Demonstrating the Mechanism and Efficacy of Water-Induced Shape Memory and the Influence of Water on the Thermal Properties of Oriented Poly(d,l-lactide)

Kaarlo Paakinaho,[1,2] Terttu Inkeri Hukka,[3] Tuuva Kastinen,[3] Minna Kellomäki[1,2]

[1]Department of Electronics and Communications Engineering, Tampere University of Technology, Hermiankatu 12, P.O. Box 692, FI-33101 Tampere, Finland
[2]BioMediTech, Biokatu 10, FI-33520, Tampere, Finland
[3]Department of Chemistry and Bioengineering, Tampere University of Technology, Korkeakoulunkatu 8, P.O. Box 541, FI-33101 Tampere, Finland
Correspondence to: K. Paakinaho (E‑mail: kaarlo.paakinaho@tut.fi)

ABSTRACT: Achieving water-induced shape-memory property in poly(D,L-lactide) (PDLLA), generated by means of advanced processing methods, opens possibilities to develop novel bioresorbable medical devices with shape-memory properties activated by the human body without external heat. The main phenomena that affect the molecular movements that enable the water-induced shape-memory effect in an oriented PDLLA in an aqueous environment at physiological temperature are related to the water driven disruption of the intermolecular dipole-dipole and/or hydrogen bonding of the oriented PDLLA chains and the subsequent decrease of the glass transition temperature (T_g) to the range of physiological temperature. The diffused water in the polymer matrix decreased the energy needed to finish the glass transition process explaining the higher shape-recovery rate of the γ-irradiated PDLLA with respect to the non-γ-irradiated PDLLA in an aqueous environment at physiological temperatures. The water-induced decrease in the T_g was thermally reversible. The efficacy of the generated shape-memory was tested with PDLLA shape-memory nails in a pullout test, in which the pullout force of the PDLLA nails increased 360% during a seven day test period *in vitro* at 37°C. © 2013 Wiley Periodicals, Inc. J. Appl. Polym. Sci. 130: 4209–4218, 2013

INTRODUCTION

The ability of a material to transform its shape because of a specific trigger is one of the most promising advanced material properties under development in the field of medical device technology. In this class of actively moving materials, shape-memory polymers are progressing rapidly because of the wide variety of tailorable properties, for example, the triggering method for shape transformation.[1] Shape memory in polymeric materials is based on the molecular movements triggered by a material-specific stimulus and driven by the entropic elastic behavior of the polymer chains. Although the shape-memory effect can be induced by light,[2] a magnetic field,[3] or chemically,[4] the activation of the molecular movements of the polymer chains is most commonly generated by an increase in the temperature of the polymer to a level where the oriented polymer chains, being fixed in an unstable temporary shape, begin to recoil back toward their nonoriented state.[3,5,6]

In medical applications, the environment where the activation occurs, that is, the human body, is sensitive to the high temperatures that might be needed to trigger these molecular movements. An advantageous approach in triggering shape memory in such a demanding environment and preventing any adverse tissue reactions caused by excessive heating is the development of polymers or polymer structures whose thermal properties are changed because of the plasticizing effect of low-molecular-weight molecules, for example, water.[7–11] Because water is always present in the physiological environment, the effect of diffused water molecules in the polymer matrix can be used to reduce the energy needed for the activation of shape memory so that it can be initiated without external energy.[12]

Until now, this type of shape-memory activation has been reported on nonbiodegradable thermoplastic polyurethanes, which undergo a significant decrease in the glass-transition temperature (T_g) as a function of increasing water content in the

polymer matrix.[13–17] The molecular mechanism that decreases the T_g is based on the ability of water to affect the hydrogen bonding between adjacent polyurethane chains and to increase the ability of the polymer chains to move. A shape-memory effect triggered by water molecules was also reported with highly tailored lactide and glycolide polymer networks.[9] In contrast to the thermoplastic polyurethanes, diffused water molecules in the polymer networks were reported not to affect the hydrogen bonding but to increase the entropy of the network domains and further decrease T_g; this enabled the initiation of a shape-memory effect at 37°C.[9]

Because of the long development time required for a new medical-grade material, a feasible way to develop medical devices with new and active properties is via the advanced processing of already existing medical materials.[18] In our earlier studies, we have shown that it is possible to generate novel shape-memory properties by means of the advanced polymer orientation processing, called *orientation programming,* of commercially available medical-grade bioabsorbable poly(D,L-lactide) (PDLLA),[19] for which tissue tolerance and degradation rates have been reported to be acceptable for possible clinical use.[20] The novelty in the shape-memory properties is that a temporary oriented structure can be generated into a linear chain polymer, which is then triggered to transform back toward the original molecular structure in a physiological environment without external energy. The triggering of the shape-memory effect of this orientation-programmed poly(D,L-lactide) (PDLLA$_{OP}$) in the physiological environment is due to the effect of water molecules that diffuse into the polymer matrix and lower the transition temperature to the range of physiological temperature.[19]

Understanding the phenomena related to the molecular movements of PDLLA in an aqueous environment at 37°C and the interactions between the diffused water molecules and the PDLLA–polymer chains are key factors in designing bioabsorbable implantable medical devices with this type of new and active property. In this article, we discuss and propose an activation mechanism for the shape transformation of PDLLA$_{OP}$ in an aqueous environment at physiological temperature and present a potential application in which this type of shape memory could be used to increase the functionality of a bioabsorbable medical device.

EXPERIMENTAL

Sample materials with shape-memory properties were manufactured by the melt extrusion of PDLLA (Boeringer Ingelheim, R207 S) with a corotating twin-screw extruder (Mini ZE 20*11.5 D, Neste Oy, Porvoo, Finland) into 6.6 ± 0.2 mm round rods. The inherent viscosity of the raw material was 1.6 dL/g, the number-average molecular weight (M_n) was 127,000 g/mol, the weight-average molecular weight (M_w) was 235,000 g/mol, and the measured residual lactide monomer content was 0.02 wt %. An orientation-programming process described in ref. 19 was used to deform the extruded rods into two types of oriented rods: round rods with a diameter of 3.2 ± 0.1 mm and grooved-shaped rods with a maximum diameter of 3.35 ± 0.1 mm. The round ones were cut to a length of 10 mm, whereas

the grooved ones, which were used as pilot devices in a pullout test, were cut to a length of 40 mm. The tips of the samples were machined to a conical shape. Both sample types were γ-irradiated for sterility with a minimum radiation dose of 25 kGy (Gamma-Service Produktbestrahlung GmbH, Radeberg, Germany).

