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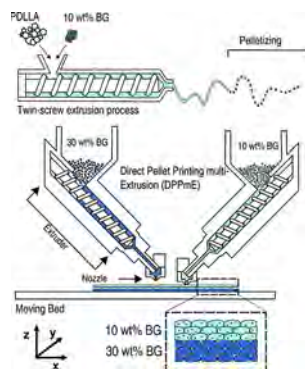
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Functionally Graded Multilayer Composites Based on Poly(D,L lactide)/Bioactive Fillers Fabricated by a 3D Direct Pellet Printing Multi-Extrusion Process

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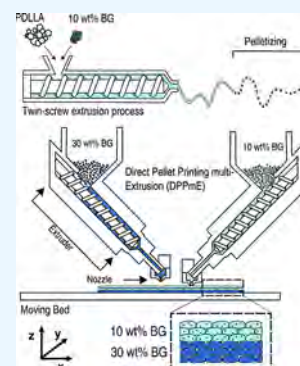
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Supporting Information

ABSTRACT: The aim of the present work was to investigate a 3D manufacturing process dealing with 3D Direct Pellet multi-Extrusion (DPPmE). Throughout this paper, various functionally graded materials (FGM) were obtained with tailored properties for bone regeneration. Therefore, an experimental investigation was performed to gain a better understanding of the structure-processing-properties relationships. A poly(D,L-lactic acid) (PDLLA) matrix and bioglass (BG) or hydroxyapatite (HA) bioactive fillers were chosen to obtain hybrid FGM in comparison to composite references. Different compositions and shape factors (from microspheres to fibers) of these bioactive fillers were used to control the PLLA matrix degradation. Then, different strategies of DPPmE were used to tailor and tune the desired gradient of properties. Interestingly, good interfaces and adhesion properties were obtained. Subsequently, rheological, size-exclusion chromatography, and porosity measurements corroborated the present findings. Besides, tensile as well as thermomechanical properties showed the advantages of the DPPmE process to fabricate FGM composites with tailored architectures.

KEYWORDS: 3D printing, multifunctional composites, biocomposite, microstructural analysis, bioglass, rheology



1. INTRODUCTION

The number of internal fixation surgeries continues to increase year by year.¹ To improve patient post-healing and avoid a second surgical intervention to remove the bone implant, numerous studies have focused on the use of resorbable polymers,² ceramics,³ and their composites.⁴

Poly(α -hydroxy ester) matrices, especially poly(L-lactic acid), poly(D-lactic acid), and their copolymer poly(D,L-lactic acid) (PDLLA), combined with bioactive fillers like bioglass (BG) or hydroxyapatite (HA) have been extensively studied for biomedical applications due to their biocompatibility, excellent mechanical properties, and controllable degradation rate.⁵

Bioglass (BG) and hydroxyapatite (HA) are inorganic osteoconductive fillers commonly used in composites for bone regeneration. BG improves both bone growth and differentiation. When BG is in contact with body fluids, a layer of HA develops on the BG surface, thus facilitating the attachment of osteoclasts and the proliferation of osteoblasts.⁶

When it comes to obtain fully dense parts, two different ways of processing poly(α -hydroxy ester)/BG composites are differentiated in the literature: solvent casting⁷ and molten manufacturing techniques (e.g., injection⁸ and compression molding⁹). The first route involves the use of toxic and costly solvents as well as energy for solvent evaporation and recycling. However, various authors have observed that in the presence of BG high-temperature processing of poly(α -hydroxy ester) can cause a significant reduction of the polymers' molecular weight

and mechanical properties.¹⁰ In our previous studies, we described how the characteristics of BG affected the degradation reaction between PLLA and BG.⁸ We demonstrated that the thermal treatment, composition, and content of BG or the extrusion temperature could reduce the hydrolytic degradation of PLLA during the thermal processing. Compared to the 45S5 composition (45 wt % SiO₂; 24.5 wt % CaO; 6 wt % P₂O₅; 24.5 wt % NaO₂), BG containing a lower amount of sodium and phosphate in its composition may exhibit a lower matrix degradation during the manufacturing step.¹¹ Hence, in order to minimize the degradation, a less reactive BG has to be chosen.¹²

On the one hand, innovative manufacturing processes like fused deposition modeling, electrospinning, or robocasting open up new possibilities to fabricate orthopedic implants based on biomaterials with an adjustable functional gradient. These systems, commonly named functionally graded materials (FGM), exhibit a structure and/or composition that gradually change in a particular direction with tailored properties. Functional gradient can be adapted to achieve a suitable

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Table 1. Properties of Bioactive Fillers

name	nature	$\rho(\text{g}/\text{cm}^3)$	$d_{50}(\mu\text{m})$	diameter-length(μm)	specific surface area (m^2/g)
HA	HA	3.14	20	-	9.5×10^{-1}
BG-MS	S53P4	2.64	60	-	3.8×10^{-2}
BG-fibers	S53P4	2.64	-	7–120	2.3×10^{-1}

66 structural strength, surface roughness, or induce bioactive, anti-
 67 inflammatory antibacterial response during implantation.¹³
 68 There exist several techniques in the literature to produce
 69 graded coatings (FGC),^{14,15} FGM with a gradient in
 70 porosity^{16–19} and 3D graded parts for orthopedic applica-
 71 tions.²⁰ Through the last years, only few authors presented the
 72 possibilities of resorbable poly(α -hydroxy ester)/bioactive
 73 fillers in FGM composites for bone tissue engineering
 74 applications. For example, Eqtesadi & Motealleh^{14,15} improved
 75 the mechanical properties of 45S5 bioglass robocast scaffolds
 76 by applying a PLA coating. Mehboob²¹ proposed a design
 77 based on finite element analysis of a FGM composite to resist
 78 the different stresses during the healing of bone fractures. They
 79 also studied the mechanical properties evolution of a multilayer
 80 FGM composites fabricated by hot-pressing immersed in a
 81 phosphate-buffers saline (PBS) solution.²⁰ Masoudi et al.,²²
 82 fabricated a bilayered membrane by electrospinning to combine
 83 guided bone and guided tissue regeneration properties.
 84 Moreover, Ma et al.,²³ presented an in vivo study of FGM
 85 with tailored mechanical properties and bioactivity of
 86 orthopedic implants fabricated by solvent casting. The
 87 principal current technologies to manufacture the FGM in
 88 the literature are freeze-drying, electrospinning, solvent
 89 coating, solvent assembling, hot-pressing, and 3D printing
 90 extrusion. However, the studies of FGM fabricated by 3D
 91 printing are focused on scaffolds with a gradient in porosity to
 92 limit the stress-shielding effect or/and with a high porous
 93 connectivity to facilitate the fluid flow through the implant.¹³
 94 Besides, preceding work²⁴ has shown that after only 14 days
 95 of in vitro tests, the mechanical properties of the composite
 96 decreased by 60%. The mechanical and morphological
 97 properties of neat PDLA specimens remained stable for 6
 98 months of immersion in a phosphate-buffered saline solution
 99 (commonly used in biological degradation simulation).
 100 Therefore, FGM PDLA/BG and/or PDLA/HA with
 101 different bioactive filler content may exhibit bioactivity and
 102 ensure the resistance during a long in vitro immersion period.
 103 On the other hand, additive manufacturing techniques
 104 present several strengths like rapid fabrication, customization,
 105 and substantial saving material. Further advantages of this
 106 manufacturing technology are that the porosity and mechanical
 107 properties of the final parts can be adjusted to respond the
 108 specifications of different medical devices. 3D Direct Pellet
 109 multi-Extrusion (DPPmE) is a Fused Deposition Modeling
 110 (FDM) technique based on an extrusion system using polymer
 111 pellets as the starting material and thus avoiding the filament
 112 preparation required for Fused Filament Fabrication (FFF).
 113 This technique democratizes the access to additive manufac-
 114 turing techniques since it expands the applicability of FDM to
 115 non-commercial materials in the filament form.^{25–27} In former
 116 studies, it has already been demonstrated that well-designed
 117 structures can be manufactured with thermal unstable
 118 polymers²⁸ and mechanical properties comparable to those
 119 of injection-molded parts.²⁹ Besides, it is necessary to pay
 120 special attention to control the rheological properties of
 121 molten materials (like viscosity modulus, zero-shear viscosity,

