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EDITORIAL

Translational study of orthopaedic biomaterials and devices

The applications of orthopaedic biomaterials, implants and devices are to stabilize, improve, protect, replace, or regenerate damaged musculoskeletal tissues both anatomically and functionally. For example: the use of permanent implants in arthroplasty, trauma, spine and tumour surgeries; the use of degradable biomaterials and tissue engineered constructs to substitute, conduct or induce tissue repair or regeneration; and the use of support devices as exoskeletons. Though biocompatibility and mechanical compatibility are still the primary requirements for medical implants and devices, research on how to improve the bioactivity of implanted materials over time has become the major focus of biomaterial research in the last decade. Recently, ideas on designing third-generation materials that stimulate specific responses in surrounding tissues at the molecular level have been proposed [1]. This special issue of the *Journal of Orthopaedic Translation* presents eight articles that introduce the latest advances and applications of orthopaedic biomaterials and devices.

Bioactive and biodegradable implants

Titanium and titanium alloy based biomaterials have been widely used to fabricate orthopaedic implants due to their good mechanical properties and biocompatibility. Considering the bio-inert nature of titanium, various materials have been coated onto the surface of the implants to improve their bioactivity [2,3]. In this issue of the journal, Ao et al reports a new approach to biochemically modifying the surface of titanium implants in order to improve the activity of mesenchymal stem cells [4]. They demonstrated that type I collagen that has been covalently immobilized onto the titanium coating promotes the migration of stem cells into the porous structure of the implant *in vitro* and enhances the osteointegration of implants *in vivo*. This type of coating with biologic macromolecules may be further combined with growth factors or antibacterial agents to promote implant fixation with biological functions or to combat implant-associated infections [5,6]. This approach has become a hot topic in the R&D of innovative biomaterials.

Biodegradable magnesium-based metal implants are a revolutionary metallic material. However, some challenges still remain, such as the rapid corrosion rate and its associated challenges with regards to its biocompatibility [7,8]. One of the major concerns is the formation of hydrogen gas cavities during *in vivo* degradation of magnesium implants. Noviana et al investigated the effect of hydrogen gas on rat mortality and found that gas cavities were rapidly formed around the site of implantation and subsequently decreased the survival rate of the rats [9]. The production of hydrogen gas may depend on the degradation rate of magnesium implants and varies in different microenvironments. More R&D efforts and related studies are desirable to address this problem.

Materials or allograft to promote tissue regeneration

The main function of tissue-repairing materials is to serve as a scaffold to promote the differentiation of osteogenic cells and vascularization. Enhanced osteogenesis can be achieved by loading growth factors and stem cells within scaffolds, or constructing tissue-engineered bone. Petta et al report on the preparation of a new composite of β-tricalcium phosphate and a thermoresponsive hyaluronan hydrogel, which can be used in the form of injectable or moldable paste [10]. Owing to its amphiphilic

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characteristic, this composite can be supplemented with small hydrophobic molecules or biologics, for example to provide controlled release of both rhBMP-2 and dexamethasone for improved osteoinductivity. Similar efforts have been made by Ding's group, who developed and tested bone graft materials in a novel perfusion bioreactor to promote bone formation [11].

Compared to partial bone and cartilage defects, the treatment of full-thickness osteochondral injury is more challenging. In a recent study, a goat femoral head was successfully regenerated using a tissue-specific biphasic scaffold fabricated with CAD/CAM and 3D printing technology [12]. It is a promising approach to regenerating a biological joint, but whether it can become a cost-effective approach that can replace osteochondral allograft transplantation—a well-accepted surgical treatment—remains for further investigation. The objective of Crist et al's study presented in this issue of the journal was to compare femoral head osteochondral autografts and allografts in a canine model [13]. The authors reported that there was a significant loss in range of motion, chondrocyte viability and articular cartilage integrity 8 weeks after implantation of both small autografts and allografts, whereas chondrocytes in the large allografts maintained their viability and structural integrity throughout the study period. A similar type of large allograft ($>$ 30 mm) was implanted into four human patients. After 4–18 months of follow-up, all patients could withstand full weight-bearing and showed no evidence of graft failure or progressive arthrosis, implying the translational potential of their proof-of-concept research.

