

MAST Biosurgery Resorbable Technology: An Overview

INTRODUCTION

The search for resorbable materials suitable for use in medical applications has led researchers to a chemical family known as alpha esters. Resorbable polymers polylactic acid (PLA) and polyglycolic acid (PGA) are each a part of this chemical category.^{7,21} These alpha ester compounds have been successfully used as suture material over the past 30 years.^{14,26} Within the last fifteen years, these resorbable polymers have also been successfully employed in various orthopaedic and craniofacial applications.^{7,11,21}

PLA VS. PGA

Years of clinical use and scientific evaluation demonstrating the safety and biocompatibility of both PLA and PGA have led to clearance by the U.S. Food and Drug Administration for use of these materials in many clinical applications.^{7,14,16,36,54,56} However, differences in tissue reactions do exist between these two commonly implanted polymers. Many scientists have suggested that the intensity of inflammatory reactions after implantation of PGA implants is more pronounced than that seen after implantation of similar devices manufactured of PLA.^{7,56} Comparative studies of PLA and PGA have demonstrated that PGA polymers exhibit a greater tissue reaction than comparable volumes of PLA.^{14,54} One study reports that PGA initiates an inflammatory tissue response 2 times that of PLA.¹⁴

Studies involving more sensitive tissues such as the dura mater further distinguish the two materials. Polymers made of PGA have been reported to become inseparable from the dura after only 2 weeks of implantation.¹⁶ PLA, however did not adhere to the dura when compared side-by-side with PGA¹⁶ nor in studies considering only the PLA material.³⁶

PLA BIOCOMPATIBILITY

PLA has been shown to be fully compatible with dural tissue.^{30,31} In animal studies, disks made of PLA were placed in direct contact with the dura after a craniotomy and evaluated over time. No adverse events were noted after histological examination of the dural tissue.^{30,31} PLA has also been shown to be biocompatible with neural tissues within the spinal cord. The proliferation of spinal cord Schwann cells is not affected by the by-products of PLA degradation.¹⁶ Studies have shown the presence of PLA to have no effect on neuronal cells, non-neuronal cells, and axon growth.¹⁶

PLA material and the products of its degradation are well tolerated by brain tissues.²⁵ Cerebral spinal fluid (CSF) is capable of buffering and eliminating increases in lactic acid by as much as 3 mM/L.^{22,37} Should a volume of PLA be inadvertently introduced subdural, the degradation of a large amount of PLA (20 grams) would only increase blood lactate levels at most by 0.2 mM/L. Even this increase of 0.2 mM/L by PLA represents a 20-fold safety factor beyond the 3 mM/L lactate increases that have been shown to occur naturally and have no effect on pH.^{22,37}

PLA has been studied in conjunction with peripheral nerves and shown to be biocompatible upon gross and histological examinations.^{36,38,45} The biocompatibility of PLA with peripheral nerve tissue has been experimentally demonstrated by the growth and subsequent reattachment of sciatic nerve stumps (5-10mm gaps) wrapped in a PLA tube.^{38,45}

PLA devices have been utilized in orthopedic and craniofacial applications without adverse effect on bone healing.^{40,41,42,44}

TABLE 1. A great deal of published literature is available which details the biocompatibility of PLA in various applications. Selected articles are organized by various clinical applications in the table below.

