Early development of a

Soft bioreactor for ex-vivo study of carpal tunnel syndrome

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Background

Carpal Tunnel Syndrome (CTS)

- Hand/wrist neuropathy
- *Extremely common,* ~15% globally[1]
- Healthcare and economic burden in billions[2]
- Unclear mechanical risk factors

Sub-Synovial Connective Tissue (SSCT)

- Fibrotic and dysregulated in CTS[3]
- Gliding tissue between carpal tunnel structures
- *No mechanical ex-vivo models for drug testing or molecular studies*

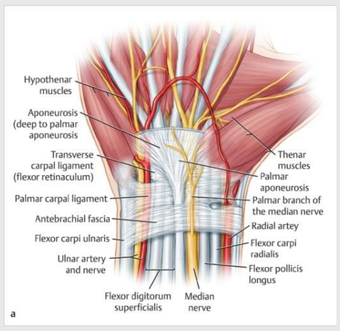
Goal: Develop, validate, and demonstrate ex-vivo model of CTS, by culturing SSCT under anatomically relevant physical stimulation (movement and pressure)

Methods

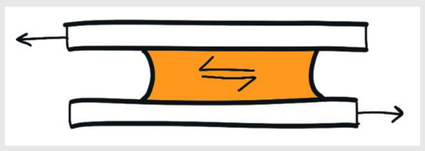
Chamber design

Simplified carpal tunnel model

Two independently moving tendons



[4]

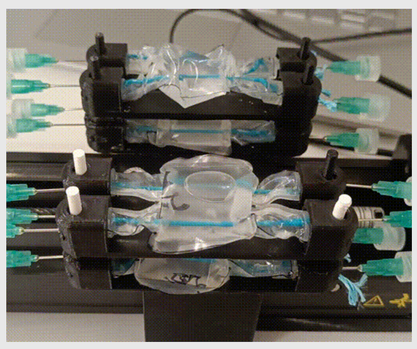


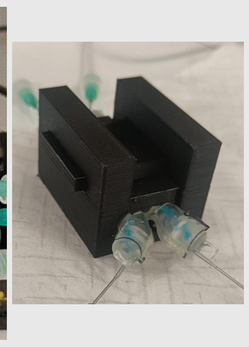
Orange = SSCT

White = Tendon

Chamber testing

- **Durability**: >70,000 shearing cycles
- **Pressure**: controlled and stable at 30-150 mmHg
  (Simulates 7 days of hand movements[5] and high pressure in CTS[6])
- **Evaporation**: rate quantified by mass





(Left) Linear actuator: Simulates tendon movement
(Right) Rigid enclosure: Constrains volume to pressurise chamber

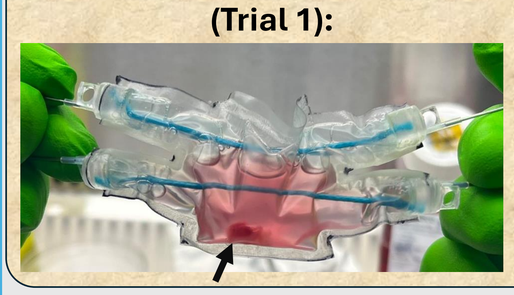
Biological validation

- Demonstrate chamber biocompatibility
- Basic data on effects of movement and pressure
- Daily PrestoBlue viability measurement

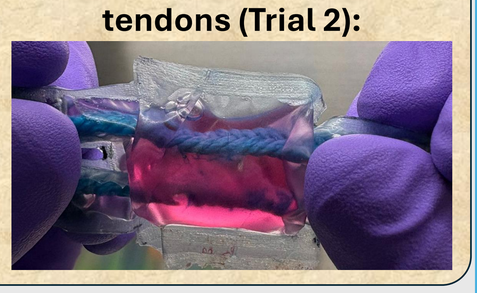
4 planned experiments:

Trial 1	n = 2	Basic cytotoxicity assessment
Trial 2	n = 2	Attachment, movement, and pressure
Trial 3	n = 4	SSCT viability vs pressure and movement
Trial 4	n = 4	Gene expression vs movement

Free-floating SSCT (Trial 1):

