POLYESTER BIOLOGICAL PATCH FOR AORTIC ROOT ENLARGEMENT AND PREPARATION METHOD THEREOF

FIELD OF THE TECHNOLOGY

[0001] This invention belongs to the technical field of biomedical materials, and particularly relates to a polyester biological patch applicable to aortic root enlargement and a preparation method thereof.

BACKGROUND

[0002] Patients with small aortic annulus often encounter the problem of prosthesis-patient mismatch (PPM) when undergoing valve replacement surgery. If left unaddressed, this condition will lead to surgical stenosis, namely obstruction of the new outflow tract formed by the implant. It not only hinders the postoperative recovery of cardiac function in patients, but also severely impairs the hemodynamic performance and durability of the prosthetic valve.

[0003] Clinically, multiple surgical procedures including Manouguian procedure, Nicks procedure, Yang procedure, Rittenhouse procedure, Mavroudis procedure and Konno-Rastan procedure can be adopted for aortic root enlargement. In recent years, the Yang procedure has attracted extensive attention. It is crucial for patients with valvular lesions combined with small-sized annulus caused by various factors, which can optimize hemodynamics and improve long-term therapeutic effects.

[0004] Clinical practices have verified that aortic root enlargement can effectively reduce the incidence of PPM. However, aortic root enlargement approaches and implant material selection are still controversial and require further optimization. At present, there is no dedicated polyester biological patch for aortic root enlargement in clinical practice. Surgeons usually cut patches from artificial blood vessels for such operations, and these conventional patches have the following defects:

[0005] (1) The coating applied on the patches for seepage prevention and accelerating endothelialization cannot withstand the high pulsating pressure at the aortic root and is prone to peeling off. (2) Poor biocompatibility and slow endothelialization. Failure to achieve rapid endothelialization may result in hemolysis, thrombosis and long-term localized calcification. (3) Excessive patch thickness (greater than 0.5 mm), leading to insufficient surgical operability and compliance, as well as poor mechanical properties. (4) Inadequate leak-proof performance. (5) The patch is a polymer woven material coated with collagen, and its leak-proof capability requires further improvement. (6) High risk of bacterial infection.

SUMMARY

[0006] The polyester biological patch for aortic root enlargement provided by the present invention is prepared via two successive chemical crosslinking steps, including primary chemical crosslinking and secondary chemical crosslinking. The primary chemical crosslinking is used to crosslink collagen molecules or collagen fibrils to obtain collagen fibrils after primary chemical crosslinking. The secondary chemical crosslinking enables the collagen fibrils after primary crosslinking to adhere to the internal voids and surface of polyester fabric, so as to form a collagen fibril coating through crosslinking reaction.

[0007] During the research, the inventors unexpectedly found that the melting points of the collagen fibril coating and the collagen fibrils after primary chemical crosslinking need to satisfy a specific difference range. By optimizing the melting point difference, the obtained polyester biological patch

features stable coating, excellent leak-proof performance, rapid endothelialization, high resistance to peeling and degradation, favorable biocompatibility, satisfactory compliance and outstanding mechanical properties.

[0008] In addition, the research proves that controlling four key mechanical parameters within specific ranges, namely maximum tensile elongation, elastic deformation rate, maximum tensile force, and the ratio of elastic deformation rate to maximum tensile elongation, can further enhance the stability of the collagen fibril coating on the polyester biological patch and optimize its leak-proof performance.

[0009] In one aspect, the present invention provides a polyester biological patch for aortic root enlargement. The patch consists of polyester fabric attached with a collagen fibril coating. The collagen fibril coating is formed by crosslinking collagen molecules or collagen fibrils (pH=7.0) through primary chemical crosslinking and secondary chemical crosslinking. The primary chemical crosslinking is performed on collagen fibrils to obtain collagen fibrils after primary chemical crosslinking. The secondary chemical crosslinking allows the collagen fibrils after primary crosslinking to adhere to the internal voids and surface of polyester fabric and form a collagen fibril coating via crosslinking. The melting point of the collagen fibrils after primary chemical crosslinking is 68.21–71.53 °C, the melting point of the collagen fibril coating is 75.13–85.88 °C, and the difference between the melting point of the collagen fibril coating and that of the collagen fibrils after primary chemical crosslinking ranges from 6.68 °C to 14.35 °C.

[0010] Preferably, the difference between the melting point of the collagen fibril coating and that of the collagen fibrils after primary chemical crosslinking is 10.04–12.36 °C.

[0011] Preferably, the maximum tensile elongation of the polyester biological patch is 28–69%, the elastic deformation rate is 13–39%, the maximum tensile force is 18–45 N, and the ratio of elastic deformation rate to maximum tensile elongation is 19–93%.

[0012] Preferably, the ratio of elastic deformation rate to maximum tensile elongation is 47–79%.

[0013] Preferably, the polyester fabric is pretreated with an alkaline solution, which is a mixed alkali solution containing 1% sodium carbonate and 0.5% Tween 20, as well as a 0.5% sodium hydroxide solution.

[0014] Preferably, the polyester fabric is pretreated by ultraviolet irradiation.

[0015] In another aspect, the present invention provides a preparation method of the polyester biological patch for aortic root enlargement, comprising the following steps:

[0016] S1: Using animal-derived collagen (preferably mammalian-derived collagen) as the raw material and glutaraldehyde as the crosslinking agent, perform primary chemical crosslinking to obtain collagen fibrils after primary chemical crosslinking with a melting point of 68.21–71.53 °C.

[0017] S2: Spray the collagen fibrils obtained in Step S1 onto polyester fabric, followed by drying to obtain polyester fabric adsorbed with collagen fibrils.

[0018] S3: Immerse the polyester fabric adsorbed with collagen fibrils into a crosslinking agent solution to obtain polyester fabric impregnated with crosslinking agent. The crosslinking agent solution is a compound solution of N-hydroxysuccinimide and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, preferably compounded at a mass ratio of 1:1, with a concentration of 5–80 mg/mL.

[0019] S4: Immerse the crosslinking agent-impregnated polyester fabric adsorbed with collagen

fibrils obtained in step S3 into a collagen fibril solution containing first chemically crosslinked collagen fibrils at a concentration of 0.1–20 mg/mL, stand for more than 2 h, and then dry to obtain the polyester biological patch with a collagen fibril coating attached thereon. The melting point range of the collagen fibril coating is 75.13–85.88 °C.

[0020] Preferably, in Step S2, the spraying density of the collagen fibrils after primary chemical crosslinking on the polyester fabric is 1–6 mg/cm².

[0021] Preferably, the polyester fabric in Step S2 is pretreated by alkali treatment or ultraviolet irradiation.

[0022] In specific embodiments, the alkali treatment includes two procedures:

[0023] ① Alkali treatment 1: Immerse polyester fabric into a mixed alkali solution containing 1% sodium carbonate and 0.5% Tween 20 at 60 °C for 25–30 minutes. Rinse the polyester fabric repeatedly with preheated ultrapure water at 60 °C until no obvious foam exists in the washing liquid, and then dry the fabric in an oven at 60 °C.

[0024] ② Alkali treatment 2: Immerse the dried polyester fabric into a 0.5% sodium hydroxide solution preheated to 99 °C for 25–30 minutes. Rinse repeatedly with room-temperature purified water until the pH value of the washing liquid reaches 6.0–7.0, spread out the polyester fabric and dry it.

[0025] In specific embodiments, the ultraviolet irradiation is conducted under the following conditions: adopt a wavelength of 312 nm, and expose the polyester fabric for 30–120 minutes with an energy of 10–90 J.

[0026] The polyester biological patch provided by the present invention can withstand the high pulsating pressure at the aortic root, and features anti-peeling coating, excellent leak-proof performance, high degradation resistance, favorable biocompatibility, satisfactory compliance and outstanding mechanical properties, which is specially applicable to aortic root enlargement surgery.

DETAILED DESCRIPTION

[0027] Unless otherwise specified, all parts mentioned in this application refer to parts by mass, all ratios refer to mass ratios, and all percentages refer to mass percentages.

[0028] Aiming at the actual clinical application demands and the physiological environment of the aortic root, the embodiments of the present invention provide a polyester biological patch for aortic root enlargement. The patch can endure the high pulsating pressure at the aortic root, with suture resistance, stable coating, low coating peeling risk, excellent leak-proof performance, rapid endothelialization, high degradation resistance, favorable biocompatibility, good compliance and superior mechanical properties.

[0029] **I. Preparation of Collagen Fibrils**

[0030] Step 1: Pretreatment of animal-derived tissues. Take fresh porcine skin tissues, remove surface fat, and soak the tissues in acetone solution at room temperature for 16 hours. Rinse with deionized water for 3 to 5 times to remove residual acetone. Then place the treated tissues into 2.0 M sodium hydroxide solution, stir at room temperature for 16 hours, and soak and rinse the materials with deionized water until neutral.

