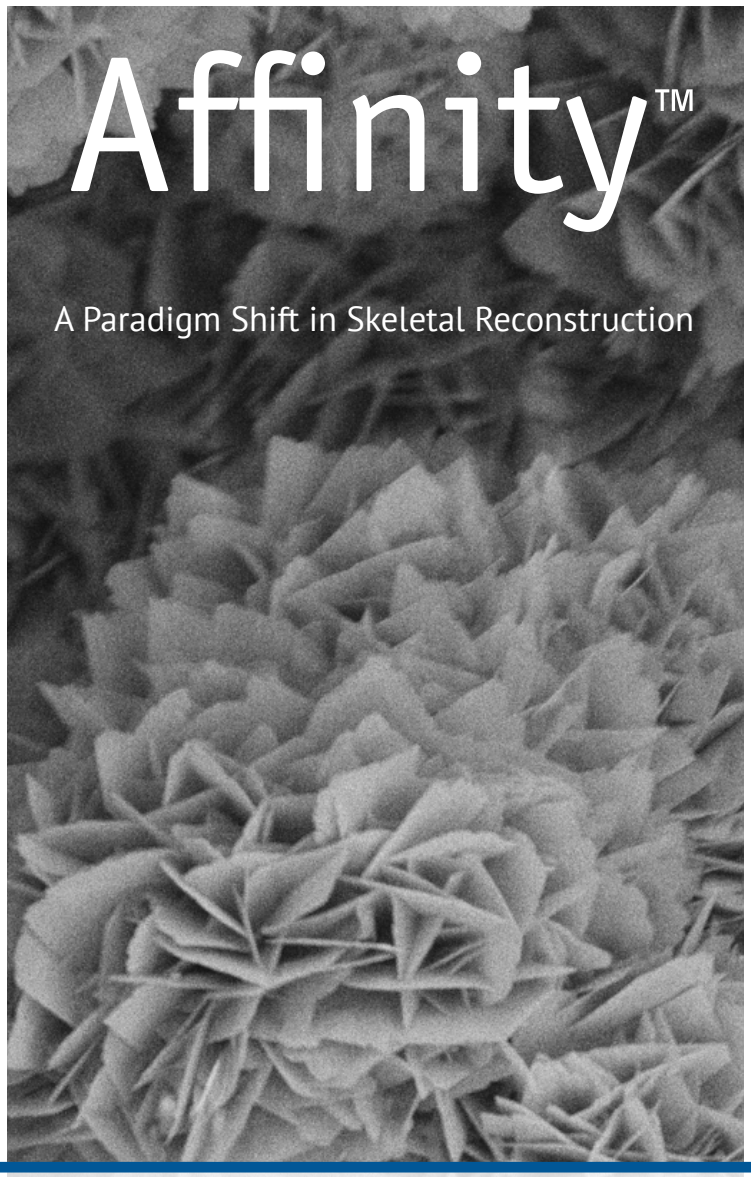
Affinity™

A Paradigm Shift in Skeletal Reconstruction



TRS

Tissue Regeneration Systems™

SKELETAL RECONSTRUCTION BREAKTHROUGH

Tissue Regeneration Systems™ (TRS™) is a start-up medical device company commercializing a breakthrough skeletal reconstruction and bone regeneration technology platform licensed from the Universities of Michigan and Wisconsin. Our technology addresses a broad range of clinical applications, and has been validated by comprehensive University, NIH and company-sponsored research initiatives spanning a period of well over a decade. This includes technology-specific studies, basic bench testing, and large animal implant studies with long-term follow-up. Several publications have resulted from this body of research that clearly demonstrate the unique attributes of our technology platform and its clinical viability. In order to fully capitalize on the product opportunities for our technology platform, TRS has chosen to pursue a corporate partnership business model. As a development and manufacturing partner, TRS makes key contributions to a collaboration.

NOVEL 3D PRINTED RESORBABLE SCAFFOLDS

TRS has a proven capability to fabricate complex, patient specific, load-bearing resorbable implant solutions using 3D printing methods.

