

# Plasma Surface Modification of Porous PLLA Films: Analysis of Surface Properties and *In Vitro* Hydrolytic Degradation

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**ABSTRACT:** The aim of this research was to investigate the effects of plasma treatment on the surface and on the *in vitro* degradation behavior of poly(L-lactide) (PLLA) films. Polymer films were prepared by solvent casting, and their surface was modified by radiofrequency plasma treatments by using oxygen and tetrafluorocarbon gas. Pristine and treated PLLA films were characterized by field emission and atomic force microscopy and by contact angle measurements. *In vitro* hydrolytic degradation studies were conducted by measurements of weight loss, water absorption, visual inspection, and thermal transitions as a function of the incubation time. As-deposited PLLA films show a uniform distribution of ring-like porous structures on the surface due to solvent evaporation. Plasma treatments produce a mass reduction following the etching of

the polymer surface. Moreover, the morphology of the porous polymer is modified by the plasma, which induces different micro/nanometric topographic reliefs as a function of the different selected plasma processing parameters. The results indicate PLLA surface become hydrophilic and the surface roughness increased with treatment time in the case of oxygen, whereas a hydrophobic behavior was induced with tetrafluorocarbon plasma treatment. However, *in vitro* degradation studies show that plasma treatments do not affect the PLLA bulk and the hydrolytic degradation properties. © 2012 Wiley Periodicals, Inc. *J Appl Polym Sci* 000: 000–000, 2012

**Key words:** biodegradable; surface modification; degradation; electron microscopy; atomic force microscopy (AFM)

## INTRODUCTION

Poly(L-lactide) (PLLA) is one of the few synthetic polymers approved for human clinical uses, as it degrades to natural metabolites.<sup>1–3</sup> It is biocompatible, biodegradable, and easily processable. In addition, the physical, chemical, mechanical, and degradation properties of these polymers can be engineered to fit particular applications.

The wide application range of PLLA results from its good physical and mechanical properties, transparency, and easy processing. However, poor hydrophilicity, which greatly affects properties and behavior of the material, is a disadvantage if we consider the greater part of the applications. The hydrophilic changes increase the biological compatibility on the surface.

The degradation behavior of a polymer has crucial impact on the long-term performance of a tissue-engineered cell/polymer construct.<sup>4,5</sup> The degrada-

tion mechanisms can be affected by various factors, such as chemical structure, molecular weight, morphology, shape and history of the specimen, as well as the conditions under which the hydrolysis is conducted.<sup>6</sup>

Biomaterial surface properties represent a key factor in the success of the engineered tissue, since they determined the kind and the strength of interactions between biological environment and materials.<sup>7,8</sup> It is well known that a specific surface pore structure enhances cell adhesion, migration, and proliferation.<sup>9</sup>

PLLA surface properties can be engineered by using different methods: such as plasma treatment, ion sputtering, grafting, oxidation, and corona discharge; they affect the chemical and physical properties of the surface layer without significantly changing bulk material properties. In particular, plasma treatment is a useful technique to enhance the hydrophilicity of biodegradable polymer films.<sup>8,10</sup>

And its main advantages of plasma treatment over other techniques are the modification of only the outer most atomic layers of a substrate, the minimization of thermal degradation and the short treatment time. Radiofrequency plasma was used because of its ability to alter the surface functionality and consequently to modulate proteins and cell behavior.

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Grafting and plasma polymerization were investigated to enhance cell adhesion and biocompatibility of PLLA<sup>11</sup> and to improve the barrier properties of PLLA films.<sup>12</sup> It is conceivable that surface modification by plasma allows modulation of the degradation properties and may provide new ways of controlling the biodegradation of polymers for a variety of applications. However, the effects of this technique on a wide range of surface properties and on the degradation of the films should be considered. It is conceivable that surface modification by plasma allows modulation of the degradation properties and may provide new ways of controlling the biodegradation of polymers for a variety of applications.

Previous researchers<sup>13,14</sup> have reported that appropriate O<sub>2</sub> plasma treatments enhance both the surface hydrophilicity and biodegradation of polymeric films, whereas for others,<sup>15,16</sup> the promotion of biodegradation was not necessarily observed, even though the surface was changed for hydrophilicity.<sup>17</sup> Tetrafluorocarbon (CF<sub>4</sub>) plasma treatments were investigated for the etching effect combined to the introduction of nanostructures onto polymer surfaces, with hydrophobic character.<sup>18</sup>

In conclusion, some previous attempts to analyze the biodegradation of aliphatic polyesters affected by O<sub>2</sub>, N<sub>2</sub>, He, and NH<sub>3</sub> plasma treatments were reported.<sup>13–17</sup> However, the results of these studies were scattered and no clear conclusions were obtained in the case of the biodegradation properties. So, in this research, we decided to investigate the influence of O<sub>2</sub> and CF<sub>4</sub> plasma treatments on the surface and *in vitro* degradation properties of PLLA polymer films, to compare and to analyze the effects of two completely different surface wettability on the degradation properties of the PLLA films.

