NEWSLETTER

Issue No 2 October 2016

The main aim of NEXT-3D project is to develop the next generation of multifunctional 3D materials for orthopaedic and dental implants. Multifunctional materials with drug delivery properties and antibacterial properties are desirable by clinicians. Research will be conducted following a multi- and inter-disciplinary research methodology designed to develop innovative biomedical materials using advanced processing technologies (3D laser printing and sintering) with market potential. The proposed research and innovative programme will lead to the advancement of knowledge in the field and to new materials with superior properties. In this NEXT 3D Newsletter describes the latest updated news about the project.

Latest News

Development of simple shapes with 3D-printing

Sooraj Nandyala and Artemis Stamboulis

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The improvement of 3D-printing processes (3DPP) technology in biomedical and tissue engineering has dramatically influenced the potential ability of making biomedical implants and scaffolds by applying data from clinical imaging and computer aided designs. In the past, Sooraj et.al have been studied and evaluated the direct bone bonding and osteointegration of the porous wedge structures by using Bonelike® graft as shown in Figure 1. The following different simple shapes /structures have been developed with our newly purchased 3D printer as shown in below. Figure 2 (a & b) show the 3D cylinder and screw models by using poly lactic acid (PLA). Further, we are also trying to make some porous structures as shown in the Figures 3(a,b). Furthermore, we will produce new PLA composite filaments biomedical applications. We have successfully developed a white PLA filament by using a filament maker as shown in Figure 4. With this approach, we can develop some complex 3D shapes and designs in the near future.

Figure 1: Porous structure developed with Bonelike graft

Figure 2: (a) Cylinder and (b) screw models developed with PLA.

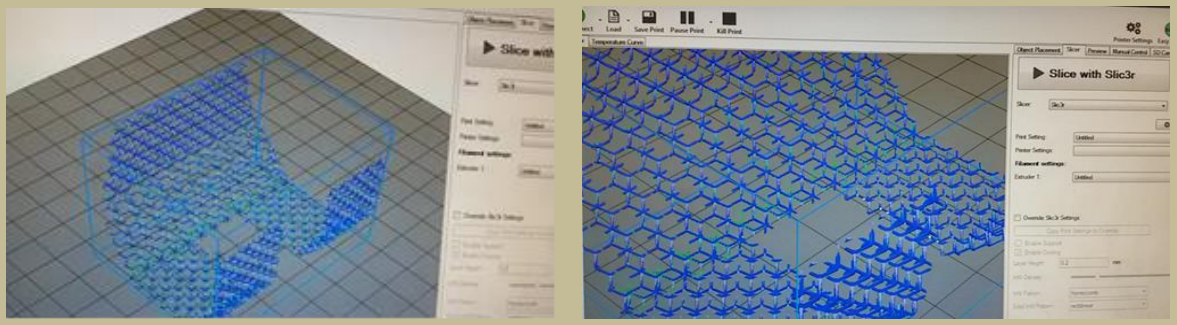

Figure 3: (a,b)Preliminary porous structured models generated by g-code format of the 3D printer.

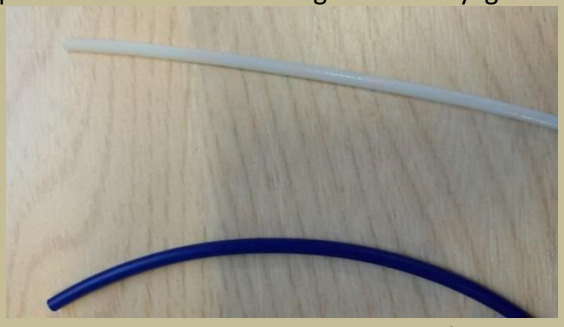

Figure 4: Developed white PLA structured models with filament maker.

Additive manufacturing of Ti6Al4V, surface treatments and peptide coating

Gabriela Melo Rodriguez, and Artemis Stamboulis

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Ti6Al4V manufactured by AM nad supplied by ADLER was mechanically mirror polished, etched and thermally treated. The microstructure obtained is shown below in Figure 1 with typical grain characteristics of additive manufacturing process.