or relaxation time/elasticity) during extrusion through the
 nozzle and after deposition in order to ensure good interlayer
 welding and the mechanical robustness of 3D-printed
 parts.^{30,31} Further, some DPPmE systems present an extrusion
 system with multiple screws, resulting in FGM-printed parts
 with different material composition and architecture. In a
 previous study of our team, we probed the successful control of
 the interfacial bonding of multimaterial systems fabricated by
 this technique.^{32,33} Despite the interesting papers dedicated in
 the recent years to 3D printing process (specially to FDM³⁴),
 there is an aperture to DPPmE and its adaptation to develop
 innovative FGM devices for medical applications.

In this work, three types of fillers, HA microspheres, BG
 microspheres, and BG fibers, were used to illustrate how the
 content, shape, and nature of the fillers affected the
 morphology, rheology, and mechanical properties of PDLA
 composites. Moreover, the 3D printing of dense FGM parts
 was carried out with special attention to the printing
 temperature to ensure a rather constant viscosity and minimize
 the matrix degradation during processing. To conclude, we
 present the post-fabrication mechanical properties of multi-
 component specimens with different bioactive filler contents to
 show the potential application of 3D DPPmE FGM for load-
 bearing orthopedic implants.

2. EXPERIMENTAL SECTION

2.1. Materials and Manufacturing Process. 2.1.1. Materials.

An amorphous poly(D,L-lactide), hereafter referred to as PDLA
 (4060D, Nature Works LLC, USA) (~ 10 €/kg), with 19.5% level of
 D isomer and a density of 1.24 g cm^{-3} was used in this work as it
 exhibited similar properties to the medical grade PDLA R207S
 (Evonik, USA) (~ 6000 €/kg). PDLA presented a weight average
 molar mass $\bar{M}_w = 136 \text{ kg mol}^{-1}$, a number average molar mass
 $\bar{M}_n = 94 \text{ kg mol}^{-1}$ and a polydispersity $\mathcal{D}_M = 1.4$ obtained by SEC
 measurements in chloroform. Rheological and molar mass details of
 R207S are given in Supporting Information A. Before extrusion and
 granulation, PDLA was dried for 4 h at 45 °C under vacuum to
 prevent hydrolytic degradation during the processing.

Particles of antibacterial bioactive glass S53P4 (BG) (XL-Sci Tech,
 USA) with a chemical composition of 53 wt % SiO_2 ; 20 wt % CaO ; 4
 wt % P_2O_5 ; 23 wt % Na_2O , as well as particles of hydroxyapatite (HA)
 (Plasma Biotol, UK), were mixed with PDLA.³⁵ For BG, two
 different particle shapes were used: microspheres and fibers. HA
 microsphere fillers are used as a reference (no chemical interaction
 between HA and PDLA is mentioned in the literature). Table 1
 summarizes the main properties of bioactive fillers. Before
 compounding, HA and BG powders were dried for 4 h at 150 °C
 under vacuum.

2.1.2. Compounding and Pelletizing of Filled PDLA. Com-
 pounding of the composite was carried out in a Haake Minilab
 Rheomax CTWS Mixing (Thermo Fisher Scientific, Cleveland, OH,
 USA) with a filling volume of 7 cm^3 at a temperature of 150 °C and a
 rotor speed of 40 rpm. The compounder can be used as an extruder or
 mixer since it combines a twin-screw extruder with a back-flow
 channel. Since no recirculation was used in this study, a short
 residence (~ 30 s) and a mixing volume of 5.5 cm^3 were fixed. PDLA
 powders micronized by Micronis (Colayrac-Saint-Cyrq, France) with
 $d_{50} = 200 \mu\text{m}$ were blended independently with BG and HA particles

178 at a total filler content of 0, 10, or 30 wt % (corresponding to 0, 5.2, or
179 17.5 vol % BG and 0, 4.2, or 14.4 vol % HA, respectively).
180 Subsequently, the extrusion filament was cut into pellets using a
181 mechanical granulation machine. The compounding and 3D printing
182 steps were made in a white room. The pellets were then dried for 4 h
183 at 45 °C under vacuum and stored in sealed desiccators with silica gel
184 until the 3D printing fabrication.

185 **2.1.3. Direct Pellet Printing Multi-Extrusion (DPPmE).** A PAM
186 Series Lx (Pollen AM, France) printer with four screw-based
187 extruders was used to prepare mono- and multicomponent tensile
188 parts. As shown in Figure 1, the specimens were fabricated by filament
189 deposition layer-by-layer system using a single-screw extruder fed
190 directly with composite pellets.³⁶

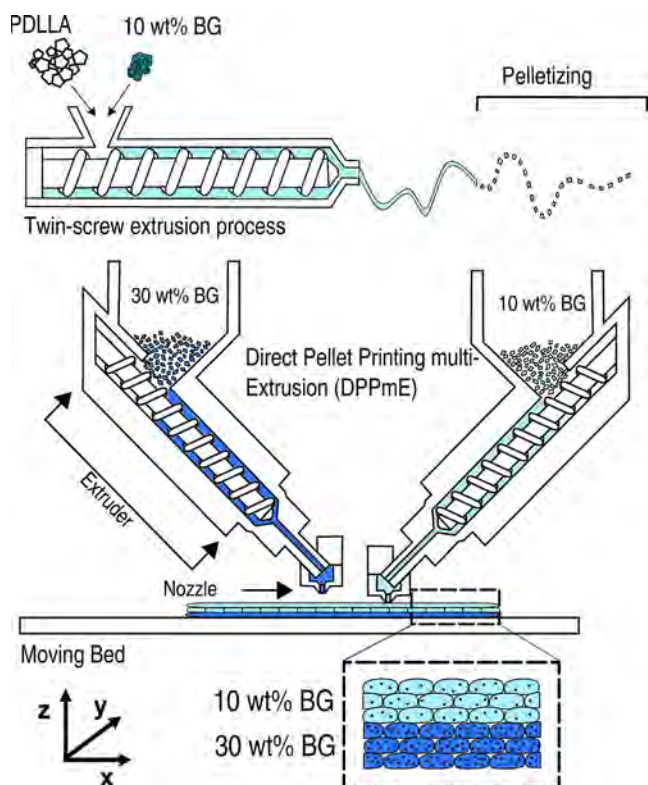


Figure 1. Schematic representation of an example of (top) the composite fabrication and (bottom) the direct pellet printing multi-extrusion process (DPPmE) with 10 and 30 wt % of BG.

