(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 February 2009 (12.02.2009)

PCT

(10) International Publication Number
WO 2009/019685 A2

(51) International Patent Classification:
A61L 27/22 (2006.01) *A61L 27/56* (2006.01)
A61L 27/24 (2006.01)

(21) International Application Number:
PCT/IL2008/001061

(22) International Filing Date: 3 August 2008 (03.08.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/935,283 3 August 2007 (03.08.2007) US

(71) Applicant *(for all designated States except US)*: **NICAST LTD.** [IL/IL]; Global Park, 2 Yodfat Street, Northern Industrial Zone, 71291 Lod (IL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MARTINEZ, Jean-Pierre Elisha** [IL/IL]; Global Park, 2 Yodfat Street, Northern Industrial Zone, 71291 Lod (IL). **DUBSON, Alexander** [IL/IL]; 36A Shapira St., 49491 Petach-tikva (IL). **SHALEV, Alon** [IL/IL]; 9 Wingate St., 43587 Raanana (IL).

(74) Agent: **DR EYAL BRESSLER LTD**; 11 Tuval St, 52522 Ramat Gan (IL).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,

[Continued on next page]

(54) Title: FIBROUS SURGICALLY IMPLANTABLE MESH

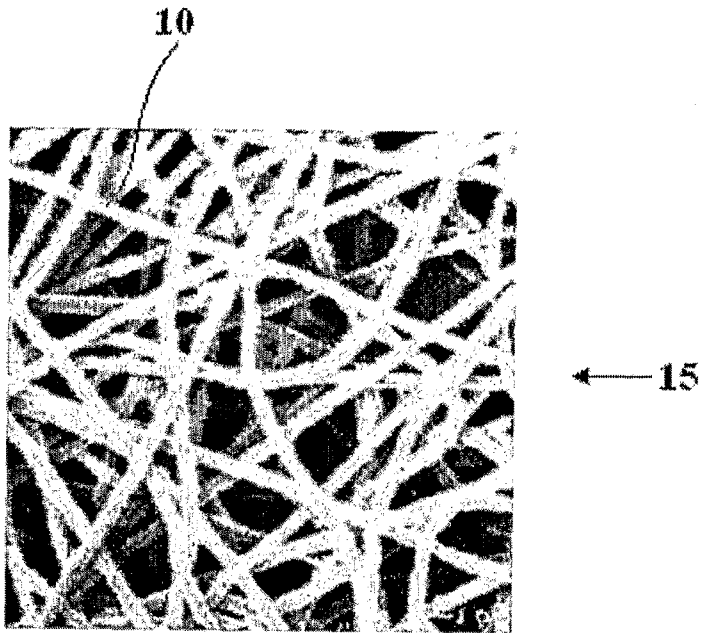

Fig. 1

(57) Abstract: A fibrous mesh surgically implantable into mammal internal cavity is disclosed. The mesh has a laminar extra-cellular-matrix-like structure. The mesh comprises a first layer characterized by porosity effective for mammal tissue infiltration into the first layer and a substantially non-porous second layer. The first layer is adapted to be surgically adhered to the mammal abdominal wall such that wall tissues infiltrate into the first layer while the second layer characterised by non-adhesion and adapted for non-traumatic contact to mammal viscera.

WO 2009/019685 A2

FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *without international search report and to be republished upon receipt of that report*

FIBROUS SURGICALLY IMPLANTABLE MESH

FIELD OF THE INVENTION

The present invention relates to a surgically implantable mesh for hernia repairing, and, more specifically, to a two-layer mesh made of polymer fibres by electrospinning.

BACKGROUND OF THE INVENTION

A hernia is a protrusion of a tissue, structure, or part of an organ through the muscular tissue or the membrane by which it is normally contained. The hernia has three parts: the orifice through which the aforesaid hernia herniates, the hernial sac, and contents of the aforesaid sac. An untreated hernia may complicate by: (a) Inflammation; (b) Irreducibility; (c) Obstruction; (d) Strangulation; and (e) Hydrocele of the hernial sac.

Inguinal hernia

By far the most common hernias (up to 75% of all abdominal hernias) are the so-called inguinal hernias. For a thorough understanding of inguinal hernias, much insight is needed in the anatomy of the inguinal canal. Inguinal hernias are further divided into the more common indirect inguinal hernia (2/3, depicted here), in which the inguinal canal is entered via a congenital weakness at its entrance (the internal inguinal ring), and the direct inguinal hernia type (1/3), where the hernia contents push through a weak spot in the back wall of the inguinal canal. Inguinal hernias are more common in men than women while femoral hernias are more common in women.

