

Next Generation VESTAKEEP® PEEK

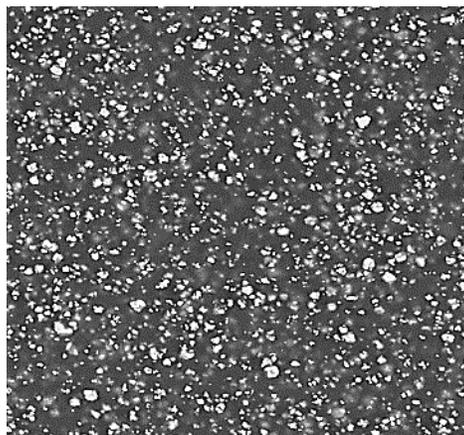
Mahrokh D, Andrew W, Subhadip B, Harsh P,
Suneel B, Jonas S, Thomas P, Ken R, Kyle M, Simon T, Marc K

Balaji Prabhu

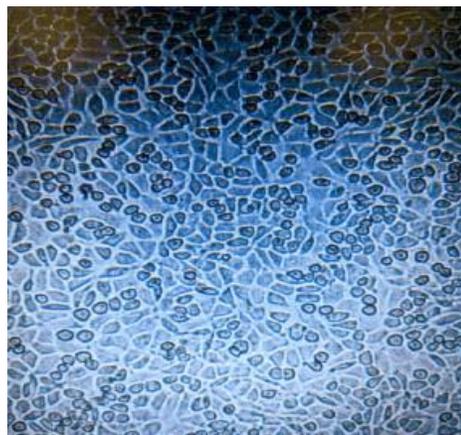
Medical Device Competence
Center (MDCC)

PEEK Meeting
Washington DC
25 April 2019

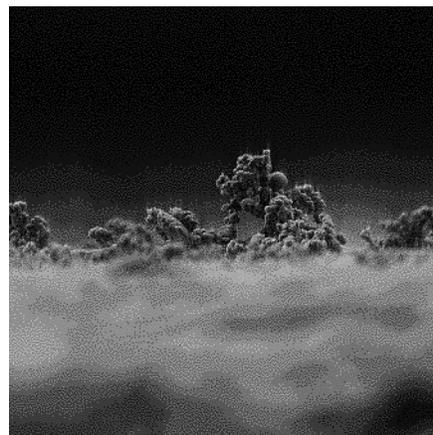
MICROSTRUCTURE



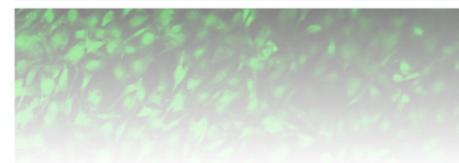
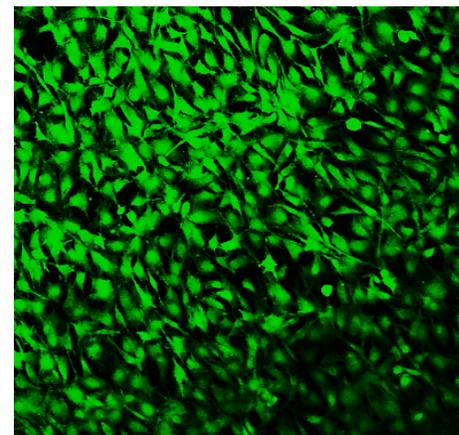
CYTOTOXICITY



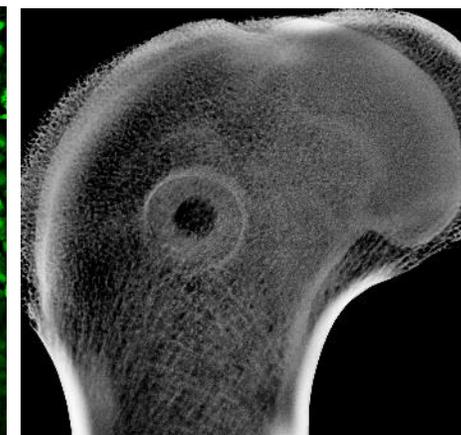
APATITE



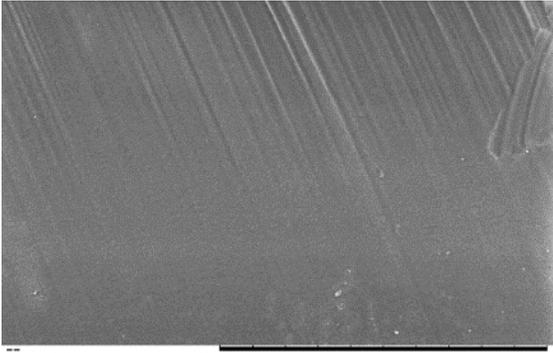
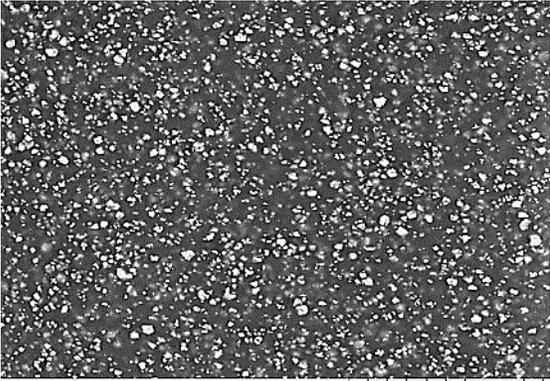
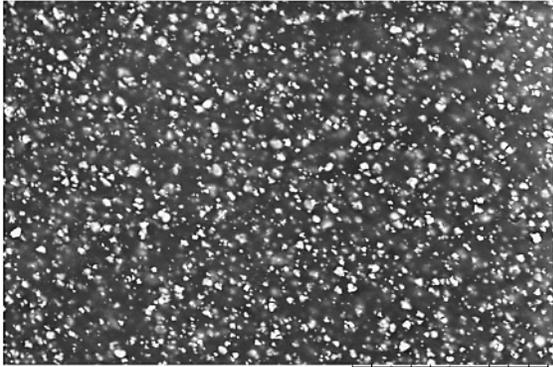
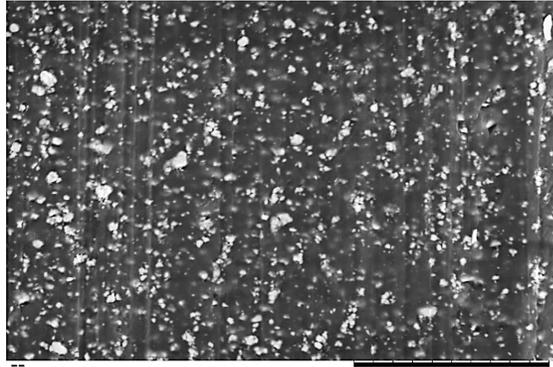
CELL CULTURE