191 All of the samples were printed using a nozzle size of 0.4 mm, a
192 $-45^{\circ}/45^{\circ}$ orientation with a layer thickness of 0.2 mm, a filament
193 width of 0.4 mm, and a printing speed of 30 mm/s inside an enclosed
194 temperature-controlled chamber in a white room environment. For
195 the clarity of this study, only results with this speed will be presented.
196 The bed temperature was set at 55 °C. For PDLLA/BG, the printing
197 temperature was set at 160 °C for the extruder and 170 °C for the
198 nozzle. For the PDLLA and PDLLA-HA composites, the temperature
199 was set at 180 and 190 °C, respectively. The different FGM
200 configurations (strategy I, II, and III) studied in this work are shown
201 in Figure 2. Prior to printing, a skirt was printed around the sample to
202 normalize the flow. For multicomponent systems, the polymer in the
203 nozzle was renewed by printing a volume support. The total printing
204 time for the tensile samples was 215 s for strategy I. Before printing
205 the new sample, the remaining melt was extruded in order to remove
206 the composite material from inside the screw. The main objective is to
207 avoid thermal degradation of the residual materials.

208 Five replicas were printed for each strategy. For the clarity purpose,
209 only results with the same filler nature will be shown for each
210 architecture.

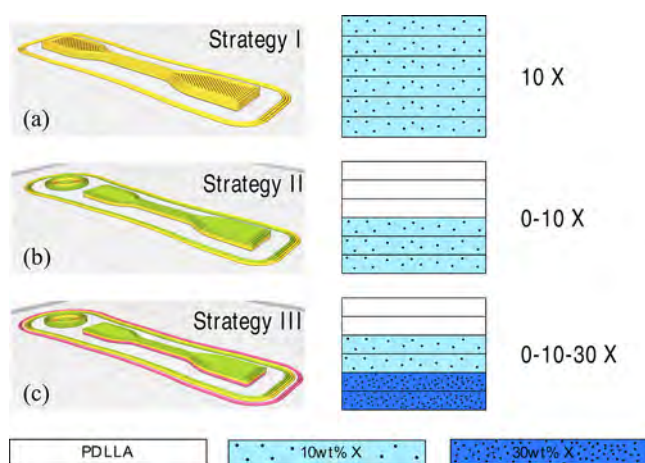


Figure 2. Tensile sample model from a 3D printing software (CURA, Ultimaker) for (a) strategy I, (b) strategy II, and (c) strategy III to print FGM composites with the corresponding layer configurations. X represents the bioactive filler (BG or HA).

211 **2.1.4. Injection Molding.** Tensile dumbbell-shaped bars were
212 prepared on a HAAKE Minijet injection molder (Thermo Fisher
213 Scientific, Cleveland, OH, USA). The injection molding (IM)
214 procedure involved a cylinder temperature at 180 °C and a mold
215 temperature at 55 °C under 800 bar of pressure for 20 s. The tensile
216 tests of dumbbell-shaped fabricated by IM were used as a reference to
217 compare with the mechanical properties of strategy I DPPmE.

218 **2.2. Methods.** **2.2.1. Rheological Analysis in the Linear**
219 **Viscoelastic Regime.** Rheological measurements in small amplitude
220 oscillatory shear (SAOS) were performed with a DHR-2 (TA
221 Instruments, USA) stress-controlled rheometer using a parallel-plate
222 geometry ($\phi = 25$ mm, gap distance 1.2 mm). Sample discs were
223 prepared by hot pressing at 140 °C for 2 min at 40 bars to minimize
224 matrix degradation.³⁷ Dynamic time (at $1 \text{ rad}\cdot\text{s}^{-1}$) and dynamic
225 frequency sweep (from 628 to $0.1 \text{ rad}\cdot\text{s}^{-1}$) measurements in the
226 linear viscoelastic regime were carried out at temperatures
227 corresponding to those in the extruder (160 °C/180 °C) and nozzle
228 (170 °C/190 °C) of DPPmE, respectively, under a continuous
229 nitrogen purge. The LVE characterization is given in [Supporting](#)
230 [Information](#).

231 **2.2.2. Size-Exclusion Chromatography (SEC) Analysis.** The
232 average molar mass in weight and number, \bar{M}_w and \bar{M}_n of PDLLA
233 before and after processing of composites was determined by size-
234 exclusion chromatography (SEC) in chloroform solvent using a tetra
235 detection system equipped with a Schimadzu SPD 20A ($\lambda = 280$ nm),
236 a Wyatt TREOS (3 angles), a ViscoStar II Wyatt and a Schimadzu
237 RID 10A. The SEC system had three columns (PL gel 5 μm Mixed C
238 300×7.5 mm, polystyrene/divinylbenzene), and the analysis
239 temperature was 30 °C. The dn/dc used for PDLLA in chloroform
240 was 0.023, and the concentration of the samples was 3 mg/mL.³⁸
241 Before the SEC analysis, the solutions were filtered with $0.45 \mu\text{m}$
242 filters to remove the BG and HA particles.

243 **2.2.3. Archimedes Method.** The procedure based on the
244 Archimedes method was applied to measure the porosity of different
245 printed parts.³⁹ A Mettler AE100 (Mettler-Toledo Inc., Columbus,
246 OH) analytical balance with a capacity of 100 g and an accuracy of
247 ± 0.01 mg was used for the mass measurements.

248 According to Archimedes' principle and by not considering the
249 open cavities, the density can be calculated as follows

$$\rho_{\text{sample}} = m_{\text{air}} \frac{\rho_{\text{liquid}}}{m_{\text{air}} - m_{\text{liquid}}} \quad (1) \quad 250$$

251 Here, ρ_{sample} is the measured sample density (g cm^{-3}), ρ_{liquid} is the
252 density of the ultra-purified water at room temperature (g cm^{-3}), m_{air}
253 is the mass of the sample in air (g) and m_{liquid} is the mass of the
254 sample in ultra-purified water (g).

255 Finally, the porosity rate of the samples was calculated according to

$$256 \quad \% \text{porosity} = \left(1 - \frac{\rho_{\text{sample}}}{\rho_{\text{theoretical}}} \right) \times 100 \quad (2)$$

257 where $\rho_{\text{theoretical}}$ is the actual density of the composite calculated from
258 additive law ($\rho_{\text{theoretical}} = \sum p_i \phi_i$, with p_i and ϕ_i the density and
259 volumetric fraction of each component).

260 **2.2.4. X-Ray Tomography.** X-ray tomography measurements were
261 conducted using a laboratory X-ray source on an EasyTom tomograph
262 (RX Solutions, France) at high resolution with a 1.5 μm voxel size on
263 small samples ($\sim 1.5 \times 1 \times 1$ mm). This tomograph was equipped
264 with an LaB6 emission tip for the X-ray source, which ensured that
265 the actual spot size was physically smaller than 1.5 μm . This way, the
266 resolution did not become modified by geometric blur. All the data
267 were reconstructed by a filtered back-projection Feldkamp algorithm.