Femoral hernia

Femoral hernias occur just below the inguinal ligament, when abdominal contents pass into the weak area at the posterior wall of the femoral canal. They can be hard to distinguish from the inguinal type (especially when ascending cephalad): however, they generally appear more rounded, and, in contrast to inguinal hernias, there is a strong female preponderance in femoral hernias. The incidence of strangulation in femoral hernias is high. Repair techniques are similar for femoral and inguinal hernia.

Umbilical hernia

Umbilical hernias are especially common in infants of African descent, and occur more in boys. They involve protrusion of intraabdominal contents through a weakness at the site of passage of the umbilical cord through the abdominal wall. These hernias often resolve spontaneously. Umbilical hernias in adults are largely acquired, and are more frequent in obese or pregnant women. Abnormal decussation of fibers at the linea alba may contribute.

Diaphragmatic hernia

Higher in the abdomen, an (internal) "diaphragmatic hernia" results when part of the stomach or intestine protrudes into the chest cavity through a defect in the diaphragm.

A hiatus hernia is a particular variant of this type, in which the normal passageway through which the esophagus meets the stomach (esophageal hiatus) serves as a functional "defect", allowing part of the stomach to (periodically) "herniate" into the chest. Hiatus hernias may be either "*sliding*," in which the gastroesophageal junction itself slides through the defect into the chest, or non-sliding (also known as *para-esophageal*), in which case the junction remains fixed while another portion of the stomach moves up through the defect. Non-sliding or para-esophageal hernias can be dangerous as they may allow the stomach to rotate and obstruct.

A congenital diaphragmatic hernia is a distinct problem, occurring in up to 1 in 2000 births, and requiring pediatric surgery. Intestinal organs may herniate through several parts of the diaphragm, posterolateral (in Bochdalek's triangle, resulting in *Bochdalek's hernia*), or anteromedial-retrosternal (in the cleft of Larrey/Morgagni's foramen, resulting in *Morgagni-Larrey hernia*, or Morgagni's hernia).

Ventral hernia may occur following surgery in the abdomen, whether the surgery is an open surgery or a laparoscopy: as a result of the intervention the abdominal wall may weaken until it is not able to sustain the abdominal pressure exercised by the viscera and creates a so-called incisional hernia.

Current medical practice in hernia repair (herniorrhaphy) often involves the use of a prosthetic (surgical) mesh, to secure the weak area under the peritoneum.

Abdominal wall hernias occur in 15-30% of patients following previous laparotomy. Laparoscopic repair of these hernias appears to be superior to open repair, but is dependent on the use of mesh material that can be safely placed in contact with the abdominal content,

especially bowel. Without a barrier between prosthetic meshes and bowel dense adhesions commonly develop, and these may cause intestinal obstruction or even erosion of the viscera and fistula formation.

It is generally advisable to repair hernias in a timely fashion, in order to prevent complications such as organ dysfunction, gangrene, and multiple organ dysfunction syndromes. Most abdominal hernias can be surgically repaired, and recovery rarely requires long-term changes in lifestyle. Uncomplicated hernias are principally repaired by pushing back, or "reducing", the herniated tissue, and then mending the weakness in muscle tissue (an operation called herniorrhaphy). If complications have occurred, the surgeon will check the viability of the herniated organ, and resect it if necessary. Modern muscle reinforcement techniques involve synthetic materials (mesh prosthesis) that avoid over-stretching of already weakened tissue (as in older, but still useful methods). The mesh is placed over the defect, and sometimes staples are used to keep the mesh in place. Evidence suggests that this method has the lowest percentage of recurrences and the fastest recovery period. Increasingly, some repairs are performed through laparoscopes.

Many patients are managed through day surgery centers, and are able to return to work within a week or two, while heavy activities are prohibited for a longer period. Patients who have their hernias repaired with mesh often recover in a number of days. Surgical complications have been estimated to be up to 10%, but most of them can be easily addressed. They include surgical site infections, nerve and blood vessel injuries, injury to nearby organs, and hernia recurrence.