The molecular weights (M_w and M_n) of PDLLA$_{OP}$ before and after γ irradiation were determined by gel permeation chromatography. Two parallel samples, with a volume of 150 μL and a concentration of 0.1 wt % in chloroform, were injected into a PLgel 5-μm Guard precolumn and two PLgel 5-μm mixed-C columns (Polymer Laboratories, Amherst, MA) at a flow rate of 1.0 mL/min. The system was composed of a detector (Waters 410 RI differential refractometer detector), a pump (Waters M515 high-pressure liquid chromatography pump), and an autosampler (Waters 717P Plus autosampler, Waters Operating Corp., Milford, CT). Universal calibration was obtained for PDLLA (Mark-Houwink parameters: $k = 5.45 \times 10^{-4}$ dl/g, $a = 0.73$), and the mean values of the results were used. The post-melt-processing lactide monomer content was measured from three parallel samples with gas chromatography (DC8000, CE Instruments, Rodano, Italy) and a flame ionization detector after chloroform dilution (Rambol Analytics Oy, Lahti, Finland) with a measuring resolution of 0.02 wt %.

The sample materials were vacuum-dried at room temperature for 7 days before measurement as dry or *in vitro* incubations. Shape recovery, measured as the radial expansion of the diameter, and water absorption were measured from six parallel samples that were incubated at either 37 ± 1 or 2 ± 1°C in a Sörensen buffer solution with a volume/weight ratio greater than 30:1 (mL/g). The incubation time was 7 days, and the pH of the buffer solution was kept within the range of 7.4 ± 0.2.

Temperature-modulated differential scanning calorimetry (MDSC; DSC Q1000, TA Instruments, New Castle, DE) was used to analyze the thermal properties of the dry and wet samples. Analyses were performed in hermetically sealed pans on six parallel 5–10 mg samples in a temperature range of 5–80°C at an amplitude of 0.5 s for a modulation period time of 40 s and at a heating rate of 1°C/min. T_g, evaluated as the extrapolated onset temperature ($T_{g\text{-onset}}$), and the enthalpy relaxation, evaluated with an interpolated baseline, were monitored for up 7 days *in vitro* at 37 ± 1°C for the non-γ-irradiated PDLLA$_{OP}$, γ-irradiated PDLLA$_{OP}$ samples, and nonoriented non-γ-irradiated PDLLA samples. In addition, γ-irradiated PDLLA$_{OP}$ samples incubated at 2 ± 1°C were also monitored for 7 days. Furthermore, a series of the γ-irradiated PDLLA$_{OP}$ samples were first incubated at 37 ± 1°C *in vitro* for 7 days and then vacuum-dried for 7 days at room temperature before MDSC analysis.

The interactions between water and the PDLLA–polymer chains were studied by Fourier transform infrared (FTIR) spectroscopy. The FTIR spectra were measured with a Spectrum One FTIR spectrometer (PerkinElmer, Shelton, CT) at a resolution of 4 cm^{-1}. For each spectrum, eight scans were carried out from 4000 to 450 cm^{-1} in transmission mode, and the resulting spectra were converted to absorbance format, after which they were processed further with a data tune-up. The repeatability in the
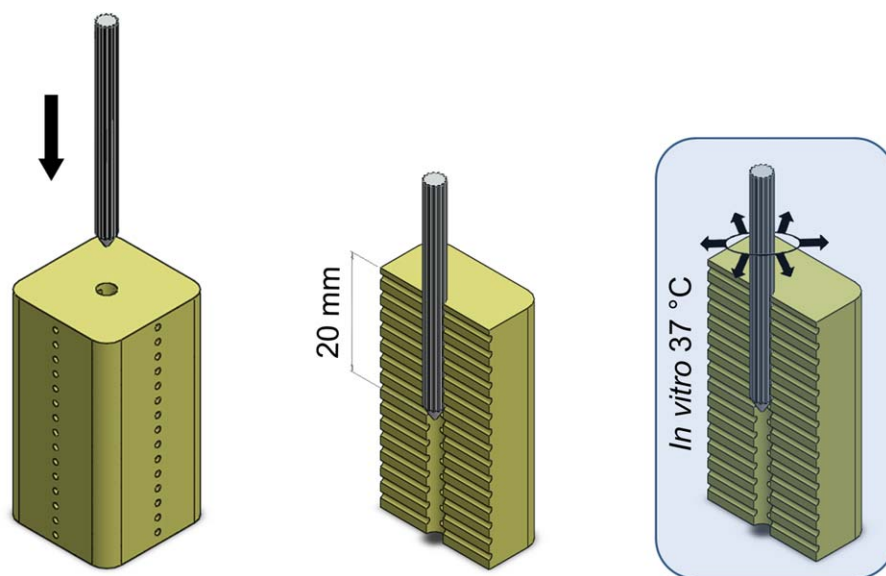
Figure 1. Principle of the pullout test *in vitro* at 37°C with the grooved-shaped, γ-irradiated PDLLA$_{OP}$ nails. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

evaluations was ± 1 cm^{-1}. Because the bands in the spectrum were too wide for circular rods to be used in the analysis and individual bands could not be analyzed, the FTIR measurements were done with thin PDLLA films. The samples were prepared by the dissolution of PDLLA in puriss-grade acetone (NF $\geq$ 99%), and the resulting solution was cast onto a film form with a film thickness between 11 and 14 μm. These two parallel samples of both non-γ-irradiated polymer films (films 1 and 2) and γ-irradiated polymer (films 1s and 2s) were scanned before vacuum drying, then vacuum-dried, and immersed in a 37°C deionized water bath, where the samples were held for up to 7 days. Films 1 and 1s were measured with FTIR spectroscopy after 1, 2, and 7 days of immersion, whereas films 2 and 2s were kept in water continuously without intervention for 7 days before analysis. To compare the IR results of the non-γ-irradiated and γ-irradiated samples, all of the IR spectra were normalized with respect to the spectrum of vacuum-dried film 1. Normalization also removed the error caused by the different thicknesses of the samples. Normalization was carried out with the signal of the asymmetric bending of the CH$_3$ group at 1454 cm^{-1}, which existed in all of the samples. This band was stated to be a suitable standard because of its isolated position in the spectrum and because its wave number does not change during water treatment and the intensity remains practically constant.[21]

The influence of the shape transformation on the pullout strength *in vitro* at 37°C was studied by the insertion of grooved-shaped γ-irradiated PDLLA$_{OP}$ nails into solid rigid polyurethane blocks (Sawbones, density = 0.32 g/cc) and the testing of the pullout force (MTS Insight 30, MTS Systems Corp., Eden Prairie, MN) as function of *in vitro* times of up to 7 days. The nails were inserted into a 3.2-mm drill hole to a depth of 20 mm. The blocks had 1-mm water channels with distances of 2.5 mm on each side. The drill holes and the PDLLA$_{OP}$ nails were rinsed with the buffer solution to ensure moist conditions

before the nails were inserted into the block. The pullout test principle with the polyurethane test blocks is presented in Figure 1.