UNIQUE BIOACTIVE MINERAL COATING

TRS has developed Affinity™, a proprietary mineral coating with unique bioactive properties that can be applied to our resorbable scaffolds, as well as to conventional orthopedic and spine implants.

SCALABLE FDA COMPLIANT MANUFACTURING

TRS has established a fully independent, FDA-compliant manufacturing facility with a certified cleanroom. Our operation can support commercial product volumes.

FDA CLEARANCE

TRS has secured FDA clearance of our 3D printed resorbable scaffold technology as well as our Affinity mineral coating.

STRONG INTELLECTUAL PROPERTY AND TRADE SECRET POSITION

TRS has an extensive patent portfolio and has also accumulated a number of important trade secrets in perfecting our technology and fabrication methods. Together, this creates meaningful protection and exclusivity for our technology platform.

PROPRIETARY BIOMIMETIC PROCESS

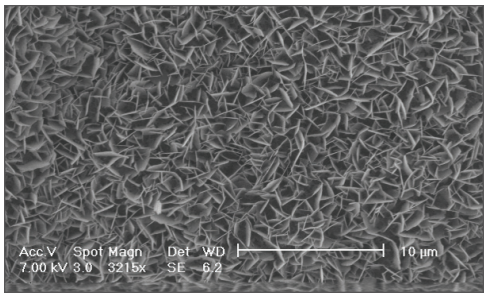
The product of 10 years of bone tissue engineering research at the University of Michigan and University of Wisconsin, Affinity is a mineral coating that is grown onto implant surfaces under physiological conditions through a proprietary biomimetic process.

PLATE-LIKE NANOSTRUCTURE

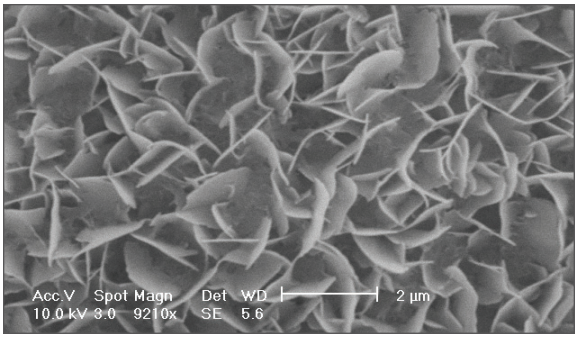
Affinity has a plate-like nanostructure that resembles living bone. Continuity is observed between the Affinity coating and newly formed mineralized bone *in vivo*.

PROMOTES OSTEOBLAST ADHESION AND FUNCTION

This nanometer topography is known to promote increased osteoblast adhesion and enhanced osteoblast function by sensitively regulating the protein interactions that lead to cell attachment.

