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MECHANICAL PROPERTIES OF 3D PRINTED PLA SCAFFOLDS FOR BONE REGENERATION

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Abstract: The growing interest in biodegradable scaffolds for bone regeneration created a need to investigate new materials suitable for scaffold formation. Poly(lactic acid) (PLA) is a polymer commonly used in biomedical engineering, e.g. in tissue engineering as a biodegradable material. However, the mechanical behavior of PLA along its degradation time is still not explored well. For this reason, the mechanical properties of PLA scaffolds affected by incubation in physiological medium needs to be investigated to show the potential of PLA to be used as a material for biodegradable scaffold formation. The purpose of this research is to determine the mechanical properties of PLA scaffolds before and after incubation, and to apply constitutive material models for further behavior prediction. Two sets of PLA scaffolds were printed by the 3D printer “Prusa i3 MK3S” and sterilized by ultraviolet light and ethanol solution. The first set of specimens was incubated in DMEM (Dulbecco’s Modified Eagle Medium) for 60, 120, and 180 days maintaining 36.5 °C temperature. The mechanical properties of the scaffolds were determined after performing the compression test in the “Mecmesin MultiTest 2.5-i” testing stand with a force applied at two different speed modes. The obtained data was curve fitted with the hyperelastic material models for a model suitability study. The second set of specimens was incubated in PBS (Phosphate Buffered Saline) for 20 weeks and used in a polymer degradation study. The obtained results show that the mechanical properties of PLA scaffolds do not decrease during incubation in physiological medium for a predicted new bone tissue formation period, though hydrolysis starts at the very beginning and increases with time. PLA as a material seems to be suitable for the use in bone tissue engineering as it allows to form biocompatible and biodegradable scaffolds with high mechanical strength, required for effective tissue formation.

Key words: scaffold, bone regeneration, poly(lactic acid) (PLA), biodegradable polymers, mechanical properties, hyperelasticity

1. INTRODUCTION

The increasing average age and the growing frequency of bone and joint disorders [1] lead to a greater need for the use of polymeric scaffolds [2], which makes the composition of a scaffold and the production methods of the ideal scaffold particularly important. Scaffolds are used in the treatment of bone fractures, especially in people with bone diseases, e.g. osteoporosis, because the bone has a reduced ability to repair itself, and scaffolds support the growth of bone tissues [3,4].

In order to create a suitable and adapted biodegradable scaffold for effective bone healing, the desired bone regeneration time should be considered, which can vary in duration and depend on many factors: human health, age, bone size, trauma, received load, etc. [5]. However, adjusting the mechanical and degradation properties of the scaffold to the required ones is not an easy task. The composition of the scaffold, its structure, manufacturing method, and the environment in which the scaffold operates are the key factors in determining whether the scaffold will maintain the desired functions over time [6]. It is well known that poly(lactic acid) (PLA) itself possesses certain mechanical properties that influence the scaffold's behavior. It is a stiff material with relatively low ductility and does not form toxic compounds during hydrolysis, therefore, it has been used in biomedicine for a long time [7]. Moreover, its mechanical properties can be modified by adjusting the printing parameters, blending with other materials, or incorporating additives such as reinforcing fibers or particles. PLA composites and manipulation of their mechanical properties by creating different scaffold compositions are widely discussed in the literature [8,9,10]. However, hydrolysis of these composites may release substances that alter pH or otherwise emerge an immune response [11]. The manufacturing method also determines the change in the properties of the scaffold and should be selected, for example, according to the desired size of the pores or the temperature resistance of the material [12].

Mechanical properties such as compressive strength, tensile strength, and elastic modulus are commonly evaluated to assess the scaffold's mechanical integrity [13]. Moreover, the mechanical strength of the 3D-printed PLA scaffold is a critical factor for successful bone regeneration. It determines the scaffold's ability to provide initial structural support and withstand mechanical forces during healing. This raises a new challenge for this study: not only to determine whether the polymer is suitable for use in the bone regeneration process and retains its mechanical properties for the required time but also to check the suitability of constitutive models to predict further material behavior [14].

Common printing techniques include fused deposition modeling (FDM), stereolithography (SLA), and selective laser sintering (SLS). Each technique has its advantages and limitations in terms of resolution, accuracy, and mechanical properties. For example, FDM-printed scaffolds tend to have anisotropic mechanical properties due to the layer-by-layer deposition process. Recently, 3D printing is increasingly used in various fields of science and industry, due to the possibility of creating models with complex shapes while maintaining high quality standards and high precision [15,16,17]. The advantage of using 3D printing in the production of scaffolds is the possibility of obtaining individual projects with a resolution in the micrometer scale and production without wasting materials. 3D printing technology allows for greater possibilities of producing scaffolds in relation to the size and distribution of pores [18,19].