SHEEP STUDY



VESTAKEEP® PEEK for Improved Osteoconductivity

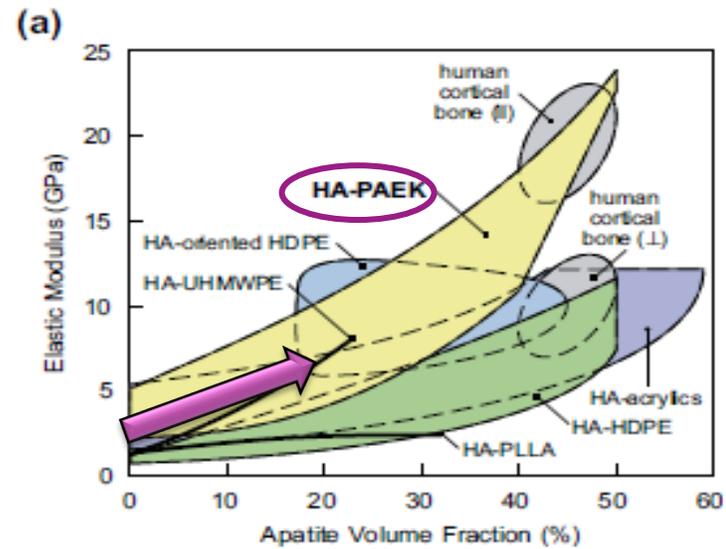
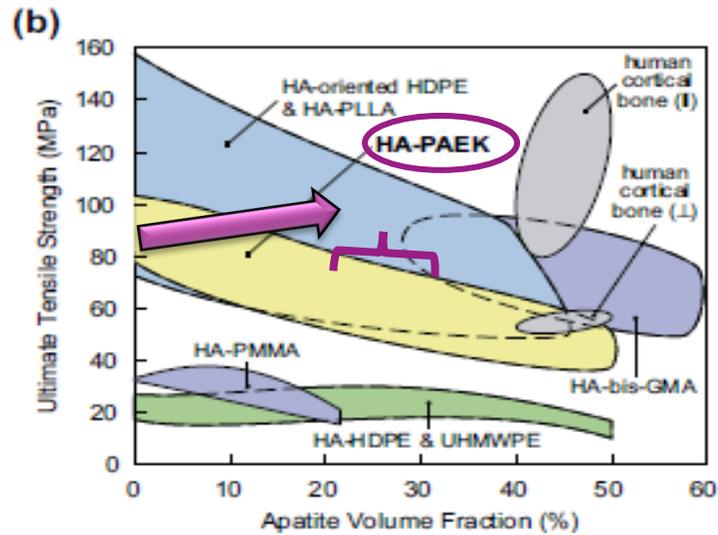
VESTAKEEP® (VIRGIN)	VESTAKEEP® COMPOSITE A	VESTAKEEP® COMPOSITE B	VESTAKEEP® COMPOSITE C
			
PEEK 0001 2015/11/25 15:51 NL D4.1 x500 200 µm	OsteoPEEK0004 2016/02/03 10:57 NL D6.2 x2.0k 30 µm	ID13M-0019 2017/03/17 14:57 NL D5.3 x2.0k 30 µm	
Microstructure	Homogenous	Homogenous	Homogenous
Elongation at Break	< 20 %*	> 40%	> 40 %
Injection Molding			
Machining			
3D Printability (FFF)			
ISO 10993-5 (Cytotoxicity)*	Pass	Pass	Pass
Osteoconductivity*	Superior to Virgin PEEK	Superior to Virgin PEEK	Superior to Virgin PEEK



Next generation PEEK + Calcium phosphate (FDA approved) compositions provide 'Improved bone-on-growth' & 'Superior Mechanical properties' - Versatile Platform for Conventional molding, Extrusion, Machining and also 3D printing

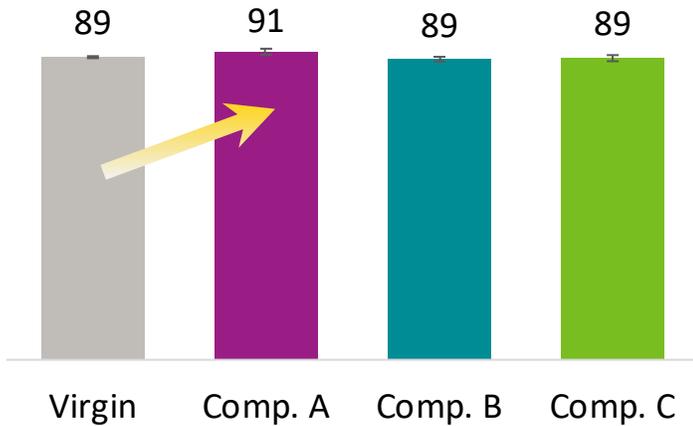
*MC3T3 cell culture

Mechanical Property: Tensile

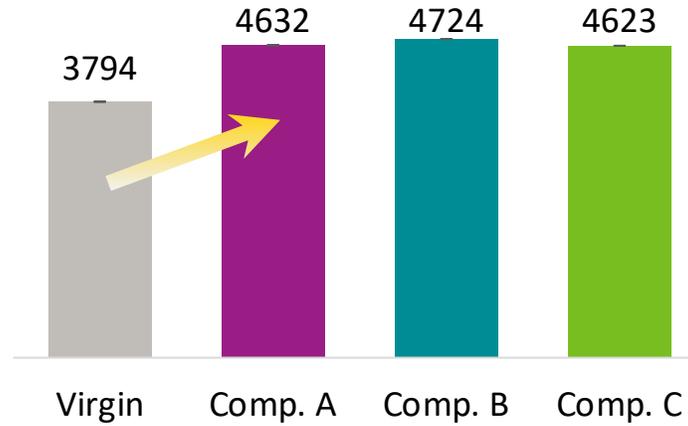


Mechanical Property: Tensile

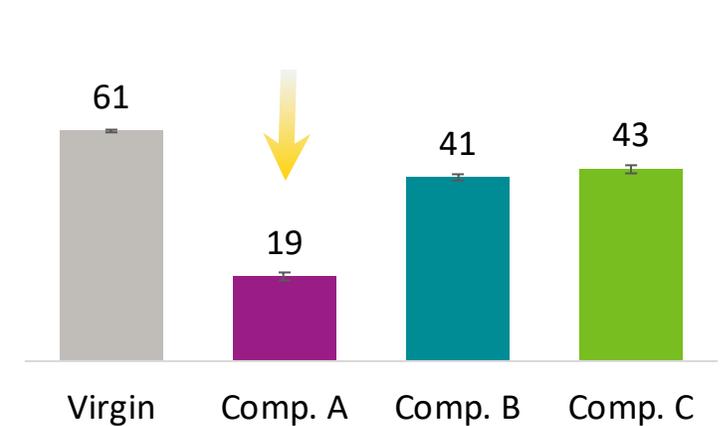
TENSILE STRENGTH (MPa)