Generally, the use of external devices to maintain reduction of the hernia without repairing the underlying defect (such as hernia trusses, trunks, belts, etc.), is not advised. Exceptions are uncomplicated incisional hernias that arise shortly after the operation (should only be operated after a few months), or inoperable patients.

The new trends for hernia repair include minimal-invasive techniques, in which the hernia defect is closed by a piece of non-absorbable mesh with minimal tension – so called "tension-free" hernia repair. The follow-up times thus far are short for such procedures, but it seems that recurrence rates of 1% or below could be expected. Also, the general recovery time has become shorter, and the patients are usually encouraged to begin their normal activities with no restrictions within a week after the operation.

To function properly, the ideal prosthetic device must allow or even induce strong adhesion to the tissues of the abdominal wall however it must be as frictionless as possible toward the visceral side, to avoid intestinal obstruction or enterocutaneous fistulae. Existing prosthetic meshes often do not meet this primary request at the satisfaction of the medical community or are difficult to handle and fix to the abdominal wall.

US Patent 6319264 ('264) discloses a flexible, fibrous hernia mesh, which is intended to be implanted to close hernia defects. The mesh has at least two functional components or layers: (1) a rapidly degradable first layer and (2) a more slowly degradable (with respect to the first layer) second layer. Using the fibrous mesh of this invention, the hernia defect can be closed so that a) the second layer supports the area until the scar tissue is strong enough (around 6 months), to prevent recurrent hernia formation, b) while the more rapid degradation of the first layer induces scar tissue formation due to inflammatory reaction, and c) the second layer isolates the first layer from the abdominal cavity, preventing tissue to tissue adhesion onto the intestines. The mesh is placed on the uncovered fascia area with its more rapidly absorbable side (the first layer) towards the fascia. The drawback of '264 is that the first layer which is in contact with the abdominal wall comprises relatively small pores, inhibiting tissue ingrowth thereby complicating the outcome.

Thus, an unmet long-felt need is to provide a bi-functional prosthetic device that is able: (a) to be strongly adhered to the tissues of the abdominal wall and (b) to non-traumatically contact to the visceral side to avoid intestinal obstruction or enterocutaneous fistulae. Existing prosthetic meshes often do not meet these basic requirements or are difficult to handle and fix to the abdominal wall.

SUMMARY OF THE INVENTION

It is hence one object of the invention to disclose a fibrous mesh surgically implantable into mammal internal cavity. The mesh has a laminar extra-cellular-matrix-like structure. The mesh comprises a first layer characterized by porosity effective for mammal tissue infiltration into the first layer and a substantially non-porous second layer.

It is a core purpose of the invention to provide the first layer adapted to be surgically adhered to the mammal abdominal wall such that wall tissues infiltrate into the first layer while the second layer characterised by non-adhesion and adapted for non-traumatic contact to mammal viscera.

Another object of the invention is to disclose the mesh effectively elastic for non-interfering with a repaired mammal cavity wall.

A further object of the invention is to disclose the mammal that is a human.

A further object of the invention is to disclose the mesh comprising electrospun fibres.

A further object of the invention is to disclose the electrospun fibers of nanometric size.

A further object of the invention is to disclose the first layer made of polyurethane.

A further object of the invention is to disclose the first layer made of collagen.

A further object of the invention is to disclose the first layer made of fibrin.

A further object of the invention is to disclose the first layer made of fibronectin,

A further object of the invention is to disclose the first layer made of vitronectin.

A further object of the invention is to disclose the first layer made of laminin.

A further object of the invention is to disclose the first layer made of protein bearing cellular adhesion peptides.

A further object of the invention is to disclose the first layer made of protein comprising arginine-glycine-aspartic acid- rich sequences.

A further object of the invention is to disclose the first layer made of protein comprising RGDS (arf-gly-asp-ser)-rich sequences.

A further object of the invention is to disclose the first layer made of proteincomprising YIGSR (Tyr-Ile-Gly-Ser-Arg)-rich sequences.

A further object of the invention is to disclose the first layer made of protein comprising CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg) -rich sequences.

A further object of the invention is to disclose the first layer comprising arginine-glycine-aspartic acid peptide linked polymer

A further object of the invention is to disclose the first layer comprising RGDS (arf-gly-asp-ser) peptide linked polymer

A further object of the invention is to disclose the first layer comprising YIGSR (Tyr-Ile-Gly-Ser-Arg) peptide linked polymer

A further object of the invention is to disclose the first layer made of protein comprising CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg) peptide linked polymer

A further object of the invention is to disclose the second layer made of polytetrafluorethylene.

