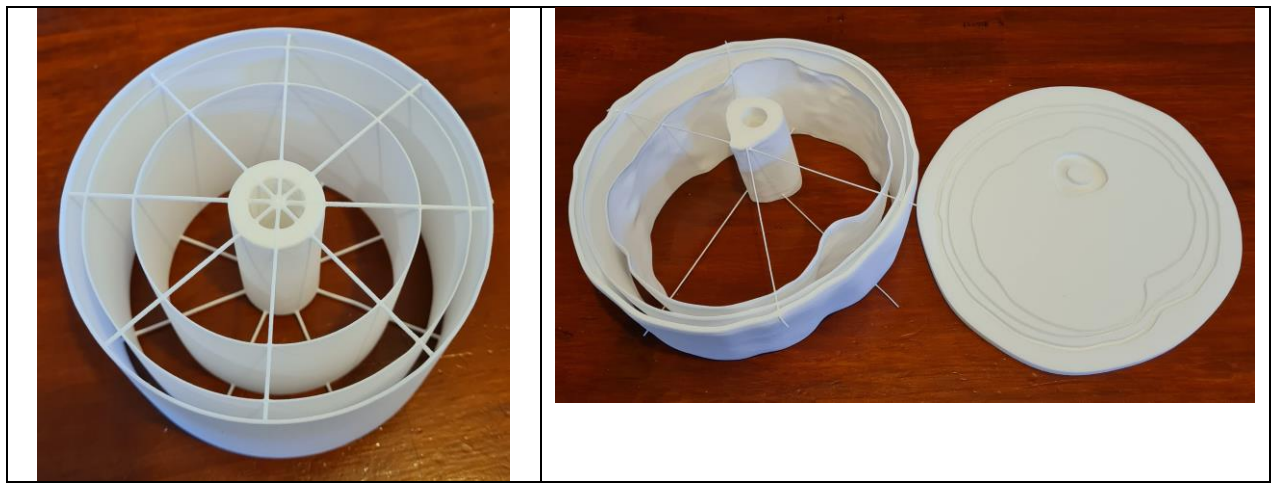


Figure 28. E9-E13 Experiments: Design of physical phantom including femur (Plastic), muscle (Gelatine), fat (Lard, pork fat), skin (Pinkysil silicone) (Credit: CI-Langton).



Figure 29. E9-E13 Experiments: Apparatus used to measure ultrasound velocity of triple-layer sample, with the complete exterior surface covered in Pinkysil to ensure physical integrity positioned within prototype DAU variable-position transducer device, with and without pseudo-socket (Credit: CI-Langton).

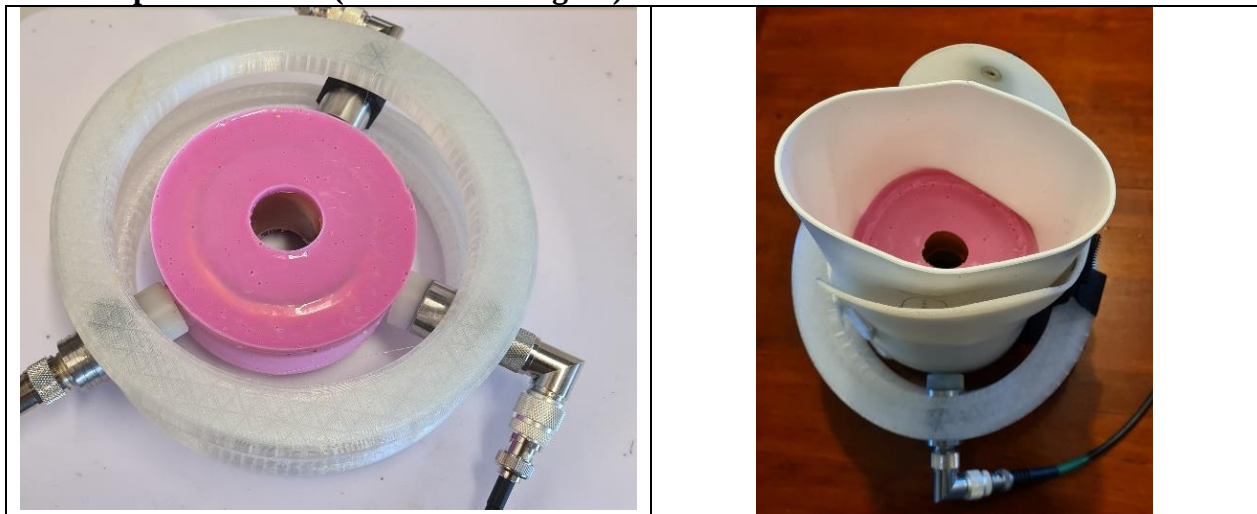


Figure 30. E9-E13 Experiments: Design of the mould of residuum from STL to CAD files to 3D print (Credit: SRF2-Perevoshchikova).

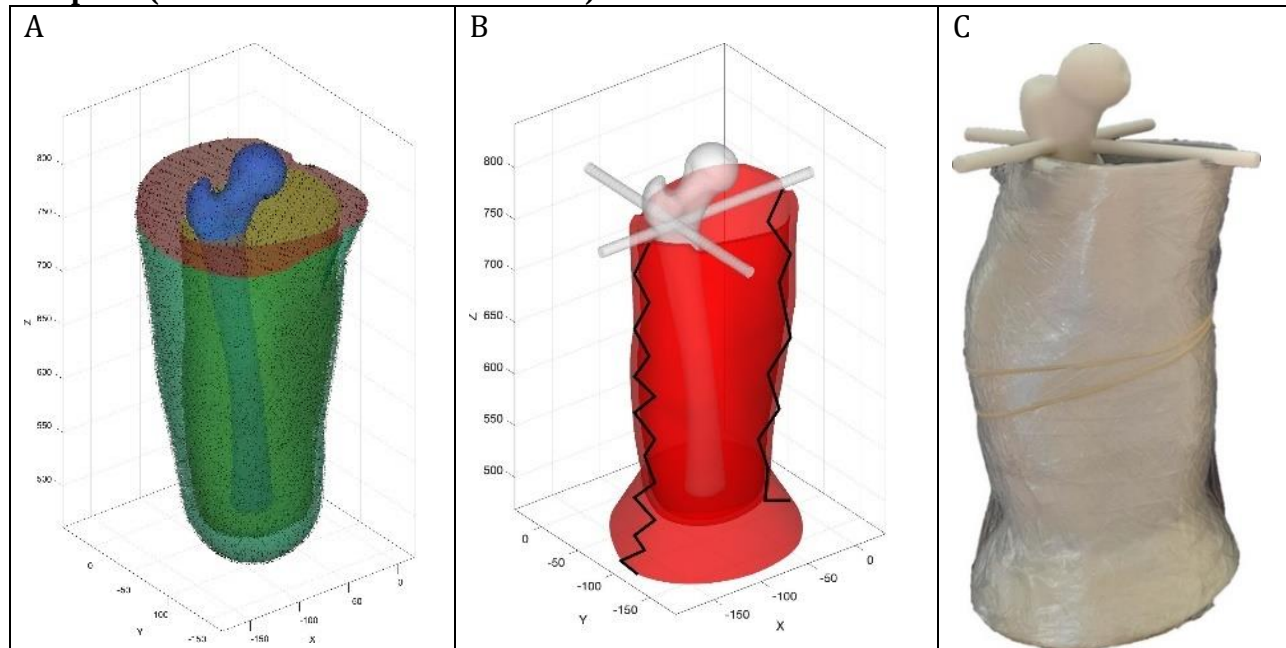


Figure 31. E9-E13 Experiments: First steps on the overview of the computational workflow to simulate the transfemoral (top) and transtibial (bottom) amputations for (Credit: SRF2-Perevoshchikova).

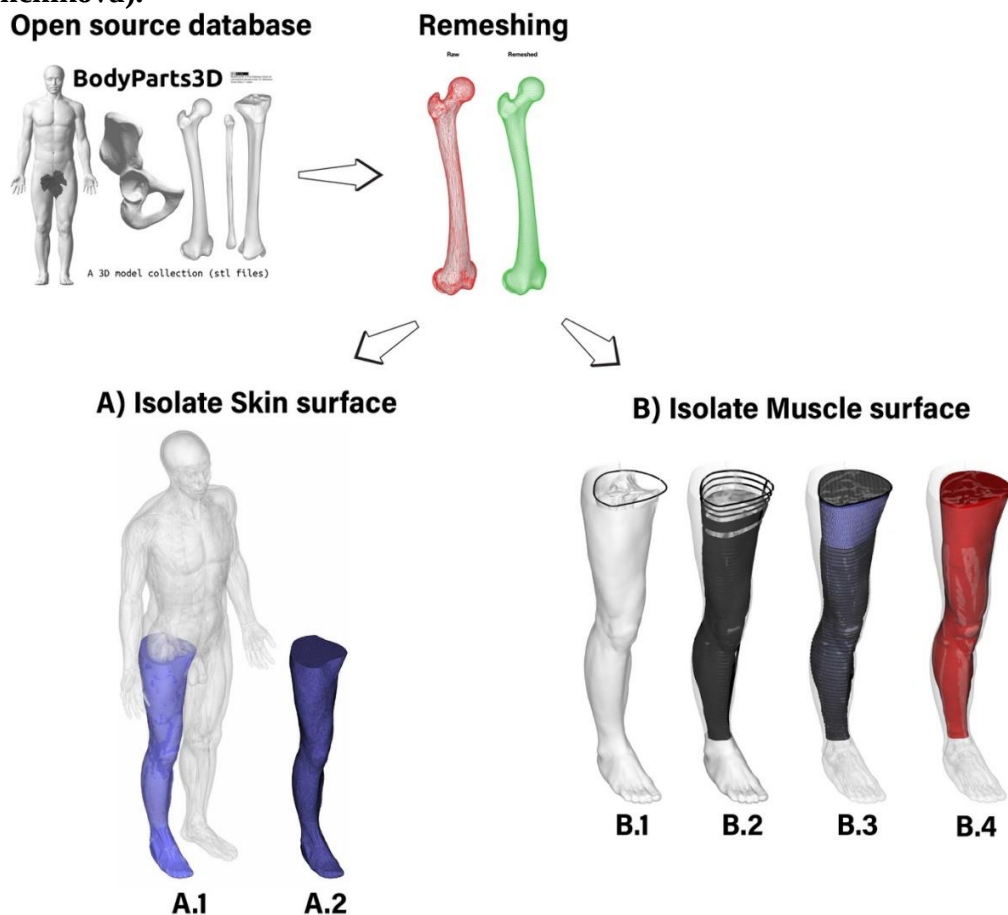


Figure 32. E9-E13 Experiments: Overview of the computational workflow to simulate the transfemoral (top) and transtibial (bottom) amputations (Credit: SRF2-Perevoshchikova, adapted from <https://github.com/SimuLimb>).

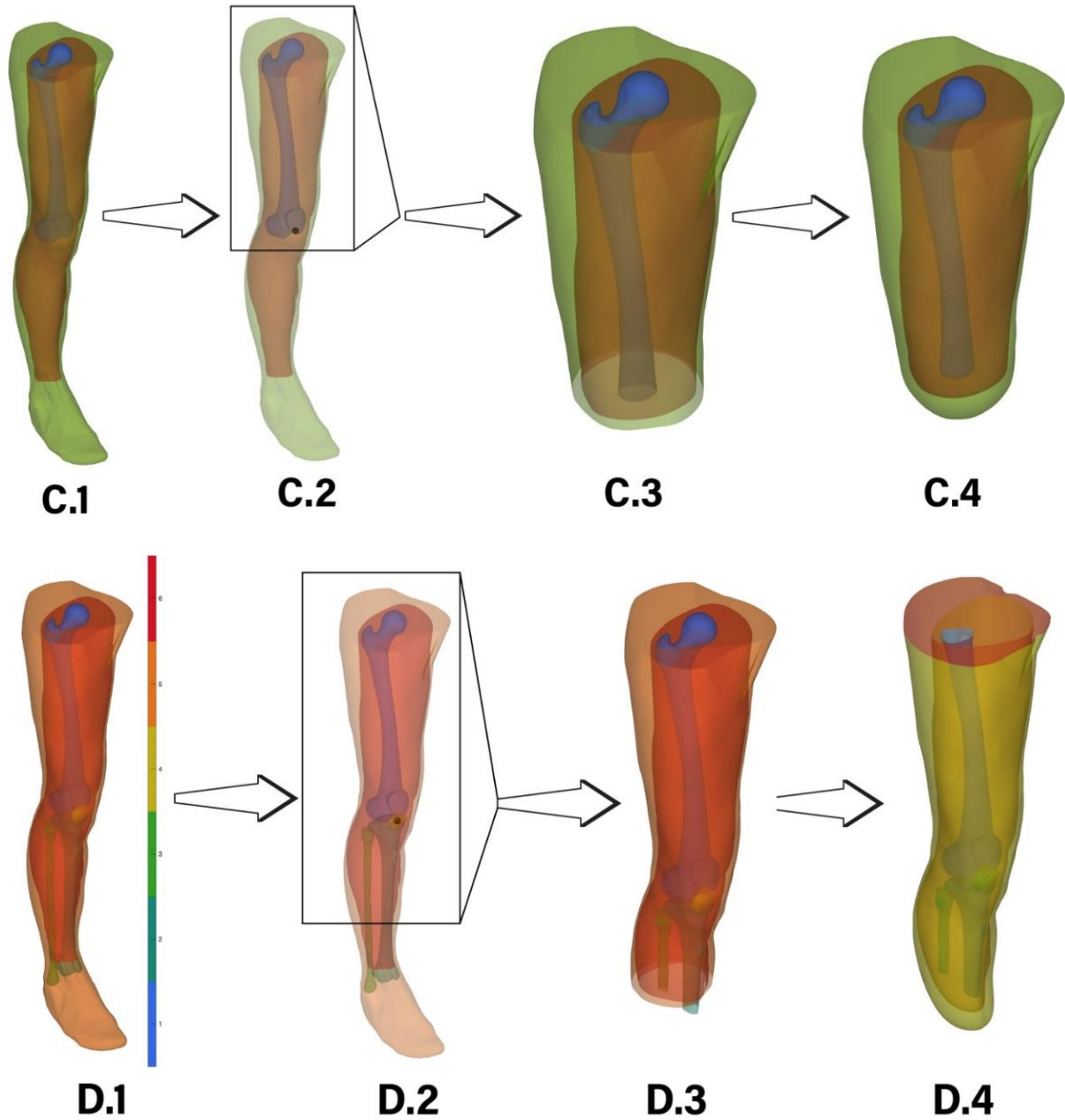


Figure 33. E14-E15 Experiments: Preparation of modelling of porcine leg including tissue compartment segmentation using mimics (Materialise) including investigating the effect of reducing the number of face Counts to find a compromise between accuracy and ability to mathematically solve. (Credit: CI-Langton)

CT Scan of Porcine Leg

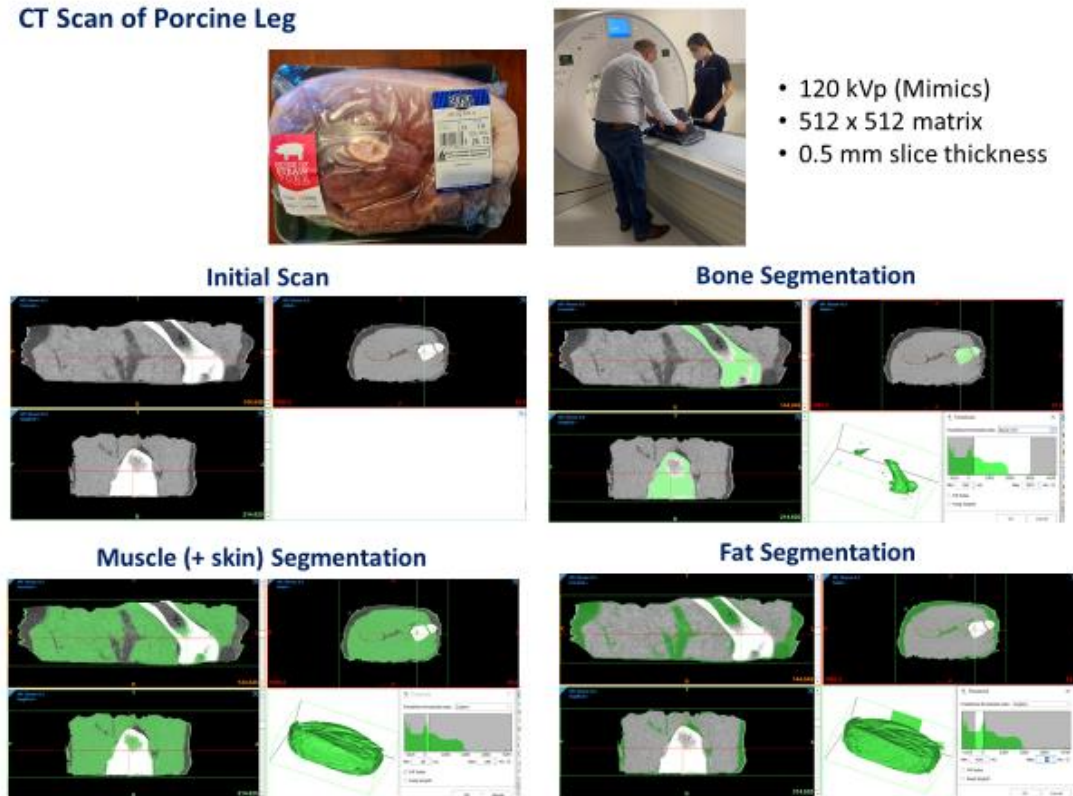


Figure 34. E14-E15 Experiments: Preliminary modelling of porcine leg (Credit: CI-Langton).

Consideration of Reduce Face Counts

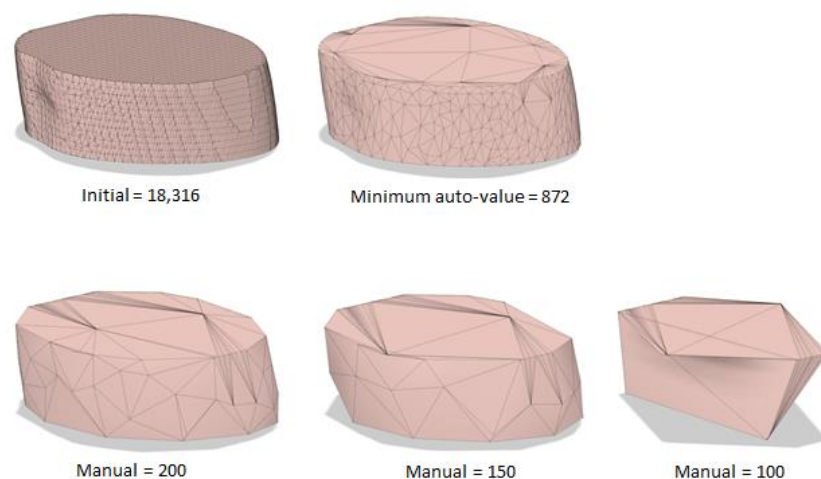


Figure 35. E17-E19 Experiments: Data flow 'a) Lower-limb CT (or MRI) scan is performed; b) Image analysis (Mimics) facilitates i) skin-surface profile and ii) number/position of transducers; c) Bespoke multi-transducer device created; d) DAU performed (Credit: CI-Langton).

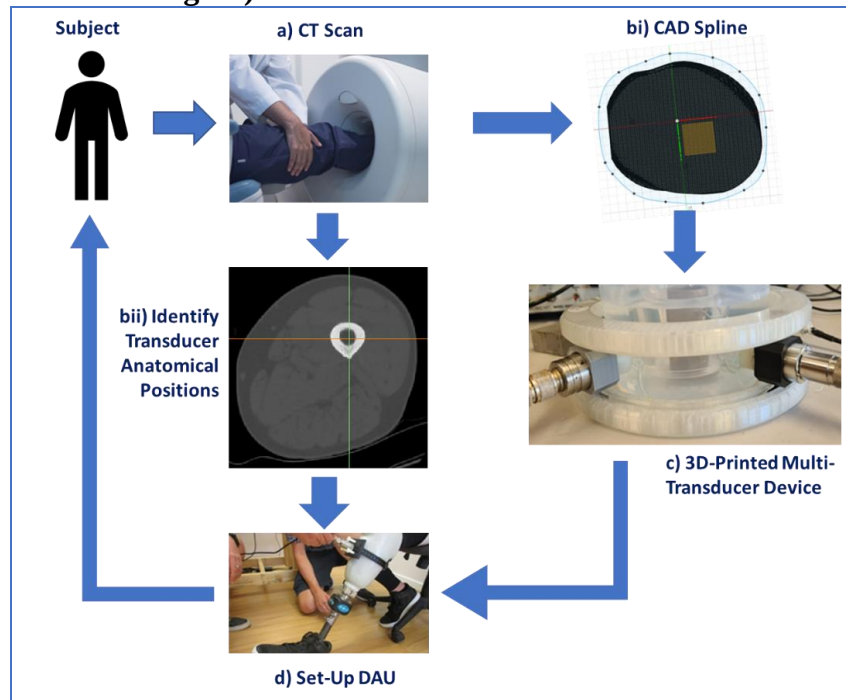


Figure 36. E17-311 Experiments: Data collection (CT scan) and analysis of aiming at segmenting to the thigh of an able-bodied participant (Credit: CI-Langton).

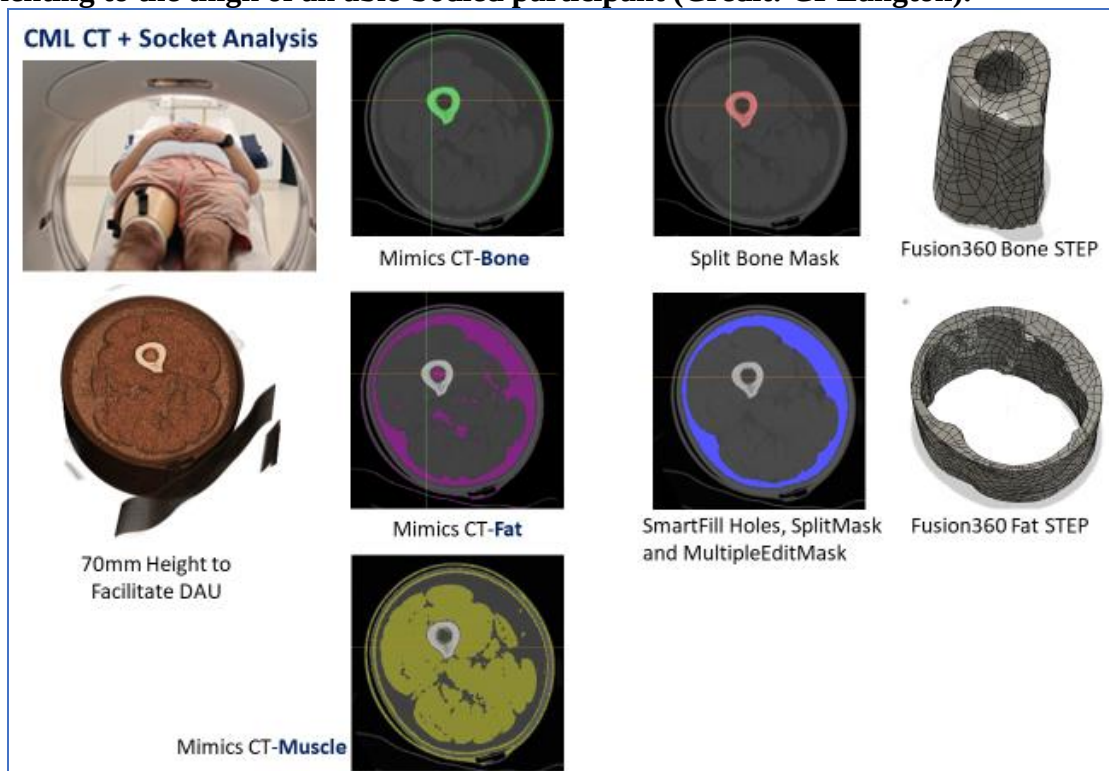


Figure 37. E17-311 Experiments: Extraction of out layer of the thigh of an able-bodied participant extracted from the (Credit: CI-Langton).

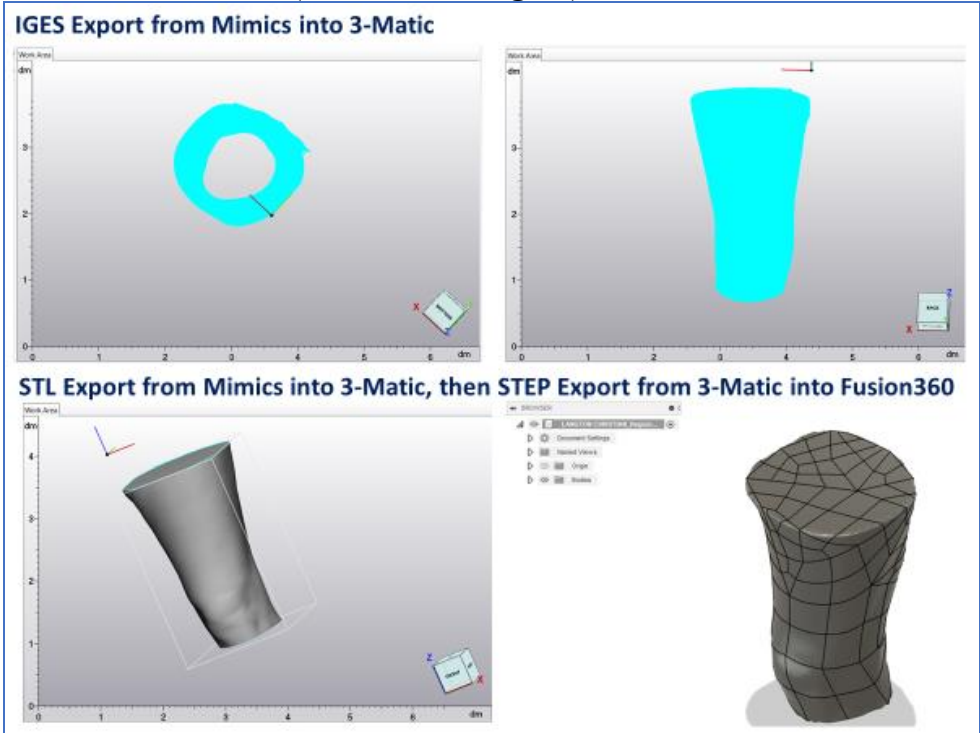


Figure 38. E17-311 Experiments: Extraction of bone, fat, and muscle of thigh of an able-bodied participant during (Credit: CI-Langton).

