Australasian Society for
Biomaterials and Tissue Engineering

WA/SA EMCR Regional Showcase 2022

Program and Abstract Book

Thursday 8th December 2022
8:45AM to 4:00PM

Contents

Australian Society for Biomaterials and Tissue Engineering

The ASBTE was formed in 1989. It provides a national focus for professionals who have interests in research, education, development and regulation of biomaterials, tissue engineering and medical devices.
Internationally, the Society is a constituent society of the International Union of Societies for Biomaterials Science and Engineering (IUSBSE) who coordinate international activities, including the World Biomaterials Congress.

The ASBTE aims to provide a forum for dissemination of research knowledge in the fields of biomaterials and tissue engineering. This is achieved through annual meetings, which also bring researchers together for generating opportunities for collaborative research. This society also strongly believes in supporting students and early-career researchers through conference and travel awards.

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Membership in the Australasian Society for Biomaterials and Tissue Engineering gives you a reduced price for our annual meeting attendance. International Biomaterials Societies also often recognise ASBTE as an affiliated society, and thus you should also get reduced rates for most of the international biomaterials meetings hosted by these societies.

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In 2023 our annual meeting will be held in Christchurch, New Zealand from the 12-14 April.

Christchurch is the largest city in the South Island of New Zealand, surrounded by the beautiful Southern Alps. It has an international airport with direct flights to/from Singapore, and also driving distance to popular towns like Queenstown, Akaroa and Wanaka. Christchurch is also known as the "Gateway to Antartic", as it houses the International Antartic Centre that provides both base facilities and a museum and visitor centre focuses on current Antartic activities. We really look forward to hosting you and your team in Christchurch, New Zealand.

We welcome submissions for topics including:
Antifouling materials, Biofabrication, Biointerfaces, Biomaterials, Biomimetic models, Clinical and commercial translation, Diagnostics and biosensing, Drug delivery, Imaging, Immunomodulatory biomaterials, Mechanobiology, Nanotechnology and nanomedicine, Scaffolds, Stem cells and cell therapy, Sustainability, Tissue engineering, Wound healing

https://www.asbte2023.co.nz/

Abstract submission

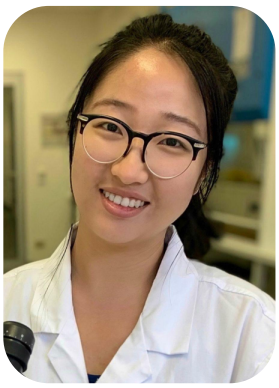
Call for abstracts open | Wednesday 9 November 2022
Submission closes | Monday 5 December 2022 at 11.59 pm NZDT
Notification of acceptance | From Wednesday 25 January 2023

Submission types:

- Oral free paper presentation | 12 minute presentation with 3 minutes for Q&A
- Rapid fire | 5 minute presentation
- Poster presentation | Visual display only

More information and abstract submission here

Showcase Organising Committee



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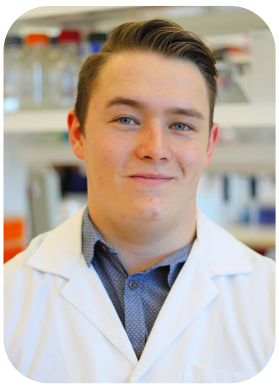

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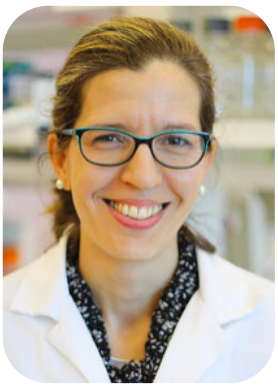

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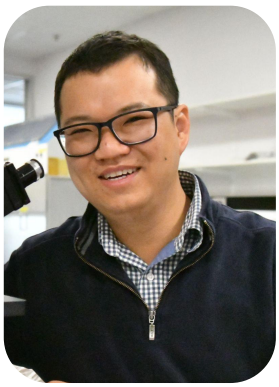

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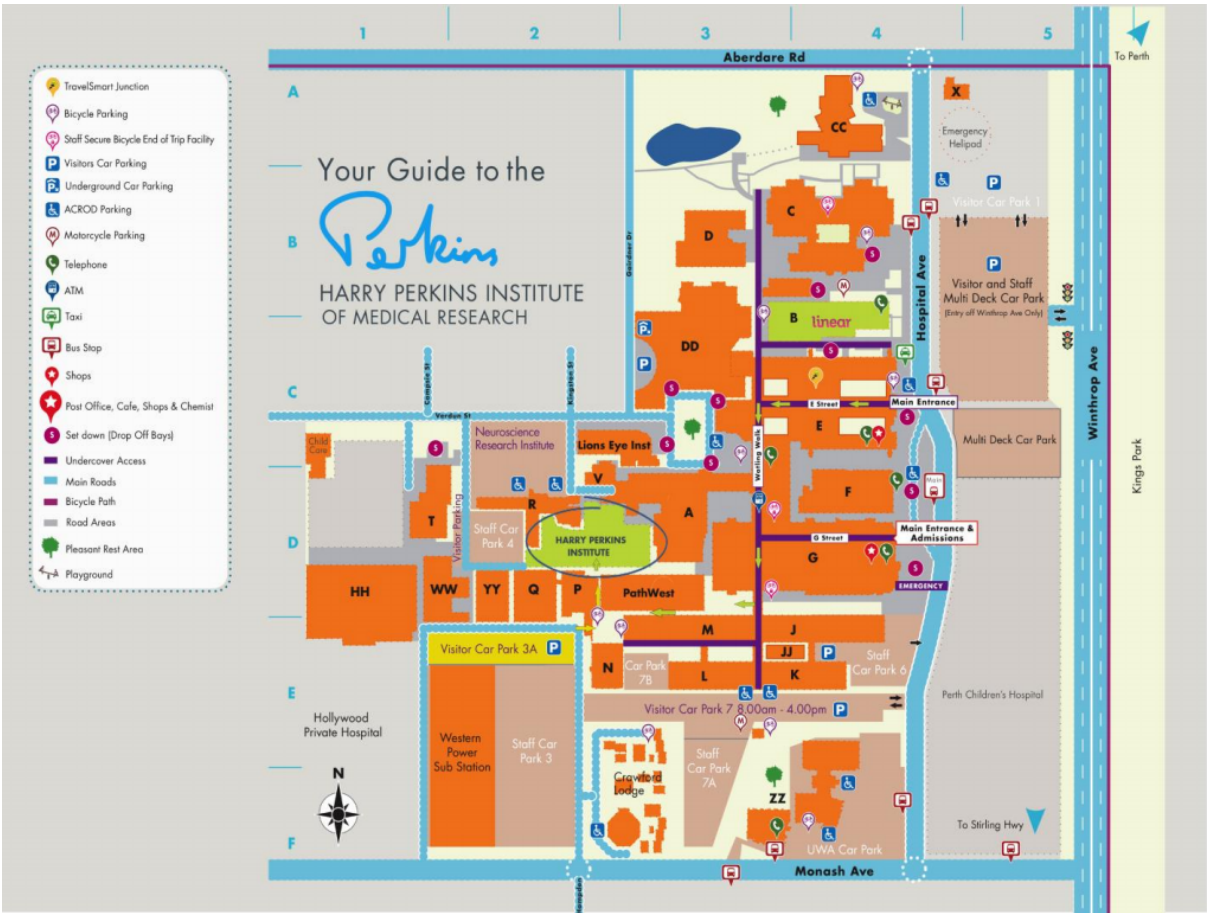