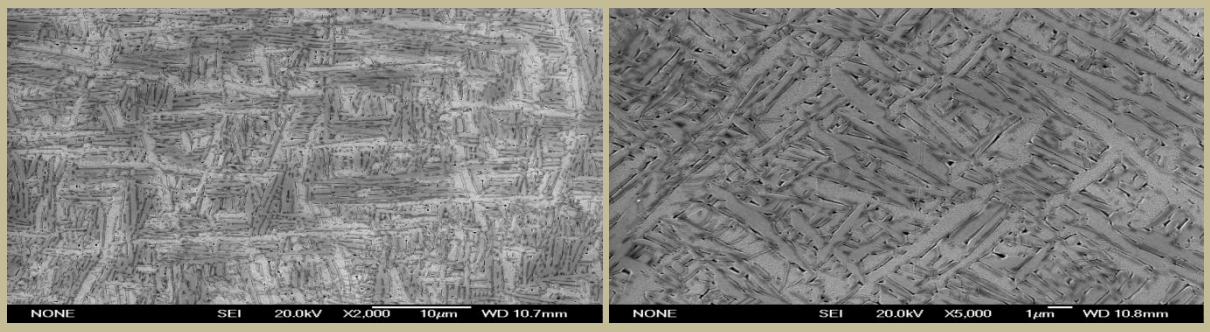

Figure 1 : Micrograph X2000 and X5000 of AM Ti6Al4V medical grade after etching with 8.8 M H_2O_2 + 0.1 M HCl at 80 °C for 30 min and thermal oxidation at 500 °C

The etching treatment affects the porosity of Ti6Al4V. α and ß grains are presented in the medical grade Ti6Al4V alloy as shown in Figure 2. It is also possible to identify both compositional grains of Ti6Al4V medical grade.

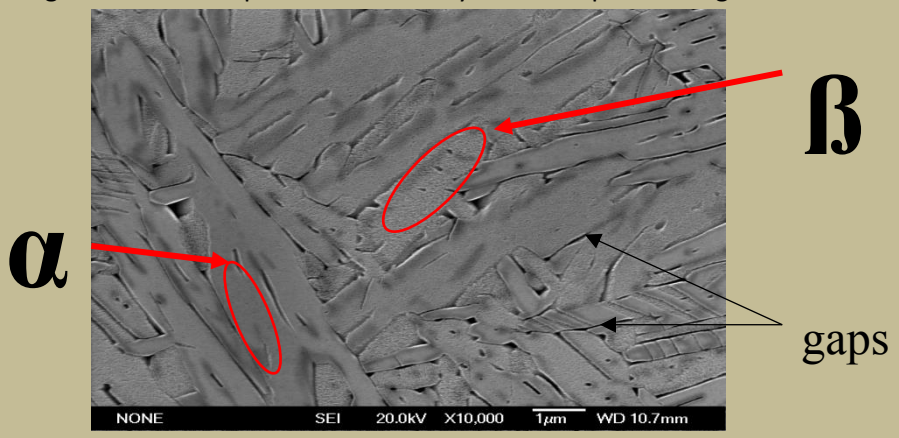

Figure 2 : Micrograph X 10000 Ti6Al4V medical grade adding manufactured after etching with 8.8 M H_2O_2 + 0.1 M HCl at 80 °C for 30 min and thermal oxidation at 500 °C

ADLER Ti6Al4V after the surface topography and oxide composition alteration was dip coated in a solution with fluorophore peptide label aptamer 5FAM-KKLPDAKKLPDAEEEEEEEE. The green colour in the sample shows (Figure 3) the presence of the label peptide on the titanium modified surfaces.

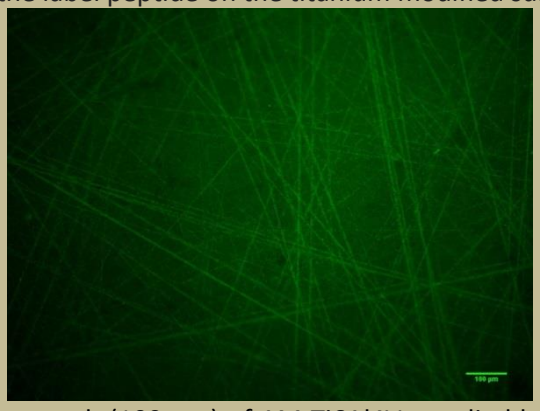

Figure 3: Fluorescence micrograph (100 µm) of AM Ti6Al4V supplied by ADLER after dip coating in SBF solution pH4 and concentration of 10 µM of label peptide aptamer.