ELASTIC MODULUS (MPa)

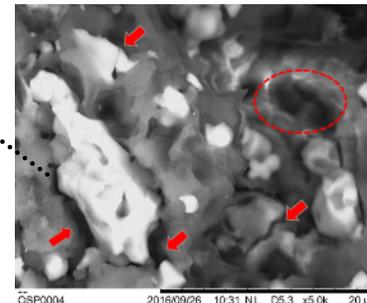


ELONGATION AT BREAK (%)

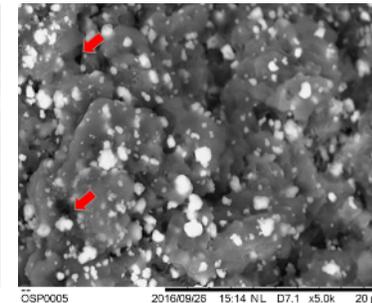


Tensile: ISO 527-A, n=10

Brittle Fracture (debonding)



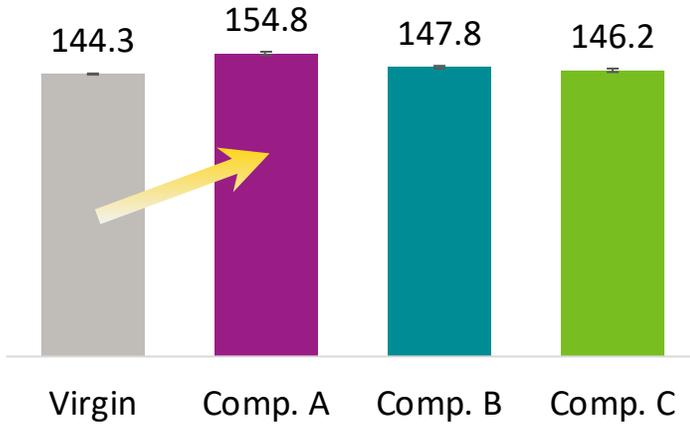
Quasi ductile



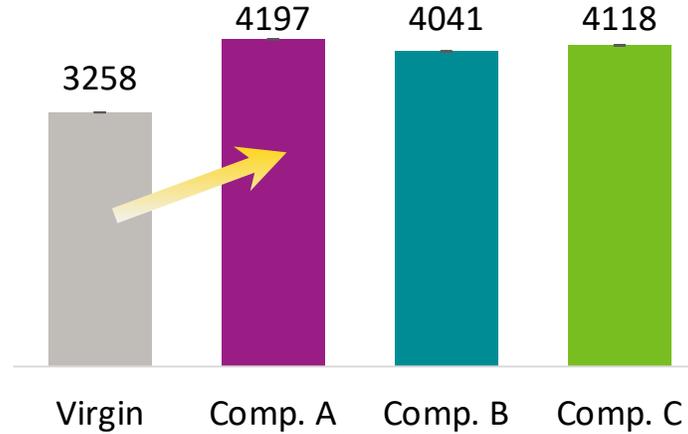
Superior Tensile properties and Ductility (Quasi ductile) with significant additive % & superior interface bonding

Mechanical Property: Flexural & Impact Strength

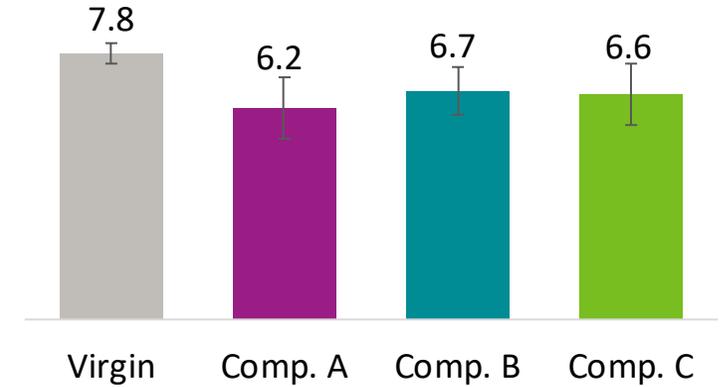
FLEXURAL STRENGTH (MPa)



FLEXURAL MODULUS (MPa)

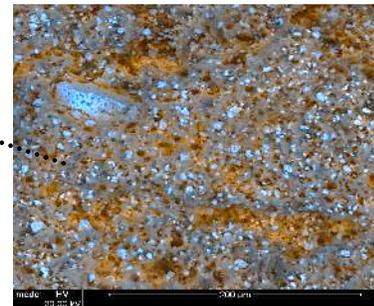


NOTCHED IMPACT (KJ/M2)

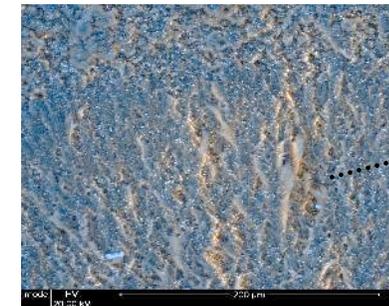


Flexural: ISO 178, n=10
Impact: ISO 180, n=5

Brittle Fracture interface (Typical)