## MATERIALS AND METHODS

### Film preparation

PLLA (I.V. 0.95–1.20 dL/g in CHCl<sub>3</sub>) was purchased from Absorbable Polymers-Lactel. The PLLA porous films were produced by solvent casting in dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>, Fluka). The films were obtained dissolving polymer granules in CH<sub>2</sub>Cl<sub>2</sub> (10% w/v) and using a magnetic stirrer at room temperature (RT) to obtain a complete polymer dissolution. The solution was cast on a Teflon<sup>®</sup> substrate and the solvent was evaporated slowly in air, at RT for 24 h to prevent the formation of air bubbles. The remaining solvent was removed in an oven at 40°C for a week. The obtained films have a circular shape and two different thickness: 0.3 mm (named thick film) and 20 μm (named thin film) and two morphological different faces: the flat lower surface, in contact with Teflon<sup>®</sup> during the casting process and the upper face, exposed to the air.

### Plasma surface treatments

The surface of PLLA films was treated by means of radiofrequency plasma method under oxygen (O<sub>2</sub>) and tetrafluorocarbon (CF<sub>4</sub>) flow using a Sistec apparatus, with Huttinger power supply at 13.56 MHz. The films were placed into the stainless steel chamber, then it was evacuated for 1 h until the pressure (P) was  $9 \times 10^{-3}$  Torr. Process parameters were selected to obtain modulated surface features, specifically roughness, morphology, and wettability, since all of these factors can affect the hydrolytic degradation of the polymeric materials. Three different plasma treatments were applied, by changing the kind of gas (O<sub>2</sub>, CF<sub>4</sub>) and the treatment time. The O<sub>2</sub> flow was maintained at 60 standard cm<sup>3</sup>/min (sccm), while CF<sub>4</sub> flow was maintained at 22 sccm. The deposition conditions were power supply 20 W, bias voltage 220 V, the pressure for O<sub>2</sub> was  $1 \times 10^{-1}$  Torr, and treatment times were 2 and 20 min, for CF<sub>4</sub> the pressure was  $8 \times 10^{-2}$  Torr and treatment time was 20 min.

### Film characterization

The plasma treatment of surfaces gave a reduction of mass due to ion etching. To study this etching effect the change of mass during the process was calculated,<sup>19</sup> the samples were weighed before ( $m_b$ ) and after ( $m_a$ ) treatment, by means of Kern ABT 220-5DM balance and the mass loss was calculated as follows:

$$\text{Change of mass} = \frac{m_b - m_a}{S_s}$$

where  $S_s$  was the sample surface.

Field emission scanning electron microscope (FESEM) Supra 25 Zeiss, Welwyn Garden City, UK, and atomic force microscope (AFM) Easy Scan AFM, Nanosurf, Liestal, Switzerland were used to characterize the morphology of the upper and lower surfaces of PLLA films. The FESEM analysis was performed on gold sputter coated samples, at an accelerating voltage of 2 kV. AFM images were recorded in a tapping mode at RT in air, using silicon cantilevers, the scan size was set at 70 and 5 μm, and the scan rate was 0.5 s/line.

Static contact angle measurements were used to investigate the wettability of pristine and treated films. The contact angles were assessed using the sessile drop method in air by a FTA1000 Analyzer (Dinwiddie Street, Portsmouth, VA). Deionized water drops of 20 μL (high-performance liquid chromatography grade water) were placed on the films, and measurements were recorded 10 s after the liquid made contact with the surface. Five independent determinations at different sites were averaged.

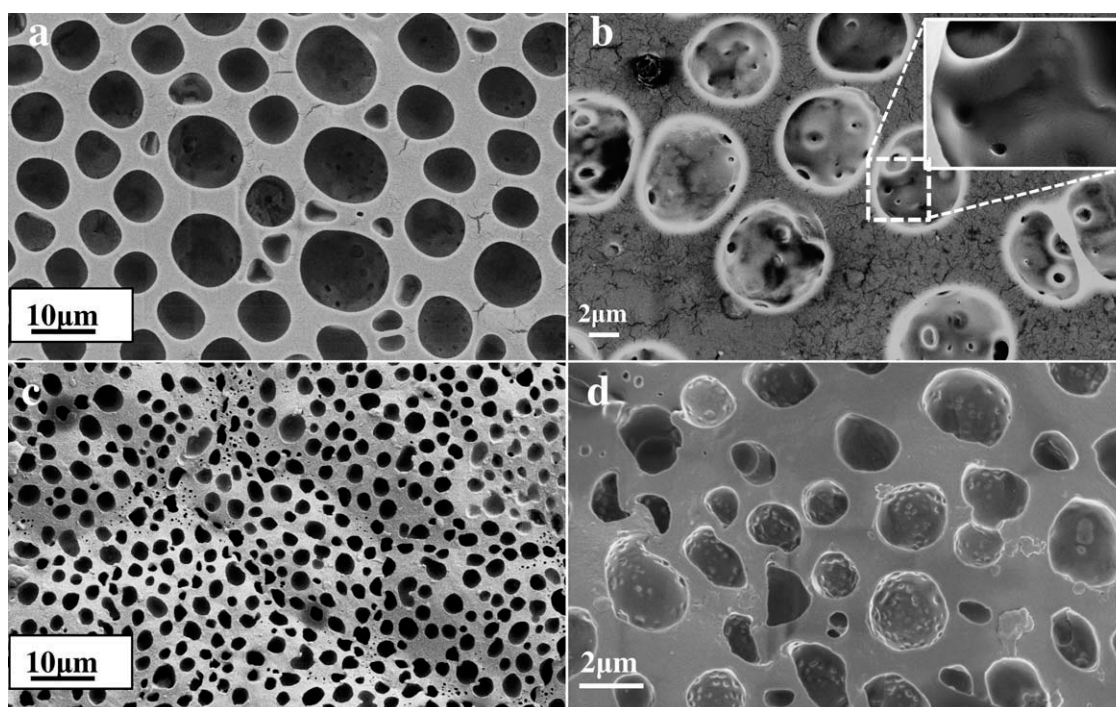


Figure 1 FESEM images of upper surfaces of PLLA thin (a,b) and thick (c,d) films.