In contrast the AM Ti6Al4V supplied by BresMedical shows a sharper grain at the endings. This microstructure is also chracteristic of additive manufacturing process as showin in Figure 4.

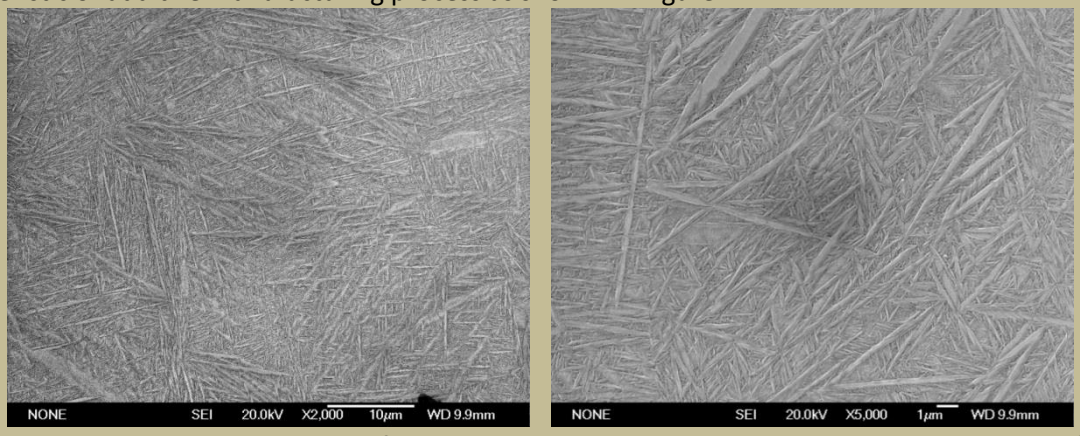

Figure 4 : Micrograph X2000 and X5000 of AM medical grade Ti6Al4V supplied by BRESMEDICAL after etching with 8.8 M H_2O_2 + 0.1 M HCl at 80 °C for 30 min and thermal oxidation at 500 °C.

α and ß grains are presented in this sample (Figure 5) of Ti6Al4V alloy. The porosity remains on the grains.

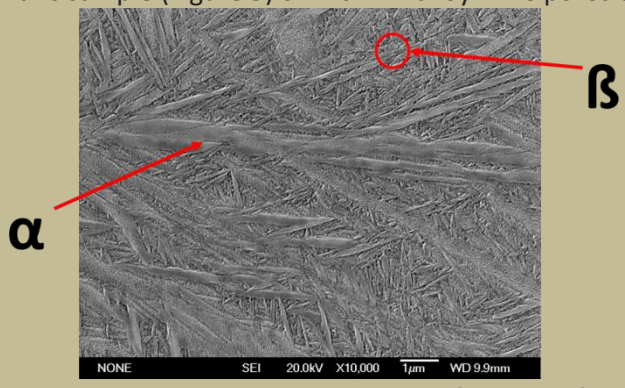

Figure 5 : Micrograph X 10000 Ti6Al4V medical grade adding manufactured after etching with 8.8 M H_2O_2 + 0.1 M HCl at 80 °C for 30 min and thermal oxidation at 500 °C.

BresMEdical Ti6Al4V after surface alterations was dip coated in a solution with fluorophore peptide label aptamer 5FAM-KKLPDAKKLPDAEEEEEEEE. The green colour in the sample shows the presence of the label peptide on the titanium modified surfaces as shown in Figure 6.

