

# BIODEGRADABLE POLYURETHANES FOR SUBSTITUTIVE MEDICINE

SYLWESTER GOGOLEWSKI

POLYMER RESEARCH, AO RESEARCH INSTITUTE, CH-7270  
DAVOS, SWITZERLAND

*[Engineering of Biomaterials, 38-43, (2004), 10]*

Interest for synthetic bioresorbable polymers as candidates for implantable devices goes back to the early 1950. Although initially the interest was purely academic, soon first implants in the form of sutures became commercially available. Gradually, the use of bioresorbable polymers for implants broadened, primarily for drug delivery, internal fixation of bone fractures and various constructs for stapling and binding soft and hard tissues.

Over the last few years there has been increasing interest in the use of bioresorbable polymers in the design of structural scaffolds which could be used as substitutes for damaged, resected or malfunctioning tissues and internal organs. Optimally, such scaffolds implanted in place of missing tissues or organs would initiate their healing and/or regeneration. The regenerative potential of the scaffolds can be intensified by loading them with autogenous and/or synthetic growth factors or by applying "tissue engineering", i.e. seeding scaffolds with autogenous or transfected cells. The candidate polymers for scaffolds that have been investigated the most extensively over the last few years are polyhydroxyacids. Recently, new aliphatic segmented polyurethanes have been attracting increased interest. Biostable medical polyurethanes have been used for years in total artificial hearts, heart valves, intraaortic balloons, mammary implants, wound dressings, pacing leads insulation, and angioplasty balloons, to mention but a few. It has been found, however, that these polyurethanes have limited long-term molecular stability in vivo. The biologically active environment of the living organisms degrades polyurethanes, mainly through hydrolytic chain scission within ester and urethane linkages in the backbone chain and oxidative attack within polyether segments - processes which can be facilitated by the presence of enzymes and cell peroxides.

The relative molecular instability of polyurethanes may, however, be deliberately exploited in the design biodegradable materials. This can be achieved by incorporating labile moieties susceptible to hydrolysis in the polymer chain. Labile moieties are based on polyols of hydroxyacids, caprolactone, polysaccharides, aminoacids, short-chain peptides and aliphatic diisocyanates. The diisocyanates of interest are aliphatic hexamethylene diisocyanate, lysine di- or triisocyanate and tetramethylene diisocyanate. The products of degradation of these polyurethanes are biocompatible and easily metabolized. Putrescine formed upon degradation of tetramethylene diisocyanate is claimed to possess a growth factor property for various cell types. The hydrophilicity, degradation rates and mechanical properties of polyurethanes can be controlled by using specific monomers and varying synthesis conditions. Polyurethanes can be made hydrophilic, hydrophobic or amphiphilic. Their mechanical properties can be adjusted according to the intended application. Hydrophilic polyurethane elastomers are preferred for the preparation of implants to be used in contact with blood or as tissue adhesion barriers. Polyurethanes

with higher amounts of hydrophobic component may be required for cancellous bone graft substitutes and for repair of articular cartilage. The ratio between the hydrophilic and hydrophobic components in amphiphilic polyurethanes may play an important role during contact of the material surface with blood proteins, cells and tissues. In the early eighties experimental biodegradable polyurethanes based on lactide diols and hexamethylene diisocyanate or on mixtures of aliphatic polyurethanes with poly(L-lactide) were used for the preparation of small-caliber vascular grafts, artificial skin, esophageal and tracheal prostheses, pericardial patches and porous membranes for the treatment of periodontitis. Vascular prostheses from these polyurethanes induced in animals the growth of functional "neo-arteries". The neo-arteries had cellular structure, compliance and biological activity similar to those of the natural vessels. Endothelial cells of the neo-artery produced prostaglandins. An "artificial skin" from biodegradable polyurethanes promoted healing of full-thickness skin wounds. Tubular microporous prostheses facilitated regeneration of resected segments of trachea and esophagus in animals. Interest in biodegradable polyurethanes gained new momentum in the late nineties. Tubular polyurethane implants that form primary scaffolding for oriented migration of fibroblasts, Schwann cells and regenerating axons, facilitated healing of large defects in the sciatic nerve. Microporous 3-D scaffolds used as bone substitutes enhanced the regeneration of critical-size segmental long bone defects and mono-, bi- and tricortical defects in the ilium. Such defects under normal circumstances do not heal in the patient's lifetime. New attractive applications of polyurethanes would be as injectable tissue augmentation materials, injectable cements for the treatment of compression fractures of osteoporotic vertebrae and as injectable hydrogels for the replacement of calcified nucleus pulposus.

## IN VIVO CHARACTERIZATION OF POLY-L/D-LACTIDE (PLDLA) 96/4 SUTURES IN THE ACHILLES TENDON OF RABBITS

JARMO KANGAS\*, ARI PAJALA\*, JUHANA LEPPILAHTI\*,  
JORMA RYHÄNEN\*, SATU LÄNSMAN\*\*, PERTTI TÖRMÄLÄ\*\*\*,  
TIMO WARIS\*, NUREDDIN ASHAMMAKHI\*

\*Department of Surgery, Oulu University Hospital, Oulu, Finland.