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Full Program

Time (AWST)	Program
08:00 – 0845AM	**Registration**
08:45 – 09:00AM	**Welcome, Acknowledgement of Country, and Opening Address** *Dr Huan Ting Ong – WA Showcase Lead* *A/Prof Khoon Lim – ASBTE President*
09:00 – 10:00AM	**Panel Discussion – Biomaterials in the Clinic: Present and Future** *Panellists: Dr Abdul Ihdayhid, Dr Elena Juan Pardo, Dr Filippo Valente, Intan Oldakowska, Prof Shirley Jansen, Prof Fiona Wood* *Moderator: Mr Michael Vernon* **Q&A:**

10:00 – 10:55AM – Session 1: Biomaterials & Tissue Engineering ***Chair: Mr Samuel Maher***		
Time (AWST)	**Name**	**Title**
10:00 – 10:25AM	Dr Andrew Stevension	Preclinical development of 3D Bioprinting for the skin regeneration
10:25 – 10:40AM	Yong Hwee (Joe) Tan	Profiling airway smooth muscle cell mechanosensation using 2D stiffness gradient hydrogels
10:40 – 10:55AM	Maria Bikuna-Izagirre	PCL-based electrospun scaffold as an in vitro human trabecular meshwork for aqueous humor outflow studies
10:55 – 11:25AM – Morning Tea – Perkins Foyer		
11:25 – 12:25PM – Session 2: Drug Delivery & Clinical Applications ***Chair: Ms Danielle Vahala***		
11:25 – 11:50PM	Dr Zlatko Kopecki	Bacteria-Activated Dual pH and Temperature Responsive Hydrogel for Targeted Elimination of Infection and Improved Wound Healing
11:50 – 12:05PM	Ebrahim Vahabli	Technological Advances to Manufacture Next-Generation Stent-Grafts
12:05 – 12:20PM	Francois Rwandamuriye	Sustained release of immunotherapy from an intraoperative hydrogel prevent cancer recurrence after surgery
12:20 – 12:25PM	Patrick Lim	Developing and validating *in-vitro* epithelial membranes for Probucol-nanoparticle delivery for inner ear therapeutics
12:25 – 01:25PM	**Lunch – Perkins Foyer**	

01:25 – 02:35PM – Session 3: Mechanobiology ***Chair: Dr Huan Ting Ong***		
01:25 – 01:50PM	Dr Matt Hepburn	Three-dimensional characterisation of cellular elasticity using quantitative micro elastography
01:50 – 02:05PM	Danielle Vahala	Mechanosensation, Proliferation and Invasion of Breast Cancer Spheroid in 3D Linearstiffness Gradient Hydrogels
02:05 – 02:20PM	Samuel Maher	Decoupling the effects of pore size and extracellular matrix stiffness on 3D stem cell mechanosensation
02:20 – 02:35PM	Sebastian Amos	Investigating the role of cell adhesion in the tumour microenvironment with a 3D cancer spheroid model
02:35 – 03:05PM	**Afternoon Tea – Perkins Foyer**	
01:25 – 02:35PM – Session 4: Characterisation Techniques & Biofabrication ***Chair: Mr George McColgan***		
03:05 – 03:20PM	Michael Vernon	Engineering Heart Valve Interfaces Using Melt Electrowriting: Biomimetic Design Strategies from Multimodal Imaging
03:20 – 03:35PM	Christopher Lamb	Investigation of parameters that impact layer bonding in melt electrowritten scaffolds
03:35 – 03:50PM	Brooke Maitland	*In situ* characterisation of melt-electrowritten scaffolds in 3D using optical coherence tomography
03:50 – 04:00PM	**Short Judging Break**	
04:00 – 04:10PM	**Closing Address and Awards Ceremony** *Dr Yu Suk Choi – ASBTE Exec Committee*	
04:10 – 06:00 PM	**Social Event – Perkins Foyer**	

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Panel Discussion:
Biomaterials in the Clinic – Present and Future

Panellists


Dr Abdul Ihdayhid


Dr Elena Juan Pardo


Dr Filippo Valente


Intan Oldakowska


Prof Shirley Jansen


Prof Fiona Wood

Moderator


Mr Michael Vernon

Submit questions on Slido

Session 1: Biomaterial & Tissue Engineering

10:00AM to 10:55AM
Chair: Mr Samuel Maher

Preclinical development of 3D Bioprinting for the skin regeneration

Nutan Chaudhari[2] Rahul Visalakshan[1] Kalani Ruberu[3] Andrew Stevenson[2] Zack Artist[5] Stephen Beirne[3] Cameron Ferris[5] Abbas Shafiee[4] Mark Fear[2] Zhilian Yue[3] Gordon Wallace[3] Fiona Wood[2] Pritinder Kaur[1]

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2 Fiona Wood Foundation, University of Western Australia, WA, Australia

3 Intelligent Polymer Research Institute, ARC Centre of Excellence for Electromaterials Science, AIIM Facility, Innovation Campus, University of Wollongong, NSW, Australia

4 Royal Brisbane & Women's Hospital, QLD, Australia

5 Inventia Life Science, NSW, Australia

INTRODUCTION:

While improving care, current therapeutic approaches for treating injury and scars remain suboptimal. Therefore, the application of cells and matrix for wound healing is complex and whilst these approaches have improved outcomes, skin regeneration remains elusive[1]. In this project, we develop a preclinical 3D bioprinting platform for printing cells combined with specialised bioinks to improve patient outcomes.

METHODS:

Porcine model and 3D bioprinting of skin: 1x1 cm full thickness excision injury, approximately 5-8 mm deep, were created on pigs and treated with the 3D bioprinted scaffolds. ReCell and Integra was used as a control. Autologous dermal fibroblasts were incorporated into the platelet lysate-based GelMA: Gelatin bioink, and 3D scaffolds were printed using 3D REDI bioprinter. Autologous keratinocytes and Laminin isoforms were added on top of the 3D bioprinter scaffolds on the Full thickness excision injury in pigs. The wound tissue was analysed using photographic assessment, Flow cytometry, general histology and cytokines profiling to track the changes in the wound healing at day 3, 7 and 2 months post-3D-bioprinting.

RESULTS & DISCUSSION:

The overall result from this project depicts the formation of bilayer organisation of the skin with improved or similar wound healing outcomes compared to the ReCell and Integra treatment wounds. Further, incorporating Laminin isoforms 521 and 525 has been shown to have a pro-proliferative effect on epidermal regeneration. The progress achieved in this study will advance current sub-optimal clinical therapeutic approaches for patients long-suffering following skin injury or disease.