### *In vitro* degradation study

The *in vitro* degradation study was carried out by placing 0.2 g of PLLA and PLLA modified surface into 10 mL of phosphate-buffered saline (PBS) solution in sealed jars, which were then placed into an incubator EN 400 (NÜVE) at  $(37.0 \pm 0.1)^\circ\text{C}$ .<sup>20</sup> Practically, before starting the hydrolysis tests,  $1.3 \times 5.0 \text{ cm}^2$  rectangular specimens from each PLLA film were prepared (the experiment was conducted in triplicate), and the initial mass of the films was recorded. Then, the samples were dipped in a flask containing 10 mL of PBS at pH 7.4, and the flasks were placed in the incubator at  $37^\circ\text{C}$ . At predetermined periods for 2 months, the specimens were picked out of the buffered solution and rinsed several times with distilled water. Then they were swabbed with blotting paper and immediately weighed to obtain the wet mass of the films,  $m_{\text{wet}}$ . After weighting, the samples were dried in an oven for a week and weighed again to obtain the dry mass left after degradation,  $m_{\text{dry}}$ . The water content and mass loss of the films were then calculated as follows:

$$\text{Water content} = \frac{m_{\text{wet}} - m_{\text{dry}}}{m_{\text{dry}}} \cdot 100$$

$$\text{Mass loss} = \frac{m_{\text{ini}} - m_{\text{dry}}}{m_{\text{ini}}} \cdot 100$$

Differential scanning calorimeter (DSC) measurements were performed on a TA Instrument Q 200

apparatus. To avoid oxidative degradation, the sample and reference pans were purged with nitrogen at a constant flow rate of  $50 \text{ mL min}^{-1}$ . The samples were heated from  $-25$  to  $220^\circ\text{C}$  at a scan rate of  $10^\circ\text{C min}^{-1}$ , then cooling at same rate and finally heated for the second time. Approximately 7 mg of each sample were used in the analysis. DSC analyses carried out on as-recovered dried samples, have shown the influence of degradation time on glass transition ( $T_g$ ), melting ( $T_m$ ), and cold crystallization ( $T_{cc}$ ) temperatures, on crystallization ( $\Delta H_c$ ) and melting ( $\Delta H_m$ ) enthalpies, as well as on crystallinity degree, calculated as follows<sup>21</sup>:

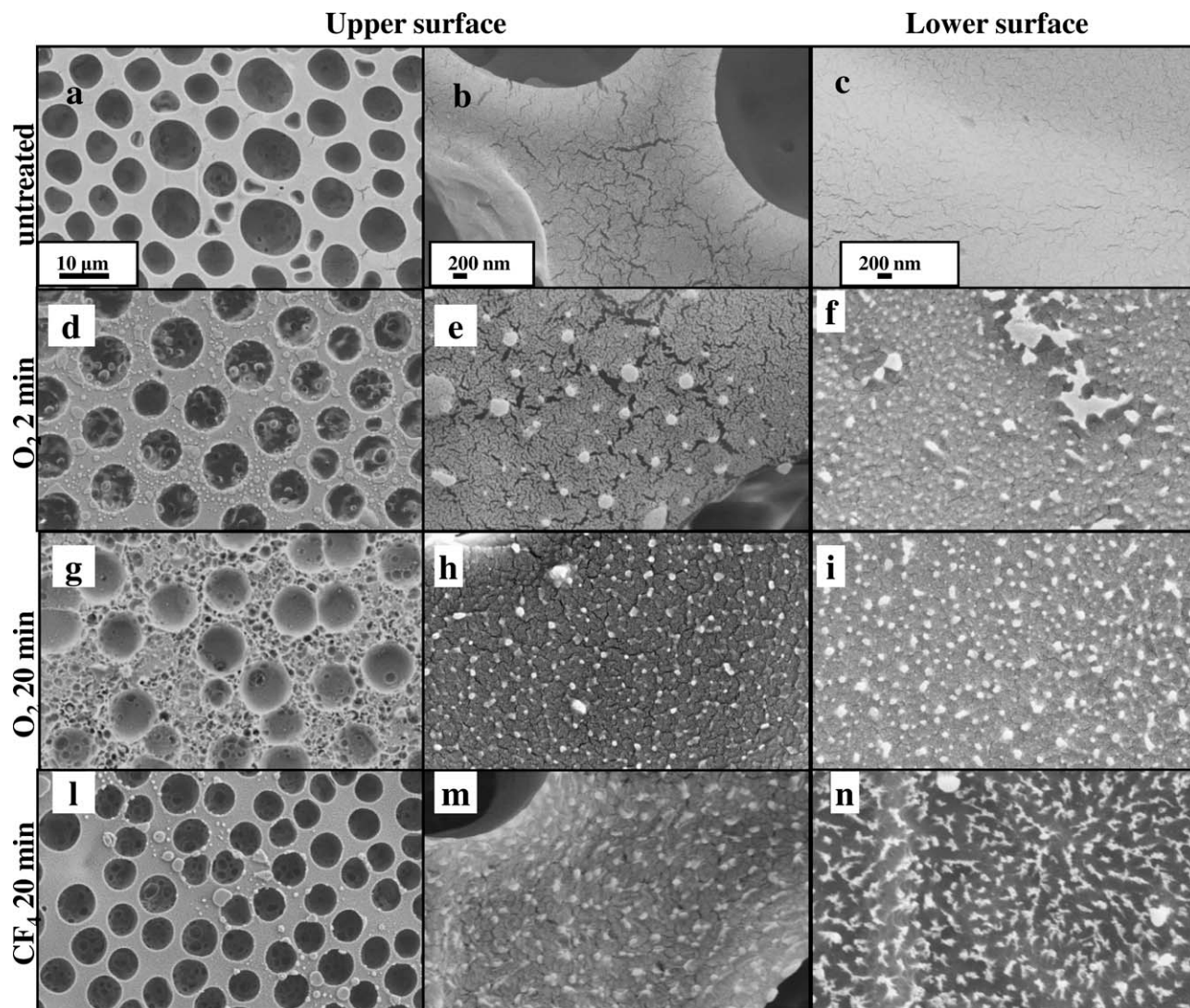
$$\chi_c(\%) = \frac{\Delta H_m - \Delta H_{cc}}{\Delta H_m^0} \cdot 100$$