Tissue Type	Conclusions	References
PLA and Tissue Reactions	PLA is biocompatible with soft tissues.	3,6,10,12,17,26,43,53,55
PLA and Human Orthopedic Procedures	PLA is biocompatible when used in orthopedic procedures in Humans.	40,41,42,44
PLA and Animal Orthopedic Procedures	PLA is biocompatible when used in orthopedic procedures in Animals.	24,33
PLA and Bone Healing	PLA is biocompatible with bone tissue and does not adversely affect bone healing.	44,49
PLA and Marrow Cells (Osteocytes)	PLA is biocompatible with bone marrow cells.	18,32,34
PLA and Craniofacial Bone Healing	PLA is biocompatible with craniofacial bone tissue and does not adversely affect craniofacial bone healing.	6,29
PLA and Mandibular Bone Healing	PLA is biocompatible with mandibular bone tissue and does not adversely affect mandibular bone healing.	4,49,50
PLA and Periodontal Bone Healing	PLA is biocompatible with periodontal bone tissue and does not adversely affect periodontal bone healing.	8,10,39
PLA and Femoral Bone Healing	PLA is biocompatible with femoral bone tissue and does not adversely affect femoral bone healing.	53,54,55
PLA and Dural Tissue	PLA is biocompatible with dural tissue.	23,30,31,35,57
Spinal Cord and Schwann Cell Biocompatibility	PLA is biocompatible with spinal cord and spinal cord Schwann cells.	16
Effect of Lactic Acid on Brain Tissue, CSF and pH	The cerebrospinal fluid is capable of buffering up to 4 times the anticipated amount of lactic acid with no change in pH. Brain tissue is biocompatible with PLA.	22,25,37
PLA and Nerve Tissues	PLA is biocompatible with peripheral nerves.	37,38,45

PLA POLYMER

PLA exists in two specific chemical forms, Poly(L-lactide) and Poly(D,L-lactide). These two forms of PLA may be joined to create a PLA co-polymer (Figure 1). Varying the ratios of the two forms of PLA will, to a great extent, determine the strength and degradation characteristics of the resulting material.

The pure PLLA form Poly(L-lactide) is characterized by a high content of crystalline particles, high strength and prolonged periods of degradation. Some studies have reported a connection between this higher crystallinity and the associated long degradation time with an increased incidence of unfavorable tissue reaction.¹¹

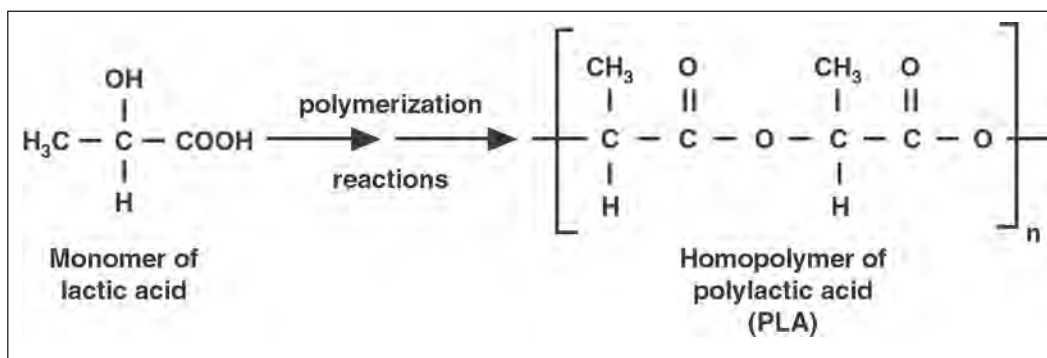


FIGURE 1. Schematic illustration of the chemical composition of polylactic acid resorbable polymers.²¹