Therefore, the purpose of this research is to investigate the mechanical properties of PLA scaffolds for bone regeneration and their changes after incubating the scaffolds in physiological medium as well as to determine the degradation of the scaffolds over time. The study addresses the change in the mechanical properties of PLA and the ability to meet the mechanical sustainability of bone tissue.

2. MATERIALS AND METHODS

The research was performed in the laboratories of Vilnius Gediminas Technical University. PLA scaffolds with 90% porosity were printed by the 3D printer "Prusa i3 MK3S" using FDM (Fused Deposition Modeling) technology. A nozzle temperature of 215 °C and a heated bed temperature of 60 °C were set for the 3D printing. This printer has a nozzle diameter of 0.4 mm. In order to ensure the favorable performance of printed products, the layer height should be adjusted to the diameter of the nozzle. This procedure affects the value of interlayer cohesion. A widely accepted mathematical model is used to determine the optimum printed layer height: $\mathrm{h} \leq 0.75 \cdot \mathrm{D}$ [20]. CAD model used to print specimens is presented in Fig. 1, and 3D printed PLA scaffolds are shown in Fig. 2. Two sets of PLA scaffolds were printed: the first set was used to determine the mechanical properties of the scaffolds, while the second one was involved in a polymer degradation study. The outer dimensions of the printed sample were checked with a micrometer. Regarding length and width dimensions, PLA revealed the accuracy with a minimum shape error of 0.05%.

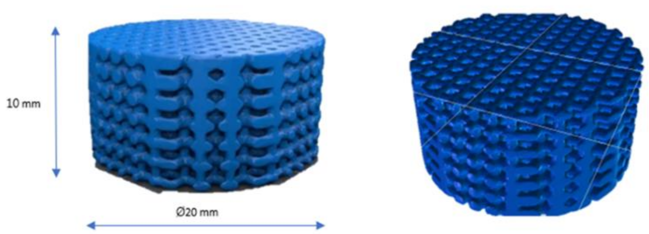

Fig. 1. CAD model, used for 3D printing of scaffold specimens

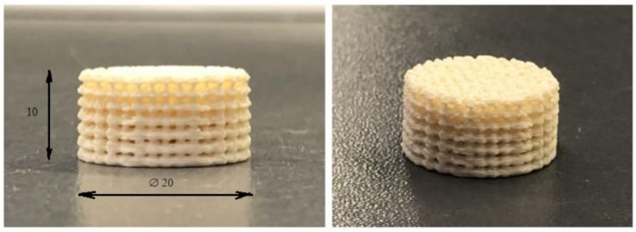

Fig. 2. 3D printed PLA scaffolds

For the more reliable scientific study, specimens must be sterilized to avoid microbial contamination. Contaminated container, specimen, or incubation medium can cause unwanted bacterial growth and formation of enzymes, which might affect PLA hydrolysis. For this reason, the printed scaffolds were sterilized using ultraviolet light and 70% ethanol solution. Such methodology was selected after analyzing method efficiency and possible impact on the mechanical properties of the polymer [21].

In order to determine the mechanical properties of PLA scaffolds, a variety of methods are used providing diverse data on the similarities of scaffold mechanical properties with the ones of natural bone tissue. Such data can be used to develop superior scaffolds for bone regeneration. The method applied in this study is scaffold incubation in physiological medium. DMEM (Dulbecco's Modified Eagle Medium) is a widely used base medium for the growth of many mammalian cells, such as fibroblasts, neurons, glial cells, human umbilical vein endothelial cells (HUVEC), muscle cells, and other cell lines. PLA scaffolds were incubated in a sterile DMEM, maintaining a temperature of 36.5 °C. 20 identical samples were printed from PLA. Specimens were separated into 4 groups and each group was incubated for a different period of time: non-incubation period, 60, 120, and 180 days (Fig. 3).

