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(54) **Titre : TISSU MULTICOUCHE ABSORBABLE RENFORCE POUR DISPOSITIFS MEDICAUX ET PROCEDE DE FABRICATION**

(54) **Title: A REINFORCED ABSORBABLE MULTILAYERED FABRIC FOR USE IN MEDICAL DEVICES AND METHOD OF MANUFACTURE**

(57) **Abrégé/Abstract:**

The present invention is directed to a multilayered fabric comprising a first absorbable nonwoven fabric and a second absorbable woven or knitted fabric, and its method of manufacture.

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ABSTRACT OF THE INVENTION

The present invention is directed to a multilayered fabric comprising a first absorbable nonwoven fabric and a second absorbable woven or knitted fabric, and its method of manufacture.

A REINFORCED ABSORBABLE MULTILAYERED FABRIC FOR USE IN MEDICAL DEVICES AND METHOD OF MANUFACTURE

FIELD OF THE INVENTION

The present invention relates to a reinforced absorbable multilayered fabric that is useful in medical devices and its method of manufacture.

BACKGROUND OF THE INVENTION

It is generally known to use multilayered fabrics in connection with medical procedures. For example, multilayered fabrics are used as all purpose pads, wound dressings, surgical meshes, including hernia repair meshes, adhesion prevention meshes and tissue reinforcement meshes, defect closure devices, and hemostats.

USP 5,593,441 to Lichtenstein et al describes a composite prosthesis preferably having a sheet of polypropylene mesh that allows tissue in-growth, such as Marlex® mesh. This reference discloses that other surgical materials that are suitable for tissue reinforcement and defect closure may be utilized, including absorbable meshes such as a polyglactin 910 (Vicryl®) mesh. The composite prosthesis of Lichtenstein et al also has an adhesion barrier, preferably a sheet of silicone elastomer. This reference generally suggests that that an oxidized regenerated cellulose such as Interceed® (TC7) absorbable adhesion barrier (commercially available from Ethicon, Inc., in Somerville, New Jersey) may be used as the adhesion barrier to produce a composite prosthesis having short term effectiveness. The composite prosthesis of Lichtenstein et al is described for use in reinforcing and repairing a weakened muscular wall while limiting the incidence of postoperative adhesions.

USP 5,686,090 to Schilder et al describes the use of a fleece in combination with a nonabsorbable or absorbable film to prevent mis-growths to adjacent tissue and to reduce adhesions. Schilder et al generally discloses that polypropylene, polyester, polyglactin, polydioxanone or poliglecaprone 25 may be used as the fleece material or the film material. The term "fleece" as used in this reference is described by its porosity, which is described as being in the range between 100 and 1000 $l/(m^2s)$ gas flow, measured with an inlet pressure of 200 Pa, a test surface of 50 cm^2 and a test thickness of 1 mm. The composite of Schilder et al is generally described as being a multilayered implant.

Additionally, multilayered fabrics are useful for tissue engineering and orthopedic applications. The recent emergence of tissue engineering offers numerous approaches to repair and regenerate damaged/diseased tissue. Tissue engineering strategies have explored the use of biomaterials that ultimately can restore or improve tissue function. The use of colonizable and remodelable scaffolding materials has been studied extensively as tissue templates, conduits, barriers and reservoirs. In particular, synthetic and natural materials in the form of foams, sponges, gels, hydrogels, textiles, and nonwovens have been used in vitro and in vivo to reconstruct/regenerate biological tissue, as well as deliver chemotactic agents for inducing tissue growth. The different forms of scaffolds may be laminated to form a multilayered tissue engineering scaffold.

However, the prior art fails to describe or suggest a reinforced absorbable multilayered fabric having a first absorbable nonwoven fabric reinforced by one or more second absorbable woven or knitted fabric.

As used herein, the term "nonwoven fabric" includes, but is not limited to, bonded fabrics, formed fabrics, or engineered fabrics, that are manufactured by processes other than weaving or knitting. More specifically, the term "nonwoven fabric" refers to a porous, textile-like material, usually in flat sheet form, composed primarily or entirely of staple fibers assembled in a web, sheet or batt. The structure of the nonwoven fabric is based on the arrangement of, for example, staple fibers that are typically arranged more or less randomly. The tensile, stress-strain and tactile properties of the nonwoven fabric ordinarily stem from fiber to fiber friction created by entanglement and reinforcement of, for example, staple fibers, and/or from adhesive, chemical or physical bonding.

Notwithstanding, the raw materials used to manufacture the nonwoven fabric may be yarns, scrims, netting, or filaments made by processes that include, weaving or knitting.