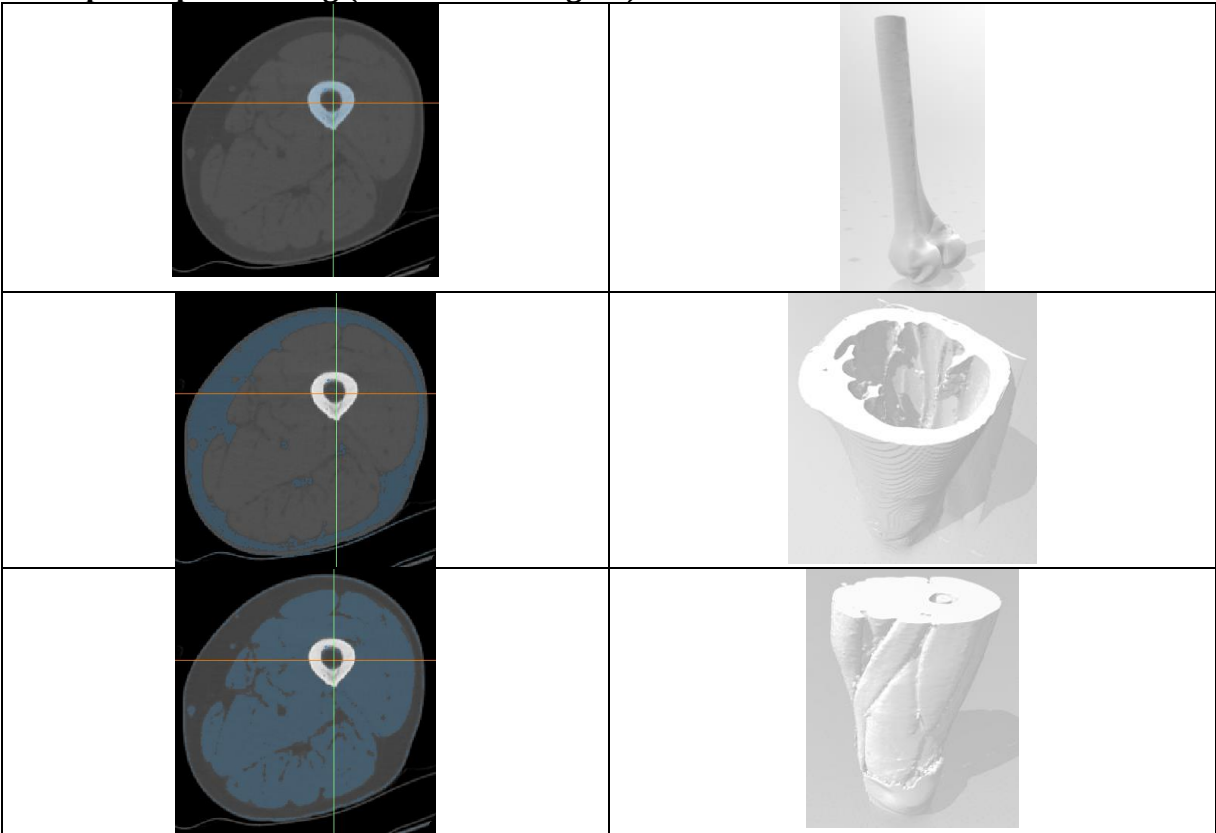


Figure 39. E23-E100 Experiments: Creation of the digital amputation of digital phantom to be used during (Credit: SRF2-Perevoshchikova).

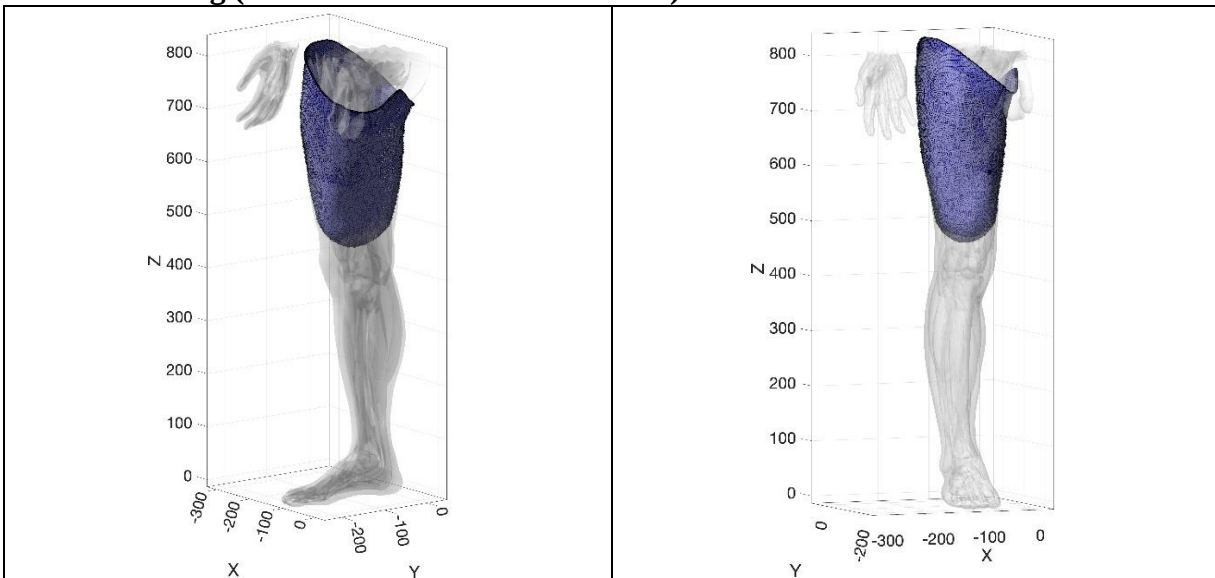
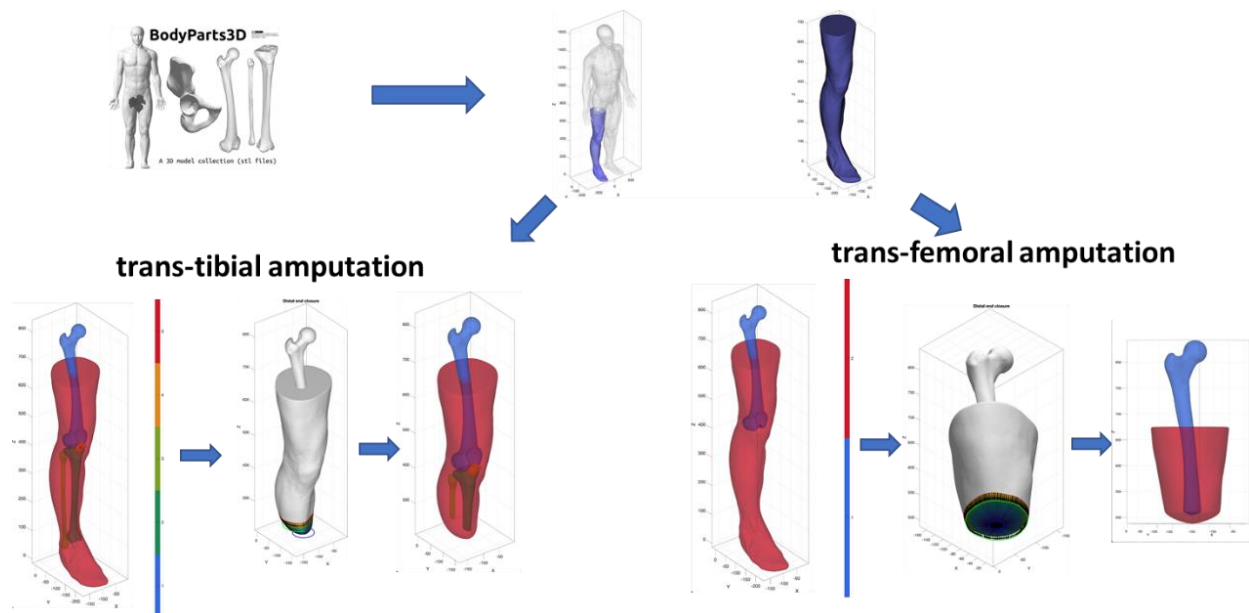


Figure 40. E23-E100 Experiments: Initial model residual limb for transtibial and transfemoral amputation using OpenSource body parts Database (<https://lifesciencedb.jp/bp3d/>) and SimuLimb toolbox (<https://github.com/SimuLimb>) (Credit: SRF2-Perevoshchikova).



- **Phase 2.3: Build prototypes (Deliverable 1)**
 - Hold series of brainstorming sessions focusing on the minimum viable product (MVP) for the In-Vivo Kinetic System 2.0 (Figure 41).
 - Design and 3D print of ultrasound probe holder to be fitted around the residuum during E17-E43 Experiments (Figure 42).
 - Design of the test rig to perform E46-E64 Experiments (Figure 43).
 - Design of 3D printed ring to hold ultrasound indenter during E23-E43 experiments (Figure 44).
 - Draft an overview of dataflow for the development of the In-Vivo Kinetic System 2.0 during E23-E100 Experiments (Figure 45).

Figure 41. Brainstorming session with the team around minimum viable product (MVP) required to build and validate the In-Vivo Kinetic System 2.0 (Credit: PI-Frossard)



Figure 42. E17-E43 Experiments: Design and trial of 3D printed ultrasound probe holder (Credit: PI-Frossard).



Figure 43. E46-E64 Experiments: Design of the test rig from whiteboard sketches for both the 'Ring' transducer track and the 'Instron' Indenter (left) to schematic for a hand-held load-cell / Faro(Absolute)-Arm implemented indenter (right) (Credit: CI-Langton).

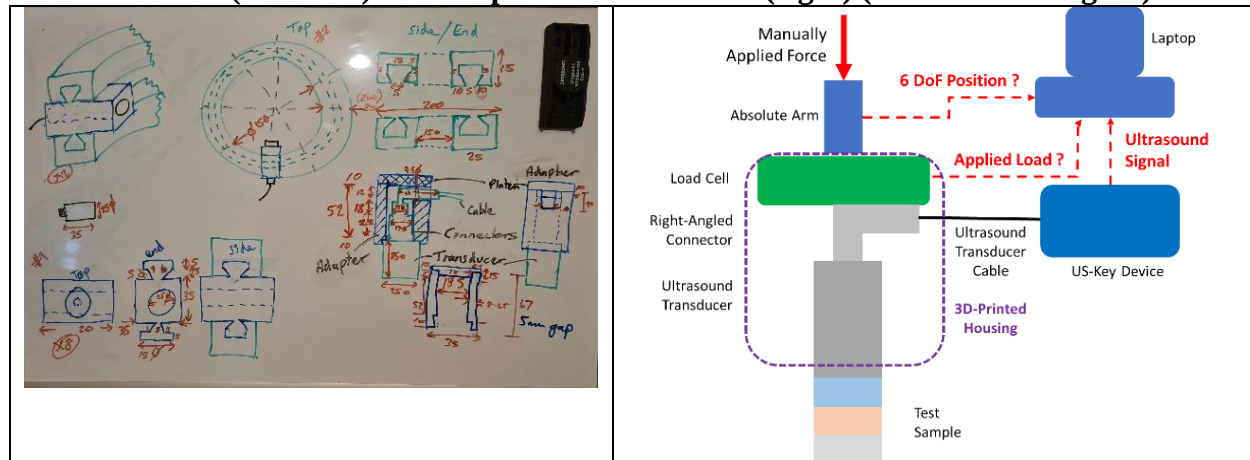


Figure 44. E23-E43 experiments: Design of 3D printed ring to hold ultrasound indenter (A: whiteboard proof of concept, B: overall envelop shape of the ring around the residuum, C, D, E: holder designs for single-element and GE-Voluson ultrasound transducers respectively) (Credit: CI-Langton).

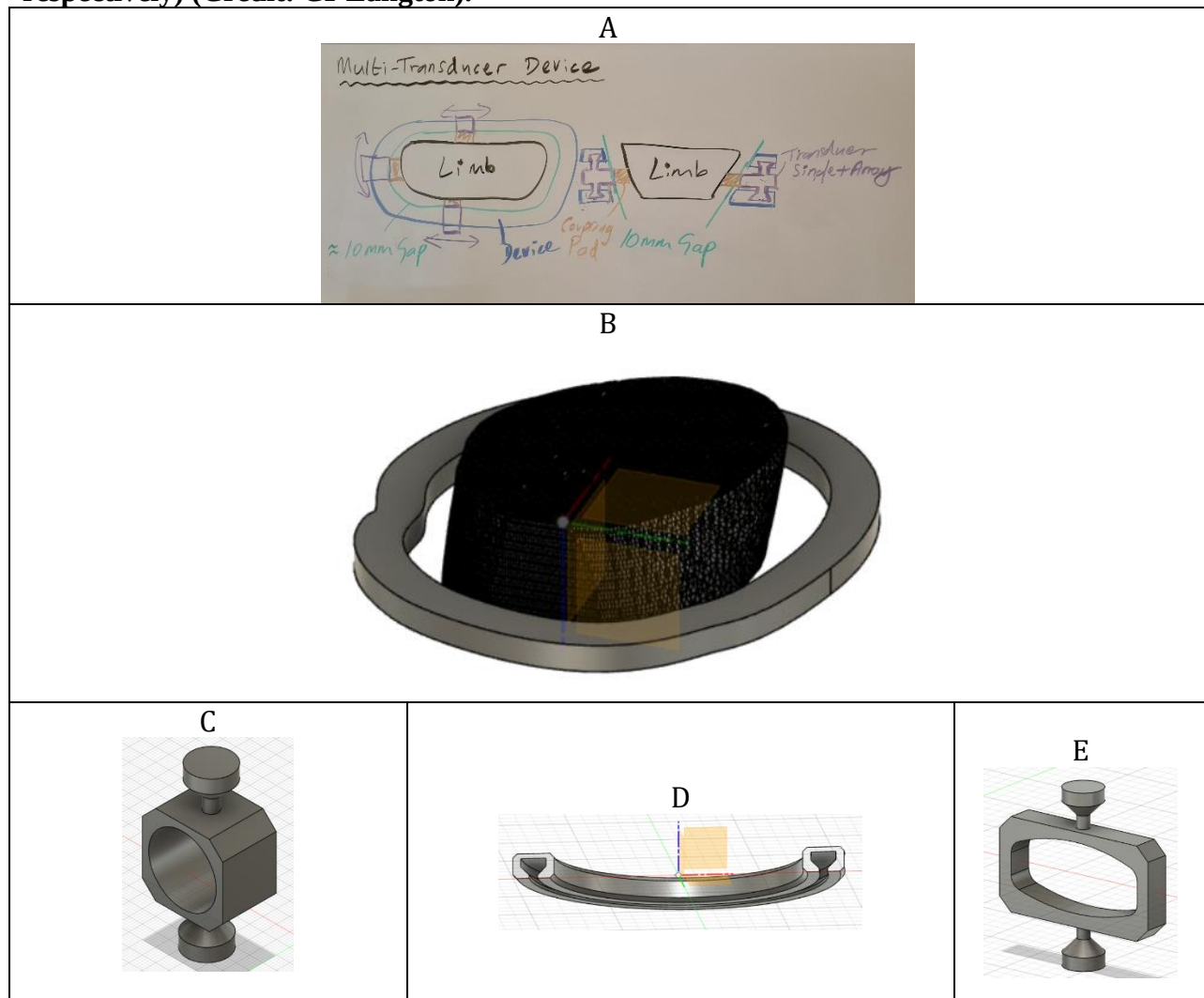
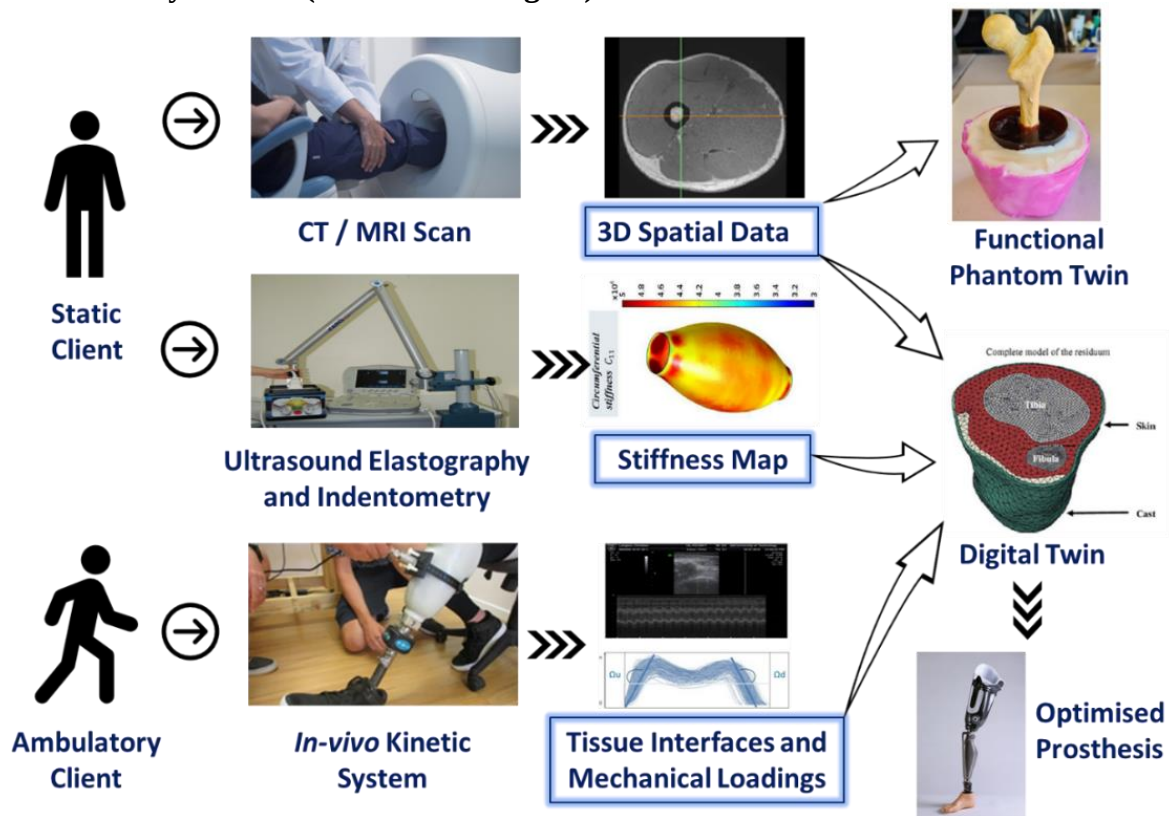


Figure 45. E23-E100 Experiments: Overview of dataflow for the development of the In-Vivo Kinetic System 2.0 (Credit: CI-Langton).



- **Phase 2.4: Proof of safety and efficacy (Deliverable 2) and Phase 2.5: Proof of utility (Deliverable 3)**
 - Prepare E23-E100 Experiments including
 - Outline of typical testing sessions (e.g., standing static with prosthesis, walking, activities of daily living).
 - Calculate the number and distribution of participants per cohorts (Table 3).
 - List the inclusion and exclusion criteria (Table 4).
 - Establish that total number of experiments (Table 5).
 - Outline of two arms involved in the proof of safety and efficacy (Table 6).
- **Phase 2.6: Design clinical trial (Deliverable 4)**
 - Transfer information gathered during E23-E100 Experiments to identify arms, design the intervention, and complete statistical power analysis of the study.

Table 3. E23-E100 experiments: Number and distribution of participants per cohorts involved in the proof of safety and efficacy In-Vivo Kinetic System 2.0.

	Socket-suspended prosthesis	Bone-anchored prosthesis	Total
Cohorts			
Transfemoral amputation	Cohort 1	Cohort 3	2
Transtibial amputation	Cohort 2	Cohort 4	2
Total	2	2	4
Number of participants			
Transfemoral amputation	15	5	20
Transtibial amputation	15	5	20
Total	30	10	40
Percentage of participants			
Transfemoral amputation	37.5	12.5	50
Transtibial amputation	37.5	12.5	50
Total	75	25	100

Table 4. E23-E100 experiments: List of inclusion and exclusion criteria for recruitment of 40 participants with unilateral transfemoral or transtibial amputation fitted with socket-suspended or bone-anchored prostheses participating to the proof of safety and efficacy In-Vivo Kinetic System 2.0.

Inclusion criteria	Exclusion criteria
1. To be a male, female or transgender with unilateral transtibial or transfemoral amputation 2. To be willing to participate to this project of research 3. To be able to be fitted with prosthetic knees (e.g., microprocessor-controlled knees) and ankles (energy-storing-and-returning feet) 4. To be willing to comply with protocol 5. To have a lower limb amputation more than 12 months prior testing 6. To have a clearance of at least 6 cm between distal end of residuum and subsequent prosthetic joint to fit the load cell. 7. To have completed rehabilitation program 8. To be free of pain and infection on the day of the recording session, 9. To weigh less than 116 kg 10. To be able to walk 200 meters	1. To have self-reported residuum pain levels greater than 4 out of 10 at testing outset 2. To have experienced a fall within the last 8 weeks before assessment 3. To present signs of infection if using bone-anchored prosthesis 2 weeks prior a testing session 4. To have mental illness or intellectual impairment 5. To not be able to give informed consent 6. To have injuries involving contralateral (intact) limb 7. To have major uncorrected visual deficit 8. To have history of epilepsy or recurrent dizziness 9. To be younger than 18 years of age or older than 80 years of age 10. To weigh more than 116 kg (prevent load cell saturation)

independently 11. To be between 18-80 years of age	
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Table 5. E23-E100 experiments: Total number of experiments for the each of the four cohorts of participants extracted from roadmap for the proof of safety and efficacy In-Vivo Kinetic System 2.0.

Cohort	First and last experiments	Number of experiments
Cohorts fitted with socket-suspended prosthesis (SSP)		
Cohort 1: Transfemoral amputation (SSP-TFA, N=15)	E23-E45	22
Cohort 2: Transtibial amputation (SSP-TTA, N=15)	E46-E68	22
Cohorts fitted with bone-anchored prosthesis (BAP)		
Cohort 3: Transfemoral amputation (BAP-TFA, N=5)	E69-E84	15
Cohort 4: Transtibial amputation (BAP-TTA, N=5)	E85-E100	15

Table 6. E23-E100 Experiments: Overview of two arms including all cohorts involved in the proof of safety and efficacy In-Vivo Kinetic System 2.0. (1) Instrument prosthesis will include usual components, iPecsLab load and DAU transducers.

Description	Control arm	Intervention arm
	Without In-Vivo Kinetic System	With In-Vivo Kinetic System
Experiments		
Standing static with prosthesis	Yes	Yes
Walking	Yes	Yes
Activities of daily living	Yes	Yes
Prosthetic fitting		
Usual prosthesis	Yes	Yes
Instrumented prosthesis (1)	No	Yes
Datasets		
Biomechanical data	Yes	Yes
Perception-of-use	No	Yes

Phase 3: Share outcomes

- **Phase 3.1: Report to stakeholders**
 - Phase 3.1.1: Submit quarterly technical report to DoD
 - Draft, review and submit four technical quarterly reports as required.
 - Phase 3.1.2: Submit yearly report to DoD
 - Draft, review and submit the yearly report as required.
- **Phase 3.2: Publish outcomes**
 - Phase 3.2.1: Publish research articles (Table 7, Table 8)

- Publish 4 abstracts in Journal of Science and Medicine in Sport (ART03, ART04, ART05, ART06) (Figure 46).
- Submit 2 manuscripts to Frontiers (ART09) and Journal of Science and Medicine in Sport (ART 07) (Figure 47).
- Drafting of 3 manuscripts to be submitted to Clinical rehabilitation (ART08), Plos One (ART10), 3D Printing in Medicine (ART11).
- Phase 3.2.2: Present research abstracts
 - Submit 3 abstracts to 13th Australasian Biomechanics Conference (ABS05, ABS06, ABS07).
- Phase 3.2.3: Present at conference as speaker
 - Present at 4 events Exercise & Sports Science Australia Webinar (PPT02), University of the Sunshine Coast Webinar (PPT03), Griffith University - Lunchbox Seminar (PPT04), Golden Key International Honour Society Seminar (PPT05) (Figure 48).

Further documents are provided in Sections 9.2, Appendix D: PDFs of all publications.

Table 7. Overview of list and status of publications including articles, abstracts and presentations.

	Presentation	Dataset	Abstract	Article	Total
Drafted	0	0	0	3	0
Submitted	1	0	5	2	0
Accepted	0	0	2	0	0
Published	4	0	0	6	0
Total accepted and published	4	0	2	6	12
Total	5	0	7	11	0

Table 8. List and status of publications including articles, abstracts and presentations.

