Biodegradable polyurethanes for substitutive medicine

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Infection, tumour resection, trauma and ageing often lead to the loss of tissues and internal organs. The number of patients who suffer from these problems is increasing while the availability of autogenous tissues for transplantation remains limited. Genetic engineering may offer a possible solution to this problem. This is, however, still at the exploratory stage and some time may pass before it gains common clinical acceptance. Yet another solution might be the use of structural tissue scaffolds having biological properties approximating those of autogenous tissues. Optimally, such scaffolds implanted in place of resected or defective tissues and organs should induce their healing and/or regeneration. This is not yet the case for state-of-the art biomaterials technology. Therefore, the scaffold’s regenerative potential needs to be enhanced, for example, by loading it with autogenous and/or synthetic growth factors or by seeding it with cells, the latter being commonly called “tissue engineering”. The form and structure of the scaffold may resemble the structure and form of the tissue or organ it is intended to substitute.

Structural tissue scaffold should be biocompatible, preferably bioresorbable or biodegradable and porous. The pores should be interconnected allowing for a flux of nutrients, ingrowth of cells, blood vessels and tissues. The size of pores having a significant impact on the scaffold’s biological functionality will depend on the intended application, i.e. there is no one “universal” pore size which suits all types of tissues to be substituted. Biodegradable aliphatic segmented polyurethanes are among the candidate materials for scaffolds. The hydrophilicity, degradation rates and mechanical properties of biodegradable polyurethanes can be controlled by using specific monomers and varying synthesis conditions and can be adjusted according to the intended application. Hydrophilic polyurethane elastomers are preferred for cardiovascular implants and tissue adhesion barriers. Polyurethanes with higher amounts of hydrophobic component may be required for cancellous bone graft substitutes and for repair of articular cartilage.

In the early eighties experimental biodegradable polyurethanes were used for the preparation of small-caliber vascular prostheses, artificial skin, esophageal and tracheal prostheses, pericardial patches and porous membranes for the treatment of periodontitis. Vascular prostheses from these polyurethanes induced the growth of functional “neo-arteries” in animals. An “artificial skin” promoted healing of full-thickness skin wounds with no scarring. Tubular microporous prostheses facilitated regeneration of resected segments of trachea and esophagus in animals. The tubular polyurethane implants with uniaxial pore orientation that formed primary scaffolding for oriented migration of fibroblasts, Schwann cells and regenerating axons, facilitated healing of large defects in the sciatic nerve.

One of the challenging problems in trauma and orthopaedic reconstructive surgery is healing of large, critical-size bone defects resulting from tumour, infections, trauma, congenital malformation and osteonecrosis. Such defects if left untreated do not heal in the patient’s lifetime. A commonly used surgical procedure to treat such defects is bone grafting using cancellous bone harvested from the ilium. Bone harvesting is traumatic, associated with high complication rates and donor site morbidity. In addition, monocortical defects in the ilium frequently present difficulties of complete bony regeneration while bicortical and tricortical defects do not heal with new bone. Hence, there is still a need for new biologically functional bone graft substitutes that could be used instead of autogenous cancellous bone graft.

Among the candidate materials for bone substitutes are biodegradable polyurethanes with controlled elasticity. Elastomeric bone substitutes do not induce the shear forces at the bone-implant interface and provide intimate contact between native bone ends and the implant. These facilitates proliferation of osteogenic cells into the implant and, in consequence promotes bone regeneration. Loading a polyurethane bone substitute with calcium phosphate ceramics preferably nanosize crystals, would provide osteoconductive properties, while impregnation with autogenous bone marrow aspirates or platelet concentrate would add an osteoinductive potential to the implant.

In the ageing population, osteoporosis and related bone fractures pose severe problem. In the US alone there are about 700,000 spine fractures, 300,000 hip fractures, 250,000 wrist fractures and 250,000 other fractures per year. Costs related to these problems were US$ 28 billion per annum (US$ 38 million/day) in 1995. The population “at risk” is estimated to be 100 million worldwide and 28 million in the US alone. Injectable polyurethane fillers - cements might potentially be used in compression fractures of vertebrae and in for the replacement of calcified disc and nucleus pulposus.