where  $\Delta H_m^0$  is the enthalpy heat of fusion for a sample that is 100% crystalline and for PLLA is  $93.6 \text{ J g}^{-1}$ .<sup>22</sup> The data were analyzed using Universal Analysis 2000 provided with the instrument. Each data represent the average value calculated from the three individual measurements.

## RESULTS AND DISCUSSION

### Film characterization

FESEM and AFM analysis were used to characterize the morphology of the upper and lower surfaces of PLLA thin and thick films. Figure 1 shows FESEM images of PLLA thin (a,b) and thick (c,d) films,



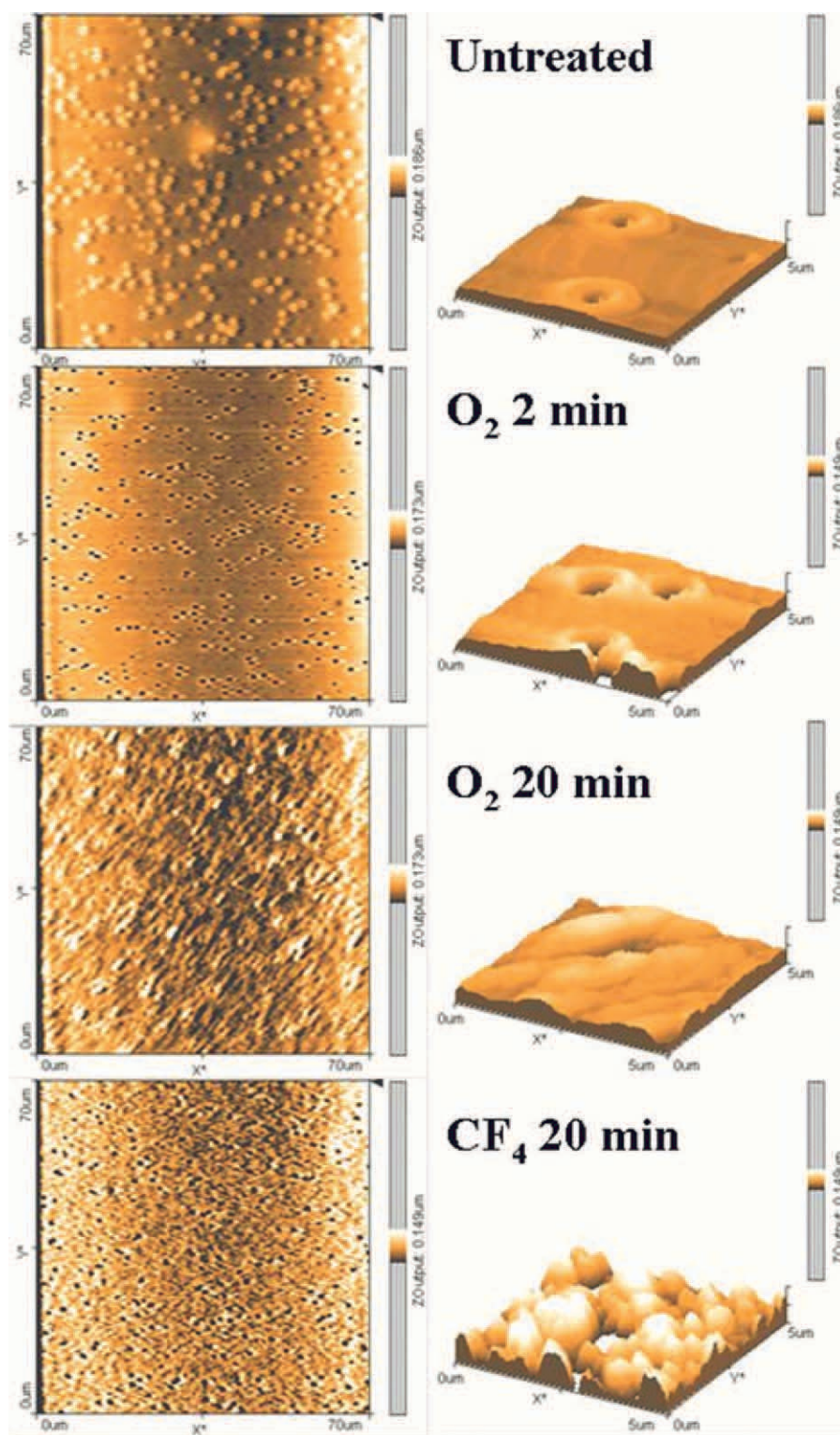
**Figure 2** FESEM images of pristine and treated PLLA upper and lower surfaces.