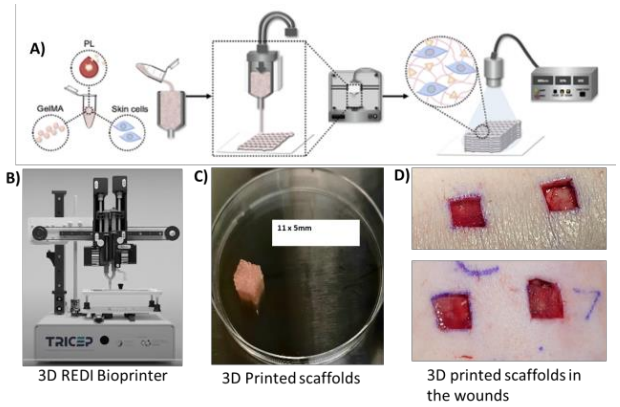

Figure 1: 3D Bioprinting on porcine skin. **A)** Extrusion-based bioprinting of platelet lysate-based GelMa:Gelatin bioink**. B)** 3D REDI Bioprinter, **C)** 3D Bioprinted scaffolds, **D)** 3D bioprinting on full-thickness excision wounds in pigs.

CONCLUSIONS:

This project explores a preclinical proof of concept wound healing in a pig model that delivers both epidermal and dermal cells in an optimised matrix directly and controllably to the wound site using 3D bioprinting technology.

ACKNOWLEDGEMENTS:

We acknowledge funding from the Medical Research Future Fund and support from the Australian National Fabrication Facility (ANFF): Materials Node & the Translational Research Initiative for Cellular Engineering and Printing (TRICEP).

REFERENCES:

1. Varkey et al. *Burns Trauma.* 2019; 7:4.
2. Daikuara et al. *Acta Biomaterialia.* 2021; 123:286-297.
3. Kaur et al. *Experimental Dermatology.* 2002. 11:387-97.

Profiling airway smooth muscle cell mechanosensation using 2D stiffness gradient hydrogels

YH. Tan[1], B. Kennedy[2], R. Sanderson[2], JY. Li[2], K. Wang[1,3], P. Noble[3], YS. Choi[1]
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[1]*University of Western Australia, Perth, AUS*;
[2]*Harry Perkins Institute of Medical Research, Perth, AUS*
[3]*Telethon Kids Institute, Perth, AUS*

INTRODUCTION:
Extracellular matrix (ECM) remodelling within the airway smooth muscle (ASM) likely contributes to airway dysfunction in obstructive disease. The role of human ASM cell (hASMC) mechanotransduction in the context of such remodelling remains unclear.

METHODS:
ASM stiffness: Porcine lungs were dissected for tracheal (N=6) smooth muscle and assessed for stiffness at different mechanical strains (0-10% in situ length ($L_{in\ situ}$)) using a custom-fabricated platform that facilitated assessment by a custom-built uniaxial compression tester (UCT).

Linear stiffness gradient hydrogel: Polyacrylamide hydrogels fabricated with a linear stiffness gradient of 2-30 kPa (approximating stiffnesses measured above) were coated with collagen I (Col), fibronectin (Fn) or laminin (Ln) and used to study changes to cell morphology, contractile and mechanomarker protein expression.

Cell culture: Primary human bronchial and tracheal smooth muscle cells (hASMC), from growth passage number 5 only, were seeded into 12-well plates with hydrogels at an initial density of 20,000 cells per gel. Mechanosensation in hASMCs was inhibited with media containing either blebbistatin (25 μM) or Y27362 (4 μM) treatment for 96 hours. Cells were seeded on Fn-coated hydrogels only. All media used for the study were changed after 48 hours and cells fixed after 96 hours.

RESULTS & DISCUSSION:
ASM stiffness: We determined physiological stiffness ranges of ASM (proximal and distal) at 0%, 5% and 10% $L_{in\ situ}$ using UCT, and derived mean tissue stiffnesses at 10% and 40% axial strain. A physiological ASM stiffness range of 2-30 kPa was observed.

hASMC mechanosensation: Cell size, nuclear size and nuclear shape (Col only) were positively correlated with substrate stiffness. Expression of contractile phenotype marker alpha-smooth muscle actin (αSMA) and mechanomarker Lamin-A were positively correlated with substrate stiffness in the presence of Col and Fn. Nuclear translocation of mechanomarker Yes-associated protein (YAP) correlated with stiffness only in the presence of Fn.

Mechanotransduction inhibition with both inhibitors resulted in disrupted cell size, shape and nuclear size. Lamin-A expression was reduced by both inhibitors, while only Y27632 induced substantial reductions in YAP nuclear translocalization.

CONCLUSIONS:
This study demonstrated the complex interplay between mechanosensation of hASMCs to ECM stiffness and proteins and their influence on contractile phenotype over mechanotransductive pathways, as well as demonstrating the potential impact of ECM remodelling in the context of obstructive disease and a conceptual mechanotransductive target for therapy.

ACKNOWLEDGEMENTS:
This work was supported by Heart Foundation Future Leader Fellowship 101173 (to YS.C), UWA fellowship support 2018/RA/1/1997/70 (to YS.C), Future Health Research and Innovation Fund WANMA 2021 (to YS.C).

PCL-based electrospun scaffold as an in vitro human trabecular meshwork for aqueous humor outflow studies

Maria Bikuna-Izagirre[1,2], Javier Aldazabal[1], Leire Extramiana[3], Javier Moreno-Montañés[3], Elena Carnero[3], Jacobo Paredes[1]
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[1]*University of Navarra, Tecnun School of Engineering, San Sebastian, SPAIN*
[2]T3mPLATE, *Harry Perkins Institute of Medical Research, QEII Medical Centre, Nedlands and UWA Centre for Medical Research, The University of Western Australia, Perth, WA, Australia*
[3]*Clinica Universidad de Navarra, Departamento de oftalmología clínica, Pamplona, SPAIN*

INTRODUCTION:

The human trabecular meshwork (TM) is responsible for the 80-90 % of the aqueous humor (AH) outflow and consequently regulates the intraocular pressure (IOP). Alterations in the TM may hinder AH outflow, increasing IOP values, which increases the risk to develop glaucoma [1]. The physiological mechanism of this malfunctioning remains unclear, and the lack of appropriate in vitro TM models make the research even more challenging. Herein, we present poly-caprolactone (PCL) based solution electrospinning (SE) nanofibrous scaffold as an in vitro TM and a custom-designed platform for further AH outflow and glaucomatous drug studies.

METHODS:

PCL scaffold fabrication and characterization: PCL (10 wt%) scaffolds were fabricated and characterized as indicated in [2].

Cell culture on scaffolds: after plasma, sterilization, and gelatin coating process [2] primary human trabecular meshwork cells (HTMC) (obtained from donors) were cultured in PCL scaffolds for 14 days. Afterwards, treatments with 15 µM dexamethasone (D) (pressure booster) and 1 µM Netarsudil (N) (pressure reducing) were applied for 5 days. Cell growth and morphology were imaged at the end of culture periods.

Perfusion studies: after drug treatments PCL scaffolds with HTMC were secured inside a perfusion chamber (Figure 1). Control, D and N treated chambers were perfused with cell media at 20 µL/min for 24 h. Outflow facility was calculated, and further imaging and genetic studies (qPCR) were performed.