Fig. 3. Incubation of scaffold specimens in DMEM

The mechanical properties of PLA scaffolds were identified after each incubation period. The compressive force of 800 N was applied to each specimen for 20 cycles at two different loading speed modes: 500 mm/min and 10 mm/min. To study the mechanical properties of PLA scaffolds, the forces acting on the place where the scaffold will be implanted should be taken into account. When a person walks or runs, the force starts to rise from zero when the weight is transferred from the rear leg to the front leg. When walking slowly, a force equal to the weight of a person acts on one leg (suppose a person weighs 80 kg, the force acting on his legs while walking would be equal to a force of 800 N). The maximum loading speed of the testing machine of 500 mm/min was chosen to simulate the mechanical load on the leg

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bone during slow walking. 10 mm/min simulates the mechanical load of the arm support. Low-cycle fatigue tests were applied. All experiments were performed in the "Mecmesin MultiTest 2.5-i" force testing stand (Fig. 4). The MultiTest-i is a versatile tensile and compression tester controlled by Emperor software running on a PC. The measurement accuracy is ±0.1% or ±0.25% of the capacity of the load cell. The loadcells measure from zero and cover the range ffrom 2 N right up to 2.5 kN.

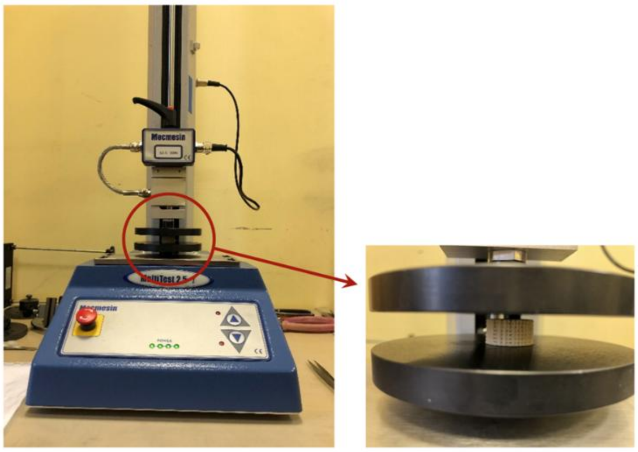

Fig. 4. Compression test performed in the "Mecmesin MultiTest 2.5-i" force testing stand

In addition, a degradation study was performed to determine PLA hydrolysis in time. For this purpose, PLA scaffolds were incubated in PBS (Phosphate Buffered Saline) solution for 20 weeks, maintaining 36.5 °C temperature. Every week specimens were taken out of a buffer, dried, and weighed by analytical scales. Additionally, the pH level was measured using a calibrated pH meter. After that, all specimens were placed in a fresh PBS buffer for further incubation. Transferring samples to fresh PBS buffer after pH measurement and drying helps to maintain a constant environment for further incubation. This ensures that any changes in the specimens are due to the experimental conditions rather than potential variations from the previous buffer. It provides a stable baseline for accurate and reliable results in medical research. Observation of the surface of the samples was carried out on a confocal microscope (Olympus Olympus Lext OLS 4000) after various incubation times in PBS solution.

3. RESULTS

3.1. Mechanical properties study

The mechanical properties study of PLA scaffolds consists of two parts: A and B, each corresponding to different compressive loading speed mode of 500 mm/min and 10 mm/min, respectively.

Study A suggests that maximum strain values in the scaffolds with respect to compressive loading increase over the incubation period. During 6 months of incubation, these values changed on average by 0.0073, and, as shown in Fig. 5A, linear and polynomial regressions of data can help to predict the increase of maximum strains during incubation over a longer period of time. The trend of the results in study B is the same: the maximum strain values of PLA samples increase over time. During 6 months of incubation, the maximum strains in PLA scaffolds changed on average by 0.0015, and regression models (Fig. 5B) suggest that these values will slightly increase along degradation time.

Stress and strain curves of study A (Fig. 6) show that the curve shifts more to the right along the x-axis with increasing incubation time but there are no other features that could be compared. Meanwhile, stress and strain curves of study B (Fig. 7) show no significant changes between incubations. Comparison of studies A and B showed no clear differences that could be distinguished (test data in Fig. 6 and 7 are marked in red).

