

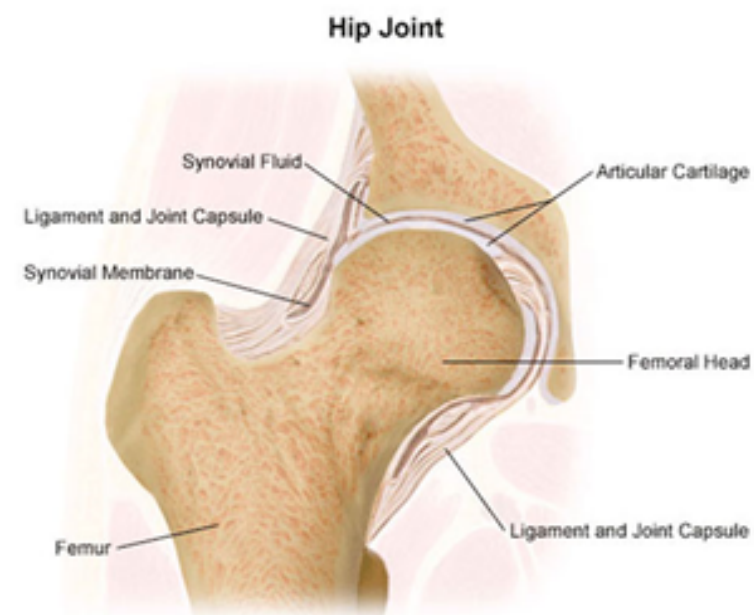
# Osteochondral scaffold innovation for early intervention of cartilage defect: from bench to clinic

Maryam Tamaddon, Chaozong Liu\*

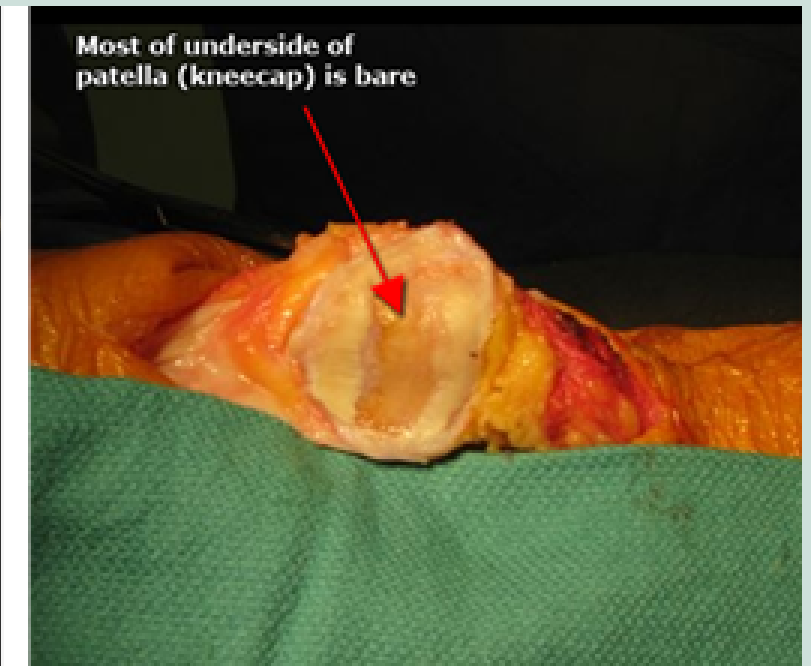
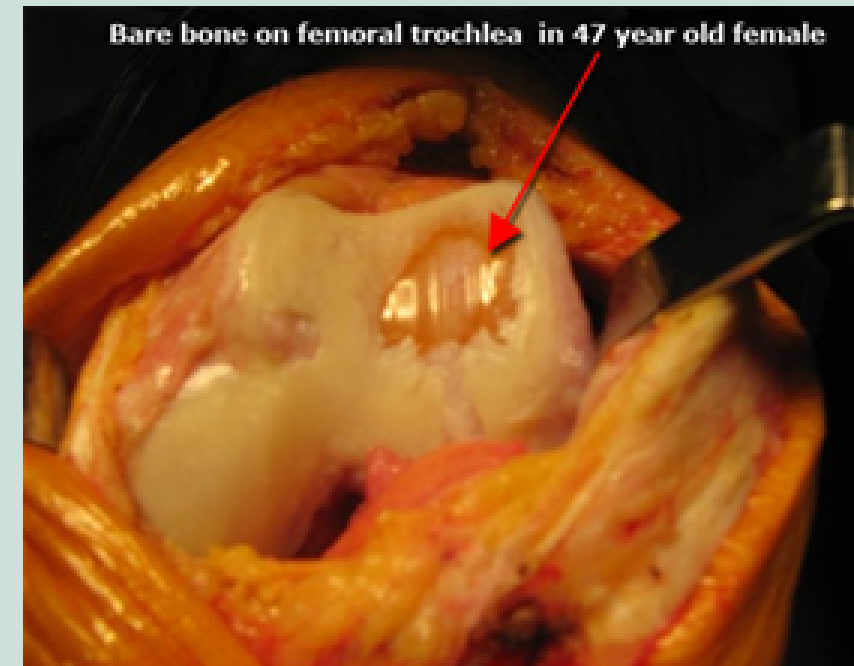
Institute of Orthopaedic & Musculoskeletal Science, University College London, Royal National Orthopaedic Hospital, Stanmore, London HA7 4LP, UK