RESULTS & DISCUSSION:

PCL scaffold as in vitro TM: fiber diameters of 770 ± 0.172 nm, pore sizes of 5.59 ± 0.28 µm^2 and a Young Modulus of 6.87 ± 0.08 MPa lead to a proper growth of HTMC and correct response to drugs on PCL scaffolds.

Perfusion studies: HTMC on PCL scaffolds presented a transmembrane pressure of 12.79 ± 0.69 mBar. Treatment with D dramatically increased it to 34.44 ± 1.72 mBar and N decreased it to 5.45 ± 0.39 mBar.

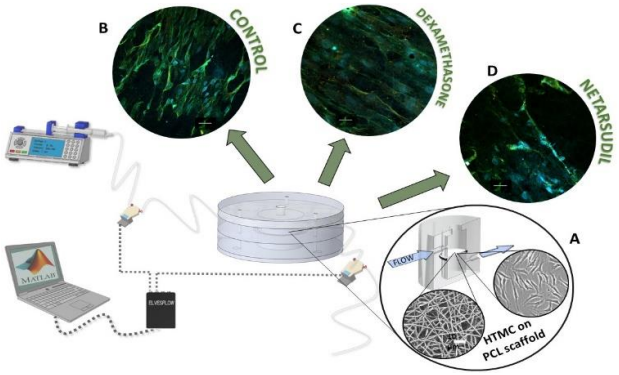

Figure 1: Perfusion platform. (A) PCL nanofibrous scaffold, HTMC and cross section of the pressure chamber. Confocal images of (B) control, (C) dexamethasone, and (D) Netarsudil. Green: phalloidin Alexa Fluor 488. Blue: DAPI.

CONCLUSIONS:

PCL nanofibrous scaffold showed to be a good platform to host HTMC and the perfusion system was able to measure drug-caused variations in the transmembrane pressure, indicating its potential for AH outflow studies.

ACKNOWLEDGEMENTS:

MBI holds Mobility Program Grant by University of Navarra. This research was supported by the Spanish government and the European Union. Project funded by Instituto Carlos III, file code PI18-01782 and European Regional Development Fund (FEDER) UE: 17259601.

REFERENCES

1. Buffault, J., Labbé, A., Hamard, P., Brignole Baudouin, F. & Baudouin, C. The trabecular meshwork: Structure, function and clinical implications. A review of the literature. *J. Fr. Ophtalmol.* 1–14 (2020). doi:10.1016/j.jfo.2020.05.002
2. Izagirre, M. B., González, E. C., Esquisabel, L. E., Aldazabal, J. & Moreno, J. Characterization of polycaprolactone based electrospun scaffold towards in vitro human trabecular meshwork model. (2020).

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Session 2: Drug Delivery & Clinical Applications

11:25AM to 12:25AM
Chair: Ms Danielle Vahala

Bacteria-Activated Dual pH and Temperature Responsive Hydrogel for Targeted Elimination of Infection and Improved Wound Healing

H. Haidari[1], K. Vasilev[2], A.J. Cowin[1], and Z. Kopecki[1]
Presenting Author: zlatko.kopecki@unisa.edu.au
[1]*Future Industries Institute, University of South Australia, Adelaide, AUS*;
[2]*Collage of Medicine and Public Health, Flinders University, Adelaide, AUS*

INTRODUCTION:

Antibacterial treatment that provides on-demand release of therapeutics that can kill a broad spectrum of pathogens while maintaining long-term efficacy, and without developing resistance or causing side effects is urgently required in clinical practice. Here, we demonstrate the development of a multi-stimuli responsive hydrogel offering the on-demand release of silver (Ag^+) ions triggered by changes in wound microenvironment.

METHODS:

Pnipam-PAA Hydrogel: Crosslinking of N-isopropyl-acrylamide with acrylic acid and loading with ultrasmall silver nanoparticles (AgNPs) to develop a dual responsive hydrogel sensitive to wound temperature and pH changes during wound infection.

Biocompatibility and Antimicrobial efficacy: The cytotoxicity was evaluated against human foreskin fibroblasts (HFFs) and keratinocytes (HaCaTs) using resazurin assay and LiveDead staining [1]. Bacterial Viability Assay and SEM were used to demonstrate effects on Gram-positive and Gram-negative bacterial cell morphology and biofilm formation [2].

Preclinical testing: *In-vivo* excisional wound infection model was used to assess the Pnipam-PAA-AgNP hydrogel efficacy against *S. aureus* (Xen29) in comparison to vehicle control and antibiotic standard. IVIS imaging and CFU analysis were used to determine treatment effects on localized infection [3]. Pnipam-PAA-AgNP hydrogel effects on wound healing, inflammation and collagen deposition were assessed.

RESULTS & DISCUSSION:

Dual-responsive hydrogel is highly sensitive to typical wound pH and temperature changes as evidenced by restricted Ag^+ ion release at acidic pH (<pH 5.5) and significantly higher release (>90%) in alkaline pH (>pH 7.4), concurrent with >95% efficacy in eliminating clinical wound pathogens both *in-vitro* and *in-vivo*.

The *in-vivo* antimicrobial efficacy and safety showed the high potency of developed Pnipam-PAA-AgNP hydrogel to clear *S. aureus* wound infection while significantly accelerating the rate of wound healing.

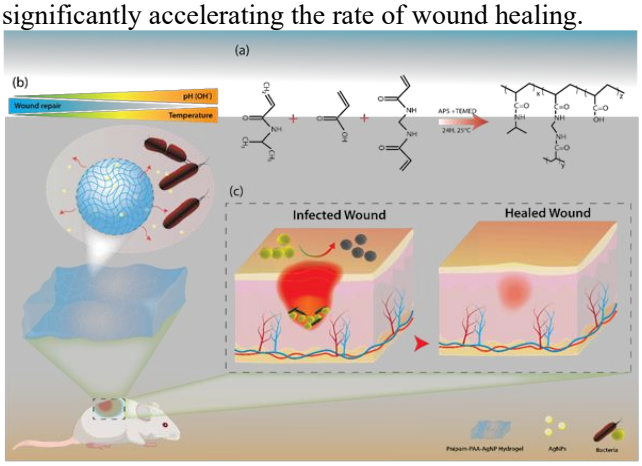

Figure 1: (a) Chemical synthesis of Pnipam-PAA hydrogel, **(b)** Schematic illustration of Pnipam-PAA-AgNP hydrogel physiochemical changes in response to localized environmental stimulus of wound infection, **(c)** The antibacterial and wound healing capacity of the developed hydrogel.

CONCLUSIONS:

The Pnipam-PAA-AgNP hydrogel offers a promising bacterial responsive delivery platform for wound management that serves as an on-demand carrier to not only reduce common silver (Ag^+) side effects but significantly boost antimicrobial efficacy reducing wound infection while promoting wound regeneration.

ACKNOWLEDGEMENTS:

Z.K. is supported by Channel 7 Children's Research Foundation Mid-Career Fellowship. The project is funded by EB Research Network Grant (#Kopecki).

REFERENCES

[1] Haidari et al., *Biomedicines* 2021; 9(9): 1182.
[2] Haidari et al., *Acta Biomaterialia* 2021;128:420-34.
[3] Haidari et al., *ACS Appl. Mater. Interfaces* 2020; 12 (37): 41011-41025.