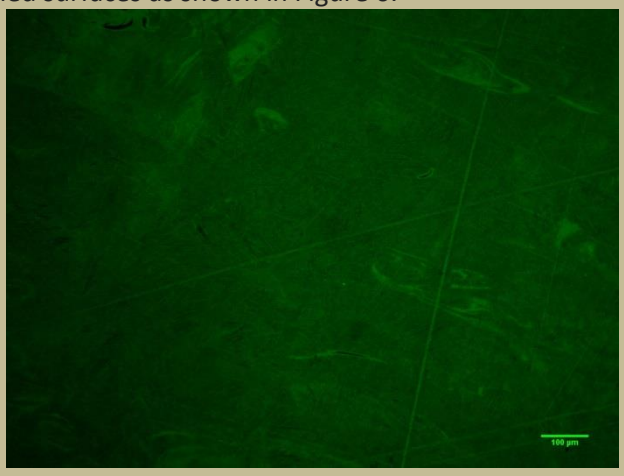

Figure 6 : Fluorescence micrograph (100 µm) on Ti6Al4V adding manufacturing by BresMedical after dip coating in SBF solution pH4 and concentration of 10 µM of label peptide aptamer.

Conclusions: Both materials processing for different companies have the composition of α and ß titanium and is possible to obtain the porosity for both cases. The topography at nano level will be important for further coatings and depositions of bioactive material such as calcium apatite including hydroxyapatite. After measured the intensities for both samples once the peptide coating is on the surface it was a notable 30% more of intensity in ADLER samples compare with the samples processing by BresMedical.

Calcium phosphate nano-coatings and nanocomposites for slow drug delivery and osteomyelitis

Besim Ben-Nissan , Innocent J. Mach, Sophie Cazalbou, and andy H Choi

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During the last two decades although many calcium phosphate based nanomaterials have been proposed for both drug delivery, and bone regeneration, their coating applications have been somehow slow due to the problems related to their complicated synthesis methods. In order to control the efficiency of local drug delivery of a biomaterial the critical pore sizes as well as good control of the chemical composition is pertinent. A variety of calcium phosphate based nano-coated composite drug delivery systems are currently being investigated. For bone repair and slow drug delivery systems, the most appropriate materials are the calcium phosphate based bone substitutes [1]. They offer easy production, drug carrying capability and supply both calcium and phosphates during dissolution. They can be easily incorporated within thin films and Nano coatings [2,3]. Due to their wide areas of applicability, the delivery of antibiotics has become a major focus in the prevention and treatment against infection during or postoperative surgical interventions. Biodegradable composite thin films Biodegradable polymer thin films loaded with gentamicin have been synthesized to act as a 'composite coatings' for metallic implants and fracture fixation devices in an attempt to prevent implant-associated infections [4-8]. Due to their tendency to uptake and release pharmaceuticals and minerals as well as the capability to degrade over time, the use of biodegradable polymer thin films is advantageous. In addition, by controlling the pore sizes and interconnectivity of these particles, the rates of drug release could be tailored to suit the treatment. In the present experimental work, hydrothermally converted coralline HAp particles containing nano and mesoporous were loaded with medically active substances, which cover both the surfaces and interconnected pores of the particles that ranged from a few hundred nanometres to micron sizes as shown in Figure 1. A schematic representation of the drug loading and release method used in the present work as shown in Figure 2.