Item	Reference	Publication	Type	Status
		(Author. Title. Journal. Year)		
1	ART01	Pitkin M, Frossard L. Loading Effect of Prosthetic Feet's Anthropomorphicity on Transtibial Osseointegrated Implant. Military Medicine. 2021. 186 (Supplement 1) p 681-687. DOI: 10.1093/milmed/usaa461	Article	Published
2	ART02	Frossard L, Lloyd D. The future of bionic limbs. Research Features. 2021. 134 p 74-77. DOI: N/A	Article	Published
3	ART03	Frossard L, Langton C, Barrett R, Lloyd D. Can A Digital Twin Of The Residuum Improve Bionic Solutions For Individuals Suffering From Limb Loss?. Journal of Science and Medicine in Sport. 2022. 25. P S4-S5. DOI: 10.1016/j.jsams.2021.11.011	Article	Published

4	ART04	Saxby D, Pizzolato C, Nasser A, Devaprakash D, Frossard L, Lloyd D. Personalized Digital Humans For Rehabilitation And Assistive Devices. Journal of Science and Medicine in Sport. 2022. 25. P S5-S6. DOI: 10.1016/j.jsams.2021.11.012	Article	Published
5	ART05	Langton C, Barrett R, Powrie R, Lloyd D, Frossard L. Development Of Dynamic Anatomical Ultrasonography To Advance Personalised Prosthetics. Journal of Science and Medicine in Sport. 2022. 25. P S6-S7. DOI: 10.1016/j.jsams.2021.11.013	Article	Published
6	ART06	Lloyd D, Perevoshchikova N, Langton C, Barrett R, Maharaj J, Frossard L. Advanced Modelling Of Residuum To Improve Bionic Limbs. Journal of Science and Medicine in Sport. 2022. 25. P S7-S8. DOI: 10.1016/j.jsams.2021.11.014	Article	Published
7	ART07	Frossard L, Langton C, Langton C, Feih S, Barrett R, Lloyd D. Next generation of diagnostic device of residuum health of individuals suffering from limb loss: A narrative review of device specifications. Journal of Science and Medicine in Sport. 2022. TBC. DOI: TBC	Article	Submitted
8	ART09	Frossard L, Conforto S, Aszmann O. Editorial: Bionics Limb Prostheses: Advances in Clinical and Prosthetic Care. Frontiers. 2022. TBC. DOI: TBC	Article	Submitted
9	ART08	TBC. Walking ability of individuals fitted with transfemoral bone-anchored prostheses: multi-centres comparative study of spatial-temporal gait characteristics. Clinical rehabilitation. 2022. TBC. DOI: TBC	Article	Drafted
10	ART10	Perevoshchikova N, Moerman K, Langton C, Lloyd D, Grimm A, Feih S, Barrett R, Smith D, Frossard L. Replicating residuum of an individual suffering from transfemoral amputation: from automated and data-driven modelling to phantom design and manufacturing. Plos One. 2022. TBC. DOI: TBC	Article	Drafted
11	ART11	Langton C, Barrett R, Powrie R, Lloyd D, Frossard L. Development of a subject-specific mechano-acoustic post-amputation lower-limb phantom-twin incorporating 3D-printed intermediate-layers. 3D Printing in Medicine. 2022. TBC. DOI: TBC	Article	Drafted
12	ABS01	Frossard L, Langton C, Barrett R, Lloyd D. Residuum health of Service Members suffering from limb loss: Digital twin and diagnostic device. Military Health System Research Symposium. 2021. MHSRS-21-03471. DOI: N/A	Abstract	Accepted

13	ABS02	Frossard L, Langton C, Barrett R, Saxby D, Perevoshchikova N, Maharaj J, Schuetz M, Powrie R, Lloyd D. Advancing Personalised Prosthetics After Amputation: From In-Vivo Monitoring To Bionic Limbs. Defence Biomarkers Symposium. 2022. In press. DOI: N/A	Abstract	Accepted
14	ABS03	Pitkin M, Park P, Frossard L, Prilutsky B. Higher index of anthropomorphicity of passive Free-Flow Foot (FFF) prosthesis as an advantage for transforming it to the powered foot prosthesis with intuitive control and sensation (Bionic FFF). Military Health System Research Symposium. 2022. MHSRS-22-05274. DOI: N/A	Abstract	Submitted
15	ABS04	Frossard L, Langton C, Perevoshchikova N, Feih S, Powrie R, Barrett R, Lloyd D. Development of a diagnostic device to maintain residuum health of Service Members suffering from limb loss: Barriers and facilitators. Military Health System Research Symposium. 2022. MHSRS-22-06886. DOI: N/A	Abstract	Submitted
16	ABS05	Perevoshchikova N, Moerman K, Langton C, Feih S, Lloyd D, Barrett R, Frossard L. Replicating Residuum Of Individuals Suffering From Trasnfemoral Amputation: From Data-Driven Modelling To Phantom Design And Manufacturing. 13th Australasian Biomechanics Conference (ABC13). 2022. TBC. DOI: TBC	Abstract	Submitted
17	ABS06	Langton C, Perevoshchikova N, Feih S, Lloyd D, Barrett R, Frossard L. A Dynamic Anatomical Ultrasonography Workflow To Advance Personalised Lower-Limb Prosthetics. 13th Australasian Biomechanics Conference (ABC13). 2022. TBC. DOI: TBC	Abstract	Submitted
18	ABS07	Langton C, Perevoshchikova N, Feih S, Lloyd D, Barrett R, Frossard L. A Mechano-Acoustic Phantom-Twin Of The Post-Amputation Lower-Limb Residuum. 13th Australasian Biomechanics Conference (ABC13). 2022. TBC. DOI: TBC	Abstract	Submitted
19	PPT01	Frossard L. Prosthetic osseointegration worldwide: from ground-breaking treatment to standard of care!. Webinar: Warrior Care in the 21st Century. 2021. . DOI: N/A	Presentation	Published
20	PPT02	Frossard L. Moving forward with bionic prostheses - Improving bionic prostheses: exercise and sports science practitioners needed!. Exercise & Sports Science Australia Webinar. 2022. . DOI: N/A	Presentation	Published

21	PPT03	Frossard L. Future of bionic limbs: What to do next?. University of the Sunshine Coast - Webinar. 2022. . DOI: N/A	Presentation	Published
22	PPT04	Frossard L. How to handle future bionic limbs?. Griffith University - Lunchbox Seminar. 2022. . DOI: N/A	Presentation	Published
23	PPT05	Frossard L. You can improve outcomes of patients using bionic limbs. Golden Key International Honour Society Seminar. 2022. . DOI: N/A	Presentation	Submitted

Figure 46. Mobility pathway including nine typical states ranging from small (e.g., bedridden, use of wheelchair or walker, two crutches without prosthesis), medium (e.g., two crutches with prosthesis, one stick, independent ambulation with pain), and large (independent ambulation without pain, participation to recreational and professional activities) mobility scales. (Credit: PI-Frossard, extracted from ART07).

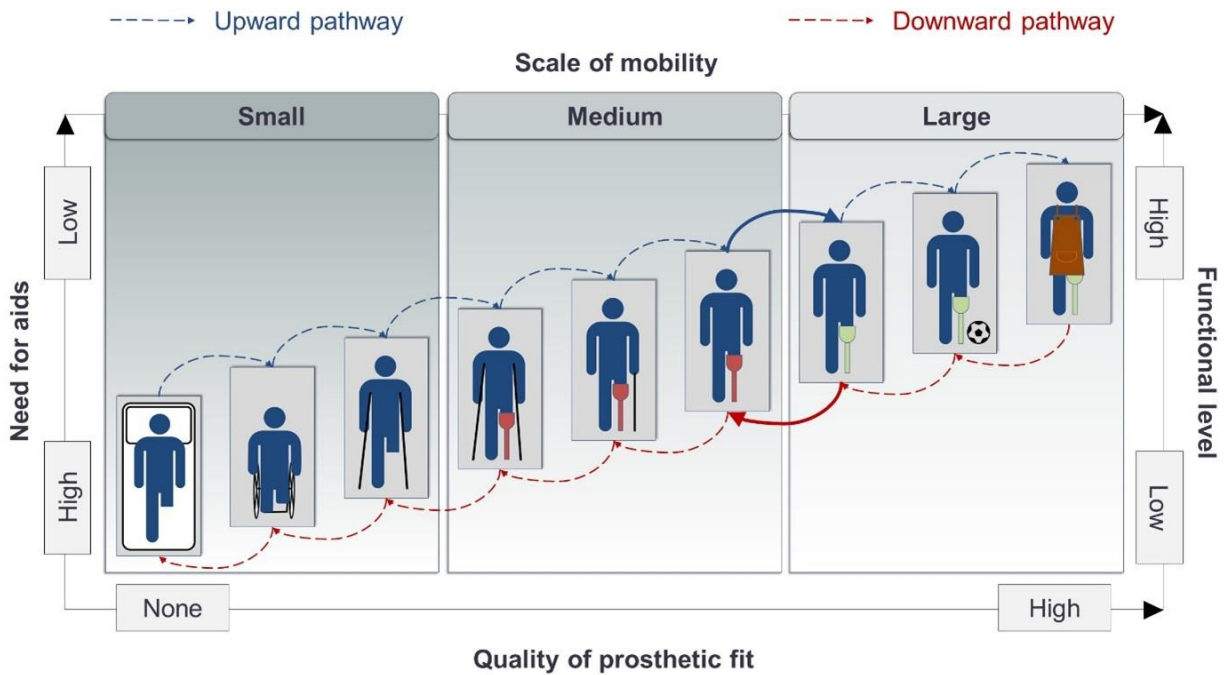


Figure 47. Overview of the next-generation diagnostic devices integrating wireless biosensors to measure mechanical constrains (e.g., PKS: Portable kinetic system), topography of the residuum tissues (e.g., DAU: Dynamic Anatomical Ultrasonography), medical imaging (e.g., MRI: Magnetic resonance imaging), and computational modelling (e.g., FEA: finite element analysis) to animate a personalised digital twin of the residuum in real-time on a handheld device accessible by all prosthetic care providers. (Credit: PI-Frossard, extracted from ART07).

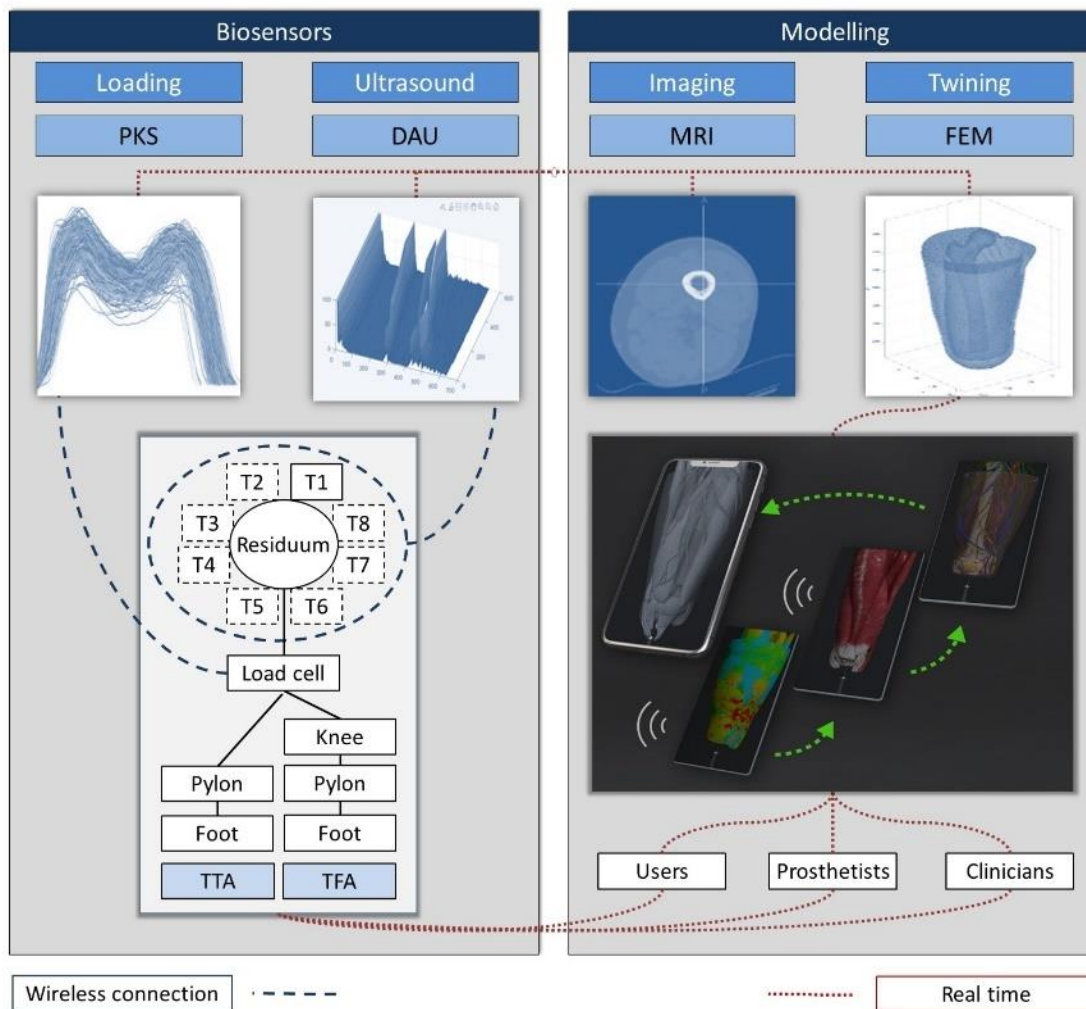


Figure 48. Present a webinar at Webinar at Warrior Care in the 21st Century.



Phase 4: Exit strategy

- Phase 4.2: Seek funding (Table 9, Table 10)
 - Phase 4.2.1: Apply for research grants
 - Win the Bionics Queensland Challenge - Bionic Mobility (2021. 1 year. AUD\$50,000) (Figure 49).
 - Receive the Australian National Member Society of the International Society for Prosthetics and Orthotics Inc (ANMS ISPO) Research Grant (2021. 1 year. AUD\$30,000) (Figure 50).
 - Apply for OPORP Clinical Research Award (2021. 3 years. AUD\$1,500,000), Clinical Translational Research Award (2021. 2 years. AUD\$1,350,000), Small Business Innovation Research Grant Applications (2021. 2 years. AUD\$1,750,000), OPORP Clinical Trial Award (2022. 3 years. AUD\$1,980,000).
 - Wait for outcome of submission for National Health and Medical Research Council Ideas Grants (2022. 3 years. AUD\$989,955), PRORP-Applied Research Award (2022. 3 years. AUD\$870,000).

Table 9. Overview of status of grants including AUD awarded for 2 grants.

	Number	Amount	Number	Amount
	(#)	(AUD\$)	(%)	(%)
Drafted	2		20	5
Submitted	3		30	43
Unsuccessful	3		30	52
Awarded	2		20	1
Total	10		100	100

Table 10. List and status of grant applications.

item	Reference	Grant	Status
		(Investigators. Title. Scheme. Year. Duration. Amount)	
1	GRT01	Frossard L, Saxby D, Schuetz M, Powrie R, Graydon C. How bionic limbs could pull more than their weight?. Bionics Queensland Challenge - Bionic Mobility. 2021. 1 year. AUD	Awarded
2	GRT02	Pitkin M, Cassidy C, Kulinets I, Frossard L, Martino G, Colvin J, Breeze J, Haas D. Kinetics of lower limb prosthesis: automated detection of vertical loading rate Numerical Standard of Anthropomorphicity of the Moment of Dorsiflexion in Prosthetic Feet for Improvement of Amputee Performance. US Department of Defence (DoD), Orthotics and Prosthetics Outcomes Research Program (OPORP), Clinical Research Award (CRA). 2021. 3 years. AUD	Unsuccessful
3	GRT03	Pitkin M, Cassidy C, Frossard L, Prilutsky B, Park H. Transforming anthropomorphic Free-Flow Foot (FFF) prosthesis to the powered foot prosthesis with intuitive control and sensation (Bionic FFF). US Department of Defence (DoD),	Unsuccessful

		Peer Reviewed Orthopaedic Research Program (PRORP) Clinical Translational Research Award (CTRA). 2021. 2 years. AUD	
4	GRT04	Pitkin M, Cassidy C, Frossard L, Prilutsky B, Park H. Anthropomorphic powered foot and ankle prosthesis with intuitive bidirectional control and sensation. National Institutes of Health (NIH), Small Business Innovation Research Grant Applications (SBIR). 2021. 2 years. AUD	Unsuccessful
5	GRT05	Byrnes J, Frossard L, Ames M, Powrie R, Berg D. Deep dive into personal experience with bionic limb: what can we learnt from a patient journey analysis?. Australian National Member Society of the International Society for Prosthetics and Orthotics Inc (ANMS ISPO) Research Grant. 2021. 1 year. AUD	Awarded
6	GRT06	Pitkin M, Cassidy C, Kulinets I, Frossard L, Martino G, Colvin J, Breeze J, Haas D. Numerical Standard of Anthropomorphicity of Prosthetic Feet for Improvement of Amputee Performance. US Department of Defence (DoD), Orthotics and Prosthetics Outcomes Research Program (OPORP), Clinical Trial Award (CTA). 2022. 3 years. AUD	Submitted
7	GRT07	Al-Dirini R, Taylor M, Frossard L, Martelli S, Dickinson A, Steer J, Cavenett S, Diment L. Transforming Prosthetic Design Using Machine Learning and 3D printing. National Health and Medical Research Council (NHMRC) Ideas Grants. 2022. 3 years. AUD	Submitted
8	GRT08	Frossard L, Feih S, Langton C, Lloyd D, Barrett R, Ware R, Schuetz M, Powrie R. handled technology to maintain residuum health of people suffering from limb loss. Collaborative Research Grants - Metro North Health. 2022. 1 year. AUD	Drafted
9	GRT09	Frossard L, Feih S, Langton C, Lloyd D, Barrett R, Moerman K, Ware R, Schuetz M, Powrie R. New adaptive interface attachment of prosthetic limb: making the best bespoke design from biosensors, computational modelling and additive manufacturing. US Department of Defence (DoD), Orthotics and Prosthetics Outcomes Research Program (OPORP), Clinical Research Award (CRA) - Level 1. 2022. 2 years. AUD	Drafted
10	GRT10	Frossard L, Langton C, Lloyd D, Barrett R, Feih S, Diamond L, Saxby D, Ware R, Polman R, Schuetz M.. Improving the life of individuals suffering from limb loss: Innovative diagnostic for residuum health to improve prosthetic fitting and reduce risk of osteoarthritis. US Department of Defense (DoD), Peer Reviewed Orthopaedic Research Program (PRORP), Applied Research Award (ARA) . 2022. 3 years. AUD	Submitted

Figure 49. Team of investigators awarded of the 2021 Bionics Queensland Mobility Challenge including Caroline Craydon bionics bone-anchored prosthesis users, CI-Ross Powrie Senior Prosthetist at Custom Prosthetics, CI-Saxby Senior Lecture at Griffith University and CI-Frossard professor of bionics at Griffith (GRT 01. Frossard L, Saxby D, Schuetz M, Powrie R, Graydon C. How bionic limbs could pull more than their weight? Bionics Queensland Challenge - Bionic Mobility. 2021. 1 year. AUD



Figure 50. Snapshot of Video about “Matthew Ames and the digital transformation of healthcare” (<https://youtu.be/TIJ2S8OoWtU>) involved in the grant awarded from Australian National Member Society of the International Society for Prosthetics and Orthotics Inc (ANMS ISPO) about Deep dive into personal experience with bionic limb: what can we learnt from a patient journey analysis? (GRT05, Byrnes J, Frossard L, Ames M, Powrie R, Berg D. 2022. 1 year. AUD



Phase 5: Post-funding tasks

- Phase 5.2: Investigate commercialization
 - Phase 5.2.1: Perform product investigations
 - Review over 35 products related to the development and commercialization of the In-Vivo Kinetic system 2.0 (Table 11, Figure 51).
 - Phase 5.2.3: Find industry partners sponsors
 - Engage with Queensland-based potential industry partners including VALD (Figure 52).

Table 11. List of products linked to the development of the In-Vivo Kinetic system 2.0 investigated .

Reference	Product	Last update
PRD 01	Adapttech	11/02/2021
PRD 02	Butterfly iQ	08/12/2021
PRD 03	Manufacturing on Demand	18/04/2021
PRD 04	Blue Phantom	07/06/2021
PRD 05	CSIRO Digital human technology	04/08/2021
PRD 06	AIXPLORER	09/08/2021
PRD 07	GUNT	01/09/2021
PRD 08	Durometer	04/09/2021
PRD 09	Hardmatic	04/09/2021
PRD 10	SkinFibroMeter	13/09/2021
PRD 11	Instron	15/09/2021
PRD 12	Open source leg	28/09/2021
PRD 13	RODIN4D	20/10/2021
PRD 14	ntopology	03/12/2021
PRD 15	LITHOZ	22/11/2021
PRD 16	Revopoint 3D	22/11/2021
PRD 17	Artec Scanner	26/11/2021
PRD 18	Artec3D	26/11/2021
PRD 19	IBMT DiPhAS Platform	29/11/2021
PRD 20	GE Healthcare Vscan Air	02/12/2021
PRD 21	Altair OptiStruct	04/12/2021
PRD 22	SIMULIA Tosca	04/12/2021
PRD 23	Slacker	13/12/2021
PRD 24	DiPhAS system	11/01/2022
PRD 25	Amputee Decision Aid	12/01/2022
PRD 26	Digital Image Correlation	28/01/2022
PRD 27	ImageJ	28/01/2022
PRD 28	MultiDIC	28/01/2022
PRD 29	Unity	04/02/2022
PRD 30	Sketchup	07/03/2022
PRD 31	VoxelCare	28/04/2022
PRD 32	Radii Device	03/05/2022
PRD 33	Cloudcompare	27/05/2022
PRD 34	OSSO	29/05/2022

PRD 35	Virtetic	31/05/2022
PRD 36	F	01/06/2022
PRD 37	Pliance	01/06/2022

Figure 51. Examples of product investigated including socket designed with ntopology, PRD 14 (left, source: <https://ntopology.com/>) and Butterfly iQ, PRD 15 (right, source: <https://www.butterflynetwork.eu/clinical-gallery>).



Figure 52. Meeting with VALD, potential industry partner in Queensland.



3.3. Opportunities for training and professional development

Nothing to Report.

3.4. Dissemination of the results to communities of interest

Nothing to Report

3.5. Plan to do during the next reporting period to accomplish the goals

The next goals to accomplish during next reporting period in accordance with SOW presented in Figure 2 including mainly, but not limited to:

- Completion of
 - Phase 2.2.3: Cross validate physical and digital phantoms
 - Phase 2.3: Build prototypes (Deliverable 1)
 - Phase 2.4: Proof of safety and efficacy (Deliverable 2)

- Phase 2.5: Proof of utility (Deliverable 3)
- Phase 2.6: Design clinical trial (Deliverable 4)
- The continue to advance
 - Phase 3: Share outcomes (Publications)
 - Phase 4: Exit strategy (Develop strategic collaborations, Seek funding)

4. Impact

4.1. Impact on the development of the principal discipline(s) of the project

In 2008, at least one in every 190 Americans was living with the loss of a limb but this number is estimated to double by 2050. The number of amputees receiving care within the VHA is more than 43,000 with an additional 5,000 amputations being performed each year. Sadly, recent conflicts have added to the growing number of individuals with traumatic lower-limb loss. US Military casualty statistics reported more than 1,230 amputations in 2010, with 24% suffering multiple limb amputations. While rehabilitation post-amputation typically aims to provide service members with a prosthetic device that returns the function and appearance of the missing limb, the life-time cost associated with continued care with prosthetic use following each amputation is estimated to range between \$US1.4 and 2.8 million. Despite advances in prosthetic technologies, socket-related problems remain an on-going source of morbidity, imposing functional limitations that often restrict return to active duty in most cases, while significantly impacting on health-related quality of life in all. Indeed, one in every two amputees will suffer from persistent limb pain main due to soft tissue breakdown with prosthetic use. The mechanical behavior of the tissues of the residuum is a critical, though poorly understood, determinant of tissue viability and subsequent ulceration and has been shown to be a more sensitive indicator of pathology than traditional clinical measures of tissue structure. Effective soft tissue ulcer prevention, therefore, requires knowledge of the mechanical properties of these tissues and their response to load.

To date, the project has already generated **new knowledge** to assist in the design of non-invasive innovative diagnostic device capable to assist the differential diagnosis of most common medical and prosthetic neuromusculoskeletal issues.

Altogether, both theoretical model and diagnostic tool will be a game-changer for multidisciplinary teams of engineers, clinicians, academics and end-users to:

- **Enable the differential diagnosis** of most common medical and prosthetic neuromusculoskeletal issues,
- **Personalize prescription of prosthetic care interventions** such as design of socket and, eventually, prosthetic components (e.g., liners, knee joint unit),
- **Guide clinical management** of prosthetic fitting by providing a quantitative method for monitoring prosthetic neuromusculoskeletal issues (e.g., tissue properties),
- **Develop educational aids or curricula** to all stakeholders involved in the clinical and prosthetic care of individuals with limb loss (e.g., fitting principle, residuum wound management).
- **Lay the foundation for research** aiming to identify new therapeutic targets and strategies for slowing or reversing processes associated with adverse consequences of prosthetic device use, including tissue breakdown in patients with limb trauma or limb loss.

Ultimately, it is anticipated that this work will **reduce the medical and prosthetic care financial burden** associated with limbs amputation (e.g., less manufacturing of sockets) while

enhancing physical function and health-related quality of life of service members with limb loss. This will be essential to assist their **return to active duty.**

Consequently, decision makers will be able to rely on the **combination of costs reduction and quality-adjusted life year increase to provide most cost-effective fitting options** for both active and non-active service members.

4.2. Impact on other disciplines

The gain of knowledge achieved so far can already be used outside the field of prosthetics. It could be anticipated that **the diagnostic tool could be extended to other areas of injury prevention and rehabilitation**, particularly those treating a range of skin damages involving mechanical loading through assistive devices. For example, this work could provide a better understanding and prevention of:

- **Effect of braces** for spine deformation and release lower limb joint loading.
- **Foot wounds care** experienced by members with diabetes that could possibly limit lower limb amputations,
- **Pressure ulcer** experienced by wheelchair bound service members,
- **Skin damage at the point of contact with external device** such as back-packs or exoskeleton armour suit used on the battlefield.

4.3. Impact on technology transfer

It is expected that this project will lead to the development of next generation of non-invasive diagnostic device to quantify the mechanical properties and viability of residuum of amputees to aid the early detection, prevention and management of neuromusculoskeletal issues (e.g., tissue degeneration, breakdown and ulceration).

To date, we believe that one way to insurance successful technology transfer and subsequent commercialization will be to reinforce already existing links between investigators and collaborations with key organization known for a) development of industrial and medical ultrasound technology, and b) forming partnerships with industry that enable this technology to be transferred to the commercial sector, including:

- **National organizations** such as the Queensland Health (as an end-user), the Queensland Department of Science, Information Technology, Innovation and the Arts (DISTIA), and
- **International organizations** such as the VALD and suppliers of prosthetic components (e.g., Ottobock, OSSUR, Ohio Willow wood),

Support will be initially sought through **Griffith Enterprise Pty Ltd**, an innovation and knowledge transfer company for Griffith University, to:

- Fund the Proof of Concept (PoC) application along with an Australian National Health & Medical Research Council (NHMRC) Development Grant as well as other State, and National and International organizations.
- Identify, protect and enable the commercialization of the medical device.
- Manage the IP assets and negotiate license agreements.
- Liaise with its contacts within the Regulatory Agencies of Australia (TGA) and FDA.

4.4. Impact on society beyond science and technology

Nothing to Report

5. Changes/Problems

5.1. Changes in approach and reasons for change

The main difficulties we have encountered in Y1 was due to new information recently published since the initial submission indicated that it will be required to cross validate the physical and digital function phantom of the residuum prior starting to build prototype (Deliverable 1), provide proof of safety and efficacy (Deliverable 2), proof of utility (Deliverable 3) and design clinical trial (Deliverable 4). However, there is lack of data in the literature about the actual mechanical and ultrasound properties of soft tissues (e.g., skin, fat, muscle, fascia). This mean that we had to investigate and test several replica materials capable to replicate human tissues to build the physical phantom. More extensive work that we anticipated had to be done during Phase 2.1 Create phantom of the residuum (Figure 2).

5.2. Changes that had a significant impact on expenditures

Principal expenditures included in the initial budget of the proposal occurred as planned (e.g., salaries). However, we choose to postpone:

- **Purchase of equipment.** We have hold on to the purchases of iPecsLab, US-Mux, EKOSCAN until completion of E1-E8 experiments and confirmation of the suitability of the device for the development of the In-Vivo Kinetic system 2.0. However, we have purchased a license for Wave 2000 (approximately \$1,525 USD) to facilitate simulation of ultrasound signal.
- **Hiring of Senior Research Fellow 3 (SRF3).** We had initially planned to hire a SRF3 to work on the integration of all hardware and software parts of the In-vivo Kinetic System 2.0. At the beginning of the grant, we anticipated to recruit Dr Jayishni Maharaj who was then working with the Griffith team as Post-doctoral Fellow. At this stage, we are planning to delay the hiring of Dr Maharaj as SRF3 by another quarter. This decision is justified by the facts that (A) we still have to complete the analysis of the E8 to E22 experiments to deliver the complete prototype of the In-Vivo Kinetic System 2.0 and (B) Dr Maharaj currently on leave until the next quarter.

5.3. Significant variations

No formal contracts variations were submitted to the DoD.

Nonetheless, we made several adjustments so that the project can progress despite issues that were beyond the control of the team of investigators related to:

- **Hiring staff.** Some of staff named in the initial application for the RF1, RF2 and RF3 were still working at Griffith but employed to work on other projects at the time of acceptance of the contract. Hiring new staff, particularly from overseas is challenging because of travel restrictions imposed by COVID19. Alternatively, we made the decision to hire:
 - Prof Laurent Frossard at 65% FTE for Year 1 and 65% FTE for Year 2 as Professor level(EPR-Level 1),
 - Prof Christian Langton at 100% FTE Year 1 and 50% FTE Year 2 as Senior Research Fellow (SRF-Level 1),
 - Dr Natalya Perevoshchikova at 50% FTE Year 1 and 100% FTE Year 2 as Research Fellow (RF2-Level 6),All level of employment and FTE commitments were made so that employment meet the budget allocation awarded.
- **Delays due to COVID19 and a flood.** Successive waves of COVID19 and a flood affected availability of staff, ability to have in-person team meeting and access to testing facilities. Alternatively, we hold regular meeting online (Figure 53, Figure 54). However, some experiments and the ethic application were delayed by several weeks.

