INTERNATIONAL ISO

First edition
2018-01

Tissue-engineered medical products — Bioactive ceramics — Method to measure cell migration in porous materials

Produits médicaux issus de l'ingénierie tissulaire — Céramiques bioactives — Méthode de mesure de la migration cellulaire dans les matériaux poreux

Reference number
ISO 19090:2018(E)

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Published in Switzerland

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Foreword

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ISO 19090 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 7, *Tissue-engineered medical products*.

Introduction

"Bioactive ceramics" are widely used in orthopaedic and dental fields due to their bioactivities and bioaffinities. Porous bioactive ceramics are designed as bone void fillers, and cell migration from tissue into their pores is an expectation for effective repair of bone defects; thus, they are one of the promising candidates for cell scaffolds for bone tissue engineering medical products.

To clarify the clinical safety and usefulness of these bioactive ceramics, physical, chemical and biological properties must be examined. In the methods used, animal tests are the ultimate and essential methods to examine biological properties of bioactive ceramics; however, numbers of both animals and animal tests must be reduced under the concept of 3R (Replacement, Reduction and Refinement)[3].

The first and most important property for porous biomaterials including bioactive ceramics is cell migration capability, because cell proliferation, differentiation, tissue formation and tissue maturation in and surroundings of porous biomaterials do not occur without cell migration.

Currently, two different cell-seeding methods are used for estimating "cell migration" property: One is dropping a cell suspension on the top surface of a porous material. This method tests the penetration ability of the "cell suspension" under gravity and estimates the number of cells that migrate into and are held within the porous material. The other method is shaking a porous material in the cell suspension. This method also tests the penetration ability of the "cell suspension" like the above method but uses shaking to drive the cells into the porous scaffolds. Both methods test the abilities of cell penetration and retention only, and do not test the intrinsic ability of the cell to migrate simulating what happens *in vivo*. Body fluid itself can sufficiently carry cells across a minor gap between the implanted material and the host bone. Accordingly, no cell migration test methods have been reported that mimic cell behaviour *in vivo*.

When porous bioceramics are implanted into bone defect, cells migrate into the pore to form new bone. In this process, migration of osteoblasts mainly plays important roles for osteoconduction. That is to say, no osteoconduction nor bone formation can occur without osteoblast migration.

Therefore, it is imperative to establish a quantifiable method to measure cell migration potential of porous bioactive ceramics in a manner similar to how cells behave *in vivo*, in order to evaluate their potential appropriately as materials for tissue-engineered medical products.