SUMMARY OF THE INVENTION

The present invention is directed to a reinforced absorbable multilayered fabric comprising a first absorbable nonwoven fabric reinforced by one or more second absorbable woven or knitted fabric, and its method of manuafacture. More particularly, the first absorbable nonwoven fabric comprises fibers comprising aliphatic polyester polymers, copolymers, or blends thereof; while the second absorbable woven or knitted fabric comprises oxidized regenerated cellulose fibers.

DETAILED DESCRIPTION OF THE INVENTION

The reinforced absorbable multilayered fabric generally comprises a nonwoven fabric and one or more reinforcement fabric. The reinforcement fabric provides a backing to which the nonwoven fabric may be attached, either directly or indirectly.

The nonwoven fabric functions as the first absorbable nonwoven fabric of the reinforced absorbable multilayered fabric described herein. The first absorbable nonwoven fabric is comprised of fibers comprising aliphatic polyester polymers, copolymers, or blends thereof. The aliphatic polyesters are typically synthesized in a ring opening polymerization of monomers including, but not limited to, lactic acid, lactide (including L-, D-, meso and D, L mixtures), glycolic acid, glycolide, ϵ-caprolactone, p-dioxanone (1,4-dioxan-2-one), and trimethylene carbonate (1,3-dioxan-2-one).

Preferably, the first absorbable nonwoven fabric comprises a copolymer of glycolide and lactide, in an amount ranging from about 70 to 95% by molar basis of glycolide and the remainder lactide.

In an alternative embodiment, the first absorbable nonwoven fabric comprises fibers comprised of aliphatic polyester polymers, copolymers, or blends thereof, alone or in combination with oxidized polysaccharide fibers.

Preferably, the nonwoven fabric is made by processes other than weaving or knitting. For example, the nonwoven fabric may be prepared from yarn, scrims, netting or filaments that have been made by processes that include, weaving or knitting. The yarn, scrims, netting and/or filaments are crimped to enhance entanglement with each other and attachment to the second absorbable woven or knitted fabric. Such crimped yarn, scrims, netting and/or filaments may then be cut into staple that is long enough to entangle. The staple may be between about 0.1 and 3.0 inches long, preferably between about 0.5 and 2.5 inches, and most preferably between about 1.0 and 1.5 inches. The staple may be carded to create a nonwoven batt, which may be then needlepunched or calendared into the first absorbable nonwoven fabric. Additionally, the staple may be kinked or piled.

Other methods known for the production of nonwoven fabrics may be utilized and include such processes as air laying, wet forming and stitch bonding. Such procedures are generally discussed in the Encyclopedia of Polymer Science and Engineering, Vol. 10, pp. 204-253 (1987) and Introduction to Nonwovens by Albin Turbank (Tappi Press, Atlanta GA 1999).

The thickness of the nonwoven fabric may range from about 0.25 to 2 mm. The basis weight of the nonwoven fabric ranges from about 0.01 to 0.2 g/in^2; preferably from about 0.03 to 0.1 g/in^2; and most preferably from about 0.04 to 0.08 g/in^2. The weight percent of first absorbable nonwoven fabric may range from about 10 to 80 percent, based upon the total weight of the reinforced absorbable multilayered fabric.

The second absorbable woven or knitted fabric functions as the reinforcement fabric and comprises oxidized polysaccharides, in particular oxidized cellulose and the neutralized derivatives thereof. For example, the cellulose may be carboxylic-oxidized or aldehyde-oxidized cellulose. More preferably, oxidized regenerated polysaccharides including, but without limitation, oxidized regenerated cellulose may be used to prepare the second absorbable woven or knitted fabric. Regenerated cellulose is preferred due to its higher degree of uniformity versus cellulose that has not been regenerated. Regenerated cellulose and a detailed description of how to make oxidized regenerated cellulose are set forth in USP 3,364,200, USP 5,180,398 and USP 4,626,253.

Examples of fabrics that may be utilized as the reinforcement fabric include, but are not limited to, Interceed® absorbable adhesion barrier, Surgicel® absorbable hemostat, Surgicel Nu-Knit® absorbable hemostat and Surgicel® Fibrillar absorbable hemostat (each available from Johnson & Johnson Wound Management Worldwide or Gynecare Worldwide, each a division of Ethicon, Inc., Somerville, New Jersey).

The reinforcement fabric utilized in the present invention may be woven or knitted, provided that the fabric possesses the physical properties necessary for use in contemplated applications. Such fabrics, for example, are described in USP 4,626,253, USP 5,002,551 and USP 5,007,916. In preferred embodiments, the reinforcement fabric is a warp knitted tricot fabric constructed of bright rayon yarn that is subsequently oxidized to include carboxyl or aldehyde moieties in amounts effective to provide the fabrics with biodegradability.