Another report is on intervertebral disc disease. Stannard et al developed a whole organ culture model of intervertebral discs in a rotating wall vessel bioreactor [14]. The annulus fibrosus was penetrated with a 20G needle to the nucleus pulposus and aspirated, which produced pathologic changes consistent with those observed in degenerative intervertebral disc disease in humans. Compared with animal models that are often time-consuming and high cost, this *in vitro* model provides a convenient way to investigate new treatment approaches, including various tissue engineering strategies [15].

Robotic devices

Recently, the demand for robotic devices has increased significantly, driven by the rapid growth of an aging population and increase in mobility disorders globally. Advancements in biomedical engineering, computer science and medical imaging technology have brought about a revolution in robotic devices [16,17]. The review in this issue of the journal by Chen et al introduces the general concept of exoskeletons and several typical lower extremity exoskeletons (LEEs) in gait rehabilitation, human locomotion assistance and human strength augmentation [18]. The limitations of current LEEs and their future research and development are discussed. The paper by Qin et al introduces the housing design and testing of a surgical robot [19]. Based on the general requirements for Class II Medical Devices, a modern surgical robot was designed and approved for use in orthopaedic surgeries in Hong Kong. This project demonstrated the successful collaboration in the multidisciplinary R&D led by orthopaedic surgeons together with mechanical and electronic engineers and industrial designers.

Limited by the issue's volume, we cannot include all of the hot topics in the research of orthopaedic biomaterials, implants and devices, such as innovations in nanobiomaterials, drug delivery systems [20] and 3D printing technology [21,22]. Although great progress has been made in recent years, success in translating orthopaedic biomaterials, implants and devices into clinical applications (or from bench to bedside) remains a challenge. Further improvements in the current academic or professional promotion systems, close collaboration among scientists, engineers, clinicians and industrial partners, and efficient communication between investigators and government regulators are key issues that need to be addressed to promote future translational studies.

Finally, we wish to reemphasize the relevant issues raised in the Editorial of the inaugural issue of the *Journal of Orthopaedic Translation* [23] with regard to scientific reports of R&D of biomaterials or implants/devices. Essential information on the testing or evaluation methods should be provided whenever possible and follow the recommended tests listed by the ISO and/or American Society for Testing Materials (ASTM). This approach will help our R&D work to be appreciated by the regulatory bodies or certified testing centres of the Food and Drug Administration in the United States or the China Food and Drug Administration (CFDA) in China, which in turn will help shorten the regulatory registration process. Apart from testing the efficacy and safety of these products, their cost-effectiveness should also be addressed for product registration. Finally, clinical trials should be conducted to collect important information for building up a solid foundation for their long-term sustainable development and clinical translation.

References

[1] Navarro M, Michiardi A, Castaño O, Planell JA. Biomaterials in orthopaedics. J R Soc Interface 2008;5:1137–58.
[2] Ramaswamy Y, Wu C, Zreiqat H. Orthopedic coating materials: considerations and applications. Expert Rev Med Devices 2009;6:423–30.
[3] Peng Z, Ni J, Zheng K, Shen Y, Wang X, He G, et al. Dual effects and mechanism of TiO_2 nanotube arrays in reducing bacterial colonization and enhancing C3H10T1/2 cell adhesion. Int J Nanomedicine 2013;8:3093–105.
[4] Ao HY, Xie YT, Yang SB, Wu XD, Li K, Zheng XB, et al. Covalently immobilised type I collagen facilitates osteoconduction and osseointegration of titanium coated implants. J Orthop Transl 2016;5:16–25.
[5] Inzana JA, Schwarz EM, Kates SL, Awad HA. Biomaterials approaches to treating implant-associated osteomyelitis. Biomaterials 2016;81:58–71.
[6] Tan HL, Ao HY, Ma R, Lin WT, Tang TT. *In vivo* effect of quaternized chitosan-loaded polymethylmethacrylate bone cement on methicillin-resistant *Staphylococcus epidermidis* infection of the tibial metaphysis in a rabbit model. Antimicrob Agents Chemother 2014;58:6016–23.
[7] Martinez Sanchez AH, Luthringer BJ, Feyerabend F, Willumeit R. Mg and Mg alloys: how comparable are *in vitro*

