AUSTRALIAN ORTHOPAEDIC ASSOCIATION

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Workforce

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Australian centre boosting biomedical engineering research and development for musculoskeletal conditions

Professor Hala Zreiqat AM

Recently, we have been celebrating the second anniversary of the Australian Research Council (ARC) Training Centre for Innovative BioEngineering. Launched at the University of Sydney in May 2018, this exciting initiative has brought together research institutions, hospitals and biotech companies to pioneer new biomedical technologies and build Australia's bioengineering workforce.

Here at the Centre we are developing a range of diagnostic and therapeutic technologies – innovative biomaterials, novel implants and wearable devices, AI-driven imaging tools, and 'smart' sensor and telemetry systems. As the Centre's name suggests, we are also doing a lot of training. Graduate and undergraduate students, postdoctoral researchers and professionals are being taught the latest technologies and research techniques. And when students complete their studies, we help them find a job.

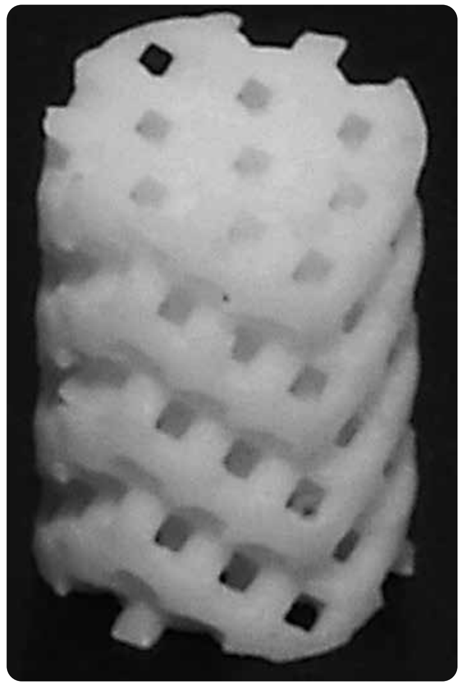
Here's a taste of the research and training we're doing.

Synthetic, customisable scaffolds to regenerate large bone defects

Due to the limitations of autografts and allografts, considerable research has been undertaken to develop synthetic bone grafts capable of repairing 'critical-sized' defects – large defects that cannot heal without intervention. But no synthetics able to bear normal loads have yet translated to the clinic.

To address this challenge, we have been developing novel ceramic materials. Ceramics are a promising bone substitute because they are light, stiff and strong. However, they are also brittle and easily fractured, and no ceramic scaffold has yet been strong enough for use in load-bearing sites such as the spine. A perennial difficulty is the trade-off between strength and bioactivity: to increase bioactivity you need more porosity, but this reduces strength.

By combining multiple strategies to improve the chemical composition and mechanical properties of our ceramics, we have succeeded in developing materials that are highly bioactive, porous and mechanically strong. Excellent bioactivity has been achieved by doping bioactive elements such as Zr, Sr, Mg, Al, and Fe into a calcium silicate backbone; this promotes bone formation without the need for additional cells or growth factors. The ceramics' strength derives from a multi-layer construction and carefully designed internal architecture.



A synthetic bioceramic scaffold

We can now fabricate our bioceramics into highly porous scaffolds with mechanical properties (stiffness $E = 15.3 \pm 2.8$ GPa; strength = 102 ± 13.2 Mpa) matching those of cortical bone. This means they have the strength to enable excellent tissue regeneration even in load-bearing sites. In preclinical load-bearing orthopaedic animal studies, some scaffolds demonstrated substantial bridging (~85%) and penetration by new bone into the scaffold structure. We are now working on optimising these bioceramics by giving them the toughness of native bone.

We are also developing a novel approach to designing and fabricating 3D scaffolds with complex shapes and architectures. Using computational modelling techniques and a new light-based 3D-printing technology we developed, our aim is the efficient and cost-effective production of bioceramic scaffolds that can be customised to a whole range of patient-specific applications.

Bioactive ceramic coatings with antimicrobial properties to increase the longevity of orthopaedic implants

Modifying the surfaces of commercially produced orthopaedic implants by coating them with another material can improve their functionality. At the Centre, we are using this strategy to address the premature failure of implants used for total hip and knee replacements. These implants typically fail within 10–15 years due to aseptic loosening and periprosthetic joint infection. This is increasingly problematic as people live longer.