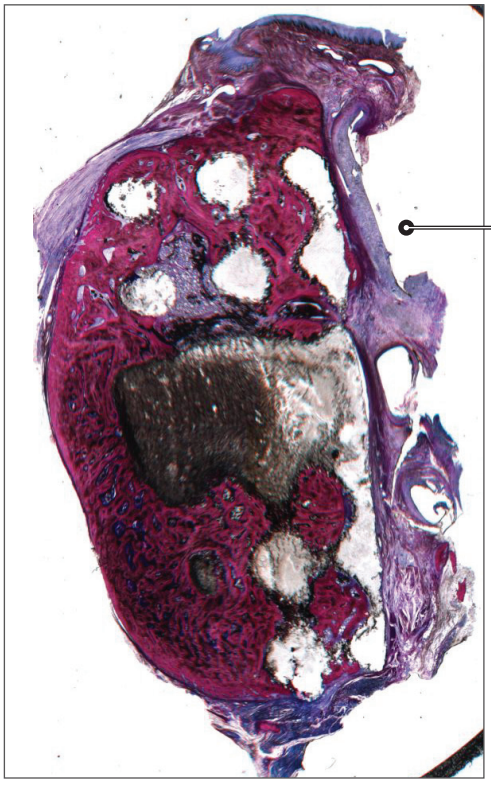


1a Affinity coating

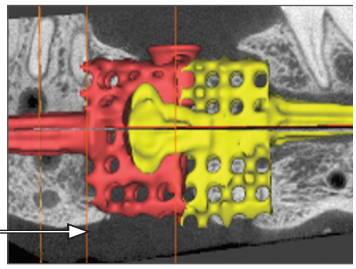


1b Affinity coating

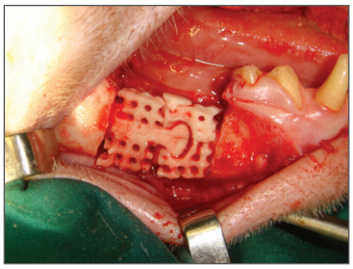
Fig. 1. Surface morphology of Affinity coating on polycaprolactone implant.



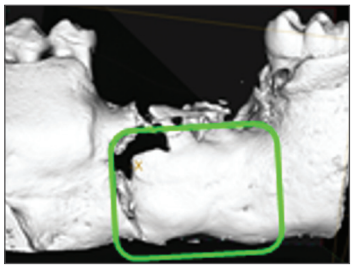
2a



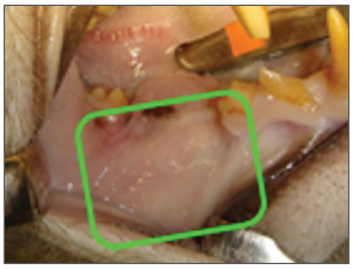
2b



2c

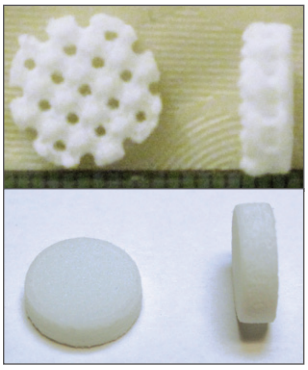


2d

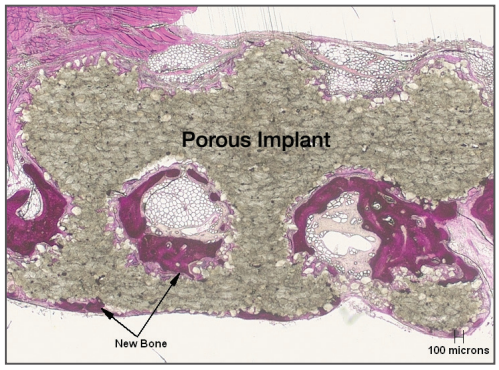


2e

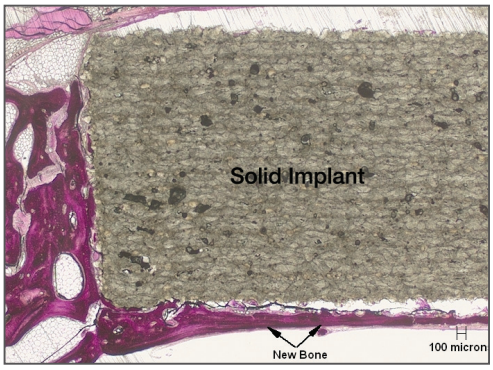
Fig. 2 (a-e). Primate segmental mandibular reconstruction and histology sections at 6 months, 2 cm defect. Histologic cross-section of the bone/implant interface (orange line) depicts bone integration through the resorbable, Affinity coated implant. 2(d) Micro-CT shows bone generation throughout implant. 2(e) Defect is well healed.



3a. Porous and solid implants with Affinity™ coating



3b

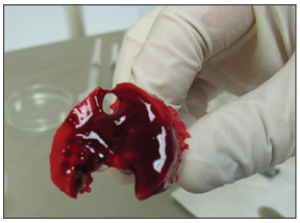


3c

Fig. 3 (a-c). New bone formation in Affinity coated porous implant and coated solid implant in a rabbit calvarial defect model at 52 weeks. Note continuity between the Affinity coating and newly formed bone.

