Turkish Journal of Clinics and Laboratory

To cite this article: Sezgic M, Serel S. The effect of poly-l-lactic acid dermal filler on tendon healing. Turk J Clin Lab 2025; 1: 140-149.

Research Article

The effect of poly-l-lactic acid dermal filler on tendon healing

Poli-l-laktik asit bileşenli dermal dolgunun tendon iyileşmesi üzerine etkisi

Melihcan Sezgiç*, Savaş Serel

Department of Plastic, Reconstructive and Aesthetic Surgery, Ankara University Faculty of Medicine, Ankara, Turkey

Abstract

Aim: Tendon healing is a slow and complex process that often results in incomplete recovery of mechanical strength. Collagen plays a key role in tendon integrity, and poly-L-lactic acid (PLLA) has been shown to enhance collagen synthesis. This study aimed to investigate the effects of PLLA-based dermal fillers on tendon healing in a rat model.

Material and Methods: Twenty four Wistar Albino female rats were divided in two groups randomly as Control group and PLLA group. In control group, right achilles tendon was cut from 4 mm proximal to its calcaneal insertion. In PLLA group, following the same procedure, PLLA-based dermal filler was injected in between 2 tendon sections. Rats were sacrified after 3 weeks and tendons were excised to examine macroscopically, biomechanically and histologically according to parameters. Histological scoring was evaluated according to Bonar Criterias.

Results: The mean macroscopic scores between the PLLA and control groups did not differ significantly (4.8 ± 0.7 vs. 4.4 ± 0.7, p = 0.178). Biomechanical analysis revealed significantly less reduction in failure load) and stiffness in the PLLA group compared to the control group (-14.0 ± 7.0 vs. -21.3 ± 6.3 N, p = 0.041; -7.1 ± 1.7 vs. -10.4 ± 2.2 N, p = 0.026; respectively). The control group had higher histological scores compared to the PLLA group (7.5 ± 1.0 vs. 5.2 ± 1.0, p = 0.004).

Conclusions: PLLA-based dermal fillers may enhance tendon healing by preserving biomechanical strength and improving histological organization, highlighting their potential as a minimally invasive treatment approach for tendon injuries.

Keywords: Collagen, poly-l-lactic acid, PLLA, tendon healing

Corresponding Author*: Melihcan Sezgiç, Department of Plastic, Reconstructive and Aesthetic Surgery, Ankara University Faculty of Medicine, Ankara, Turkey
Orcid: 0000-0002-8213-8526
E-mail: mlh_s@yahoo.com
Doi: 10.18663/tjcl.1591774
Received: 26.11.2024 accepted: 14.03.2025

Öz

Amaç: Tendon iyileşmesi, genellikle mekanik gücün tam olarak geri kazanılamadığı yavaş ve karmaşık bir süreçtir. Kollajen, tendon bütünlüğünde kilit bir rol oynar ve poli-L-laktik asidin (PLLA) kollajen sentezini artırdığı gösterilmiştir. Bu çalışmada, PLLA bazlı dermal dolgu maddelerinin sıçan modelinde tendon iyileşmesi üzerindeki etkilerini araştırmayı amaçladı.

Gereç ve Yöntemler: Yirmi dört Wistar Albino dişi sıçan, Rastgele Kontrol Grubu ve PLLA Grubu olmak üzere iki gruba ayrıldı. Kontrol grubunda, sağ Aşil tendonu, kalkaneal yapışma yerinin 4 mm proksimalinden kesildi. PLLA grubunda ise aynı işlem uygulandıktan sonra iki tendon ucu arasına PLLA bazlı dermal dolgu enjekte edildi. Sıçanlar 3 hafta sonra sakrifiye edilerek tendonlar makroskopik, biyomekanik ve histolojik olarak parametrelere göre incelendi. Histolojik skorlama, Bonar kriterlerine göre yapıldı.

Bulgular: PLLA ve kontrol grupları arasında ortalama makroskopik skor açısından anlamlı bir fark bulunmadı (4.8 ± 0.7 vs. 4.4 ± 0.7, p = 0.178). Biyomekanik analiz, PLLA grubunda yük taşıma kapasitesinde ve sertlikteki azalmanın kontrol grubuna kıyasla anlamlı derecede daha az olduğunu gösterdi (sırasıyla; -14.0 ± 7.0 vs. -21.3 ± 6.3 N, p = 0.041; -7.1 ± 1.7 vs. -10.4 ± 2.2 N, p = 0.026). Histolojik değerlendirmede, kontrol grubunun histolojik skorlarının PLLA grubuna göre daha yüksek olduğu belirlendi (7.5 ± 1.0 vs. 5.2 ± 1.0, p = 0.004).

Sonuç: PLLA bazlı dermal dolgular, biyomekanik dayanıklılığı koruyarak ve histolojik organizasyonu iyileştirerek tendon iyileşmesini artırabilir ve bu da tendon yaralanmaları için minimal invaziv bir tedavi yaklaşımı olarak potansiyellerini vurgular.

Anahtar Kelimeler: Kollajen, poli-l-laktik asit, PLLA, tendon iyileşmesi

Introduction

Tendon injuries are a frequent and significant clinical challenge within the musculoskeletal system, often leading to substantial functional deficits and a high risk of long-term disability (1). In particular, flexor tendon injuries pose a unique challenge due to their complex anatomy, limited vascular supply, and the high risk of adhesion formation following surgical intervention (2). Generally, tendon healing progresses through the phases of inflammation, proliferation, and remodeling, but attaining full histological and biomechanical restoration remains challenging (3). Despite the body's intrinsic regenerative capacity, the specialized structure of tendons—characterized by a parallel arrangement of collagen fibers and relatively poor vascularity—often results in suboptimal healing outcomes, including reduced strength and persistent stiffness (4, 5).