268 **2.2.5. Scanning Electron Microscopy (SEM) Analysis.** SEM
269 micrographs were taken on uncoated samples using a Supra 55
270 microscope (Zeiss, Oberkochen, Germany). The specimens were first
271 cryo-fractured in liquid nitrogen and then observed at low
272 acceleration voltage (1 kV) under high vacuum mode.

273 **2.2.6. Mechanical and Thermomechanical Characterization.**

274 **2.2.6.1. Tensile Testing.** In accordance with ASTM D638, tensile tests
275 were performed on dumbbell-shaped bars with dimensions of $l_0 = 20$
276 mm, $b = 4.2$ mm, and $h = 1.2$ mm for DPPmE and $l_0 = 20$ mm, $b = 4.2$
277 mm, and $h = 2$ mm for IM parts. The measurements were conducted
278 on a universal AGSX 5 kN (Shimadzu Corporation, Ltd., Kyoto,
279 Japan) tensile tester with a crosshead speed of 1 mm/min.

280 **2.2.6.2. Dynamic Mechanical Analysis (DMA).** DMA analysis was
281 performed on hot-pressed and 3D-printed rectangular samples ($h =$
282 0.6 mm, $b = 4.5$ mm, and $l = 12$ mm). Temperature sweep tests were
283 carried out on a DMA Q800 (TA Instruments, USA) in tensile mode
284 at a frequency of 1 Hz and a strain of 0.05%. Storage and loss moduli
285 were determined as functions of temperature from 30 to 120 $^{\circ}\text{C}$ at a
286 heating rate of 2 $^{\circ}\text{C}/\text{min}$.

3. RESULTS

3.1. Dispersion and Microstructural Properties of 3D-Printed Filled Composites (Strategy I).

287 The purpose of
288 this section is to investigate the dispersion properties of BG
289 and HA fillers in PDLLA matrix after compounding and 3D
290 printing. Micro-computed tomography (μCT) and SEM
291 analysis were therefore used to analyze the filler dispersion in
292 the PDLLA matrix. The filler content of each specimen was
293 calculated by image analysis using ImageJ. As shown in Table
294 2, the printed parts presented a slight difference between the
295 compounding filler content and that calculated by ImageJ from
296 the printed parts. For the following section, we have
297 considered the value of the filler content as calculated from
298 the image analysis of the printing parts. The mean values of
299 porosity were measured by Archimedes' method. Interestingly,
300

Table 2. Quantified Porosity and Filler Content of Strategy I^a

sample	wt %	$\rho_{\text{theoretical}}(\text{gcm}^{-3})$	$\rho(\text{gcm}^{-3})$	%porosity
PDLLA	0	1.24	1.22	1.7
PDLLA10-HA	13	1.35	1.28	2.8
PDLLA30-HA	28	1.49	1.47	1.1
PDLLA10-BG-MS	13	1.33	1.26	3.1
PDLLA30-BG-MS	25	1.39	1.36	2.2
PDLLA10-BG-fibers	7.0	1.28	1.23	1.8
PDLLA30-BG-fibers	25	1.46	1.36	1.7

^aWith an error bar of its standard deviation for theoretical density, experimental density and porosity (i.e., 0.03% and 0.1% respectively) and 1%, for wt %.

and according to the porosity study, the specimens of different
301 filler content and nature had a very low porosity (between 1
302 and 3%).

303
304 **3.1.1. Particle Dispersion and Anisotropy from μCT Analysis.** Two methods were employed to quantify the particle
305 dispersion from μCT images: the free-space length (L_f)⁴⁰ and
306 the degree of anisotropy⁴¹ (DA) technique. Both procedures
307 quantified the particle dispersion in the matrix by taking into
308 account the effect of particle size, their content and facilitated
309 the detection of possible defaults during the 3D printing
310 process such as particle aggregation and internal porosity.

311 The free-space length (L_f) has been described by Khare et
312 al.⁴⁰ as the length of the largest observation volume for which
313 the most probable number of contained particles is zero.⁴⁰ As
314 L_f is rather equal to the theoretical free space length of the
315 Poisson distribution (L_p) (i.e., a completely random
316 distribution of particles into the matrix) for the different
317 composites presented in this study, we considered that the
318 particles were dispersed homogeneously. As previously
319 described, the L_f method gives quantitative information of
320 the level of particle dispersion. Although L_f can be calculated
321 for fibres, this technique is more appropriate for calculating the
322 dispersion of spherical particles in the matrix. Moreover, the
323 DA value, with [0,1] boundaries (0 means the dispersion is
324 completely isotropic and 1 extremely orientation in the
325 structure), was used to describe the type of particle orientation
326 as well as the organization using the plugin of ImageJ namely
327 "BoneJ".^{41,42} Therefore, the DA was calculated from the radius
328 of the ellipsoid (D1, D2, and D3) fitted with the mean
329 intercept length (MIL vectors) points as
330

$$331 \quad \text{DA} = 1 - \frac{1}{R_z^2} / \frac{1}{R_x^2} \quad (4)$$

332 with $R_z > R_y > R_x$.

333 Table 3 summarizes the obtained DA results from the
334 printed parts and the particle dispersion properties in the

Table 3. Quantified Dispersions With the Free-Space Length and MIL Vectors

sample	L_f	L_p	DA	R_x	R_y	R_z
PDLLA10-HA	42	52.69	0.06	6.7	6.7	6.6
PDLLA30-HA	34	35	0.06	10.5	10.0	10.0
PDLLA10-BG-MS	50	56	0.14	5.7	5.4	5.3
PDLLA30-BG-MS	42	48	0.08	4.5	4.4	4.3
PDLLA10-BG-fibers	105	65	0.39	8.2	7.9	6.3
PDLLA30-BG-fibers	60	41	0.37	7.3	7.1	5.8

335 printed parts (L_f and L_p). Furthermore, Figure 3a and 3b
336 illustrates the 3D BG-fibres and BG-MS dispersion with 10 wt
337 % in the PDLLA matrix, respectively. BG fibres form an
338 orthotropic structure (i.e., a planar alignment particle on the
339 plane perpendicular to the Z direction), whereas BG
340 microspheres present a homogeneous dispersion. The radius
341 of the ellipsoid in the printing plane was longer than the length
342 in the Z direction ($R_z < R_x, R_y$) and as a result, the filament
343 extrusion induced an alignment of BG fibres in the direction
344 parallel to the nozzle. In the case of the microspheres, the
345 distribution can be considered as completely random (DA ~
346 0).⁴¹

347 **3.1.2. Microstructural Analysis of Printed Composites.**
348 Figure 4 shows the cross-section of strategy I for BG-MS, BG-
349 fibers, and HA fillers. PDLLA/BG and PDLLA/HA printed

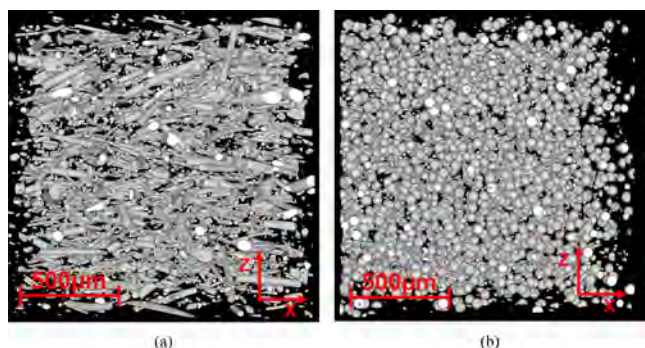


Figure 3. 3D structure of the printed composite reconstructed from μ CT images (matrix hidden) for (a) PDLA-10-BG-fibers and (b) PDLA-10-BG-MS.