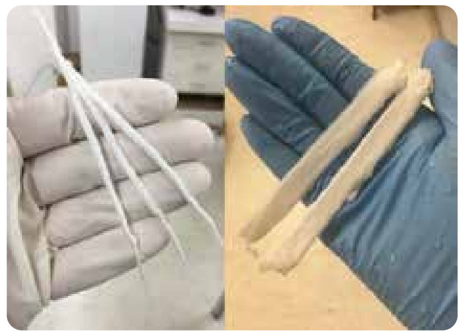
Using the plasma-spray coating technique, we can spray coatings made from our novel bioceramics onto the bone-contacting surfaces of implants. Coatings can be tens of nanometres to hundreds of micrometres in thickness, offering many options. Since our bioceramics significantly improve integration with bone and initial evidence suggests that they have antimicrobial properties that deter bacterial adhesion and growth, we are hoping this strategy will reduce aseptic loosening and infection.

Knee implant plasma sprayed with our novel ceramics

We are currently learning more about the relationship between coating microstructures (eg porosity and phase distribution in three dimensions) and mechanical properties (eg adhesion and biocompatibility) in order to optimise this technology.

Synthetic scaffolds to heal injured tendons and ligaments

There is an immense clinical need for readily available, off-the-shelf, mechanically strong synthetic scaffolds to repair ruptured tendons and ligaments. This is a significant engineering challenge, however, with materials to date exhibiting poor cell and tissue ingrowth, which eventually compromises their strength.



Synthetic tendon/ligament scaffolds

At the Centre, we have developed a novel fibre-reinforced hydrogel scaffold that mimics the hierarchical structure of native human tendons and ligaments. This synthetic scaffold exhibits an equilibrium water content of 70 wt %, similar to that of human tendon, and a tensile strength of (77.0–81.8 MPa) which matches the range found in the human Achilles' tendon. We also have promising in vivo results. Implanted into full-thickness rat patellar tendon defects, our scaffolds showed excellent collagenous tissue ingrowth after six weeks.

This ongoing work demonstrates the potential viability of our novel scaffolds for off-the-shelf biosynthetic tendon-graft material.

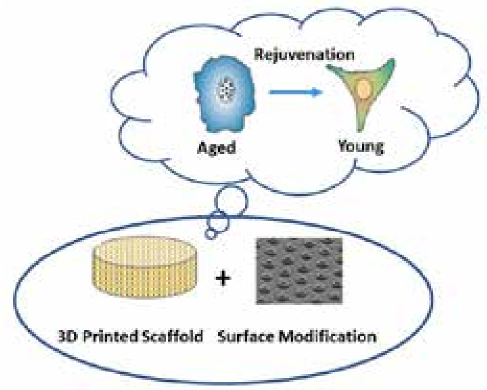
Bone regeneration and senescence

The single greatest risk factor for human diseases is age. Amongst other things, it contributes to the body's declining capacity to repair and regenerate bone tissue. We are investigating how to reverse this decline.

Firstly we demonstrated that our bioceramic scaffolds can significantly improve bone-regeneration capacity in aged animals. These findings indicated a feasible biomaterial strategy to promote bone tissue regeneration in the elderly.

Now we are investigating how to modify our bioceramics to address the particular problem of cellular senescence. Cellular senescence is a permanent state of cell cycle arrest, and it has emerged as one of the fundamental mechanisms of ageing.

Our research is providing deep insights into how chemical, physical and biological cues in aged bone tissue contribute to the development of the cellular senescent phenotype. Armed with this knowledge, we are manipulating the nanostructure and composition of our bioceramics to simulate a 'young' bone microenvironment. This should produce 'young' physical and chemical cues, which in turn should correct age-altered cell fingerprints, including cell shape.



By manipulating nanostructure and composition we will simulate a "young" bone niche. This will provide "young" physical and chemical cues to correct ageing-altered cell properties, rejuvenating aged cells and improving the regenerative capacity of the aged skeleton.

Ultimately we plan to develop a new class of biomaterial implants that provide cues to rejuvenate aged bone cells and thereby enhance elderly people's bone health.

Computer-aided analysis and visualisation of musculoskeletal images for orthopaedic surgery

When diagnosing and planning treatment for musculoskeletal conditions, orthopaedic specialists and surgeons routinely use images generated by positron emission tomography (PET), computed tomography (CT) and magnetic resonance (MR). These images help with, for example, quantifying and localising a tumour, deciding precisely where to place an implant, or determining the margins for surgical resection.

But using these images is time-consuming, and there is considerable intra- and inter-surgeon variability in how effectively they are used. If these images could be visualised so that complex and native 3D structures were easier to discern, such as a tumour without occlusion by surrounding structures, it would bring significant advantages.

At the Centre we are working with hospital and industry partners to develop an advanced computer-aided approach to help specialists and surgeons plan orthopaedic procedures. It involves an AI-driven image-segmentation algorithm, using state-of-the-art deep neural networks, that automatically detects and delineates tumours from surrounding structures on images. The segmentation output is then fed into our 3D volume-rendering algorithm, and finally presented to the surgeon via a HoloLens mixed-reality headset. As the pictures illustrate, using our approach a tumour can be clearly depicted without obstruction from surrounding anatomical features.