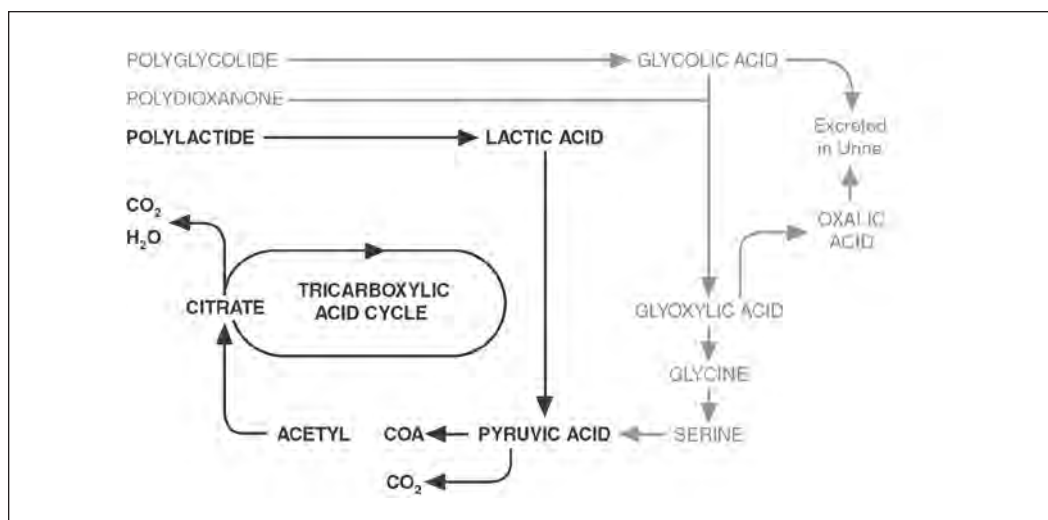


FIGURE 2. Schematic illustrating the *in vivo* degradation of resorbable polymers including PLA.²¹

The D,L-Lactide is, in contrast, characterized by lower strength and quicker rates of degradation.^{9,21,29}

By combining L-lactide and D,L-lactide, a single copolymer may be created which provides relatively high strength and an appropriate degradation rate for most musculoskeletal applications.

MAST Biosurgery has chosen a polymer composed of medical grade 100% amorphous 70:30 Poly(L-lactide-co-D,L-lactide). This copolymer is produced from a mixture of 70% L-lactide and 30% D,L-lactide polymers. This material is noncrystalline, and is characterized by a degradation time of 12-18 months, depending on the anatomical location of the implant.

PLA DEGRADATION

The degradation of PLA occurs in two phases—Hydrolysis and Metabolization (Figure 2).^{7,21} Hydrolysis occurs as body fluids (H₂O) enter the implant, chemically reacting with the polymer and breaking the polymer chains. Metabolization occurs as the single lactic acid molecules are finally metabolized in the liver into CO₂ and H₂O.

During degradation, the material loses strength in a predictable fashion. Any factors, including sterilization technique, implant size and geometry, manufacturing processes, etc., can alter the strength and degradation characteristics of implants manufactured from PLA.

MAGNETIC RESONANCE IMAGING (MRI)

PLA is non ferrous, and does not adversely impact the quality of post-operative images at the site of

the implanted material. Many studies have successfully utilized MRI scanning to evaluate the *in vivo* tissue response of PLA implants.^{12,42,47,55,56} No signal scatter has been reported when utilizing MRI scanning techniques in the presence of PLA implants.^{12,42,47,55,56} As PLA does not disrupt the MRI scan, it is possible to monitor bone healing in the presence of PLA implants.⁵⁵ PLA implants are visible on MRI images and show up as homogeneous low signal intensity (SI) black structures easily distinguished from the high SI gray-white of bone tissue.¹²

MAST BIOSURGERY POLYMER

A great deal of time and effort has been invested in gaining an understanding of the PLA polymers, the factors that play a role in the material's properties, and the performance of resulting medical devices. The material utilized in the fabrication of MAST implants is created by carefully controlling all facets of the production, including proprietary manufacturing processes to optimize the performance of the implant.

The manufacturing process of other commercialized forms of 70:30 Poly(L-lac-tide-co-D,L-lactide) may not necessarily result in the ideal resorption period. Complete strength loss has been noted to occur in products with as little as 6 weeks of saline immersion if processing criteria were not carefully adhered to.

STRENGTH DURING DEGRADATION

Research conducted by Claes et al.,⁹ characterized the strength of PLA materials during degradation. In that study, *in vivo* degradation was simulated by

both real-time aging of the material in a 37°C buffered saline bath, and accelerated aging in a 70°C buffered saline bath. The MAST polymer has been similarly evaluated under both accelerated and real-time simulated conditions. Testing conducted by MAST confirmed degradation performance similar to that found by Claes et al. ⁹

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