[0031] Step 2: Preparation of crude collagen extract. Crush and homogenize the rinsed materials in 0.5 M acetic acid. Extract collagen at a temperature of 18 °C for 72 hours by adding pepsin at a mass ratio of tissue to pepsin of 20:1. Centrifuge the extracting solution to collect the supernatant, stir evenly and perform clarification and filtration to control the turbidity below 30, so as to obtain the

crude collagen extract.

[0032] Step 3: Purification. Perform ultrafiltration on the crude collagen extract via a tangential flow filtration (TFF) system, concentrate the solution to 3 mg/mL, and then dialyze with 20 mM acetic acid solution with a dialysis volume 20 times of the original solution to obtain purified collagen molecules.

[0033] Step 4: Collagen fibrillogenesis. Take a certain volume of purified collagen molecules, add phosphate buffer solution (volume ratio of 0.2M Na_2HPO_4 : 0.2M NaH_2PO_4 =7:3, v:v) with a volume of 1/10 of the collagen solution. Mix evenly to adjust the pH value to 7.0, and place the mixture at 30 °C for 6 hours to obtain collagen fibrils.

[0034] The above four steps can be implemented by any existing technical means as long as the corresponding technical objectives are achieved.

[0035] **II. Preparation of Collagen Fibrils after Primary Chemical Crosslinking**

[0036] S1: Primary chemical crosslinking. Add the collagen fibrils prepared in the above steps into glutaraldehyde aqueous solutions of different concentrations, mix evenly, stir overnight at 30 °C, and centrifuge to collect precipitates. Rinse the precipitates for 2 to 3 times with phosphate buffer solution (pH =7.0) to obtain collagen fibrils after primary chemical crosslinking.

[0037] The concentration of the glutaraldehyde aqueous solution is 0.003%–0.04%. The difference among Embodiment 1 to Embodiment 8 lies in the concentration of glutaraldehyde aqueous solution adopted.

[0038] The melting points (recorded as Melting Point 1) of the collagen fibrils after primary chemical crosslinking prepared in Embodiment 1 to Embodiment 8 are determined by differential scanning calorimetry (DSC). The specific test method is as follows: Transfer the samples into an aluminum crucible for DSC testing and seal the crucible. Conduct scanning under nitrogen atmosphere with a heating rate of 10 K/min within the temperature range of 25–100 °C which covers the melting range of the samples.

[0039] **Embodiments 1 to 8**

[0040] The main differences between Embodiments 1 to 8 and the measured Melting Point 1 are shown in the following table:

Table 1: Differences and Measured Melting Point 1 of Embodiments 1 to 8

Group	Concentration of glutaraldehyde aqueous solution	Melting Point 1 (°C)	Group	Concentration of glutaraldehyde aqueous solution	Melting Point 1 (°C)
Embodiment 1	0.003%	68.21	Embodiment 5	0.008%	69.67
Embodiment 2	0.005%	68.67	Embodiment 6	0.01%	70.33
Embodiment 3	0.006%	68.98	Embodiment 7	0.02%	70.98
Embodiment 4	0.007%	69.35	Embodiment 8	0.04%	71.53

[0041] It can be concluded from Table 1 that the Melting Point 1 of the collagen fibrils after primary chemical crosslinking prepared in Embodiment 1 to Embodiment 8 ranges from 68.21 °C to 71.53 °C.

[0042] **III. Adhesion of Collagen Fibrils after Primary Chemical Crosslinking to Polyester Fabric**

[0043] S2: Uniformly spray the collagen fibrils after primary chemical crosslinking obtained in Step S1 onto polyester fabric with a spraying density of 1–6 mg/cm². After spraying, dry the fabric in an oven at 30–35 °C to obtain polyester fabric adsorbed with collagen fibrils.

[0044] S3: Fully immerse the polyester fabric adsorbed with collagen fibrils into the secondary

crosslinking agent solution and stand at room temperature for 20 minutes to obtain crosslinking agent-impregnated polyester fabric adsorbed with collagen fibrils. The preparation method of the secondary crosslinking agent solution is as follows: Weigh N-hydroxysuccinimide (NHS) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) at a mass ratio of 1:1, and dissolve them in phosphate buffered saline (PBS, pH=7.2) to prepare the crosslinking agent solution. The concentration of both NHS and EDC is 5–80 mg/mL.

[0045] S4: Secondary chemical crosslinking. Prepare a collagen fibril solution with a concentration of 0.1–20 mg/mL using the collagen fibrils after primary chemical crosslinking and PBS solution (pH = 7.2).

[0046] Immerse the crosslinking agent-impregnated polyester fabric adsorbed with collagen fibrils into the above collagen fibril solution, stand at room temperature for more than 2 hours (preferably overnight), and fully dry at 30–35 °C. The collagen fibrils undergo secondary crosslinking to form a collagen fibril coating attached to the internal voids and surface of polyester fabric, thus obtaining the polyester biological patch for aortic root enlargement.

[0047] The melting point of the coating (recorded as Melting Point 2) is determined by DSC. The test method is as follows: Transfer the prepared polyester biological patch and pure polyester fabric into aluminum crucibles for DSC testing and seal the crucibles. Conduct scanning under nitrogen atmosphere with a heating rate of 10 K/min within the temperature range of 25–100 °C. The melting point of the collagen fibril coating is obtained by excluding the background peak of polyester fabric.

[0048] Dehydrate the polyester biological patch with collagen fibril coating via glycerol replacement: immerse the patch in 100% glycerol to fully replace the water molecules inside the polyester fabric with glycerol, so as to complete desiccation.

[0049] Embodiment 9 to Embodiment 56 are prepared by adopting collagen fibrils with different crosslinking degrees from Embodiment 1 to Embodiment 8, and adjusting the spraying density, crosslinking agent concentration, collagen fibril solution concentration and drying temperature.

[0050] **Embodiments 9 to 56**

[0051] Based on the III. Adhesion Of Primary Chemically Crosslinked Collagen Fibrils To Polyester Fabrics, the main differences of Embodiments 9 to 56, Melting Point 2, and the measured difference values between Melting Point 2 and Melting Point 1 are shown in Table 2 below:

Table 2 Main Difference and Related Melting Point of Embodiments 9 to 56

Group	Embodiment for Preparing Collagen Fibrils	Spraying Density in Step S2 (mg/cm²)	Crosslinker Concentration in Step S3 (mg/mL)	Concentration of Collagen Fibril Solution in Step S4 (mg/mL)	Drying Temperature in Step S2 and Step S4 (℃)	Melting Point 1 (℃)	Melting Point 2 (℃)	Difference Between Melting Point 2 and Melting Point 1 (℃)
Embodiment 9	Embodiment 1	1	5	1	30	68.21	72.28	4.07
Embodiment 10	Embodiment 1	2	20	5	32	68.21	78.48	10.27
Embodiment 11	Embodiment 1	1.5	5	1	31	68.21	75.13	6.92
Embodiment 12	Embodiment 1	3	50	10	33	68.21	80.86	12.65
Embodiment 13	Embodiment 1	4	50	6	34	68.21	79.2	10.99
Embodiment 14	Embodiment 1	6	40	5	35	68.21	78.63	10.42
Embodi	Embodime	3	50	10	30	68.67	81.02	12.35

ment 15	nt 2							
Embodiment 16	Embodiment 2	1	20	2	31	68.67	77.32	8.65
Embodiment 17	Embodiment 2	2	50	8	32	68.67	79.79	11.12
Embodiment 18	Embodiment 2	1.5	40	5	33	68.67	78.8	10.13
Embodiment 19	Embodiment 2	4	40	6	34	68.67	79.49	10.82
Embodiment 20	Embodiment 2	6	50	12	35	68.67	81.03	12.36
Embodiment 21	Embodiment 3	3	50	9	30	68.98	80.81	11.83
Embodiment 22	Embodiment 3	4	50	12	31	68.98	81.60	12.62
Embodiment 23	Embodiment 3	2	50	8	33	68.98	80.13	11.15
Embodiment 24	Embodiment 3	1.5	40	5	33	68.98	78.22	9.24
Embodiment 25	Embodiment 3	1	5	1	34	68.98	71.61	2.63
Embodiment 26	Embodiment 3	6	50	10	35	68.98	80.56	11.58
Embodiment 27	Embodiment 4	1	40	6	30	69.35	79.52	10.17
Embodiment 28	Embodiment 4	1.5	50	12	31	69.35	81.78	12.43
Embodiment 29	Embodiment 4	2	40	5	32	69.35	78.52	9.17
Embodiment 30	Embodiment 4	3	50	10	33	69.35	80.94	11.59
Embodiment 31	Embodiment 4	4	40	6	34	69.35	79.84	10.49
Embodiment 32	Embodiment 4	2	20	1	35	69.35	75.07	5.72
Embodiment 33	Embodiment 5	1	50	12	30	69.67	83.35	13.68
Embodiment 34	Embodiment 5	1.5	40	5	31	69.67	78.6	8.93
Embodiment 35	Embodiment 5	1	80	12	32	69.67	88.19	18.52
Embodiment 36	Embodiment 5	3	50	8	32	69.67	80.01	10.34
Embodiment 37	Embodiment 5	1	5	1	34	69.67	73.93	4.26
Embodiment 38	Embodiment 5	6	60	10	35	69.67	84.34	14.67
Embodiment 39	Embodiment 6	1	60	12	30	70.33	84.15	13.82
Embodiment 40	Embodiment 6	1.5	60	10	31	70.33	85.34	15.01
Embodiment 41	Embodiment 6	4	20	1	32	70.33	76.17	5.84
Embodiment 42	Embodiment 6	3	40	6	33	70.33	78.97	8.64
Embodiment 43	Embodiment 6	4	50	10	34	70.33	81.11	10.78
Embodiment 44	Embodiment 6	6	20	2	35	70.33	76.61	6.28
Embodiment 45	Embodiment 7	1	5	1	30	70.98	75.17	4.19
Embodiment 46	Embodiment 7	1.5	20	4	31	70.98	77.66	6.68
Embodiment 47	Embodiment 7	2	80	12	32	70.98	89.59	18.61