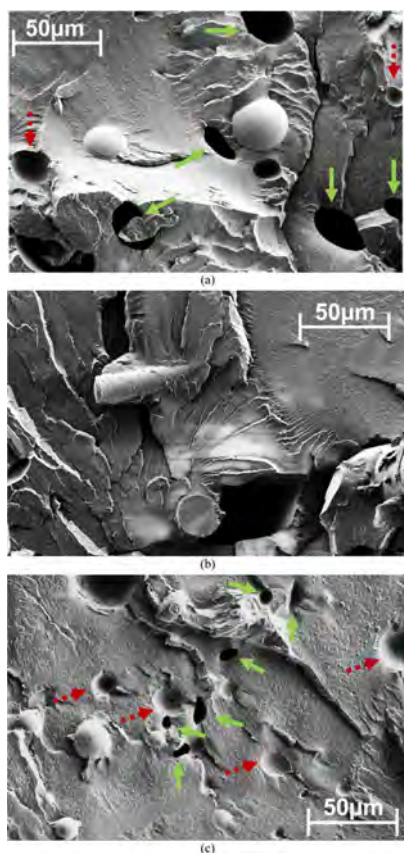


Figure 4. Scanning electron micrograph of cryo-fractured cross sections of strategy I composites (a) PDLA-10-BG-MS, (b) PDLA-10-BG-fibers, and (c) PDLA-10-HA. Red dashed arrows represent the hole of particle loosening and green solid the smaller pores inside the filament.

350 samples exhibited good particle/matrix wetting, with the
351 presence of intra-filament pores (between 10 and 25 μ m),
352 which are specific to composite parts fabricated by a 3D
353 printing extrusion process.⁴³ However, as indicated with red
354 dashed arrows in Figure 4a,c, the BG and HA particles
355 presented a loosening owing to a low adhesion with the
356 surrounding PDLA. HA and BG particles showed the same
357 behavior: good wetting of particles by the PDLA matrix with
358 poor adhesion.

359 **3.2. Investigation of Melt Rheological Properties of**
360 **Filled PDLA Materials.** 3D printing involving material

361 extrusion in the molten state can induce some polymer
362 degradation. The choice of printing parameters must strike a
363 balance between reducing this degradation, ensuring good
364 welding between adjacent printed filaments, and avoiding the
365 maximum torque limits of the screw-extrusion of DPPmE. The
366 3D-printing extrusion process conditions were optimized by a
367 rheological characterization in the linear viscoelastic (LVE)
368 domain. As observed in our previous works,⁸ the degradation
369 kinetics of PDLA is influenced by the presence of BG fillers.
370 Indeed, in the molten state, the presence of BG increases the
371 polymer degradation since the R-Si-O- on the surface of BG
372 catalyzed the ester bond scission of PDLA chains.⁸ Figure 5
373 shows the thermal stability investigated by analyzing the
374 evolution of the relative viscosity (η_r) (Equation 3).

$$\eta_r(t) = \frac{\eta^*(t)}{\eta^*(t=0)} \quad (3) \quad 375$$

376 PDLA and PDLA-HA (Figure 5a) composites showed a
377 slight decrease in the relative viscosity due to the hydrolytic
378 degradation of PDLA.⁴⁴ Interestingly, HA fillers on PDLA-
379 HA composites seem to reduce the hydrolytic degradation
380 since they can absorb the remaining moisture enclosed into the
381 matrix. However, compared with PDLA and PDLA-HA, the
382 BG-based composites presented a higher continuous decrease
383 of the relative viscosity over time.

384 Figures 5b and 5c show that, by reducing the temperature of
385 the thermal stability test from 180 to 160 $^{\circ}$ C, the PDLA-BG
386 composite yielded a smaller decrease of η_r . Therefore, the
387 extruder temperature of DPPmE was set to 160 $^{\circ}$ C for BG
388 composites in order to reduce the polymer degradation during
389 the 3D printing process. Moreover, η_r was also affected by the
390 filler content and shape of the BG particles (e.g., with 30 wt %,
391 the viscosity decreased faster than with 10 wt % of BG).
392 Finally, owing to the high specific surface of BG fibers,
393 composites filled with BG fibers presented a higher decrease in
394 relative viscosity compared to those filled with microspheres
395 (MS). Based on the obtained results, it is really clear that it is
396 possible to decrease the degradation amount of the PDLA
397 matrix by reducing the printing temperature and decreasing the
398 surface contact of BG with the PDLA matrix. Figure 5d
399 presents an overview of the complex viscosity modulus of neat
400 PDLA and its filled composites with HA and BG-MS as a
401 function of the angular frequency. Interestingly, by reducing
402 the printing temperature of PDLA/BG composites up to 20
403 $^{\circ}$ C, we were able to limit the matrix degradation and achieve a
404 similar viscosity to neat PDLA at 190 $^{\circ}$ C.

3.3. Investigation of the Filler Effect and FGM

405 **Structure.** 3.3.1. *Microstructural Analysis of Printed Multi-*
406 *component FGM (Strategy II and III).* Figure 6 shows the
407 cross-section of FGM multicomponent with strategy II (0–10
408 BG-fibers) and strategy III (0–10–30 HA). They exhibit the two
409 examples of interface adhesion between different components
410 and layers. In some cases, SEM images of multicomponent
411 systems presented almost any porosity between layers and
412 filaments (Figure 6a), whereas other samples exhibited inter-
413 filament pores (50–100 μ m) (Figure 6b). Interestingly,
414 specimens fabricated following strategies II and III showed
415 good interface adhesion, regardless of the filler content of the
416 adjacent layers. Hence, the optimization of processing
417 parameters (e.g., printing temperature, printing speed, infill
418 density, or infill pattern) made it possible to achieve systems
419