Technological Advances to Manufacture Next-Generation Stent-Grafts

Ebrahim Vahabli [1,2,4], Shirley Jansen [1,3], Elena De-Juan-Pardo [2,4], Barry Doyle [1,2]
Presenting Author: Ebrahim.vahabli@research.uwa.eu.au, HDR
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[2]*University of Western Australia, Perth, Western Australia, Australia*
[3]*Curtin University, Perth, Western Australia, Australia*
[4]*T3mPLATE, Harry Perkins Institute of Medical Research, QEII Medical Centre, Nedlands, Perth, Western Australia, Australia*

INTRODUCTION:

Diseases of the aorta can affect any segment of the vessel, from the aortic root to the bifurcation, and typically manifest as either the formation of an aneurysm or dissection. The endovascular treatment of aortic disorders has gained wide acceptance due to the reduced physiological burden to the patient compared to open surgery, and ongoing stent graft evolution has made aortic repair an option for patients with more complex anatomies.

Despite their use as a modern-day life-saving device, stent grafts are still typically fabricated using traditional methods. Device complications jeopardize patient outcomes, and as such, more engineering assessment is required to fully understand the current limitations and design solutions to create the next-generation device.

METHODS:

Although we can see progress in the newer versions of commercial stent-grafts, traditional fabrication techniques have not been capable of solving device-related complications. That is why the technology paradigm should eventually shift to advanced manufacturing techniques. With the emergence of 4D-printing and smart materials, unprecedented features, including adaptive shape changes and remote battery-free self-monitoring, can be defined in next-generation stent grafts.

DISCUSSION:

The technical assessment of stent graft failure modes reveals that the reoccurrence of lethal complications cannot be easily avoided through established techniques. We discuss and review the application of novel techniques to manufacture next-generation endovascular implants in this work.

CONCLUSIONS:

The ideal stent graft has yet to be constructed. However, they must be versatile enough to address complex anatomic intricacies while being compatible with standard angiographic techniques.

We will likely see more use of hybrid smart materials capable of controlled responses combined with real-time monitoring capabilities. Based on current evidence, future stent grafts may overcome established complications from existing designs by activating interconnected biological and mechanical dynamic elements, so the device can fully integrate into the body enabling the device to sense, respond and adapt to the changing environment. Functional structures within the stent graft could effectively seal and heal aortic pathologies such as aortic dissections.

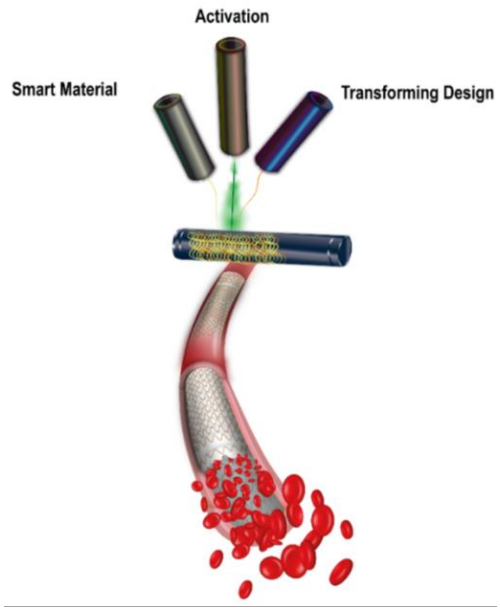

Figure 1: A schematic of 4D printing process to manufacture next-generation stent-grafts

ACKNOWLEDGMENTS:

E.V. gratefully acknowledges the Australian Government Research Training Program PhD Scholarship from The University of Western Australia.

REFERENCES

[1] Vahabli E et al. Advanced Healthcare Materials, 2022; 11, 2200271

Sustained release of immunotherapy from an intraoperative hydrogel prevent cancer recurrence after surgery

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INTRODUCTION:

Surgery is often the first-line treatment option for many solid cancers, usually in combination with chemotherapy and/or radiotherapy. However, relapse of the primary tumour after surgery is common and associated with a poor prognosis. Here, we aimed to develop a hydrogel, which could be easily applied locally during oncological surgery, with the goal to attract and activate immune cells into the tumour resection site to eradicate any remaining tumour cells and prevent post-surgical cancer recurrence.

METHODS:

Hydrogels: Hydrogels were prepared by modification of hyaluronic acid (HA). Bulk, and micro-scale, mechanical properties of the hydrogels were characterised using uniaxial compression testing, and optical coherence elastography, respectively.

Degradation and release kinetics: Degradation speed of the hydrogel and release kinetics of the immunotherapy drug were assessed *in vitro* and *in vivo*, using fluorescence imaging.

Mouse model: A mouse model of incomplete tumour resection [1] was used to assess the efficacy of the hydrogel-loaded immunotherapy by implanting the hydrogel in the resection site.

Mechanism of action. The underlying immunological mechanism of the immunotherapy was assessed using cytokine blocking studies, flow cytometry, and RNA sequencing.

RESULTS & DISCUSSION:

A hyaluronic acid-based hydrogel could be feasibly applied in the wound bed after cancer surgery. The immunotherapy from the hydrogel, placed in the tumour resection site, prevented tumour recurrence in multiple mouse models. Mechanistically, the immunotherapy induced a transient IFNα response that reshaped the tumour microenvironment by attracting inflammatory immune cells and depleting T regs from the tumour microenvironment. In addition, RNAseq data show that a pre-existing gene expression signature predicts response to the immunotherapy-loaded hydrogel. Finally, the hydrogel delivery platform was safe for use in canine cancer patients, easily usable by the surgeon, while the immunotherapy induced a measurable systemic immune response.

CONCLUSIONS:

The surgically optimized hydrogel provides a safe and effective drug delivery approach to prevent relapse of solid tumours following surgery and can be translated in real-world oncological settings.

ACKNOWLEDGEMENTS:

FX. R. is supported by an Australian Government PhD scholarship and Abbie Basson PhD top-up scholarship. This work was funded by grant APP1184331 from Cancer Australia/The Kids' Cancer Project. The authors acknowledge the facilities, and the scientific and technical assistance offered by Diana Patalwala at the National Imaging Facility at the Centre for Microscopy, Characterisation & Analysis, The University of Western Australia, a facility funded by the University, State, and Commonwealth Governments.

REFERENCES

[1] Rwandamuriye FX et al. J. Vis. Exp., e60882 (2020)

Developing and validating *in-vitro* epithelial membranes for Probucol-nanoparticle delivery for inner ear therapeutics

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INTRODUCTION:

Drug permeation through the ears round window membrane (RWM) poses as a signidicnat barreir for the delivery of therapeutic agents into the inner ear. Constructing an *in-vitro* platform that mimics the RWM's physiological characteristics may aid in screening the permeability of a novel treatment for hearing loss, Probucol-nanoparticles.

METHODS:

In-vitro platform: HaCaT epithelial cells were cultured on Transwell plates until a confluent monolayer membrane was achieved. This was validated with immunofluorescence (IF) of zonula occludens 1 (ZO-1) tight junction protein and measuring the paracellular permeability of dextrans (4, 40, and 70kDa).