Embodiment 48	Embodiment 7	3	20	2	33	70.98	76.24	5.26
Embodiment 49	Embodiment 7	4	50	10	34	70.98	84.14	13.16
Embodiment 50	Embodiment 7	6	60	12	35	70.98	87.46	16.48
Embodiment 51	Embodiment 8	1	80	12	30	71.53	89.99	18.46
Embodiment 52	Embodiment 8	2	50	10	31	71.53	81.15	9.62
Embodiment 53	Embodiment 8	1.5	60	12	32	71.53	85.88	14.35
Embodiment 54	Embodiment 8	3	80	12	33	71.53	89.35	17.82
Embodiment 55	Embodiment 8	6	50	10	34	71.53	81.57	10.04
Embodiment 56	Embodiment 8	4	20	2	35	71.53	76.88	5.35

[0052] It can be seen from Table 2 that:

[0053] (1) The polyester patches obtained in Embodiments 9 to 14 adopt the primary chemically crosslinked collagen fibrils prepared in Embodiment 1, wherein Melting Point 1 of the coating is 68.21 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 9 to 14 ranges from 72.28 °C to 80.86 °C, and the difference value between Melting Point 2 and Melting Point 1 is 4.07–12.65 °C.

[0054] (2) The polyester patches obtained in Embodiments 15 to 20 adopt the primary chemically crosslinked collagen fibrils prepared in Embodiment 2, wherein Melting Point 1 of the coating is 68.67 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 15 to 20 ranges from 77.32 °C to 81.03 °C, and the difference value between Melting Point 2 and Melting Point 1 is 8.65–12.36 °C.

[0055] (3) The polyester patches obtained in Embodiments 21 to 26 adopt the primary chemically crosslinked collagen fibrils prepared in Embodiment 3, wherein Melting Point 1 of the coating is 68.98 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 21 to 26 ranges from 71.61 °C to 81.60 °C, and the difference value between Melting Point 2 and Melting Point 1 is 2.63–12.62 °C.

[0056] (4) The polyester patches obtained in Embodiments 27 to 32 adopt the primary chemically crosslinked collagen fibrils prepared in Embodiment 4, wherein Melting Point 1 of the coating is 69.35 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 27 to 32 ranges from 75.07 °C to 81.78 °C, and the difference value between Melting Point 2 and Melting Point 1 is 5.72–12.43 °C.

[0057] (5) The polyester patches obtained in Embodiments 33 to 38 adopt the primary chemically crosslinked collagen fibrils prepared in Embodiment 5, wherein Melting Point 1 of the coating is 69.67 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 33 to 38 ranges from 73.93 °C to 88.19 °C, and the difference value between Melting Point 2 and Melting Point 1 is 4.26–18.52 °C.

[0058] (6) The polyester patches obtained in Embodiments 39 to 44 adopt the primary chemically crosslinked collagen fibrils prepared in Embodiment 6, wherein Melting Point 1 of the coating is 70.33 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 39 to 44 ranges from 76.17 °C to 85.34 °C, and the difference value between Melting Point 2 and Melting Point

1 is 5.84–15.01 °C.

[0059] (7) The polyester patches obtained in Embodiments 45 to 50 adopt the primary chemically crosslinked collagen fibrils prepared in Embodiment 7, wherein Melting Point 1 of the coating is 70.98 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 45 to 50 ranges from 75.17 °C to 89.59 °C, and the difference value between Melting Point 2 and Melting Point 1 is 4.19–18.61 °C.

[0060] (8) The polyester patches obtained in Embodiments 51 to 56 adopt the primary chemically crosslinked collagen fibrils prepared in Embodiment 8, wherein Melting Point 1 of the coating is 71.53 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 51 to 56 ranges from 76.88 °C to 89.99 °C, and the difference value between Melting Point 2 and Melting Point 1 is 5.35–18.46 °C.

[0061] In summary, when Melting Point 1 is in the range of 68.21–71.53 °C, Melting Point 2 of the coating of the polyester patches obtained in Embodiments 9 to 56 ranges from 71.61 °C to 89.99 °C, and the difference value between Melting Point 2 and Melting Point 1 is 2.63–18.61 °C.

[0062] **Coating peeling test of patches in Embodiment 9 to Embodiment 56**

[0063] The collagen content before and after the pulsatile flow test can directly reflect the stability of the coating. Infrared intensity serves as another indirect characterization method for collagen content. Comparing the intensity of the characteristic infrared peaks of collagen on the patches before and after the pulsatile flow test can also indirectly reflect the coating stability.

[0064] The polyester biological patches prepared in the above Embodiments 9 to 56 were respectively subjected to pulsatile flow tests in accordance with the standard ISO 5840. Each polyester biological patch with a length of 4 cm and a width of 1 cm was sewn onto a pulsatile flow platform. After 90 days of pulsation under standard physiological conditions, the collagen content and infrared transmittance of collagen of the patches before and after the test were compared to evaluate the stability of the collagen fibril coating under pulsating flow. The test results are shown in Table 3.

Table 3 Changes Of Collagen Coating Content Of Patches Before And After Pulsatile Flow Test (Embodiments9 To 56)

Group	Collagen Content (mg/cm^2)			Collagen Infrared Transmittanc (%)		
	Before Pulsation	After Pulsation	Difference	Before Pulsation	After Pulsation	Difference
Embodiment 9	0.596	0.495	0.101	83.27	84.65	1.38
Embodiment 10	0.805	0.794	0.011	77.35	77.39	0.04
Embodiment 11	0.653	0.639	0.014	82.55	82.94	0.39
Embodiment 12	1.220	1.132	0.088	69.62	70.14	0.52
Embodiment 13	0.932	0.918	0.014	64.31	64.55	0.24
Embodiment 14	0.892	0.822	0.07	74.69	74.73	0.04
Embodiment 15	1.259	1.220	0.039	66.62	66.98	0.36
Embodiment 16	0.752	0.744	0.008	78.46	78.49	0.03
Embodiment 17	1.035	1.02	0.015	62.52	62.71	0.19
Embodiment 18	0.894	0.881	0.013	74.69	74.98	0.29
Embodiment 19	0.985	0.957	0.028	74.85	74.89	0.04
Embodiment 20	1.260	1.171	0.089	66.05	66.51	0.46
Embodiment 21	1.190	1.113	0.077	60.55	60.59	0.04
Embodiment 22	1.460	1.368	0.092	63.25	63.60	0.35
Embodiment 23	1.096	1.020	0.076	61.38	62.03	0.65
Embodiment 24	0.783	0.773	0.010	77.92	77.99	0.07
Embodiment 25	0.583	0.403	0.180	83.56	84.69	1.13