Figure 53. Virtual team meeting to prepare E1-E8 Experiments (Credit: PI-Frossard).

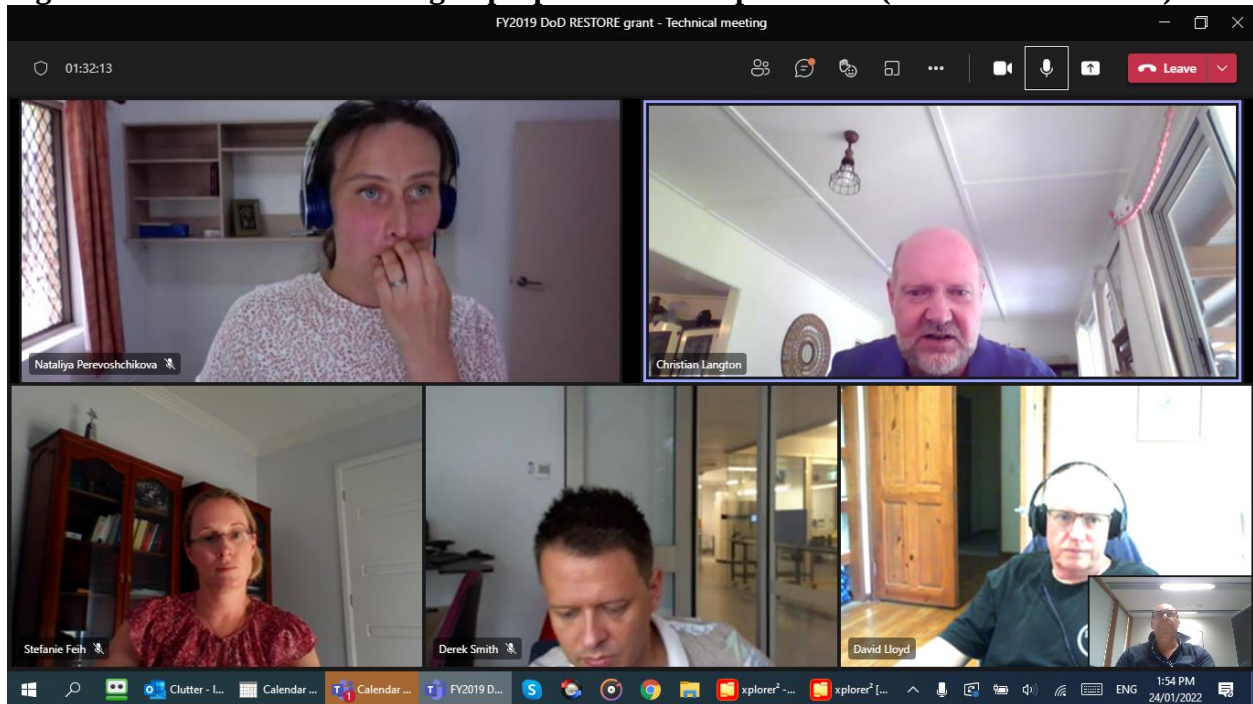
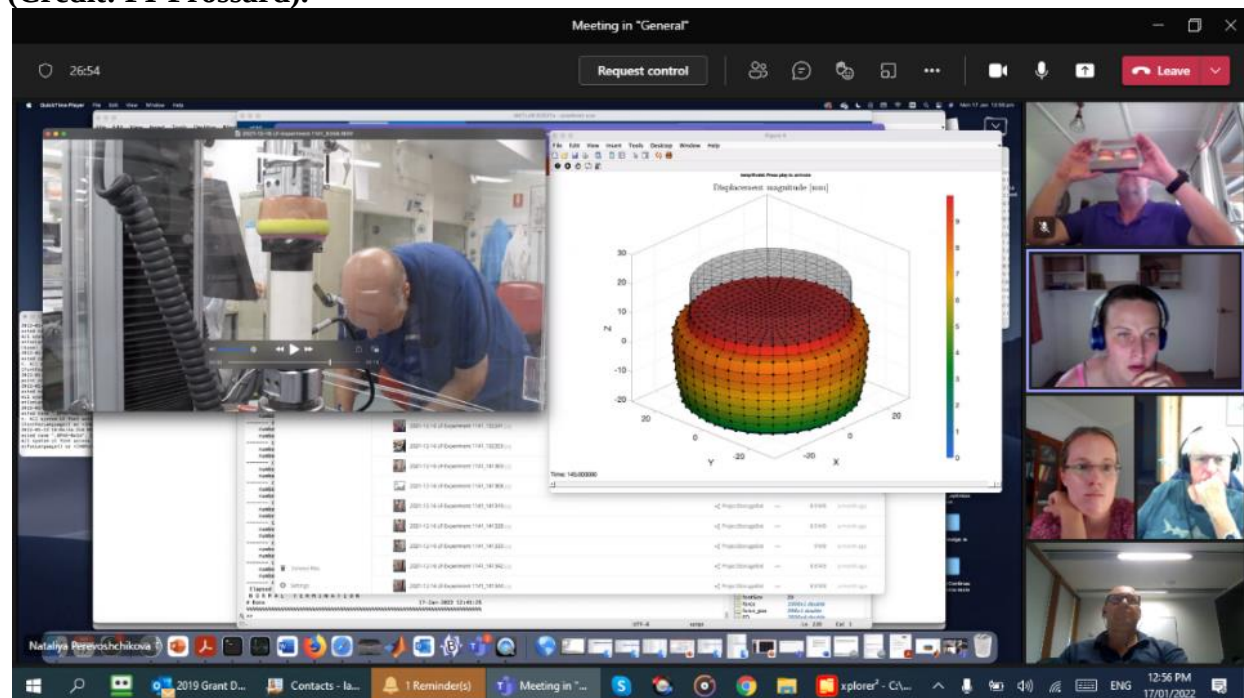


Figure 54. Virtual team meeting to discuss outcomes of E8-1141a and 1141b Experiments (Credit: PI-Frossard).



5.4. Significant changes in use or care of human subjects

Nothing to Report

5.5. Significant changes in use or care of vertebrate animals

Nothing to Report

5.6. Significant changes in use or care of biohazards, and/or of select agents

Nothing to Report

6. Products

6.1. Publications, conference papers, and presentations

- **Journal publications**

1. Pitkin M, Frossard L. Loading Effect of Prosthetic Feet's Anthropomorphicity on Transtibial Osseointegrated Implant. *Military Medicine*. 2021. 186 (Supplement 1) p 681-687. DOI: 10.1093/milmed/usaa461. Status of publication: Published. Acknowledgement of federal support: Yes. (ART01)
2. Frossard L, Lloyd D. The future of bionic limbs. *Research Features*. 2021. 134 p 74-77. DOI: N/A. Status of publication: Published. Acknowledgement of federal support: N/A. (ART02)
3. Frossard L, Langton C, Barrett R, Lloyd D. Can A Digital Twin Of The Residuum Improve Bionic Solutions For Individuals Suffering From Limb Loss?. *Journal of Science and Medicine in Sport*. 2022. 25. P S4-S5. DOI: 10.1016/j.jsams.2021.11.011. Status of publication: Published. Acknowledgement of federal support: Yes. (ART03)
4. Saxby D, Pizzolato C, Nasser A, Devaprakash D, Frossard L, Lloyd D. Personalized Digital Humans For Rehabilitation And Assistive Devices. *Journal of Science and Medicine in Sport*. 2022. 25. P S5-S6. DOI: 10.1016/j.jsams.2021.11.012. Status of publication: Published. Acknowledgement of federal support: Yes. (ART04)
5. Langton C, Barrett R, Powrie R, Lloyd D, Frossard L. Development Of Dynamic Anatomical Ultrasonography To Advance Personalised Prosthetics. *Journal of Science and Medicine in Sport*. 2022. 25. P S6-S7. DOI: 10.1016/j.jsams.2021.11.013. Status of publication: Published. Acknowledgement of federal support: Yes. (ART05)
6. Lloyd D, Perevoshchikova N, Langton C, Barrett R, Maharaj J, Frossard L. Advanced Modelling Of Residuum To Improve Bionic Limbs. *Journal of Science and Medicine in Sport*. 2022. 25. P S7-S8. DOI: 10.1016/j.jsams.2021.11.014. Status of publication: Published. Acknowledgement of federal support: Yes. (ART06)
7. Frossard L, Langton C, Langton C, Feih S, Barrett R, Lloyd D. Next generation of diagnostic device of residuum health of individuals suffering from limb loss: A narrative review of device specifications. *Journal of Science and Medicine in Sport*. 2022. TBC. DOI: TBC. Status of publication: Submitted. Acknowledgement of federal support: Yes. (ART07)
8. Frossard L, Conforto S, Aszmann O. Editorial: Bionics Limb Prostheses: Advances in Clinical and Prosthetic Care. *Frontiers*. 2022. TBC. DOI: TBC. Status of publication: Submitted. Acknowledgement of federal support: Yes. (ART09)

- **Books or other non-periodical, one-time publications.**

Nothing to Report

- **Other publications, conference papers, and presentations.**

9. Frossard L, Langton C, Barrett R, Lloyd D. Residuum health of Service Members suffering from limb loss: Digital twin and diagnostic device. *Military Health System Research Symposium*. 2021. MHSRS-21-03471. DOI: N/A. Status of publication: Accepted. Acknowledgement of federal support: Yes. (ABS01)

10. Frossard L, Langton C, Barrett R, Saxby D, Perevoshchikova N, Maharaj J, Schuetz M, Powrie R, Lloyd D. Advancing Personalised Prosthetics After Amputation: From In-Vivo Monitoring To Bionic Limbs. Defence Biomarkers Symposium. 2022. In press. DOI: N/A. Status of publication: Accepted. Acknowledgement of federal support: Yes. (ABS02)
11. Pitkin M, Park P, Frossard L, Prilutsky B. Higher index of anthropomorphicity of passive Free-Flow Foot (FFF) prosthesis as an advantage for transforming it to the powered foot prosthesis with intuitive control and sensation (Bionic FFF). Military Health System Research Symposium. 2022. MHSRS-22-05274. DOI: N/A. Status of publication: Submitted. Acknowledgement of federal support: No. (ABS03)
12. Frossard L, Langton C, Perevoshchikova N, Feih S, Powrie R, Barrett R, Lloyd D. Development of a diagnostic device to maintain residuum health of Service Members suffering from limb loss: Barriers and facilitators. Military Health System Research Symposium. 2022. MHSRS-22-06886. DOI: N/A. Status of publication: Submitted. Acknowledgement of federal support: Yes. (ABS04)
13. Perevoshchikova N, Moerman K, Langton C, Feih S, Lloyd D, Barrett R, Frossard L. Replicating Residuum Of Individuals Suffering From Trasnfemoral Amputation: From Data-Driven Modelling To Phantom Design And Manufacturing. 13th Australasian Biomechanics Conference (ABC13). 2022. TBC. DOI: TBC. Status of publication: Submitted. Acknowledgement of federal support: Yes. (ABS05)
14. Langton C, Perevoshchikova N, Feih S, Lloyd D, Barrett R, Frossard L. A Dynamic Anatomical Ultrasonography Workflow To Advance Personalised Lower-Limb Prosthetics. 13th Australasian Biomechanics Conference (ABC13). 2022. TBC. DOI: TBC. Status of publication: Submitted. Acknowledgement of federal support: Yes. (ABS06)
15. Langton C, Perevoshchikova N, Feih S, Lloyd D, Barrett R, Frossard L. A Mechano-Acoustic Phantom-Twin Of The Post-Amputation Lower-Limb Residuum. 13th Australasian Biomechanics Conference (ABC13). 2022. TBC. DOI: TBC. Status of publication: Submitted. Acknowledgement of federal support: Yes. (ABS07)

- **Presentations.**

16. Frossard L. You can improve outcomes of patients using bionic limbs. Golden Key International Honour Society Seminar. 2022. DOI: N/A. Status of publication: Published. Acknowledgement of federal support: N/A. (PPT05)

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Nothing to Report

- **Other Products**

Nothing to Report

7. Participants & Other Collaborating Organizations

7.1. Individual contributions on the project

All Principal Investigators and Co-Investigators included in the initial proposal have sustained their involvement and contributed to the development of the project during Y0 and Y1.

Each participant has been involved accordingly to the time commitment and contributions to revised SOW as indicated in the initial proposal (Table 12).

The details for the individual contribution presented in Table 12 are based on the 65 net working days at 7.25 hours per day corresponding to a maximum of 145 hours of effort per person month worked accordingly to Griffith University's Manual of Policies and Procedure.

Further individual contribution to overall project could be found in Sections 9.2, Appendix B: Overview of Y1 activity.

Unfortunately, CI-Huang will be unavailable to work on the project for the next 12 months.

Table 12. Individual contributions to the development of the project during Y0 and Y1. PI: Principle Investigator, CI: Co-Investigator, AD: administrative collaborator, FTE: Full time employment)

PI / PRF (LF)	
Name:	Prof Laurent Frossard (PhD)
Project Role:	Project manager, Leading Researcher (Loading)
Researcher Identifier	0000-0002-0248-9589
Nearest person month worked:	16.965 (522 Working days x 0.65 FTE=2,460 Hours)
Contribution to Project:	Prof Laurent Frossard (PhD) has contributed to the completion of 565 tasks
Funding Support:	- Frossard L, Saxby D, Schuetz M, Powrie R, Graydon C. How bionic limbs could pull more than their weight?. Bionics Queensland Challenge - Bionic Mobility. 2021. AUD\$50,000 - Byrnes J, Frossard L, Ames M, Powrie R, Berg D. Deep dive into personal experience with bionic limb: what can we learnt from a patient journey analysis?. Australian National Member Society of the International Society for Prosthetics and Orthotics Inc (ANMS ISPO) Research Grant. 2021. AUD\$30,000
CI1 (CL)	
Name:	Prof Christian Langton (BSc Jt Hons Iii, MSc, PhD, DSc)
Project Role:	Leading Researcher (Ultrasound)
Researcher Identifier	0000-0002-3647-4027
Nearest person month worked:	0.000 (522 Working days x 0 FTE=0 Hours)
Contribution to Project:	Prof Christian Langton (BSc Jt Hons Iii, MSc, PhD, DSc) has contributed to the completion of 335 tasks
Funding Support:	Nothing to report
CI2 (DL)	
Name:	Prof David Lloyd (BSc (Merit), PhD)
Project Role:	Leading Researcher (Modeling)

Researcher Identifier	0000-0002-0824-9682
Nearest person month worked:	5.220 (522 Working days x 0.2 FTE=757 Hours)
Contribution to Project:	Prof David Lloyd (BSc (Merit), PhD) has contributed to the completion of 287 tasks
Funding Support:	- Improving Donor Site Musculotendon Regeneration following Quadrupled Semitendinosus Anterior Cruciate Ligament Reconstruction through Autologous Conditioned Plasma Therapy. Arthrex. 2019-2022. AUD\$68,000 - ARC Centre for Medical Implant Technology. Australian Research Council, Industrial Transformation Training Centres. 2020-2024. AUD\$4,000,000 - Sidestep & Landing Analyser. Vald Performance and Australian Innovation Connection. 2019-2022. AUD\$200,000 - iTraining for the human Achilles tendon. Australian Research Council (ARC) Industry Linkage Project. 2016-2022. AUD\$870,000 (US\$590,000) - Development and testing of a novel neural restoration technology for people with spinal cord injury (BioSpine). Motor Accident Insurance Commission, Queensland Government. 2019-2022. AUD\$2,000,000 - Exercise as medicine for heart failure: A novel intervention to improve outcomes. Australian National Health and Medical Research Council. 2019-2022. AUD\$674,903 - Exercise as medicine for heart failure: A novel intervention to improve outcomes. Australian National Health and Medical Research Council. 2019-2022. AUD\$674,903 - The Digital Athlete Australia. Wu Tsai Human Performance Alliance. 2022-2024. AUD\$275,000 - Osteoarthritis compass: Predicting personalized disease onset and progression with future capacity for clinical use. Australian National Health and Medical Research Council. 2021-2024. AUD\$860,231
CI3 (RB)	
Name:	Prof Rod Barrett (PhD)
Project Role:	Leading Researcher (Integration)
Researcher Identifier	0000-0002-1784-1629
Nearest person month worked:	5.220 (522 Working days x 0.2 FTE=757 Hours)
Contribution to Project:	Prof Rod Barrett (PhD) has contributed to the completion of 266 tasks
Funding Support:	- The Digital Athlete Australia. Wu Tsai Human Performance Alliance. 2022-2024. AUD\$275,000 - Validation of a novel field-test for assessing anterior cruciate ligament injury risk. Innovation Connections, Australian Government. 2020-2022. AUD 200,000 (USD 150,000) - Development and testing of a novel neural restoration technology for people with spinal cord injury (BioSpine).

	Motor Accident Insurance Commission, Queensland Government. 2019-2022. AUD\$2,000,000 Digitally-enabled neural rehabilitation for spinal cord injury. Motor Accident Insurance Commission (MAIC). 2019-2022. AUD 137,000 (USD 100,000)
CI4 (RB)	
Name:	Prof Robert Ware (BSc (Hons I), PhD)
Project Role:	Bio-statistician
Researcher Identifier	0000-0002-6129-6736
Nearest person month worked:	5.220 (522 Working days x 0.2 FTE=757 Hours)
Contribution to Project:	Prof Robert Ware (BSc (Hons I), PhD) has contributed to the completion of 93 tasks
Funding Support:	- Chronic Musculoskeletal Conditions in Children and Adolescents. Australian Cerebral Palsy Musculoskeletal Health Network Medical Research Future Fund (MRFF). Department of Health. 01/2022-12/2026. - Cerebral Palsy SYNERGY Network to Protect, Repair and improve Outcomes. National Health and Medical Research Council Australia. 01/2021-12/2025. - Does LOng peripheral intraVENous catheter with retractable coiled tip guidewire optimise first insertion success rate for patients with Difficult IntraVenous Access: a randomised controlled trial (LOVE-DIVA). Emergency Medicine Foundation. 01/2022-12/2024. - Preventing adverse events during paediatric cancer treatment: A multi-site hybrid randomised controlled trial of innovative catheter lock solutions. Cancer Council Queensland. 01/2022-12/2025. - ACTIVE STRIDES-CP: Randomised trial of Intensive Rehabilitation (Combined Intensive Gait and Cycling Training) for children with moderate to severe bilateral cerebral palsy. National Health and Medical Research Council Australia. 01/2021-12/2025. - Activating pharmacists to reduce medication related problems: the ACTMed stepped wedge randomised controlled trial. Medical Research Future Fund (MRFF). Department of Health. 01/2021-12/2024. - OCD BOUNCE- Building community-based treatment capacity for children and young people across NSW. Mindgardens Neuroscience Network. 01/2021-12/2022. “Protect PIVs”: A pilot randomized controlled trial of a novel antimicrobial dressing in peripheral intravenous catheters (PIVs). 3M Foundation. 01/2021-12/2025. - Single versus double hamstring tendon graft in anterior cruciate ligament reconstruction in the paediatric patient: a single blind randomised controlled trial. Smith & Nephew Pty Ltd. 01/2021-12/2025.

	• School Readiness child outcomes of early neuroprotection/early neurorehabilitation for infants at high risk of Cerebral Palsy- in the first 2,000 days. Medical Research Future Fund (MRFF). Department of Health. 01/2021-12/2025. • EASY Health - Enhancing Access to Services for Your Health. National Disability Insurance Agency. 07/2020-06/2023. • Early Moves: A prospective cohort study to identify an early biomarker for cognitive impairment. National Health and Medical Research Council Australia. 01/2020-12/2024. • Difficult peripheral intravenous catheter insertion: Australian considerations for sustainable implementation of ultrasound guided procedures. National Health and Medical Research Council Australia. 01/2020 – 12/2022. AUS • Wearing masks to reduce traffic-related air pollution exposure and improve children’s respiratory health. National Health and Medical Research Council Australia. 01/2019-12/2022. AUS • A tiered approach to the diagnosis of Foetal Alcohol Spectrum Disorder in remote Indigenous primary care settings. National Health and Medical Research Council Australia. 01/2020-12/2023. AUS • Improving access to treatment for children with anxiety disorders: A randomised controlled non-inferiority trial of positive search training. National Health and Medical Research Council Australia. 01/2019-12/2022. AUS • Prediction of childhood Brain Outcomes in infants born preterm using neonatal MRI and concurrent clinical biomarkers - PREBO-6. National Health and Medical Research Council Australia. 01/2019-12/2023. AUS • Can Exercise Delay Transition to Active Therapy in Men with Low Grade Prostate Cancer? A Multi-Centre Randomized Controlled Trial. National Health and Medical Research Council Australia. 01/2018-12/2022. AUS
CI5 (MS)	
Name:	Dr Michael Schuetz
Project Role:	Orthopedic surgeon
Researcher Identifier	0000-0003-2808-0631
Nearest person month worked:	0.261 (522 Working days x 0.01 FTE=38 Hours)
Contribution to Project:	Dr Michael Schuetz has contributed to the completion of 75 tasks
Funding Support:	• Frossard L, Saxby D, Schuetz M, Powrie R, Graydon C. How bionic limbs could pull more than their weight?. Bionics Queensland Challenge - Bionic Mobility. 2021. 1 year. AUD • Engineering of Nanostructured Surfaces for Enhanced Antibacterial Activity. Australian Research Council. 2023 –

	2026. AUD
<u>PI6 (PH)</u>	
Name:	Dr Pei Huang
Project Role:	Rehabilitation specialist
Researcher Identifier	TBC
Nearest person month worked:	0.261 (522 Working days x 0.01 FTE=38 Hours)
Contribution to Project:	Dr Pei Huang has contributed to the completion of 26 tasks
Funding Support:	Nothing to report
<u>PI7 (RP)</u>	
Name:	Ross Powrie (CPO)
Project Role:	Prosthetist
Researcher Identifier	N/A
Nearest person month worked:	0.261 (522 Working days x 0.01 FTE=38 Hours)
Contribution to Project:	Ross Powrie (CPO) has contributed to the completion of 73 tasks
Funding Support:	- Frossard L, Saxby D, Schuetz M, Powrie R, Graydon C. How bionic limbs could pull more than their weight?. Bionics Queensland Challenge - Bionic Mobility. 2021. 1 year. AUD - Byrnes J, Frossard L, Ames M, Powrie R, Berg D. Deep dive into personal experience with bionic limb: what can we learnt from a patient journey analysis?. Australian National Member Society of the International Society for Prosthetics and Orthotics Inc (ANMS ISPO) Research Grant. 2021. 1 year. AUD
<u>SRF2 (CL)</u>	
Name:	Prof Christian Langton (BSc Jt Hons Iii, MSc, PhD, DSc)
Project Role:	Leading Researcher (Ultrasound)
Researcher Identifier	0000-0002-3647-4027
Nearest person month worked:	26.100 (522 Working days x 1 FTE=3,785 Hours)
Contribution to Project:	Prof Christian Langton (BSc Jt Hons Iii, MSc, PhD, DSc) has contributed to the completion of 220 tasks
Funding Support:	Nothing to report
<u>SRF2 (NP)</u>	
Name:	Dr Nataliya Perevoshchikova (PhD)
Project Role:	Senior Research Fellow (Modeling)
Researcher Identifier	TBC
Nearest person month worked:	19.575 (522 Working days x 0.75 FTE=2,838 Hours)
Contribution to Project:	Dr Nataliya Perevoshchikova (PhD) has contributed to the completion of 203 tasks
Funding Support:	N/A
<u>AD1 (MN)</u>	
Name:	Marretta Mann
Project Role:	Senior Manager, Grant

Researcher Identifier	N/A
Nearest person month worked:	3.825 (522 Working days x 0.146551724137931 FTE=555 Hours)
Contribution to Project:	Marretta Mann has contributed to the completion of 17 tasks
Funding Support:	N/A
<u>AD2 (LA)</u>	
Name:	Lynette Farquhar
Project Role:	Senior Manager, Research Grants
Researcher Identifier	N/A
Nearest person month worked:	2.700 (522 Working days x 0.103448275862069 FTE=392 Hours)
Contribution to Project:	Lynette Farquhar has contributed to the completion of 12 tasks
Funding Support:	N/A
<u>AD3 (RG)</u>	
Name:	Ridhima Gulati
Project Role:	Research Grants, Officer
Researcher Identifier	N/A
Nearest person month worked:	4.725 (522 Working days x 0.181034482758621 FTE=685 Hours)
Contribution to Project:	Ridhima Gulati has contributed to the completion of 21 tasks
Funding Support:	N/A
<u>AD4 (DM)</u>	
Name:	Deborah Marshal
Project Role:	Senior Manager, Communication
Researcher Identifier	N/A
Nearest person month worked:	1.575 (522 Working days x 0.0603448275862069 FTE=228 Hours)
Contribution to Project:	Deborah Marshal has contributed to the completion of 7 tasks
Funding Support:	N/A
<u>AD5 (KK)</u>	
Name:	Kathy Kruger
Project Role:	Senior Manager, Communication
Researcher Identifier	N/A
Nearest person month worked:	1.575 (522 Working days x 0.0603448275862069 FTE=228 Hours)
Contribution to Project:	Kathy Kruger has contributed to the completion of 7 tasks
Funding Support:	N/A
<u>AD6 (JW)</u>	
Name:	Jane Way
Project Role:	Human Resources, Officer
Researcher Identifier	N/A
Nearest person month worked:	1.575 (522 Working days x 0.0603448275862069 FTE=228 Hours)
Contribution to Project:	Jane Way has contributed to the completion of 7 tasks, including:
Funding Support:	N/A

7.2. Change in the active other support of the PD/PI(s)

The list of current funding support for each PIs and Cis is provided in Table 12.