RESULTS

Effect of the Melt Processing, Orientation Programming, and γ Irradiation on the Molecular Weight and Thermal Properties

The molecular weights after melt processing and orientation programming were as follows: $M_n = 116,000$ g/mol and $M_w = 222,000$ g/mol. After γ irradiation, the values were as follows: $M_n = 56,000$ g/mol and $M_w = 109,000$ g/mol. No change in the lactide monomer content (0.02 wt %) occurred during the melt processing. The orientation-programming process affected both $T_{g\text{-onset}}$ and the enthalpy relaxation of PDLLA. During the orientation programming, the measured $T_{g\text{-onset}}$ of PDLLA increased from about 50°C to about 56°C and at the same time generated an enthalpy relaxation peak to the T_g zone. The subsequent γ irradiation decreased $T_{g\text{-onset}}$ by about 1°C but did not have a significant effect on the area of the enthalpy relaxation peak of the oriented PDLLA (Figure 2).

Shape Recovery

The shape recovery of PDLLA$_{OP}$ toward the original nonoriented shape was initiated at 37°C in an aqueous environment for both the non-γ-irradiated and γ-irradiated samples. The γ-irradiated PDLLA$_{OP}$ had a faster shape-recovery rate than the non-γ-irradiated sample, and the recovery rate accelerated after a 3-day incubation at 37°C, whereas the recovery rate of the non-γ-irradiated PDLLA$_{OP}$ remained constant. During the 7-day incubation period, the shape recoveries at 37°C in an aqueous environment were 6% for the non-γ-irradiated PDLLA$_{OP}$ and 46% for the γ-irradiated PDLLA$_{OP}$ (Figure 3). No shape transformation was detected for the γ-irradiated PDLLA$_{OP}$ in an aqueous environment at 2°C. The shape recovery of the γ-irradiated PDLLA$_{OP}$, measured as the radial
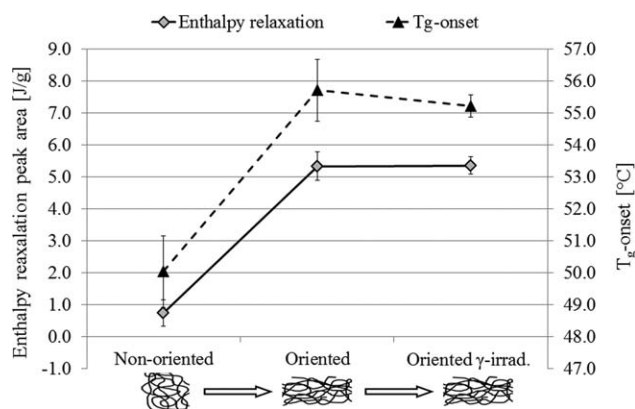
Figure 2. Effect of the orientation programming and γ irradiation on the enthalpy relaxation and T_g of PDLLA (n = 6).

expansion of the diameter, was unsymmetrical, as presented in Figure 4. The radial expansion was faster at the ends of the rods, which seemingly curved outward after 4 days of incubation. After the 7-day incubation, the shape recovery measured from the ends of the γ-irradiated PDLLA$_{OP}$ rods was 59%.

Water Absorption and Changes in the Thermal Properties in an Aqueous Environment

The submersion of the polymer samples into the buffer solution enabled the diffusion of water into the oriented PDLLA$_{OP}$ polymer matrix. Both the incubation temperature and the molecular weight had an effect on the absorption of water, which leveled at an incubation temperature of 37°C to 1 wt % for the γ-irradiated PDLLA$_{OP}$ and about 0.7 wt % for the non-γ-irradiated PDLLA$_{OP}$. The water absorption at an incubation temperature of 2°C for the γ-irradiated PDLLA$_{OP}$ was slower than at 37°C. During the 7-day *in vitro* period, water absorption slowly increased up to about 0.6 wt % (Figure 5).

The overall changes in the thermal properties of the PDLLA measured with MDSC at different stages from processing to shape transformation in a 37°C aqueous environment for the γ-irradiated samples are presented in Figure 6. The effects of
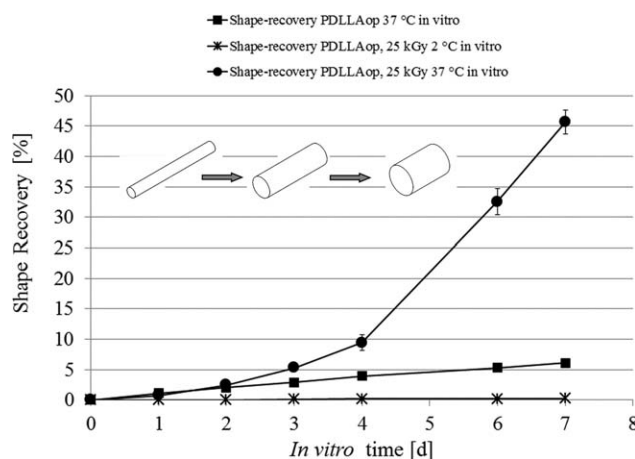

Figure 3. Shape recovery of PDLLA$_{OP}$ toward the nonoriented shape measured *in vitro* as a radial expansion of the diameter from the middle of the sample (*n* = 6).

orientation programming and the plasticizing effect of water was observed clearly as a change in the shape in the MDSC curves. For the sake of clarity, only the total curves are presented and later discussed. After the non-γ-irradiated PDLLA$_{OP}$ samples were submerged into the 37°C aqueous environment, $T_{g\text{-onset}}$ decreased 10°C from its initial value and leveled at 45°C during the 7-day incubation period, whereas $T_{g\text{-onset}}$ of the non-γ-irradiated PDLLA decreased 8°C and leveled to 42°C. $T_{g\text{-onset}}$ for the γ-irradiated PDLLA$_{OP}$, however, decreased 15°C and leveled at 40°C (Figure 7). The *in vitro* temperature had a clear effect on the T_g drop. $T_{g\text{-onset}}$ for the γ-irradiated PDLLA$_{OP}$ decreased 9°C to 46°C during the 7-day *in vitro* period at a temperature of 2°C. $T_{g\text{-onset}}$ of the γ-irradiated PDLLA$_{OP}$ shifted back toward its original value when the diffused water was removed by vacuum drying. The original dry T_g of the oriented form was not fully reached as the $T_{g\text{-onset}}$ leveled at 51°C, but $T_{g\text{-onset}}$ of the nonoriented PDLLA ($\sim$50°C) was reached, which showed that the change in T_g was thermally reversible.

In Figure 8, the calculated values of the enthalpy relaxation peak areas are presented as a function of the *in vitro* time. The diffusion of water into the polymer matrix did not have such a straightforward effect on the enthalpy relaxation of PDLLA$_{OP}$ as on T_g. During the 7-day incubation period at 37°C, the enthalpy relaxation peak area for the non-γ-irradiated PDLLA$_{OP}$ remained unchanged, whereas the enthalpy relaxation peak area for the γ-irradiated PDLLA$_{OP}$ decreased by 50%. The diffused water had a powerful effect on the thermal properties of the PDLLA$_{OP}$ even at an incubation temperature of 2°C. As shown in Figure 8, the enthalpy relaxation peak area decreased 23% after a 7-day incubation period at 2°C. After incubation at 37°C, the vacuum drying only minutely increased the peak size of the enthalpy relaxation of the γ-irradiated PDLLA$_{OP}$ compared to those analyzed wet; this indicated a nonreversible morphological change due to molecular movements in the aqueous environment at 37°C. The non-γ-irradiated PDLLA showed an aging-type behavior when it was incubated at 37°C, as the enthalpy relaxation peak area increased sixfold during the first 24 h, after which significant changes were observed.