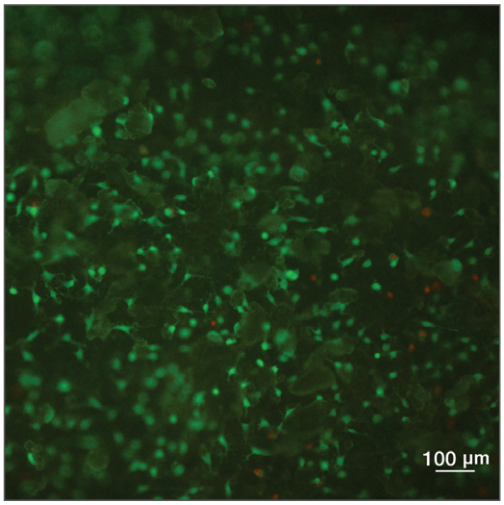
RAPID CELL ATTACHMENT

Intraoperatively added autologous cells attach within minutes to the Affinity coating. Early biological fixation protects against the micro-motion that may allow fibrous integration, and provides defense against biofilm formation during the "race for the surface."

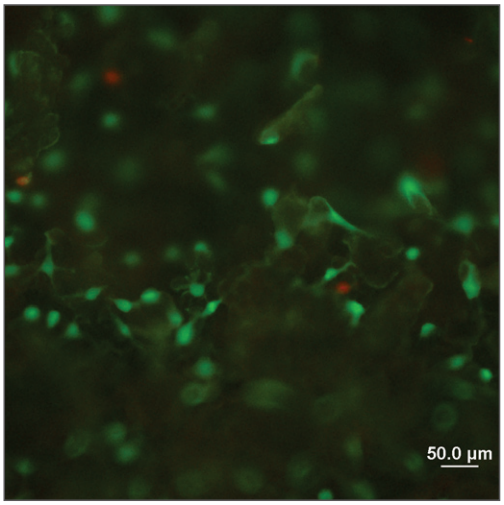


4a

Fig. 4 (a-c). Biological solutions such as blood can be readily added to Affinity coated implants to enable cell or protein binding. Stem cells attach and spread on the coating within minutes, with a high survival percentage (green = viable, red = not viable).



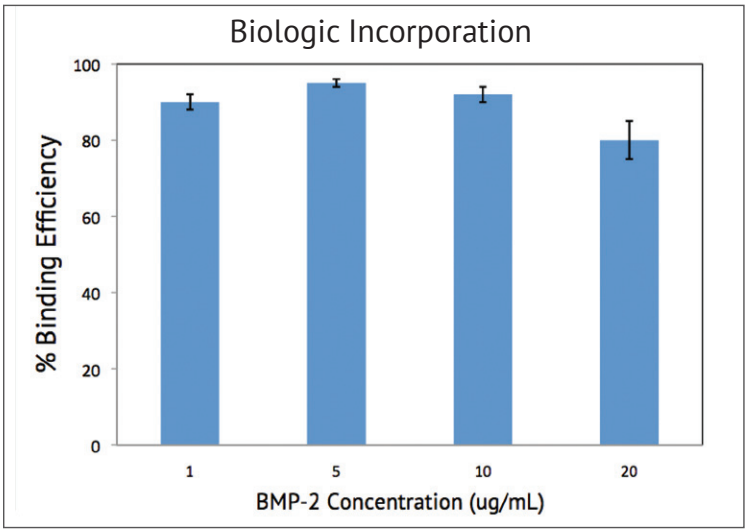
4b



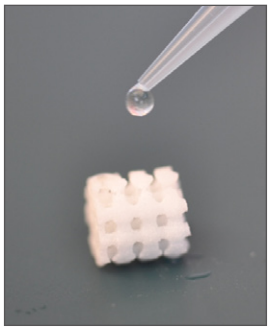
4c

HIGH BINDING EFFICIENCY WITH AUTOLOGOUS BIOLOGICS

The Affinity coating may be easily functionalized with autologous cells or proteins during surgery, enabling the potential of these intraoperatively captured biologics to be realized.