In recent years, there has been growing interest in harnessing the potential of tissue engineering and regenerative medicine approaches to optimize tendon repair. Biodegradable and biocompatible polymers, such as poly-L-lactic acid (PLLA), have emerged as promising materials in the development of scaffolds, implants, and drug delivery systems (6, 7). PLLA is well-known for its relatively low immunogenicity, controlled degradation profile, and capacity to support cell adhesion and proliferation—features that make it attractive for various orthopedic and soft tissue applications (8, 9). PLLA has gained substantial attention in aesthetic medicine as a dermal filler, primarily for its ability to stimulate collagen synthesis and promote tissue remodeling (10, 11). This unique mechanism of action, which leads to gradual volumization and neocollagenesis, may also provide potential benefits for tendon healing. By supporting extracellular matrix (ECM) deposition and enhancing the proliferation and differentiation of resident cells, PLLA-based fillers or scaffolds could theoretically contribute to the restoration of structural integrity and functional capacity in injured tendons (12, 13).

Although initial findings suggest that PLLA can facilitate soft tissue repair, there remains a notable gap in the literature regarding its efficacy and safety specifically in tendon healing. Further investigation is therefore necessary to elucidate the molecular and cellular pathways through which PLLA exerts its effects and to determine whether these positive outcomes observed in soft tissue augmentation translate effectively to tendon tissues (12, 13). Hence, this study aimed to investigate the effects of PLLA on a rat tendon healing model.

Material and methods

This experimental study was conducted in 2017 at Ankara University Faculty of Medicine's Experimental Animals and Research Laboratory and was approved by the Local Ethics

Committee for Animal Experiments of Ankara University (Date: 05.03.2024 - No: 2024/03-21).

Study Design

A total of 26 female Wistar albino rats (mean weight: 308 ± 48 g) were included in this study. Of these, 2 rats were dedicated to a pilot assessment to familiarize the researchers with the regional anatomy. The remaining 24 rats were then randomly divided into a control group (n = 12) and an experimental (PLLA) group (n = 12).

In the control group, an incision was made in the right Achilles tendon. The paratenon and skin were subsequently sutured without the application of any additional material. Following a three-week recovery period, tendon samples were collected from all 12 rats. Macroscopic measurements of tendon thickness were performed. Histological analysis was conducted on 6 of these rats, while the remaining 6 underwent complete excision of both left and right muscle–bone–tendon units for biomechanical testing.

For the control group, an incision was made in the right Achilles tendon, with the paratenon and skin subsequently sutured. After three weeks, tendon samples were obtained, and macroscopic evaluations of tendon thickness were carried out for all 12 rats. Samples for histological examination were collected from 6 rats, while the remaining 6 underwent complete excision of the left and right muscle-bone-tendon units, which were then assessed via biomechanical testing.

In the experimental group, the right Achilles tendon was transected in the same manner, but a PLLA-based dermal filler (Sculptra) was injected into the transection site prior to closing the paratenon and skin. After three weeks, the same procedures were carried out: macroscopic measurements of tendon thickness were recorded for all 12 rats; 6 rats provided tissue samples for histological evaluation, and the remaining 6 underwent excision of both left and right muscle–bone–tendon units for biomechanical analysis.

Preparation of PLLA Dermal Filler

A vial of Sculptra (containing 367.5 mg powder: 150 mg Poly-L-Lactic Acid, 90 mg sodium carboxymethylcellulose, and 127.5 mg nonpyrogenic mannitol) was used as the filler material (Figure 1a). To prepare, 5 mL of 0.9% saline was added to the vial, which was then gently swirled and allowed to stand for 3 hours at room temperature before use. This procedure ensured uniform hydration of the PLLA particles.

Surgical Procedure

All surgeries were performed under sterile conditions. Prior to surgery, each rat was anesthetized using an appropriate combination of ketamine (45 mg/kg) and xylazine (5 mg/kg), administered intramuscularly. The surgical area was shaved, disinfected with povidone-iodine, and draped using sterile technique to minimize contamination. A longitudinal incision was made approximately 4 mm proximal to the calcaneal insertion of the right Achilles tendon (Figure 1a). The skin and subcutaneous tissues were carefully incised to expose the Achilles tendon (Figure 1c) and its paratenon. The plantaris tendon was transected to prevent internal splinting (Figure 1d). A full-thickness cut was made on the Achilles tendon ~4 mm proximal to the calcaneal insertion (Figure 1e).

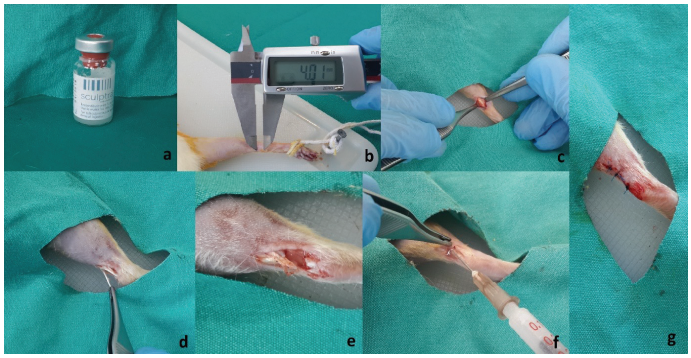

Figure 1.a) PLLA based dermal filler (Sculptra®), **b)** Planning the incision, **c)** exposure of right achilles tendon, **d)** Transection of plantaris tendon, **e)** Transection of achilles tendon, **f)** Sculptra injection, **g)** Closure of the incision.

