TWO-YEAR FOLLOW-UP OF BIOABSORBABLE PLLA CAGES FOR LUMBAR INTERBODY FUSION: IN VITRO AND IN VIVO DEGRADATION

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Introduction: Current cage devices considerably exceed the stiffness of the spinal segment, which may lead to stress-shielding, migration of the cage, and pseudarthrosis. In order to avoid these material related complications, a poly (L-lactic acid) cage device (PLLA cage) has been designed with limited stiffness compared to current cage devices and which will be absorbed on the long term. Biomechanical in vitro testing demonstrated that the PLLA cage is mechanically sufficient directly after implantation [1] and radiographic evaluation in an in vivo investigation disclosed that interbody fusion could be obtained after 6 months follow-up [2]. In the last three decades the use of biodegradable PLLA osteosynthesis devices has gained an increasing interest and have mainly been used in non weightbearing conditions due to their attributed limited mechanical properties [3]. The use of PLLA spinal cages to induce lumbar interbody fusion under high load bearing conditions has not yet been investigated. Under the high load bearing conditions in the current investigation, the degradation kinetics of the PLLA cage may be increased as the rate of polymer degradation is influenced by the degree of dynamic loading. The aim of this investigation was therefore to describe the in vitro degradation of bioabsorable PLLA cages and the in vivo degradation under high load bearing conditions in a lumbar interbody fusion goat model. In addition, the segments with the PLLA cages were subjected to radiologic, macroscopic and microscopic evaluation after 3, 6, 12, and 24 months of implantation.

Materials and Methods: The PLLA (Purac BV, Gorinchem, The Netherlands) was injection molded into two types of transparent cages with an open box configuration (10x10x18 mm): a stiff PLLA cage (axial compression stiffness: 4 kN/mm) with a wall thickness of 1.5 mm and a flexible PLLA cage (axial compression stiffness: 2 kN/mm) with a wall thickness of 0.75 mm. Inherent viscosities after Gas Plasma sterilization of the stiff and flexible PLLA cages were 2.64 ± 0.23 dl/gm and 2.45 ± 0.15 dl/gm, respectively. In vitro evaluation: The PLLA cages were placed in sealed glass jars filled with PBS at 37°C ± 1°C. For 4, 8, 12, 26, 52, and 73 weeks of incubation, six PLLA cages were removed and tested for inherent viscosities. In vivo evaluation: Eighteen Dutch milk goats (2-3 years old, 50 kg) underwent a lumbar interbody fusion (L3-L4) procedure using a retroperitoneal approach. The stiff (n=6) and flexible (n=12) PLLA cages were packed with autologous cancellous bone and randomly implanted. After 3, 6, 12, and 24 months, the animals were sacrificed and the lumbar spine dissected. Anteroposterior and lateral contact radiographs of the lumbar spine were performed. Remnants of the PLLA cages were collected from one sagittal part without disrupting the integrity of the cage, when solid, and subjected to the degradation experiments. In addition, specimens were undecalcified embedded in methylmethacrylate. The specimens were sectioned into sections of 6 μm thickness and stained with Haemotoxin and Eosin.

Results: In vitro degradation: The flexible PLLA cages disclosed 12% reduction of inherent viscosity at 4 weeks, 36% at 12 weeks, and 87% at 73 weeks of incubation in PBS. Accordingly, the stiff PLLA cage showed 13% reduction of inherent viscosity at 4 weeks, 44% at 12 weeks, and 90% at 73 weeks of incubation (Fig. 1). Radiological evaluation: No evidence of collapse of the operated spinal segment in both PLLA groups was observed after the follow-up periods. After 3 months, ingrowth of trabecular bone was observed [1]. Hereafter, radiological fusion of the spinal segments was observed in 89% (16/18) of the specimens. Macroscopic findings: After 3 months, the PLLA cages were intact and had maintained their geometrical shape (height: 10 mm). The flexible PLLA cages showed formation of radial micro-cracks without displacement. After 6 months, the stiff and flexible PLLA cages were also intact and solid (height: 10 mm). The PLLA cages disclosed a whitish aspect with microcracks and the flexible cage showed a slight bending deformation. At 12 months, the stiff and flexible PLLA cages were brittle and had been disintegrated entirely into fragments with a grayish aspect (Fig. 2). At 24 months, no PLLA could be observed macroscopically.

Microscopic findings: After 3 months, the wall thickness of the stiff and flexible PLLA cage had increased to a mean of 1.64 ± 0.09 mm and 1.01 ± 0.09 mm, respectively. After 6 months, the wall thickness of the stiff and flexible PLLA cages measured a mean of 1.83 ± 0.23 mm and 0.99 ± 0.0 mm, respectively. Very sparse birefringent PLLA fragments could be observed in the extracellular space of the quiescent fibrous tissue, enveloping the implants during the follow-up periods. After 12 and 24 months, the PLLA caged had lost their geometrical shape and had been disintegrated into multiple birefringent fragments of different sizes with interposition of quiescent fibrous tissue. No adverse tissue reactions could be observed. In vivo degradation: After 12-months, an adequate amount of PLLA could only be retrieved from one specimen in the flexible PLLA group. In the stiff PLLA group, the amount of retrieved PLLA was too sparse for separate inherent viscosity determination, and were therefore pooled. After 24 months, no PLLA could be retrieved. The flexible PLLA cages disclosed 69% reduction of inherent viscosity at 12 weeks, 81% at 24 weeks, and 90% at 52 weeks of implantation. The stiff PLLA cages showed a 64% reduction of inherent viscosity at 12 weeks, 72% at 24 weeks, and 93% at 52 weeks of implantation (Fig. 1).

Fig. 1. Inherent viscosities of PLLA cages as a function of the incubation/implantation periods.

Fig. 2. Stiff PLLA cages after 3, 6, 12 and 24 months of implantation.

Discussion: The flexible and stiff PLLA cages showed a similar decline in inherent viscosity curves during follow-up. However, in vivo degradation was more pronounced compared to the in vitro inherent viscosities during 12 months follow-up. This might be due to the high load bearing conditions of the PLLA cages besides the in vivo enzymatic activity. After 3 and 6 months follow-up, the PLLA cages disclosed signs of degradation, but maintained their original geometrical shape and height. After 12 and 24 months follow-up, no collapse of the spinal segment was observed despite the fact that the PLLA cages had been disintegrated into multiple fragments and did not contribute to carry the spinal load anymore. After 24 months, the PLLA cage was mainly absorbed. The fibrous tissue surrounding the PLLA implants showed no signs of adverse tissue reactions. However, longer follow-up periods are mandatory to investigate the local tissue response and the total absorption of the PLLA cages on the long term.


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