Nanoparticle production: Polymer-bile acid formulations F1 (Probucol loaded) and F2 (control) were processed through the Buchi Mini Spray Dryer B-290 to produce the nanoparticles. Physico-chemical analyses were used to determine nanoparticle's thermal, chemical, size, and electrokinetic stability, in addition to drug loading.

Permeation assay: The epithelial membranes were treated with 0.6mg/ml F1 and F2 nanoparticles for 24 hours. Cell culture media from apical and basolateral chambers were analysed through high-performance liquid chromatography (HPLC) detecting for the presence of Probucol.

RESULTS & DISCUSSION:

Membrane confluency and integrity: IF showed positive staining of ZO-1 at intercellular borders indicating that characteristic tight junctions had between cells in the monolayer. A significant decrease in the paracellular flux of dextrans molecules was further detected in the cultured inserts in comparison to blanks. This suggests confluency of the membrane through it's ability to form a tight barrier preventing leakage between cells.

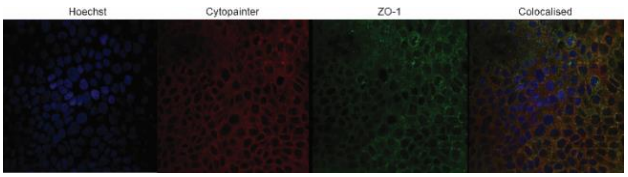

Figure 1. Fluorescence confocal laser scanning images at 40x of HaCaT inserts

Nanoparticle characterization: Physico-chemical analysis of nanoparticles identified characteristics conducive for drug delivery. However, improvements can still be made to surface characteristics such as charge and size uniformity to enhance bioavailability.

Nanoparticle permeation: Following 24 hour treatment, HPLC did not detect Probucol in the basolateral chamber, however it was present in the apical chamber. This suggests that Probucol-nanoparticles did not permeate through the membrane. We hypothesise that inadequate treatment time may be a limiting factor by not allowing sufficient time for the nanoparticles to be intracellularly trafficked

CONCLUSIONS:

This study provides early proof of concept for developing an *in-vitro* model of the RWM. Multiple improvements have been identified in this pilot model which can be utilized in further studies to more accurately represent the RWM's permeation characteristics.

ACKNOWLEDGEMENTS:

The work was partially supported by the European Union Horizon 2020 Research Project and Innovation Program under the Marie Skłodowska-Curie Grant Agreement No. 872370, the Curtin Faculty ORS-WAHAI Consortium, and the Australian National Health and Medical Research (APP9000597). Al-Salami H is currently receiving funding from Beijing Nat-Med Biotechnology Co., Ltd. and Glanis PTY Ltd.

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Session 3: Mechanobiology

01:25PM to 02:35PM
Chair: Dr Huan Ting Ong

Three-dimensional characterisation of cellular elasticity using quantitative micro elastography

Presenting Author: matt.hepburn@uwa.edu.au, ECR
Matt S. Hepburn[1,2], Alireza Mowla[1,2], Jiayue Li[1,2], Samuel Maher[3], Danielle Vahala[3], Sebastian Amos[3], Farzan Navaeipour[1,2], Yu Suk Choi[3], and Brendan F. Kennedy[1,2]
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INTRODUCTION:

The mechanical properties of cells and the extracellular matrix (ECM) are increasingly recognised as critical regulators of cell functions including growth and differentiation [1]. However, whilst it is established that accurate measurement of cell mechanical properties should be performed in a three-dimensional (3-D) environment, techniques available to quantify mechanical properties on the microscopic scale are typically limited to two-dimensional (2-D) surface characterisation or analysing cells in isolation. Optical coherence elastography (OCE) holds potential to characterize the mechanical properties of cells in 3-D within their microenvironment [2]. Quantitative micro-elastography (QME) is a variant of compression-based OCE that maps elasticity throughout a sample volume with micro-scale resolution over millimetre fields of view [3]. In this work, we present the development of Quantitative micro-elastography (QME) to characterise the elasticity of cells and the ECM in 3-D biomaterials.

METHODS:

Encapsulating cells in hydrogels: We analyzed the elasticity of 3-D methacrylated gelatin (GelMA) hydrogels (6.5% weight-to-volume) with encapsulated human adipose-derived stem cells (ASCs) (ASC-F-SL, Zen Bio). Crosslinked hydrogels containing cells were placed in standard media and incubated for fourteen days at 37°C and 5% CO2 to ensure cell growth and spread. ASCs and TAZ- (a mechanosensitive transcription factor which regulates cell volume) activated ASCs were encapsulated in hydrogels under the same conditions.

QME measurements: QME measurements were performed using a fiber-based spectral-domain OCT system (TEL320, Thorlabs Inc., USA).

Signal processing: To improve the resolution of cellular-scale features in QME, we extend a framework developed by our group for analyzing spatial resolution in compression OCE.

RESULTS & DISCUSSION:

Our results demonstrate that QME can reveal elevated elasticity in local regions surrounding cells and can distinguish between different cell types (**Figure 1**). Furthermore, we demonstrate the ability of QME to characterise intra-cellular elasticity in both cells and cell spheroids.

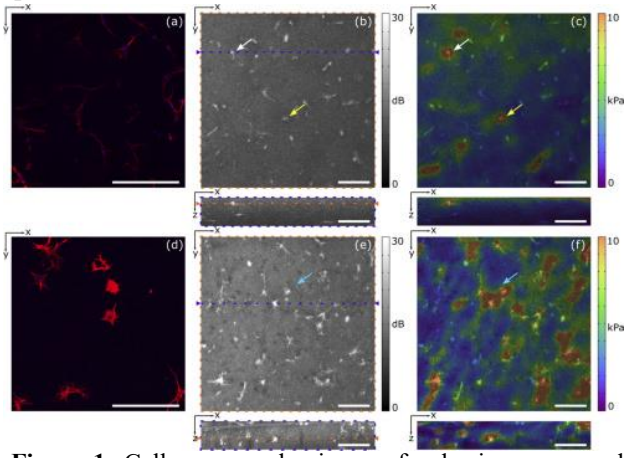

Figure 1: Cells measured using confocal microscopy and dual-arm QME. Representative confocal microscopy of GelMA with (a) ASCs and (d) TAZ activated ASCs with cell nuclei shown in blue, and actin filaments in red. (b) OCT and (c) OCT/QME overlay images of ASCs. (e) OCT and (f) OCT/QME overlay images of ASCs with TAZ activation. The arrows indicate example regions where individual cells have elevated elasticity. Scale bars represent 250 µm.

CONCLUSIONS:

We believe QME has potential to bridge the gap between the large body of existing research in 2-D substrates and how mechanical properties influence cell behaviour *in vivo*.

REFERENCES

[1] B. Ladoux and R. M. Mège, *Nature Reviews Molecular Cell Biolology*, vol. 18, pp. 743–757, 2017.
[2] K. V. Larin and D. D. Sampson, *Biomedical Optics Express*, vol. 82, pp. 1172–1202, 2017.
[3] K. M. Kennedy, *et al*, *Scientific Reports*, vol. 5, 15538, 2015.