7.3. Other organizations involved as partners

Not applicable

8. Special Reporting Requirements

8.1. Collaborative awards

Not Applicable

8.2. QUAD charts

As requested, the update QUAD chart is included in Section 9.3 Appendix C: QUAD chart

9. Appendices

9.1. Appendix A: Detailed SOW

9.2. Appendix B: Overview of Y1 activity

9.3. Appendix C: QUAD chart

9.4. Appendix D: PDFs of all publications

Phase	Task	Pre		During										Post	
		Y0	Y0	Y1	Y1	Y1	Y1	Y2	Y2	Y2	Y2	Y2	Y2	Y3	Y3
		Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q1	Q2
1	Phase 1: Kick-off tasks														
1.1	Create project management structure														
1.1.1	Manage project														
1.1.2	Plan study														
1.1.3	Collect data														
1.1.4	Analyse data														
1.1.5	Publish outcomes														
1.1.6	Commercialise product														
1.1.7	Promote output														
1.2	Hire staff														
1.2.1	Appoint of PRF (Frossard L)														
1.2.2	Appoint of RF1 (Langton C)														
1.2.3	Appoint of RF2 (Perevoshchikova N)														
1.2.4	Appoint of RF3														
1.2.5	Appoint of Study Coordinator														
1.2.6	Engage with Clinical Trial Monitor														
1.3	Develop collaboration														
1.3.1	Attract key experts														
1.4	Purchase equipment														
1.4.1	Purchase iPecsLab														
1.4.2	Purchase US-Mux for DAU														
1.4.3	Purchase ultrasound transducers for DAU														
1.5	Obtain ethics approval														
1.5.1	Obtain ethics approval from GUG														
1.5.2	Obtain ethics approval from DoD														
2	Phase 2: Key developments and deliverables														
2.1	Plan experiments														
2.1.1	Establish roadmap for experiments														
2.2	Create phantom of residuum														
2.2.1	Create physical phantom														
2.2.2	Create digital phantom														
2.2.3	Cross validate physical and digital phantoms														
2.3	Build prototypes (Deliverable 1)														
2.3.4	Incorporate 8-tranducer US-Mux														
2.3.5	Develop of neuromusculoskeletal modelling														
2.3.6	Develop of digital twin of residuum														
2.3.7	Test In-vivo Kinetic system 2.0														
2.4	Proof of safety and efficacy (Deliverable 2)														
2.4.1	Test device in military operational environment														
2.4.2	Recruit participants (TTA=6, TFA=6)														
2.4.3	Collect loading and DAU data														
2.4.4	Conduct statistical analysis														
2.5	Proof of utility (Deliverable 3)														
2.5.1	Confirm utility in military operational environment														
2.5.2	Recruit participants (TTA=12, TFA=12)														
2.5.3	Collect loading and DAU data														
2.5.4	Conduct statistical analysis														
2.6	Design clinical trial (Deliverable 4)														
2.6.1	Complete analytical planning study														
2.6.2	Write protocol for the Research Level 3 clinical trial														
2.6.3	Conduct equivalence study														
2.6.4	Assess disruption in service delivery														

[illegible]

Level - Item	Date	Date	Percentage completion			Key contributors												2022-Y1 <----> 2022-Q2
	Start	End	Before	Achieved	To date	PI1	CI1	CI2	CI3	CI4	CI5	CI6	CI7	RF1	RF2			
						LF	CL	DL	RB	RW	MS	PH	RP	CL	NP			
1 - Phase 1: Kick-off tasks	22/06/2016	31/12/2023																
1.1 - Manage project	22/06/2016	31/12/2023																
1.1.1 - Manage contract	13/10/2020	18/10/2020																
1.1.1.1 - Prepare contract	13/10/2020	01/07/2021		100	100	X												
1.1.1.2 - Sign contract	01/07/2021	05/07/2021		100	100	X												
1.1.1.3 - Award grant	05/07/2021	10/07/2021		100	100	X												
1.1.2 - Manage project charter	01/07/2020	31/12/2023																
1.1.2.1 - Create project charter	18/07/2021	30/09/2021		100	100	X												
1.1.2.2 - Update project charter for 2021-Q3 report	01/07/2020	11/09/2021		100	100	X	X	X	X	X	X	X	X	X				
1.1.2.3 - Review project charter for 2021-Q3 report	11/09/2021	19/09/2021		100	100			X	X									
1.1.2.4 - Approve project charter for 2021-Q3 report	19/09/2021	27/09/2021		100	100	X												
1.1.2.5 - Print project charter for 2021-Q3 report	27/09/2021	30/09/2021		100	100	X												
1.1.2.6 - Update project charter for 2021-Q4 report	01/10/2021	12/12/2021		100	100	X												
1.1.2.7 - Review project charter for 2021-Q4 report	12/12/2021	20/12/2021		100	100		X	X	X	X	X	X	X					
1.1.2.8 - Approve project charter for 2021-Q4 report	20/12/2021	28/12/2021		100	100	X	X	X	X									
1.1.2.9 - Print project charter for 2021-Q4 report	28/12/2021	31/12/2021		100	100	X												
1.1.2.10 - Update project charter for 2022-Q1 report	01/01/2022	12/03/2022		100	100	X												
1.1.2.11 - Review project charter for 2022-Q1 report	12/03/2022	20/03/2022		100	100		X		X	X				X				
1.1.2.12 - Approve project charter for 2022-Q1 report	20/03/2022	28/03/2022		100	100			X										
1.1.2.13 - Print project charter for 2022-Q1 report	28/03/2022	31/03/2022		100	100	X												
1.1.3 - Manage dashboard	01/07/2020	31/12/2023																
1.1.3.1 - Create dashboard	27/09/2021	30/09/2021		20	20	X												
1.1.3.2 - Update dashboard for 2021-Q3 report	01/07/2020	11/09/2021		20	20	X	X	X	X	X	X	X	X	X				
1.1.3.3 - Review dashboard for 2021-Q3 report	11/09/2021	19/09/2021		20	20			X	X									
1.1.3.4 - Approve dashboard for 2021-Q3 report	19/09/2021	27/09/2021		20	20	X												
1.1.3.5 - Print dashboard for 2021-Q3 report	27/09/2021	30/09/2021		20	20	X												
1.1.3.6 - Update dashboard for 2021-Q4 report	01/10/2021	12/12/2021		100	100	X												
1.1.3.7 - Review dashboard for 2021-Q4 report	12/12/2021	20/12/2021		100	100		X	X	X	X	X	X	X					
1.1.3.8 - Approve dashboard for 2021-Q4 report	20/12/2021	28/12/2021		100	100	X	X	X	X									
1.1.3.9 - Print dashboard for 2021-Q4 report	28/12/2021	31/12/2021		100	100	X												
1.1.3.10 - Update dashboard for 2022-Q1 report	01/01/2022	12/03/2022		100	100	X												
1.1.3.11 - Review dashboard for 2022-Q1 report	12/03/2022	20/03/2022		100	100		X		X	X				X				
1.1.3.12 - Approve dashboard for 2022-Q1 report	20/03/2022	28/03/2022		100	100			X										
1.1.3.13 - Print dashboard for 2022-Q1 report	28/03/2022	31/03/2022		100	100	X												
1.1.4 - Manage team	01/07/2020	31/12/2023																
1.1.4.1 - Create team plan	18/07/2021	30/09/2021		100	100	X												
1.1.4.2 - Update team plan for 2021-Q3 report	01/07/2020	11/09/2021		100	100	X	X	X	X	X	X	X	X	X				
1.1.4.3 - Review team plan for 2021-Q3 report	11/09/2021	19/09/2021		100	100			X	X									
1.1.4.4 - Approve team plan for 2021-Q3 report	19/09/2021	27/09/2021		100	100	X												
1.1.4.5 - Print team plan for 2021-Q3 report	27/09/2021	30/09/2021		100	100	X												
1.1.4.6 - Update team plan for 2021-Q4 report	01/10/2021	12/12/2021		100	100	X												
1.1.4.7 - Review team plan for 2021-Q4 report	12/12/2021	20/12/2021		100	100		X	X	X	X	X	X	X					
1.1.4.8 - Approve team plan for 2021-Q4 report	20/12/2021	28/12/2021		100	100	X	X	X	X									
1.1.4.9 - Print team plan for 2021-Q4 report	28/12/2021	31/12/2021		100	100	X												
1.1.4.10 - Update team plan for 2022-Q1 report	01/01/2022	12/03/2022		100	100	X												
1.1.4.11 - Review team plan for 2022-Q1 report	12/03/2022	20/03/2022		100	100		X		X	X				X				
1.1.4.12 - Approve team plan for 2022-Q1 report	20/03/2022	28/03/2022		100	100			X										
1.1.4.13 - Print team plan for 2022-Q1 report	28/03/2022	31/03/2022		100	100	X												
1.1.5 - Create team registry (Version 01)	29/06/2021	04/07/2021																
1.1.5.1 - Update team registry (Version 02)	04/07/2021	09/07/2021		100	100	X	X	X	X	X	X	X	X	X				
1.1.5.2 - Update team registry (Version 03)	23/07/2021	28/07/2021		100	100	X	X	X	X	X	X			X	X			
1.1.5.3 - Update team registry (Version 04)	02/08/2021	07/08/2021		100	100	X	X	X	X	X	X			X	X	X		
1.1.5.4 - Update team registry (Version 05)	03/08/2021	08/08/2021		100	100	X	X	X	X	X	X			X	X	X		
1.1.5.5 - Update team registry (Version 06)	04/08/2021	09/08/2021		100	100	X	X	X	X	X	X			X	X	X		
1.1.5.6 - Update team registry (Version 07)	19/08/2021	24/08/2021		100	100	X	X	X	X	X	X			X	X	X		
1.1.5.7 - Update team registry (Version 08)	19/08/2021	24/08/2021		100	100	X	X	X	X	X	X			X	X	X		
1.1.5.8 - Update team registry (Version 09)	19/08/2021	24/08/2021		100	100	X	X	X	X	X	X			X	X	X		

1.1.5.9 - Update team registry (Version 10)	19/08/2021	24/08/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.5.10 - Update team registry (Version 11)	20/08/2021	25/08/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.5.11 - Update team registry (Version 12)	23/08/2021	28/08/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.5.12 - Update team registry (Version 13)	10/09/2021	15/09/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.5.13 - Update team registry (Version 14)	20/09/2021	25/09/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.5.14 - Update team registry (Version 15)	22/09/2021	27/09/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.5.15 - Update team registry (Version 16)	15/10/2021	20/10/2021		100	100	X											
1.1.5.16 - Update team registry (Version 17)	05/11/2021	10/11/2021		100	100	X											
1.1.5.17 - Update team registry (Version 18)	06/12/2021	11/12/2021		100	100	X											
1.1.5.18 - Update team registry (Version 19)	07/12/2021	12/12/2021		100	100	X											
1.1.5.19 - Update team registry (Version 20)	09/03/2022	14/03/2022		100	100	X											
1.1.6 - Manage stakeholders	01/07/2020	31/12/2023															
1.1.6.1 - Create stakeholder plan	18/07/2021	30/09/2021		100	100	X											
1.1.6.2 - Update stakeholder plan for 2021-Q3 report	01/07/2020	11/09/2021		100	100	X	X	X	X	X	X	X	X	X	X		
1.1.6.3 - Review stakeholder plan for 2021-Q3 report	11/09/2021	19/09/2021		100	100			X	X								
1.1.6.4 - Approve stakeholder plan for 2021-Q3 report	19/09/2021	27/09/2021		100	100	X											
1.1.6.5 - Print stakeholder plan for 2021-Q3 report	27/09/2021	30/09/2021		100	100	X											
1.1.6.6 - Update stakeholder plan for 2021-Q4 report	01/10/2021	12/12/2021		100	100	X											
1.1.6.7 - Review stakeholder plan for 2021-Q4 report	12/12/2021	20/12/2021		100	100		X	X	X	X	X	X					
1.1.6.8 - Approve stakeholder plan for 2021-Q4 report	20/12/2021	28/12/2021		100	100		X	X	X								
1.1.6.9 - Print stakeholder plan for 2021-Q4 report	28/12/2021	31/12/2021		100	100	X											
1.1.6.10 - Update stakeholder plan for 2022-Q1 report	01/01/2022	12/03/2022		100	100	X											
1.1.6.11 - Review stakeholder plan for 2022-Q1 report	12/03/2022	20/03/2022		100	100		X		X	X			X				
1.1.6.12 - Approve stakeholder plan for 2022-Q1 report	20/03/2022	28/03/2022		100	100			X									
1.1.6.13 - Print stakeholder plan for 2022-Q1 report	28/03/2022	31/03/2022		100	100	X											
1.1.7 - Create stakeholders registry (Version 01)	18/05/2021	23/05/2021															
1.1.7.1 - Update stakeholders registry (Version 02)	18/07/2021	23/07/2021		100	100	X	X	X	X	X	X	X	X	X	X		
1.1.7.2 - Update stakeholders registry (Version 03)	11/09/2021	16/09/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.7.3 - Update stakeholders registry (Version 04)	07/12/2021	12/12/2021		100	100	X											
1.1.7.4 - Update stakeholders registry (Version 05)	09/03/2022	14/03/2022		100	100	X											
1.1.8 - Manage risks	01/07/2020	31/12/2023															
1.1.8.1 - Create risk plan	18/07/2021	30/09/2021		100	100	X											
1.1.8.2 - Update risk plan for 2021-Q3 report	01/07/2020	11/09/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.8.3 - Review risk plan for 2021-Q3 report	11/09/2021	19/09/2021		100	100			X	X								
1.1.8.4 - Approve risk plan for 2021-Q3 report	19/09/2021	27/09/2021		100	100	X											
1.1.8.5 - Print risk plan for 2021-Q3 report	27/09/2021	30/09/2021		100	100	X											
1.1.8.6 - Update risk plan for 2021-Q4 report	01/10/2021	12/12/2021		100	100	X											
1.1.8.7 - Review risk plan for 2021-Q4 report	12/12/2021	20/12/2021		100	100		X	X	X	X	X	X					
1.1.8.8 - Approve risk plan for 2021-Q4 report	20/12/2021	28/12/2021		100	100		X	X	X								
1.1.8.9 - Print risk plan for 2021-Q4 report	28/12/2021	31/12/2021		100	100	X											
1.1.8.10 - Update risk plan for 2022-Q1 report	01/01/2022	12/03/2022		100	100	X											
1.1.8.11 - Review risk plan for 2022-Q1 report	12/03/2022	20/03/2022		100	100		X		X	X	X		X				
1.1.8.12 - Approve risk plan for 2022-Q1 report	20/03/2022	28/03/2022		100	100			X									
1.1.8.13 - Print risk plan for 2022-Q1 report	28/03/2022	31/03/2022		100	100	X											
1.1.9 - Create risks registry (Version 01)	18/05/2021	23/05/2021															
1.1.9.1 - Update risks registry (Version 02)	18/07/2021	23/07/2021		100	100	X	X	X	X	X	X	X	X	X	X		
1.1.9.2 - Update risks registry (Version 03)	11/09/2021	16/09/2021		100	100	X	X	X	X	X	X		X	X	X		
1.1.9.3 - Update risks registry (Version 04)	07/12/2021	12/12/2021		100	100	X											
1.1.9.4 - Update risks registry (Version 05)	09/03/2022	14/03/2022		100	100	X											
1.1.10 - Manage finances	01/07/2020	31/12/2023															
1.1.10.1 - Create financial plan	27/09/2021	30/09/2021		100	100	X											
1.1.10.2 - Update financial plan for 2021-Q3 report	01/07/2020	11/09/2021		100	100	X	X	X	X				X	X			
1.1.10.3 - Review financial plan for 2021-Q3 report	11/09/2021	19/09/2021		100	100			X	X								
1.1.10.4 - Approve financial plan for 2021-Q3 report	19/09/2021	27/09/2021		100	100	X											
1.1.10.5 - Print financial plan for 2021-Q3 report	27/09/2021	30/09/2021		100	100	X											
1.1.10.6 - Update financial plan for 2021-Q4 report	01/10/2021	12/12/2021		100	100	X											
1.1.10.7 - Review financial plan for 2021-Q4 report	12/12/2021	20/12/2021		100	100		X	X	X	X	X	X					
1.1.10.8 - Approve financial plan for 2021-Q4 report	20/12/2021	28/12/2021		100	100		X	X	X								
1.1.10.9 - Print financial plan for 2021-Q4 report	28/12/2021	31/12/2021		100	100	X											
1.1.10.10 - Update financial plan for 2022-Q1 report	01/01/2022	12/03/2022		100	100	X											
1.1.10.11 - Review financial plan for 2022-Q1 report	12/03/2022	20/03/2022		100	100		X		X	X	X		X				
1.1.10.12 - Approve financial plan for 2022-Q1 report	20/03/2022	28/03/2022		100	100			X									

[illegible]

4 of 10

5 of 10

6 of 10

7 of 10

3.1.1.9 - Update quarterly report registry (Version 10)	15/09/2021	20/09/2021		100	100	X	X	X	X	X	X		X	X	X	
3.1.1.10 - Update quarterly report registry (Version 11)	15/09/2021	20/09/2021		100	100	X	X	X	X	X	X	X	X	X	X	
3.1.1.11 - Update quarterly report registry (Version 12)	07/12/2021	12/12/2021		100	100	X									X	
3.1.1.12 - Update quarterly report registry (Version 13)	08/12/2021	13/12/2021		100	100	X									X	
3.1.1.13 - Update quarterly report registry (Version 14)	09/12/2021	14/12/2021		100	100	X									X	
3.1.1.14 - Update quarterly report registry (Version 15)	10/12/2021	15/12/2021		100	100	X									X	
3.1.1.15 - Update quarterly report registry (Version 16)	10/12/2021	15/12/2021		100	100	X	X	X	X	X	X	X	X	X	X	
3.1.1.16 - Update quarterly report registry (Version 17)	11/12/2021	16/12/2021		100	100	X	X	X	X	X	X	X	X	X	X	
3.1.1.17 - Update quarterly report registry (Version 18)	09/03/2022	14/03/2022		100	100	X										
3.1.1.18 - Update quarterly report registry (Version 19)	10/03/2022	15/03/2022		100	100	X										
3.1.1.19 - Update quarterly report registry (Version 20)	11/03/2022	16/03/2022		100	100	X										
3.2 - Publish outcomes	13/02/2019	01/07/2022														
3.2.1.2 - Prepare data (Sub 1, Rd 1) for Mil Med-Effetct of AI on TTA-BAP (ART01)	13/02/2019	18/11/2020		100	100	X										
3.2.1.5 - Wait reviewers report (Sub 1, Rd 1) for Mil Med-Effetct of AI on TTA-BAP (ART01)	05/05/2020	04/08/2020		100	100	X										
3.2.1.6 - Draft illustrations and manuscript (Sub 1, Rd 2) for Mil Med-Effetct of AI on TTA-BAP (ART01)	04/08/2020	07/09/2020		100	100	X										
3.2.1.7 - Submit manuscript (Sub 1, Rd 2) for Mil Med-Effetct of AI on TTA-BAP (ART01)	07/09/2020	12/09/2020		100	100	X										
3.2.1.8 - Wait reviewers report (Sub 1, Rd 2) for Mil Med-Effetct of AI on TTA-BAP (ART01)	07/09/2020	12/09/2020		100	100	X										
3.2.1.9 - Draft illustrations and manuscript (Sub 1, Rd 3) for Mil Med-Effetct of AI on TTA-BAP (ART01)	04/10/2020	09/10/2020		100	100	X										
3.2.1.10 - Submit manuscript (Sub 1, Rd 3) for Mil Med-Effetct of AI on TTA-BAP (ART01)	04/10/2020	09/10/2020		100	100	X										
3.2.1.11 - Wait reviewers report (Sub 1, Rd 3) for Mil Med-Effetct of AI on TTA-BAP (ART01)	04/10/2020	22/10/2020		100	100	X										
3.2.1.12 - Proof read accepted version (Sub 1, Rd 3) for Mil Med-Effetct of AI on TTA-BAP (ART01)	22/10/2020	24/10/2020		100	100	X										
3.2.1.13 - Publish (Sub 1, Rd 3) for Mil Med-Effetct of AI on TTA-BAP (ART01)	18/11/2020	27/01/2021														
3.2.1.15 - Complete publication pathway study (Sub 1, Rd 1) for Res Features-Future of bionics limb (ART02)	27/08/2020	21/09/2020		100	100	X										
3.2.1.16 - Choose review (Sub 1, Rd 1) for Res Features-Future of bionics limb (ART02)	21/09/2020	26/09/2020		100	100	X										
3.2.1.17 - Draft illustrations and manuscript (Sub 1, Rd 1) for Res Features-Future of bionics limb (ART02)	02/10/2020	20/12/2020		100	100	X										
3.2.1.18 - Submit manuscript (Sub 1, Rd 1) for Res Features-Future of bionics limb (ART02)	20/12/2020	07/01/2021		100	100	X										
3.2.1.19 - Publish (Sub 1, Rd 1) for Res Features-Future of bionics limb (ART02)	07/01/2021	27/02/2021		100	100	X										
3.2.1.30 - Accept invitation (Sub 1, Rd 1) for JSaMS-Digital twin and bionics (ART03)	01/06/2021	17/06/2021		100	100	X										
3.2.1.31 - Check submission guideline (Sub 1, Rd 1) for JSaMS-Digital twin and bionics (ART03)	17/06/2021	02/07/2021		100	100	X		X	X							
3.2.1.32 - Draft (Sub 1, Rd 1) for JSaMS-Digital twin and bionics (ART03)	02/07/2021	24/09/2021		100	100	X	X	X	X					X		
3.2.1.33 - Submit (Sub 1, Rd 1) for JSaMS-Digital twin and bionics (ART03)	24/09/2021	25/09/2021		100	100	X	X	X	X					X		
3.2.1.34 - Receive acceptance (Sub 1, Rd 1) for JSaMS-Digital twin and bionics (ART03)	25/09/2021	30/09/2021		100	100	X	X	X	X					X		
3.2.1.45 - Accept invitation (Sub 1, Rd 1) for JSaMS-Ultrasound DAU (ART05)	01/06/2021	17/06/2021		100	100	X										
3.2.1.46 - Check submission guideline (Sub 1, Rd 1) for JSaMS-Ultrasound DAU (ART05)	17/06/2021	06/08/2021		100	100	X	X							X		
3.2.1.47 - Draft (Sub 1, Rd 1) for JSaMS-Ultrasound DAU (ART05)	06/08/2021	07/09/2021		100	100	X	X							X		
3.2.1.48 - Submit (Sub 1, Rd 1) for JSaMS-Ultrasound DAU (ART05)	07/09/2021	12/09/2021		100	100	X	X							X		
3.2.1.49 - Receive acceptance (Sub 1, Rd 1) for JSaMS-Ultrasound DAU (ART05)	07/09/2021	10/09/2021		100	100	X	X							X		
3.2.1.60 - Accept invitation (Sub 1, Rd 1) for JSaMS-Twinning (ART06)	01/06/2021	17/06/2021		100	100	X										
3.2.1.61 - Check submission guideline (Sub 1, Rd 1) for JSaMS-Twinning (ART06)	17/06/2021	06/08/2021		100	100	X		X	X							
3.2.1.62 - Draft (Sub 1, Rd 1) for JSaMS-Twinning (ART06)	06/08/2021	14/09/2021		100	100	X		X	X							
3.2.1.63 - Submit (Sub 1, Rd 1) for JSaMS-Twinning (ART06)	14/09/2021	15/09/2021		100	100	X		X	X							
3.2.1.64 - Receive acceptance (Sub 1, Rd 1) for JSaMS-Twinning (ART06)	15/09/2021	16/09/2021		100	100	X		X	X							
3.2.1.75 - Accept invitation (Sub 1, Rd 1) for JSaMS-Digital human (ART04)	01/06/2021	17/06/2021		100	100	X										
3.2.1.76 - Check submission guideline (Sub 1, Rd 1) for JSaMS-Digital human (ART04)	17/06/2021	06/08/2021		100	100	X		X	X							
3.2.1.77 - Draft (Sub 1, Rd 1) for JSaMS-Digital human (ART04)	06/08/2021	07/09/2021		100	100	X		X	X							
3.2.1.78 - Submit (Sub 1, Rd 1) for JSaMS-Digital human (ART04)	07/09/2021	08/09/2021		100	100	X		X	X							
3.2.1.79 - Receive acceptance (Sub 1, Rd 1) for JSaMS-Digital human (ART04)	08/09/2021	09/09/2021		100	100	X		X	X							
3.2.1.90 - Complete publication pathway study (Sub 1, Rd 1) for JSaMS-IKS-Barriers and Facilitators (ART07)	02/03/2022	03/03/2022		100	100	X	X	X	X					X		
3.2.1.91 - Choose review (Sub 1, Rd 1) for JSaMS-IKS-Barriers and Facilitators (ART07)	03/03/2022	04/03/2022		100	100	X	X	X	X					X		
3.2.1.92 - Prepare data (Sub 1, Rd 1) for JSaMS-IKS-Barriers and Facilitators (ART07)	04/03/2022	09/03/2022		100	100	X	X	X	X					X		
3.2.1.105 - Complete publication pathway study (Sub 1, Rd 1) for Clin Rehab-Walking ability TFA-BAP vs CTL (ART08)	22/12/2020	27/12/2020		100	100	X										
3.2.1.106 - Choose review (Sub 1, Rd 1) for Clin Rehab-Walking ability TFA-BAP vs CTL (ART08)	27/12/2020	28/12/2020		100	100	X										
3.2.1.107 - Prepare data (Sub 1, Rd 1) for Clin Rehab-Walking ability TFA-BAP vs CTL (ART08)	28/12/2020	19/02/2022		100	100	X	X	X	X					X		
3.2.1.108 - Draft illustrations and manuscript (Sub 1, Rd 1) for Clin Rehab-Walking ability TFA-BAP vs CTL (ART08)	19/02/2022	01/07/2022		100	100	X										
3.2.1.120 - Prepare data (Sub 1, Rd 1) for Frontier-Editorial bionics and rehab (ART09)	17/01/2022	12/04/2022		100	100	X										
3.2.1.165 - Draft (Sub 1, Rd 1) for MHSRS-Digital twin (ABS01)	22/01/2021	27/02/2021		100	100	X										
3.2.1.166 - Submit (Sub 1, Rd 1) for MHSRS-Digital twin (ABS01)	27/02/2021	04/03/2021		100	100	X										
3.2.1.167 - Receive acceptance (Sub 1, Rd 1) for MHSRS-Digital twin (ABS01)	15/07/2021	20/07/2021		100	100	X	X	X	X					X		
3.2.1.168 - Present (Sub 1, Rd 1) for MHSRS-Digital twin (ABS01)	16/08/2021	21/08/2021		100	100	X		X	X							
3.2.1.180 - Accept invitation (Sub 1, Rd 1) for Biomarkers-Symposium-In-vivo monitoring for bionics (ART10)	01/06/2021	17/06/2021		100	100	X										
3.2.1.181 - Check submission guideline (Sub 1, Rd 1) for Biomarkers-Symposium-In-vivo monitoring for bionics (ART10)	17/06/2021	22/06/2021		100	100	X										
3.2.1.182 - Draft (Sub 1, Rd 1) for Biomarkers-Symposium-In-vivo monitoring for bionics (ART10)	17/06/2021	14/08/2021		100	100	X	X	X	X					X		

9 of 10

10 of 10

Innovative In-Vivo Kinetic System to Facilitate Rehabilitation and Maintenance Residuum

Health After Limb Loss

DM190659

W81XWH-21-1-0215

PI: Laurent Frossard

Org: Griffith University

Requested Amount: \$969,182

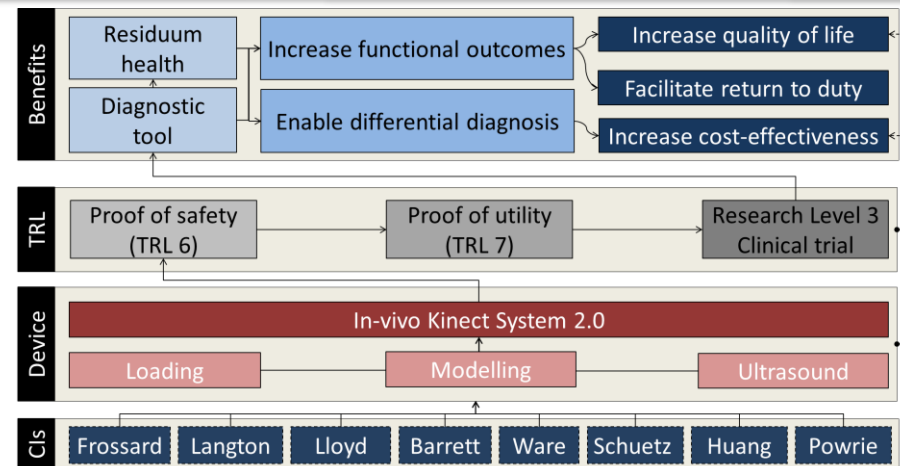


Study Aim

- This project aims at equipping rehabilitation specialists with the In-vivo Kinetic system 2.0 capable to diagnose common issues compromising residuum health of Service Members and Veterans that is essential for their return to duty and quality of life.