Computed tomography (CT) and positron emission tomography (PET) images, visualised in conventional 2D views (showing the corona views) and the 3D computer-aided visualisation counterpart. A soft-tissue sarcoma tumour is identifiable in both (a) CT and (b) PET images but lacks quantification and clarity. Our algorithm segmented the tumour region, providing quantitative information for diagnosis and enabling a 3D visualisation (c) that clearly articulates the tumour region in the context of its anatomical structures.

Bioelectronic devices

Bioelectronic devices are systems designed to deliver therapy through electrical stimulation or to monitor signals from biological tissues. Applications such as wound monitoring, pain management, electrical stimulation of muscle and neural tissues to enhance healing, and the recording of myoelectrical signals for improved control of prosthetic limbs are now being explored. However, the biosensors and biostimulators used in current systems are predominantly attached to the epidermal surface covering musculoskeletal tissue, resulting in poor specificity and signal strength.

We are exploring the printability of biocompatible conductive nanoparticles for electrode contact, combined with soft substrate and encapsulation materials. The electrode contacts are being designed to interface with the tissue close to the prosthetic limb or, in the case of wound monitoring devices, around the wound. This involves testing the material properties of the nanoparticles as well as testing the mechanical and electrical properties of the printed conductive electrodes and their integration with the external measurement system. By using innovative additive manufacturing technologies, our aim is to move beyond mass-produced one-size-fits-all devices towards automated fabrication tailored to the specific needs and anatomy of the individual.

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GENERAL ARTICLES

How AOA is shaping ethic al conduct within the healthcare sector

AOA CEO AND AEHA CHAIR Adrian Cosenza

AEHA PROJECT OFFICER Talysa Trevallion

The practice of ethical standards and behaviours is of particular importance at this time, and will continue to be of significance in achieving improved patient care post COVID-19.

Thanks to AOA's leadership as chair of the Alliance, and the involvement of multiple organisations in the healthcare sector, the Australian Ethical Health Alliance (AEHA) has made considerable progress in delivering ethical implementation activities, with the aim to improve patient care in the Australian community.

Over the past six months, AEHA has continued to encourage ethical conduct in the healthcare sector in numerous capacities. In particular, AOA – as AEHA chair – has led two AEHA Steering Committee meetings, where implementation plans were tracked and progress discussed. AEHA has contributed to the APEC Vision for 2025 and encouraged further flexibility in the model of the Australian Consensus Framework, incorporating high-level principles. Two working groups – the Communications and Media Working Group and the AEHA Symposium Working Group – were established and met on two occasions; through these meetings a number of awareness and communication activities, including a social media strategy, were progressed, and planning for an inaugural AEHA Symposium with the theme, 'Making Ethics Matter', proceeded (rescheduled to mid 2021).

AEHA also continues to be recognised for its leadership and progress on the global stage. AEHA was recently invited to be one of the first signatories to a global rollout of the IFC Ethical Principles in Health Care (or EPiHC) by the International Finance Corporation (IFC) of the World Bank Group. In addition, the Journal of Internal Medicine has accepted an AEHA academic publication, which is currently in press.

AOA was among six AEHA member organisations that recently participated in the first stage of a pilot on the Guide to Implementing the ACF and Self-Evaluation Form, which assessed the practicality and effectiveness of the document. Through this process, positive and valuable feedback was gathered on the practicality of implementing the ethical activities, and two further pilots are scheduled for progression in the latter half of the year.

AOA has played a significant role in contributing to the journey to more ethical behaviour in the healthcare sector, including within the orthopaedic community. The AOA Board receives reports on the progress of AEHA's implementation activities through the AOA Ethics Implementation Progress Report, with the aim to better implement the ACF principles into AOA's processes, policies and culture, alongside reports on the implementation of the AOA *Ethical Framework*.

Through AOA's leadership role within the Alliance, AOA continues to foster strong relationships with government, industry, healthcare institutions, medical colleges, specialties, patient groups and education providers – a key aim of the *AOA Strategic Plan 2019–2021*.

The membership should be proud to be the leader of a movement for improved ethical conduct and collaboration in the healthcare sector. By encouraging a commitment to ethical practice, AOA, with the support of the AEHA community, looks forward to strengthening healthcare delivery in the Australian community.

For more information on AEHA and the ACF, please visit the AEHA website: **ethicalhealth.org.au**

As part of AEHA's continued leadership recognition, the Australian Healthcare and Hospital Association's *The Health Advocate* recently published the following article that positively profiles the Australian Consensus Framework and the work on the initiative.