Changes in the Spectroscopic Properties in an Aqueous Environment

The main changes in the FTIR spectra of the PDLLA films, which were immersed in water after vacuum drying, were seen in the intensities and locations of the peaks created by the IR absorptions of the OH bonds of the water molecules absorbed into the polymer matrix (3651–3657 and 1625–1630 cm^{-1}),[22,23] the OH bonds of the polymer (3547–3569 cm^{-1}),[24] and the C=O bonds of the polymer (1748–1765 cm^{-1} and the overtone at 3504–3509 cm^{-1}).[24,25] The increase in the intensities and the shifting of the bands were the most significant during the first day of immersion, after which the positions of the bands moved only slightly or remained unaltered. These observations corresponded to the results of the mass change measurements and differential thermal analysis, as presented previously. The ν(OH) absorption band of water shifted to a lower wave number in water-treated films 1, 1s (Figure 9), 2, and 2s from approximately 3656–3660 to 3652–3653 cm^{-1} after the 1st day and to approximately 3651–3652 cm^{-1} after 7 days of immersion. This
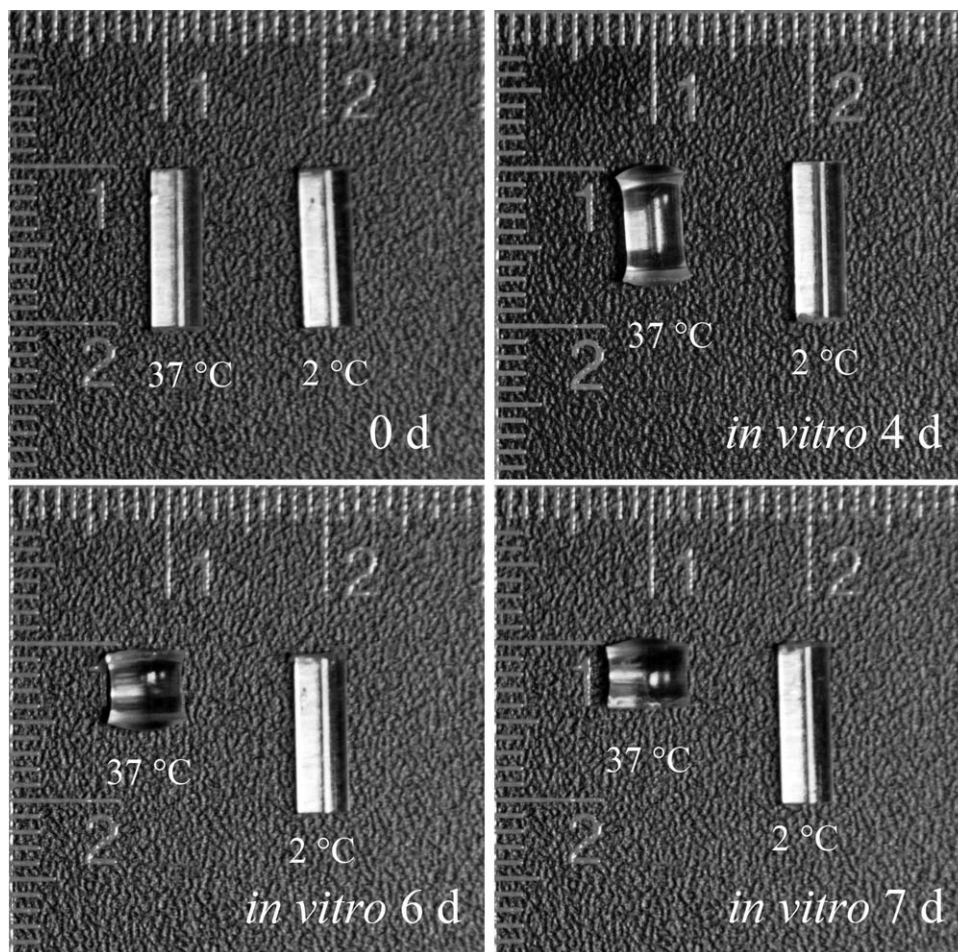
Figure 4. Comparison of the shape transformation of the γ-irradiated PDLLA$_{OP}$ *in vitro* at 37 and at 2°C (the scale is in millimeters).

indicated that the amount of intermolecular hydrogen bonding between the water molecules increased with the immersion time and that the increase in intensity corresponded to the amount of water absorbed in the polymer matrix during the immersion period. Furthermore, the FTIR spectra indicated that the $v(OH)$ PDLLA absorption band, which originated from the OH groups

Figure 5. Water absorption measured as the weight increase of the PDLLA$_{OP}$ *in vitro* ($n = 6$).

of the original polymer, shifted to a higher wave number when the polymer was immersed in water for 1 day, that is, from 3565 to 3568 cm^{-1} in film 1 and from 3548 to 3568 cm^{-1} in film 1s. The intensity of the peak was very small and corresponded to a small number of OH end groups; there were no monomers present in the original polymer material. The $v(OH)$ PDLLA peak was shifted only by 1 cm^{-1} during the 2nd day of immersion and remained constant until the 7th day of immersion. The intensity increased slightly until the 2nd day but remained unchanged after that.
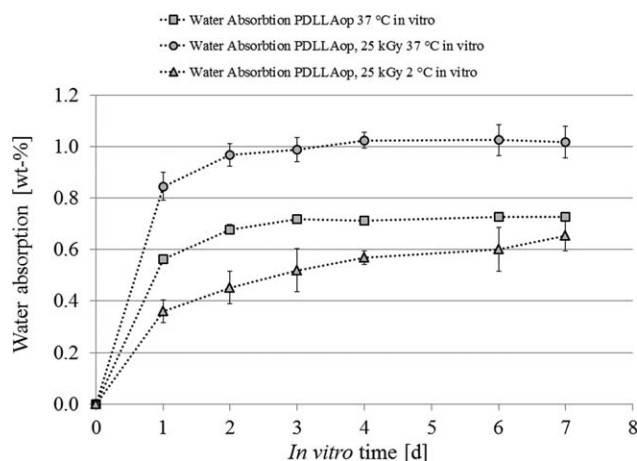
The absorption band at 3505 cm^{-1} was associated with an overtone of carbonyl stretching vibrations [$v(C=O)$] of the polymer that occurred in the range 1765–1748 cm^{-1}. In the non-γ-irradiated high-molecular-weight films, the position of this overtone peak shifted only slightly (by 1 cm^{-1}) to a lower wave number after 1 day of immersion and remained unaltered until the 7th day of immersion (Figure 9). The shift was interpreted as a hydrogen-bonding interaction between the C=O groups of the PDLLA–polymer and water; this made the stretching vibrations of this group slightly easier energetically. The intensity of the peak increased during the first 2 days to a level where it stayed for the rest of the *in vitro* period of 7 days. In the case of the γ-irradiated films, the peak shifted 2 cm^{-1} during the 1st day and 3 cm^{-1} in total during the 7 days of immersion. The
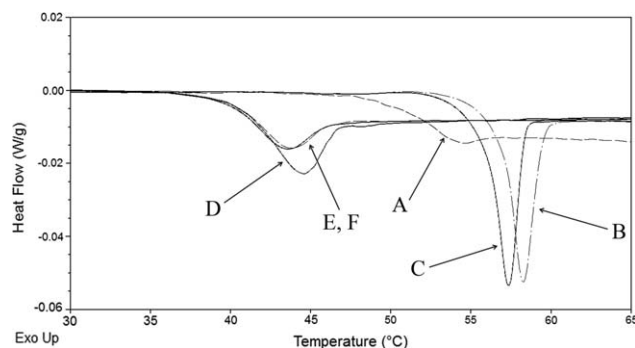
Figure 6. MDSC curves presenting the changes in the thermal properties from melt processing to shape transformation *in vitro* at 37°C: (A) PDLLA (nonoriented), (B) PDLLA$_{OP}$, (C) γ-irradiated PDLLA$_{OP}$, (D) γ-irradiated PDLLA$_{OP}$ *in vitro* at 37°C 1 days, and the γ-irradiated PDLLA$_{OP}$ *in vitro* at 37°C for (E, solid line) 3 and (F, dashed line) 7 days.