In an alternative embodiment, the second absorbable woven or knitted fabric comprises oxidized polysaccharide fibers in combination with fibers comprised of aliphatic polyester polymers, copolymers, or blends thereof.

The second absorbable woven or knitted fabric preferably comprises oxidized regenerated cellulose and may have a basis weight ranging from about 0.001 to 0.2 g/in^2, preferably in the range of about 0.01 to 0.1 g/in^2, and most preferably in the range of about 0.04 to 0.07 g/in^2.

The first absorbable nonwoven fabric is attached to the second absorbable woven or knitted fabric, either directly or indirectly. For example, the nonwoven fabric may be incorporated into the second absorbable woven or knitted fabric via needlepunching, calendaring, embossing or hydroentanglement, or chemical or thermal bonding. The staple of the first absorbable nonwoven fabric may be entangled with each other and imbedded in the second absorbable woven or knitted fabric. More particularly, for methods other than chemical or thermal bonding, the first absorbable nonwoven fabric may be attached to the second absorbable woven or knitted fabric such that at least about 1% of the staple of the first absorbable nonwoven fabric are exposed on the other side of the second absorbable woven or knitted fabric, preferably about 10-20% and preferably no greater than about 50%. This ensures that the first absorbable nonwoven fabric and the second absorbable woven or knitted fabric remain joined and do not delaminate under normal handling conditions. The reinforced absorbable multilayered fabric is uniform such that substantially none of the second absorbable woven or knitted fabric is visibly devoid of coverage by the first absorbable nonwoven fabric.

One method of making the multilayered fabric described herein is by the following process. Absorbable polymer fibers, having a denier per fiber of about 1 to 4, may be consolidated to about 80 to 120 denier multifilament yarn and then to about 800 to 1200 denier yarns, thermally crimped and then cut to a staple having a length between about 0.75 and 2.0 inch. The staple may be fed into a multiroller dry lay carding machine one or more times and carded into a uniform nonwoven batt, while humidity is maintained between about 20-60% at a room temperature of 15 to 24°C. For example, the uniform nonwoven batt may be made using a single cylinder roller-top card, having a main cylinder covered by alternate rollers and stripper rolls, where the batt is doffed from the surface of the cylinder by a doffer roller and deposited on a collector roll. The batt may be further processed via needlepunching or any other means such as calendaring.

Thereafter, the first absorbable nonwoven fabric may be attached to the second absorbable woven or knitted fabric by various techniques such as needlepunching. The reinforced absorbable multilayered fabric may then be scoured by washing in an appropriate solvent and dried under mild conditions for 10- 30 minutes.

It is desirable to control process parameters such as staple length, opening of the staple, staple feed rate, and relative humidity. For example, the consolidated yarns may have from about 5 to 50 crimps per inch, and preferably from about 10 to 30 crimps per inch. Efficient cutting of the crimped yarns is desirable, as any long and incompletely cut staple tends to stick on the carding machine and cause pilling. A preferred range of the staple length is from about 05 to 2.5 inches, and more preferably from about 1.0 to 1.5 inches.

To optimize uniformity and minimize the build-up of static electricity, the relative humidity may be controlled during batt processing, preferably during carding to form the uniform nonwoven batt. Preferably, the nonwoven batt is processed using a dry lay carding process at a relative humidity of at least about 20% at a room temperature of about 15 to 24°C. For example, the nonwoven batt is processed at a relative humidity of from about 40% to 60%.

The multilayered fabric is scoured using solvents suitable to dissolve any spin finish. Solvents include, but are not limited to, isopropyl alcohol, hexane, ethyl acetate, and methylene chloride. The multilayered fabric is then dried under conditions to provide sufficient drying while minimizing shrinkage.

The reinforced absorbable multilayered fabric may have an average thickness of between about 0.5 and 3.0 mm, preferably between about 1.00 and 2.5 mm, and most preferably between about 1.2 and 2.0 mm. The reported thickness is dependent upon the method of thickness measurement. Preferred methods are the ASTM methods (ASTM D5729-97 and ASTM D1777-64) conventionally used for the textile industry in general and non-woven in particular. Such methods can be slightly modified and appropriately adopted in the present case as described below. The basis weight of the reinforced absorbable multilayered fabric is between about 0.05 and 0.25 g/in^2, preferably between about 0.08 and 0.2 g/in^2, and most preferably between about 0.1 and 0.18 g/in^2. The reinforced absorbable multilayered fabric is uniform such that there is no more than about 10% variation (relative standard deviation of the mean) in the basis weight or thickness across each square inch.