Embodiment 26	1.108	1.075	0.033	60.65	61.36	0.71
Embodiment 27	0.994	0.98	0.014	72.78	72.8	0.02
Embodiment 28	1.556	1.554	0.002	61.57	62.25	0.68
Embodiment 29	0.865	0.852	0.013	76.19	76.23	0.04
Embodiment 30	1.225	1.137	0.088	66.24	66.78	0.54
Embodiment 31	1.136	1.100	0.036	70.48	70.64	0.16
Embodiment 32	0.682	0.578	0.104	79.4	80.41	1.01
Embodiment 33	1.562	1.515	0.047	61.94	62.88	0.94
Embodiment 34	0.869	0.846	0.023	74.98	75.09	0.11
Embodiment 35	1.992	1.833	0.159	58.81	60.57	1.76
Embodiment 36	1.213	1.177	0.036	69.96	70.25	0.29
Embodiment 37	0.607	0.390	0.217	83.12	84.27	1.15
Embodiment 38	1.961	1.927	0.134	60.68	62.45	1.77
Embodiment 39	1.852	1.834	0.018	60.79	61.55	0.76
Embodiment 40	1.874	1.725	0.149	62.31	64.45	2.14
Embodiment 41	0.723	0.517	0.206	77.15	79.19	2.04
Embodiment 42	0.931	0.903	0.028	74.25	74.36	0.11
Embodiment 43	1.320	1.229	0.091	63.39	63.95	0.56
Embodiment 44	0.736	0.629	0.107	79.26	80.32	1.06
Embodiment 45	0.694	0.589	0.105	81.15	83.19	2.04
Embodiment 46	0.758	0.749	0.009	78.18	78.21	0.03
Embodiment 47	2.325	2.163	0.162	52.03	53.81	1.78
Embodiment 48	0.726	0.607	0.119	79.21	81.37	2.16
Embodiment 49	1.723	1.707	0.016	61.10	61.81	0.71
Embodiment 50	2.215	2.053	0.162	58.71	60.14	1.43
Embodiment 51	2.358	2.159	0.199	50.03	51.32	1.29
Embodiment 52	1.356	1.214	0.142	63.64	64.67	1.03
Embodiment 53	1.985	1.937	0.048	60.23	60.28	0.05
Embodiment 54	2.059	1.799	0.26	59.51	61.24	1.73
Embodiment 55	1.420	1.376	0.044	63.73	64.42	0.69
Embodiment 56	0.750	0.530	0.22	78.70	79.88	1.18

[0065] (1) It can be seen from Table 3 that among the polyester patches obtained in Embodiments 9 to 14, the coating of the polyester patch from Embodiment 9 exhibits relatively large variations in collagen content and collagen infrared transmittance before and after the pulsatile flow test. Combined with Table 2, it can be observed that Embodiment 9 has a low Melting Point 2 and a small difference between Melting Point 2 and Melting Point 1.

[0066] Combined with Table 2, excluding the polyester patch of Embodiment 9 from Embodiments 9 to 14, when Melting Point 1 is 68.21 °C, the optimized range of Melting Point 2 is 75.13–80.86 °C, and the optimized range of the difference between Melting Point 2 and Melting Point 1 is 6.92–12.65 °C.

[0067] (2) It can be seen from Table 3 that the coatings of polyester patches obtained in Embodiments 15 to 20 all show minor variations in collagen content and collagen infrared transmittance before and after the pulsatile flow test.

[0068] Combined with Table 2, for the polyester patches obtained in Embodiments 15 to 20, when Melting Point 1 is 68.67 °C, the optimized range of Melting Point 2 is 77.32–81.03 °C, and the optimized range of the difference between Melting Point 2 and Melting Point 1 is 8.65–12.36 °C.

[0069] (3) It can be seen from Table 3 that among the polyester patches obtained in Embodiments 21 to 26, the coating of the polyester patch from Embodiment 25 has relatively large variations in collagen content and collagen infrared transmittance before and after the pulsatile flow test. Combined

with Table 2, Embodiment 25 features a low Melting Point 2 and a small difference between Melting Point 2 and Melting Point 1.

[0070] Combined with Table 2, excluding the polyester patch of Embodiment 25 from Embodiments 21 to 26, when Melting Point 1 is 68.98 °C, the optimized range of Melting Point 2 is 78.22–81.60 °C, and the optimized range of the difference between Melting Point 2 and Melting Point 1 is 9.24–12.62 °C.

[0071] (4) It can be seen from Table 3 that among the polyester patches obtained in Embodiments 27 to 32, the coatings of polyester patches from Embodiments 27 to 31 all present slight variations in collagen content and collagen infrared transmittance before and after the pulsatile flow test. By comparison, the polyester patch of Embodiment 32 has low Melting Point 2 and a small difference between Melting Point 2 and Melting Point 1.

[0072] Combined with Table 2, for the polyester patches obtained in Embodiments 27 to 32, when Melting Point 1 is 69.35 °C, the optimized range of Melting Point 2 is 78.52–81.78 °C, and the optimized range of the difference between Melting Point 2 and Melting Point 1 is 9.17–12.43 °C.

[0073] (5) It can be seen from Table 3 that among the polyester patches obtained in Embodiments 33 to 38, the coatings of polyester patches from Embodiments 33–34 and 34 exhibit minor variations in collagen content and collagen infrared transmittance before and after the pulsatile flow test, indicating favorable coating stability. Comparative analysis shows that the coatings of Embodiments 35 and 37 have Melting Point 2 values and Melting Point 2–Melting Point 1 differences at the extreme limits; meanwhile, the Melting Point 2 and corresponding difference value of Embodiment 38 are close to the upper extreme limit.

[0074] Combined with Table 2, excluding Embodiments 35 and 37–38 from Embodiments 33 to 38, when Melting Point 1 is 69.67 °C, the optimized range of Melting Point 2 is 78.60–83.35 °C, and the optimized range of the difference between Melting Point 2 and Melting Point 1 is 8.93–13.68 °C.

[0075] (6) It can be seen from Table 3 that among the polyester patches obtained in Embodiments 39 to 44, the coatings of polyester patches from Embodiments 39 and 42–43 achieve superior stability. Combined with Table 2, it is concluded that when Melting Point 1 of the coating is 70.33 °C, the optimized range of Melting Point 2 is 78.97–84.15 °C, and the optimized range of the difference between Melting Point 2 and Melting Point 1 is 8.64–13.82 °C.

[0076] (7) It can be seen from Table 3 that among the polyester patches obtained in Embodiments 45 to 50, the coatings of polyester patches from Embodiments 46 and 49 show superior stability. Combined with Table 2, it is concluded that when Melting Point 1 of the coating is 70.98 °C, the optimized range of Melting Point 2 is 77.66–84.14 °C, and the optimized range of the difference between Melting Point 2 and Melting Point 1 is 6.68–13.16 °C.

[0077] (8) It can be seen from Table 3 that among the polyester patches obtained in Embodiments 51 to 56, the coatings of polyester patches from Embodiments 53 and 55 exhibit superior stability. Combined with Table 2, it is concluded that when Melting Point 1 of the coating is 71.53 °C, the optimized range of Melting Point 2 is 81.57–85.88 °C, and the optimized range of the difference between Melting Point 2 and Melting Point 1 is 10.04–14.35 °C.

[0078] In summary, by comparing Table 2 and Table 3, the inventors surprisingly found that when Melting Point 1 is within 68.21–71.53 °C, both Melting Point 2 and the difference between Melting Point 2 and Melting Point 1 must satisfy specific numerical ranges to produce polyester patches with

highly stable coatings. Based on the conclusions (1) to (8) above, the following findings are drawn:

[0079] When Melting Point 1 ranges from 68.21 °C to 71.53 °C, Melting Point 2 ranges from 75.13 °C to 85.88 °C, and the difference between Melting Point 2 and Melting Point 1 ranges from 6.68 °C to 14.35 °C, the probability of preparing polyester patches with stable coatings is high.

[0080] When Melting Point 1 ranges from 68.21 °C to 71.53 °C and the difference between Melting Point 2 and Melting Point 1 ranges from 10.04 °C to 12.36 °C, all obtained polyester patches possess extremely stable coatings.

[0081] Subsequent tests were carried out on the polyester biological patches prepared by Embodiments 11–12, 16, 22, 24, 28–29, 33–34, 39, 42, 46, 49 and 53 (hereinafter collectively referred to as the 14 optimized embodiments), all of which satisfy the range of 10.04–12.36 °C for the difference between Melting Point 2 and Melting Point 1.

[0082] **Physical Performance**

[0083] (1) Appearance and thickness

[0084] Visual observation was conducted on the polyester biological patches obtained from 14 optimized embodiments, and the patch surfaces were free of stains, foreign matters, tears, abrasions and particulate matter.

[0085] The thickness of the polyester biological patches from the 14 optimized embodiments was measured to be 0.35±0.15 mm by using a thickness gauge and general measuring tools..

[0086] (2) Mechanical properties and overall water permeability test

[0087] Mechanical tests were conducted on the polyester biological patches from the 14 optimized embodiments to determine four mechanical parameters, namely the maximum tensile elongation, elastic deformation rate, maximum tensile force, and the ratio of elastic deformation rate to maximum tensile elongation. The determination methods for maximum tensile elongation and maximum tensile force refer to existing literature (Li C C, Liu L, Wang S, et al. Comparison of Mechanical Properties Between Allogeneic and Animal-derived Patches[J]. Beijing Biomedical Engineering, 2021). The elastic deformation rate was measured by conventional methods in this field. Specifically, it was calculated according to the elastic deformation section of the tensile curve obtained during the test for maximum tensile elongation.