A further object of the invention is to disclose the second layer made of fluor based polymer.

A further object of the invention is to disclose the second layer made of polyvinylidene fluoride.

A further object of the invention is to disclose the second layer made of a hydrophobic material.

A further object of the invention is to disclose the second layer made of polyester.

A further object of the invention is to disclose the second layer made of polypropylene (to be checked).

A further object of the invention is to disclose the second layer made of polyformaldehyde (to be checked).

A further object of the invention is to disclose the second layer made of silicone rubber.

A further object of the invention is to disclose the second layer made of poly(ethylene glycol).

A further object of the invention is to disclose the second layer made of acrylic acid or acrylate polymers.

A further object of the invention is to disclose a method of repairing a tissue aperture. The aforesaid method comprises the steps of: (a) providing an implantable mesh of a laminar extra-cellular-matrix-like structure comprising a first layer characterized by a predetermined porosity and a substantially non-porous second layer; (b) inserting the mesh into a mammal cavity; and (c) tightly attaching the mesh to a mammal cavity wall.

It is a core purpose of the invention to provide the step of attaching the mesh further comprises a step of attaching the first layer to a mammal cavity wall such that wall tissues are able to infiltrate into the first layer and the second layer is in non-traumatic contact to mammal viscera.

A further object of the invention is to disclose the aperture that is a hernia.

A further object of the invention is to disclose the hernia selected from the group consisting of an inguinal hernia, a femoral hernia, an umbilical hernia, a diaphragmatic hernia or an incisional hernia.

BRIEF DESCRIPTION OF THE DRAWINGS

In order to understand the invention and to see how it may be implemented in practice, a plurality of embodiments is adapted to now be described, by way of non-limiting example only, with reference to the accompanying drawings, in which

Fig. 1 is a microphotograph of the artificial nano-fiber mesh; and

Fig. 2 is a photograph of the microsection of the two-layer mesh.

DETAILED DESCRIPTION OF THE INVENTION

The following description is provided, alongside all chapters of the present invention, so as to enable any person skilled in the art to make use of said invention and sets forth the best modes contemplated by the inventor of carrying out this invention. Various modifications, however, are adapted to remain apparent to those skilled in the art, since the generic principles of the present invention have been defined specifically to provide a fibrous mesh surgically implantable into mammal internal cavity and a method of repairing a tissue aperture.

The term 'hernia' hereinafter refers to a protrusion of a tissue, structure, or part of an organ through the muscular tissue or the membrane by which it is normally contained. The hernia has three parts: the orifice through which the aforesaid hernia herniates, the hernial sac, and contents of the aforesaid sac.

The term 'extra-cellular matrix (ECM)' hereinafter refers to an extracellular part of animal tissue that usually provides structural support to the cells in addition to performing various other important functions. The extracellular matrix is the defining feature of connective tissue in animals.

The term 'viscus' (plural: viscera) hereinafter refers to an internal organ of an animal (including humans), in particular an internal organ of the thorax or abdomen.

The term 'porosity of a porous medium' hereinafter refers to a fraction of void space in the material, where the void may contain, for example, air or water. The porosity ϕ is defined by the ratio:

$$\phi = \frac{V_V}{V_T}$$

where V_V is the volume of void-space (such as fluids) and V_T is the total or bulk volume of material, including the solid and void components. Porosity is a fraction between 0 and 1, typically ranging from less than 0.01 for solid granite to more than 0.5 for peat and clay.

Reference is now made to Fig. 1, presenting an artificial nano-fiber mesh 15 produced by means of electrospinning. The polymer nano-fibers 10 form ECM-like structure. The aforesaid artificial mesh when surgically attached to herniated wall of a mammal wall, e.g. a herniated human abdominal wall, enables wall tissues to infiltrate into the mesh. It should be emphasized that EMC-like structures provide open pores (gaps between nano-fibers 10) with no real pore walls as for the pores formed in other known implantable materials. Thus, the artificial meshes of similar structure are applicable for hernia repair more effectively.