Additionally, the nonwoven fabric may comprise biologically active agents, such as hemostatic agents. Hemostatic agents that may be used include, without limitation, procoagulant enzymes, proteins and peptides, either naturally occurring, recombinant, or synthetic. More specifically, prothrombin, thrombin, fibrinogen, fibrin, fibronectin, Factor X/Xa, Factor VII/VIIa, Factor IX/IXa, Factor XI/XIa, Factor XII/XIIa, tissue factor, von Willebrand Factor, collagen, elastin, gelatin, synthetic peptides having hemostatic activity, derivatives of the above and any combination thereof, may be utilized. Preferred hemostatic agents are thrombin and/or fibrinogen and fibrin.

Alternatively, the reinforced absorbable multilayered fabric may contain bioactive agents to aid in the repair or regeneration of tissue. Examples of bioactive agents include cell attachment mediators, such as peptide-containing variations of the "RGD" integrin binding sequence known to affect cellular attachment, biologically active ligands, and substances that enhance or exclude particular varieties of cellular or tissue ingrowth. Examples of such substances include integrin binding sequence, ligands, bone morphogenic proteins, epidermal growth factor, IGF-I, IGF-II, TGF-β I-III, growth differentiation factor, parathyroid hormone, vascular endothelial growth factor, hyaluronic acid, glycoprotein, lipoprotein, bFGF, TGF-beta superfamily factors, BMP-2, BMP-4, BMP-6, BMP-12, sonic hedgehog, GDF5, GDF6, GDF8, PDGF, recombinant human growth and differentiation factor 5 (rhGDF-5), small molecules that affect the upregulation of specific growth factors, tenascin-C, fibronectin, thromboelastin, thrombin-derived peptides, heparin-binding domains, and the like.

Bioactive agents may also include biologically derived substance selected from the group consisting of demineralized bone matrix (DBM), platelet rich plasma, bone marrow aspirate and bone fragments, all of which may be from autogenic, allogenic, or xenogenic sources.

In other embodiments, the reinforced absorbable multilayered fabric may contain an inorganic filler. The inorganic filler may be selected from alpha-tricalcium phosphate, beta-tricalcium phosphate, calcium carbonate, barium carbonate, calcium sulfate, barium sulfate, hydroxyapatite, and mixtures thereof. In certain embodiments the inorganic filler comprises a polymorph of calcium phosphate such as a phosphate glass.

In yet another embodiment, the reinforced absorbable multilayered fabric can be seeded or cultured with appropriate cell types prior to implantation for the targeted tissue. Cells which can be seeded or cultured on the matrices of the current invention include, but are not limited to, bone marrow cells, stromal cells, stem cells, embryonic stem cells, chondrocytes, osteoblasts, osteocytes, osteoclasts, fibroblasts, pluripotent cells, chondrocyte progenitors, endothelial cells, macrophages, leukocytes, 5 adipocytes, monocytes, plasma cells, mast cells, umbilical cord cells, , postpartum derived cells, mesenchymal stem cells, epithelial cells, myoblasts, and precursor cells derived from adipose tissue.

The cells can be seeded on the multilayered fabric for a short period of time, e.g. less than one day, just prior to implantation, or cultured for longer a period, e.g. greater than one day, to allow for cell proliferation and matrix synthesis within the seeded fabric prior to implantation.

Additionally, the nonwoven fabric may comprise pharmacologically and biologically active agents, including but not limited to, wound healing agents, antibacterial agents, antimicrobial agents, growth factors, analgesic and anesthetic agents.

When used as a tissue scaffold, the reinforced absorbable multilayer fabric may be seeded or cultured with appropriate cell types prior to implantation for the targeted tissue.

The reinforced absorbable multilayered fabric can be used as a scaffold in tissue repair and regeneration applications. Examples of tissue repair and regeneration include rotator cuff repair, repair of damaged knee cartilage, and regeneration of skin, muscle, or bone lost due to disease or injury.

The method for using the reinforced absorbable multilayered fabric is to: first prepare a repair site for implantation, and then dispose the fabric at the site of repair. The fabric may be attached to the site of repair with sutures, tacks, or any of a number of biocompatible glues.

Example 1. Nonwoven PGL fabric with ORC fabric.

Poly (glycolide-co-lactide) (PGL, 90/10 mol/mol) was melt-spun into fiber. A multi-filament yarn was consolidated, crimped and cut into staple having a length of 1.75 inches. The staple was carded to create a nonwoven batt and then compacted to a thickness of about 1.25 mm and a density of about 98.1 mg/cc. The nonwoven fabric was then needlepunched into a knitted carboxylic-oxidized regenerated cellulose (ORC) fabric, available from Ethicon, Inc., under the tradename Interceed®, to secure the nonwoven fabric to the ORC fabric. The final multilayered fabric comprised about 60 weight percent of the nonwoven fabric.