larger shift toward lower energy could be interpreted as an increased opportunity for hydrogen bonding to take place between the C=O groups and water after γ irradiation; this shortened the polymer chains and increased the flexibility of the chains compared to before γ irradiation. Because the intensity of the overtone peak was very small, more attention should be paid to the actual $v(C=O)$ peak.

When the films were immersed in water, the peaks within the strong, broad, and split $v(C=O)$ stretching band of PDLLA at 1748–1765 cm^{-1} [Figure 10(a,c)] shifted to lower wave numbers by 1–7 cm^{-1}. The shift was clearer for the γ-irradiated films where the polymer chains had become shorter. The direction of the shift indicated that the stretching of the C=O bond became easier with the presence of water and could be interpreted as an increase in the hydrogen-bonding interaction between water molecules and the C=O groups of the polymer. During the first 2 days, the intensity of the band increased pronouncedly, especially in the non-γ-irradiated films, but it increased only slightly after that. Such an increase in intensity indicated that more C=O groups became hydrogen-bonded when the amount of water increased and the saturation level was approached or achieved within the immersion period.
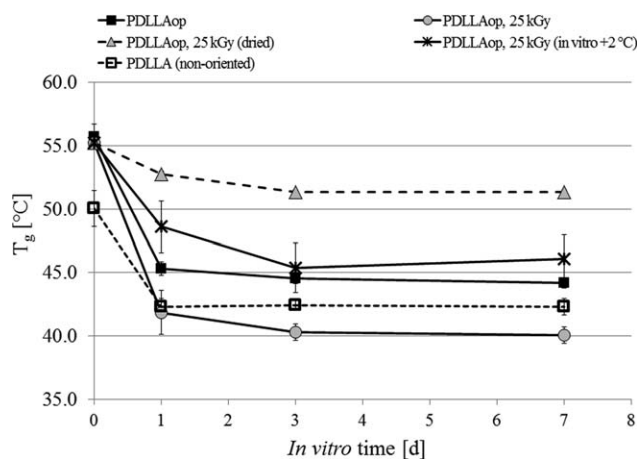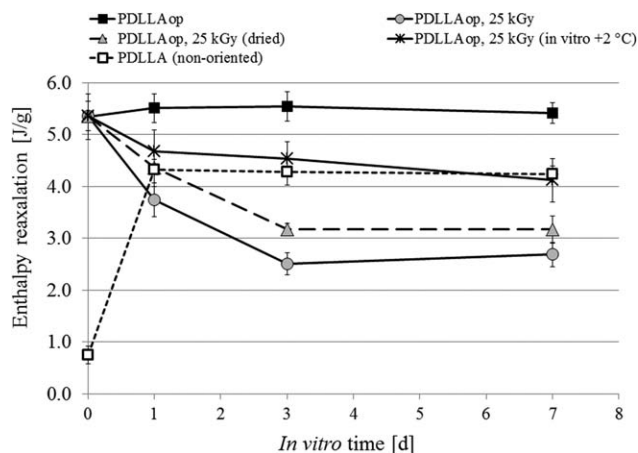

Figure 8. Enthalpy relaxation changes of the PDLLA$_{OP}$ and PDLLA *in vitro* ($n = 6$).

Moreover, the intensity of the peak at the lowest wave number, that is, at 1748–1750 cm^{-1}, increased with respect to the highest wave-number peak at 1765 cm^{-1}.

The weak band appearing at approximately 1626 cm^{-1} after immersion in water for 1 day [Figure 10(b,d)] was due to the H—O—H bending of free water. This band was removable from the films through their drying in an oven at 37°C; this supported the assignment for free water, that is, absorbed water. When we studied the spectral lines carefully, we observed that even in the non-vacuum-dried films, there was some water that absorbed infrared light at a slightly lower wave number than after immersion.
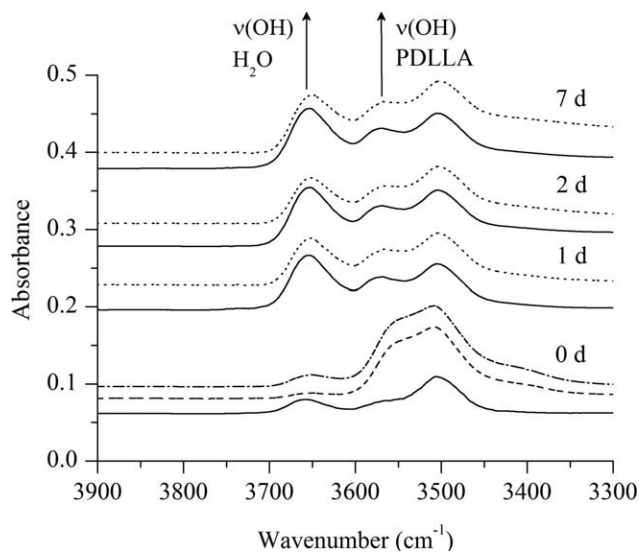