obtained by using two different detectors to better analyze the film morphology, Figure 1(a,c) shows the aspect of samples, the surfaces show a regular porous morphology due to the solvent evaporation. This specific polymer surface topography is obtained as a result of the solvent evaporation, and it could be attributed to the evaporation temperature (40°C) and the high-evaporation rate of the selected CH<sub>2</sub>Cl<sub>2</sub>, used in film preparation, as previously described in literature.<sup>23-25</sup> The surface of thin films was flat with a nonuniform pore diameter (ranged from 1 to 10 μm) and distribution [Fig. 1(a)], while the surface of thick PLLA [Fig. 1(c,d)] was wavy, the pore shape and distribution were irregular, with pore diameter ranged from 0.5 to 3 μm. Figure 1(b,d) shows the internal pore wall morphology of the PLLA thin and thick films, respectively. Thin film shows a pore distribution not only on the surface but also on the pore walls, while thick PLLA films [Fig. 1(d)] show pore walls with an irregular

roughness on the inner surface, but without the presence of holes. The FESEM analysis highlights the presence of the same pore structure on the surface of thin and thick PLLA films, however pores have different diameters, induced by the different polymer solution/surface ratio during the evaporation step in the film casting process.

#### Surface modifications

The change of mass to the exposed surface area due to the plasma process parameters (gas and time) was measured, to check the ion etching effects of plasma treatments to the films. For treatments of 20 min, the oxygen gas results in a higher mass reduction, twice respect to CF<sub>4</sub>. Moreover, the mass change increases with treatment time, with 0.274 mg/cm<sup>2</sup> for 20 min of oxygen treatment and 0.044 mg/cm<sup>2</sup> for 2 min of treatment. This result means that the etching effect increases with the time of the

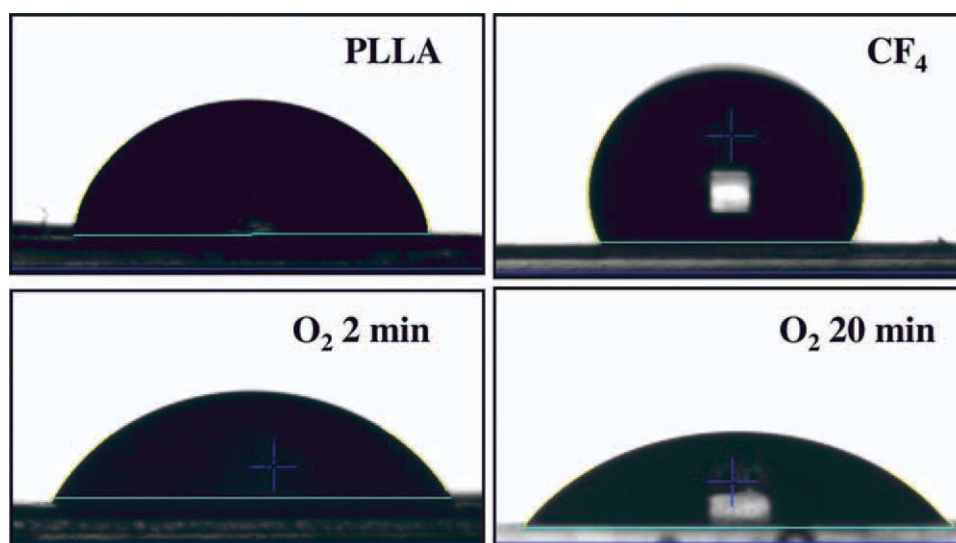


**Figure 3** AFM images of pristine and treated PLLA surfaces. Two-dimensional images: scan size: 70  $\mu\text{m}$ , 3D images scan size: 5  $\mu\text{m}$ . [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

treatment. This aspect is important to analyze when considering the morphological modification analyzed by FESEM and AFM.

Figure 2 shows the effects of different plasma process parameters on the surface morphology studied

by FESEM images and confirmed by AFM analysis (Fig. 3). The etching effect of the plasma treatments is clearly visible even at low magnification [Fig. 2(a,d,g,l)], the treated samples with  $\text{O}_2$  plasma for 2 min show an increase in surface roughness with



**Figure 4** Contact angle images of pristine and treated PLLA surfaces. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

emergence of micro- and nanopillars with nonuniform distribution [Fig. 2(d–f)]. The treatment effect is also visible on the inner pores that increase their size as the surface ones. Increasing the processing time (20 min), the micrometer-sized structures disappear and the nanoscale topography are distributed more evenly. Twenty minutes of  $O_2$  plasma treatment induces the presence of new pores on the upper PLLA surface [Fig. 2(g)]. The effect of  $CF_4$  plasma results in an increase in surface roughness, the foil-like protuberances have homogeneous distribution and different shape, dimension, and density compared with oxygen plasma treatment.