In the control group, the paratenon and skin were sutured with 5/0 atraumatic round needle Prolene and surgery was terminated. In the PLLA group, approximately 0.1 mL of the prepared PLLA filler (Sculptra) was injected into the gap formed by the retraction of the proximal part of the tendon (Figure 1f). The paratenon and skin were then sutured in the same fashion as in the control group (Figure 1g).

In postoperative period, no external immobilization (splint or cast) was applied, and the rats were allowed free mobilization in their cages. Skin sutures were removed after 1 week.

Macroscopic Examination

Three weeks after surgery, all 24 rats were sacrificed using carbon dioxide (CO_2) inhalation. The right Achilles tendon in each rat was exposed along the previous incision line. Tendon morphology was assessed macroscopically using the scoring criteria described by Stoll et al. (14) and modified by Zhang et al. (15). A maximum score of 14 points indicated a healthy tendon appearance (Table 1).

Table 1. Macroscopic evaluation criteria (adapted from Zhang et al8)

	POINTS			
CRITERIA	3	2	1	0
Loading/Lameless	-	-	Hind leg fully loaded	NOT fully loaded
Tendon-Skin Connection(Slidability)	-	-	Slidable	Adhesion(+), NOT fully slidable
Tendon rupture	-	-	Non-existing	Existing
Inflammation	-	-	Non-existing	Existing(swelling, redness and edema)
Tendon Surface at the defect area	-	-	Intact, smooth	Firm, rough
Adjacent tendon properties	-	-	Unchanged	Changed(colour, thickness and surface)
Swelling/Redness of tendon	-	No swelling, redness	Palpable swelling, no redness	Palpable swelling and redness
Tendon-Paratendineum-Fascia Connection	-	-	Slidable	Adhesion(+), NOT slidable
Shape of tendon	Normal	Slightly thickened	Moderately thickened	Intensely thickened
Colour of tendon	-	-	Bright white	Translucent, dull white
M.gastrocnemius tendon strains	-	-	Normal, conjoined	Adhesion (+)
Higher the score the better tendon quality(Max :14, Min :0 pts)				

Biomechanical Evaluation

Biomechanical testing was carried out within 2 hour after the excision in the electro-mechanical testing device (Shimadzu AGS-X 1N-10kN Tensile Testing Machine, Columbia, MD, U.S.A.) located in the Biomedical Engineering department of Ankara University Faculty of Engineering (Figure 2). Six rats were randomly selected from both groups for biomechanical examination. For these selected rats, the incision was made from the calcaneus to the thigh, and the Achilles tendon was excised with the foot and distal 2/3 triceps surae muscle. In addition, the intact left achilles tendons were excised as muscle-bone-tendon unit also, for comparative test (Figure 3). The excised tendons were wrapped in gauze and soaked with a ringer's lactate solution, then held until testing. Before the test, tendon thickness and length was measured with a digital caliper (Watano) in the healing area. No stretching and adjustment was made to the tendons before the test, and the room temperature was at a constantly set at 25 °C. The free ends of the tendons were fixed with anti-slip plates and the speed of the test device was adjusted to 10 mm/min. With the help of the computer software that the test device was linked, the force/rupture graph curve was created. Also, load to failure (LF, N) and tendon stiffness (TS, N/mm) values was calculated separately for each tendon. Tendon stiffness value was calculated from the linear part of the force/rupture graph.

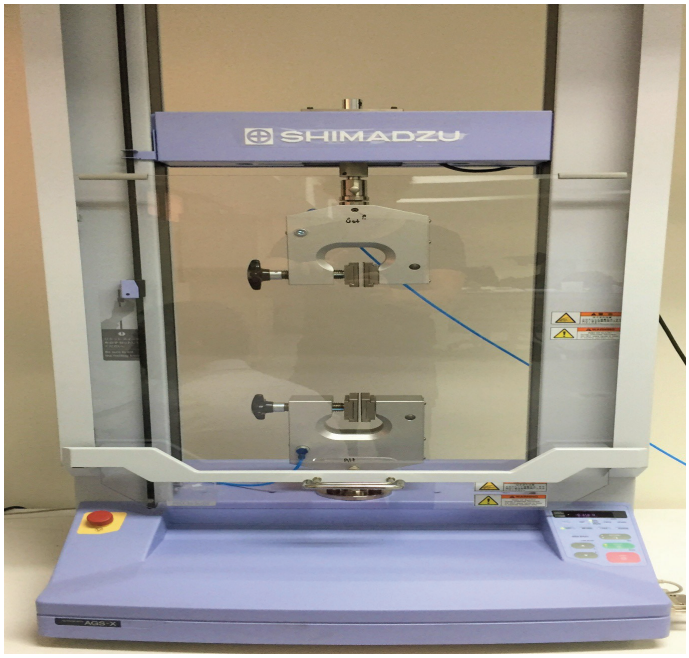

Figure 2. Shimadzu AGS-X 1N-10kN tensile test machine.