Figure 9. FTIR spectra of film 1 (solid lines) and film 1s (dotted lines) in the region of 3900–3300 cm^{-1} before (0 days) and after immersion in water for 1, 2, and 7 days. The spectrum of film 1 after drying *in vacuo* (the lowest line) was used as a reference for normalization. The dash-dotted line (—··—) represents film 1s before γ-irradiation, and the dashed line (——) directly below it is the same film after γ irradiation and vacuum drying but before exposure to water. The directions of the changes in the intensities due to water treatment are indicated with arrows.
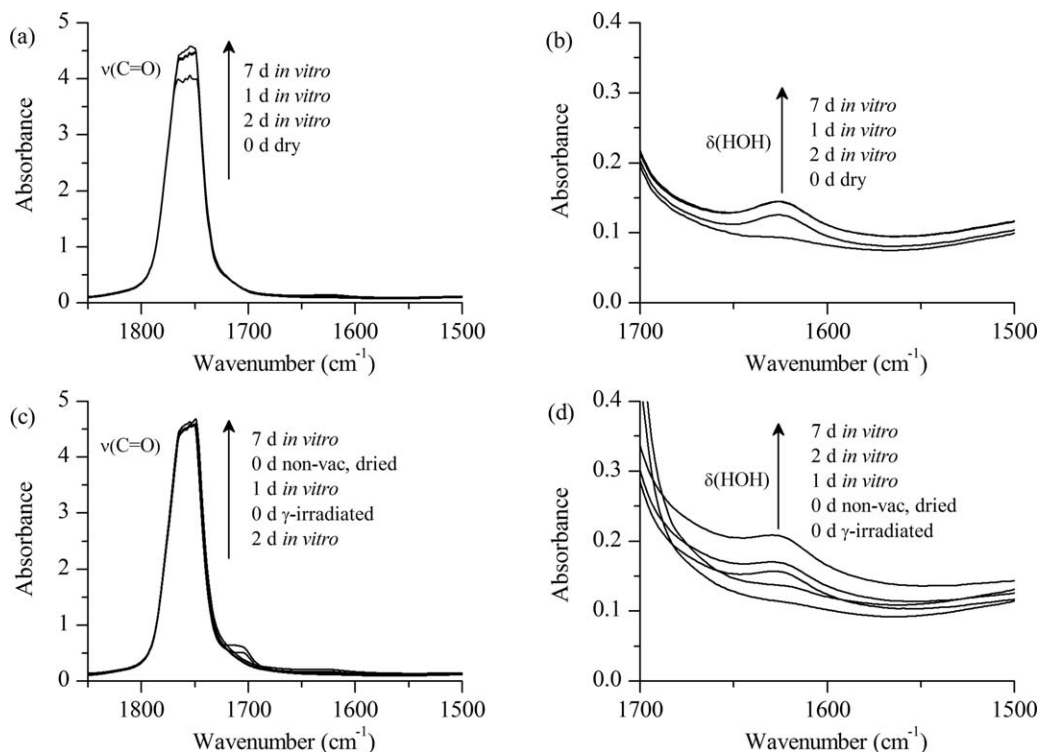

Figure 7. $T_{g\text{-onset}}$ changes of the PDLLA$_{OP}$ and PDLLA *in vitro* ($n = 6$).

Figure 10. FTIR spectra of film 1 in the regions of (a) 1850–1500 and (b) 1700–1500 cm^{-1} and the γ-irradiated film 1s in the same regions of (c) 1850–1500 and (d) 1700–1500 cm^{-1}.

Effect of the Shape-Memory Effect on the Pullout Force of PDLLA Nails

Figure 11 presents the increase of the pullout force as function of the time *in vitro* at 37°C for the γ-irradiated PDLLA$_{OP}$ nails. The initial pullout strength of the nails was maintained up to the first test point (1 day). The shape-transformation tendency of the PDLLA$_{OP}$ nails in a tight drill hole generated a 110% increase in the pullout force during a 3-day incubation period, and after 7 days, the pullout force had increased 360%. During the shape-transformation, the PDLLA$_{OP}$ nails were visually observed to expand where they could, simultaneously contract-
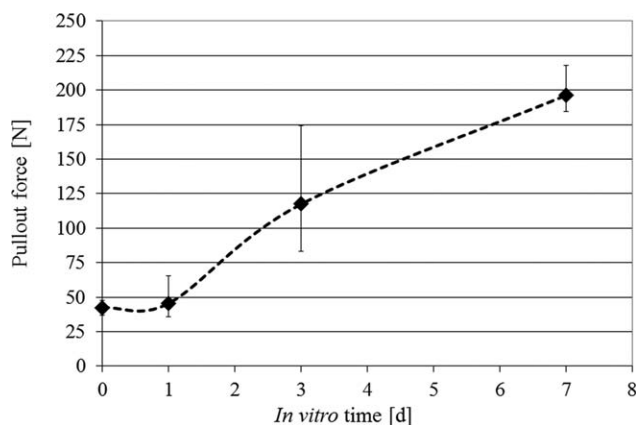
ing in the direction of their longitudinal axis, mainly outside the test blocks. Also, the tips of the nails expanded in a manner similar to the rods presented in Figure 4.

DISCUSSION

The temporary shape for PDLLA was generated by the forcing of the linear polymer chains, which were randomly organized after melt extrusion, to a more organized and oriented morphology. When the PDLLA was deformed at a temperature above its T_g and subsequently cooled, the polymer chain entanglements that determined the permanent shape were preserved. The change in the polymer's morphology due to this procedure was detected as an enthalpy relaxation peak in the glass-transition zone. As a result of the morphological transformation, the analyzed T_g value and the T_g range increased. As a perspective of thermal analysis, the phenomenon was similar to a typical aging process in polymers, in which the segmental mobility drives the polymers toward volume relaxation and a reduction in free volume.[26–29] The difference from an aging process was that the smaller enthalpy and free volume in the PDLLA$_{OP}$ was caused by an active stretching of the polymer chains. This strain-induced oriented morphology required more energy to finish the glass-transition process than the original nonoriented structure.[30,31]

The diffusion of water into the oriented polymer matrix significantly changed the thermal properties of both the non-γ-irradiated and γ-irradiated PDLLA$_{OP}$. A notable effect of the diffusion of water was a decrease in T_g of the polymer–water complex. As a result, $T_{g\text{-onset}}$ decreased and leveled to 45°C for the

Figure 11. Increase of the pullout force of the γ-irradiated PDLLA$_{OP}$ nails *in vitro* at 37°C ($n = 3$; the error bars show the minimum and maximum values).

non-γ-irradiated PDLLA$_{OP}$ and 40°C for the γ-irradiated PDLLA$_{OP}$, after a constant level of water in the polymer matrix had been reached. As shown in Figure 5, the higher molecular weight non-γ-irradiated PDLLA$_{OP}$ was more resistant to the diffusion of water at 37°C than the γ-irradiated PDLLA$_{OP}$; this led to a lower plasticization of the non-γ-irradiated PDLLA$_{OP}$. At 2°C, the water absorption of the γ-irradiated PDLLA$_{OP}$ was significantly weaker than it was at 37°C and resulted in a significantly smaller T_g drop due to a smaller number of diffused water molecules in the polymer matrix than at 37°C. A similar result regarding the stabilization of the water content and the effect of the molecular weight on T_g of PDLLA was also reported by Steendam et al.[7] The removal of water from the polymer matrix by the vacuum drying of the samples at room temperature increased $T_{g\text{-onset}}$ to the range of the $T_{g\text{-onset}}$ of the nonoriented PDLLA but not to the range of the initial dry T_g of the PDLLA$_{OP}$ because of the orientation-programming-derived shifting of the glass-transition zone. This result indicates that the change in T_g was thermally reversible with PDLLA.