[0088] An overall water permeability test was performed on the polyester biological patches obtained from the 14 optimized embodiments in accordance with YY/T 0500-2021. Circular specimens with a diameter of 3 cm were cut from the patches. The volume of water permeating through each patch within 1 min under a pressure of 16 kPa was collected to calculate the overall water permeability. The unit of overall water permeability is expressed as mL/(cm²·min).

[0089] The test results of mechanical properties and overall water permeability are presented in Table 4.

Table 4 Mechanical properties and overall water permeability of polyester biological patches in optimized embodiments

14 Optimized Embodiments	Maximum Tensile Elongation	Elastic Deformation Rate	Maximum Tensile Force	Ratio of Elastic Deformation Rate to Maximum Tensile Elongation	Overall Water Permeability （ml/（cm²·min））
Embodiment 11	69%	13%	27N	19%	3.28
Embodiment 12	37%	20%	19N	54%	0.21
Embodiment 16	34%	15%	31N	44%	1.62
Embodiment 22	41%	36%	18N	88%	2.39

Embodiment 24	36%	25%	29N	69%	0.83
Embodiment 28	37%	20%	19N	54%	0.66
Embodiment 29	30%	28%	20N	93%	4.32
Embodiment 33	38%	30%	21N	79%	0.15
Embodiment 34	56%	39%	22N	70%	0.27
Embodiment 39	56%	39%	45N	70%	0.24
Embodiment 42	28%	21%	35N	75%	0.37
Embodiment 46	30%	14%	34N	47%	0.34
Embodiment 49	45%	15%	44N	33%	1.86
Embodiment 53	37%	18%	31N	49%	0.93

[0090] It can be seen from the above table that the polyester biological patches prepared from the 14 optimized embodiments have a maximum tensile elongation ranging from 28% to 69%, an elastic deformation rate ranging from 13% to 39%, a maximum tensile force ranging from 18 N to 45 N, and a ratio of elastic deformation rate to maximum tensile elongation ranging from 19% to 93%. Their overall water permeability is between 0.15 and 4.32 mL/(cm²·min).

[0091] With reference to Table 2, the overall water permeability of the patches from Embodiments 12, 24, 28, 33–34, 39, 42, 46 and 53 is less than 1 mL/(cm²·min). Under such conditions, the inventors surprisingly found that the ratio of elastic deformation rate to maximum tensile elongation of the polyester biological patches falls within the range of 47% to 79%.

[0092] **Chemical Performance**

[0093] (1) Heavy metal and trace element detection

[0094] Test solutions were prepared in accordance with Method 3 for the preparation of water extraction test solutions specified in YY/T 1814-2022 *Surgical Implants—Synthetic Non-absorbable Patches—Hernia Repair Patches*. The extraction operation was carried out at an extraction ratio of 6 cm2/mL under extraction conditions of 70℃±2℃ for 24±2h, and the total area of each test specimen was calculated based on both sides. The prepared test solutions were taken, and each trace element was determined by Inductively Coupled Plasma Mass Spectrometry (ICP-MS) as described in General Chapter 0412 of the *Chinese Pharmacopoeia (2020 Edition)*. The polyester biological patches obtained from the 14 optimized embodiments were tested. Experimental results showed that the total content of nickel, cobalt, copper, arsenic, mercury, lead and chromium in the extraction solutions of the polyester biological patches from the 14 optimized embodiments did not exceed 1 μg/mL; the cadmium content did not exceed 0.1 μg/mL; the color of the extraction solutions was no darker than that of the lead standard reference solution at a concentration of 1 μg/mL.

[0095] (2) Collagen Content

[0096] The collagen content of the polyester biological patches obtained from the 14 optimized embodiments was determined in accordance with the method specified in Appendix A of YY/T 0954-2015 *Acellular Surgical Implants — Type I Collagen Implants*, where k (conversion factor) was 7.46. All test results met the acceptance criteria. The collagen content calculated based on the total area of both front and back surfaces ranged from 0.5 to 3.0 mg/cm².

[0097] (3) Infrared Absorption Spectrum

[0098] Fourier-transform infrared (FTIR) characterization was performed on the polyester biological patches from the 14 optimized embodiments using an IRXross Fourier-transform infrared spectrometer (Shimadzu). Infrared spectra were recorded over the wavenumber range of 4000–400 cm^{-1} with a scanning resolution of 4 cm^{-1}. The characteristic absorption peaks of the patches fell within two wavenumber ranges: 1647.72–1664.28 cm^{-1} and 1548.22–1563.78 cm^{-1}, respectively.

[0100] (4) Ethylene Oxide Residue

[0101] After measurement, the ethylene oxide residue content of each polyester biological patch obtained from the 14 optimized embodiments was all no more than 10 μg/g.

[0102] **IV. Pretreatment 1: Alkali Treatment of Polyester Fabric**

[0103] Preparation of Solution 1: Weigh 20 g of sodium carbonate powder and dissolve it in 1990 mL sterile water for injection, then add 10 g of Tween 20 to prepare a mixed alkaline solution containing 1% sodium carbonate and 0.5% Tween 20 (referred to as "Solution 1"). Add a magnetic stir bar, stir thoroughly, and set aside for later use. Preparation of Solution 2: Weigh 10 g of sodium hydroxide powder into a 2000 mL glass bottle to prepare a 0.5% sodium hydroxide solution (referred to as "Solution 2"). Measure 2000 mL sterile water for injection with a graduated cylinder and add it to the glass bottle. Add a magnetic stir bar, stir thoroughly, and set aside for later use.

[0104] ① Alkaline Treatment 1: Immerse the polyester fabric in Solution 1 heated to 60 °C for 25–30 min. Afterwards, repeatedly rinse the polyester fabric with ultrapure water preheated to 60 °C until no obvious foam is observed in the washing liquid, then place the fabric in an oven and dry at 60 °C.

[0105] ② Alkaline Treatment 2: Immerse the dried polyester fabric in Solution 2 preheated to 99.0 °C for 25–30 min. Then repeatedly rinse the fabric with room-temperature purified water until the pH of the washing liquid reaches 6.0–7.0 (tested with a pH meter). Spread the rinsed polyester fabric flat in a 15 cm petri dish and dry in an oven at 60 °C to obtain alkali-treated polyester fabric.

[0106] With reference to the III. Adhesion of Collagen Fibrils after Primary Chemical Crosslinking to Polyester Fabric, the alkali-treated polyester fabric is adopted to prepare the polyester patches of Embodiments 57–66. The melting point of the coating is measured via DSC (recorded as "Melting Point 3").

[0107] **Embodiments 57–66**

[0108] The difference between Melting Point 2 and Melting Point 1 of the polyester biological patches obtained from the 14 optimized embodiments falls within the range of 10.04–12.36 °C. The polyester biological patches of Embodiments 57–66 are prepared with alkali-treated polyester fabric. The polyester biological patches of Embodiments 57–66 were compared with 10 embodiments whose difference between Melting Point 2 and Melting Point 1 was outside 10.04–12.36 °C. The key differences and detailed measured melting point data are shown in Table 5 below.

Table 5 Key Differences and Measured Melting Points of Embodiments 57–66

Group	Difference	Corresponding Melting Point 2 (°C)	Difference between Melting Point 2 and Melting Point 1 (°C)	Melting Point 3 (°C)	Difference between Melting Point 3 and Melting Point 1 (°C)
Embodiment 57	Alkali-treated polyester fabric adopted compared with Embodiment 11	75.13	6.92	79.58	11.37
Embodiment 58	Alkali-treated polyester fabric adopted compared with Embodiment 12	80.86	12.65	80.42	12.21
Embodiment 59	Alkali-treated polyester fabric adopted compared with Embodiment 16	77.32	8.65	80.07	11.40

Embodiment 60	Alkali-treated polyester fabric adopted compared with Embodiment 22	81.60	12.62	81.04	12.06
Embodiment 61	Alkali-treated polyester fabric adopted compared with Embodiment 24	78.22	9.24	81.11	12.13
Embodiment 62	Alkali-treated polyester fabric adopted compared with Embodiment 28	81.78	12.43	81.20	11.85
Embodiment 63	Alkali-treated polyester fabric adopted compared with Embodiment 29	78.52	9.17	80.74	11.39
Embodiment 64	Alkali-treated polyester fabric adopted compared with Embodiment 33	83.35	13.68	80.33	10.66
Embodiment 65	Alkali-treated polyester fabric adopted compared with Embodiment 34	78.60	8.93	80.61	10.94
Embodiment 66	Alkali-treated polyester fabric adopted compared with Embodiment 39	84.15	13.82	81.71	11.38

[0109] As indicated by the melting point measurement results in Table 5, the range of the difference between Melting Point 3 and Melting Point 1 of the collagen fibril coating on polyester biological patches prepared with alkali-treated polyester fabric is closer to 10.04–12.36 °C.