Histological Analysis

The remaining 6 rats from each group (n=6 per group) were used for histological examination. Tendons were fixed in 10% phosphate buffered formaldehyde for 24 hours, then washed under tap water. Dehydration was performed using graded ethanol series (75%, 96%, 100%). Tissues were made transparent with xylene after dehydration. After incubation for 3 hours in a 60 °C oven with liquid paraffin, it was buried in hard paraffin blocks. From the

paraffin blocks, 4 µm sections was taken with Leica® RM 2125RT "sliding" microtome. Also, in terms of comparison with the intact tendon section, the same procedure was applied to the sample taken from the left Achilles tendon of the rat and samples were taken. Hematoxylin-Eosin and Alcian Blue dyes were applied to the tissue sections. The prepared slides were examined with Zeiss ® Axio Scope A1 light microscope by one blinded investigator. Slide photos were provided with the help of Sysmex Pannoramic 250 Flash III digital pathology screening device located in the Pathology Department of Ankara University Medical Faculty.

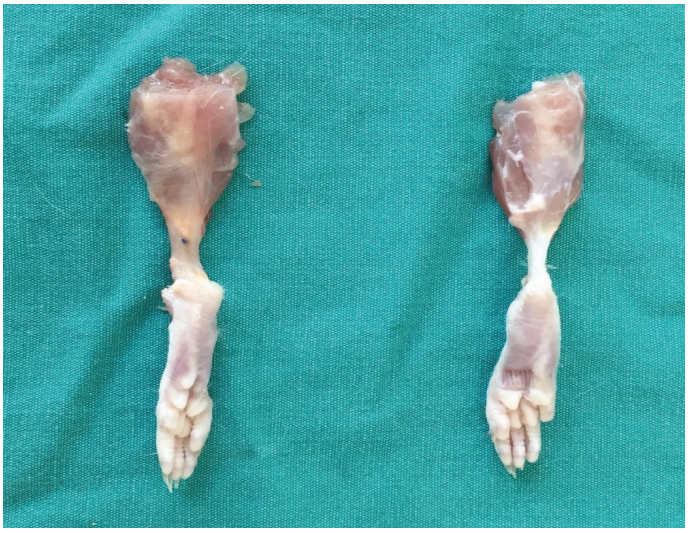

Figure 3. Excised muscle-bone-tendon unit (left: injured, right: healthy).

For the assesment of prepared microscopic slides, The Bonar Criteria (Table 2) was used which was described by Maffulli et al (16). Tenocytes were evaluated according to spindle form, increased rounding, increased size and the amount of cytoplasm. The ground substance was scored using alcian blue dye. While evaluating collagen, demarcation and organization of the fibers were taken into account. Therefore, parameters of separation of fibers, loss of demarcation and tendon structure were examined. Vascularity was scored by examining the capillary vascular clumps between the collagen fibers in the tendon tissue.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS program. The normality of numerical data distribution was assessed using the Kolmogorov-Smirnov test. Data were presented as mean ± standard deviation and median (min-max). Comparisons between two groups were performed using the Mann-Whitney U test. For comparisons involving more than two groups, the ANOVA test (post-hoc: Bonferroni) was used for normally distributed data, and the Kruskal-Wallis H test (post-hoc: Dunn's test) was used for non-normally distributed data. For biomechanical examination, Wilcoxon test was used to test whether the distribution of the two variables is the same, taking into account the dimensions of the differences between the paired groups. A p-value of $P < 0.05$ was considered statistically significant for all analyses.

Table 2. The Bonar Criteria (adapted from Maffulli et al9)

VARIABLES	Tenocytes	Ground Substance	Collagen	Vascularity
Grade 0 (0 point)	Insignificant elongated spindle shaped nuclei with no obvious cytoplasm at light microscopy	No stainable ground substance	Collagen arranged in tightly cohesive well-demarcated bundles with a smooth dense birght homogenous polarization pattern with normal crimping	Insignificant blood vessels coursing between bundles
Grade 1 (1 point)	Increased roundness (nucleus becomes more ovoid to round in shape without remarkable cytoplasm)	Stainable mucin between fibers but bundles still discrete	Diminished fiber polarization(seperation of individual fibers with maintenance of demarcated bundles)	Occasional cluster of capillaries, less than one per 10 high-power fields
Grade 2 (2 point)	Increased roundness and size(the nucleus is round, slightly enlarged and a small amount of cytoplasm is visible)	Stainable mucin between fibers with loss of clear demarcation of bundles	Bundle changes(seperation of fibers without demarcation of fibers giving rise to expansion of the tissue overall and clear loss of polarization pattern)	1-2 clusters of capillaries per 10 high power fields
Grade 3 (3 point)	Nucleus is round, large with abundant cytoplasm and lacuna formation(chondroid change)	Abundant mucin throught with inconspicuous collagen staining	Marked seperation of fibers with complete loss of architecture	Greater than 2 clusters per 10 high power fields
0 pt :Normal tendon, 12 pt: most abnormal tendon				

Results

Macroscopic Findings

On the 21st day of the study, the macroscopic morphology of the tendons was examined. Under normal conditions, healthy tendons appear white, feature a smooth surface, and exhibit no adhesion to surrounding tissues. In contrast, the operated tendons exhibited a dull white, thickened appearance, along with multiple adhesions extending to the paratenon, fascia, and subcutaneous tissue. Although both the control and PLLA groups exhibited thickening and adhesions involving the paratenon, fascia, and subcutaneous tissue in the Achilles tendons, the PLLA group showed relatively less thickening compared to the control group. However, the mean macroscopic scores between the PLLA and control groups did not differ significantly (4.8 ± 0.7 vs. 4.4 ± 0.7, p = 0.178) (Table 3).