Example 2. Nonwoven PGL fabric with ORC fabric.

Poly (glycolide-co-lactide) (PGL, 90/10 mol/mol) was melt-spun into fiber. A multi-filament yarn was consolidated, crimped and cut into staple having a length of 1.75 inches. The staple was carded to create a nonwoven batt and then compacted to a thickness of about 1.22 mm and a density of about 103.4 mg/cc. The nonwoven fabric was then needlepunched into a knitted carboxylic-oxidized regenerated cellulose fabric (ORC), available from Ethicon, Inc., under the tradename Surgicel NuKnit®, to secure the nonwoven fabric to the ORC fabric. The final multilayered fabric comprised about 25 weight percent of the nonwoven fabric.

Example 3. Nonwoven PGL fabric with ORC fabric.

Poly (glycolide-co-lactide) (PGL, 90/10 mol/mol) was melt-spun into fiber. A multi-filament yarn was consolidated, crimped and cut into staple having a length of 1.75 inches. The staple was carded to create a nonwoven batt and then compacted a felt having a thickness of about 1.1 mm and a density of about 102.8 mg/cc. The nonwoven fabric was then needlepunched into a knitted carboxylic-oxidized regenerated cellulose fabric (ORC), available from Ethicon, Inc., under the tradename Surgicel®, to secure the nonwoven fabric to the ORC fabric. The final multilayered fabric comprised about 60 weight percent of the nonwoven fabric.

Example 4. Nonwoven PGL fabric with ORC fabric.

Poly (glycolide-co-lactide) (PGL, 90/10 mol/mol) was melt-spun into fiber. A 80 denier multifilament yarn was consolidated into a 800 denier consolidated yarn. The consolidated yarn was crimped at approximately 110 °C. The crimped yarn was cut into staple having a length of about 1.25" in length. 20 g of the crimped staple was accurately weighed and laid out uniformly on the feed conveyor belt of a multi-roller carding machine. The environmental conditions (temp: 21°C /55% RH) were controlled. The staple was then carded to create a nonwoven batt. The batt was removed from the pick-up roller and cut into 4 equal parts. These were re-fed into the carder perpendicular to the collection direction. After this second pass the batt was weighed (19.8 g: 99% fabric yield) and then compacted into a felt. The compact felt was precisely laid onto an ORC fabric and firmly attached via 2 passes in the needlepunching equipment. The multilayered fabric was trimmed and scoured in 3 discrete isopropyl alcohol baths to remove spin finish and any machine oils. The scoured multilayered fabric was dried in an oven at 70 °C for 30 minutes, cooled and weighed.

The “thickness” of the multilayered fabric was measured as described herein. The measurement tools were:

(1) Mitutoyo Absolute gauge Model number ID-C125EB [Code number-- 543-452B]. The 1" diameter foot was used on the gauge.

(2) A magnetic holder was used to lock in place and set the caliper up to the die platen.

(3) Two metal plates ~ 2.75" x 2" x 0.60", weighing between 40.8g to 41.5g [combined total of ~82.18g].

The multilayered fabric was placed on a platen surface that is a smooth and machined surface. The two metal plates were placed on top of each other on the multilayered fabric and gently pressed at their corners to make sure the multilayered fabric is flat. The gauge foot was placed onto the top of the metal plates and was then re-lifted and re-placed, at which time a reading was made.

12 - 1” X 1” pieces were die-cut from the scoured multilayered fabric and accurately weighed. The thickness of each 1” X 1” piece was measured 4 -5 times in different areas of the metal plate in order to obtain a reliable average. The weight and thickness of each piece is shown in Table 1. The values indicate that the coverage of both layers is similar in all directions.

TABLE 1

Sample #	Sheet #1		Sheet #2	
	Weight (g)	Thickness (mm)	Weight (g)	Thickness(mm)
1	.132	1.53	.13	1.58
2	.132	1.58	.124	1.57
3	.131	1.59	.13	1.62
4	.129	1.55	.134	1.64
5	.126	1.58	.126	1.56
6	.125	1.5	.131	1.59
7	.129	1.56	.136	1.7
8	.127	1.52	.131	1.62
9	.132	1.55	.131	1.57
10	.123	1.58	.136	1.58
11	.128	1.58	.135	1.65
12	.13	1.51	.133	1.55
Average	**0.1287**	**1.5525**	**0.1314**	**1.6025**
Std. Dev	**0.0029**	**0.031**	**0.0037**	**0.044**
CV (%)	**2.304**	**2.002**	**2.837**	**2.767**

Example 5. Effect of humidity on processing of polyglactin 910 staple.