Approach

- Deliverable 1. Prototype of In-vivo Kinetic system 2.0** including loading and ultrasound measurements as well as neuromusculoskeletal modelling
- Deliverable 2. Proof of safety and efficacy (TRL-6)** to determine ability to safely and accurately estimate the loading and tissue deformation
- Deliverable 3. Proof of utility (TRL-7)** to determine the ability to measure differences in tissue deformation in response to loading constraints
- Deliverable 4. Design of clinical trial** including complete written description of scientific rationale and research activities for the clinical trial.



Overview of the development of In-vivo Kinetic system 2.0 integrating loading and Ultrasound measurements as well as neuromusculoskeletal modelling as diagnostic tool for of residuum health of current and former Service Members.

Timeline and Cost

Timeline and Cost												
Task	Pre	Funding period								Post		
		Year 1				Year 2						
		1	2	3	4	5	6	7	8	9	10	
Proof of concept of In-vivo Kinetic system 1.0 (TRL-5)	✓											
Ethics approval	✓											
Deliverable 1: Prototype of In-vivo Kinetic system 2.0												
Deliverable 2: Proof of safety and efficacy (TRL-6)												
Deliverable 3: Proof of utility (TRL-7)												
Deliverable 4: Design clinical trial												
Reports to DoD												
Publish outcomes												
Implement Research Level 3 clinical trial												
Investigate commercialization												
Estimated Budget (\$K)												

Goals/Milestones

Pre funding period – Feasibility and pre-requisite

✓ Proof of Concept (TRL-5)

✓ Ethical clearance

Q1-Q6 Goal: Prototype

□ Incorporate loading and DAU measurements as well as modelling

Q4-Q8 Goal: Proof of safety and efficacy (TRL-6)

□ Collect loading and DAU data with participants (TTA=6, TFA=6)

□ Compare kinetic and 3D motion analysis data

Q4-Q8 Goal: Proof of utility (TRL-7)

□ Collect kinetic data with participants (TTA=12, TFA=12)

□ Compare kinetic data with basic and advanced components

Q7-Q8 Goal: Design clinical trial

□ Conduct analytical planning study

□ Write protocol for the Research Level 3 clinical trial

Post funding period – Implementation

□ Conduct Research Level 3 clinical trial

Budget Expenditure : Maximum projected expenditure: \$969,182

Loading Effect of Prosthetic Feet's Anthropomorphicity on Transtibial Osseointegrated Implant

Mark Pitkin, PhD^{*,†}; Laurent Frossard, PhD^{‡,§,||,¶}

ABSTRACT

Introduction:

Osseointegrated implants for direct skeletal attachment of transtibial prosthesis carry risks that are yet to be fully resolved, such as early loosening, mechanical failure of percutaneous and medullary parts of implant, periprosthetic issues, and infections. Underloading could lead to early loosening and infection. Overloading might compromise the bone–implant interface. Therefore, Goldilocks loading regimen applied by transtibial bone-anchored prostheses is critical for safe and efficient development of osseointegration around the implant during rehabilitation and beyond. We hypothesized that Goldilocks loading could be achieved when ambulating with a so-called anthropomorphic prosthetic ankle showing moment–angle relationship similar to a sound ankle.

Materials and Methods:

Quantitative characteristics of the moment–angle curve of the sound ankle during dorsiflexion phase of a free-pace walking were extracted for 4 able-bodied participants (experiment 1). A slope of the moment–angle curve (stiffness) was calculated twice: for the first half and for the second half of the moment–angle curve. The difference of stiffnesses (those at the second half minus at the first half) was called the index of anthropomorphicity (IA). By definition, positive IA is associated with concave shape of the moment–angle curve, and the negative IA is associated with convex shape. In experiment 2, the same recordings and calculations were performed for 3 participants fitted with transtibial osseointegrated fixation during walking with their usual feet and the Free-Flow Foot (Ohio Willow Wood). The Free-Flow Foot was selected for its anthropomorphicity demonstrated in the previous studies with amputees using traditional socket attachment.

Results:

The IA was 5.88 ± 0.93 for the able-bodied participants, indicating that the stiffness during the first part of the dorsiflexion phase was substantially fewer than during the second parts, as the calf muscles resisted to angulation in ankle substantially less than during the second part of dorsiflexion phase. For amputees fitted with Free-Flow Foot, IA was 2.68 ± 1.09 and -2.97 ± 2.37 for the same amputees fitted with their usual feet.

Conclusions:

Indexes of anthropomorphicity, while of different magnitude, were positive in control able-bodied group and in the amputee group wearing Free-Flow Foot, which was qualitatively associated with concave shape of their moment–angle curves. The 3 usual feet worn by the participants were classified as nonanthropomorphic as their individual moment–angle curves were convex and the corresponding IAs were negative. Furthermore, this study showed that a foot with anthropomorphic characteristics tends to decrease maximal loads at the bone–implant interface as compared to the nonanthropomorphic feet and possibly may minimize the risks to compromise the integrity of this interface.

INTRODUCTION

Over 2.2 million U.S. patients are projected to have limb loss by 2020, with the number rising to 3.6 million by 2050.¹

In military medicine, advances in combat casualty care have increased survival rates of battlefield injuries, including high-energy open tibial fractures.² Through 2015, over 1,600 service members have had a major limb amputation as the result of combat wounds sustained in Iraq and Afghanistan.³ Over 20% of these members have lost more than 1 limb.⁴

Compensatory Synergy in Prosthetic Gait

Every step on a leg prosthesis requires the amputee to create a bending moment in the prosthetic ankle in order to overcome its resistance to flexion-dorsiflexion. To achieve it, the amputee generates by the stump a pair of equal and opposite forces applied to the socket (Fig. 1 (a) and (b)).⁵ When a prosthetic ankle is excessively resistive to angulation, a larger bending moment is required from the stump, and a correspondingly greater loading is applied back to it from the socket. This is illustrated with the convex moment–angle

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Poster presentation at the 2019 Military Health System Research Symposium, Kissimmee, FL, MHSRS-19-00186.

The views expressed in this article are those of the author and do not necessarily represent the official position or policy of the U.S. Government, the Department of Defense, or the National Institutes of Health.

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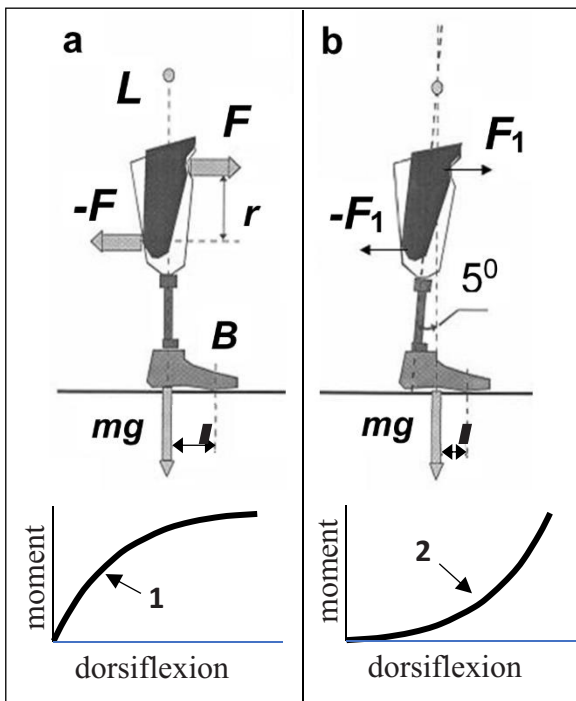


FIGURE 1. Upper panel—example of lean and bulbous transtibial residuum, where compressive and frictional forces from the socket contribute to immune dysregulation.¹² Lower panel—pair of forces F , $-F$ (a) and F_1 , $-F_1$ (b), which the amputee has to generate by the stump to dorsiflex the prosthetic ankle with convex (1) or concave (2) shape of its moment of resistance to dorsiflexion.⁵

graph in Fig. 1, indicating that the initiation of the angulation requires greater moment than its progression.

Conversely, if the ankle moment–angle graph is concave (Figs. 1, 2), allowing for almost free initial dorsiflexion, the force couple F_1 , $-F_1$ (Fig. 1 (b)) and corresponding loads on the stump are lower than F , $-F$ (Fig. 1 (a)).⁵

To decrease excessive loads from the socket walls, the wearer intuitively avoids bending the rigid ankle unit, which synergistically decreases the knee stance-flexion angle in the involved leg even though the anatomical knee joint is intact, resulting in increased gait asymmetry with the uninvolved leg.⁶ Another compensatory locomotor strategies include asymmetric loading of the limbs, altering kinematic parameters, and developing abnormal trunk motion.^{7–9} Relying heavily on their intact limb during ambulation, trans-tibial amputees have an increased risk of developing osteoarthritis in the knee of their intact limb.^{10–12}

Amputee patients who have endured battle trauma have a disproportionately high prevalence of skin problems on their stumps compared with civilian patients.^{13,14} These issues are experienced by 73.9% of patients who became amputees because of mine explosion and by 80.3% of patients who became amputees because of gunshot.¹¹ The skin in the socket of a prosthesis must withstand the compressive and frictional forces for which it is poorly adapted (Fig. 1, upper panel).^{10–12,15,16}

Some of these shortcomings could be alleviated by direct skeletal attachment where the socket is replaced by an osseointegrated fixation including a percutaneous part (abutment) that enables attachment of bone-anchored prosthesis. However, the surgical implantations of osseointegrated fixation carry risks that are yet to be fully resolved. For example, consistent excessive bending of the abutment because of nonregulated ankle resistance to angulation may compromise the bone–implant interface, leading to early loosening, mechanical failure of percutaneous and medullar parts of implant.¹⁷ Underloading could also lead to early loosening and infection.

Therefore, Goldilocks loading regimen applied by transtibial bone-anchored prostheses is critical for safe and efficient development of osseointegration around the fixation during rehabilitation and beyond (Fig. 2).

The purpose of the study was to verify a hypothesis that Goldilocks loading can be achieved with a so-called anthropomorphic prosthetic ankle, being defined as showing moment–angle relationship that resembles those generated by a sound ankle.^{5,6} To quantitatively compare the moment–ankle graphs, we developed a numerical parameter called index of anthropomorphicity (IA). We developed a technique for its calculation using 2 consecutive slopes of each moment–ankle graph (ankle stiffnesses).¹⁸

Specifically, the difference of these stiffnesses (those at the second half minus at the first half) has been called the IA. By definition, positive IA is associated with concave shape of the moment–angle curve, and the negative IA is associated with the convex shape.

A guidance for designing prosthetic feet suggests to mimic the stiffness of the anatomical ankle (anthropomorphic) to minimize the damaging moment on the residuum or the osseointegrated fixation as compared to nonanthropomorphic prostheses (Fig. 2).^{7,19}

Unfortunately, it is not seen in the majority of the current prostheses lead to overloading of amputees' residuum, with serious, which negatives consequences.

We believe that properly attuned stiffness of an anthropomorphic prosthetic ankle could significantly mitigate the risks of commonly experienced adverse events, particularly loosening, periprosthetic issues, and, possibly, infections.

In the long term, we plan to demonstrate experimentally an urgent need to develop regulations for the prosthetic feet performance and suggest the IA as the first numerical criterion of safe body–prosthesis interface.

MATERIALS AND METHODS

Ethics Review Statement

Gait study with able-bodied subjects was approved by Sinai IRB, New England Sinai Hospital, 150 York St., Stoughton, MA 02072, USA. Gait study with amputee subjects was approved by Queensland University of Technology IRB, 2 George St, Brisbane, 4000 QLD, Australia.

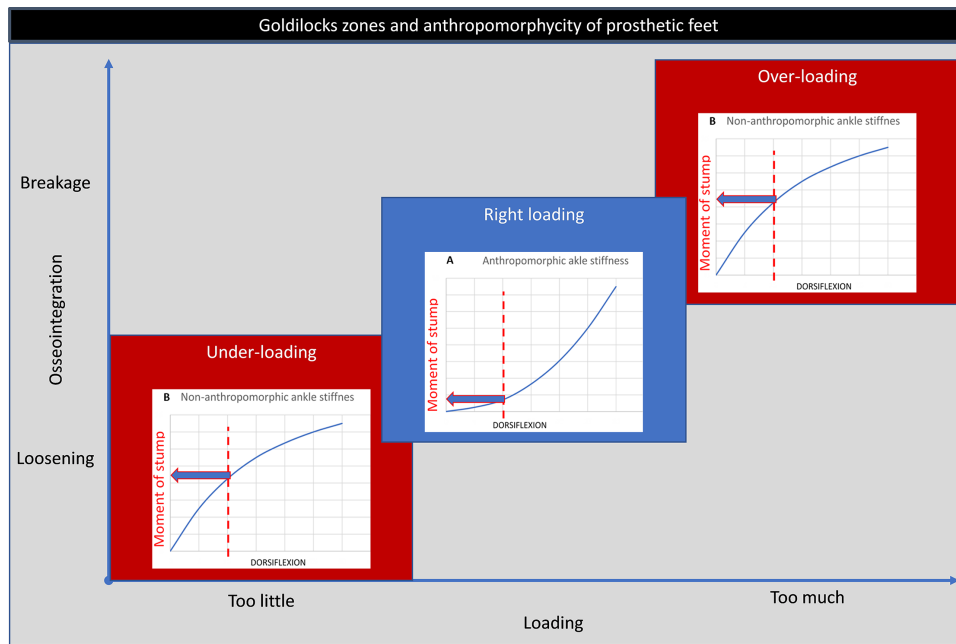


FIGURE 2. Potential relationship between Goldilocks zone and anthropomorphicity of prosthetic feet characterized by stiffness curve with concave shape for anthropomorphic prosthetic ankles (A) and convex stiffness curve nonanthropomorphic ankles (B).¹⁸

Study Design

The observational case series involves 2 experiments focusing on able-bodied and individuals with transtibial amputation. The sampling frequency for the recording on the 3D kinematic and kinetic data for experiment 1 was 200 Hz and that on the 2D kinematic data for experiment 2 was 60 Hz. In both experiments, participants were encouraged to take as much rest as needed between walking trials.

Experiment 1: Control Arm With Able-bodied Participants

The stiffness characteristics of sound ankle were extracted for 4 able-bodied participants (2 males, 2 females, 25 ± 2.5 years, 1.71 ± 0.12 m, 68 ± 1.72 kg). Participants were recruited by New England Sinai Hospital between January and April 2014.

Able-bodied participants walked 3 trials at self-selected speed in the Gait lab equipped with 6 cameras (Vicon Motion Analysis System, Oxford, UK) and 2 Kistler force plates (Kistler Instrument Corp., Novi, MI, USA). Dorsiflexion angle data were extracted from the 3D motion capture with the video and force plate sampling frequency of 200 Hz and using the Modified Helen Hayes full body reflective 9-mm marker set. Bending moment data were calculated using inverse dynamics.

Experiment 2: Intervention Arm With Participants With Transtibial Amputation

The experiment 2 was primarily designed to measure directly the load applied on the residuum of individuals with transtib-

ial osseointegrated implant during daily activities. One of the objectives of this experiment was to analysis kinetic data applied during daily activities performed in a nonexperimental environment. This reduced opportunities to record complementary kinematic data using a typical 3D motion capture. Alternatively, each trial was video recorded to assist a retrospective visual inspection, when needed. These footages were sufficient to determine the angle of dorsiflexion but not the speed of walking. Alternatively, we provided the cadence and other spatiotemporal characteristics.

The stiffness characteristics of the prosthetic feet was extracted for 3 participants with transtibial amputation fitted with press-fit osseointegrated fixation (2 males, 1 female, 58 ± 17 years, 1.76 ± 0.17 m, 83.46 ± 24.84 kg). Participants were recruited by prosthetists in Brisbane, Australia, between May and July 2017.

First, participants 1, 2, and 3 walked 5 trials with their own prostheses including RUSH foot (RUSH), Trias 1C30 foot, and Triton Vertical shock 1C6 foot (both by Otto Bock), respectively. Then, participants walked with the Free-Flow Foot (Ohio Willow Wood).¹⁸ The Free-Flow Foot was selected because of its stiffness curve's concavity, which is also observed in the ankle in the norm (Fig. 3).^{20,21}

The individual cadence, duration of GC and support phases ranged from 40 ± 1 strides/min to 52 ± 1 strides/min, 1.158 ± 0.02 s to 1.488 ± 0.034 s, and $61 \pm 1\%$ GC to $68 \pm 2\%$ GC with usual foot as well as 45 ± 1 strides/min to 51 ± 1 strides/min, 1.175 ± 0.016 s to 1.46 ± 0.029 s, and $61 \pm 1\%$ GC to $64 \pm 2\%$ GC with Free-Flow Foot, respectively.¹⁹

No marker set was used for experiment 2. Dorsiflexion angle data was collected using a digital camera (Canon, IXUS, USA) recording the 2D sagittal view on the prosthetic side. We clicked frame-by-frame on body landmarks (Center knee joint, Centre ankle joint, toe) using Kinovea angle tool to determine the ankle angle between the long axis of the leg and the foot.²² Bending moment was recorded at the sampling rate of 200 Hz using iPecsLab (RTC, USA) portable kinetic system including a tri-axial transducer embedded between the percutaneous part and ankle unit (Fig. 3).^{23,24}

Characterization of Ankle Stiffness

In both experiments, the ankle stiffness was characterized following the 12-step process we have recently published.¹⁸ This

automated data-based criterion process eliminated all subjective detections of key variables characterizing stiffness, and, therefore eliminated interrater variability in data extraction.

First, the shape of the stiffness curve was identified based on the isolation of the flat foot phase, the recognition of the curvature and the identification of the point of inflection of the stiffness curve. This point of inflection was the maximum point above or below the reference line between the lowest and highest point of the stiffness curve for convex and concave curve, respectively. Then, the stiffness variables were extracted. The overall ankle stiffness (K0) was to the slope of the line reference line. K1 and K2 were the slopes of the regression lines of stiffness curve before and after the point of inflection. The IA was calculated using $IA = K2 - K1$.

RESULTS

Mean dorsiflexion angle, bending moment and regression lines for K0, K1, K2, and IA of moment–angle curves exerted by sound ankle of able-bodied and prosthetic ankle of participants with osseointegrated prostheses fitted with Free-Flow Foot and their usual feet are presented in Fig. 4.

DISCUSSION

Outcomes

- Bending moments applied to the implant progressed by 73.27 ± 29.62 Nm for usual feet and by 54.99 ± 13.37 Nm for Free-Flow Foot. The averaged maximal bending moments generated by Free-Flow Foot decreased by 25% corresponding to 18 Nm that is well and truly larger than load measurements errors.^{18,25}
- Ankle stiffnesses in control group of the able-bodied participants were all positive with an $IA = 5.88 \pm 0.93$.
- Ankle stiffnesses the Free-Flow Foot demonstrated concave shape and were positive: $IA = 2.68 \pm 1.09$ confirming the Free-Flow Foot's classification as an anthropomorphic foot.
- Correspondingly, the 3 usual feet wore by the subjects were classified as nonanthropomorphic as their individual ankle stiffnesses demonstrated convex shape and were negative: $IA = -2.97 \pm 2.37$.

Interpretation

The study demonstrated that it is possible to differentiate angle of dorsiflexion and bending moment profile using IA between feet with different design characteristics. The study showed that a foot with anthropomorphic characteristics tends to decrease maximal loads. This could possibly minimize the risks and increase the longevity of the bone–implant interface while reducing rate of revisions without modifying existing technology of osseointegration. This study also revealed that a prosthetic foot with anthropomorphic characteristics could generate a stiffness profile that is comparable with an able-bodied ankle. This might suggest that an anthropomorphic foot, like to Free-Flow, could generate loading characteristics

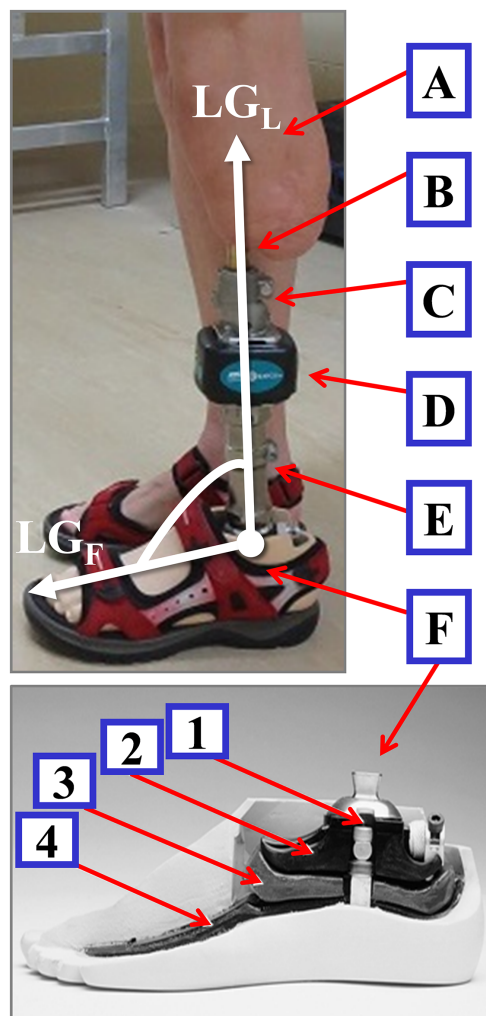


FIGURE 3. Example of long axes of the leg (LG_L) and foot (LG_F) used to determine ankle angle of dorsiflexion of the instrumented transtibial bone-anchored prosthesis attached to residuum (A) and percutaneous part of osseointegration fixation (B) including connector (C), transducer (D), pylon (E), and multi-axial rolling Free-Flow Foot (Ohio Willow Wood) (F) with anthropomorphic moments of dorsiflexion, inversion/eversion, and axial rotation featuring screw for adjustment of initial stiffness (1), tibial surface of rolling contact (2), cushion (3), and base talar surface of rolling (4).¹⁹

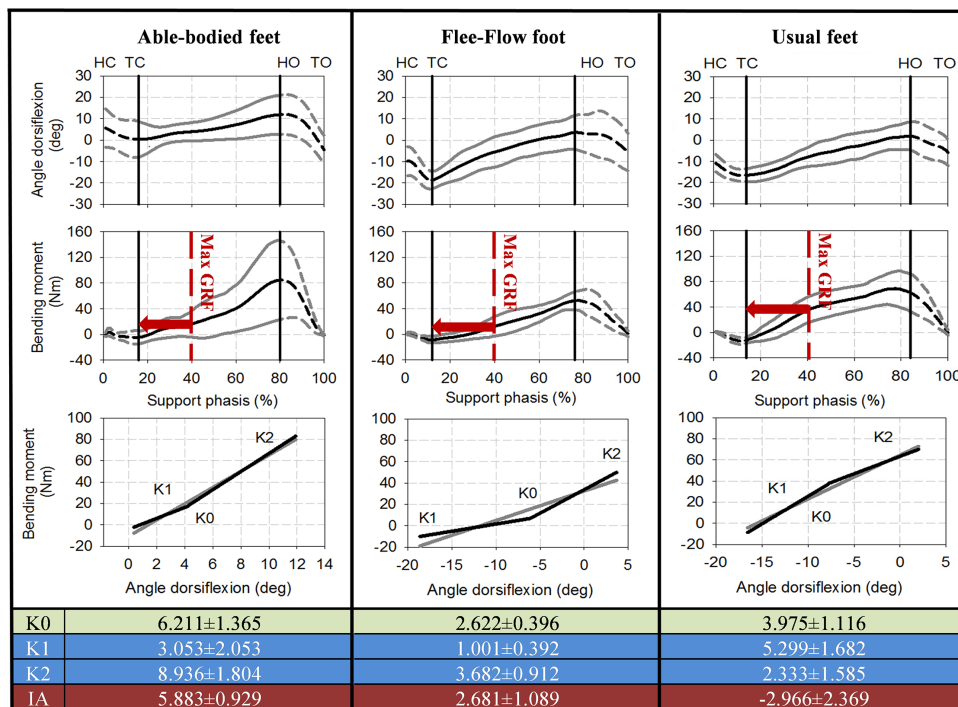


FIGURE 4. Angle of dorsiflexion and bending moment and regression lines for K0 and IA = K2–K1 of moment–angle curves for able-bodied (A) and participants with osseointegrated prostheses with Free-Flow (B) and their own feet (C). Upper graphs: averaged moment–angle diagrams in able-bodied and amputee subjects wearing either their own prosthetic feet or the Free-Flow foot. Lower table: values of K1, K2, and IA = K2–K1. HC, heel contact; TC, toe contact; HO, heel off; TO, toe off.

attuned with expected bone loading and therefore could potentially promote osseointegration. Such foot could then increase safety of the treatment provided. However, this hypothesis remained to be validated depending if the stiffness applied by anthropomorphic foot is, indeed, within the most favorable Goldilocks zone.

Limitations

This study presented the typical limitations of a retrospective preliminary study comparing kinematic and kinetic data collected with 2 small and unrelated series.

As we reported Frossard et al. (2019),¹⁸ the interpretation of differences in stiffness outcomes between prostheses was limited mainly because of unknown effects of confounders (e.g., individual length of residuum, distal position of transducer, short acclimation with Free-Flow Foot, foot size, and footwear).¹⁸ Unknown are also differences in spatiotemporal gait characteristics (e.g., speed of walking, walking base, step, and stride length), kinematics (e.g., trunk bending, knee flexion, and hip range of movement) and kinetics (e.g., knees and hips joint power) information.²⁶

Furthermore, the comparison on stiffness between series of able-bodied and individuals with transtibial amputation was limited by the discrepancies in measurements of ankle angle of dorsiflexion (e.g., automated 3D Vicon motion capture vs. manual 2D Kinovea movement analysis) and bending

moment (e.g., inverse dynamics using fixed force plates vs. direct measurement using wearable load cell).

Generalization

Generalization of the outcomes must be considered carefully giving the intrinsic shortcoming of a case-series study. Nonetheless, this study provided initial benchmark stiffness profile involving 42% of existing population with transtibial amputation fitted with press-fit fixation worldwide.