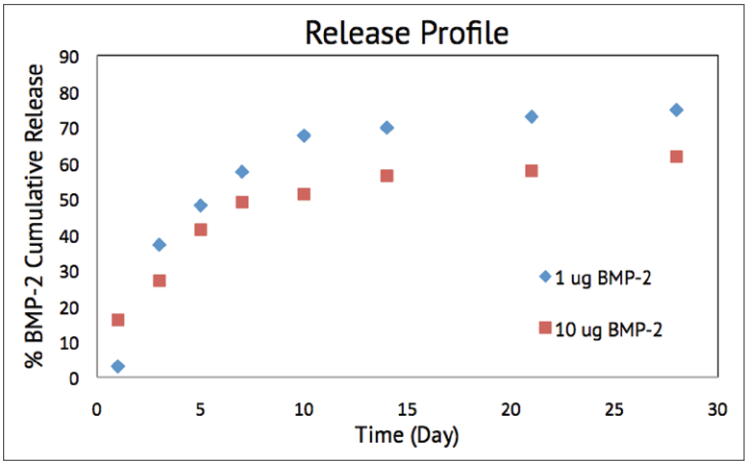
5a. High binding efficiency of BMP-2 on Affinity coating with different BMP-2 concentrations. Note binding efficiency is nearly 100%.



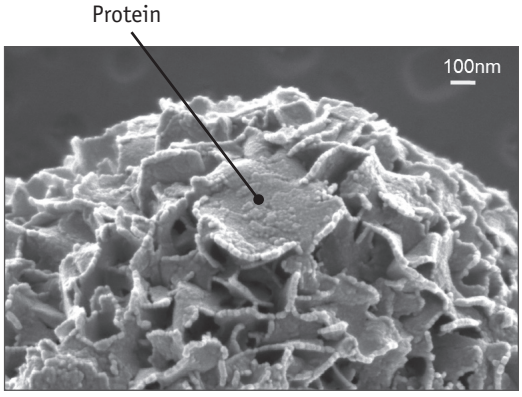
5b. Intraoperative biologic incorporation into Affinity coating.

CUSTOMIZED RELEASE KINETICS

By systematically varying the dissolution rate, composition and topography, Affinity may be engineered to create a controlled delivery system allowing for predictable release kinetics and bone generation.



6a. Proteins scuh as BMP-2 are released from within the nano-porous Affinity coating, resulting in a controllable, sustained release profile. Note near linear release with no burst effect.



6b. Protein binding on Affinity coating.

MAINTAINS LONG TERM PROTEIN STABILITY

The Affinity nanometer porosity maintains the stability of bound proteins, even during device sterilization. The coating slowly releases proteins locally as it resorbs, and leaves bone in its place.

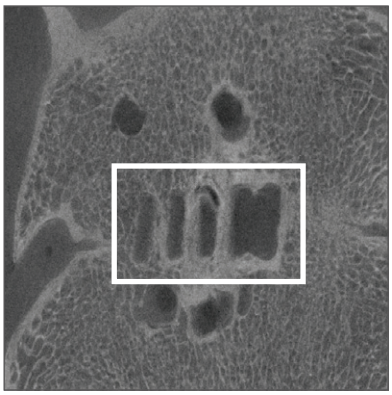
ENRICHES DESIRED BIOLOGIC ELEMENTS

The TRS Affinity coating serves as an affinity column to enrich desired biologic elements and select out undesired elements.