*6th TERMIS World Congress, Maastricht, November 2021*

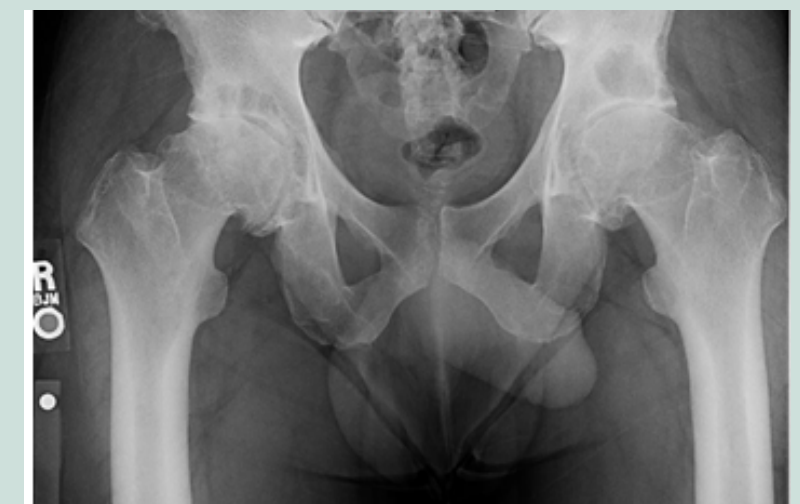
# Joint Disease Results in Cartilage Damages



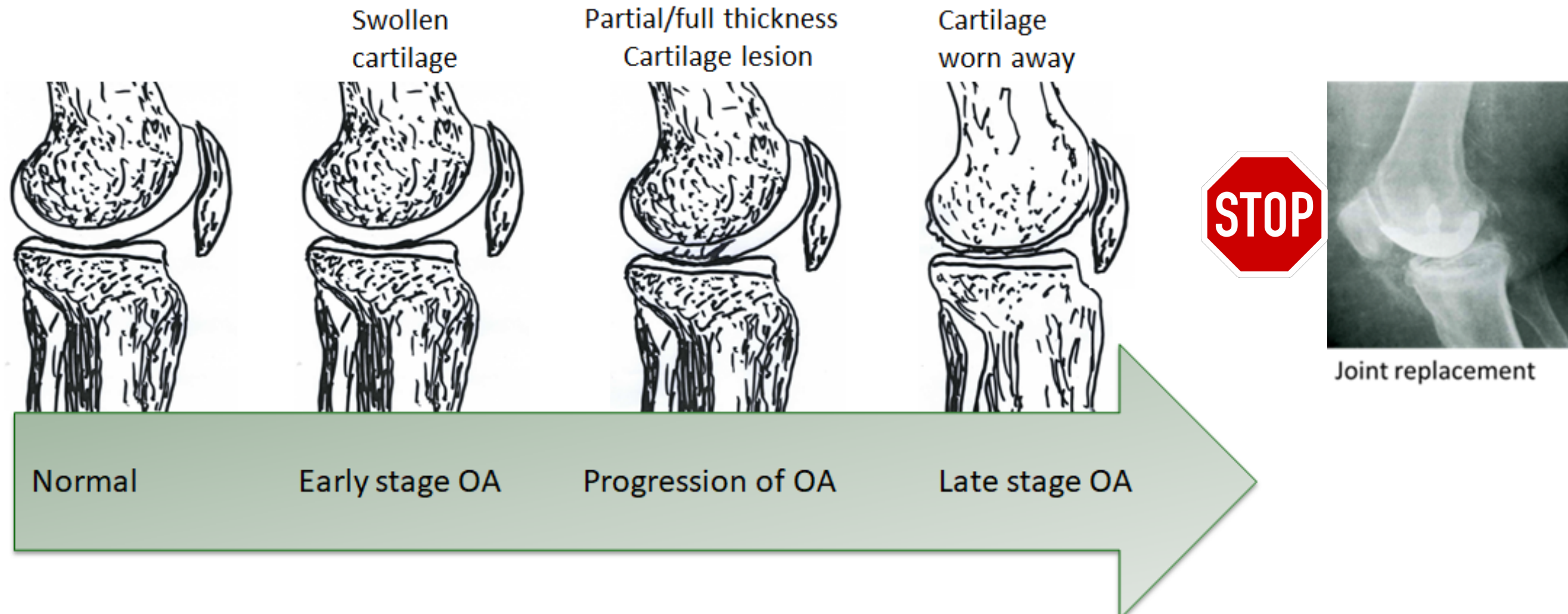
- Distribute joint loads over wide area
- Allow relative movement of joint with minimal friction and wear



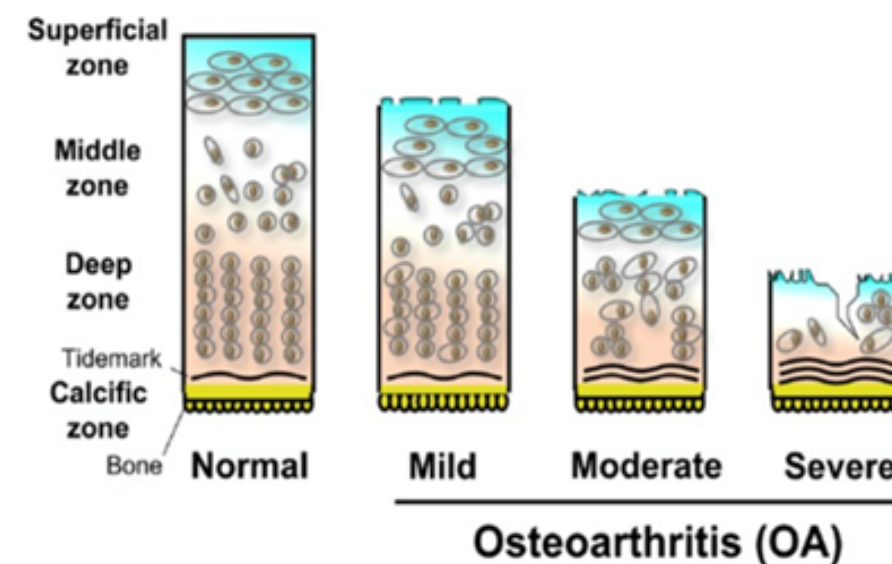
- (1) Joint space narrowing
- (2) Osteophytes
- (3) Subchondral sclerosis
- (4) Subchondral cysts
- (5) Structural damage