Biomechanical Findings

In the control group, the mean LF value was higher in the healthy tendon group compared to the injured tendon group (45.7 ± 9.9 vs. 24.3 ± 5.8 N, p = 0.027). Similar findings were observed in the PLLA group (Healthy tendon: 41.5 ± 12.5 vs. Injured tendon: 27.5 ± 7.4 N, p = 0.028) (Table 4).

Table 3. Distribution of macroscopic scores in control and PLLA groups.

	PLLA group		Control group		
	Mean ± SD	Median (min - max)	Mean ± SD	Median (min - max)	P-value*
Macroscopic Score	4.8 ± 0.7	5.0 (4.0 - 6.0)	4.4 ± 0.7	4.0 (4.0 - 6.0)	0.178

Abbreviations: Max, Maximum; Min, Minimum; SD, standart deviation. *Mann Whitney U Test.

Table 4. Distribution of load to failure and tendon stiffness values in control and PLLA groups.

	PLLA group		Control group	
	Mean ± SD	Median (min - max)	Mean ± SD	Median (min - max)
Load to failure, N				
Healthy tendon	41.5 ± 12.5	37.5 (30.0 - 64.0)	45.7 ± 9.9	46.5 (35.0 – 62.0)
Injured tendon	27.5 ± 7.4	25.5 (20.0 - 37.0)	24.3 ± 5.8	23.5 (17.0 - 32.0)
P-value*	0.028		0.027	
Tendon stiffness, N/mm				
Healthy tendon	14.2 ± 1.8	13.9 (11.8 - 16.9)	15.4 ± 2.1	15.2 (12.5 - 18.0)
Injured tendon	7.1 ± 0.9	6.8 (6.2 - 8.2)	4.9 ± 0.6	5.0 (4.1 - 5.6)
P-value*	0.027		0.028	

Abbreviations: Max, Maximum; Min, Minimum; SD, standart deviation.*Wilcoxon Test

In the control group, the mean TS value was higher in the healthy tendon group compared to the injured tendon group (15.4 ± 2.1 vs. 4.9 ± 0.6 N/mm, p = 0.028). Similar results were noted in the PLLA group (Healthy tendon: 7.1 ± 0.9 N/mm, p = 0.027) (Table 4).

To quantify the biomechanical deficit resulting from tendon injury, the differences (Δ) in LF and TS values were calculated by subtracting the injured tendon measurements from the corresponding healthy tendon measurements. Table 5 provides a comparative overview of these differences for both the PLLA and control groups. In the PLLA group compared to control groups, the mean ΔLF (-14.0 ± 7.0 vs. -21.3 ± 6.3 N, p = 0.041) and mean ΔTS (-7.1 ± 1.7 vs. -10.4 ± 2.2 N, p = 0.026) levels was lower (Table 5).

Histological Findings

Before initiating the primary experimental analyses, histological examinations of healthy tendons were performed. The observations revealed spindle-shaped tenocyte nuclei, organized collagen fibers, and negligible capillary clusters, indicative of normal tendon architecture (Figure 4).

Table 5. Comparison of decrease in load to failure and tendon stiffness values between the control and PLLA groups.

	PLLA group		Control group		P-value*
	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	
ΔLoad to failure, N	-14.0 ± 7.0	-12.5 [(-27) - (-6)]	-21.3±6.3	-19.5 [(-32) - (-16)]	0.041
ΔTendon stiffness, N/mm	-7.1 ± 1.7	-7.2 [(-9.8) - (-5.1)]	-10.4±2.2	-10.4 [(-13.9) - (-7.2)]	0.026

Abbreviations: Max, Maximum; Min, Minimum; SD, standart deviation. *Mann Whitney U Test.

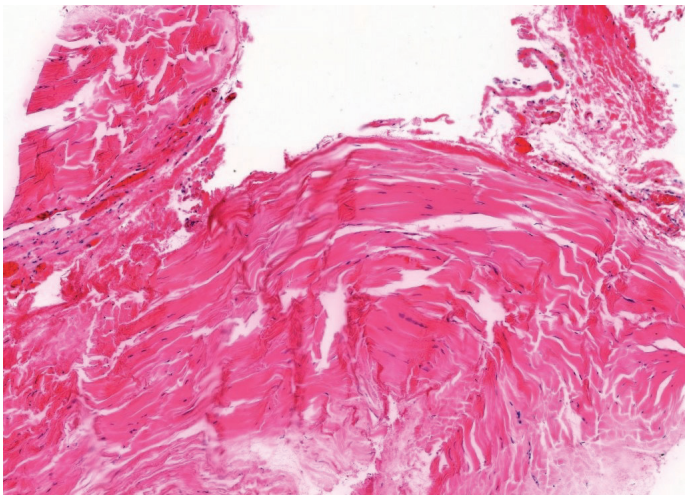

Figure 4. Microscopic slide of healthy tendon; Spindle shaped tenocyte nuclei, no obvious cytoplasm, organized collagen fibers.

Tenocyte morphology was found to be impaired in both groups of injured tendons. Notably, the control group displayed a higher rate of lacuna formation—suggestive of cartilage transformation—and rounding of tenocyte nuclei compared with the PLLA group (Figure 5a, b).