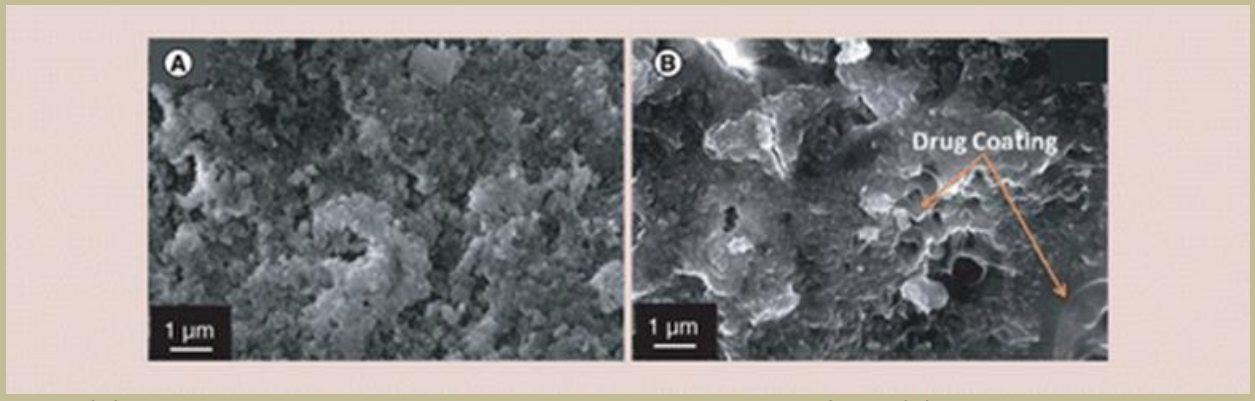

Figure 1: (A) Hydrothermal converted coralline hydroxyapatite surface. (B) Gentamicin-coated coralline hydroxyapatite surface.

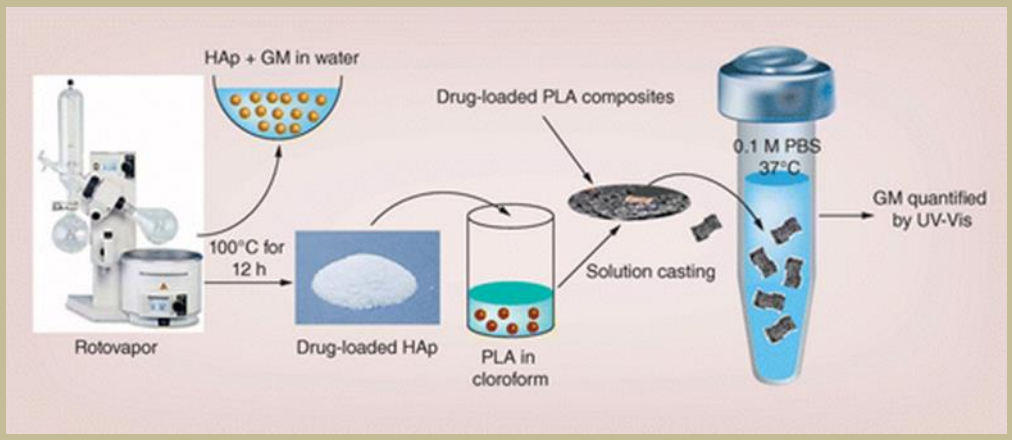

Figure 2: Schematic representation of the drug loading and release method used in the work.