# Osteoarthritis – Treatment Options



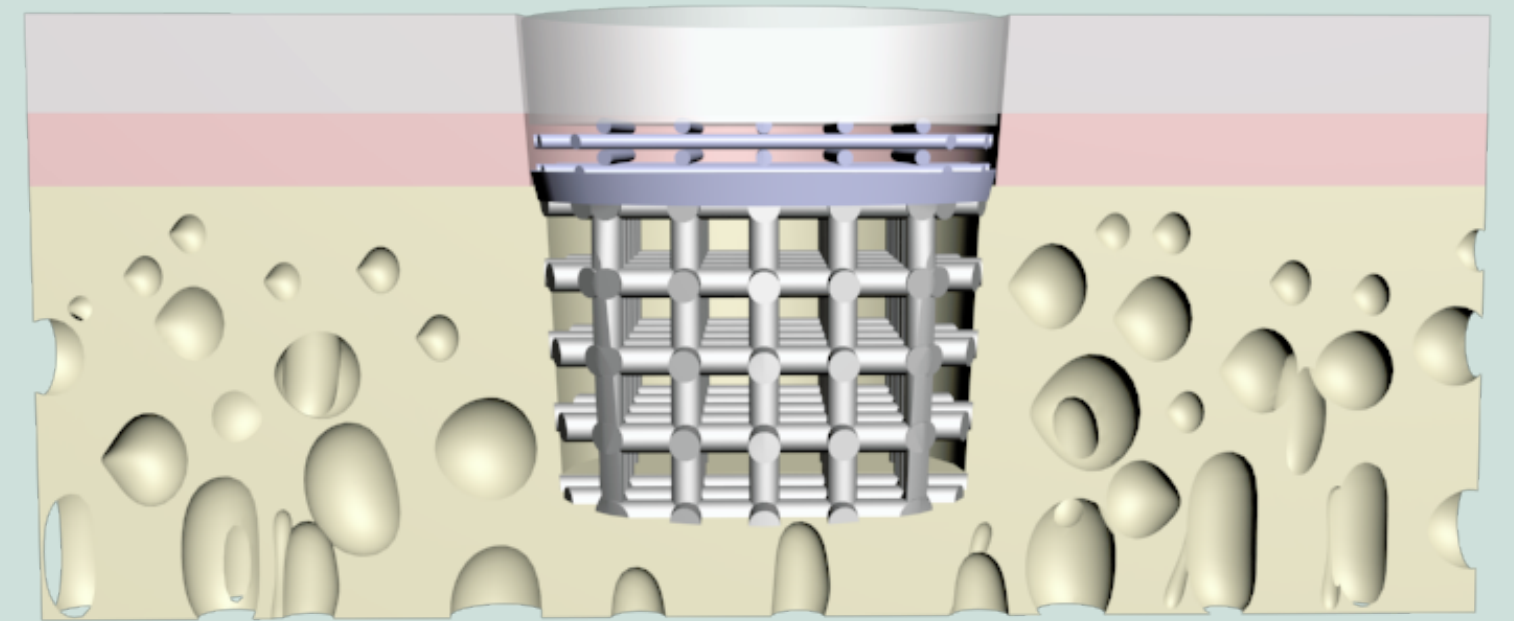
- Intervention of OA at early stage of progression