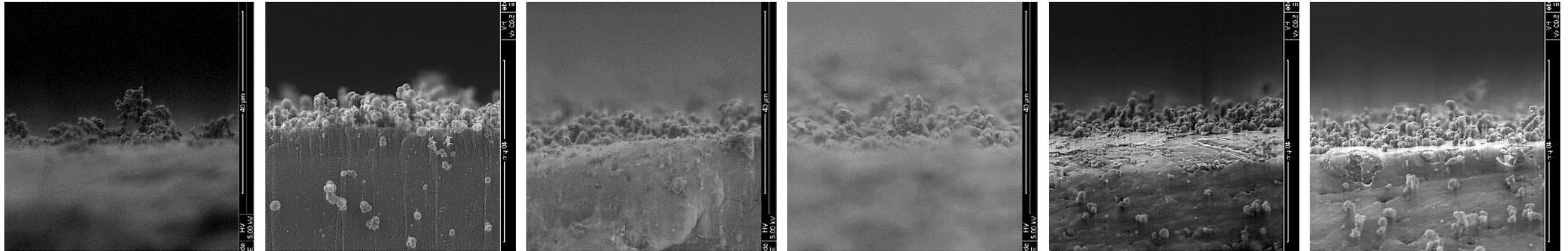
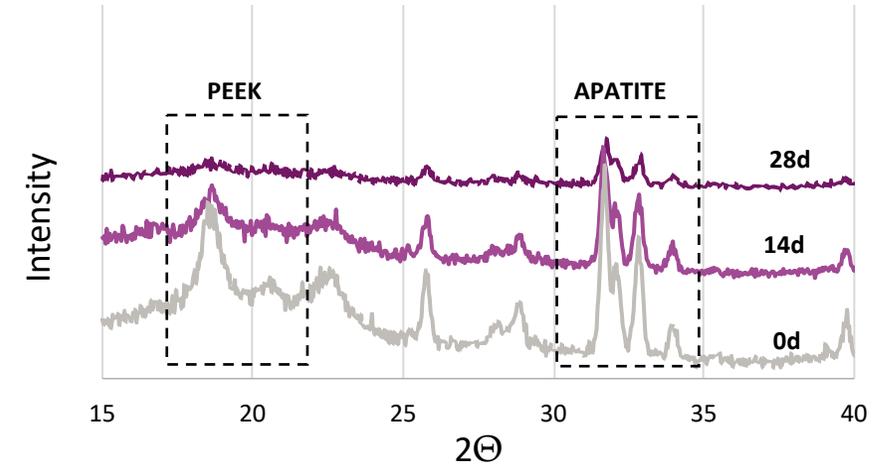
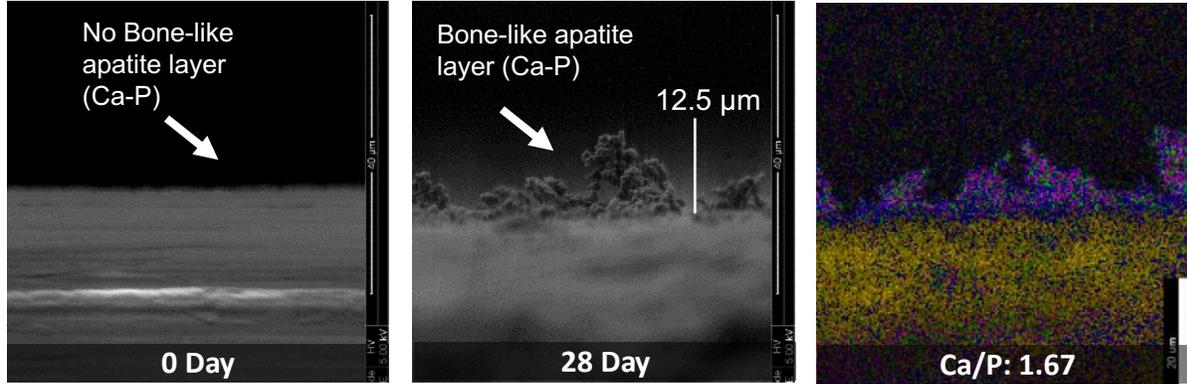
Quasi ductile Interface



Superior Flexural and impact properties even with significant additive % and without any agglomeration

In vitro study: Apatite formation in simulated body fluid solution

VESTAKEEP®
COMPOSITE A



More than 50 formulations assessed to understand apatite growth in-vitro

METHOD
10x10x2mm submersed at 37°C in SBF:
SBF: NaCl, NaHCO₃, Na₂HPO₄·2H₂O CaCl₂HCL
Apatite crystals evaluated at 0, 7, 14, and 28 days via SEM and XRD

In-vitro study: ISO 10993-5: Cytotoxicity

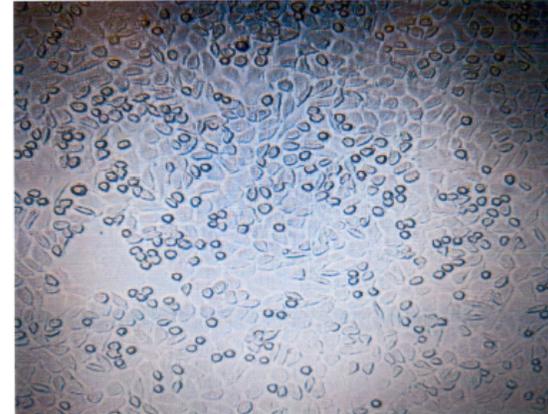
VESTAKEEP® (Virgin)



VESTAKEEP® Composite A



VESTAKEEP® Composite B



VESTAKEEP® Composite C



Identification	Results (Pass/Fail)	Scores			
		1	2	3	Average
Virgin	Pass	0	0	0	0
Composite A	Pass	0	0	0	0
Composite B	Pass	0	0	0	0
Composite C	Pass	0	0	0	0
(-Ve) Control – Polypropylene Pellets		0	0	0	0
(+Ve) Control – Latex Natural Rubber		4	4	4	4
Media Control		0	0	0	0

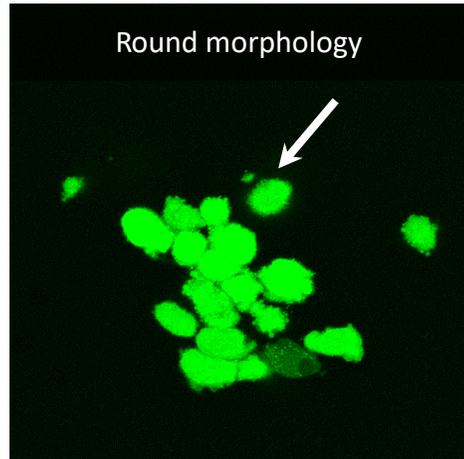
Virgin PEEK and PEEK composites – Both PASS cytotoxicity

