Live 3-D printing of osteogenic scaffolds into bone defects

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At the 47th Annual Meeting of the American Association for Dental Research (AADR), held in conjunction with the 42nd Annual Meeting of the Canadian Association for Dental Research (CADR), Venu G. Varanasi (University of Texas at Arlington College of Nursing and Health Innovation and Texas A&M University College of Dentistry, Dallas), presented an oral session titled "Live 3D Printing of Osteogenic Scaffolds Into Bone Defects." The AADR/CADR Annual Meeting is in Fort Lauderdale, Fla., USA from March 21-24, 2018.

Severe traumatic injuries to the cranium have been challenging to heal due to the large missing bone volume. Typically, metal or plastic implants are used. But, these implants can take a long time to be customized for fit and often take a longer than desired time to support bone fixation. This can often lead to multiple revision surgeries if the defect is not properly healed. Moreover, the tissue that adjoins the implant can improperly heal. For the effective treatment of these defects and injuries, it is necessary to reduce the time and improve the accuracy of implantable bone scaffold substitutes. Further, the microarchitecture and materials chemistry of the scaffold must enhance tissue regeneration and growth to hasten the healing process.

"Our goal is to heal the defect or fracture site rapidly, as if nothing ever happened", said Dr. Varanasi. "We want to develop these methods and materials so that someday we can treat certain types of bone defects like they are dental fillings. Principally, these become out-patient procedures where the patient goes home to heal with the support of their loved ones

and with reduced medical expenses owed to extended hospital stays."

The efficacy of bone scaffold substitutes is limited by the rate of bone formation, scaffold-defect mismatch and scaffold displacement during implantation. However, additive in-situ 3D printing can overcome these limitations by printing scaffolds that conform to the dimensions of the defect site.

"In our laboratory," said Dr. Varanasi "we tested several nanobiosilica-based 3D scaffolds with adequate 3D printing properties to potentially improve implantability and rapid bone healing capability. We hypothesized that these scaffolds formed the intended porosity and chemistry for bone and vascular healing. " His lab used a human periosteum cell culture model and a rat cranial defect animal model to illustrate the efficacy of this scaffold and live 3D printing method for potential clinical translation.

The biosilica-biopolymer scaffold was prepared by mixing Laponite (Lp) with methacrylated gelatin (MAG). Sucrose was used to increase viscosity and reduce gelation of the printing ink. IRGACURE 2529 was used as a crosslinking agent. During printing, crosslinking was initiated by UV light at the tip of the printer nozzle and scaffolds were in-situ 3D printed directly into calvaria bone defects using varied Laponite concentration to determine optimal bone density and chemical structure.

Scaffolds were fabricated into a mesh design with dimensions matching that of formed defects and after four weeks, cranial bone samples were extracted. Evaluation by micro-CT showed that nearly 55% of the bone defect was healed after four weeks for higher Lp- rich-MAG scaffolds versus lower Lp-containing MAG scaffolds. Empty control defects only had 11% of the defect filled with bone after four weeks. Histological staining showed that the scaffolds recruited cells into their structure to regenerate the intra-bony layers needed to initiate the healing process.

The results showed that 3D in-situ printing of bone regenerating scaffolds did improve the delivery of regenerative and reconstructive biomedical devices for the proper and rapid healing of bone fractures. The method allows for the absorption of blood and growth factors into the scaffold as it is being constructed within the defect. This provides an advantage in that cells from within the initial hematoma become incorporated into the scaffold structure, thus, giving the operator flexibility to use the printed scaffold as a structural support that stimulates healing," said Dr. Varanasi.

Dr. Varanasi credits the progress made on this work by the research team including mentees Taha Azimaie, Azhar Ilyas, Tugba Cebe, Neelam Ahuja, Ritesh Bhattacharjee, and Felipe Monte as well as close collaboration with Drs Philip Kramer and Likith Reddy (Texas A&M University) and Drs. Marco Brotto and Pranesh Aswath (University of Texas at Arlington). Jim Havelka has served as a senior business mentor. "This project would not have made the strides it made without their efforts. I was just fortunate to have these team members to help develop this work", Dr. Varanasi said.

Dr. Varanasi will now pursue this pioneering work further as part of the Bone-Muscle Group at the University of Texas at Arlington College of Nursing and Health Innovation, and, in collaboration with the University of Texas at Arlington College of Engineering, Texas A&M University College of Engineering, and College of Dentistry. Dr. Varanasi is now underway to identify commercialization and scientific development to help bring this emerging technology to serve patients in the clinic.

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