- Disruption of cartilage and it is non-reversible

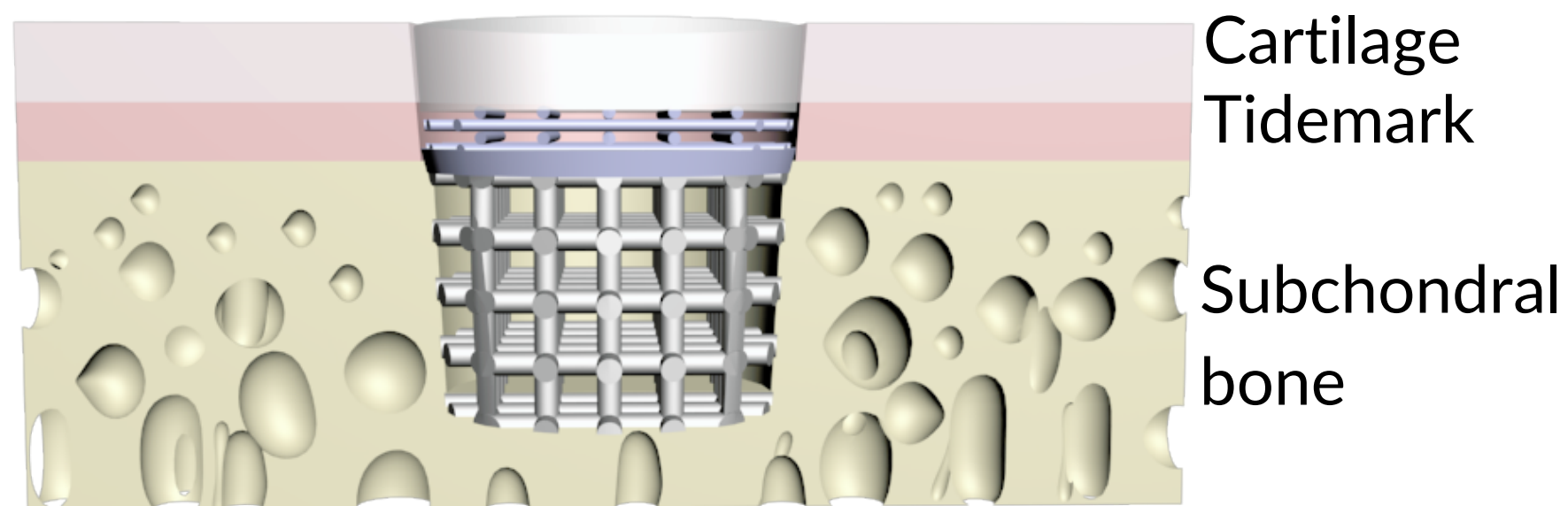


# Biomimetic Osteochondral Scaffold – UCL Stanmore Approach



# Concept

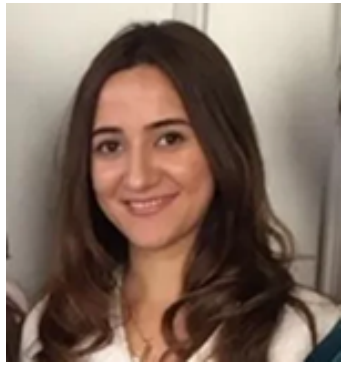
- Simultaneous regeneration of cartilage and underlining subchondral bone



- A conical hole is punched through the subchondral plate;
- An osteochondral scaffold with pre-defined size and shape is inserted into the defect;
- Recruit MSCs from bone marrow and provide the template to promote appropriate tissue ingrowth



# Concept Development



2014

EPSRC MeDe Innovation Feasibility Study (£50k)

- Clinical specification
- Fabrication and optimisation;
- In vitro evaluation

2015

ARUK-IKC PoC study (£100k)

- In vitro biological performance
- Small scale short term safety and efficacy animal study (10 sheep, 12 weeks);
- Market analysis.
- IP protection



2017

Innovate UK via Newton Fund (£998k) + MoST (10m CNY)

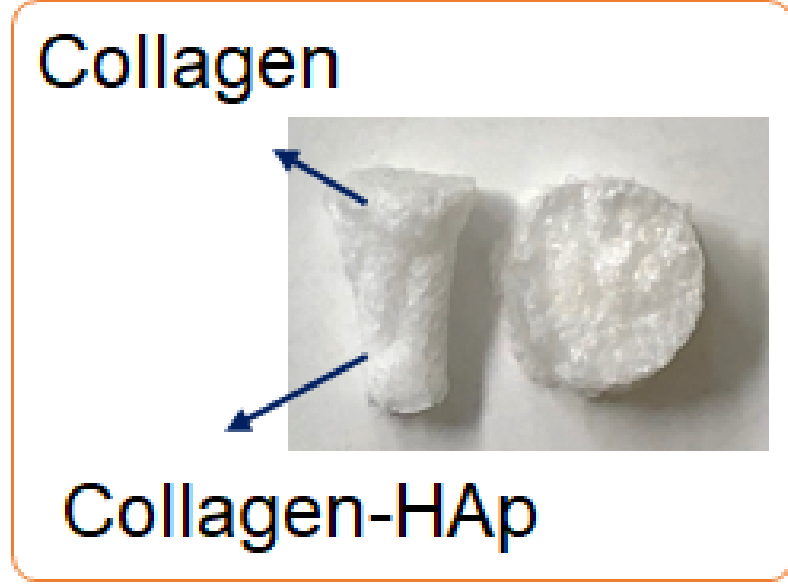
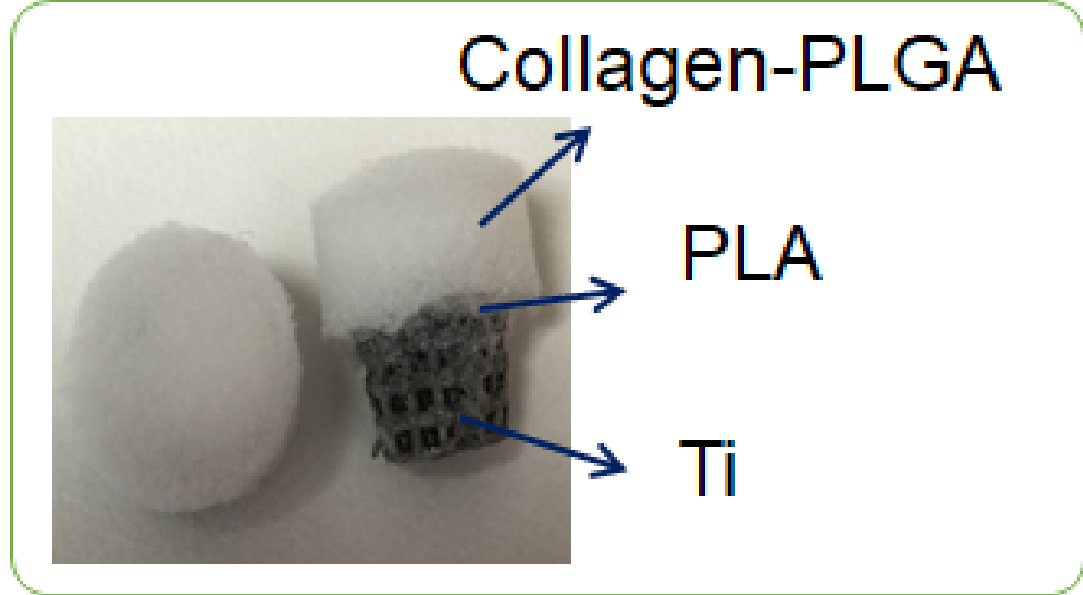
- Clinical stratified specifications
- Translation of lab protocols;
- GMP manufacturing
- Surgical tools
- Large scale, long-term safety and efficacy animal study (sheep & rabbits)
- Human tissue explant as disease-relevant model
- Market analysis