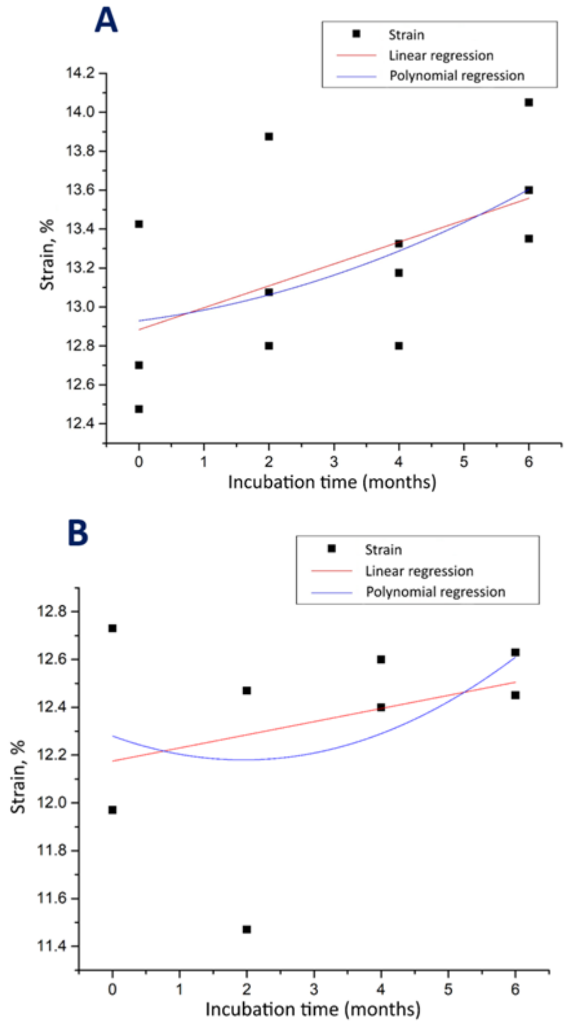

Fig. 5. Maximum strain values in the scaffolds with respect to compressive loading at two different loading speed modes: 500 mm/min (A) and 10 mm/min (B)

In addition, constitutive material models were curve fitted to the test data for further analysis and the possibility to predict the mechanical behavior of PLA scaffolds with respect to incubation time. Various constitutive models suitable for the prediction of material behavior are described in the literature [22]. Due to the nonlinear stress and strain feature, the classical linear elastic model is not suitable for large deformations. Thus, taking into account the nature of this biodegradable polymer, common hyperelastic material models were used: the 2nd order reduced polynomial model and the Mooney-Rivlin model. The development of such models makes it possible to predict the mechanical behavior of a biodegradable scaffold during its life cycle. The stress

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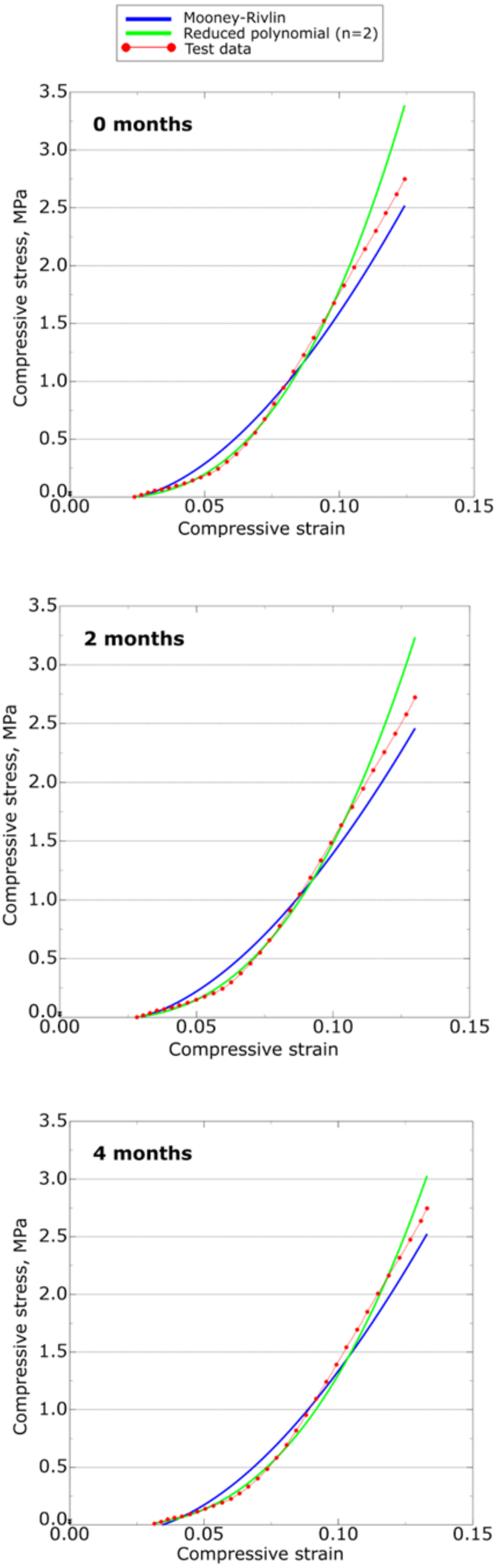
and strain diagrams for both studies are presented in Fig. 6 and 7, showing the fitted Mooney-Rivlin (blue line) and reduced polynomial (green line) curves.