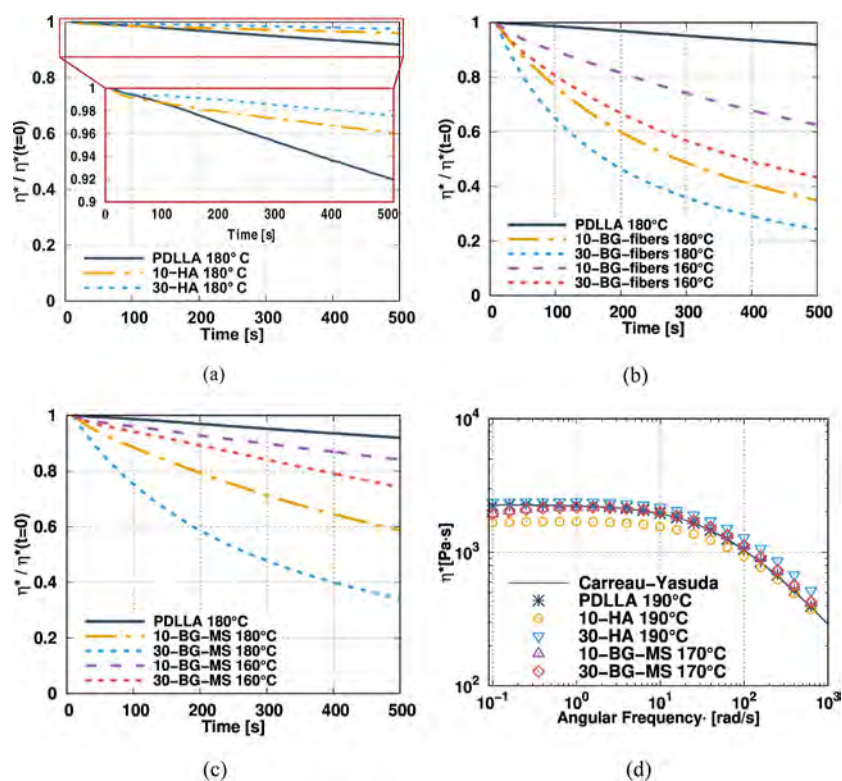


Figure 5. Time evolution of the relative viscosity at 1 rad/s of (a) HA-based composites at 180 °C; (b) BG-fiber-based composites at 160 and 180 °C; (c) BG-MS-based composites at 160 and 180 °C; (d) example of the complex viscosity modulus as a function of the angular frequency of neat PDLLA, PDLLA/HA, and PDLLA/BG-MS composites at the corresponding nozzle temperatures with the Carreau-Yasuda model fitting of PDLLA.

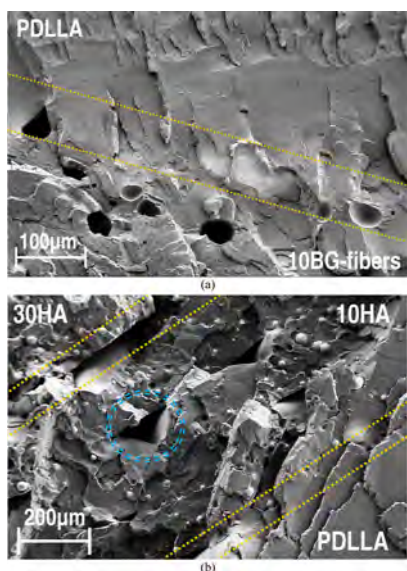


Figure 6. Scanning electron micrograph of cryo-fractured cross sections of the composites taken in the bulk of FGM (a) PDLLA-0-10 BG fibers and (b) PDLLA-0-10-30 HA. Blue solid circle represents the pore between the filaments and the yellow dashed line the interface between different components.

(SEC). The \bar{M}_w values of PDLLA extracted from the 425
composites after the extrusion-compounding step and those 426
of the PDLLA after the 3D printing are compared in Figure 7. 427 17

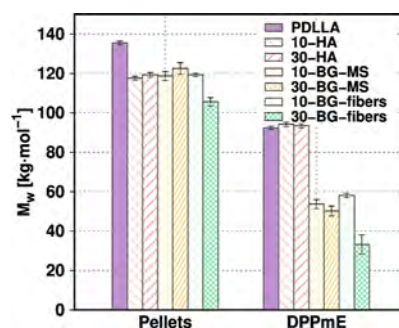


Figure 7. Evolution of the average molar mass (\bar{M}_w) for pellets and printed parts following strategy I with various biocompatible fillers.

A reduction of \bar{M}_w revealed the occurrence of PDLLA 428
degradation during the extrusion-pelletizing steps and the 429
DPPmE process. This reduction in \bar{M}_w after extrusion- 430
pelletizing was similar for all composites except for the 30 wt 431
% BG fibers, which presented a lower \bar{M}_w value. As observed in 432
our previous studies,⁸ the addition of BG increased the matrix 433
degradation, especially when the surface contact of PDLLA/ 434
BG was increased (high filler content or shape factor). 435

As shown in Figure 7, compared with the pellets, the 436
PDLLA/BG specimens displayed a 50% reduction in \bar{M}_w . 437
However, even if \bar{M}_w decreased for the printed parts, the 438
molecular weight remained constant for parts printed under 439

420 with no visual interface or delamination between different 421
layers.

422 **3.3.2. Effect of Filler and DPPmE on the Molar Mass of**
423 **PDLLA.** The average molecular weight values of the pellets and
424 specimens were measured by size exclusion chromatography

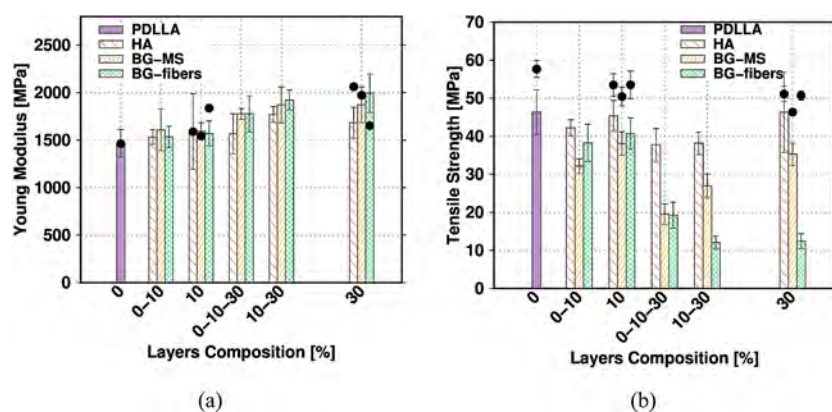


Figure 8. Evolution of (a) E_t (MPa) and (b) σ_{max} (MPa) of composites based on HA, BG-MS, and BG-fibers with various filler content and multicomponent systems. The dots represent the values of injected parts with the same composition.

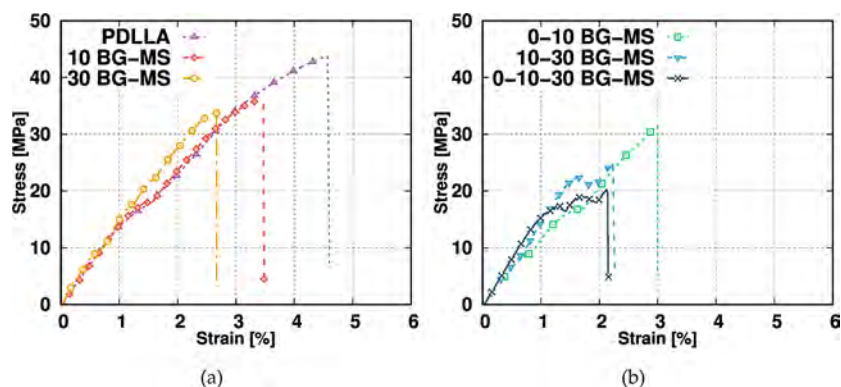


Figure 9. Stress–Strain of BG-MS 3D-printed FGM composites in (a) strategy I and (b) strategy II and III systems.