Figure 3 shows the topographical view in 2D (scan size:  $70\ \mu\text{m}$ ) and 3D (scan size:  $5\ \mu\text{m}$ ) of upper PLLA untreated and treated surfaces. The etching effect of  $O_2$  plasma can be seen in the formation of nanopillar like structure, 2 min of treatment was sufficient to create the specific nanostructure with the distribution that becomes more regular with 20 min of treatment. The 3D images at  $5\ \mu\text{m}$  scan size show the effect of plasma treatments on the holes of the film.

Water static contact angle measurements were performed to study the plasma treatment effects on surface wettability. The untreated PLLA has a water contact angle of  $83^\circ \pm 3^\circ$  that decreases with  $O_2$  treatment (Fig. 4) up to  $50^\circ \pm 4^\circ$  for 20 min of plasma

exposure, while increase to  $113^\circ \pm 4^\circ$  in case of  $CF_4$  treatment. The different wetting behavior of the PLLA-treated films is due to different morphology induced by plasma treatments, and to the functional groups introduced on the surface as a result of different gas used in the plasma treatments, as previously reported.<sup>8,26</sup>

#### *In vitro* degradation study

The changes in the general aspect of samples upon hydrolysis could be first of all visually judged, as revealed in Figure 5(a) significant change in the sample opacity could be observed. The modification of the opacity of each sample can be explained by various phenomena occurring along the degradation. Indeed, the changes in appearance are directly related to the light diffusion through the material. Such diffusion can be altered by an evolution in crystallinity of the polymer matrix. Since the hydrolytic degradation of the polyester chains is known to take place in the amorphous phase of the matrix,<sup>27</sup> this phenomenon is expected to increase the PLLA crystallinity, which is translated by an increase in the overall opacity of the samples. Moreover, the samples become brittle and broke in two or three large pieces after 49 days.



**Figure 5** Photograph of pristine and treated PLLA films before and after 21 and 49 days of *in vitro* degradation. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

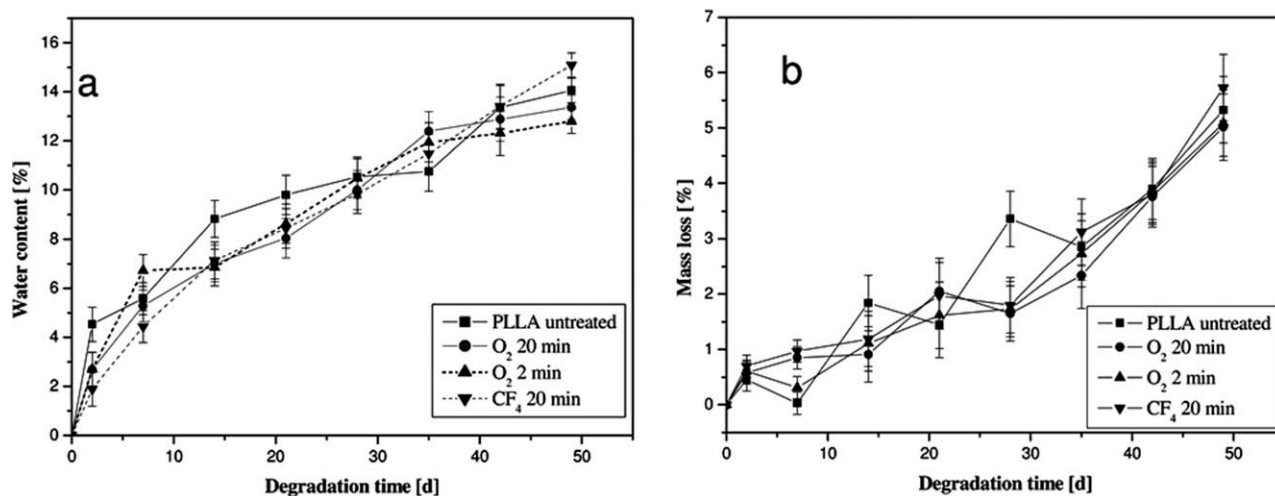


Figure 6 Water content (a) and mass loss (b) of pristine and treated PLLA films during *in vitro* degradation study.

Figure 6 shows the water content and the mass loss of PLLA films during *in vitro* degradation study. The water absorption [Fig. 6(a)] does not appear to

be influenced by the surface treatments except in the first moments: the samples treated with CF<sub>4</sub> have a water absorption below the O<sub>2</sub> treated and pristine