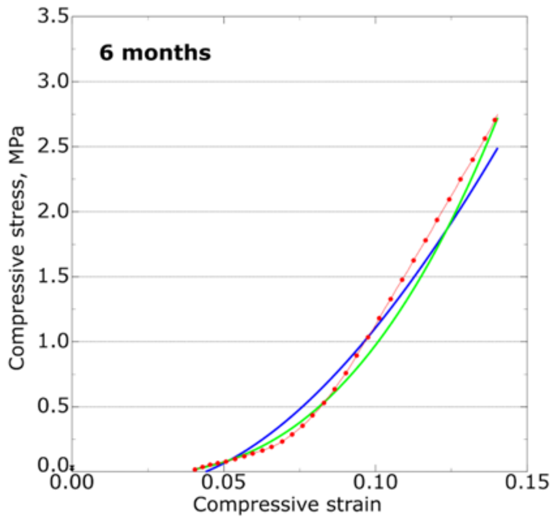
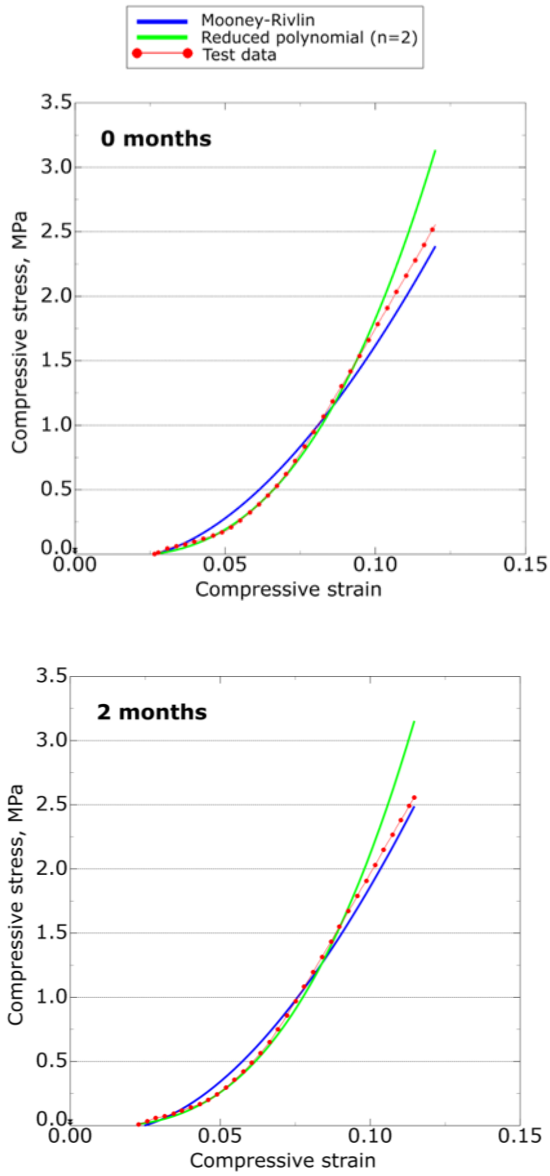


Fig. 6. Study A: stress and strain test data curve fitted with the hyperelastic material models (loading speed is 500 mm/min): 0 months – unincubated samples; 2, 4 and 6 months – incubation period



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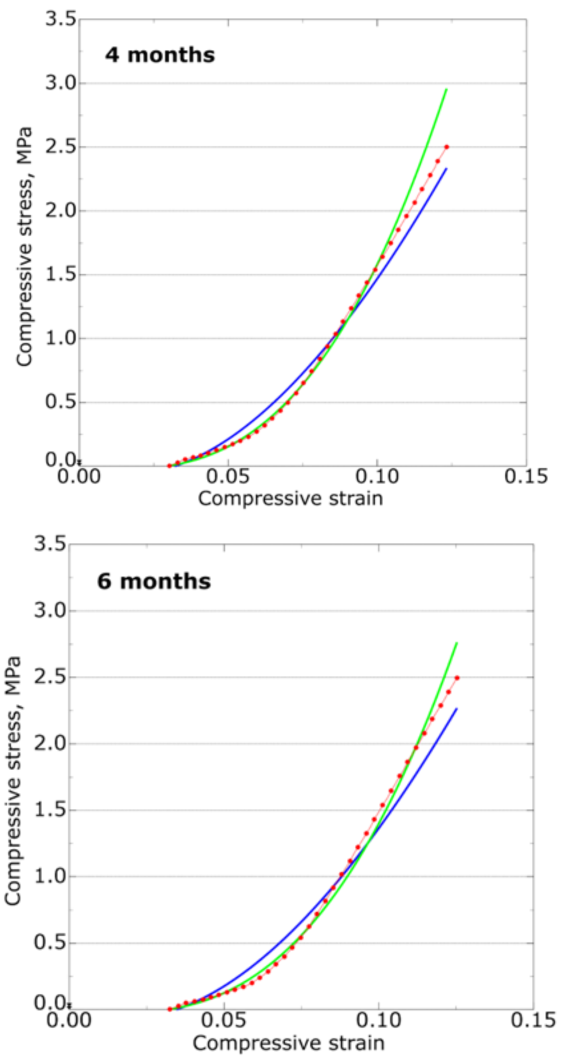