[0110] **Coating Delamination Performance of Patches from Embodiments 57–66**

[0111] Pulsatile flow tests were carried out on the polyester biological patches prepared in Embodiments 57–66 respectively, and the test results are listed in Table 6.

Table 6 Changes of Coating on Patches from Embodiments 57–66 Before and After Pulsatile Flow Test

Group	Difference in collagen content before and after pulsatile flow (mg/cm²)	Difference in infrared transmittance of collagen before and after pulsatile flow (%)
Embodiment 57	0.004	0.08
Embodiment 58	0.024	0.03
Embodiment 59	0.006	0.11
Embodiment 60	0.013	0.05
Embodiment 61	0.002	0.08
Embodiment 62	0.007	0.04
Embodiment 63	0.003	0.15
Embodiment 64	0.004	0.07
Embodiment 65	0.022	0.63
Embodiment 66	0.013	0.32

[0112] It can be seen from the above table that polyester biological patches made from alkali-treated polyester fabric exhibit less coating delamination and higher coating stability.

[0113] **Mechanical Property and Overall Water Permeability Test of Patches from Embodiments 57–66**

[0114] Overall water permeability tests were performed on the polyester biological patches obtained from Embodiments 57–66, and the test results are shown in Table 7.

Table 7 Mechanical Property and Overall Water Permeability Test Results of Patches from Embodiments 57–66

Group	Ultimate tensile elongation	Elastic deformation rate	Maximum tensile force	Ratio of elastic deformation rate to ultimate tensile elongation	Overall water permeability (mL/(cm²·min))
Embodiment 57	31%	17%	43 N	55%	0.32
Embodiment 58	47%	30%	36 N	64%	1.06
Embodiment 59	48%	24%	27 N	50%	0.87
Embodiment 60	52%	27%	31 N	52%	0.33
Embodiment 61	55%	42%	22 N	76%	0.95
Embodiment 62	48%	30%	19 N	63%	1.38
Embodiment 63	35%	20 N	25 N	57%	0.71
Embodiment 64	57%	32%	33 N	56%	0.87
Embodiment 65	33%	23%	40 N	70%	0.61
Embodiment 66	28%	16%	36 N	57%	0.85

[0115] The table above shows that all patches from Embodiments 57–66 have low overall water permeability.

[0116] Comprehensive analysis of Table 5 to Table 7 leads to the following conclusion: polyester biological patches fabricated from alkali-treated polyester fabric have a difference between Melting Point 3 and Melting Point 1 ranging from 10.66 to 12.21 °C (closer to 10.04–12.36 °C), the ratio of elastic deformation rate to ultimate tensile elongation is 50–76% (within the range of 47–79%), the collagen fibril coating has high stability, and the overall water permeability is low.

[0117] **V. Pretreatment 2: Ultraviolet Irradiation of Polyester Fabric**

[0118] **Embodiments 67–71**

[0119] Polyester fabric was exposed under a wavelength of 312 nm with energy ranging from 10 to 90 J for 30–120 min to obtain UV-irradiated polyester fabric. Referring to Section II Adhesion of Primary Chemically Crosslinked Collagen Fibrils to Polyester Fabric, the UV-irradiated polyester fabric was adopted to prepare polyester biological patches of Embodiments 67–71. The melting point of the collagen fibril coating was measured via Differential Scanning Calorimetry (DSC), recorded as "Melting Point 4".

[0120] **Embodiments 67–71**

Table 8 Key Differences and Measured Melting Points of Embodiments 67–71

Group	Difference	Energy (J)	Exposure Time (min)	Corresponding Melting Point 2 (°C)	Difference between Melting Point 2 and Melting Point 1 (°C)	Melting Point 4 (°C)	Difference between Melting Point 4 and Melting Point 1 (°C)

Embodiment 67	UV-irradiated polyester fabric adopted compared with Embodiment 11	10	120	75.13	6.92	78.53	10.32
Embodiment 68	UV-irradiated polyester fabric adopted compared with Embodiment 12	15	30	80.86	12.65	79.13	10.92
Embodiment 69	UV-irradiated polyester fabric adopted compared with Embodiment 16	20	60	77.32	8.65	80.12	11.45
Embodiment 70	UV-irradiated polyester fabric adopted compared with Embodiment 22	25	120	81.60	12.62	80.81	11.83
Embodiment 71	UV-irradiated polyester fabric adopted compared with Embodiment 24	30	120	78.22	9.24	80.44	11.46
Embodiment 72	UV-irradiated polyester fabric adopted compared with Embodiment 28	35	30	81.78	12.43	80.60	11.25
Embodiment 68	UV-irradiated polyester fabric adopted compared with Embodiment 29	40	45	78.52	9.17	81.16	11.81
Embodiment 69	UV-irradiated polyester fabric adopted compared with Embodiment 33	60	60	83.35	13.68	81.77	12.10
Embodiment 70	UV-irradiated polyester fabric adopted compared with Embodiment 34	80	100	78.60	8.93	80.23	10.56
Embodiment 71	UV-irradiated polyester fabric adopted compared with Embodiment 39	90	120	84.15	13.82	81.20	10.87

[0121] According to the melting point measurement results shown in Table 8, the range of the difference between Melting Point 4 and Melting Point 1 of the collagen fibril coating on polyester biological patches prepared with UV-irradiated polyester fabric is closer to 10.04–12.36 °C.

[0122] **Coating Delamination Performance of Patches from Embodiments 67–71**

[0123] Pulsatile flow tests were conducted on the polyester biological patches of Embodiments 67–71, and the test results are summarized in Table 9.

Table 9 Changes of Coating on Patches from Embodiments 67–71 Before and After Pulsatile Flow Test

Group	Difference in collagen content before and after pulsatile flow	Difference in infrared transmittance of collagen before and after pulsatile flow
Embodiment 67	0.003	0.13
Embodiment 68	0.004	0.12
Embodiment 69	0.008	0.09
Embodiment 70	0.015	0.03

Embodiment 71	0.012	0.11
Embodiment 72	0.002	0.24
Embodiment 68	0.013	0.23
Embodiment 69	0.008	0.02
Embodiment 70	0.003	0.09
Embodiment 71	0.004	0.43

[0124] The table above demonstrates that the coating of polyester biological patches from Embodiments 67–71 shows less delamination and higher stability compared with patches fabricated from polyester fabric without UV irradiation.

[0125] **Mechanical Property and Overall Water Permeability Test of Patches from Embodiments 67–71**

[0126] Overall water permeability tests were performed on the polyester biological patches obtained from Embodiments 67–71, and the test results are listed in Table 10.

Table 10 Mechanical Property and Overall Water Permeability Test Results of Patches from Embodiments 67–71

Group	Ultimate tensile elongation	Elastic deformation rate	Maximum tensile force	Ratio of elastic deformation rate to ultimate tensile elongation	Overall water permeability (mL/(cm²·min))
Embodiment 67	32%	19%	18 N	58%	0.29
Embodiment 68	34%	21%	43 N	62%	0.62
Embodiment 69	45%	24%	32 N	54%	0.31
Embodiment 70	46%	22%	35 N	47%	0.53
Embodiment 71	62%	44%	29 N	71%	0.74
Embodiment 72	34%	18%	25 N	52%	0.63
Embodiment 68	55%	30%	33 N	55%	1.15
Embodiment 69	42%	29%	42 N	68%	0.51
Embodiment 70	56%	27%	19 N	49%	0.71
Embodiment 71	35%	26%	36 N	73%	0.93

[0127] The table above indicates that all patches from Embodiments 67–71 exhibit low overall water permeability.

[0128] Comprehensive analysis of Table 8 to Table 10 draws the following conclusion: polyester biological patches made from UV-treated polyester fabric have a difference between Melting Point 4 and Melting Point 1 ranging from 10.32 to 12.10 °C (closer to 10.04–12.36 °C), the ratio of elastic deformation rate to ultimate tensile elongation is 47–73% (within the range of 47–79%), the coating stability is improved, and the overall water permeability is increased.

[0129] **VI. Animal Experiment**

[0130] Sheep have heart size and body weight similar to human beings, as well as comparable hemodynamic characteristics and laboratory test indicators. Their coagulation system is similar to humans, or slightly more prone to coagulation, so sheep are widely selected as animal models for heart valve replacement and vascular replacement surgeries. Sheep have docile temperaments, easy management, low postoperative infection risk, simple long-term feeding control, and high long-term survival rates. Therefore, sheep were chosen as experimental animals in this study. Aortic replacement

combined with aortic root enlargement surgery was performed on each single animal to evaluate the in vivo safety and efficacy of the aortic root enlargement patch.