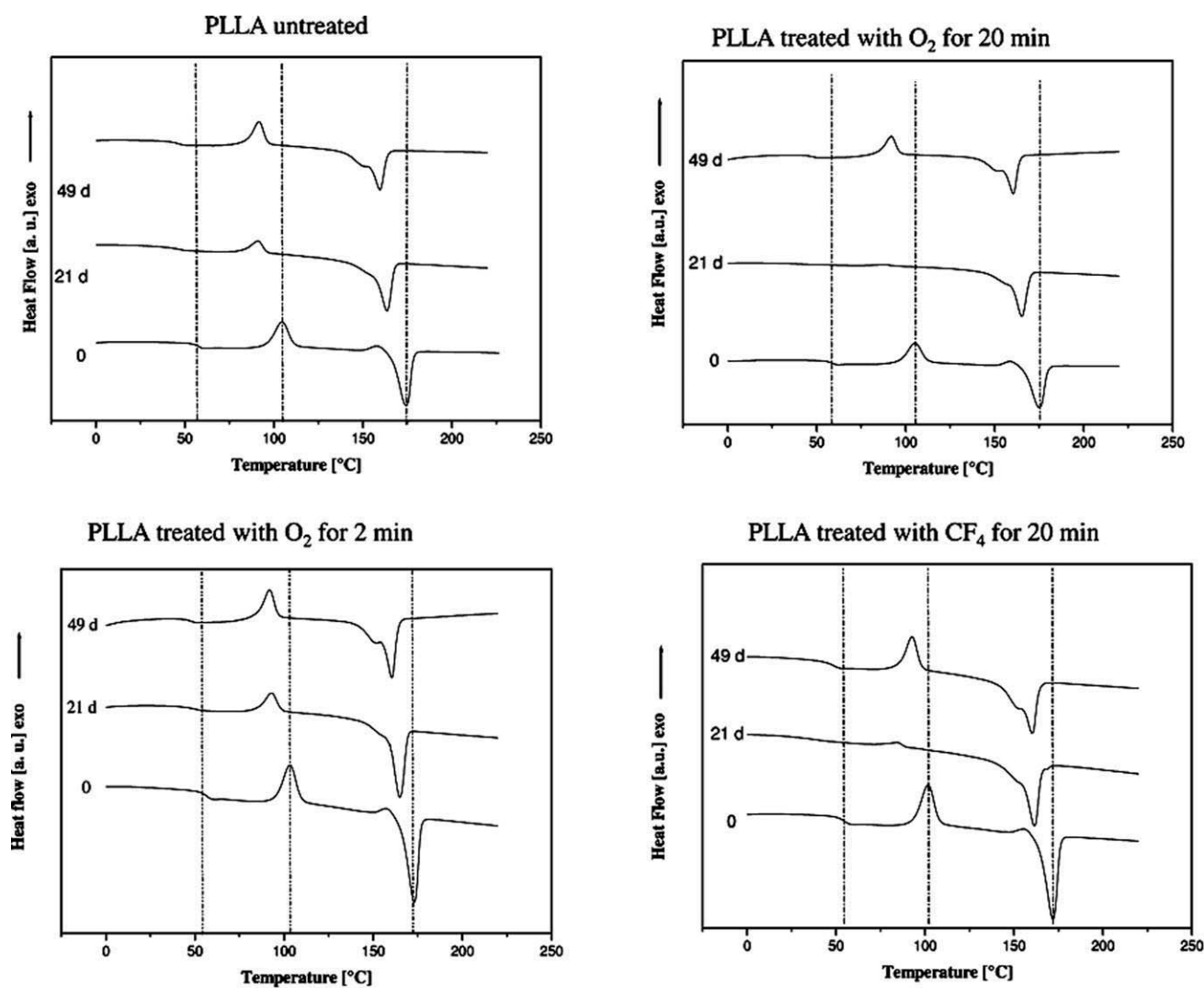


Figure 7 DSC thermograms of pristine and treated PLLA films obtained by second heating curves.

**TABLE I**  
**Thermal Properties of Pristine and Treated PLLA Films During *In Vitro* Degradation Study**

	0 days			21 days			49 days		
	First heating scan								
Samples	$T_g$ (°C)	$T_m$ (°C)	$\chi_c$ (%)	$T_g$ (°C)	$T_m$ (°C)	$\chi_c$ (%)	$T_g$ (°C)	$T_m$ (°C)	$\chi_c$ (%)
PLLA	44 ± 2	172.0 ± 0.5	46.1 ± 0.5	57 ± 2	166 ± 2	59 ± 5	59 ± 3	163 ± 1	62 ± 2
O <sub>2</sub> 2 min	45 ± 1	172.3 ± 0.1	43.2 ± 0.2	50 ± 5	166 ± 1	57 ± 4	60 ± 2	163.0 ± 0.3	63 ± 2
O <sub>2</sub> 20 min	48 ± 5	175 ± 4	49 ± 5	57 ± 1	167 ± 1	57 ± 1	57 ± 1	163 ± 1	63 ± 3
CF <sub>4</sub> 20 min	46 ± 4	172 ± 1	46 ± 5	46 ± 1	164 ± 2	55 ± 4	–	161.2 ± 0.2	60 ± 2
	Cooling scan								
Samples	$T_c$ (°C)	$\Delta H_c$ (J/g)		$T_c$ (°C)	$\Delta H_c$ (J/g)		$T_c$ (°C)	$\Delta H_c$ (J/g)	
PLLA	94.2 ± 0.6	4.4 ± 0.5		91 ± 4	27 ± 3		87 ± 3	13 ± 4	
O <sub>2</sub> 2 min	95 ± 1	4.0 ± 0.5		94 ± 2	27 ± 5		90 ± 1	22 ± 4	
O <sub>2</sub> 20 min	95 ± 2	3.8 ± 0.7		94.8 ± 0.2	35 ± 3		89 ± 2	20 ± 6	
CF <sub>4</sub> 20 min	95.5 ± 0.5	4.6 ± 0.5		91 ± 2	31 ± 4		88 ± 3	18 ± 5	
	Second heating scan								
Samples	$T_m$ (°C)	$T_{cc}$ (°C)	$\chi_c$ (%)	$T_m$ (°C)	$T_{cc}$ (°C)	$\chi_c$ (%)	$T_m$ (°C)	$T_{cc}$ (°C)	$\chi_c$ (%)
PLLA	173 ± 1	104 ± 1	19 ± 2	163 ± 4	90 ± 5	42 ± 3	158 ± 2	91.0 ± 0.6	28 ± 4
O <sub>2</sub> 2 min	172 ± 1	103 ± 1	19 ± 3	165 ± 3	92 ± 4	39 ± 6	160 ± 1	90 ± 2	34 ± 2
O <sub>2</sub> 20 min	173 ± 2	104 ± 2	19 ± 3	166 ± 1	90 ± 2	49 ± 1	160.3 ± 0.3	91 ± 3	32 ± 4
CF <sub>4</sub> 20 min	172 ± 1	102 ± 1	19 ± 1	165 ± 2	88 ± 4	48 ± 3	158 ± 2	91 ± 3	30 ± 4