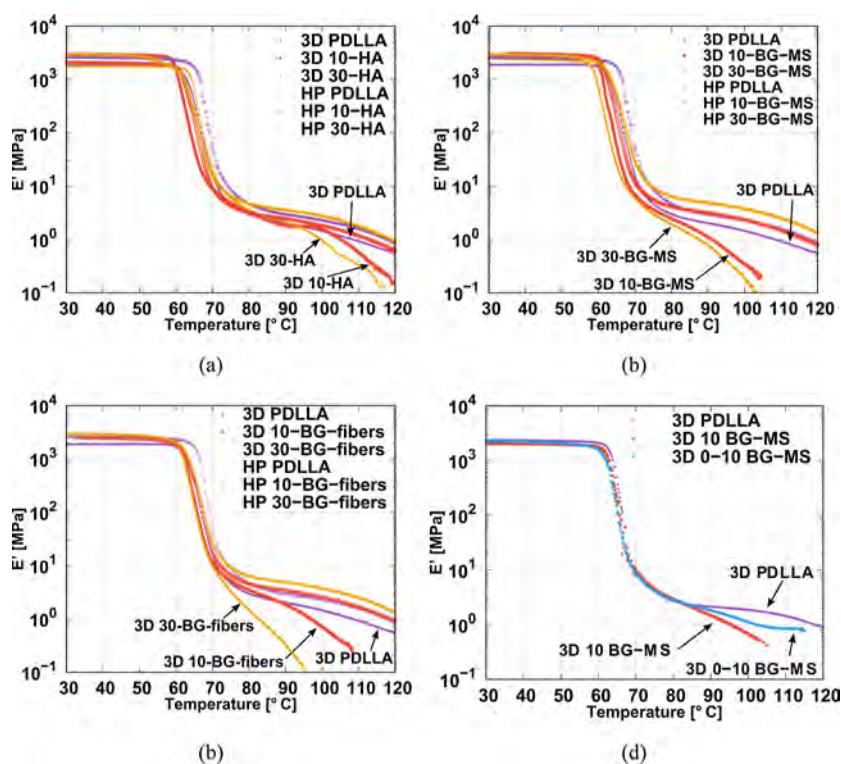


Figure 10. Evolution of E' (MPa) as a function of the temperature for DPPmE (3D) and hot-pressed (HP) samples of (a) HA, (b) BG-MS, (c) BG-fibers, and (d) for DPPmE PDLLA, 10-BG, and strategy II 0–10 BG-MS.

440 similar conditions, confirming a good repeatability of the
441 process. This degradation was thus mainly due to the chemical
442 reaction between PDLA and BG in the molten state.

443 Interestingly, even at high filler contents, printed parts based
444 on HA presented a value of \bar{M}_w close to that of printed
445 PDLA, confirming a low interaction between HA and
446 PDLA. Thus, multicomponent FGM (strategy II and III)
447 combine a bioactive composite with a component presenting a
448 low matrix degradation after processing.

449 **3.3.3. Mechanical and Thermomechanical Properties.**

450 **3.3.3.1. Tensile Testing.** Figure 8a,b displays the evolution of
451 the tensile modulus (E_t) and maximum tensile strength (σ_{\max})
452 as functions of the filler contents and manufacturing strategy.
453 Surprisingly, the Young moduli of the printed parts were close
454 to those observed for injected parts with the same
455 composition. Moreover, multicomponent specimens presented
456 an intermediate modulus between the values of the different
457 constitutive layers.

458 Furthermore, the tensile strength of strategy I systems was
459 rather constant for almost all the different composites; only the
460 one with 30 wt % of BG fibers presented a decreased strength
461 (Figure 8b). However, compared to IM, DPPmE specimens
462 exhibited a lower tensile strength. It seems that the residual
463 stress and polymer chains orientation induced by the process
464 in formers may enhance the tensile strength properties. FGM
465 based on strategy II with HA or 0–10 BG fibers and MS
466 displayed a tensile strength slightly lower than that observed
467 for strategy I systems. However, FGM based on strategy II and
468 III containing 30 wt % of BG exhibited a decreased tensile
469 strength compared to the 0–10 assembly. Lap shear tests
470 confirmed a good adhesion between different components as
471 the fracture occurred in a stress concentration location instead
472 of at the interface between different components (cf.
473 Supporting Information B).

474 As can be seen in Figure 9a,b, a stress fluctuation occurred in
475 the stress/strain curve, suggesting that micro-cracking took
476 place on the interfaces during the tensile tests, thus initiating
477 the breaking of the sample.^{45,46} This fluctuation was more
478 pronounced for multicomponent specimens, especially with a
479 0-10-30 configuration. Thus, even if we considered good
480 interfacial adhesion between layers of different filler content,
481 the layers presenting the worst mechanical properties
482 promoted the fracture of the FGM specimens. For the clarity
483 of this study, we show only the results with BG-MS on Figure 9
484 (since they show higher values of σ_{\max} than BG-fibers).

485 **3.3.3.2. Thermomechanical Properties and Validation of**
486 **FGM Design.** As shown in Figure 10, DPPmE and hot-pressed
487 samples of each content and filler presented the same elastic
488 modulus at a temperature below T_α (the temperature of α
489 relaxation associated with the glass transition). The hot-
490 pressed samples were prepared to eliminate any effect of
491 orientation induced during IM parts. They showed the classical
492 behavior of filled systems, that is, a higher plateau modulus in
493 comparison with PDLA when the filler content is increased.
494 However, for the DPPmE specimens, the rubbery plateau
495 displayed a shift to lower temperatures, and the length of the
496 plateau was reduced for systems containing BG particles. In
497 addition, highly filled systems presented an even shorter
498 domain (e.g., samples with 30 wt % of BG-fibers did not show
499 a plateau as the value of E' decreased continuously as a
500 function of temperature). As a result, the shortening of the
501 rubbery plateau highlighted the matrix degradation induced by
502 the DPPmE process, whatever the nature of the filler.

Figure 10d shows an example of the thermomechanical
properties of the 0–10 BG-MS configuration with the medical
grade PDLA matrix (R207S). The medical grade PDLA and
its composites presented a slightly longer rubbery plateau than
the industrial grade PDLA. Interestingly, the FGM with the
0–10 BG-MS configuration presented a rubbery plateau value
in between the ones of its two own layers. Therefore, the
thermomechanical properties of FGM were improved
compared to 10-BG-MS while preserving the bioactive
properties.

4. DISCUSSION

In this work, the evolution of the relative viscosity is a suitable
tool to probe the thermal sensitivity of PDLA and its
filled composites at the molten state and longer residence
time, simulating the process conditions. In the case of the BG
composites, the viscosity presented a significant decrease with
time due to matrix degradation. At high temperatures, the
silicate groups on the surface of the BG were associated with
counterions and accelerated the PDLA degradation.⁸ Thus,
the thermally induced PDLA degradation could be limited by
reducing the screw and nozzle temperatures for the PDLA-
BG composites. For PDLA and the PDLA/HA composites,
the evolution of the relative viscosity reflected a higher thermal
stability compared to PDLA/BG composites. Moreover, SEC
and DMA measurements confirmed the matrix degradation
obtained by the rheological analysis.