METHOD: Polymer Extracted in (MEM) 72 h at 37 °C
 After 72 cell, media is filtered, added to cell monolayers L-929 (mouse fibroblasts) in the tissue culture plates in triplicate and incubated for additional 24 h. Cells are examined and scored wrt +ve and -ve controls

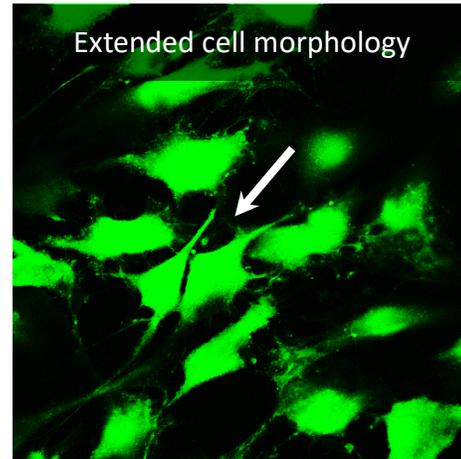


In-vitro: Cell Culture Studies (Day 1)

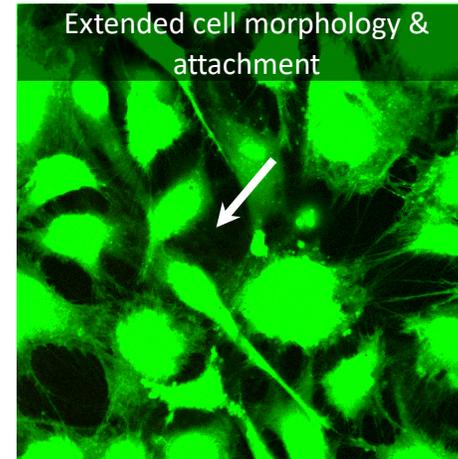
VESTAKEEP® (Virgin)



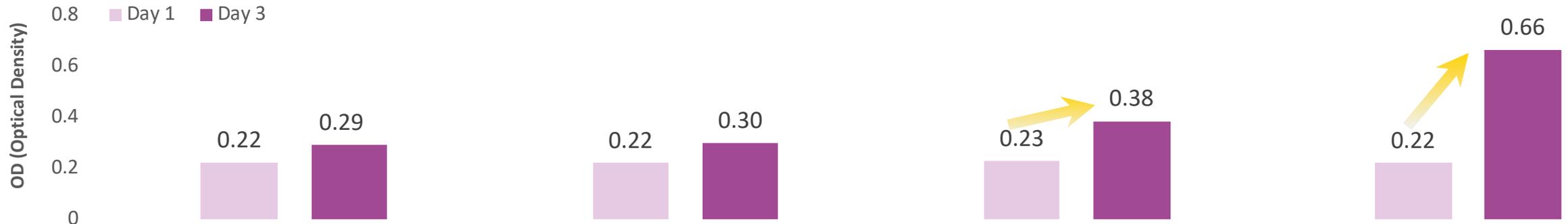
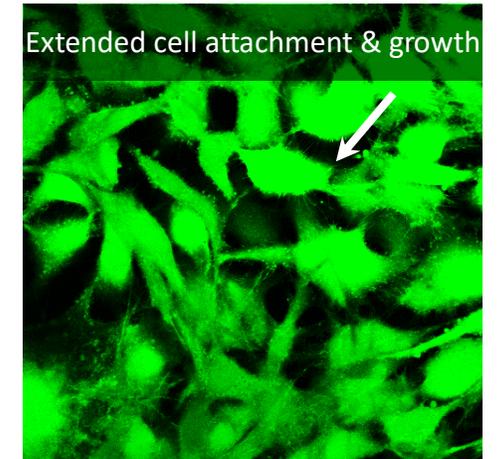
VESTAKEEP® Composite A



VESTAKEEP® Composite B



VESTAKEEP® Composite C



Cell Culture Studies with MC3T3 Mouse Osteoblasts show Improved Cellular Attachment & Proliferation