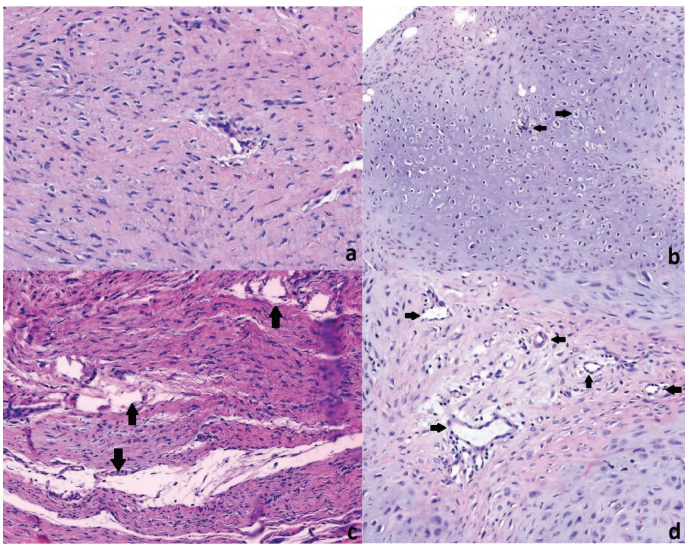

Figure 5. a) Increased roundness of tenocytes (Grade 1), **b)** Lacunae formation (sign of cartilage transformation), **c)** Separation of collagen fibers, **d)** Increased vascularity(arrows show capillary vessels)

Additionally, both groups exhibited a comparable degree of collagen fiber irregularity and separation (Figure 5c). When evaluating the intermediate material, mucin staining was observed to be more intense in the control group than in the PLLA group. Moreover, an increased capillary clusters was similarly noted in both groups (Figure 5d).

The control group had higher histological scores compared to the PLLA group (7.5 ± 1.0 vs. 5.2 ± 1.0, p = 0.004) (Table 6).

Discussion

This study is among the rare investigations highlighting the clinical efficacy of PLLA in tendon injuries. Our findings suggest that PLLA application may provide certain histological and biomechanical advantages in tendon repair, although its effects on macroscopic tendon morphology remain statistically insignificant.

Although there was no significant difference in the macroscopic score between the PLLA group and the controls, the PLLA group exhibited relatively better macroscopic tendon morphology. Moreover, tendons in the control group exhibited greater thickness and edema compared to those in the PLLA group. Previous studies suggest that in tendon repair models using PLLA, the tendon maintains its macroscopic integrity, with a smooth layer of connective tissue covering its surface (17, 18). In a study conducted on rabbits with a medial collateral ligament model, it was reported that the newly formed tissue obtained using a PLLA scaffold was macroscopically covered with normal connective tissue but initially appeared thicker (hypertrophic) compared to the normal tendon (17). This thickening was observed in the early phase due to the presence of dense fibrotic tissue around the scaffold but showed a tendency to resolve as the tissue matured over time. A study on animals implanted with a double-layered PLLA scaffold reported that the repair site was externally covered by a thin and uniform membrane, with no evident signs of significant inflammation (18). These results suggest that PLLA effectively integrates tendon ends, ensures structural integrity, and facilitates the formation of a macroscopically organized morphology.

Table 6. Comparison of histological scores between the control and PLLA groups.

	PLLA group		Control group		P-value*
	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	
Bonar Scores	5.2 ± 1.0	5.5 (4.0 - 6.0)	7.5 ± 1.0	7.5 (6.0 – 9.0)	0.004

Abbreviations: Max, Maximum; Min, Minimum; SD, standart deviation. *Mann Whitney U Test.

Various studies have emphasized the beneficial role of PLLA in preventing adhesion formation, which is an unfavorable complication in tendon healing. A previous study demonstrated that a double-layered PLLA fiber scaffold significantly reduced macroscopic adhesions and preserved a gliding space around the tendon (19). Another study assessed electrospun PLA and poly(ε-caprolactone) (PCL) membranes with varying degradation kinetics to investigate their anti-adhesive effects in Achilles tendon repair. The findings revealed that the electrospun PLA membrane group exhibited significantly superior anti-adhesive properties and tendon repair potential compared to the PCL membrane group (20). In this study, both the control and PLLA groups exhibited thickening and adhesions in the Achilles tendons, involving the paratenon, fascia, and subcutaneous tissue. However, it is well established that macroscopic changes in tissue healing occur later than microscopic alterations. Therefore, a longer waiting period between procedures may influence the observed results.

The observation that healthy tendons demonstrate significantly higher LF and TS values than injured tendons is an anticipated outcome, given that tendon injuries impair mechanical properties, thereby reducing both strength and stiffness (21). On the other hand, we found that the biomechanical deficits (ΔLF and ΔTS) were significantly lower in the PLLA-treated group compared to the control group. This suggests that PLLA treatment may mitigate the loss of mechanical properties following tendon injury. Similar outcomes have been reported in previous research. Gould et al. demonstrated that PLLA mesh augmentation in patellar tendon repair enhanced biomechanical stability, resulting in reduced gap formation and increased load-to-failure compared to repairs without augmentation (22). Additionally, studies have shown that PLLA scaffolds can promote tendon regeneration by providing structural support and facilitating cell proliferation, thereby improving the mechanical integrity of the healing tendon (23). Furthermore, a study evaluating a layered PLLA scaffold for infraspinatus tendon defects in a rabbit model supports these findings. The study demonstrated that PLLA scaffolds facilitated cell migration, promoted tissue regeneration, and ultimately restored biomechanical properties comparable to reattached tendons at 8 and 16 weeks postoperatively. Although tendon stiffness did not show significant improvement, the fact that PLLA-treated tendons achieved a failure load similar to native infraspinatus tendons suggests that PLLA-based scaffolds can effectively bridge tendon defects and contribute to mechanical restoration over time (24). Another study compared three biodegradable materials—poly-N-acetyl-D-glucosamine (chitin), PCL, and PLA—for tendon reconstruction in a rabbit model. The results indicated that PLA and chitin/p-CL composite tendons exhibited good initial strength and promoted fibrous tissue ingrowth, while chitin tendons degraded rapidly, leading to early strength loss. Notably, PLA-based implants supported the formation of both type I and type III collagen, which are essential for tendon regeneration (25). These findings align with our results, suggesting that PLLA scaffolds provide structural integrity during tendon healing and may enhance mechanical recovery by promoting extracellular matrix deposition.