80 denier polyglactin 910 consolidated yarn was crimped and cut into 1.75 inch staple. Room temperature was maintained between 21-22 °C and the relative humidity was controlled by a room humidifier and varied from 36-60%. No additional means of static control were employed for this series of runs. Crimped staple was carded into a batt approximately 32"x8". The percent of staple incorporated into the batt after two passes through the carding machine, i.e., the yield, increased with increasing humidity, and the quality of the batt improved with yield.

Table 2: Effect of Relative Humidity on Processing

Staple Weight (g)	%RH	Batt Weight (g)	Yield %	Batt Quality*
27	36	17	63	3.5
27	38-45	18.4	68	4.0
20.9	40	13.8	66	3.0
20.1	49	14.9	74	4.5
33	49	24.4	74	5.0
25.5	60	21.9	86	5.0

*Quality was rated on a scale of 1-5 based on visual inspection.

1=large areas devoid of polyglactin 910, streaking pilling

3=some small bare spots devoid of polyglactin 910 or very thin spots with minimal polyglactin 910 coverage

5=Uniform by visual inspection – no bare spots, no very thin spots, no pilling

Example 6. Effect of Staple Length on processing of polyglactin 910 staple.

80 denier polyglactin 910 consolidated yarn was crimped and cut into 1.25", 1.5" and 1.75" long staple. Room temperature was maintained between 69-71°F and the relative humidity was controlled at ~55% by a room humidifier. No additional means of static control were employed for this series of runs. Crimped staple was carded into a batt approximately 32" x 8".Table 3: Effect of staple length on batting quality and yield at 55%RH

Staple Length (in)	Staple Weight (g)	Batt Weight (g)	% Yield	Batt Quality*
1.75	25	13.94	56	4.0
1.75	25	16.0	64	5.0
1.5	30.7	28.0	91	ND
1.5	25	21.8	87	ND
1.25	25	24.1	96	5.0
1.25	25	24.2	97	5.0

*Quality was rated on a scale of 1-5 based on visual inspection.

1+large areas devoid of polyglactin 910, streaking, pilling

3=some small bare spots devoid of polyglactin 910 or very thin spots with minimal polyglactin 910 coverage

5=Uniform by visual inspection – no bare spots, no very thin spots, no pilling.

Example 7. Poly (glycolide-co-lactide) (PGL, 90/10 mol/mol) was melt-spun into fiber. A 80 denier multifilament yarn was consolidated into a 800 denier consolidated yarn. The consolidated yarn was crimped at approximately 110 °C. The crimped yarn was cut into staple having a length of about 1.25" in length. 44 g of the crimped staple was accurately weighed after conditioning the yarn for about 30 minutes in a high humidity environment (>55% RH). The yarn was laid out uniformly on the feed conveyor belt of a multi-roller carding machine. The feed time (5minutes) was accurately controlled to within 30-45 seconds. The environmental conditions (temp: 21°C /25% RH) were recorded. Static bars were employed near the 2nd Randomiser roller as well as near the steel pick up roller and were turned on during the run to minimize the detrimental impact of static generation on the uniformity and yield of the resulting batt. The staple was then carded to create a nonwoven batt. Two vacuum inlets were strategically placed near the two edges of the 2nd Randomizer roller to control the width of the ensuing batt. The batt was removed from the pick-up roller and weighed (41g: 91% yield). The uniform batt was precisely laid onto an ORC fabric and firmly attached via a single pass in the needlepunching equipment. The needle penetration depth was controlled at 12 mm. The multilayered fabric was trimmed and scoured on a rack (along with other similarly produced sheets) suspended in a tank containing isopropyl alcohol to remove spin finish and any machine oils. The scoured multilayered fabric (matrix sheet) was calendered to remove excess solvent and dried in an oven at 70°C for app. 30 minutes, cooled and weighed.

Example 8.

The matrix sheet as described has an off-white/beige color on both sides. One side may be described as the non-woven side where as the other side as the knitted fabric side. For certain application, it may be vital to identify the non-woven versus knitted surfaces of the matrix. Under difficult environmental conditions, the similarity in color and texture (to some extent) makes it difficult to identify one side from the other. Several means were employed to impart sidedness to the matrix sheet, which enables the observer to distinguish the 2 sides apart. These means include physical (stitching/knitting, braiding, pleating, etc), thermo-mechanical (heat, heat embossing; laser etching; etc) and chromic (use of a dye) means may be employed to achieve sidedness. The following examples describe some of the means:

8a) The matrix sheet was modified on the knitted fabric side by attaching a 1mm wide 4 inch long braided tape of the polyglactin 910 fiber. The tapes although successful in imparting sidedness add to the amount of the longer resorbing Polyglactin 910.