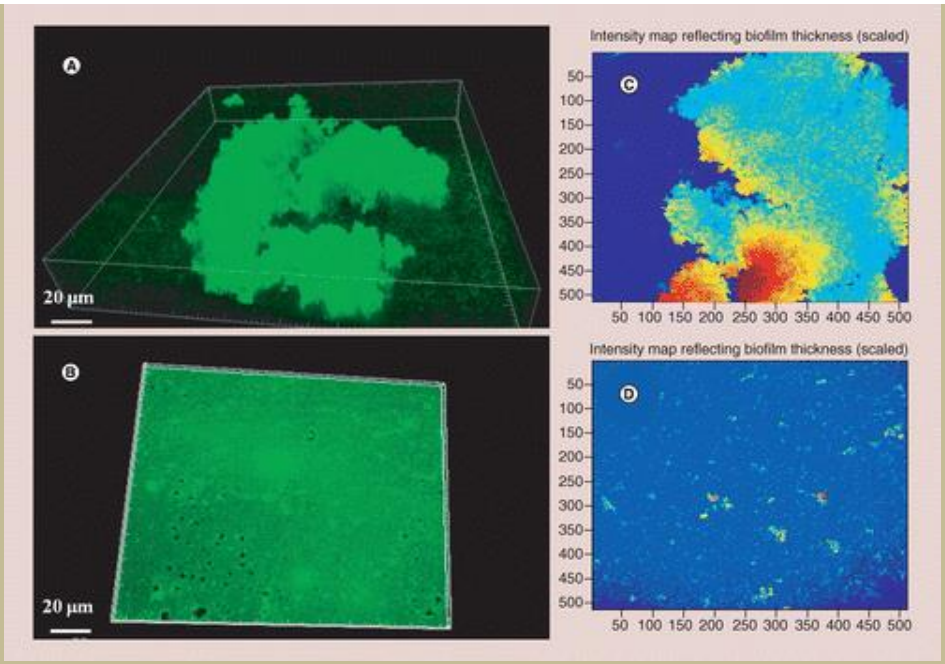

Figure 3 : Confocal microscopy images showing 24 h biofilm growth of Staphylococcus aureus. Biofilm growth on (A) PLAHAp, (B) PLAHApGM films and their intensity map reflecting biofilm thickness in (C & D), respectively, where (B & D) reflects the effectiveness of the gentamicin-loaded composites. GM: Gentamicin; HAp: Hydroxyapatite; PLA: Polylactic acid.

In summary, all of the PLA and PLA/HAp gentamicin loaded thin films under experimental conditions exhibited significant ability to prevent bacterial growth even at high concentration of bacterial. The prolonged ability to release drug from these films was tested by subjecting films for 4 weeks under the same experimental conditions. It was observed that even after releasing drugs for 4 weeks, films were still able to release enough gentamicin to prevent microbial activities.

Infection Studies - Clinical cases

Periprosthetic infections are frequently caused by coagulase-negative Staphylococci (CoNS). These bacteria are often resistant to methicillin. Culture remains the gold standard but it requires often few days to obtain a result. Thus a rapid test could be interesting to adapt sooner the antibiotic strategy. RT-PCR (Cepheid®) has been previously validated to detect Staphylococcus aureus and the presence of Meca gene, which traduces a methicillin resistance. The purpose of this study was to evaluate the detection methicillin resistance by this RT-PCR technique, of CoNS isolated from articular prosthesis.

Further, in the treatment of prosthetic joint infection often requires the prosthesis replacement. However, the question is it requires a two-stage better than a one-stage revision? This is still controversial and criteria proposed for choosing one or another strategy is not universally accepted. The success of treatment depends mainly on the surgeon's experience. Some of the updated clinical case studies have been reported in the following link : **http://www.boneandjoint.org.uk/search/procs/giordano**

Dissemination of Results

Publications

1. Besim Ben-Nissan, Innocent Macha, Sophie Cazalbou and Andy H Choi, Calcium phosphate nanocoatings and nanocomposites, part 2: thin films for slow drug delivery and osteomyelitis, Nanomedicine, March 2016 ,Vol. 11, No. 5, Pages 531-544 , DOI 10.2217/nnm.15.220.

2- Periprosthetic Knee Infection treated by computed assisted guidance (CAS) revisions ina one-stage procedure: A series of 41 patients, G. Giordano, G. Gracia, J. Remi, G. Krin, J. Lourtet, M.P. Felice, A. Bicart-See, L. Gauthie, P. Marlin, E. Bonnet, Orthopaedic Proceedings December 2015 97-B: 96-96.

3- The use of massive prostheses in periprosthetic infection : One stage and two stage experience of 33 patients, G. Giordano, G. Gracia, J. Lourtet, M.P. Felice, A. Bicart-See, L. Gauthie, P. Marlin, E. Bonnet, Orthopaedic Proceedings December 2015 97-B: 60-60.

Posters

1- Zeinab Salary, Cédric Charvillat , Parastoo Jamshidi, Artemis Stamboulis, Moataz Atallah, David Grossin, Besim Ben-Nissan, Olivier Marsan, Additive manufacturing of Bio-ceramics for bone repair, 10th World Biomaterials Congress (WBC), which will be held in Montreal May 17-22, 2016. (Poster Presentation).

Upcoming Events

4th International Conference on Biomedical Engineering and Systems (ICBES17), Rome, Italy – 5-6,2017.
http://icbes.net/

11th World Biomaterials Congress – Glasgow, Scotland, - 19-24 May, 2020.

Job Opportunities

At present there are no available job opportunities. If you are interested in submitting your CV, please contact Dr. Sooraj Nandyala, Project Manager, at s.h.nandyala@bham.ac.uk for future consideration.

Next 3D website

http://www.birmingham.ac.uk/research/activity/metallurgy-materials/next-3d/index.aspx

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