Tendon healing is a complex process involving cellular proliferation, extracellular matrix remodeling, and vascularization. In this study, we observed that PLLA-treated tendons exhibited improved histological organization compared to the control group, with reduced signs of degenerative changes. These findings suggest that PLLA scaffolds may support a more favorable regenerative environment, potentially by modulating cellular behavior and matrix organization. Previous research has demonstrated that PLLA scaffolds enhance wound healing by promoting fibroblast proliferation and neocollagenesis (26, 27). PLLA has also been recognized as a deep tissue regenerator, as it increases fibroblast activity and collagen production through a controlled inflammatory response (28, 29). Neocollagenesis begins within the first month, peaks around the sixth month, and continues up to nine months before PLLA particles are completely eliminated (29, 30). This progressive collagen formation suggests that PLLA could play a significant role in the

maturation phase of tendon healing, which extends beyond the early inflammatory and proliferative stages. In our study, lacuna formation, a marker of severe degeneration, was observed in two control samples, and cell rounding was more pronounced in the control group. Additionally, mucin staining intensity was higher in the control group, suggesting greater extracellular matrix disorganization, while collagen fiber separation was similar in both groups. These findings align with previous studies indicating that collagen fiber organization is primarily a late-stage remodeling event, which may not be fully developed in the early healing phase (31-34). Rat tendon healing studies have shown that major histological changes occur within the first two weeks post-injury, making our three-week evaluation period appropriate for early-stage assessment (35).

This study has some limitations. First, the follow-up period was limited to three weeks, focusing on the early phase of tendon healing. Since PLLA-induced neocollagenesis continues for up to nine months, its long-term effects on tendon remodeling and mechanical strength remain unknown. Second, while histological scoring was performed, quantitative methods such as collagen fiber alignment analysis or molecular markers were not included. Third, the rat tendon model may not fully replicate human tendon healing, given species differences in biomechanics and load-bearing capacity. Finally, the long-term degradation profile and potential dose-dependent effects of PLLA dermal fillers remain unclear. Future studies incorporating extended follow-up periods, advanced quantitative assessments, and large-animal or clinical models are needed to fully elucidate PLLA's role in tendon healing.

Conclusion

This study demonstrates that PLLA improves tendon healing by reducing adhesions, preserving biomechanical strength, and enhancing histological organization. PLLA-treated tendons exhibited lower histological degeneration scores, healthier tenocyte morphology, and lower lacuna formation, contributing to improved tissue remodeling. PLLA's well-documented ability to stimulate fibroblast activity and neocollagenesis makes it a promising candidate for tendon regeneration. Additionally, its injectable form provides a minimally invasive alternative to traditional tendon repair strategies, allowing for post-injury application without the need for open surgery.

Funding

The authors declared that this study has received no financial support.

Conflicts of Interest

The authors declare they have no conflicts of interest.

Ethics Approval

The study was approved by the Ankara University Animal Experiments Ethics Committee.

Availability of Data and Material

The data that support the findings of this study are available on request from the corresponding author.

Authors' contribution

Concept – M.S. and S.S., Design- S.S.; Supervision - S.S.; Data collection and/or processing – M.S. and S.S., Analysis and/or interpretation - M.S. and S.S., Writing – M.S.; Critical review- S.S. All authors read and approved the final version of the manuscript.

References

1. de Putter CE, Selles RW, Polinder S, Panneman MJ, Hovius SE, and van Beeck EF. Economic impact of hand and wrist injuries: health-care costs and productivity costs in a population-based study. J Bone Joint Surg Am. 2012;94(9):e56.
2. Tang JB. Clinical outcomes associated with flexor tendon repair. Hand Clin. 2005;21(2):199-210.
3. Docheva D, Muller SA, Majewski M, and Evans CH. Biologics for tendon repair. Adv Drug Deliv Rev. 2015;84:222-39.
4. Sharma P and Maffulli N. Tendon injury and tendinopathy: healing and repair. J Bone Joint Surg Am. 2005;87(1):187-202.
5. Wong JK, Cerovac S, Ferguson MW, and McGrouther DA. The cellular effect of a single interrupted suture on tendon. J Hand Surg Br. 2006;31(4):358-67.
6. Lui PP. Stem cell technology for tendon regeneration: current status, challenges, and future research directions. Stem Cells Cloning. 2015;8:163-74.
7. Capuana E, Lopresti F, Ceraulo M, and La Carrubba V. Poly-l-Lactic Acid (PLLA)-Based Biomaterials for Regenerative Medicine: A Review on Processing and Applications. Polymers (Basel). 2022;14(6)
8. Lee KWA, Chan LKW, Lee AWK, Lee CH, Wong STH, and Yi KH. Poly-d,l-lactic Acid (PDLLA) Application in Dermatology: A Literature Review. Polymers (Basel). 2024;16(18)
9. Yang G, Rothrauff BB, and Tuan RS. Tendon and ligament regeneration and repair: clinical relevance and developmental paradigm. Birth Defects Res C Embryo Today. 2013;99(3):203-22.
10. Oh S, Lee JH, Kim HM, et al. Poly-L-Lactic Acid Fillers Improved Dermal Collagen Synthesis by Modulating M2 Macrophage Polarization in Aged Animal Skin. Cells. 2023;12(9)