# Product Development



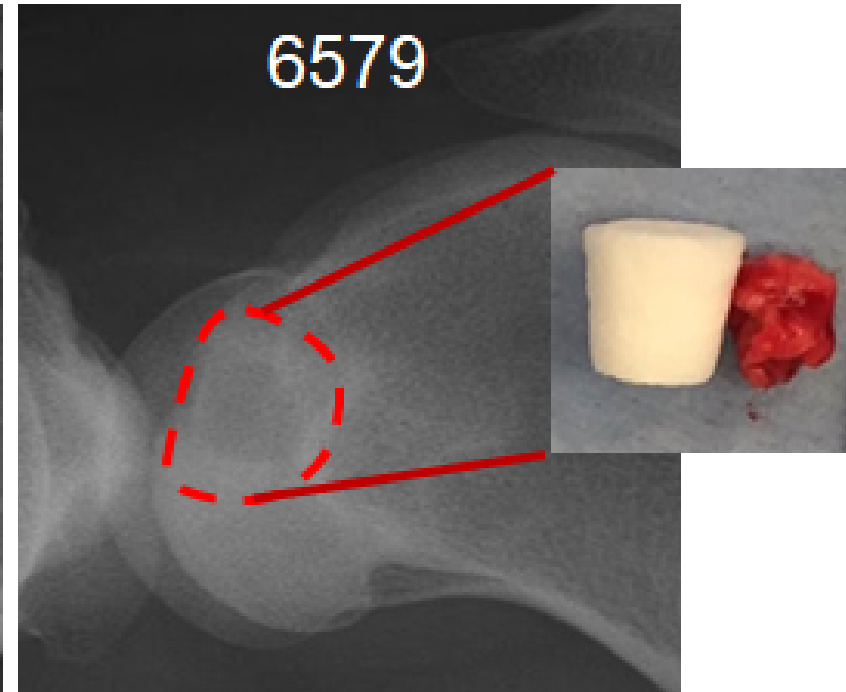
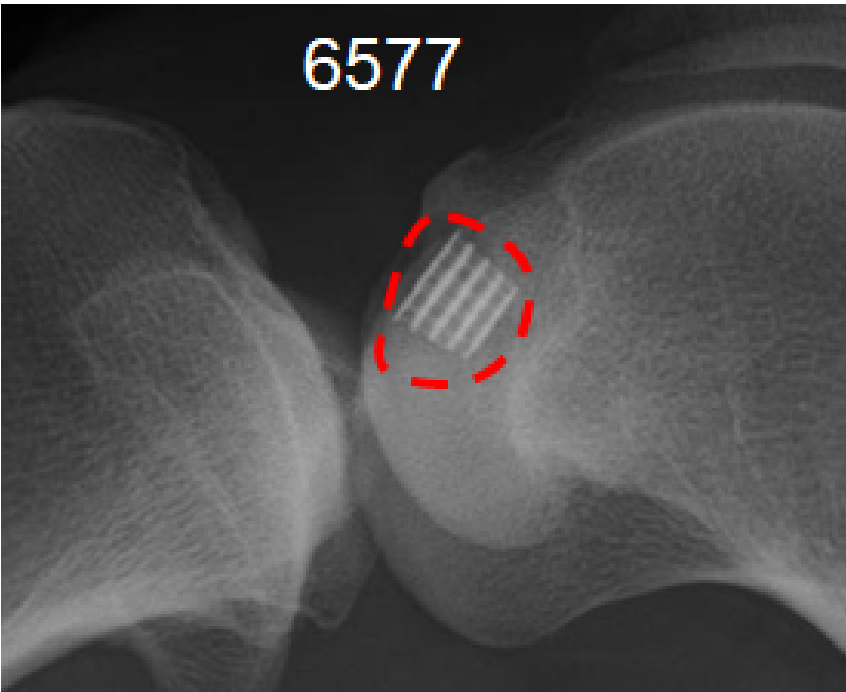
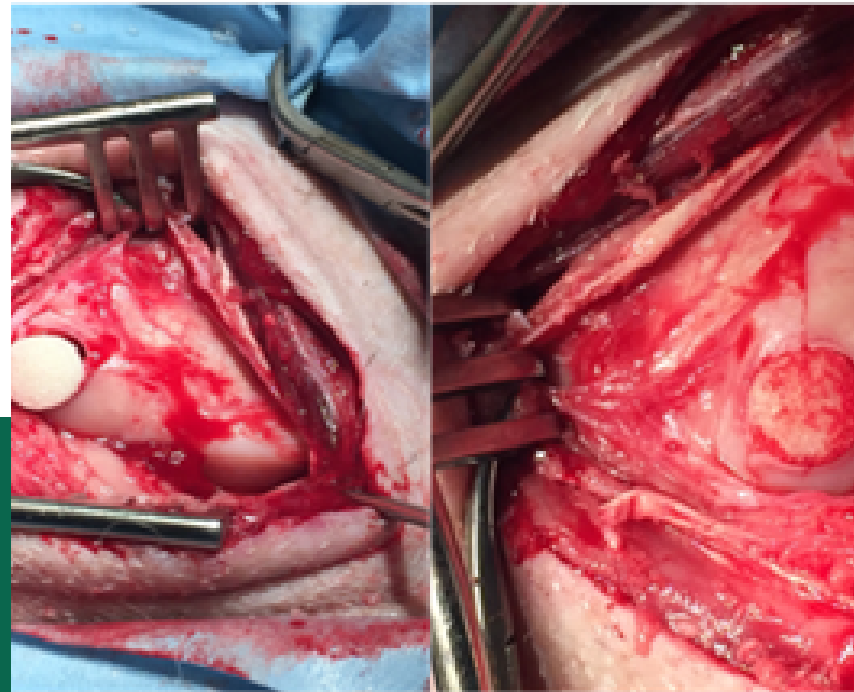
# Osteochondral scaffold – sheep condyle model