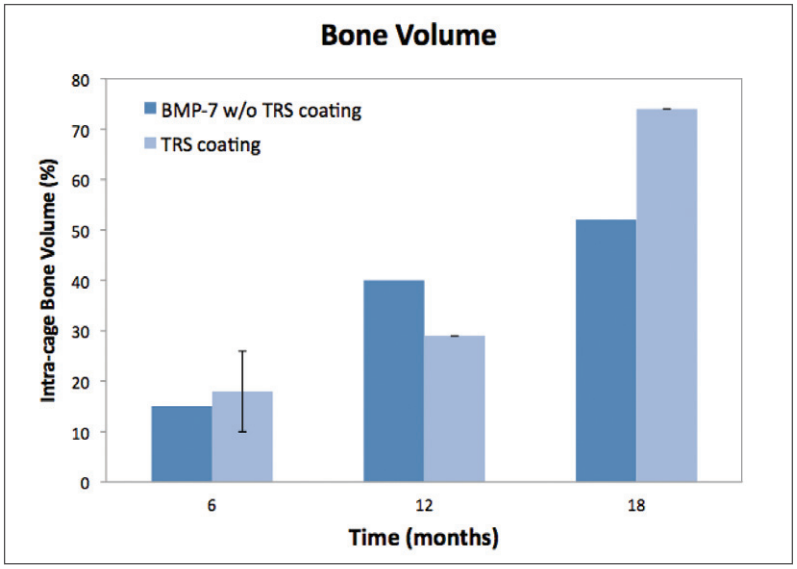
EFFICIENT BONE REGENERATION

In a large animal spine fusion study, the Affinity™ coated spinal cage (without orthobiologics) demonstrated comparable bone generation to an uncoated cage delivering BMP-7, suggesting the potential to support bone regeneration between endplates without the need for additional bone grafting materials.

7a



7b



7c

Fig. 7 (a-c). Intervertebral cage for anterior cervical discectomy and fusion in a porcine model. The Affinity coated implant showed complete bony bridging, with comparable bone generation to the uncoated cage loaded with a collagen sponge releasing BMP-7.

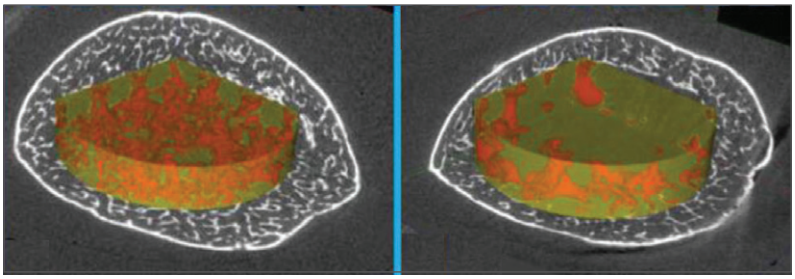


Fig. 8. Micro-CT analysis of bone formation (red areas) in coated scaffold (left) and uncoated (right). Both were seeded with BMP-7 transduced human gingival fibroblasts.

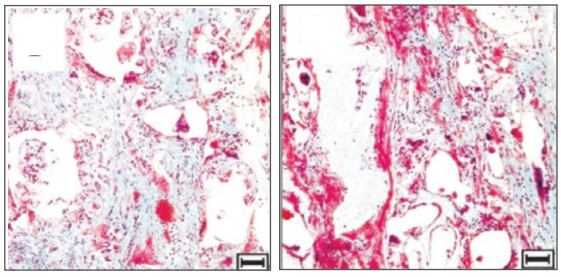
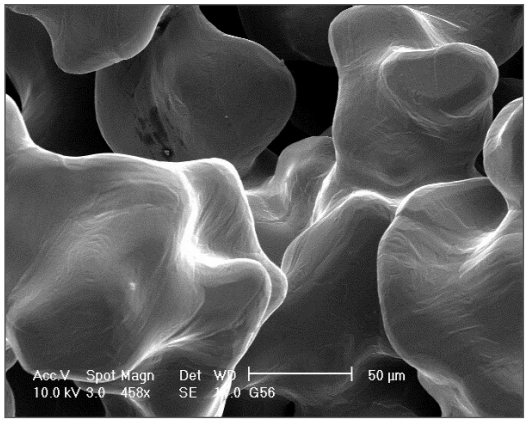


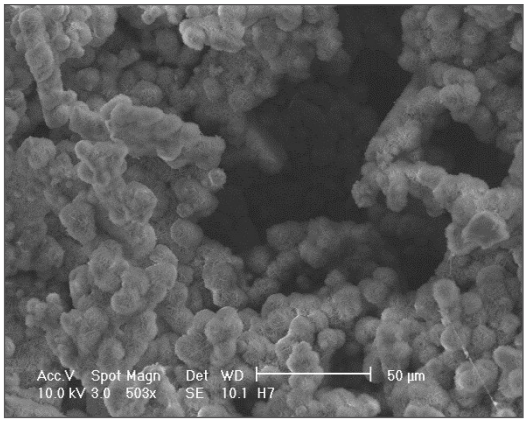
Fig. 9. Compared to the uncoated version (left), TRS Affinity coating supports bone ingrowth and enhanced osteoid matrix deposition (right) at 14 weeks post-implantation in rat calvarial defect model.