8 b) A web made of dyed nylon fiber was placed under the knitted fabric and the non-woven batt during the needle-punching step. The web is secured to the knitted fabric side due to the needling process. The web affords excellent sidedness and if available in an absorbable material, could be used to make completely resorbable, implantable matrix sheets. The web (mesh) can be secured similarly on the non-woven side. Other means of securing the web may be thermo-mechanical in nature. Inclusion of such a web can be for the reason of mechanical enforcement as well. In such cases the web could be secured on either side or even between the two layers. Such a reinforced structure may have multiple applications.

8 c) The small amount of Polyglactin 910 that resides on the knitted fabric side (due to the needle-punching step) of the matrix sheet can be thermally modified to create sidedness. This can include heating under pressure such that a shiny film of Polyglactin 910 is formed. Other options include heat embossing a discernible pattern. Both approaches achieve sidedness but may result in thermal degradation of the polymer/construct

8 d). The knitted ORC fabric, prior to the needle-punching step is pleated (vertical or horizontal pleats). The pleats are stabilized by using heat and pressure. The pleated fabric is then used in place of the regular fabric for the rest of the process as described in Example 7. The resulting matrix sheet has distinct stripes that achieve the sidedness.

8 e) Dyed Polyglactin 910 creates matrix sheet that is colored on the non-woven side and off-white/beige on the other. This construct achieves sidedness. A dye can be used similarly by employing a dyed suture thread etc. on the knitted side. The suture (braided into a tape or used as is) may be sewed in or thermally bonded.

Example 9. Rotator cuff repair using reinforced absorbable multilayered fabric.

In the case of a rotator cuff problem, the surgeon first looks at the extent of an injury using an arthroscope. Then, under general anesthesia, the patient undergoes open surgery to repair the tear.

After the anesthetic has been administered and the shoulder has been prepared, a cosmetic incision is made over the top front corner of the shoulder. This incision allows access to the seam between the front and middle parts of the deltoid muscle. Splitting this seam allows access to the rotator cuff without detaching or damaging the important deltoid muscle, which is responsible for a significant portion of the shoulder's power. All scar tissue is removed from the space beneath the deltoid and the acromion (part of the shoulder blade to which the deltoid attaches). Thickened bursa and the rough edges of the rotator cuff and humerus (upper arm bone) are also smoothed to make sure that they pass smoothly beneath the acromion and deltoid.

The edges of the cuff tendons are identified and the quality and quantity of the cuff tissue is determined. The goal of the repair is to reattach good quality tendon to the location on the arm bone from which it was torn. A groove or trough is fashioned in the normal attachment site for the cuff. To support the tendon and aid in healing, the surgeon sutures a patch of reinforced absorbable multilayered fabric into place over it. Sutures (lengths of surgical thread) draw the edge of the tendon securely into the groove to which it is to heal.

The surgeon then completes the surgery by closing the deltoid muscle and the skin incision. Over time, the body creates new tissue in the area that matches surrounding tissue. The body also absorbs the implanted patch in two to four months.

Example 10. Knee cartilage repair using reinforced absorbable multilayered fabric.

First, the surgeon examines the knee through an arthroscope - a small device that allows the doctor to see into your knee joint. If a lesion is detected, a surgical procedure is performed.

After the anesthetic has been administered and the knee has been prepared, a cosmetic incision is made through the skin over the top front corner of the patella. First, the damaged cartilage is removed. The reinforced absorbable multilayered fabric is then implanted into the lesion. The fabric may be attached to the lesion site with sutures, tacks, or any of a number of biocompatible glues.

The surgeon then completes the surgery by closing the skin incision. Cartilage cells migrate into and multiply in the implanted fabric, and the cell/fabric implant intergrates with surrounding cartilage. With time, the cells will mature and fill-in the lesion with hyaline cartilage.

Example 11: Tissue repair using_reinforced absorbable multilayered fabric.

Goat cartilage was harvested from femoral condyles of 1 to 1-1/2 year old goat knees. A first set of 5-millimeter diameter discs were made from the cartilage using a punch. The cartilage discs were washed in phosphate buffered saline (PBS) containing antibiotic and antimycotics, then rinsed in PBS. Separately, a second set of 5-millimeter diameter discs were made from ORC/Polyglactin multilayered fabric formed as described in Example 1 and sterilized by Ethylene Oxide (EtO).

