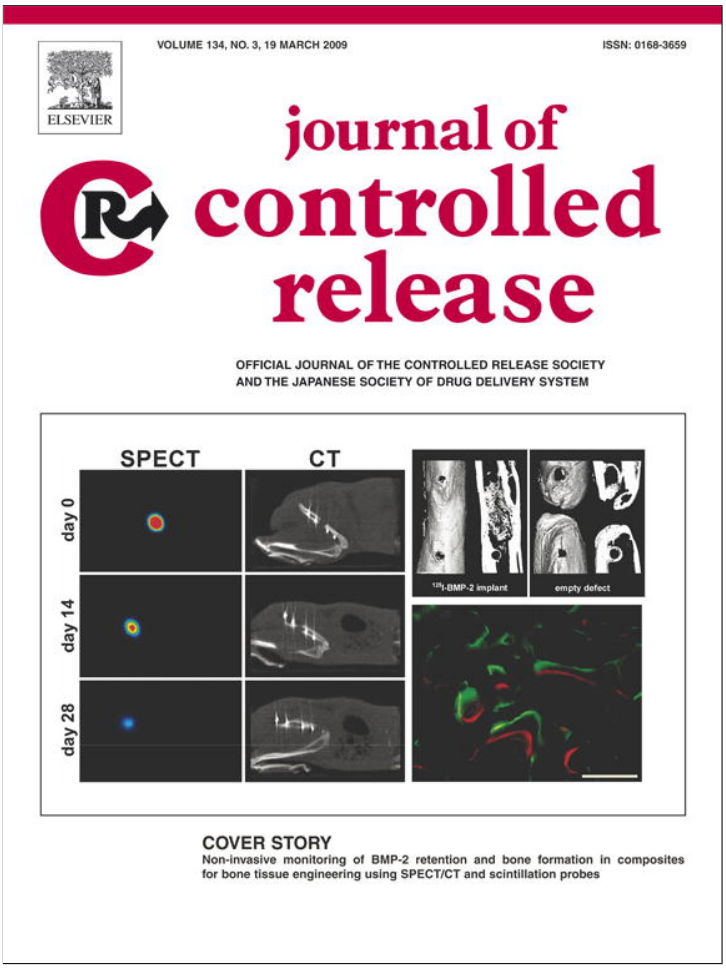

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Cover Story

Non-invasive monitoring of BMP-2 retention and bone formation

Over the past decades, the role of growth factors in bone regeneration has gained increasing interest. Many growth factors involved in the natural process of bone healing have been identified. Advances in recombinant DNA technology have enabled large scale production of such growth factors for research and therapeutic applications. Despite their promising effects on the regeneration process, administration of growth factors in orthopedic applications remains complicated by their short biological half-lives and rapid local clearance. To overcome these problems, controlled delivery systems have been utilized to maximize growth factor-based bone regeneration. Although many vehicles for growth factor delivery are currently under development and appear promising, optimization of their pharmacokinetic and biological actions is still a big challenge. A particular hurdle to overcome is the discrepancy found between *in vitro* and *in vivo* release profiles. A profile identified *in vitro* as optimally reflecting endogenous concentrations during spontaneous healing may not have the same favorable kinetics *in vivo* and thus become inefficient at stimulating bone formation. In the absence of *in vitro–in vivo* correlations, optimization of drug release profiles from the delivery vehicles requires *in vivo* monitoring of both growth factor release and its subsequent effect on bone formation.

In the study by Kempen et al. in this issue [1], nuclear medicine and radiological techniques were explored for non-invasive monitoring of drug release and bone formation at ectopic and orthotopic locations. Single photon emission computed tomography (SPECT) and a scintillation probe setup were used to determine local retention profiles of the radiolabeled osteoinductive protein BMP-2. Micro-computed tomography (μCT) was used for monitoring bone formation in the delivery vehicle. Sequential use of two nuclear medicine techniques was able to provide detailed release profiles that correlate well bone formation. There were no significant differences between the non-invasive and *ex vivo* analysis of isotope activity and localization after 8 weeks of follow up. At the same time, non-invasive μCT imaging showed the onset and extent of the bone formation at both locations over time.

From a perspective of controlled drug delivery and bone regeneration, the non-invasive sequential measurements provided detailed profiles of the growth factor release as well as bone formation in a limited number of animals. This combination of non-invasive techniques over a prolonged period of time will provide essential information on the roles of growth factors during bone regeneration and the optimization of drug delivery vehicles enhancing regeneration. One of the main strengths of the approach taken by Kempen et al. is that it can easily establish *in vitro–in vivo* correlations for various drugs making the development of new delivery systems easier and more efficient.

Reference

[1] D.H.R. Kempen, M.J. Yaszemski, A. Heijink, T.E. Hefferan, L.B. Creemers, J. Britson, A. Maran, K.L. Classic, W.J.A. Dhert, L. Lu, Non-invasive monitoring of BMP-2 retention and bone formation in composites for bone tissue engineering using SPECT/CT and scintillation probes, J. Control. Release 134 (2009)10.1016/j.jconrel.2008.11.023.

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