Fig. 7. Study B: stress and strain test data curve fitted with the hyperelastic material models (loading speed is 10 mm/min): 0 months – unincubated samples; 2, 4 and 6 months – incubation period

The Mooney-Rivlin hyperelastic model is commonly used when modeling the nonlinear behavior of high-strain uncompressed materials [23]. It is important to understand that this model does not provide any specific insight into the behavior of the material. It is only a curve of various polynomial data that allows to predict further behavior of the polymer. Fig. 6 and 7 show that the reduced polynomial model is less accurate than the Mooney-Rivlin model. The material parameters C10 and C01 of the Mooney-Rivlin model as well as C10 and C20 of the reduced polynomial model were examined for each specimen (Tables 1 and 2).

Tab. 1. Study A: material parameters of the Mooney-Rivlin and reduced polynomial models

Incubation time, months	Mooney-Rivlin		2nd order reduced polynomial	
	C10	C01	C10	C20
0	–26.8901	26.1858	–0.1948	59.5980
2	–26.0619	25.2424	–0.2288	50.9024
4	–26.8167	26.0130	–0.2104	49.6285
6	–25.3135	24.3870	–0.2692	36.4299

Tab. 2. Study B: material parameters of the Mooney-Rivlin and reduced polynomial models

Incubation time, months	Mooney-Rivlin		2nd order reduced polynomial	
	C10	C01	C10	C20
0	–28.8934	28.0161	–0.2577	63.2575
2	–30.3108	29.5503	–0.2734	55.4032
4	–27.7097	26.8852	–0.2747	53.5780
6	–27.5727	26.7106	–0.3015	50.5683

The regression of the Mooney-Rivlin material parameter C10 for studies A and B are shown in Fig. 8. The coefficients obtained during this curve fitting reveal that the material is unstable for all strains because the sum of the coefficients is below zero. However, with these coefficients, it is still possible to model a longer-term incubation stress and strain curves and predict further mechanical behavior of the scaffolds.

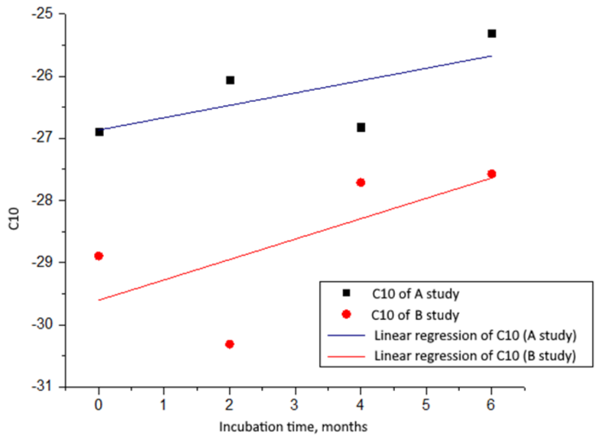

Fig. 8. Evolution of Mooney-Rivlin material parameter C10 in time

3.2. PLA degradation study

The results of the PLA degradation study show that on average the scaffolds lost about 10% of their weight during the incubation time of 20 weeks. The scatter of the results and their regression is shown in Fig. 9. By modelling further PLA degradation, it can be estimated that PLA would lose up to 20% of its weight over the next 14 weeks of incubation.