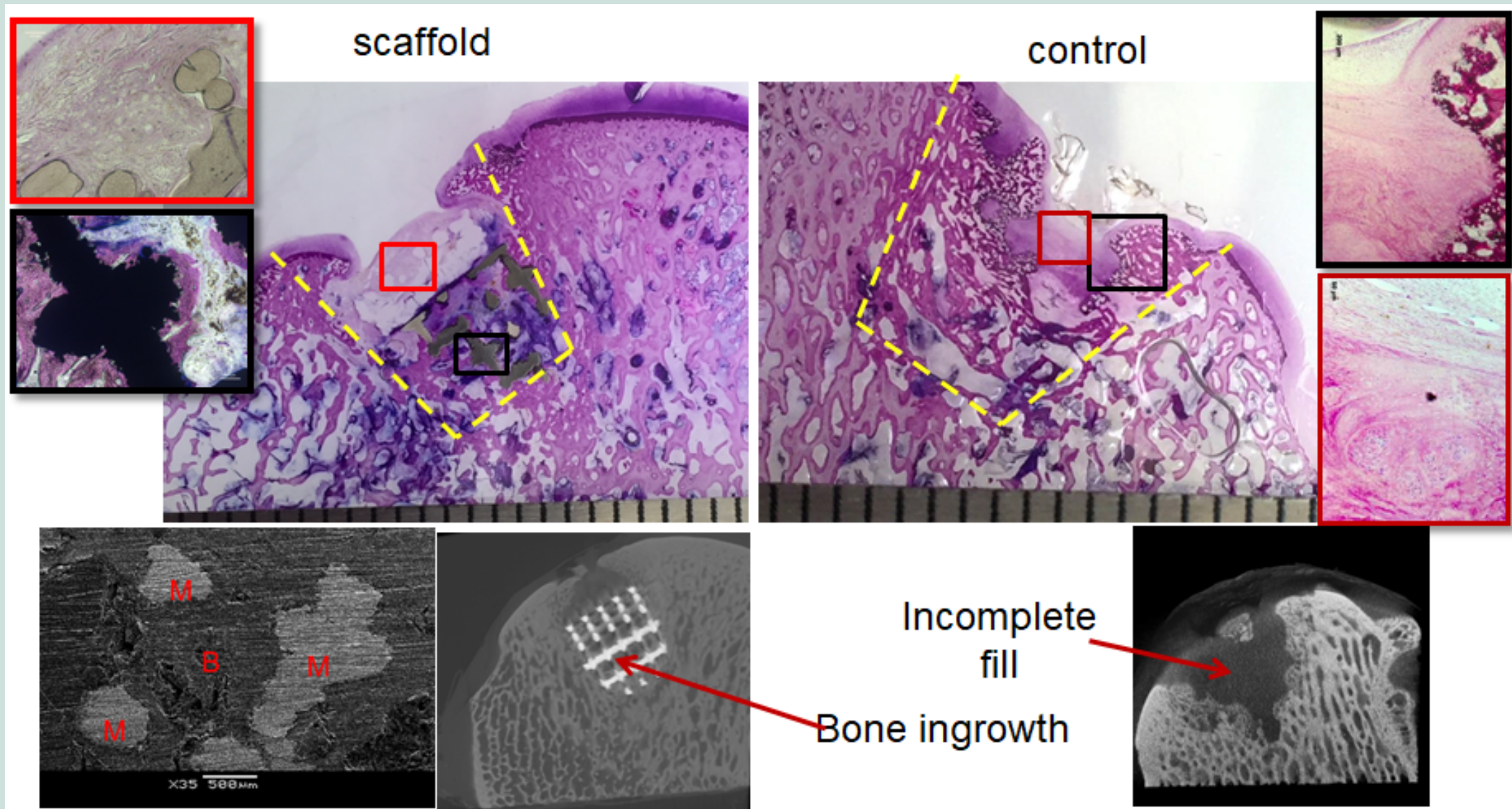
Scaffold was implanted in the sheep condyle

The scaffold form a stable fixation in the bone

The control scaffold shrank upon contact with blood and could not fill in the joint