METHOD - MC3T3 MOUSE OSTEOBLASTS

Cell density: 20,000/cm²

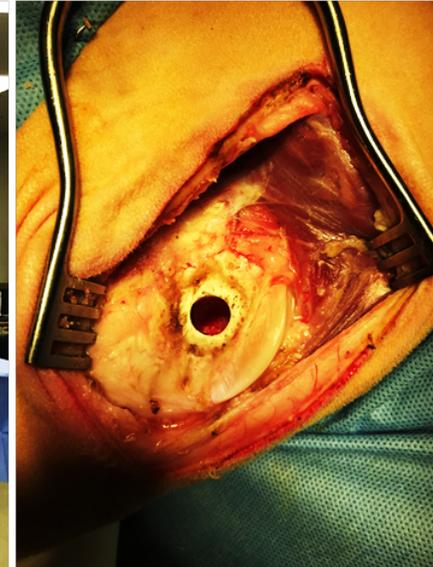
Cell media: α-mem media + vitamin C

Assay: MTS for cell attachment and proliferation

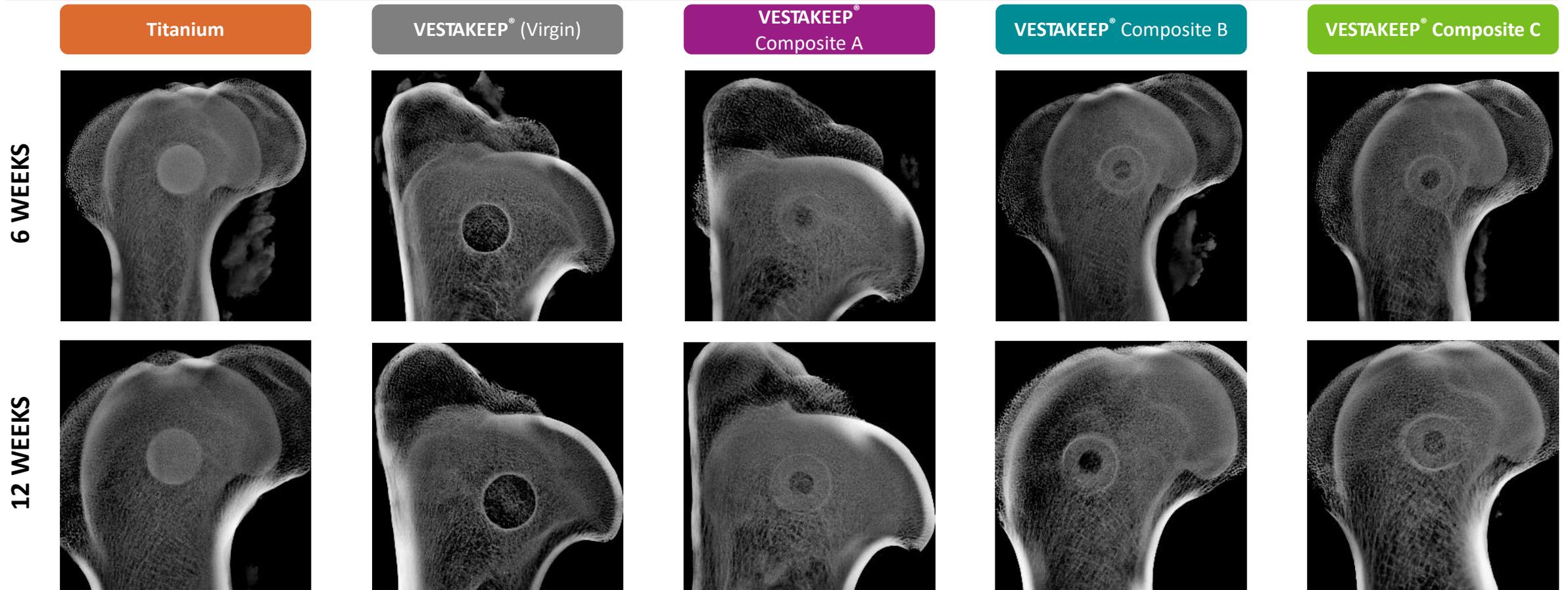
Live/Dead assay for cell morphology

In-vivo Study: Sheep Study

- **20** Sheep (Suffolk Crossbred Female 3yrs old)
- **4** implants / animal (Left & Right Humerus & Femur)
- **80** dowels (10 X 15 cm each)
- **6 & 12** week time points
- Rate of osseointegration in a critical bone defect
- Radiographic, biomechanical, micro-CT, & histological analysis



In-vivo Study: Sheep Study - Radiographic Analysis



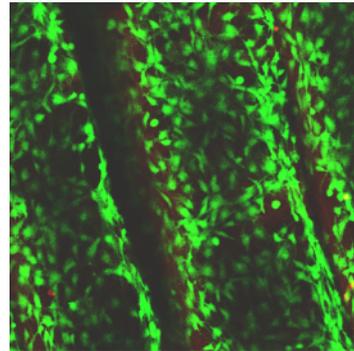
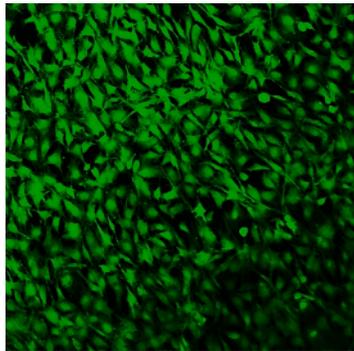
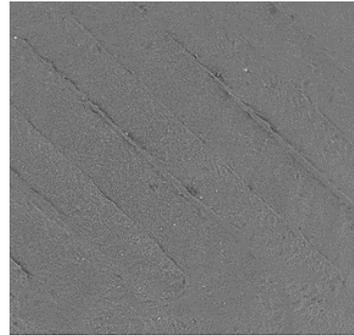
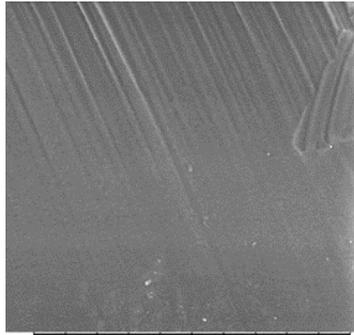
Preliminary analysis show **NO** infection and sign of improved fixation and healing

METHOD
Faxitron:
33-37 kV ; 3.00 s; 1.00mA

Advanced Processing: 3D Printing (Fused Filament Fabrication)



CELL CULTURE (DAY 1: MOUSE OSTEOBLASTS)



Injection Molded
VESTAKEEP® Composite

3D Printed
VESTAKEEP® Composite

MECHANICAL PROPERTY (VESTAKEEP® COMPOSITE)

FLEXURAL STRENGTH (MPa)

142

143

Injection Molded

3D Printed

TENSILE STRENGTH (MPa)

83

81

Injection Molded

3D Printed

FLEXURAL MODULUS (MPa)

4415

4670

Injection Molded

3D Printed

ELASTIC MODULUS (MPa)

4674

3930

Injection Molded

3D Printed



VESTAKEEP composites made into filament form and 3D printed shows comparable properties in initial evaluations

Versatile Platform for your applications...



PELLETS



VESTAKEEP® OsteoComposite



STOCK SHAPES



FILAMENTS





EVONIK

POWER TO CREATE

Apatite formation via Immersion test

In vitro bioactivity testing @ PHMD

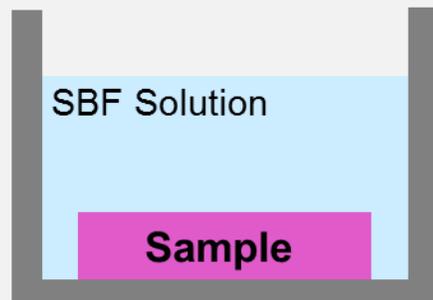
Background

- ❑ **Goal:** To evaluate osseointegration potential.
- ❑ **Hypothesis:** Apatite formation in SBF is an indication of bone bonding potential of an implant material adjacent to living bone.
- ❑ **SBF (Simulated body fluid):** The SBF will be prepared by mixing two solutions (A and B) as mentioned in Table

SBF Solution (Invibio Patent)

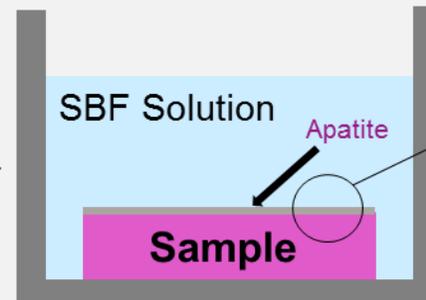
Starting materials	Weight of starting materials (g/L)	
	Solution A	Solution B
NaCl	6.129	6.129
NaHCO ₃	5.890	-
Na ₂ HPO ₄ ·2H ₂ O	0.498	-
CaCl ₂	-	0.540
HCL (1.00M)	0.934 (mL/L)	0.934 (mL/L)