PLLA films, for the first 7 days, and then they have a similar pattern to the other samples. The weight loss [Fig. 6(b)] is an index of water soluble oligomer amount and monomer formed as a result of hydrolysis and released from the PLLA crystalline residues. Mass loss from the films is found to be relatively low during the degradation test. All PLLA films lost <10% wt of their initial mass after 64 days, while the water content is found to have increased of 15% wt. A slightly decrease of the initial medium pH (from 7.4 to 7.0) in 2 months during the hydrolytic degradation experiments confirms the low amount of mass loss.

The DSC analysis (Fig. 7 and Table I) has shown the influence of degradation time on thermal transitions as well as on the enthalpies and the crystallinity. Analyzing the data obtained from the DSC curves during the first heating (Table I), it is seen that the different plasma surface treatments do not affect the thermal properties of the material. The melting temperature was about 172°C for neat PLLA and PLLA treated with a percentage of crystallinity around 50% for all systems. After degradation, the glass transition  $T_g$  became more difficult to be observed in the first heating scan. During the hydrolytic degradation, the  $T_m$  decreases from 172°C to 163°C after 49 days while the crystallinity increases from 50 to 60%. This effect occurs because the PLLA degradation process has as consequence the formation of new crystals, which can be melted with lower energy and temperature.<sup>23</sup> After degradation (Table I), the crystallization temperature, measured in the cooling scan changes from 94°C to 89°C; this can be explained by the degradation of PLLA amorphous part that promotes the mobility of the chains allowing the crystallization at the lower temperature.<sup>24</sup> The solvent casting method used to obtain the films

allowed a complete crystallization, so the thermograms do not present  $T_{cc}$  in the first heating scan. However, in the second heating, the crystallization enthalpy ( $\Delta H_c$ ) occurred, due to the fast cooling rate that hinders the complete crystallization.<sup>24</sup> During the second heating scan, a decrease of melting and cold crystallization temperatures of about 15°C is revealed. During the hydrolytic degradation process, the melting peak changes the shape significantly (Fig. 7), with a presence of a shoulder at lower temperature.<sup>25</sup> This indicates the coexistence of  $\alpha$ -form and  $\alpha'$ -form crystals in the PLLA film. According to the previous study,<sup>28</sup>  $\alpha$ -form crystals transferred to  $\alpha'$ -form crystals melt at higher temperature while the pre-existing  $\alpha$ -form crystal melt at lower temperature. The maximum of crystallinity obtained around the third week of degradation was attributed to the decreased lattice disorder of the PLLA crystalline residues. After this period, the decrease of  $\chi_c$  was ascribed to the decrease of molecular weight of the crystalline residues, which enhanced the effect of the surface having a large surface energy.<sup>29</sup> Since the samples show a small weight loss [Fig. 6(b)] upon hydrolysis, such an increase in crystallinity cannot be ascribed to a decrease of the relative content in amorphous phase. This increase has to be attributed to an effective crystallization occurring during hydrolysis. One possible mechanism that would allow for such crystallization would imply both the decrease in the PLLA molecular weight and a plasticization of PLLA by water and buffer molecules as well as by lactic acid oligomers that would give sufficient mobility to the polymer chains to organize and crystallize further.<sup>23</sup> It is evident that the thermal behavior of treated PLLA films is quite similar to the untreated PLLA film, underlining that the plasma surface treatment changes the polymer



surface properties, but it does not affect the bulk properties and the hydrolytic degradation process. In conclusion, the characteristic thermal transitions of the polymer matrix were not affected by the different process parameters used.

### CONCLUSIONS

This article showed the development and characterization of biodegradable porous PLLA films performed by solvent casting process. The results obtained highlight the presence of the micrometric pore structure on the film surface, with their shape and size affected by the film process.

This study demonstrated that plasma treatment is able to modulate PLLA surface properties: inducing surface nanostructure with different shape, which affects the hydrophilic/hydrophobic behaviors, without changing PLLA bulk properties. Furthermore, the hydrolytic degradation behavior of PLLA films is not influenced by the plasma process applied.

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