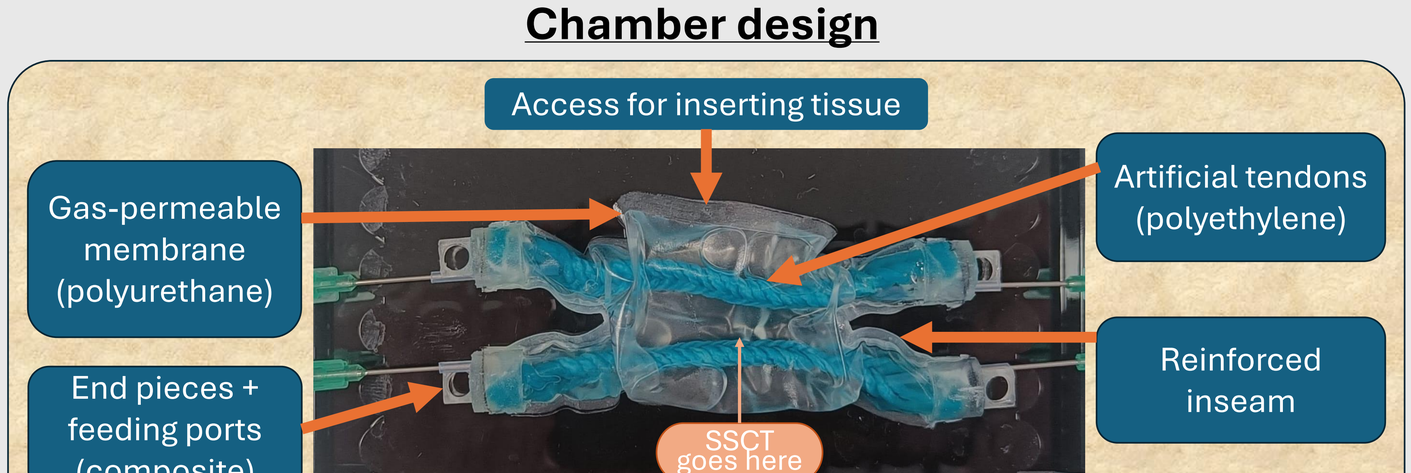


SSCT sutured between tendons (Trial 2):



Results

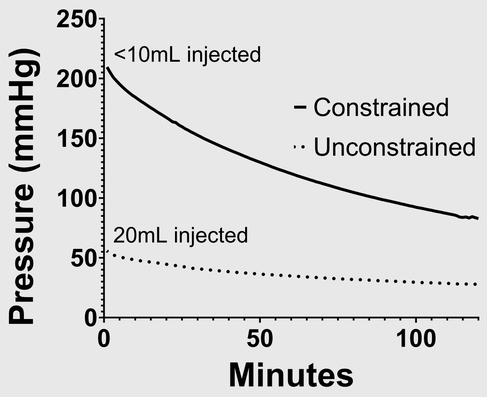
Chamber design



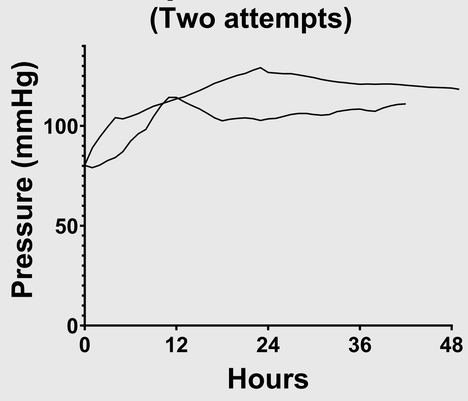
Chamber testing

- **Durability:** Chamber modified until 70,000+ cycles reached reliably
- **Pressure:** Quick pressure decay, controlled using syringe pump
  Automatic pressure control system currently being designed
- **Evaporation:** ~2.5 mL/day, requires daily medium change

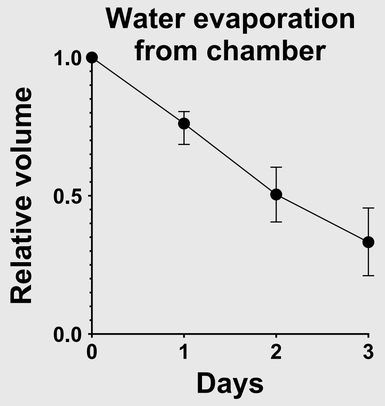
Chamber must be constrained to reach high pressure



Active pressure control (Two attempts)



Water evaporation from chamber



Biological validation

2 of 4 trials completed to-date

- **Trial 1:** Tissue viable and stable for 7 days.
  Chamber not cytotoxic.
- **Trial 2:**
  - Viability drop in mechanically stimulated tissue (reasons unclear)
  - Failure of pressurised chamber
  - Protocols improved

Normalised tissue viability (Trial 2)

Conclusions and future plans

- Successful chamber design
- Mechanical tissue stimulation
- Challenges with pressure
- Early viability data
- mRNA-seq in upcoming experiments

Future direction of platform

- Drug screening
- Molecular analysis
- SSCT mechanical properties
- Anatomical wrist robot

[7] Musculoskeletal robot arm, Uni of Salford

Acknowledgments and references

I would like to thank my supervisors, NHS staff, and my colleagues at the Botnar Research Centre for their support throughout the project.

Humanoid Bioreactor Project:

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