The fabric discs were placed in between two cartilage discs and bonded together with bovine fibrin glue. Constructs were implanted subcutaneously in SCID mice. Six weeks following implantation, samples were collected and processed for histology. Histological slides were assessed for repair tissue in the fabric discs by Hematoxylin /Eosin and Safranin O staining.

Results showed that cells had migrated into the scaffolds and formed new repair tissue. At this time point the repair tissue was fibrous in nature.

Example 12: Tissue repair using_reinforced absorbable multilayered fabric having a bioactive agent

Constructs for SCID implantation were prepared similar to that described for Example 11 with the exception that the ORC/Polyglactin composites were loaded with 2.5 micrograms of recombinant human growth and differentiation factor 5 (rhGDF-5) and lyophilized. Constructs were implanted in SCID mice and processed similar to Example 11. Histological slides were assessed for repair tissue in scaffolds by Hematoxylin/Eosin and Safranin O staining.

Results showed that cells had migrated into the scaffolds and formed new repair tissue. In the presence of the growth factor new cartilage like repair tissue was formed within the scaffolds. This repair tissue stained positive for Safranin O a stain specific for sulfated proteoglycans.

While the examples demonstrate certain embodiments of the invention, they are not to be interpreted as limiting the scope of the invention, but rather as contributing to a complete description of the invention. All reinforcement fabrics described in the examples below are the nonsterile materials of the corresponding commercial products referred by their tradenames.

We claim:

1. A multilayered fabric comprising a first absorbable nonwoven fabric and two or more second absorbable woven or knitted fabric as a reinforcement backing to the first absorbable nonwoven fabric, where the first absorbable nonwoven fabric comprises fibers comprised of aliphatic polyester polymers or copolymers of one or more monomers selected from the group consisting of lactic acid, lactide, glycolic acid, glycolide, ϵ-caprolactone, p-dioxanone, and trimethylene carbonate, and wherein the lactide is selected from the group consisting of L-, D-, meso and D, L mixtures of lactide, and wherein the weight of said first nonwoven fabric is from 10% to 80% of the total weight of the multilayered fabric, and wherein the two or more second absorbable woven or knitted fabric comprises oxidized regenerated cellulose.

2. The multilayered fabric of claim 1, wherein the first absorbable nonwoven fabric comprises staple having a length from about 0.5 to 2.5 inches.

3. The multilayered fabric of claim 1 or 2, wherein the first absorbable nonwoven fabric has a basis weight of about 0.01 to 0.2 g/in^2; and the two or more second absorbable woven or knitted fabric has a basis weight of about 0.001 to 0.2 g/in^2.

4. The multilayered fabric of any one of claims 1 to 3, further comprising a bioactive agent selected from the group consisting of integrin binding sequence, ligands, bone morphogenic proteins, epidermal growth factor, IGF-I, IGF-II, TGF-β I-III, growth differentiation factor, parathyroid hormone, vascular endothelial growth factor, hyaluronic acid, glycoprotein, lipoprotein, bFGF, TGF-beta superfamily factors, BMP-2, BMP-4, BMP-6, BMP-12, sonic hedgehog, GDF5, GDF6, GDF8, PDGF, recombinant human growth and differentiation factor 5, tenascin-C, fibronectin, thromboelastin, thrombin-derived peptides, heparin-binding domains, demineralized bone matrix, platelet rich plasma, bone marrow aspirate, and bone fragments.

5. The multilayered fabric of any one of claims 1 to 4, further comprising cells selected from the group consisting of bone marrow cells, stromal cells, stem cells, embryonic stem cells, chondrocytes, osteoblasts, osteocytes, osteoclasts, fibroblasts,

pluripotent cells, chondrocyte progenitors, endothelial cells, macrophages, leukocytes, adipocytes, monocytes, plasma cells, mast cells, umbilical cord cells, postpartum derived cells, mesenchymal stem cells, epithelial cells, myoblasts, and precursor cells derived from adipose tissue.

6. A method for making the multilayered fabric according to any one of claims 1 to 5, comprising the steps of:

(a) crimping absorbable polymer fibers or yarns in the range of about 10 to 30 crimps per inch;

(b) cutting the crimped fibers or yarns to a staple length between about 0.1 and 2.5 inch;

(c) carding the staple to form the first absorbable nonwoven fabric;

(d) attaching the first absorbable nonwoven fabric to the two or more second absorbable woven or knitted fabric; while

(e) maintaining the humidity of the environment for step (c) to about 20 to 60%, at a room temperature of about 15 to 24°C.