MECHANOSENSATION, PROLIFERATION AND INVASION OF BREAST CANCER SPHEROID IN 3D LINEARSTIFFNESS GRADIENT HYDROGELS

Danielle Vahala[1], Marta Sacchi[1], Sebastian Amos[1], Chrissie Astel[1], Bram Soliman[2], Khoon Lim [2], Yu Suk Choi [1]
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INTRODUCTION:
Breast cancer remains one of the largest health concerns with 2.3 million women diagnosed in 2020 and 685 000 deaths globally. Tumour development is accompanied by increased ECM deposition over time (temporal) while creating a spatial stiffness gradient from the core (soft) to the periphery (stiff). Increased tissue stiffness leads to inappropriate cellular responses including highly invasive and migratory phenotypes. Cancer mechanosensation is predominately studied using 2D platforms with discontinuous, discrete stiffnesses which limits recapitulation of the dynamic 3D properties of the tumour microenvironment. The primary aims of this study are to recapitulate the spatio-temporal stiffening of tumour tissue by developing a 3D linear stiffness gradient hydrogel with on-demand stiffening and encapsulate cancer spheroids to investigate tumour growth and mechanosensation.

METHODS:
Hydrogels were fabricated using allylated gelatins (GelAGE) with
spatially and temporally controlled UV exposure via transparency gradient photomasks. MCF7 cells were suspended within pre-polymerised GelAGE and cultured for 10-days with live-cell imaging.

RESULTS & DISCUSSION:
When the spatial gradient was established at day 0 spheroids exhibited restricted expansion with no change to cell number and greater mechanosensitivity compared to a delayed spatial gradient established after spheroid growth (day 5). Interestingly, Lamin-A level increased with stiffness (2 to 13.1kPa) whilst the stiffest condition (16.8kPa) showed significantly lower levels of Lamin-A. Only when spheroids were grown in dense network however did they display significant levels of YAP. This combined with Lamin-A data suggests spheroids grown within a stiff matrix at day 0 and experiencing the highest degree of compression, could be entering premetastatic state favouring more deformable and migratory phenotype.

CONCLUSION:
The development of a hydrogel with a pathophysiologically relevant gradient stiffness and integration of spheroid culture has improved on current in-vitro platforms to study cell-matrix interactions and allowed for greater investigation into cancer growth and mechanosensation.

Decoupling the effects of pore size and extracellular matrix stiffness on 3D stem cell mechanosensation

Samuel J. Maher[1], Chrissie Astell[1], Sebastian E. Amos[1], Vihara Ellepola[1], Yongsung Hwang[2], Jennifer Young[3, 4], Yu Suk Choi[1]

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INTRODUCTION:

The microenvironment provides a vast array of signalling cues to cells that regulate cell behaviour and phenotype, all of which play a vital role in homeostasis. Given the complexity and ever-changing presentation of the extracellular matrix (ECM) *in vivo*, it remains challenging to identify the primary drivers of mechanosensitive response in 3D. As such, this study aims to develop and utilise tuneable hydrogel platforms to draw conclusions about the independent effects of pore size and ECM stiffness on 3D stem cell mechanosensation.

METHODS:

Human adipose-derived stem cells encapsulated in phototunable gelatin methacryloyl hydrogels were cultured for six days at either a static or gradient stiffness allowing for equal or variable expansion, respectively. Following this, hydrogels were 'on-demand' stiffened using UV photomasks to a desired stiffness and after a further two days, observations of cell morphology and protein expression were made.

RESULTS & DISCUSSION:

Cell volume was successfully limited by hydrogel stiffness with cells being significantly larger in areas of lower substrate stiffness. Furthermore, the gradient expansion model (varied expansion with same mechanosensation) showed a significant decrease in nuclear localisation of both YAP and MRTFa. In contrast, the equal expansion model (same expansion with differential mechanosensation) showed no significant changes in cell morphology or mechanomarker expression. However, in both platforms, a correlation between cell volume and nuclear mechanomarker localisation was observed.

CONCLUSIONS:

The current results from this platform suggest that 3D mechanosensation is controlled by volume expansion, not stiffness. The findings of this study may prove useful in controlling stem cell fate for regenerative medicine purposes.

ACKNOWLEDGEMENTS:

This research was supported by an Australia Government Research Training Program Scholarship. This work was funded by NHMRC #1098449 & WANMA from the WA Department of Health.

Investigating the role of cell adhesion in the tumour microenvironment with a 3D cancer spheroid model

Sebastian E. Amos[1], Hyunbin D. Huh[2], Matt S. Hepburn[3], Jiayue Li[3], Alireza Mowla[3]
Brendan F. Kennedy[3], Hyun Woo Park[2] and Yu Suk Choi[1]
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[2]*Yonsei University, Seoul, KOR;*
[3]*Harry Perkins Institute of Medical Research, Perth AUS*

INTRODUCTION:

The remarkable phenotypic plasticity of cancer cells permits the negotiation of mechanical challenges presented by the metastatic cascade, such as extreme confinement, pinch point constrictions, anoikis and shear stress. However, the mechanisms that drive these shifts remain incompletely understood. Moreover, existing paradigms in cancer metastasis research incompletely characterise observed cancer cell behaviour, especially changes to cell adhesion and deformability in invading or circulating tumour cells, for example. Here, we explore the role of a novel set of endogenous haematopoietic transcriptional regulators that reprogram cell adhesion and mechanosensitivity in primary tumour growth with a 3D pancreatic cancer cell spheroid model.

METHODS:

Cells: A pancreatic cancer cell line (SUIT-2) was transfected with adhesion-dependent plasticity (ADP) factors to convert adherent cells into adhesion-independent cells without lineage-specific differentiation by eliciting spontaneous cell rounding, cell-matrix dissociation, and anoikis resistance.

3D microenvironment: Adherent and suspended phenotype SUIT-2 cells were encapsulated in 3D gelatin methacryloyl hydrogels crosslinked to form either a soft (normal) or stiff (cancerous) condition. Encapsulated cells were cultured for 7 days to form spheroids before fixation, staining and imaging. Quantitative micro-elastography was also performed to visualise the intra-spheroidal distribution of elasticity.

Analysis: 3D confocal datasets were analysed with a custom GPU-accelerated ImageJ/FIJI plugin. Briefly, the nuclei were segmented while each whole spheroid was gated and used to generate a core, peripheral and cytoplasmic region of interest (ROI). The nuclear objects and spheroid ROIs were used to conduct region-restricted analyses of fluorescent proteins and volumetric measurements.

RESULTS & DISCUSSION:

Volumetric measurements: Suspended-type spheroids grew significantly larger and more elongated than their adherent-type counterparts. They also contained significantly more nuclei, and nuclear volume was greater.

Intensity measurements: Spheroids with suspended-type cells expressed more nuclear Ki-67 and YAP, while Lamin-A/C was also higher in the whole, core and peripheral ROIs. Notably, the expression of vimentin, a marker associated with the epithelial-mesenchymal transition (EMT), was significantly reduced in suspended-type spheroids, demonstrating that ADP is a novel, EMT-adjacent paradigm.

Quantitative micro-elastography: Stress distribution closely matched the expression of the cytoskeletal protein filamentous actin (F-actin). In suspended-type spheroids, the intra-spheroidal distribution of mechanical stress and F-actin expression was centralised to the core. In contrast, elasticity and F-actin expression were largely peripheral in adherent-type spheroids.