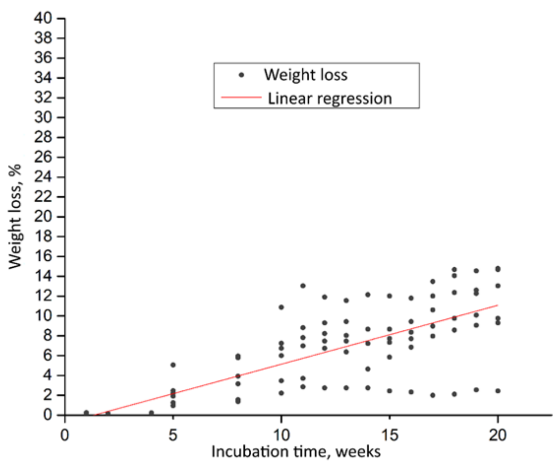

Fig. 9. PLA weight loss over time

The observed degradation is quite high, which possibly occurs due to the erosion of the scaffolds. However, the present study confirms that while PLA scaffolds degrade, no toxic compounds that would cause an adverse reaction in the human body or during cell growth in vitro are produced. In addition, the pH level measured throughout the study did not change much and remained in the range of 7.0 to 7.4. No precipitation or color change was observed as well.

Figure 10 shows the surface of printed scaffolds conditioned at different times. Fig. 10a shows a PLA sample before incubation in solution. Printed paths have an even surface. There are no widenings in the print paths overlapping subsequent layers, which is visible in samples after incubation in the solution. The surface area of the samples after 5 and 10 weeks was similar (Fig. 10b and c). The 3D printing paths are of equal size and the scaffold walls have the regular shape of the FDM filament extruder. The first changes in the shape of the scaffold walls are visible after 15 weeks. The walls of the scaffolds have narrowing, especially in the spaces where the filament does not lean against the wall from the lower layer (Fig. 10e). In addition, there are pits on the surface, which additionally indicate the degradation process (Fig. 10f). Extending the incubation time of the printed scaffolds resulted in further degradation (Fig. 10d). The walls of the scaffolds were irregular, with large narrowings, and the last layer separated.

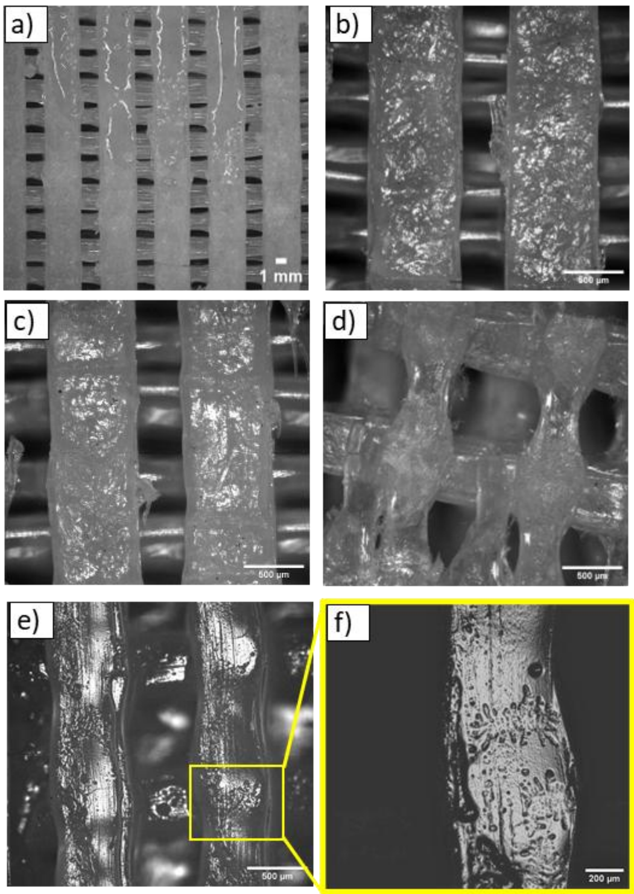

Fig. 10. Surface of printed scaffolds after different incubation time in PBS solution: a) 0 weeks, b) 5 weeks, c) 10 weeks, d) 20 weeks, e, f) 15 weeks

4. DISCUSSION

PLA polymer and other copolymers of this material have been widely studied for many years and have a wide range of applications [24]. Although the polymer is being studied at a fundamental level, further research is needed for a more complete understanding of its material properties. This paper presents a way to study the mechanical properties of PLA by manipulating environmental conditions such as temperature, incubation medium, or incubation time. The study confirms that PLA scaffolds are very strong and can withstand extremely high loads.

The results obtained during the present study suggest that the PLA scaffolds did not lose their mechanical strength over incubation time unlike the PLA-PCL copolymer, which was studied by Vieira et al. [9]. In their study, the authors found that under incubation conditions similar to ours the Mooney-Rivlin model parameters of PLA-PCL change much faster, and the material parameters of scaffolds incubated for 16 weeks are twice as big as the ones of non-incubated specimens. Also, comparing the results published by Tew and Bhatia [25] with the ones in the Vieira's study [9], the most suitable mathematical model for describing the behavior of polymers was identified to be the Mooney-Rivlin. Some experiments that determined the accuracy of this model and its possible further applications for the prediction of the material behavior can also be found in the literature [9,23,25,32].