Prior to printing, the melt in the extrusion zone was
extruded in order to eliminate residual material which can be
degraded with time. However, the rheological measurements
highlighted the thermal instability of high-filled BG composites
(30 wt %), and as a result, the BG specimens presented a more
significant decrease in the molar mass of the matrix and a loss
of mechanical properties. As observed by the SEC analysis, the
molar mass was rather stable for successive printing,
confirming the repeatability of the process with thermally
unstable composites.

The microstructural analysis by SEM confirmed good
particle-PDLA wetting for the BG-fibers, the BG-MS, and
the HA microspheres. Compared to HA, BG showed a better
interaction with the matrix; a thin layer of PDLA adhered to
the surface of BG. This difference may be due to the chemical
reaction described in our previous work.⁸ The detection of
filler detaching from the cryo-fractured cross-section of SEM
confirmed a low adhesion with the surrounding PDLA.

Analysis of the μ -CT images of printed parts revealed that
DPPmE enabled a homogeneous distribution of the particles in
the PDLA matrix. For the microspherical fillers, the free space
length (L_f) confirmed the good dispersion. Besides, for the
fiber fillers, the degree of anisotropy indicated a particle
alignment along the printing direction, which may induce an
improvement of the mechanical properties on the beneficial
orientation.⁴⁷ Even if, in general, the SEM images showed that
the layers presented good interfacial adhesion; we observed a
slight porosity (between 1 and 3%) after porosity measure-
ments by Archimedes' method. In addition, the pores observed
in the SEM micrographs, with a size between 10 and 100 μm ,
indicated a fluctuation of flow rate during the extrusion.

Compared to parts fabricated by injection molding, the
presence of internal pores in the 3D-printed parts induced a
decrease in tensile strength. Besides, the value of the standard
deviation of mechanical properties was higher for the 3D-
printed parts.

564 Interestingly, the thermomechanical properties of the hot-
565 pressed PDLA-BG composites presented the classical
566 behavior of filled systems: the storage modulus increased for
567 a higher filler content. However, the printed samples presented
568 a decrease in E' and a shortening of the rubbery plateau, which
569 indicated some degradation of the matrix. Thus, the pre-
570 processing step of compounding had a smaller effect than the
571 DPPmE process.

572 The second objective of this article was to study the
573 possibilities of 3D-printed multicomponent parts with
574 bioactive filler for load-bearing implants. First, multicompo-
575 nent systems with two (strategy II) and three (strategy III)
576 content types were more difficult to process as the thermal
577 stability of more than one composite in different extruders
578 needed to be controlled for alternative printing. As observed by
579 SEM, an incomplete healing of the adjacent layers led to a
580 visible interface between the two layers. However, the FGM
581 interface exhibited good properties as for lap-shear on
582 bicomponent 3D-printed parts, the fracture occurred in stress
583 concentration location of bulk material (Supporting Informa-
584 tion A). Tensile tests revealed that the printed FGM with a
585 composition of 0-10-30 and 10-30 wt % of BG presented poor
586 tensile strength, whereas samples with the same composition of
587 HA showed a behavior close to that of systems printed with
588 strategy I. The fracture mechanisms of PDLA/BG and
589 PDLA/HA composites were driven by the micro-cavitation
590 and particle debonding.

591 Furthermore, system manufactured following the strategy II
592 with 0-10 wt % (even BG or HA) presented good mechanical
593 properties. Dynamic mechanical analysis revealed that the
594 FGM strategy increased the thermomechanical properties since
595 the rubbery plateau displayed a behavior between the 3D-
596 printed PDLA and the 10 BG-MS. Hence, the strategy II
597 systems containing 0-10 wt % of BG seemed to introduce a
598 different approach for the fabrication of FGM by 3D printing,
599 as they contained a bioactive layer and a layer with a low-
600 degraded matrix. Otherwise, the presence of HA in hybrid
601 HA/BG FGM composites seems to play an interesting role to
602 balance mechanical properties. The printed PDLA layers
603 played a role of mechanical support for the bioactive PDLA-
604 BG layers.

5. CONCLUSIONS

605 The aim of this work was to study the rheological,
606 microstructural, and mechanical properties of PDLA-BG
607 and PDLA-HA composites when processed by DPPmE
608 multi-screw extrusion. This innovative manufacturing techni-
609 que presented the advantage of producing functionally graded
610 materials (FGM) with tailored properties for bone regener-
611 ation.

612 First, a significant influence of the processing temperature
613 was detected by rheological analysis. Indeed, the molar mass
614 measured by SEC revealed that DDPmE caused significant
615 polymer degradation due to the chemical reactions of BG and
616 HA. Thus, in order to assure a repeatability of the final
617 properties and reduce the polymer degradation, the residence
618 time and temperature of PDLA in the extrusion mechanism
619 had to be controlled.

620 Microspheres and fibres fillers were used to create a system
621 presenting bioactive and mechanical properties.

622 The HA and BG fillers were homogeneously distributed
623 within the PDLA matrix in 3D printed systems as confirmed
624 by SEM and μ -CT analyses. The filler particles exhibited a

good wetting with the surrounding matrix. Interestingly, the
625 non-detection of an interface between adjacent layers of
626 systems based on strategies I, II, and III by SEM analysis
627 confirmed solid welding during 3D DPPmE. Moreover, they
628 presented low internal porosity. The addition of BG reduced
629 the tensile strength of the composite and increased the Young
630 modulus. Besides, the addition of HA did not lead to a notable
631 impact on the mechanical properties. Although the tensile
632 strength of the systems fabricated with strategies II and III was
633 slightly lower when compared with the respective composites,
634 we believe that the combination of BG and HA layers of
635 different content will, under in vivo conditions, present good
636 bioactivity and a higher mechanical resistance during
637 implantation. 638

639 Finally, this study showed the potential of DPPmE multi-
640 extrusion for the manufacturing of orthopaedic implants with
641 bioactive fillers while assuring good mechanical properties and
642 complex geometries. Even if the effect of hydrolytic
643 degradation of PDLA matrix in the molten state was
644 minimized by the experimental protocol, the contact of BG
645 fillers with PDLA still influenced the molar masses of PDLA
646 at high processing temperatures. Hence, the authors believe
647 that FGM combining a low-degraded (with HA fillers) and a
648 bioactive layer (with BG fillers) is a key to tune the bioactivity
649 during in vivo implantation. Further investigations of FGM
650 systems based on PDLA and bioactive fillers immersed in
651 phosphate-buffered saline (PBS) solution will be performed to
652 study the evolution of the morphological, microstructural, and
653 mechanical properties of systems produced by DPPmE. 653

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at
654 <https://pubs.acs.org/doi/10.1021/acsapm.2c01475>. 655

656 Comparison between the physico-chemical properties of
657 industrial and medical grade PDLA, lap-shear results,
658 FTIR spectroscopy to describe the degradation mech-
659 anisms, rheological investigation of the linear viscoelastic
660 regime, and additional data of mechanical and
661 thermomechanical properties of DPPmE parts (PDF) 662

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