Apatite Formation in SBF Solution

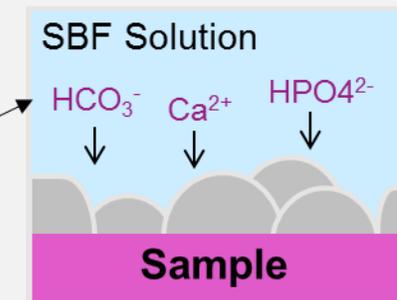


Immersion of sample in 3 mL SBF solution @37°C

Incubation Period
~ upto 4 weeks

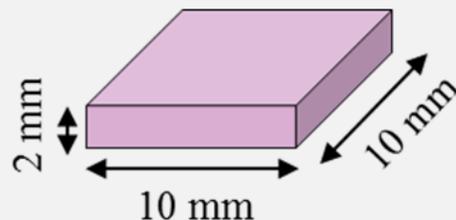


Amorphous calcium phosphate (ACP) or Apatite deposition on sample surface



Mechanism of carbonated ACP or Apatite deposition on sample surface

CNC Machined Samples

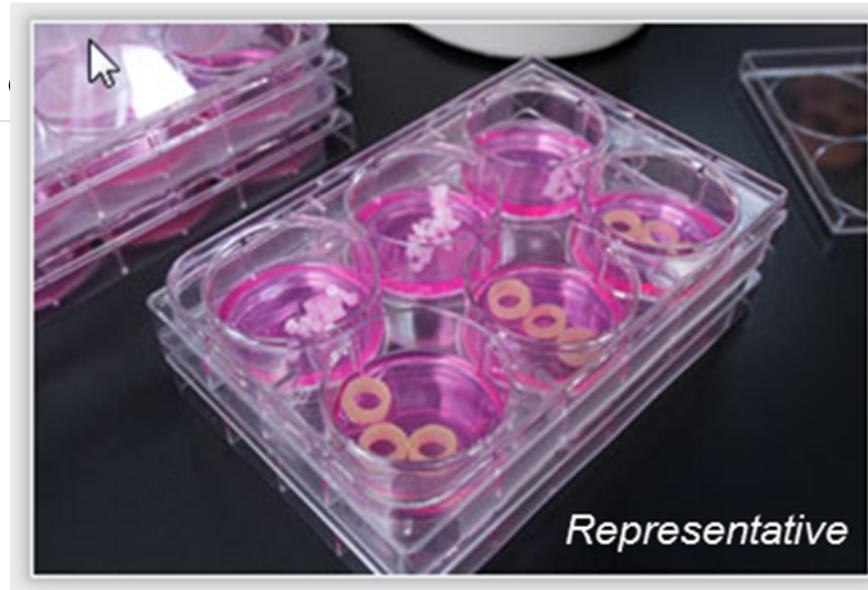


Flexural

- Flexural
 - Radius bending punch: 5mm
 - Radius pad: 5mm
 - Width between supports: 61.44mm
 - Pre-load: 10N
 - Start E-Modulus: 0.05%
 - End E-Modulus: 0.25%
 - Speed, E-Modulus: 2mm/min
 - Test Speed: 2mm/min
- Tensile
 - Clamping length: 50mm
 - Measured length: 20mm
 - Pre-Load: 5N
 - Speed Pre-Load: 1mm/min
 - Speed Modulus: 1mm/min
 - Start E-Modulus: 0.05%
 - End E-Modulus: 0.25%
 - Test Speed: 5mm/min
- Impact
 - Pendelum: 1J
 - Velocity: 3.458m/s

ISO 10993-5 MEM Elusion Test

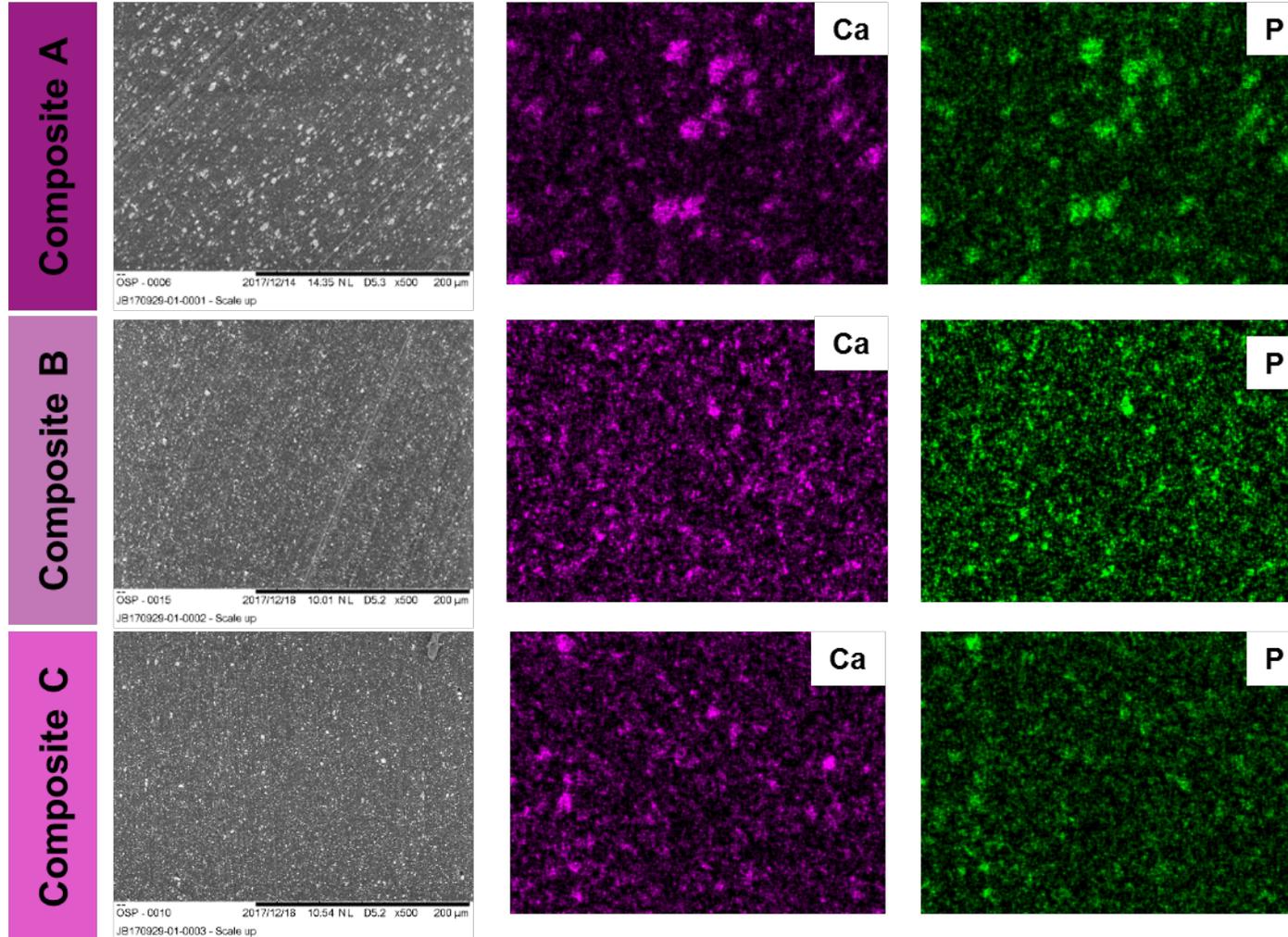
- Polymers extracted in minimum essential media (MEM) 72 h at 37 °C.
- After 72 cell, media is filtered and added to cell monolayers L-929 (mouse fibroblasts) in the tissue culture plates in triplicate and incubated for additional 24 h.
- Cells are examined and scored based on controls.