The experimentally determined nonlinear behavior of the material in the present study increases the importance of computational modeling, which can help to understand how the scaffold will behave in a given environment, and to optimize the application of the scaffold for the use in the medical field. A number of developed mechanical behavior models are used to predict the behavior of a material under different loads and environments [22]. These models, if used correctly, can provide insights into the response and subsequent behavior of the required material. Due to the strong interest in this field from both science and industry, the computational modeling of material behavior is and will become more important in the future.

Despite all the advantages of process optimization and microstructural characterization, there is still a lack of an understanding of the mechanical behavior of porous scaffolds while in the human body [6]. One of the unique properties of biodegradable polymers is their ability to degrade under biologically favorable conditions [26]. Degradation, which is a major reason for the successful use of PLA for medical applications, depends on the molecular weight and microstructure of the material, the degree of crystallinity, and the applied chemical and mechanical loading.

While comparing the results obtained during the present study with the ones published in [9] where PLA-PCL composite scaffolds lost 20% of their weight in 28 weeks and a greater change in mechanical properties was observed, it can be concluded that PLA scaffolds degrade at a similar rate but do not lose their mechanical strength. Also, a comparison with the study published by Guo et al. [27] can be made, in which PLA weight loss of 83% after 240 days of incubation in physiological medium was observed. Compared to the results obtained in the present study, the degradation of PLA differs significantly, and by following our estimated degradation model, we can expect up to 20% of PLA degradation over the next 100 days of incubation. However, with the prolonged incubation, the degradation described by linear regression can progress to become exponential thus increasing to significantly higher numbers.

The surface of printed scaffolds can undergo changes over time when incubated in a phosphate-buffered saline (PBS) solution. The specific changes observed depend on several factors, including the material composition of the scaffold, the printing technique used, and the environmental conditions during incubation. Initially, the degradation process was slow, which is confirmed by the literature. Weight loss of conditioned samples was small after 10 weeks, and there were no significant differences on the surface, similar behavior of scaffolds is in the work [27,29]. In the work [29], it was noticed that the parallel arrangement of beams in a layer of the printed scaffold, and the arrangement of successive layers at an angle of 90°, may contribute to faster degradation. In paper [30], a PLA scaffold was studied and compared to a PLA composite with 316L powder. Degradation was tested after 1 week and 1 month. Already after a week, the first defects between the printed layers were noticed, which increased with the extension of the incubation time. In the work of Zhu et al. [31], in which pure PLA was compared with PLA with PEG addition, the biodegradation process in PBS solution after 4, 8 and 24 hours was studied. It was noted that the biodegradation of PLA is a slow process, as no changes were observed after 24 hours. This work also noted a longer biodegradation time as mentioned in Section 3.2. the first changes in the samples were noticed after 15 weeks.

5. CONCLUSION

A study of the mechanical properties of PLA scaffolds for bone regeneration revealed that maximum strain values in the scaffolds with respect to compressive loading of 800 N increases over the incubation period. During study A (loading speed of 500 mm/min), it was found that the deformation of scaffolds changed from 12.87% to 13.67% after 6 months of incubation. In study B (loading speed of 10 mm/min), the deformation of scaffolds changed from 12.35% to 12.54%. Such differences are indeed small. The stress-strain curves look similar and do not differ much over all incubation times, though a slight shift along the x-axis of the curve in study A was observed. This suggests that PLA scaffolds did not change their mechanical properties during incubation much. Such results and the coefficients obtained from the curve fitted Mooney-Rivlin model allow to state that the change in the mechanical properties of the material is insignificant and would not affect the effective bone formation.

The degradation study confirms that PLA degrades and loses an average of 10% of its weight during 20 weeks of incubation and that the hydrolysis does not release any toxic compounds. As the pH did not change much and remained neutral (in the range of 7.0 to 7.4), no precipitants or changes of solution color were observed throughout the study.

To summarize, it can be concluded that the mechanical properties of PLA scaffolds do not change much during incubation in physiological medium and such scaffolds could support an effective formation of bone tissue, which lasts for about 6 months. PLA would degrade in the human body over a longer period of time than the required one for the bone formation, and would not impair cell development as it does not form any toxic compounds.

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