More generalizable is the methodology presented here to evidence ankle stiffness profile.¹⁸ This information should be considered and, possibly, educate the design of subsequent studies focusing on characterization of transtibial BAP. For example, the range of differences angle of dorsiflexion and bending moment might informed the sample size required to reach sufficient statistical power.^{21,27}

Altogether, this study provided initial evidence of worthiness of the IA that could possibly be integrated in ISO 22523, ISO 22675, ISO 10328, and the WHO Standards for Prosthetics and Orthotics, as the first quantitative standard of the prosthesis' performance.^{28–31}

Future Studies

Future longitudinal studies could compare ankle stiffness with various prosthetic constructs (e.g., components, alignment)

for a larger cohort of individuals fitted with a transtibial prosthesis.^{32,33} This could provide a better understanding of intra- and intervariability inherent to design of components and daily activities.^{34,35}

Subsequent cross-sectional studies could establish a link between ankle stiffness outcomes and additional 3D biomechanical (e.g., dynamics, kinematics, joint work, and power), physiological (e.g., EMG of residuum muscles, metabolic energy consumption, development of osseointegration, and skin damages), and participants' experience (e.g., PEQm, TAPES-M) information.

CONCLUSIONS

This work was an initial effort toward providing benchmark of stiffness data exerted by feet with and without anthropomorphic designs. Altogether, this study should be considered as a stepping stone for manufacturers of components, prosthetic care providers, and decision-makers developing international standards and guidelines toward better evidence-based prescription of safe prosthetic components to growing population of individuals with transtibial amputation fitted with osseointegrated fixation worldwide.

FUNDING

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The future of bionic limbs

Artificial limbs are essential to improve the quality of life of people living without limbs. Bionic limbs such as bone-anchored prostheses use implants directly inserted into the living bone for more stability. However, this technology still causes adverse events. Dr Laurent Frossard, Adjunct Professor of Bionics, and Professor David Lloyd, Professor of Biomechanical Engineering, combine biomechanics and computational modelling to develop a new integrated, wearable and non-invasive diagnostic device relying on the design of a digital twin of the residuum, which may ultimately improve the quality of life of people suffering from limb loss.

Over 2.2 million Americans are currently living with limb loss, and this number may double by 2050. The main causes of amputations are disease (such as diabetes) and trauma (car accidents or military conflicts). Limb amputation requires a lifetime of care. For each amputation, the cost of prosthetic care has been estimated to range between \$1.4 and \$2.8 million over a lifetime.

The everyday use of artificial limbs is critical to the wellbeing of these individuals. Orthopaedic surgeons, rehabilitation specialists and prosthetists work together and make bespoke recommendations with the intention to maximise comfort, stability and mobility of prosthetic fittings. However, this is not without difficulty.

CHALLENGES OF CURRENT PROSTHETIC ATTACHMENT

Prosthetic fittings that allow sustained high-levels of daily activities are difficult to achieve. Indeed, skin, nerves, muscles and bones of the residuum (also called the stump) may

be compromised by acute and chronic skin issues, oedema, neuroma, muscle contractures, or fractures. This makes daily prosthetic loading difficult to withstand. Moreover, sockets are challenging to fit around stumps with incongruous shapes. Patients living in hot conditions are particularly disadvantaged because perspiration due to heat and humidity makes sockets difficult to wear. Challenges with prosthetic fittings lead to frequent and, too often, permanent prosthesis abandonment in 25–57% of cases.

ROLE OF BIONIC SOLUTIONS

Alternatively, individuals experiencing overwhelming socket issues can be fitted with bionic limbs. A bionic solution is a technological platform relying on three interconnected pillars: the engine, the chassis, and the power-assisted steering wheel.

Advanced prosthetic components (the engine), such as microprocessor-controlled robotic-like artificial joints, are the central part of bionic solutions. Suitable attachment to the residuum (the chassis) can be achieved through direct skeletal attachment using osseointegrated implants, rather than a socket. The inner part of the implant is inserted into the living bone. The outer part protrudes from the skin of the residuum, enabling external attachment of the bone-anchored prosthesis.

Intuitive control of advanced components (the power-assisted steering wheel) can be achieved using sensors harvesting physiological signals from the brain, nerves or muscles. Bionic limbs therefore have physical connections with all sorts of body parts like the brain, nerves, muscles, skin and bone.

STRENGTHS OF BIONIC LIMBS

Promising life-changing benefits of bionic limbs showed by long-term efficacy studies are compelling for



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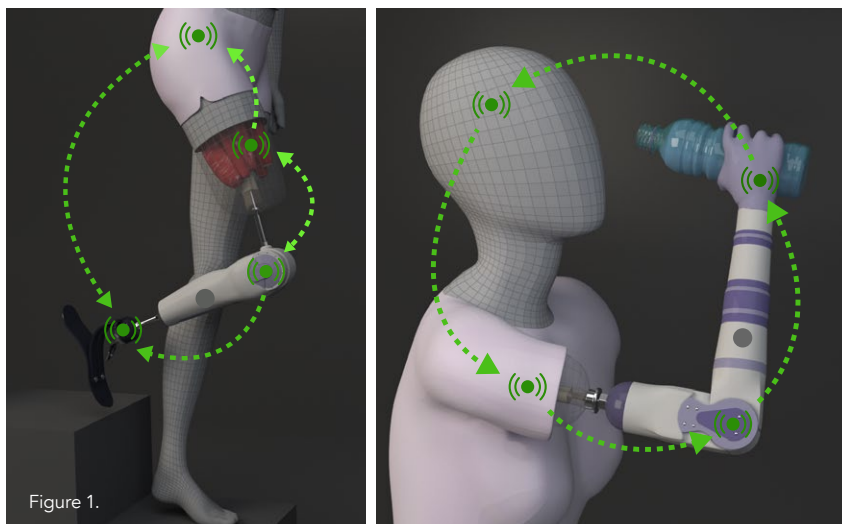


Figure 1.

patients. The direct attachment of the prosthesis through an osseointegrated implant has immediate benefits. It eliminates all typical burden associated with a socket, particularly the residuum's skin problems. It eases attachment and removal of the prosthesis. It also provides a much more comfortable sitting position and allows a much larger range of movements.

There is overwhelming evidence that bionic limbs attached to osseointegrated implants significantly improve mobility. Users walk faster for longer bouts of daily and recreational activities. This is especially obvious for young and active individuals. Users of osseointegrated

Bionic limbs can potentially cause issues with implant stability, bone fracture, breakage of the implant parts and infection. All these adverse events have several common negative effects. They cause pain. They significantly disturb the lifestyle because they limit usage of the prosthesis for prolonged duration. They also cost money paid either by the healthcare system or the users themselves as out-of-pocket expenses.

A NEED TO IMPROVE

Efforts must be made to lessen severity and incidence of adverse events of bone-anchored bionic prostheses. Prostheses must become safer and more accessible to a large population

The digital twin of the residuum is a virtual replica living inside the computer.

implants report that they feel that their prosthesis is more like a part of their body; they experience a phenomenon called osseoperception. Practically, they can feel more vibrations. This helps to feel where the prosthetic foot is on the ground and the type of surface the person is walking on. Dr Frossard has published studies showing that when compared to typical socket prostheses, bone-anchored bionic prostheses significantly improved quality of life by about 17%.

WEAKNESSES OF BIONIC LIMBS

Occurrence and severity of adverse events with bone-anchored bionic prostheses are yet to be fully resolved.

worldwide. Significant reduction of the risks is a prerequisite for unequivocal approval from international governing bodies such as the FDA. Safer treatment will also warrant a more successful development of the next generation of brain-activated neuroprostheses.

A NEW RADICAL APPROACH

Dr Frossard and Prof Lloyd believe that one way to address the current shortcomings of bone-anchored bionic prostheses is to have a radical new approach relying on the design of a 'digital twin' of the residuum, to assess residuum health under real-life conditions. Indeed, adverse events

primarily depend on residuum health, which is usually assessed through physical examinations, medical tests and imaging modalities. This is not sufficient to examine the effects of the prosthesis while wearing it.

This is why Dr Frossard and Prof Lloyd are currently developing an integrated, wearable and non-invasive diagnostic device. By computing physiological measures related to residuum health and creating a virtual replica (digital twin) of the residuum, the diagnostic device could improve care of patients and facilitate their rehabilitation.

FEATURES OF THE DIAGNOSTIC DEVICE

Different sensors assess the mechanical constraints applied by the bone-anchored bionics on the residuum and measure the resulting movements of the tissues (bone, muscle, tendon, fat, skin) within the residuum. The back end of the device consists of the software integrating all this information into a personalised digital twin of the residuum. Basically, the digital twin of the residuum is a virtual replica living inside the computer. It corresponds to the high-fidelity physics-based model of the different tissues constituting the residuum. The front end of the device consists of a handheld device (such as a smartphone) that provides a visual animation of the model in real time so that patients and clinicians equipped with the device and see can how movements impact the inside of the body.

IMPROVING REHABILITATION FOR PATIENTS

The diagnostic device provides a radically new and empowering experience for patients. It can help them monitor how their loading positions stimulate specific zones of the implant in real time using a friendly-user interface and guide them to adopt pain-free positions. By improving stability, it can reduce risks of loosening, fractures and infections. It can also allow patients to better inform clinicians about how a treatment or intervention feels. Altogether, this new approach can increase the quality of life of individuals suffering from limb loss.

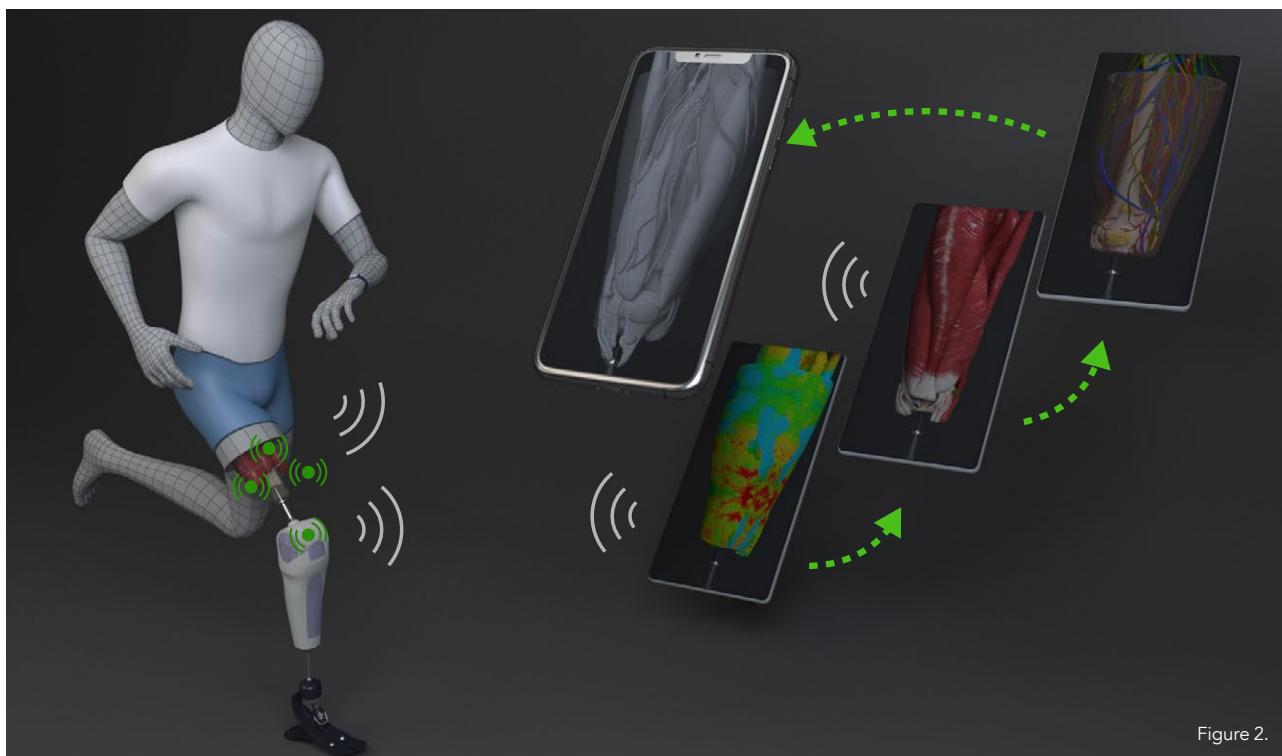


Figure 2.

MAKING THE UNKNOWN VISIBLE TO CLINICIANS

The digital twin provides detailed personal records on residuum health, osseointegration and adverse events. The diagnostic device therefore creates tremendous opportunities to extend precision medicine: by assisting clinicians

DEVELOPING THE NEXT GENERATION OF BIONIC LIMBS

The digital twin enables the simulation of specific effects from a particular intervention before actually doing the intervention. It allows us to predict outcomes and, possibly, anticipate the likeliness of adverse events. It can

The digital twin will also allow new neuroprostheses to reverse the current dynamics between the users and their prosthesis. At the moment, despite advances in microprocessors controlling the prosthesis, users must adapt to the functions of their prostheses. With the new neuroprostheses, it will work the other way around: the prostheses will respond to the individual command of the users.

The diagnostic device provides a radically new and empowering experience for patients.

in detecting residuum issues during rehabilitation and beyond, it helps them make more accurate decisions. In the long term, the accumulation of data contributes to developing models that can predict adverse events such as unfavourable bone remodelling or elevated inflammatory response.

REDUCING HEALTHCARE EXPENSES

The diagnostic device could potentially improve cost-effectiveness of bionic solutions by reducing over-prescription when considering care interventions. By improving residuum health, the diagnostic device could also reduce the lifetime financial burden on healthcare system of treatments due to poor residuum health of patients.

enable immediate adjustments to residuum loading, stresses and strains, and therefore potentially improve long-term residuum health.

The use of a digital twin is essential to develop intuitive control of advanced components using sensors harvesting physiological signals from the brain, nerves or muscles. The aim is to enable patients to control bionic limbs by merely thinking about the action they want to perform. The diagnostic device can enable safer developments of personalised neuroprostheses by making the link between the command (like the contraction of muscles) and the functions of the prosthesis (such as ascending stairs, grabbing an object).

Dr Frossard and Prof Lloyd's work is essential to opening up access to new bionic solutions, improving safety and mobility as well as, ultimately, improving the quality of life of individuals suffering from limb loss.

To find out more: https://eprints.qut.edu.au/view/person/Frossard,_Laurent.html



Behind the Research



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Dr David Lloyd



Research Objectives

The team are developing accurate personalised digital twins of humans and devices that operate in real-time by combining data from laboratory-based instrumentation, multimodal medical imaging and wireless wearable devices. These technologies are being applied to a range of medical diagnostics required for personalised surgical planning, implant design and manufacture, and assistive devices.

Detail

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Bio

Adjunct Professor Laurent Frossard
Chief Scientist Officer at
YourResearchProject

Dr Laurent Frossard is a bionic limbs scientist passionate about developing ground-breaking prosthetic solutions to improve life of individuals suffering from limb loss. He is internationally recognised as a researcher and independent expert for his unique expertise in bionic limbs. He approaches bionic solutions from an all-rounded perspective integrating prosthetic biomechanics, clinical

benefits, service delivery and health economics. Dr Frossard has over 25 years of experience both in academia and private industries in Australia, Canada and Europe working with more than 100 organisations worldwide. He is currently the Director and Chief Scientist Officer at YourResearchProject Pty Ltd and Adjunct Professor at the Griffith University, Queensland University of Technology and University of Sunshine Coast in Australia.

Professor David Lloyd BSc, PhD, FISB
Professor of Biomechanical Engineering

David Lloyd is a Professor of

Biomechanical Engineering and Director of the Griffith Centre of Biomedical and Rehabilitation Engineering. He has published over 250 full scientific articles (16,300 citations, 66 h-index, Google Scholar), and received over \$AUD 34M in research funding with many awards such as the Fellow of the International Society of Biomechanics, 2020 Geoffrey Dyson Award, and The Australian 2019 Biophysics Field Leader. Prof Lloyd and his team develop personalised digital twins of humans for medical technologies to assist surgical planning as well as implant design and neuro-assistive devices.

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Personal Response

What sparked your passion for bionic limbs?

“ I have always been fascinated by the magic of computers and the mystery of the human body. Bionics is a way to combine these two passions. I feel privileged to work in the field of bionics that can ultimately transform lives of people suffering from limb loss. ”



concentrations of circulating IGF-I system components: a preliminary study. *Growth Horm IGF Res* 2012; 22(5):151-157. <https://doi.org/10.1016/j.ghir.2012.04.007>

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I008

Bone and calcium metabolism markers as an indicator of skeletal adaptation and stress fracture risk in military personnel

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Introduction: Bone is in a constant state of remodelling to remove old or damaged bone and form new bone. This process of bone resorption and formation is 'coupled' to preserve bone size, structure, and mass. Several physiological challenges—typical of military training and employment—can disturb bone metabolism including high levels of physical activity and energy and sleep restriction. Accumulation of damaged bone during exercise stimulates targeted remodelling, a process where the resorption of damaged bone can cause pores in the cortical bone and eventually stress fracture. Bone resorption also plays an important role in maintaining circulating calcium homeostasis during exercise. These changes in bone metabolism can lead to an (mal) adaptive bone response with implications for stress fracture risk and long-term skeletal health.

Approach: This presentation will provide an overview of the role of markers of bone and calcium metabolism as indicators of skeletal adaptation and stress fracture risk in military personnel. The physiological processes of bone resorption and bone formation, and the role and accuracy of using biomarkers to reflect these processes, will first be reviewed. An overview of emerging novel markers of bone and calcium metabolism will also be provided. Finally, a critical review of military and non-military studies will be provided to identify the utility of these biochemical markers in monitoring the responses to exercise, nutritional interventions, and energy and sleep restriction, with implications for skeletal (mal) adaptation and stress fracture risk.

Discussion/conclusions: Several established circulating and urinary biomarkers are available for measuring bone resorption, bone formation, and calcium metabolism. Bone resorption and bone formation are complex temporal processes and consideration needs to be given to the underlying processes each biomarker represents. Novel methods of measuring calcium isotopes with isotope mass ratio spectrometry appear promising for measuring whole-body bone calcium balance with implications for quantifying bone gain or loss during acute interventions. Laboratory studies show that the individual stressors associated with military training, including high-intensity exercise and energy and sleep restriction all have independent effects on bone formation, bone resorption, or both, in men and women. Biomarkers of bone and calcium metabolism are responsive to military training in both men and women, but it is unclear how these processes relate to the observed structural changes in bone. The implications of changes in bone resorption, bone formation, and calcium metabolism for stress fracture risk and long-term skeletal health is not clear.

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I009

Other physical and functional markers of bone stress injury

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Introduction: The purpose of the talk is to identify the physical and behavioural characteristics likely to be associated with bone stress injury. Over the past decades many risk factors for bone stress injury have been reported for athlete and military populations. The data on which those reports have been based, however, has not always been of the highest quality. The result has been a plethora of suspects but a dearth of certainty around the biological, morphological, behavioural, and functional characteristics that should be the focus of preventative and therapeutic measures for bone stress injury. This presentation will round off the symposium on Biomarkers for Bone Health and Metabolism by addressing risk factors of particular relevance to bone stress injury.

Approach: The literature will be reviewed to examine the gamut of risk factors that have been identified to have an association with incidence of bone stress injury in athletes and military recruits (e.g., age, sex and hormone status, race, bone mass and morphology, lean mass and strength, biomechanical anomalies, footwear, medications, sleep, diet, tobacco, alcohol, training type and intensity). Heterogeneity of findings will be discussed and the risk factors that have been determined from the highest quality evidence identified.

Discussion/conclusions: It is well recognised that the primary risk factor for bone stress injury in athletic and military populations is too much training, too soon. In fact, the inherent ability of bone to adapt to increases in habitual loading will avert tissue failure under normal circumstances. When the rate or magnitude of increase in loading is very great however, the accumulation of microdamage in bone tissue can outstrip the rate of tissue adaptation. While this behavioural characteristic is by far the most influential risk factor for bone stress injury, a number of other physical and behavioural attributes likely increase that risk. As a clinical trial aiming to inflict BSI in order to examine risk factors would be ethically unacceptable, risk factor data has historically been collected from observational studies, limiting the ability to make causal inferences or parse out complex interactions. It is nevertheless abundantly clear that when rapidly increased loading is unavoidable, such as during recruit training, optimising modifiable factors of risk such as physical fitness and nutrition prior to doing so would be based on sound principles of bone physiology.

Acknowledgements: Funding for some of the data was provided by US Army MPMC DAMD17-98-1-8519 and the Defence Health Foundation (Australia).

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I010

Can a digital twin of the residuum improve bionic solutions for individuals suffering from limb loss?

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Introduction: Rehabilitation specialists need to improve differential diagnosis of the neuromusculoskeletal health issues of the residuum experienced by former and active Service Members suffering from limb loss¹. The development of a portable and non-invasive diagnostic device seeks to help maintain residuum health and support bionic solutions. Here, we outline the latest developments of an In-vivo Kinetic system 2.0 (Fig. 1), a diagnostic device that combines:

- Measurements of the mechanical loading applied to the site of amputation using portable wireless sensors²,
- Measurement of the tissue distribution within the residuum made by the newly developed Dynamic Anatomical Ultrasonography,
- Neuromusculoskeletal modelling or “digital twinning” of the residuum for a real-time personalized animation of the residuum during static and dynamic loading conditions³.

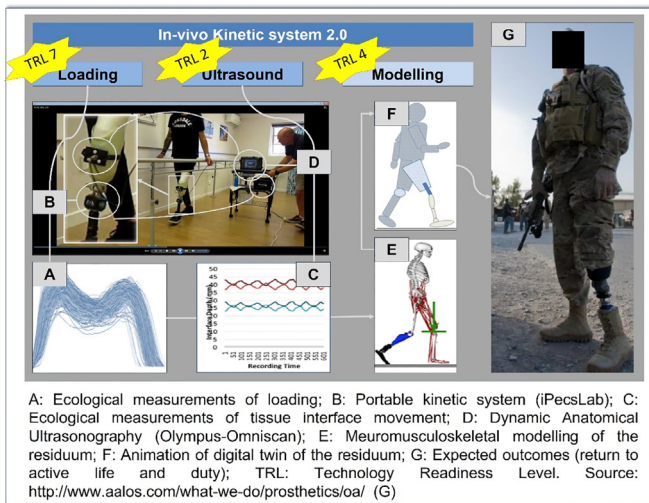


Fig. 1. Overview of In-vivo Kinetic system 2.0 relying on digital twin of the residuum that could enable innovative prosthetic care pathways for Service Members and Veterans with lower limb amputation.

Technology readiness levels (TRL) were estimated at 7, 2, and 4 for the loading, ultrasound, and modelling parts, respectively. Thus, demonstrating feasibility to develop an integrated, wearable and non-invasive In-vivo Kinetic system 2.0 capable of performing patient-specific differential diagnosis of residuum health under real world conditions⁴.

However, barriers inherent to biosensors (e.g., ultrasound measurements, synchronisation), the creation of a digital twin (e.g., tissues mechanical property) and integration (e.g., discrepancies of TRLs) continue to be challenging. The clinical roll-out of the device will require overcoming these issues and consideration of discrepancies between the skills of practitioners and siloed health care organizations.

Discussion/future directions: This system will provide unparalleled holistic insight into residuum health and productively disrupt the current model of health care. Hopefully, this diagnostic device will facilitate restoration of mobility, return to active duty, and, ultimately, improve life of the growing population suffering from limb loss considering bionic solutions.

Acknowledgements: This work was supported by the FY19 Defense Medical Research and Development Program through the Joint Program Committee 8 / Clinical and Rehabilitative Medicine Research Program Restoring Warfighters with Neuromusculoskeletal Injuries Research Award (RESTORE) under Award No. W81XWH2110215-DM190659. Opinions, interpretations, conclusions, and recommendations are those

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1011

Personalized digital humans for rehabilitation and assistive devices

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Introduction: Understanding the influence of whole-body activity (e.g., physical training) on the biophysics at organ-, tissue-, and sub-tissue-levels is important for designing optimal physical training/rehabilitation and effective control of assistive devices. The Griffith Centre of Biomedical and Rehabilitation Engineering (GCORE) has developed mature rehabilitation and assistive device technologies underpinned by the Personalized Digital Human (PDH).

Method framework: The PDH is a physics-based digital twin of the human (and devices), which includes representation of an individual's bones, articulations, muscles, and other soft tissues. Coupled with peripheral muscle excitation (e.g., electromyograms), PDH encodes muscle activations specific to the individual (e.g., sensitive to training and disease) and task (e.g. sensitive to control task)¹.

Examples: To analyze human performance, PDH quantifies mechanical parameters such as net loading to the body, organ (e.g., whole bone; Fig. 2), joint, tissue (e.g., ligament; Fig. 1)², and sub-tissue (e.g., local strain in tendon; Fig. 1)¹. Within a control system³, PDH predicts muscle activations that produce target mechanics (e.g., torque on rehabilitation ergometer), compliment an assistive device (e.g., torque above motor-driven assistance), sensory afferents that augment/simulate sensory experience (e.g., haptics), and safety margins (e.g., critical stresses) (Fig. 2).

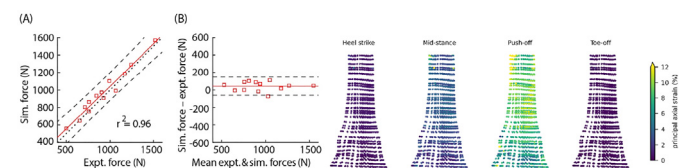


Fig. 1. (Left) Anterior cruciate ligament (ACL) force model where measured (Expt. force) and simulated (Sim. force) ACL forces are (A) highly correlated with (B) minimal bias. The ACL model can function in real-time to provide biofeedback to control ACL loading². (Right) Real-time visual feedback of Achilles tendon strain, based on PDH, was implemented in Javascript three.js (r100) and visualized on a mobile phone via internet browser (Mozilla Firefox)¹.

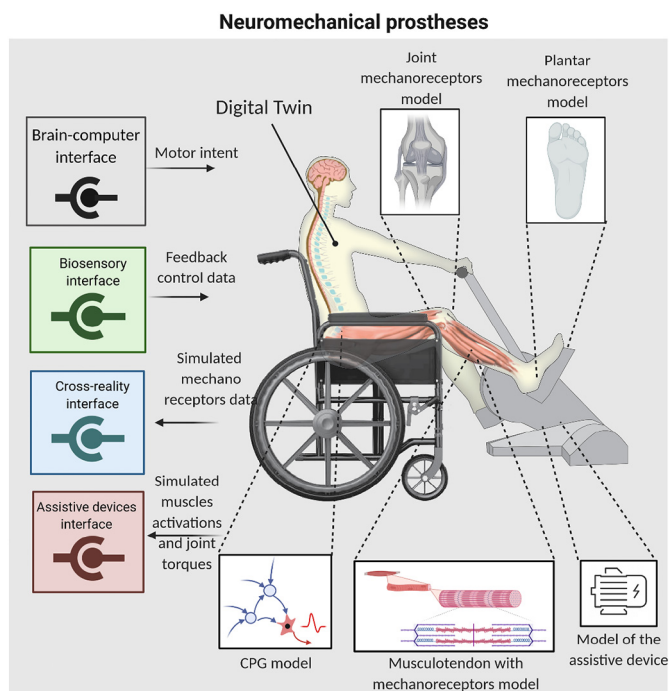


Fig. 2. The PDH used within a control system to interpret sensor data, model the internal states of the human, provide augmented sensory afferents, and perform safety checks on the loading of musculoskeletal tissues³.