- METHOD:** POLYMER EXTRACTED IN (MEM) 72 h at 37 °C
- After 72 cell, media is filtered, added to cell monolayers L-929 (mouse fibroblasts) in the tissue culture plates in triplicate and incubated for additional 24 h.
 - Cells are examined and scored wrt +ve and -ve controls

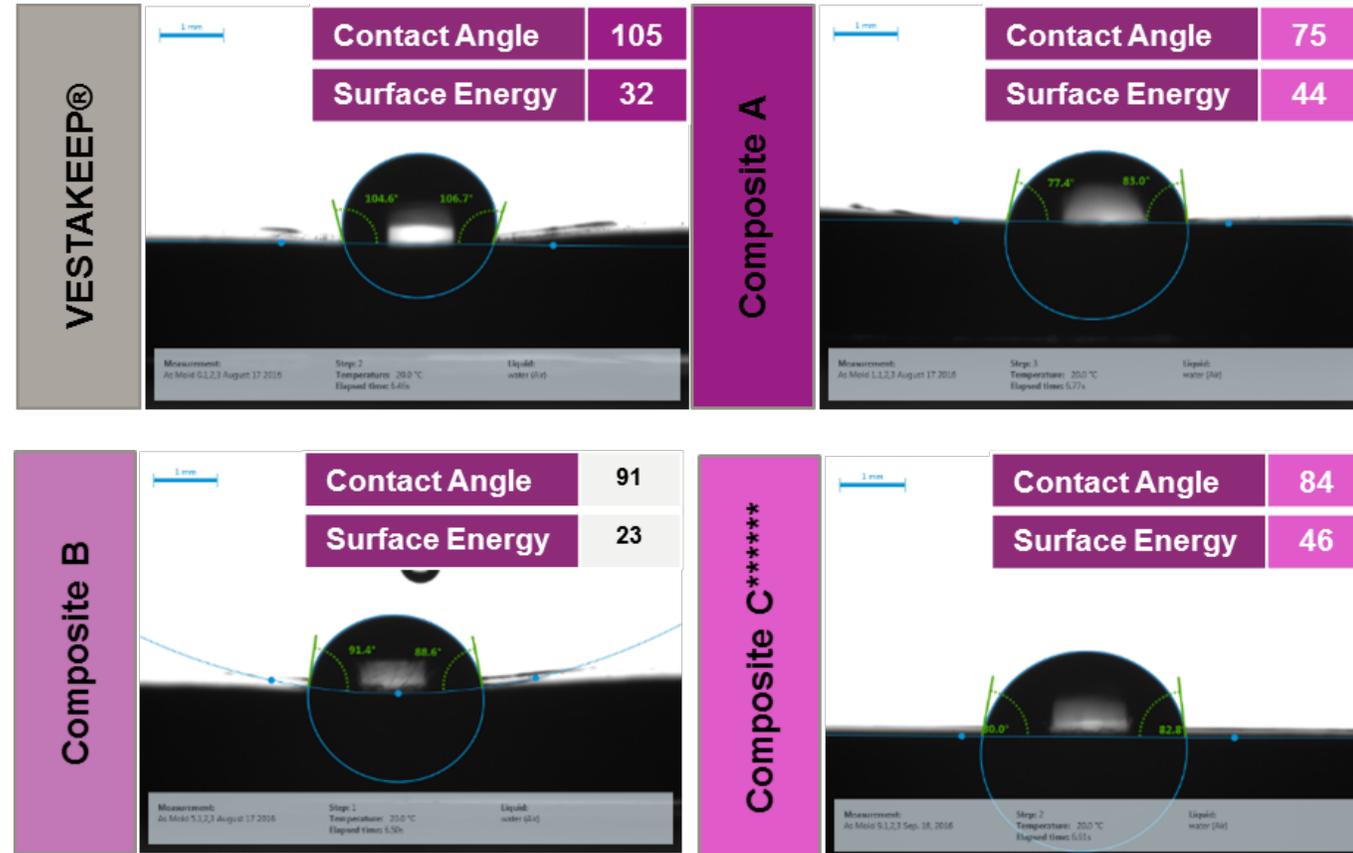
SEM observation: Morphology

Elemental mapping: Distribution of elements



Contact angle

- Composite materials showed decreased contact angle measurements compared to VESTAKEEP® (Virgin)
- Sample Size: Each composite was tested in triplicate
- Liquid Phase: Water and Diiodomethane were used as the two liquid phases in order to calculate the surface energy of each sample.
- Liquid Dosing: Dosing the liquid phase was automated and allowed to flow from capillary tube and deposit onto the sample surface with minimal gravitational interaction.
- Angle Measurement: Contact angle measurements were acquired automatically when the liquid phase released from the capillary tube and came into contact with the sample surface forming a hemispherical deposition.
- Calculation: Contact angles and subsequent surface energies were calculated within Kruss' ADVANCE software using the OWRK method.



PEEK Printing Parameters

- Filament Material: Vestakeep 4000
- Filament Diameter: 1.75 mm
- Machine: 3NTR A4v3
- Nozzle Diameter: 0.4 mm
- Nozzle Temperature: 410°C
- Print Bed Temperature: 135°C
- Print Bed Material: Glass
- Print Chamber Temperature: 75°C
- Print Speed: 25 mm/s
- Layer Height: 100 µm