As presented in Figure 8, the changes in the enthalpy relaxation peak in an aqueous environment at 37°C were significantly affected by γ irradiation. Although T_g of the non-γ-irradiated PDLLA$_{OP}$ decreased, its enthalpy relaxation peak was not affected by the diffused water. However, the enthalpy relaxation peak area of the γ-irradiated PDLLA$_{OP}$ was significantly decreased because of the effects of the diffused water. During the 7-day incubation period at 37°C, the enthalpy relaxation peak area of the γ-irradiated PDLLA$_{OP}$ leveled to 50% of its initial value. It was intriguing that the enthalpy relaxation of the γ-irradiated PDLLA$_{OP}$ changed in an aqueous environment at a temperature as low as 2°C. This change showed that chain movements on a molecular level were possible even at very low temperatures. As shown in the macroscopic scale presented in Figures 3 and 4, these molecular movements were still too small to generate a measurable shape transformation. On the basis of the results of this study, the molecular movements seen on the macroscopic scale for the γ-irradiated PDLLA$_{OP}$ were the result of two thermal changes that occurred in an aqueous environment at 37°C: a decrease in T_g and a simultaneous decrease in the enthalpy relaxation. As T_g of the polymer decreased near the physiological temperature because of the diffusion of water, the probability of molecular movements at 37°C increased,[32] and the simultaneous increases in the enthalpy and free volume enabled the glass-transition process to finish with a lower amount of energy.[26] In addition, as previously shown, the initiation of the T_g range for the γ-irradiated PDLLA$_{OP}$ was below the physiological temperature, even though the analyzed $T_{g\text{-onset}}$ was above the physiological temperature.[19] The significantly slower shape transformation of the non-γ-irradiated PDLLA$_{OP}$ in a 37°C aqueous environment could be explained by the lower concentration of plasticizing water and the lower enthalpy of the polymer because the polymer chains could not move as easily as with the γ-irradiated PDLLA$_{OP}$. After immersion, the enthalpy relaxation peak, which still remained in the non-γ-irradiated PDLLA$_{OP}$, caused the observed T_g value to shift to a higher temperature because of a longer relaxation time than with the γ-irradiated PDLLA$_{OP}$.[33] This phenomenon led to a

paradoxical result, in which the whole T_g range shifted, even though the initiation of the glass-transition process would have been nearly at the same temperature range.[19,34] The removal of water from the polymer matrix had only a minor effect on the enthalpy relaxation of the γ-irradiated PDLLA$_{OP}$; this indicated that the change in enthalpy was due to a permanent change of morphology after a low energy barrier because the chain movements were achieved within the polymer–water complex. Thus, after 3 days of incubation at 37°C, the reduced activation energy and $T_{g\text{-onset}}$ of the γ-irradiated PDLLA$_{OP}$ led to an accelerated shape transformation. Similar results regarding the activation of the shape recovery and the shape-recovery rate were reported by Choi et al.[35] with amorphous polymer networks, in which the structural relaxation controlled the activation of the recovery, whereas the viscoelastic properties strongly influenced the response after activation.

The molecular mechanism behind the water-induced shift of the glass-transition zone studied by FTIR spectroscopy showed that the diffusion of water to the polymer matrix, even though the amount was relatively small, affected the intermolecular dipole–dipole and/or hydrogen bonding of the PDLLA chains. The most significant changes in the intensities and shifting of the bands occurred during the 1st day *in vitro*. In the FTIR spectra of the PDLLA, these changes were seen in the intensities and locations of the peaks created by the IR absorptions of the OH bonds of the water molecules absorbed into the polymer matrix,[22,23] the OH bonds of the polymer,[24] and the C═O bonds of the polymer.[24,25] When the water molecules diffused between the polymer chains, they both separated the chains and interacted with them. As a result, the slightly stronger interaction (dipole–dipole and/or hydrogen bonding) between the polar OH groups and other polar groups of the original polymer was disrupted. Therefore, the IR absorption (i.e., stretching) of the chain end O─H bonds became slightly more difficult energetically. This effect most probably competed and overlapped with the hydrogen-bonding interaction between the water molecules and the OH end groups of the polymer; this had a tendency to move the stretching band slightly back to a lower wave number and to increase the intensity of the peak. The former interaction, however, was expected to have a stronger effect on the peak shift, that is, toward higher wave numbers. Furthermore, the ν(C═O) stretching band shifted clearly to lower wave numbers in the immersed γ-irradiated films. Similar results were obtained for the C═O stretching modes of not only polylactide[36] but also polyamide and polyurethane after the sorption of water. When one water molecule, known as firmly bound water, is hydrogen-bonded to two C═O groups at a time, the C═O absorption appears at a lower wave number than when only one water molecule is hydrogen-bonded to one C═O group.[13,37] The weak and removable band appearing at about 1626 cm^{-1} after 1 day of soaking in water was due to the H─O─H bending of free water. In previous studies,[10,38] the different fractions of water adsorbed in hydrophilic materials were assigned. One fraction, so-called bound water, which corresponds to the first water layer in contact with the adsorbing solid, absorbs at a lower wave number ($\sim$1640 cm^{-1}). The other fraction, which corresponds to the absorbed water layers

on top of the first layer, absorbs at a higher wave number ($\sim$1656 cm^{-1}). In the case of polyurethane, it has been shown that the bound water causes a decrease in T_g of the polymer.[13,17] In addition, the absorbed water in the polymer matrix weakens the hydrogen bonding between the chains and causes a significant decrease in T_g. Our findings on the interaction of PDLLA with water were in agreement with the results of polyurethane shape-memory polymers and show that a similar type of change in the thermal properties due to the diffusion of water could also be applied to generate a water-induced shape-memory effect with PDLLA.

Even though the shape-transformation rate of PDLLA$_{OP}$ in an aqueous environment was slow compared to thermally stimulated shape-memory polymers[5] or to highly tailored lactide and glycolide polymer networks,[9] this type of shape memory can be successfully used to increase the functionality and fixation reliability of bioabsorbable medical devices such as nails, pins, or suture anchors. The efficacy of water-induced shape memory was successfully demonstrated in a pullout test with grooved-shaped nails, in which the initial pullout strength and the fixation stability was due to the tight fitting of the grooved-shaped nails, and the longer stability and the increasing fixation strength were due to the shape-memory effect activated by the 37°C aqueous environment. This type of approach in combination with the implant design and water-induced shape memory could be used to simplify surgical procedures by replacing screw-type medical devices, such as threaded suture anchors or screws for bone fracture fixation, with expandable plugs or nails, which could be easily inserted into a drill hole and make the threading procedure to the bone redundant. A potential strategy could also be to use this type of shape-memory property to increase the functionality of already existing medical devices, such as bioabsorbable screws used in the anterior cruciate ligament reconstructions, in which the slow radial expansion of the device would be an advantageous property in providing reliable long-term fixation strength despite changes in the mechanical properties of the surrounding tissues.