\*\*Department of Ophthalmology, Oulu University Hospital, Oulu, Finland.

\*\*\*Institute of Biomaterials, Tampere University of Technology, Tampere, Finland.

**Keywords:** Achilles, polylactide, tendon repair, suture

*[Engineering of Biomaterials, 38-42, (2004), 10-11]*

## Background

Common Achilles tendon ruptures are usually not fixed by absorbable sutures due to limitations in their strength properties. Modern technology has made it possible to develop bioabsorbable sutures with prolonged strength retention.

## Aim

To evaluate histologically tissue reactions and biodegradation of poly-L/D-lactide (PLDLA) sutures implanted in Achilles tendon of rabbits.

## Material and methods

Fifteen rabbits were operated on and killed within a time schedule of 2, 6 and 12 weeks, with 5 rabbits in per period. PLDLA monofilament sutures (Tampere University of Technology, Tampere, Finland) were implanted inside the rabbit medial gastrocnemius tendon for biocompatibility testing. Polyglyconate (4.0) monofilament sutures (MaxonR, Cyanamid of Great Britain Ltd., Gosport, UK) with the same diameter were implanted in the contralateral tendon. The histology was studied in hard-resin embedded samples and the thickness of the capsule membrane was determined histomorphometrically.

## Results

PLDLA have significantly smaller capsule formation around each fiber in tendon than MaxonR sutures. The mean capsule thicknesses in each follow-up period can be seen in TABLE 1.

## Conclusions

In present study, by 12 weeks the PLDLA sutures implanted intratendineously formed thinner fibrous capsule than MaxonR sutures of same diameter. The suture materials were not degraded by 12 weeks.

## Acknowledgements

Research funds from the Technology Development Center in Finland (TEKES, Biowaffle Project 40274/03 and MFM Project 424/31/04), the European Commission (EU Spare Parts Project QLK6-CT-2000-00487), the Academy of Finland (Project 73948) and the Ministry of Education (Graduate School of Biomaterials and Tissue Engineering) are greatly appreciated.

	2 weeks	6 weeks	12 weeks
PLDLA	5.26	11.66	10.63
Maxon <sup>R</sup>	13.22	80.97	17.59

TABLE 1.



# RESORBABLE MULTIFUNCTIONAL ANTIBIOTIC RELEASING TACKS

JOHANNA TIAINEN\*, KAISA KNUUTILA\*\*, MINNA VEIRANTO\*\*, ESA SUOKAS\*\*\*, TIMO WARIS\*, PERTTI TÖRMÄLÄ\*\*, OUTI KAARELA\*, NUREDDIN ASHAMMAKHI\*

\*DEPARTMENT OF SURGERY, OULU UNIVERSITY HOSPITAL, OULU, FINLAND.

\*\*INSTITUTE OF BIOMATERIALS, TAMPERE UNIVERSITY OF TECHNOLOGY, TAMPERE, FINLAND.

\*\*\*LINVATEC BIOMATERIALS LTD., TAMPERE, FINLAND.

## Abstract

The aim of this study was to compare the pullout forces of recently developed bioabsorbable ciprofloxacin-releasing and plain self-reinforced polylactide/polyglycolide (SR-PLGA) 80/20 tacks in human cadaver parietal bones. Parietal bone pieces (approximately 6 x 20 cm) were collected from five human male cadavers (29-77 years of age). Fifty plain SR-PLGA 80/20 tacks (diameter = 2 mm, length = 6.0 mm) and 50 ciprofloxacin-releasing SR-PLGA 80/20 tacks of similar dimensions were applied to drill holes using a special tack-shooter without tapping the drill holes. The force needed to pull the tacks from human parietal cadaver bones was measured using a universal tensile testing machine. The tack pullout speed was 10 mm/min. Means and standard deviations (SDs) were calculated and analyzed using the Student t test (SPSS version 10.0 for Windows). The pullout forces of the ciprofloxacin-releasing and plain tacks were 147 +/- 10.3 N and 141.4 +/- 12.6 N respectively (insignificant difference, P<0.001). The main cause of failure was the breakage of tack barbs (95% in the both cases). Ciprofloxacin-releasing SR-PLGA tacks have a pullout strength similar to corresponding plain conventional SR-PLGA tacks and they can be applied in cranial bone fixation.

**Keywords:** Bioabsorbable, ciprofloxacin, osteofixation, tack  
[Engineering of Biomaterials, 38-43, (2004), 11]

## Acknowledgements

Research funds from the Technology Development Center in Finland (TEKES, Biowaffle Project 40274/03 and MFM Project 424/31/04), the European Commission (EU Spare Parts Project QLK6-CT-2000-00487), the Academy of Finland (Project 73948) and the Ministry of Education (Graduate School of Biomaterials and Tissue Engineering) are greatly appreciated.