11. Ao YJ, Yi Y, and Wu GH. Application of PLLA (Poly-L-Lactic acid) for rejuvenation and reproduction of facial cutaneous tissue in aesthetics: A review. Medicine (Baltimore). 2024;103(11):e37506.
12. Brebels J and Mignon A. Polymer-Based Constructs for Flexor Tendon Repair: A Review. Polymers (Basel). 2022;14(5)
13. Chen R, Chen F, Chen K, and Xu J. Advances in the application of hydrogel-based scaffolds for tendon repair. Genes Dis. 2024;11(4):101019.
14. Stoll C, John T, Conrad C, et al. Healing parameters in a rabbit partial tendon defect following tenocyte/biomaterial implantation. Biomaterials. 2011;32(21):4806-15.
15. Zhang B, Luo Q, Kuang D, Ju Y, and Song G. Mechano-growth factor E peptide promotes healing of rat injured tendon. Biotechnol Lett. 2016;38(10):1817-25.
16. Maffulli N, Longo UG, Franceschi F, Rabitti C, and Denaro V. Movin and Bonar scores assess the same characteristics of tendon histology. Clin Orthop Relat Res. 2008;466(7):1605-11.
17. Nishimoto H, Kokubu T, Inui A, et al. Ligament regeneration using an absorbable stent-shaped poly-L-lactic acid scaffold in a rabbit model. Int Orthop. 2012;36(11):2379-86.
18. Inui A, Kokubu T, Makino T, et al. Potency of double-layered poly L-lactic acid scaffold in tissue engineering of tendon tissue. Int Orthop. 2010;34(8):1327-32.
19. Wang W, He N, Yao Z, et al. An Integrative Dual-Layer Poly-L-Lactic Acid Fibrous Membrane Prevents Peritendinous Adhesions. Front Bioeng Biotechnol. 2020;8:387.
20. Song Z, Shi B, Ding J, et al. A comparative study of preventing postoperative tendon adhesion using electrospun polyester membranes with different degradation kinetics. Science China Chemistry. 2015;58:1159-68.
21. Xu Z, Xu W, Zhang T, and Luo L. Mechanisms of tendon-bone interface healing: biomechanics, cell mechanics, and tissue engineering approaches. J Orthop Surg Res. 2024;19(1):817.
22. Gould HP, Rate WRt, Harrell RA, Abbasi P, and Fillar AL. Effect of Poly-L-Lactic Acid Mesh Augmentation on Cyclic Gap Formation in Transosseous Patellar Tendon Repair: A Biomechanical Study. J Knee Surg. 2023;36(12):1224-29.
23. Zhang J, Wang W, Zhang X, Yang L, and Zhang J. Research progress of biodegradable polymers in repairing Achilles tendon injury. Frontiers in Materials. 2022;9:815930.
24. Inui A, Kokubu T, Fujioka H, et al. Application of layered poly (L-lactic acid) cell free scaffold in a rabbit rotator cuff defect model. Sports Med Arthrosc Rehabil Ther Technol. 2011;3:29.
25. Sato M, Maeda M, Kurosawa H, Inoue Y, Yamauchi Y, and Iwase H. Reconstruction of rabbit Achilles tendon with three bioabsorbable materials: histological and biomechanical studies. J Orthop Sci. 2000;5(3):256-67.
26. Jouybar A, Seyedjafari E, Ardeshirylajimi A, et al. Enhanced Skin Regeneration by Herbal Extract-Coated Poly-L-Lactic Acid Nanofibrous Scaffold. Artif Organs. 2017;41(11):E296-E307.
27. Kim KL, Han DK, Park K, et al. Enhanced dermal wound neovascularization by targeted delivery of endothelial progenitor cells using an RGD-g-PLLA scaffold. Biomaterials. 2009;30(22):3742-8.
28. Ballin AC, Brandt FS, and Cazzaniga A. Dermal fillers: an update. Am J Clin Dermatol. 2015;16(4):271-83.
29. Lowe NJ. Optimizing poly-L-lactic acid use. J Cosmet Laser Ther. 2008;10(1):43-6.
30. Goldberg D, Guana A, Volk A, and Daro-Kaftan E. Single-arm study for the characterization of human tissue response to injectable poly-L-lactic acid. Dermatol Surg. 2013;39(6):915-22.
31. Movin T, Gad A, Reinholt FP, and Rolf C. Tendon pathology in long-standing achillodynia. Biopsy findings in 40 patients. Acta Orthop Scand. 1997;68(2):170-5.
32. Maffulli N, Barrass V, and Ewen SW. Light microscopic histology of achilles tendon ruptures. A comparison with unruptured tendons. Am J Sports Med. 2000;28(6):857-63.
33. Maffulli N, Reaper J, Ewen SW, Waterston SW, and Barrass V. Chondral metaplasia in calcific insertional tendinopathy of the Achilles tendon. Clin J Sport Med. 2006;16(4):329-34.
34. Hapa O, Cakici H, Gideroglu K, Ozturan K, Kukner A, and Bugdayci G. The effect of ethanol intake on tendon healing: a histological and biomechanical study in a rat model. Arch Orthop Trauma Surg. 2009;129(12):1721-6.
35. Muller SA, Durselen L, Heisterbach P, Evans C, and Majewski M. Effect of a Simple Collagen Type I Sponge for Achilles Tendon Repair in a Rat Model. Am J Sports Med. 2016;44(8):1998-2004.