CONCLUSIONS

The shape memory of PDLLA$_{OP}$ in an aqueous environment at 37°C was triggered by the combined effect of water molecules and thermal activation. The main phenomena affecting the molecular movements in an aqueous environment at physiological temperature were as follows: (1) the diffusion of water into the polymer matrix, (2) the disruption of the intermolecular dipole–dipole and/or hydrogen bonding of the oriented-programmed PDLLA chains due to the diffused water, (3) the decrease in T_g of PDLLA$_{OP}$ to the range of physiological temperature due to the intermolecular disruption of molecular bonding, and (4) the decrease in the energy needed to finish the glass-transition process, that is, enthalpy relaxation. The appliance of this type of shape-memory property in absorbable medical devices opens possibilities for the development of novel active implant technologies to increase the reliability of fixation devices and the ease of operation techniques.

REFERENCES

1. Lendlein, A.; Shastri, V. P. *Adv. Mater.* **2010**, *22*, 3344.

2. Lendlein, A.; Jiang, H.; Junger, O.; Langer, R. *Nature* **2005**, *434*, 879.

3. Behl, M.; Lendlein, A. *Mater. Today* **2007**, *10*, 20.

4. Huang, W. M.; Zhao, Y.; Wang, C. C.; Ding, Z.; Purnawali, H.; Tang, C.; Zhang, J. L. *J. Polym. Res.* **2012**, 19.

5. Lendlein, A.; Langer, R. *Science* **2002**, *296*, 1673.

6. Behl, M.; Lendlein, A. *Soft Matter* **2007**, *3*, 58.

7. Steendam, R.; van Steenbergen, M. J.; Hennink, W. E.; Frijlink, H. W.; Lerk, C. F. *J Controlled Release* **2001**, *70*, 71.

8. Siemann, U. *Thermochim. Acta* **1985**, *85*, 513.

9. Pierce, B. F.; Bellin, K.; Behl, M.; Lendlein, A. *Int. J. Artif Organs* **2011**, *34*, 172.

10. Blasi, P.; D'Souza, S. S.; Selmin, F.; DeLuca, P. P. *J Controlled Release* **2005**, *108*, 1.

11. Fan, K.; Huang, W. M.; Wang, C. C.; Ding, Z.; Zhao, Y.; Purnawali, H.; Liew, K. C.; Zheng, L. X. *Express Polym. Lett.* **2011**, *5*, 409.

12. Hancock, B. C.; Zografi, G. *Pharm. Res.* **1994**, *11*, 471.

13. Yang, B.; Huang, W. M.; Li, C.; Li, L. *Polymer* **2006**, *47*, 1348.

14. Huang, W. M.; Yang, B.; An, L.; Li, C.; Chan, Y. S. *Appl. Phys. Lett.* **2005**, *86*, 114105.

15. Wang, Y.; Li, Y.; Luo, Y.; Huang, M.; Liang, Z. *Mater. Lett.* **2009**, *63*, 347.

16. Wang, W.; Jin, Y.; Su, Z. *J. Phys. Chem. B* **2009**, *113*, 15742.

17. Leng, J.; Lv, H.; Liu, Y.; Du, S. *Appl. Phys. Lett.* **2008**, 92.

18. Sun, L.; Huang, W. M.; Wang, C. C.; Zhao, Y.; Ding, Z.; Purnawali, H. *J. Polym. Sci. Part A: Polym. Chem.* **2011**, *49*, 3574.

19. Paakinaho, K.; Heino, H.; Pelto, M.; Hannula, M.; Törmälä, P.; Kellomäki, M. *J. Mater. Sci.: Mater. Med.* **2012**, *23*, 613.

20. Tschakaloff, A.; Losken, H. W.; von Oepen, R.; Michaeli, W.; Moritz, O.; Mooney, M. P.; Losken, A. *Int. J. Oral Maxillofac. Surg.* **1994**, *23*, 443.

21. Davis, E. M.; Theryo, G.; Hillmyer, M. A.; Cairncross, R. A.; Elabd, Y. A. *Am. Chem. Soc. Appl. Mater. Interfaces* **2011**, *3*, 3997.

22. Braun, B.; Dorgan, J. R.; Dec, S. F. *Macromolecules* **2006**, *39*, 9302.

23. Silverstein, R., M.; Webster, F., X.; Kiemle, D. Spectrometric Identification of Organic Compounds; Wiley: New York, **2005**.

24. Gonçalves, C. M. B.; Coutinho, J. A. P.; Marrucho, I. M. In Poly(lactic acid): Synthesis, Structures, Properties,

Processing, and Applications; Auras, R. A., Lim, L., Selke, S. E. M., Tsuji, H., Eds.; Wiley: Hoboken, NJ, **2010**; p 97.

25. Zhang, J.; Duan, Y.; Sato, H.; Tsuji, H.; Noda, I.; Yan, S.; Ozaki, Y. *Macromolecules* **2005**, *38*, 8012.

26. Pan, P.; Zhu, B.; Inoue, Y. *Macromolecules* **2007**, *40*, 9664.

27. Hutchinson, J. M.; Smith, S.; Horne, B.; Gourlay, G. M. *Macromolecules* **1999**, *32*, 5046.

28. Rault, J. *J. Non-Cryst. Solids* **2006**, *352*, 4946.

29. Bailey, N. A.; Sandor, M.; Kreitz, M.; Mathiowitz, E. *J. Appl. Polym. Sci.* **2002**, *86*, 1868.

30. Lee, S. C.; Han, J. I.; Jeong, Y. G.; Kwon, M. *Macromolecules* **2010**, *43*, 25.

31. Stoclet, G.; Seguela, R.; Lefebvre, J.; Rochas, C. *Macromolecules* **2010**, *43*, 7228.

32. Hancock, B. C.; Shamblin, S. L.; Zografi, G. *Pharm. Res.* **1995**, *12*, 799.

33. Matsuoka, S.; Bair, H. E. *J. Appl. Phys.* **1977**, *48*, 4058.

34. Höhne, G. W. H.; Hemminger, W. F.; Flammersheim, H. Differential Scanning Calorimetry, 2nd ed.; Springer-Verlag: Berlin, **2003**.

35. Choi, J.; Ortega, A. M.; Xiao, R.; Yakacki, C. M.; Nguyen, T. D. *Polymer* **2012**, *53*, 2453.

36. Zhang, J.; Sato, H.; Tsuji, H.; Noda, I.; Ozaki, Y. *J. Mol. Struct.* **2005**, *735*, 249.

37. Puffr, R.; Šebenda, J. *J. Polym. Sci. Part C: Polym Symp* **1967**, *16*, 79.

38. Herrera-Gómez, A.; Velázquez-Cruz, G.; Martín-Polo, M. O. *J. Appl. Phys.* **2001**, *89*, 5431.