CONCLUSIONS:

While ADP factors are proposed mediators of circulating tumour cell survival, these data highlight the role of adhesion in tumour spheroid growth under 3D confinement and demonstrate a dramatic reprogramming of cancer mechanics that elucidate the role of adhesion in primary tumour growth.

ACKNOWLEDGEMENTS:

This work was supported by a WANMA from the Western Australian Department of Health (Y.S.C), a UWA RIGG (Y.S.C and H.W.P), and a Hackett Postgraduate Scholarship and an Australian Government Research Training Program Scholarship (S.E.A). The authors also thank the Centre for Microscopy, Characterisation and Analysis at UWA.

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Session 4: Characterisation Techniques & Biofabrication

03:05PM to 03:50PM
Chair: Mr George McColgan

Engineering Heart Valve Interfaces Using Melt Electrowriting: Biomimetic Design Strategies from Multimodal Imaging

Michael J. Vernon[1,2,3], Jason Lu[1,3], Benjamin Padman[4], Christopher Lamb[1,3], Ross Kent[5], Petra Mela[6], Barry Doyle[2,3], Abdul Rahman Ihdayhid[7,8], Shirley Jansen[7,9], Rodney J. Dilley[1] and Elena M. De-Juan-Pardo[1,3]

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INTRODUCTION:

The aortic heart valve has multiple heterogeneous regions, each of which helps enable the valve's crucial function. The interfaces between these regions not only physically join these regions but, importantly, contribute to their orchestrated interplay and function. Here we explore the ability of melt electrowriting (MEW) to engineer complex interfaces for heart valve scaffolds using a biomimetic approach.

METHODS:

Multimodal Imaging of Porcine Tissue: Micro-computed tomography, second harmonic generation imaging and focused ion beam - scanning electron microscopy were used to characterize the collagen orientation and density in porcine aortic valves to be used as inspiration for biomimetic heart valve design.

Multiphasic MEW Scaffold Interface Fabrication and Characterization: Three interfacing methods of multi-phasic MEW scaffolds (overlapping, suturing and continuous) were investigated for their morphological, tensile and flexural properties. Scaffolds were fabricated from medical-grade poly(ε-caprolactone) using an in-house-built MEW device.

Bio-inspired Heart Valve Interface Scaffold Design, Fabrication and Characterization: Based on the findings of the multimodal imaging and interface characterization investigations, a bio-inspired heart valve interface scaffold was designed, fabricated via MEW and mechanically characterized biaxially under physiologically relevant tensile strains.

RESULTS & DISCUSSION:

Multimodal Imaging of Porcine Tissue: Collagen orientation, density and recruitment was revealed in previously unexplored regions of the aortic valve including the commissure, inter-leaflet triangle, and the interfaces between them.

Multiphasic MEW Scaffold Interface Fabrication and Characterization: Continuous interfaces demonstrated superior properties with respect to print accuracy and flexural properties.

Bio-inspired Heart Valve Interface Scaffold Design, Fabrication and Characterization: A multiphasic scaffold was fabricated with continuous interfaces, gradient porosities, variable layer numbers across regions and tailored fiber orientations based on the previously analyzed tissue. When characterized under physiologically relevant tensile strains, the scaffold exhibited similar behavior to porcine heart valves with respect to yield strain, hysteresis, and relaxation behavior.

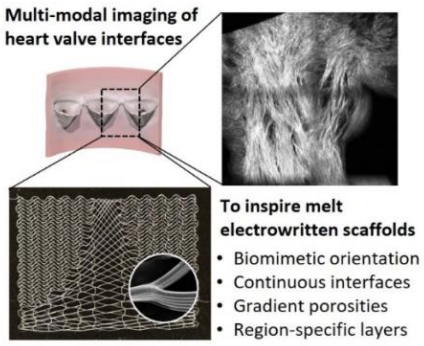

Figure 1: Bioinspired Design Approach. Overview of process used to design bioinspired heart valve interface scaffold. Showing regions of interest analyzed using multimodal imaging, and corresponding scaffold.

CONCLUSIONS:

This work demonstrates the ability of a bio-inspired approach for MEW scaffold design to address the functional complexity of biological tissues.

ACKNOWLEDGEMENTS:

We also acknowledge the facilities and assistance of Microscopy Australia at CMCA UWA, a facility funded by the University, State and Commonwealth Governments.

Investigation of parameters that impact layer bonding in melt electrowritten scaffolds

Christopher Lamb [1,2], Paul Dalton[4], Brendan Kennedy[2,3], Adrian Keating [2], Elena M. De-Juan-Pardo [1,2]

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In situ characterisation of melt-electrowritten scaffolds in 3D using optical coherence tomography

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INTRODUCTION:

Recent developments in melt electrowriting (MEW), a high-resolution additive manufacturing technology, have led to increases in scaffold complexity. However, MEW scaffolds are currently characterised *ex situ*, which causes time–consuming iterations of characterisation and fabrication that limit scaffold throughput and more widespread use of the technology. For the first time, an *in situ* method to characterize the 3D microstructure of MEW scaffolds using optical coherence tomography (OCT) is described.

METHODS:

Ten medical grade poly(ε-caprolactone) (PCL) MEW scaffolds were manufactured with varied designs. Images were acquired with a benchtop spectral-domain OCT system. Calculations of microstructural features are performed on OCT data using a custom algorithm developed on MATLAB software. The same scaffolds were imaged with scanning electron microscopy (SEM). Statistical analysis was performed by an unpaired t-test.

RESULTS & DISCUSSION:

OCT calculations of fibre diameter and scaffold thickness are within an average of 0.31 and 1.79 µm, respectively, of corresponding SEM–derived calculations, however, this difference did reach significance ($p<0.05$, n=20 diameter & n=4 thickness). Similarly, OCT calculations of pore size are within 1% of SEM measurements, however, this reached significance ($p<0.05$, n=10).

Additionally, the 3D capabilities of OCT enable the non-destructive characterisation of scaffolds with depth–varying microstructures, overcoming some main limitations of SEM.

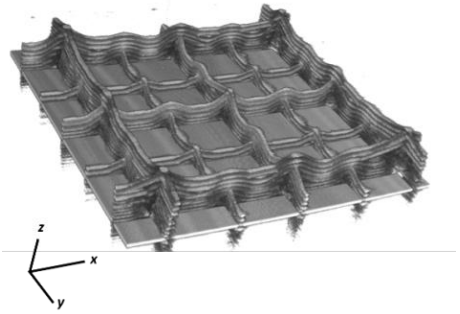

Figure 1: 3D-OCT imaging. 3D reconstruction of MEW scaffold with depth-varying pore size from OCT data.

Finally, *in situ* characterisation is achieved by integrating the OCT scanner within an MEW printer, enabling the scaffold microstructure to be evaluated and optimized during manufacture. *In situ* fibre diameter measurements facilitate the changing of input parameters to optimize scaffold print, and *in situ* 3D renders enable insight into scaffold quality features such as wall stacking.

CONCLUSIONS:

This new capability represents an important step toward achieving an efficient fabrication–characterisation cycle with the guaranteed scaffold quality and reproducibility required to validate the manufacturing process.

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