Discussion/future directions: Currently, we are developing direct fusion of PDH with prosthesis design to optimize amputee residuum health⁴. Further, PDH could readily be extended to become the personalized digital soldier, with extensive scope for use in monitoring training loads, improving rehabilitation efficacy, and designing equipment to better interface with humans.

Acknowledgements: The PDH is the result of numerous nationally-competitive and industry grants for over 2 decades.

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I012

Development of dynamic anatomical ultrasonography to advance personalised prosthetics

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^bCustom Prosthetics, Australia

Introduction: Ultrasound is routinely used by rehabilitation specialists to establish differential diagnosis of the residuum's neuromusculoskeletal issues experienced by former and active Service Members suffering from limb loss¹. Ultrasound offers real-time, non-ionizing, unspecialised facility assessment. Conventional imaging modalities record a qualitative static image. More fundamental signal/data display modalities such as the raw radio-frequency signal and A-mode are rarely utilised, although offer

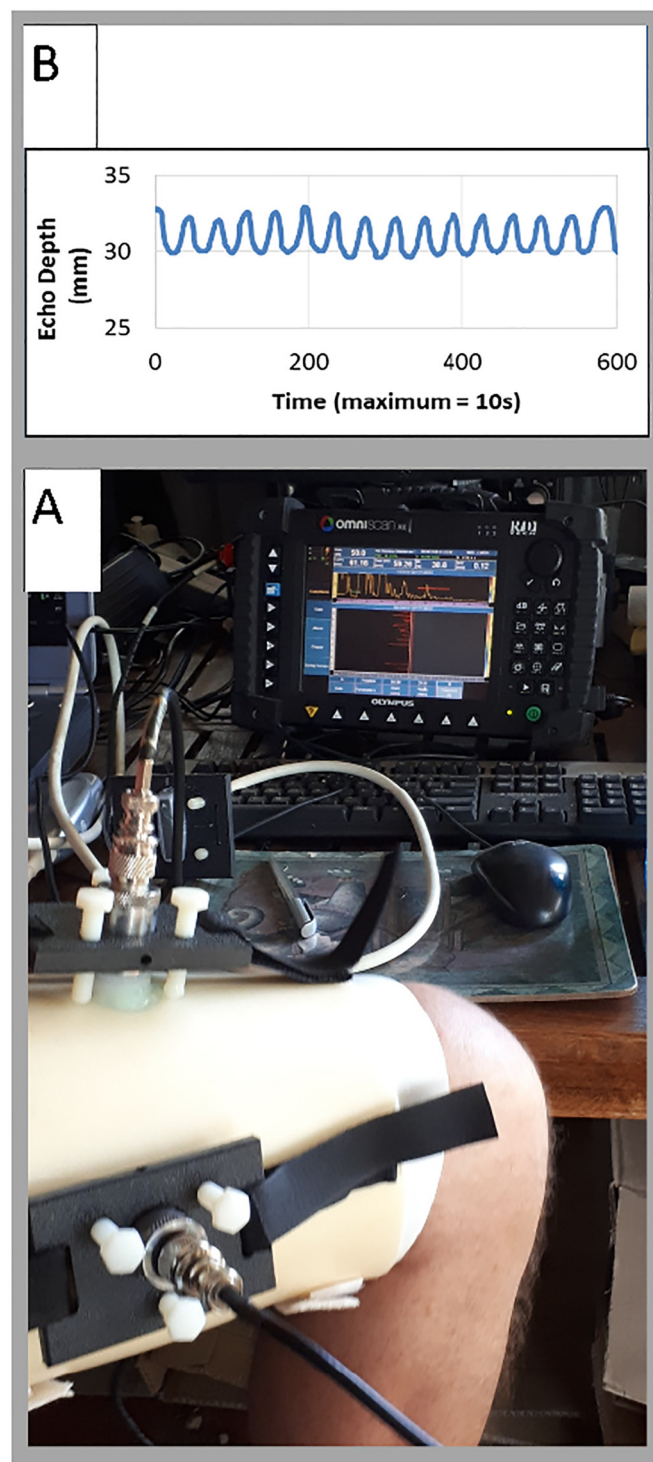


Fig. 1. Photograph of a custom pseudo socket incorporating two ultrasound transducers attached to an asymptomatic subject (A), along with echo depth of the femur during limb motion (B).

specialised opportunities, particularly for quantitative tissue characterisation, when the subject is mobile, and when several anatomical locations need to be synchronously assessed.

Our aim is to develop a wearable ultrasound biosensor system that provides real-time assessment of various anatomical compartment dimensions within a post-amputation residual lower limb of former and active Service Members, termed Dynamic Anatomical Ultrasonography (DAU).

Methods and results: The Olympus Omniscan MX is a highly-portable and rugged ultrasound instrument aimed primarily at the industrial sector. It incorporates the facility to connect up to eight individual single-element ultrasound transducers.

A custom pseudo prosthetic socket was created for an asymptomatic subject, to which were attached two 1 MHz, 19 mm diameter ultrasound transducers, as shown in Fig. 1A. Ultrasound signal data was recorded for a defined measurement period of 10 seconds as the subject repeatedly lifted and lowered their thigh. Utilising the semi-automated time-gate signal detection facility, the depth of the femur bone surface was recorded, shown in Fig. 1B.

Discussion/future directions: We have demonstrated the ability to monitor motions of the femur; of particular note is that measurements were obtained through the socket and silicone liner in addition to the overlying soft tissues. It is hypothesised that knowledge of the dynamic behaviour of the various tissue compartments will improve our understanding of the biomechanics associated with the residual limb of individuals suffering from limb loss and, furthermore, facilitate the fitting and development of bionics prostheses for former and active Service Members².

Our long-term aim is to investigate whether a combination of ultrasound and mechanical load biomarker data, fed into a 'Digital Twin' computational simulation will improve socket design, restore mobility, facilitate return to active duty, and, ultimately, enhance users' quality of life.

Acknowledgements: This work was supported by the FY19 Defense Medical Research and Development Program through the Joint Program Committee 8 / Clinical and Rehabilitative Medicine Research Program Restoring Warfighters with Neuromusculoskeletal Injuries Research Award (RESTORE) under Award No. W81XWH2110215-DM190659. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the FY19 Defense Medical Research and Development Program.

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<http://dx.doi.org/10.1016/j.jsams.2021.11.013>

1013

Advanced modelling of residuum to improve bionic limbs

David G. Lloyd^a, Nataliya N. Perevoshchikova^a, Christian M. Langton^a, Rod S. Barrett^a, Jayishni N. Maharaj^a, Laurent A. Frossard^a

^aGriffith Centre of Biomedical and Rehabilitation Engineering, Griffith University, Australia

Introduction: Military personnel can suffer limb loss and subsequently use bionic limbs affixed to their residuum. The residuum's different musculoskeletal tissues undergo continual

adaptation due to stress-strains experienced during daily activities, affecting residuum health. These stress-strains depend on the interface between the prosthesis and residuum, it is therefore critical to assess the residuum's internal stress-strains during daily activities to optimise prosthesis design and use. A framework is presented to create a *Digital Twin* of an amputee's residuum that operates in real-time and validated using a phantom of the residuum¹.

Methods and results: The current workflow used for real-time Achilles' tendon (AT) strain is being translated for use with the residuum² (Fig. 1). Dynamic Anatomical Ultrasonography³ is used to measure the unloaded and loaded 3D shape of the AT or residuum (Fig. 1A) to generate unloaded and loaded solid meshes (Fig. 1B). Since the external loading state of AT or residuum is known, material properties can be inversely determined, and internal stress-strain distribution ascertained using finite element models (FEM) (Fig. 1C).

Next a range of loads are applied to the AT or residuum FEM that generate a matrix of corresponding stress-strains (Fig. D). A Machine Learning (ML) model is trained to link all loading and stress-strains states (Fig. E). Operationally, external loading, e.g., real-time residuum loading measured using prosthesis-embedded load-cell, are applied to the ML model to estimate the AT or residuum stress-strain, which is rendered in real-time on a smart phone (Fig. 1G and 2B).

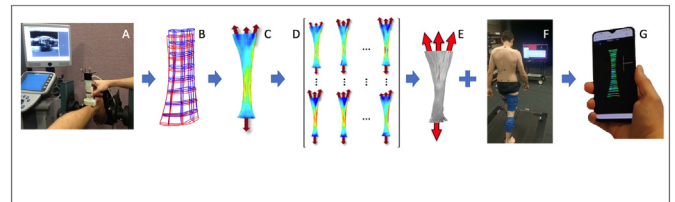


Fig. 1. Workflow to generate real-time Achilles' tendon stress-strain in daily activities that is being translated for use with the amputee's residuum.

Workflow validation uses a phantom of the residuum and its internal structures of known material properties. The phantom, placed in the Dynamic Anatomical Ultrasonography rig (Fig. 2A), has forces applied to phantom's femur and socket, and 3D shape changes of the different tissues measured.

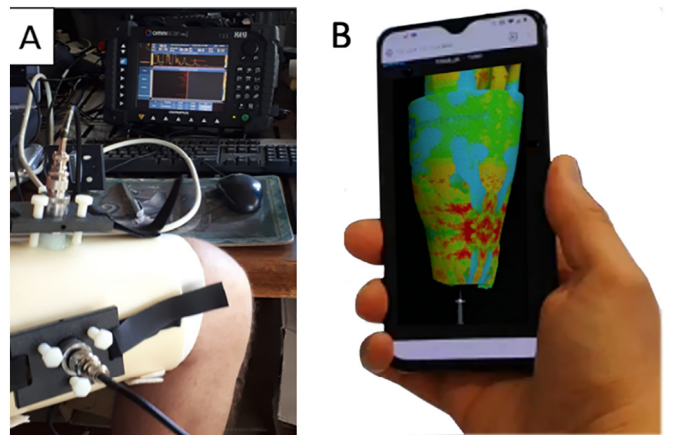


Fig. 2. (A) Dynamic Anatomical Ultrasonography to measure residuum 3D shape changes and (B) residuum tissues stress-strain rendered on smart phone.

Discussion/future directions: This workflow generates AT stress-strain in real-time while a person is walking and is being translated for use in estimating residuum stress-strain during daily

specialised opportunities, particularly for quantitative tissue characterisation, when the subject is mobile, and when several anatomical locations need to be synchronously assessed.

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1013

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David G. Lloyd^a, Nataliya N. Perevoshchikova^a, Christian M. Langton^a, Rod S. Barrett^a, Jayishni N. Maharaj^a, Laurent A. Frossard^a

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adaptation due to stress-strains experienced during daily activities, affecting residuum health. These stress-strains depend on the interface between the prosthesis and residuum, it is therefore critical to assess the residuum's internal stress-strains during daily activities to optimise prosthesis design and use. A framework is presented to create a *Digital Twin* of an amputee's residuum that operates in real-time and validated using a phantom of the residuum¹.

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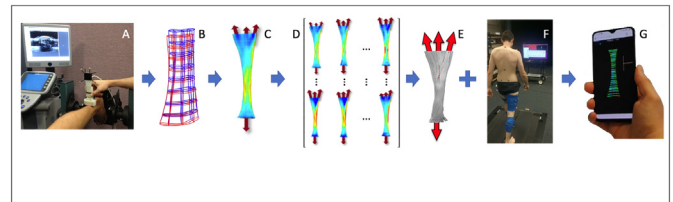


Fig. 1. Workflow to generate real-time Achilles' tendon stress-strain in daily activities that is being translated for use with the amputee's residuum.

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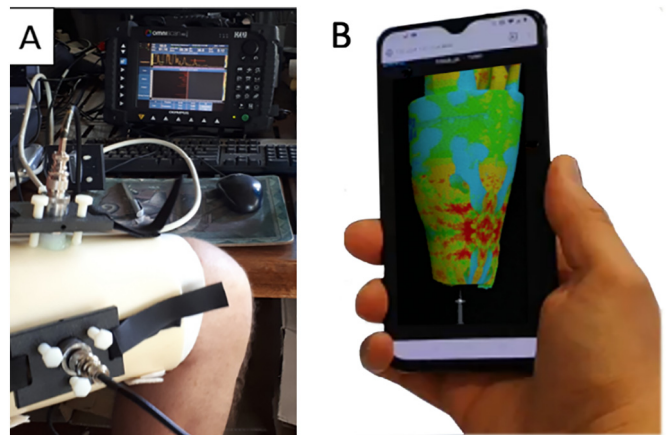


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Discussion/future directions: This workflow generates AT stress-strain in real-time while a person is walking and is being translated for use in estimating residuum stress-strain during daily

activities, enabling personalised prosthesis design and use for military personnel.

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<http://dx.doi.org/10.1016/j.jsams.2021.11.014>

I014

Modelling of fatigue, activity, and terrain in field environments for decision support

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Introduction: Current methods to assess human activity recognition (HAR) and fatigue do not account for environmental factors and noise which occur down range. Wearable sensors and machine learning (ML) models offer the promise of determining fatigue in the field however the number of sensors and comparison to gold standards are problematic when translating to the field. Fatigue can be quantified as the level of performance to perform a task relying on a cascade of overlapping redundant systems, influenced by physical, central and psychological factors¹. The complexity of fatigue makes ML a promising computational approach². This work investigates using an ML model with single wearable sensor to predict cognitive and physical fatigue in an outdoor environment.

Methods: There are challenges moving into the field including logistics, validation, battery power, equipment size, assessment distractions and validation protocols. The research used a novel protocol to collect data for clinical comparison and computational model training in an unstructured environment with varying fatigue levels with self-pacing.

The trail was segmented by terrain surface, slope or obstacle using observation, satellite imagery and GPS. Sensor data was collected from a Zephyr BioHarness (Medtronic, Minneapolis, USA). Activity was voluntary and self-paced so transitions could not be determined a priori. Terrain included slope, crossing obstacles (cross river or climb fence) and surfaces including road, gravel, clay, mud, long grass. A goal was set to run 100 km with 10,000 feet of ascent within 25 hours to trigger goal assessment with possible action crisis, which required each one-hour cycle to complete 4 km trail in 35 minutes. Mental load used a software tool implementing the NASA Multi Attribute Test. Clinical comparison was performed against, Stroop, Jump Height, Finger Tap Test (FTT), Trail Making A (PVSAT), spatial memory. Separate convolutional neural networks were developed and trained to predict HAR, physical fatigue and cognitive fatigue.

Results: HAR results for 5 features accuracy 0.98 and minimum class precision for one-off activity 0.802. Fatigue prediction accuracy was highest for FTT right hand (R^2 0.71) and Jump Height (R^2 0.78).

Discussion/conclusions: This experiment showed a single sensor and ML model can achieve accurate results for HAR, cognitive fatigue and physical fatigue equivalent to gold standard tests performed in clinic. Additionally, a field environment can be calibrated to enable translational real world dataset noise and equipment acceptable to an operator. Further research is required for more individuals, terrain and equipment carriage, sleep deprivation, dehydration, and recovery cycles.

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<http://dx.doi.org/10.1016/j.jsams.2021.11.015>

I015

A novel method to assist clinical management decisions following mTBI using wearable sensors and machine learning

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Introduction: The consequences of traumatic brain injury (TBI) significantly affect athletic populations, military personnel, and the general public around the world. Mild TBI (mTBI) accounts for 95% of all TBIs, up to 50% of patients with these “mild” injuries will struggle to perform tasks that would typically be trivial for weeks/months post-injury¹. Some patients present with functional impairments due to a predominantly physiological cause, while others suffer due to a primarily vestibular issue. Best practice is to prescribe an individualised treatment plan based on the underlying source of symptomology², but this process is currently highly reliant on the availability of an adequately trained clinician. Laboratory studies using electrocardiography (ECG) and force plates have identified differences between mTBI patients and healthy controls^{3,4}, but no research has investigated whether physiological and biomechanical data can differentiate between subgroups of mTBI patients requiring different treatment modalities. The purpose of this exploratory study was to evaluate whether a convolutional neural network could accurately classify mTBI patients who present with different symptom profiles using features within physiological and biomechanical data collected during an exertional protocol.

Methods: A cross-sectional design enabled evaluation of a deep learning model trained with ECG and accelerometry (ACC) data to classify patients identified to have predominantly physiological (n = 12) or vestibular symptomology (n = 5) by an expert clinician. Time-series ECG and ACC data were acquired using a Zephyr BioHarness (Medtronic, Minneapolis, USA) during a validated exertional protocol on a treadmill performed in a real-world clinical environment. Three temporal slices of the ECG and ACC signals were defined at different stages of the protocol to standardise data inputs

Introduction: Rehabilitation specialists need to improve differential diagnosis of the neuromusculoskeletal health issues of the residuum experienced by former and active Service Members suffering from limb loss¹. The development of a portable and non-invasive diagnostic device seeks to help maintain residuum health and support bionic solutions. Here, we outline the latest developments of an In-vivo Kinetic system 2.0 (Fig. 1), a diagnostic device that combines:

- Measurements of the mechanical loading applied to the site of amputation using portable wireless sensors²,
- Measurement of the tissue distribution within the residuum made by the newly developed Dynamic Anatomical Ultrasonography,
- Neuromusculoskeletal modelling or “digital twinning” of the residuum for a real-time personalized animation of the residuum during static and dynamic loading conditions³.

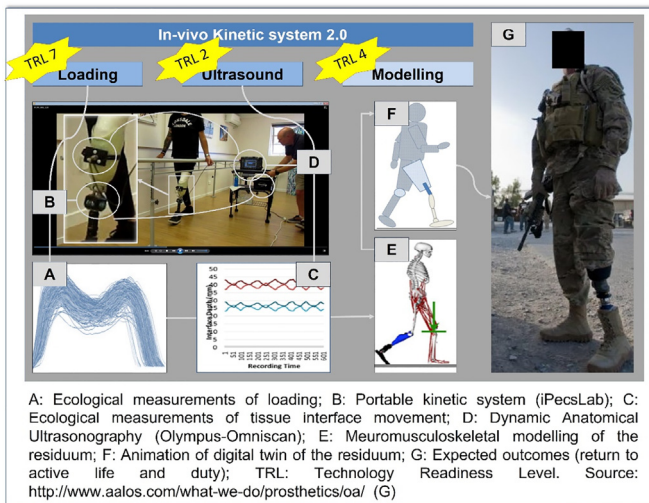


Fig. 1. Overview of In-vivo Kinetic system 2.0 relying on digital twin of the residuum that could enable innovative prosthetic care pathways for Service Members and Veterans with lower limb amputation.

Technology readiness levels (TRL) were estimated at 7, 2, and 4 for the loading, ultrasound, and modelling parts, respectively. Thus, demonstrating feasibility to develop an integrated, wearable and non-invasive In-vivo Kinetic system 2.0 capable of performing patient-specific differential diagnosis of residuum health under real world conditions⁴.

However, barriers inherent to biosensors (e.g., ultrasound measurements, synchronisation), the creation of a digital twin (e.g., tissues mechanical property) and integration (e.g., discrepancies of TRLs) continue to be challenging. The clinical roll-out of the device will require overcoming these issues and consideration of discrepancies between the skills of practitioners and siloed health care organizations.

Discussion/future directions: This system will provide unparalleled holistic insight into residuum health and productively disrupt the current model of health care. Hopefully, this diagnostic device will facilitate restoration of mobility, return to active duty, and, ultimately, improve life of the growing population suffering from limb loss considering bionic solutions.

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of the author and are not necessarily endorsed by the FY19 Defense Medical Research and Development Program.

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1011

Personalized digital humans for rehabilitation and assistive devices

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Introduction: Understanding the influence of whole-body activity (e.g., physical training) on the biophysics at organ-, tissue-, and sub-tissue-levels is important for designing optimal physical training/rehabilitation and effective control of assistive devices. The Griffith Centre of Biomedical and Rehabilitation Engineering (GCORE) has developed mature rehabilitation and assistive device technologies underpinned by the Personalized Digital Human (PDH).

Method framework: The PDH is a physics-based digital twin of the human (and devices), which includes representation of an individual's bones, articulations, muscles, and other soft tissues. Coupled with peripheral muscle excitation (e.g., electromyograms), PDH encodes muscle activations specific to the individual (e.g., sensitive to training and disease) and task (e.g. sensitive to control task)¹.

Examples: To analyze human performance, PDH quantifies mechanical parameters such as net loading to the body, organ (e.g., whole bone; Fig. 2), joint, tissue (e.g., ligament; Fig. 1)², and sub-tissue (e.g., local strain in tendon; Fig. 1)¹. Within a control system³, PDH predicts muscle activations that produce target mechanics (e.g., torque on rehabilitation ergometer), compliment an assistive device (e.g., torque above motor-driven assistance), sensory afferents that augment/simulate sensory experience (e.g., haptics), and safety margins (e.g., critical stresses) (Fig. 2).

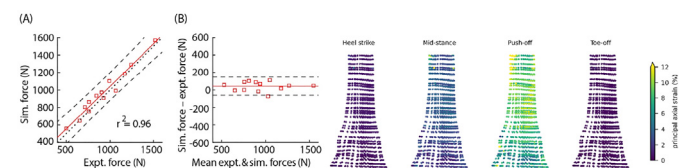


Fig. 1. (Left) Anterior cruciate ligament (ACL) force model where measured (Expt. force) and simulated (Sim. force) ACL forces are (A) highly correlated with (B) minimal bias. The ACL model can function in real-time to provide biofeedback to control ACL loading². (Right) Real-time visual feedback of Achilles tendon strain, based on PDH, was implemented in Javascript three.js (r100) and visualized on a mobile phone via internet browser (Mozilla Firefox)¹.

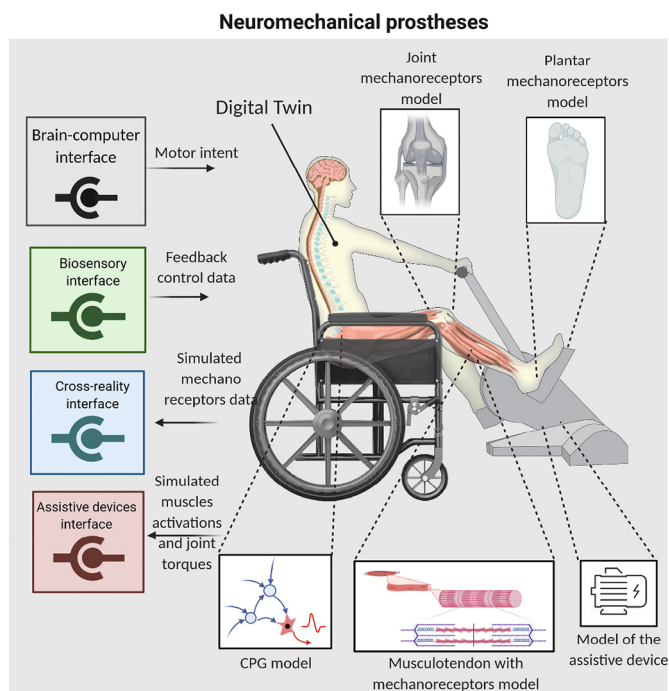


Fig. 2. The PDH used within a control system to interpret sensor data, model the internal states of the human, provide augmented sensory afferents, and perform safety checks on the loading of musculoskeletal tissues³.

Discussion/future directions: Currently, we are developing direct fusion of PDH with prosthesis design to optimize amputee residuum health⁴. Further, PDH could readily be extended to become the personalized digital soldier, with extensive scope for use in monitoring training loads, improving rehabilitation efficacy, and designing equipment to better interface with humans.

Acknowledgements: The PDH is the result of numerous nationally-competitive and industry grants for over 2 decades.

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Development of dynamic anatomical ultrasonography to advance personalised prosthetics

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Introduction: Ultrasound is routinely used by rehabilitation specialists to establish differential diagnosis of the residuum's neuromusculoskeletal issues experienced by former and active Service Members suffering from limb loss¹. Ultrasound offers real-time, non-ionizing, unspecialised facility assessment. Conventional imaging modalities record a qualitative static image. More fundamental signal/data display modalities such as the raw radio-frequency signal and A-mode are rarely utilised, although offer

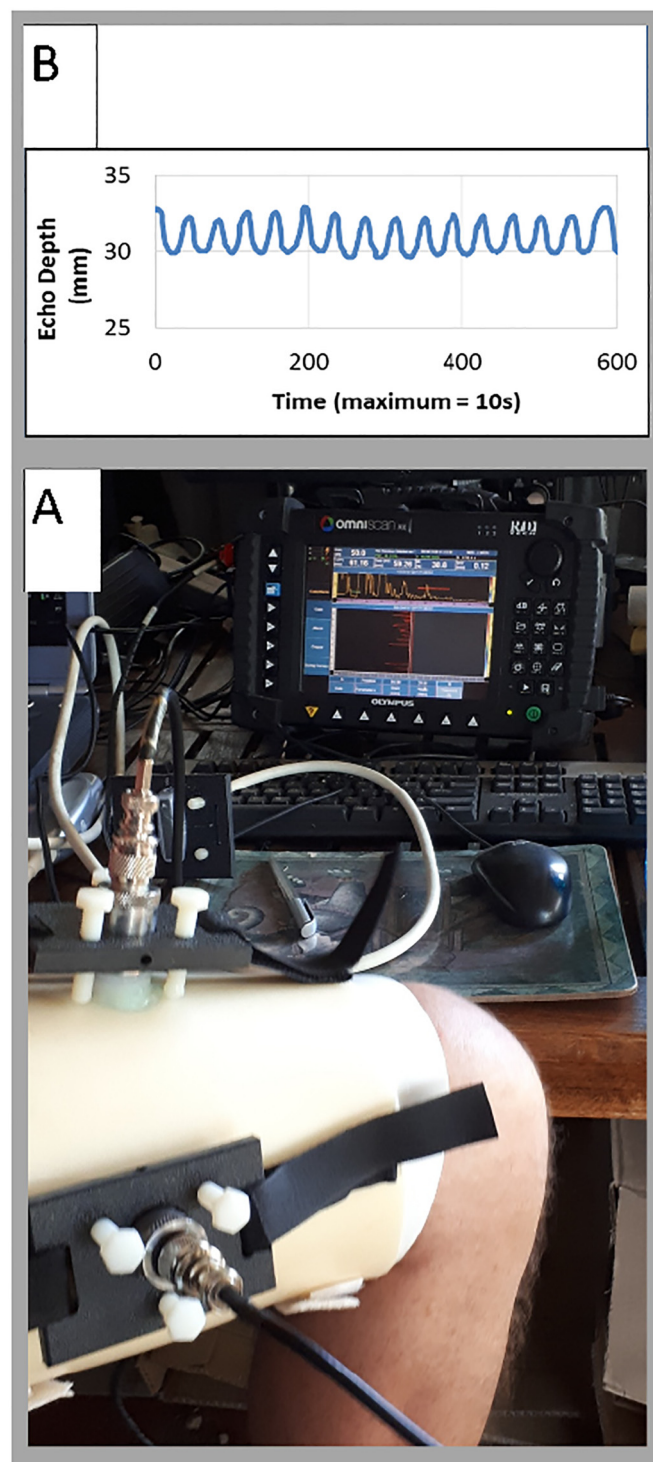


Fig. 1. Photograph of a custom pseudo socket incorporating two ultrasound transducers attached to an asymptomatic subject (A), along with echo depth of the femur during limb motion (B).