[0131] **1. Test Design and Grouping**

[0132] This is a single-arm trial including 6 male sheep with unrestricted monthly age and body weight of 60–90 kg. Thoracotomy was performed on each animal. The polyester biological patches obtained from Embodiment 10, Embodiment 15 and Embodiment 21 among the 14 optimized embodiments were used to complete aortic replacement combined with aortic root enlargement surgery.

[0133] Animals were housed in suspended stainless steel cages, fed at least twice daily, and provided with municipal tap water for ad libitum drinking. Feeding environment parameters: temperature 16–28 °C, relative humidity 40–70% RH, air exchange frequency ≥8 times per hour, 12-hour light/12-hour dark full-spectrum fluorescent light cycle.

[0134] The facility conditions, cage quality, feed, drinking water and all environmental indicators for animal experiments comply with GB 14925-2023 *Laboratory Animal Environment and Facilities*. Animal management and feeding meet the relevant provisions of the *Guide for the Care and Use of Laboratory Animals*. Facilities and equipment will not cause accidental injury to animals. Cages are regularly cleaned and disinfected to maintain a clean and comfortable environment. Animal drinking and feeding devices are safe, reliable, convenient, clean and hygienic.

[0135] **2. Experimental Protocol**

[0136] (1) Preoperative Preparation

[0137] One week of adaptive feeding before surgery: 12 h light-dark cycle, room temperature 22±6 °C, humidity 40–70%. Animals were fasted for 12–16 h before surgery with free access to water. CT scanning was adopted to measure the aortic annulus diameter of each animal before surgery.

[0138] Scopolamine Hydrobromide Injection (0.01 mg/kg, intramuscular injection) was administered to reduce respiratory secretions. Isoflurane was inhaled via mask, followed by tracheal intubation connected to isoflurane supply. Venous access was established, and an electrocardiograph monitor was connected to monitor heart rate, blood pressure and blood oxygen saturation.

[0139] (2) Surgical Procedures

[0140] Standard surgical procedures were followed, starting with aortic root enlargement surgery repaired by the aortic root patch.

[0141] a. Transthoracic color Doppler echocardiography was performed per routine inspection standards, and preoperative data were recorded.

[0142] b. The animal was placed in the right lateral decubitus position. The chest was disinfected routinely and covered with sterile drapes. Left thoracotomy was conducted through the fourth rib, and systemic heparinization was performed to expose the heart.

[0143] c. Cardiopulmonary bypass (CPB) was established routinely, a left heart drainage tube was placed, the ascending aorta was clamped, and cold blood cardioplegia solution was perfused through the aortic root and/or left/right coronary arteries. Ice slush was applied to cool the heart surface.

[0144] d. An oblique incision was made on the ascending aorta, aortic leaflets were resected, and the annulus diameter was measured. The aortic oblique incision was extended downward from the right wall to the junction of the left and non-coronary leaflets without cutting the left atrium, mitral annulus or anterior leaflet root. The patch was then used to enlarge the aortic root. A valve sizer was adopted to measure the enlarged aortic valve diameter, and enlargement data were recorded.

[0145] e. Bioprosthetic aortic valve of appropriate size was selected and sutured for fixation.

[0146] f. Electrical defibrillation was performed to restore heart beat after aortic declamping. Cardiopulmonary bypass was terminated after stable vital signs. Heparin was neutralized with protamine, all perfusion catheters were removed, and hemostasis was achieved on the wound surface.

[0147] g. Transesophageal echocardiography was conducted to examine the function of the surgically implanted bioprosthetic aortic valve and hemodynamic conditions.

[0148] h. After confirming no active bleeding in the thoracic cavity, a thoracic drainage tube was placed, and the thorax was closed layer by layer with interrupted sutures. The drainage tube was connected to a drainage bottle.

[0149] i. Jugular vein and femoral artery puncture sheaths were removed, and compression hemostasis was maintained for at least 10 min.

[0150] j. The tracheal intubation was removed after the sheep recovered spontaneous breathing, corneal reflex, stable blood pressure and heart rhythm, followed by 30 min observation under natural body position.

[0151] (3) Postoperative Management

[0152] After successful surgery, experimental animals were sent back to the animal housing room for continuous observation and feeding after resuscitation. Feed and water were provided regularly. The animal status was closely monitored throughout postoperative care, pain signs were observed, and appropriate analgesics were administered when necessary.

[0153] Ceftiofur Sodium was injected intramuscularly at 5 mg/kg twice a day for 7 consecutive days after surgery, with complete records kept.

[0154] Heparin Sodium Injection was administered intravenously during surgery at a dose of 1.5 mg/kg or 100–200 U/kg to maintain activated clotting time (ACT) >500 s.

[0155] Warfarin Sodium Tablets combined with Aspirin were administered starting on the day of surgery with an initial dose of 5 mg + 100 mg. The Warfarin Sodium dosage was adjusted according to International Normalized Ratio (INR) results to maintain INR within 1.0–2.5. The anticoagulation regimen was adjusted per physician's requirements in case of hemorrhage or other adverse events.

[0156] **3. Observation Indicators**

[0157] (1) General Condition

[0158] Food intake, mental state, living habits, defecation and urination; presence of dyspnea, oliguria, abnormal behaviors and other symptoms.

[0159] (2) Blood Examinations

[0160] Blood gas analysis, routine blood test, blood biochemistry, coagulation function and immunological tests, to evaluate hemolysis, inflammatory and immune responses of animals after device implantation.

[0161] (3) Transthoracic Echocardiography

[0162] Observe vegetation, abnormal blood flow around the valve and annulus; measure left ventricular volume, transvalvular pressure gradient, aortic valve flow velocity and left ventricular ejection fraction (LVEF); observe and record the size of each cardiac chamber and regurgitation degree of each valve.

[0163] (4) CT Scan

[0164] CT scanning was used to measure aortic annulus diameter data of animals before and after

surgery.

[0165] (5) Gross Anatomy and Pathological Examination

[0166] All animals reaching or failing to reach the test endpoint in this experiment underwent gross anatomy and pathological examination. Blood was collected via femoral vein puncture under general anesthesia for routine blood, liver and kidney function tests. Systemic heparinization at 3 mg/kg was performed to prevent post-mortem blood coagulation which may be confused with thrombosis formed inside the bioprosthetic heart valve. Animals were euthanized via exsanguination under general anesthesia. The tissue surrounding the implanted bioprosthetic heart valve was observed for morphological changes, adhesion and fibrous capsule formation, with photos taken for documentation. Gross visual inspection and photography were conducted to record leaflet morphological changes, thrombosis and calcification of the bioprosthetic heart valve. If thrombosis was present, the wet weight of thrombus and its coverage ratio on the implant surface were recorded. Prosthesis morphology and deformation were documented. The bioprosthetic heart valve and surrounding tissues were collected to prepare pathological sections for microscopic pathological observation. Samples were taken from the bioprosthetic heart valve and its surrounding 3 mm tissue area, fixed in 10% neutral buffered formalin for 10–14 days, embedded in paraffin, sectioned and stained with Hematoxylin-Eosin (H.E.). Organ dissection was performed on the heart, lung, spleen, liver, kidney, brain and other visceral organs. Gross inspection was carried out first to observe the surgical thoracic incision, infarction lesions and abnormal pathological changes, with photos taken for recording.

Table 11 Evaluation and Observation Schedule

Item	Pre-operation	Immediate post-implantation	Post-op Day 1	Post-op Day 3	Post-op Week 1	Post-op Week 4	Post-op Week 12	Post-op Week 26
Physical Examination[1]	√	√	√	√	√	√	√	√
Routine Blood Test	√	√	√	√	√	√	√	√
Blood Biochemistry	√	√	√	√	√	√	√	√
Blood Gas Analysis[2]	√	√						
Hemolysis Test	√					√	√	√
Five Coagulation Assays	√					√	√	√
Immunological Test[3]	√					√	√	√
Echocardiography[4]	√	√				√	√	√
CT Scan	√	√				√	√	√
Angiography						√	√	√
Pathological Anatomy						√[5]		√

Implant Analysis[6]						√		√
Other Complications or Adverse Events[7]	√							

[0167] Notes: 1) Body weight, gender, body temperature, heart rate, respiratory frequency, etc. 2) Performed preoperatively, intraoperatively and immediately after surgery. 3) C-reactive protein detection. 4) Transvalvular pressure gradient, regurgitation, paravalvular leakage and cardiac function. Echocardiography evaluation was conducted preoperatively, intraoperatively, immediately post-operation and at scheduled follow-up time points and test endpoints. Only transthoracic and transesophageal echocardiography were performed at interval follow-up points. Preoperative abdominal ultrasound was used to examine liver and kidney function and exclude abnormal animal models. Abdominal ultrasound was performed before scheduled dissection to assess liver and kidney function. 5) 9 animals in test group and control group respectively; 3 animals were sacrificed at Week 4 for gross observation of intimalization and pathological examination; 6 animals underwent gross anatomical sampling after hematology, ultrasound and angiography examinations at Week 26. 6) Gross visual inspection: pannus formation, tissue ingrowth, thrombosis, calcification, displacement or detachment of bioprosthetic valve, accurate positioning relative to blood flow (attention to device angulation, bending and kinking), morphological and structural component changes of bioprosthetic valve, endothelialization, etc. Histopathology: inflammation, calcification, thrombosis, rejection and other unexpected tissue-device interactions at major visceral organs and implantation site, endothelialization, etc. Additional tests: structural changes and calcification of bioprosthetic valve, calcium content quantification. 7) Such as myocardial infarction, severe arrhythmia, embolism, bioprosthetic valve dysfunction.