and *in vivo* corrosion rates? A review. Acta Biomater 2015;13:16—31.
[8] Wang J, Witte F, Xi T, Zheng Y, Yang K, Yang Y, et al. Recommendation for modifying current cytotoxicity testing standards for biodegradable magnesium-based materials. Acta Biomater 2015;21:237—49.
[9] Noviana D, Paramitha D, Ulum MF, Hermawan H. The effect of hydrogen gas evolution of magnesium implant on the postimplantation mortality of rats. J Orthop Transl 2016;5:9—15.
[10] Petta D, Fussell G, Hughes L, Buechter DD, Sprecher CM, Alini M, et al. Calcium phosphate/thermoresponsive hyaluronan hydrogel composite delivering hydrophilic and hydrophobic drugs. J Orthop Transl 2016;5:57—68.
[11] Ding M, Henriksen SS, Theilgaard N, Overgaard S. Assessment of activated porous granules on implant fixation and early bone formation in sheep. J Orthop Transl 2016;5:38—47.
[12] Ding C, Qiao Z, Jiang W, Li H, Wei J, Zhou G, et al. Regeneration of a goat femoral head using a tissue-specific, biphasic scaffold fabricated with CAD/CAM technology. Biomaterials 2013;34:6706—16.
[13] Crist BD, Stoker AM, Pfeiffer FM, Kuroki K, Cook CR, Franklin SP, et al. Optimising femoral-head osteochondral allograft transplantation in a preclinical model. J Orthop Transl 2016;5:48—56.
[14] Stannard JT, Edamura K, Stoker AM, O'Connell GD, Kuroki K, Hung CT, et al. Development of a whole organ culture model for intervertebral disc disease. J Orthop Transl 2016;5:1—8.
[15] Silva-Correia J, Correia SI, Oliveira JM, Reis RL. Tissue engineering strategies applied in the regeneration of the human intervertebral disk. Biotechnol Adv 2013;31:1514—31.
[16] Pazzaglia M, Molinari M. The embodiment of assistive devices—from wheelchair to exoskeleton. Phys Life Rev 2015 Dec 2. http://dx.doi.org/10.1016/j.plrev.2015.11.006. pii: S1571—0645(15)00211-0. [Epub ahead of print].
[17] Karthik K, Colegate-Stone T, Dasgupta P, Tavakkolizadeh A, Sinha J. Robotic surgery in trauma and orthopaedics: a systematic review. Bone Joint J 2015;97-B:292—9.
[18] Chen B, Ma H, Qin LY, Gao F, Chan KM, Law SW, et al. Recent developments and challenges of lower extremity exoskeletons. J Orthop Transl 2016;5:26—37.
[19] Qin LY, Wen JZ, Chui CS, Leung KS. Housing design and testing of a surgical robot developed for orthopaedic surgery. J Orthop Transl 2016;5:72—80.
[20] Rejinold NS, Jayakumar R, Kim YC. Radio frequency responsive nano-biomaterials for cancer therapy. J Control Release 2015;204:85—97.
[21] Skardal A, Atala A. Biomaterials for integration with 3-D bioprinting. Ann Biomed Eng 2015;43:730—46.
[22] Ma R, Lai YX, Li L, Tan HL, Wang JL, Li Y, et al. Bacterial inhibition potential of 3D rapid-prototyped magnesium-based porous composite scaffolds—an *in vitro* efficacy study. Sci Rep 2015;5:13775.
[23] Qin L. Translational medicine in orthopaedics. J Orthop Trans 2013;1:3—5.

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