ENHANCES OSSEOINTEGRATION OF METAL SURFACES

The unique nanoscale architecture of the Affinity coating may be applied to virtually any underlying implant surface (such as plasma sprayed titanium), reaching all pores of complex scaffolds and improving upon the degree of osseointegration into micro-structured implants.



10a



10b

Fig. 10 (a,b). Surface morphology of porous titanium before and after Affinity coating was applied.

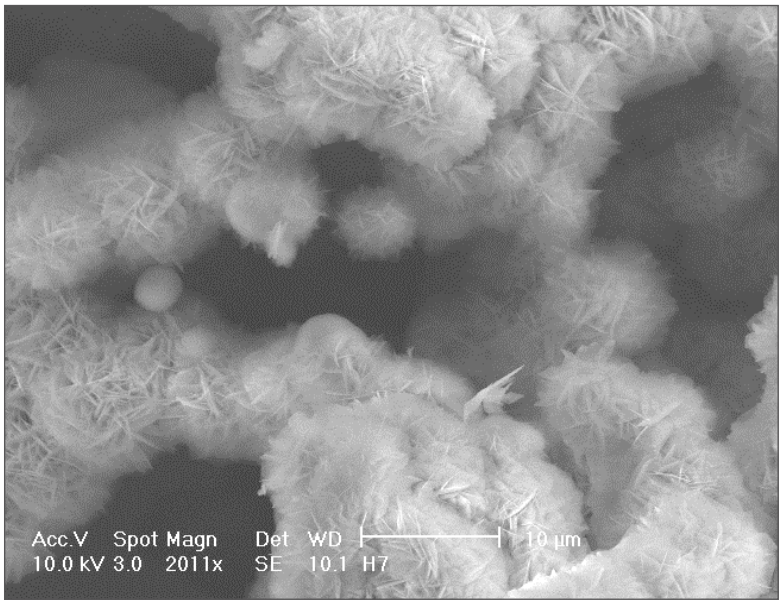


Fig. 10c. Higher magnification of coated titanium

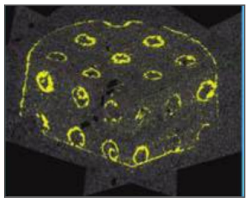
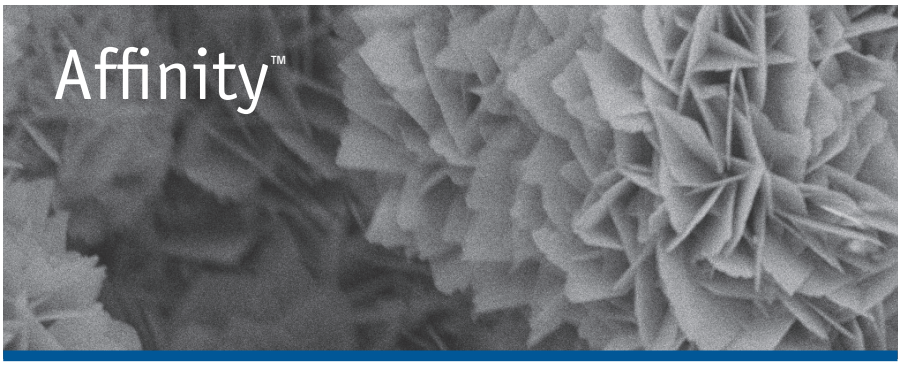


Fig. 11. Micro-CT analysis of coated implant demonstrates Affinity coating (yellow color) has reached all pores of complex scaffolds.



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9. Saito E. , et al. ADV HEALTHCARE MATER in press, 2015. (Fig. 8)
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