[0168] (6) Processing and Analysis of Cardiac Specimens

[0169] The left atrium and left ventricle were incised to observe the valve placement position from the endocardial surface. Tissue samples from the ventricular wall and surrounding area of the aortic valve were collected, stored fresh or refrigerated at 4 °C, and delivered for testing on the day of sacrifice at test endpoint or within 24 h of accidental death. Whole visceral inspection was performed with focus on surface changes of the valve, thrombosis, infection and necrosis of each organ. Routine light microscopy sampling covered the left ventricle, left atrium, aorta, aortic root, tissue surrounding the aortic valve and the bioprosthetic heart valve.

Table 12 Dissection Sampling and Microscopic Examination List for Safety Evaluation Group

Tissue / Organ	Tissue Collection	Fixation	Histopathological Examination
Implanted Patch and Bioprosthetic Valve	√	F	√
Left Atrium, Left Ventricle	√	F	√
Aorta, Aortic Root	√	F	√
Tissue Surrounding Aortic Valve	√	F	√
Liver	√	F	√
Spleen	√	F	√

Lung	√	F	√
Kidney	√	F	√
Brain	√	F	√
Any Gross Abnormal Lesions (if present)	√	F	√

[0170] **4. Results of Animal Experiment**

[0171] (1) Aortic root enlargement surgery was performed on animals using polyester biological patches from Embodiment 10, Embodiment 15 and Embodiment 21 among the 14 optimized embodiments. No anastomotic bleeding or fluid exudation occurred during or after surgery.

[0172] (2) All animals maintained good general conditions during survival feeding with normal body temperature, food intake, defecation and spontaneous activity. No dyspnea, oliguria, obvious weight loss, fever, anorexia, mania or other abnormal behaviors were observed. All animals survived until the test endpoint without complications such as myocardial infarction, severe arrhythmia, embolism or bioprosthetic valve dysfunction.

[0173] No abnormal results were found in routine blood tests (including plasma free hemoglobin, white blood cell count, neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count, red blood cell count, hemoglobin, hematocrit, platelet count), blood biochemistry (total bilirubin, direct bilirubin, alanine transaminase, aspartate transaminase, C-reactive protein, alkaline phosphatase, glutamyl transferase, total protein, albumin, creatinine, uric acid, blood urea nitrogen) and coagulation tests (prothrombin time, thrombin time, activated partial thromboplastin time).

[0174] Electrolyte, liver and kidney function values at all follow-up time points after cardiac radiofrequency ablation surgery were almost within normal ranges. The INR value of coagulation remained around 1.0 preoperatively and during follow-up. No abnormalities were detected in the quantity, morphology and quality of whole blood cells. Test results of white blood cells, red blood cells, hemoglobin, platelets and other indicators remained stable without significant abnormal routine blood parameters. No clinical significant liver or kidney dysfunction was observed; individual values slightly higher or lower than the reference range had no clinical significance. No laboratory test results with clinical significance were identified before surgery and prior to test endpoint sacrifice.

[0175] The above text describes preferred specific embodiments of the present invention in detail. It should be understood that a person of ordinary skill in the art can make numerous modifications and variations based on the conception of the present invention without creative labor. Therefore, all technical solutions that can be obtained by those skilled in the art through logical analysis, reasoning or limited experiments based on the conception of the present invention and the prior art shall fall within the protection scope defined by the claims.

CLAIMS

What is claimed is:

1. A polyester biological patch applicable for aortic root enlargement, characterized in that the polyester biological patch is a polyester fabric coated with a collagen fibril coating; the collagen fibril coating is formed by collagen fibrils via primary chemical crosslinking and secondary chemical crosslinking;

the primary chemical crosslinking refers to chemically crosslinking collagen fibrils to obtain collagen fibrils after primary chemical crosslinking;

the secondary chemical crosslinking refers to attaching the collagen fibrils after primary chemical crosslinking to internal voids and surface of the polyester fabric and performing crosslinking to form the collagen fibril coating;

a melting point of the collagen fibrils after primary chemical crosslinking is 68.21–71.53 °C, a melting point of the collagen fibril coating is 75.13–85.88 °C, and a difference range between the melting point of the collagen fibril coating and that of the collagen fibrils after primary chemical crosslinking is 6.68–14.35 °C.

2. The polyester biological patch applicable for aortic root enlargement according to Claim 1, characterized in that the difference range between the melting point of the collagen fibril coating and that of the collagen fibrils after primary chemical crosslinking is 10.04–12.36 °C.

3. The polyester biological patch applicable for aortic root enlargement according to Claim 1, characterized in that a maximum tensile elongation range of the polyester biological patch is 28–69%, an elastic deformation rate range is 13–39%, a maximum tensile force range is 18–45 N, and a ratio of elastic deformation rate to maximum tensile elongation ranges from 19% to 93%.

4. The polyester biological patch applicable for aortic root enlargement according to Claim 3, characterized in that the ratio of elastic deformation rate to maximum tensile elongation ranges from 47% to 79%.

5. The polyester biological patch applicable for aortic root enlargement according to any one of Claims 1 to 4, characterized in that the polyester fabric is pre-treated with alkali.

6. The polyester biological patch applicable for aortic root enlargement according to Claim 5, characterized in that the alkali solutions are a mixed alkali solution containing 1% sodium carbonate and 0.5% Tween 20, and a 0.5% sodium hydroxide solution.

7. The polyester biological patch applicable for aortic root enlargement according to any one of Claims 1 to 4, characterized in that the polyester fabric is pre-irradiated with ultraviolet.

8. A method for preparing a polyester biological patch applicable for aortic root enlargement, characterized by comprising the following steps:

S1: using animal-derived collagen as raw material and glutaraldehyde as crosslinker, conducting primary chemical crosslinking to obtain collagen fibrils after primary chemical crosslinking with a melting point of 68.21–71.53 °C;

S2: spraying the collagen fibrils after primary chemical crosslinking obtained in Step S1 onto polyester fabric, followed by drying to obtain polyester fabric adsorbed with collagen fibrils;

S3: immersing the polyester fabric adsorbed with collagen fibrils in a crosslinker solution to obtain crosslinker-impregnated polyester fabric adsorbed with collagen fibrils; the crosslinker solution

is a compound solution of N-hydroxysuccinimide and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, preferably compounded at a mass ratio of 1:1 with a concentration of 5–80 mg/mL;

S4: immersing the crosslinker-impregnated polyester fabric adsorbed with collagen fibrils obtained in Step S3 into a collagen fibril solution with collagen fibrils after primary chemical crosslinking at a concentration of 0.1–20 mg/mL, standing for more than 2 h, and drying to obtain the polyester biological patch attached with collagen fibril coating, wherein a melting point range of the collagen fibril coating is 75.13–85.88 °C.

9. The method according to Claim 8, characterized in that in Step S2, a spraying density of the collagen fibrils after primary chemical crosslinking on the surface of the polyester fabric is 1–6 mg/cm².

10. The method according to Claim 8, characterized by further comprising a pretreatment step of alkali treatment or ultraviolet irradiation on the polyester fabric;

Wherein the alkali treatment includes:

① alkali treatment 1: immersing the polyester fabric in a mixed alkali solution containing 1% sodium carbonate and 0.5% Tween 20 at 60 °C for 25–30 min, repeatedly rinsing the polyester fabric with ultrapure water preheated to 60 °C until no obvious foam exists in the washing liquid, and drying in an oven at 60 °C;

② alkali treatment 2: immersing the dried polyester fabric in a preheated 0.5% sodium hydroxide solution at 99 °C for 25–30 min, repeatedly rinsing with room-temperature purified water until the pH of the washing liquid is 6.0–7.0, spreading out the polyester fabric and drying it;

the ultraviolet irradiation comprises: adopting a wavelength of 312 nm, and exposing the polyester fabric under an energy range of 10–90 J for 30–120 min.