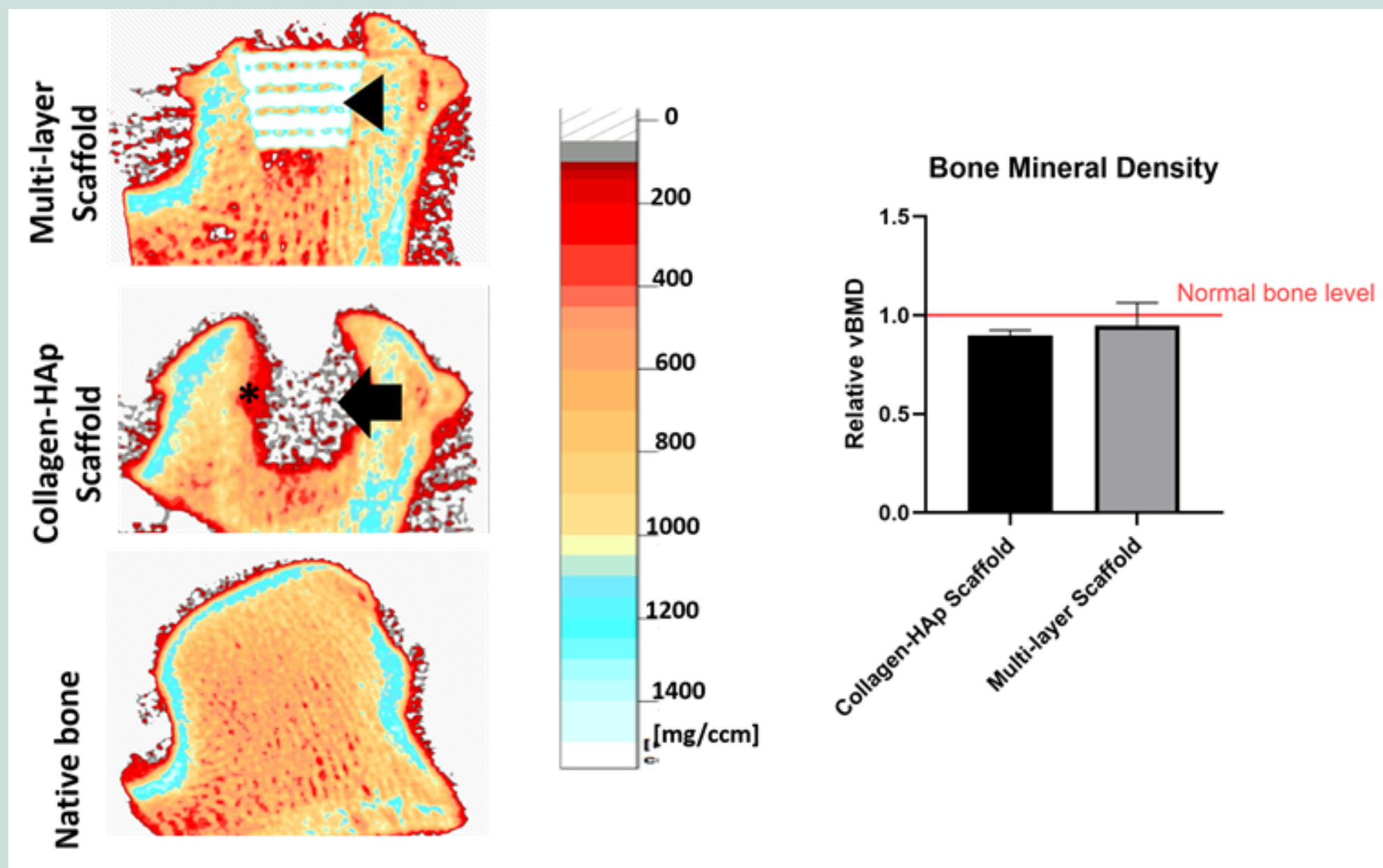






# Improved bone formation

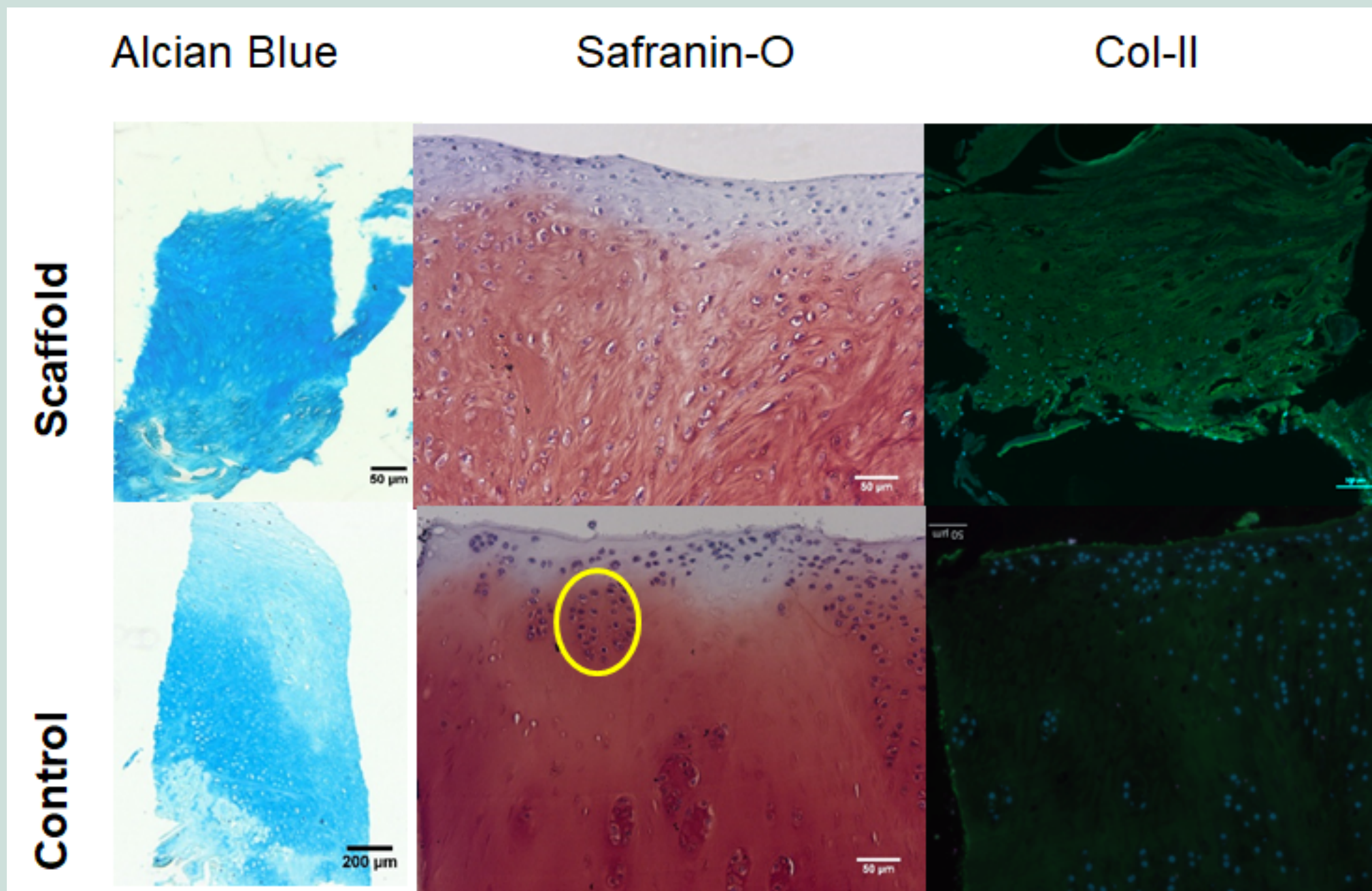
- Extensive bone ingrowth and integration in Ti layer, while fibrous tissue observed instead of bone in control



# Improved bone formation

- Consistently higher values of bone mineral density in scaffold groups compared to control groups





Improved  
cartilage  
formation

- Formation of hyaline-like cartilage in scaffold group

24 October 2017

Ref: KP/21875

Dr Chaorong Liu  
Royal National Orthopaedic Hospital  
Brockley Hill, Stanmore  
London  
HA7 4LP

Dear Dr Liu

Outline application for an Arthritis Research UK Priorities in Clinical Research award

Thank you for your application to the priorities in clinical research call entitled 'A first-in-man study to assess short-term safety and efficacy of a novel osteochondral scaffold in early repair of cartilage defects'. Applications have now undergone review by the Arthritis Research UK Treatment Subcommittee. The purpose of the review is to identify at an early stage those proposals which the charity wish to invite to full application and those that will not be invited.

Outline applications were assessed on scientific quality, strategic relevance and remit, quality of the research design and feasibility of the work proposed.

I am pleased to inform you that after careful consideration the Treatment Subcommittee have recommended that your outline go through to a full application in this round.

The subcommittee were of the opinion that this was an exciting proposal with the potential to provide a novel intervention for a large number of patients and potentially provide good value for money for the health services. The panel members were impressed by the significant patient involvement in the development of the proposal and the plans described to disseminate the results following the completion of the study.

Additionally, the subcommittee have some recommended amendments and further comments for your consideration while preparing the full application. These are as follows:

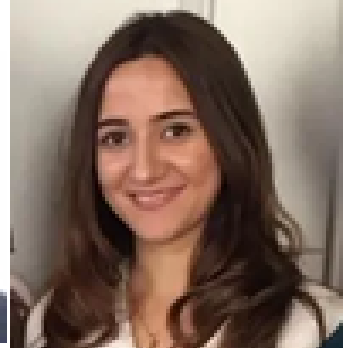
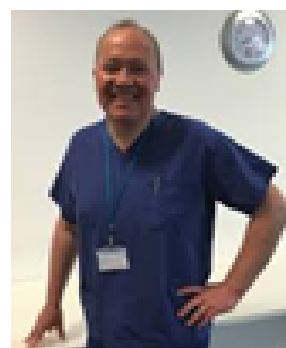
# COWALK - From Animals to Human

## First in human study



- 20 Patients
- RNOH
- 01 Oct 2019 ~ 30 Sep 2023

The subcommittee were of the opinion that this was an exciting proposal with the potential to provide a novel intervention for a large number of patients and potentially provide good value for money for the health services. The panel members were impressed by the significant patient involvement in the development of the proposal and the plans described





The biomimetic osteochondral scaffold has been developed via an ARUK-IKC PoC award. It has a gradient architecture and varied mechanical strength to reflect the hierarchical nature of the osteochondral unit.

The in vivo sheep condyle model evaluation have demonstrated the resultant scaffold achieved stable mechanical fixation and could provide support to the overlying cartilage.

Development of osteochondral scaffold for intervention of osteoarthritis progression is still a grand challenge. An ideal scaffold should recapitulates the physical environment found in vivo to promote appropriate tissue ingrowth

**COLLABORATION IS  
KEY TO ACHIEVING  
TRANSLATION!**

## Perspective Summary



**UCL**

# Acknowledgements

# VERSUS ARTHRITIS

**Medical  
Technologies**  
INNOVATION AND KNOWLEDGE CENTRE

**MeDe**  
Innovation  
EPSRC Centre for  
Innovative Manufacturing  
in Medical Devices



Horizon 2020  
European Union funding  
for Research & Innovation