Reference is now made to Fig. 2, showing a microsection of a two-layer mesh 25 usable for repairing a tissue aperture, e.g. for repairing a hernia, specifically, an inguinal hernia, a femoral hernia, an umbilical hernia, a diaphragmatic hernia or an incisional hernia. The aforesaid mesh comprises two layers 20 and 30. As seen in Fig. 2, the layer 20 is characterized by a high value of porosity while the layer 30 is non-porous and has a smooth outer surface. In accordance with the preferable embodiment of the current invention, the layer 20 is provided with the porosity ranged between 72 and 80%, and the pore sizes of 10-100 μm, as measured using a capillary flow parameter. The mesh comprises a plurality of open pores. The meshes with the open pores of sizes selected from the group consisting of 10-20 μm, 20-30 μm, 30-40 μm, 40-50 μm, 50-60 μm, 60-70 μm, 70-80 μm, 80-90 μm, 90-100 μm, and any combination thereof are in the scope of the current invention,

The two-layer mesh 25 is surgically implanted into a mammal cavity to be attached to a herniated cavity wall, e.g. a human abdominal wall, so that the layer 20 adheres to wall tissues while the layer 30 is in contact to the viscera. The highly porous layer 20 enables the abdominal wall tissues to infiltrate thereinto and more reliably fixate the mesh 25 at the

hernia. More extended infiltration of the wall tissue into the layer 20 reduces a risk of recrudescence.

As said above, the layer 30 has the smooth surface and provides non-traumatic contact to the viscera. The non-porous hydrophobic surface of the layer 30 provides inadhesion relative to the viscera that prevents trauma of internals. Tissues of the internals slide over the layer 30 and do not penetrate thereinto.

An additional anti-traumatic effect is achieved by high elastic property of the electrospinningly made two-layer mesh. The electrospinning technology provides implantable materials characterized by the elasticity reaching a value of 500%. Thus, the implanted mesh 25 becomes an integral part of the abdominal wall and is deformed therewith.

The proposed mesh 25 is applicable by means minimally invasive methods. The aforesaid mesh can be inserted into the human abdominal cavity through a lumen of an endo-/laparoscope in a folded form. The mesh 25 unbends in the abdominal cavity due to an inherent property of shape memory.

In accordance with the current invention, the layer 20 is made of a material providing cellular adhesion such as hydrophilic materials, e.g. materials from the PUR family, biological materials e.g. natural ECM components e.g. collagen, fibrin, fibronectin, vitronectin and laminin and their composites and all material/protein bearing cellular adhesion peptides, natural or synthetic, such as RGD (arginine-glycine-aspartic acid), RGDS (arf-gly-asp-ser), YIGSR (Tyr-Ile-Gly-Ser-Arg) and/or CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg). Also cell adherence may be induced or enhanced by addition of materials which promote cellular electrostatic attraction such as poly-lysine. Also tissue ingrowth can be promoted and/or enhanced by addition and/or linking biochemicals known to promote/ induce cell proliferation e.g. growth factors. Also viability of the infiltrated tissues can be enhanced by addition and/or linking biochemicals known to promote and /or enhance angiogenesis et neo-vascularization. As the pore size is thought to be important for cell migration and tissue infiltration, it may be controlled using degradable and/or bio absorbable and/or soluble materials combined with the main structural material, e.g. PLA, PGA, and PEC.

The layer 30 is made of material known for their anti-adhesion properties, such as PTFE, PVDF and all fluor based polymer, and/or hydrophobic materials, PE, PP, Delrin, silicone

rubber, and hydrophilic materials such as poly (ethylene glycol), acrylic acid used alone or a composite of various materials and/or interpenetrating polymer networks and/or copolymers. Also biological materials known to "repel" cells and to avoid their attachment, and their derivatives, such albumin or heparin may be used for this purpose. The structure of the material may be a film layer or an electro-spun nano-fiber structure with very low porosity and/or nanometric pore size, or a gel containing the raw material and water prepared during the device production or at the theater of surgery or in situ.

In accordance with the current invention, the fibrous mesh surgically is implanted into human internal cavity, e.g the abdominal cavity. The aforesaid mesh has a laminar extra-cellular-matrix-like structure and comprises the layer 20 characterized by a porosity effective for human tissue infiltration thereinto and the substantially non-porous layer 30.

The layer 20 is adapted to be surgically adhered to the abdominal wall such that wall tissues infiltrate into the layer 20 while the layer 30 characterised by non-adhesion and adapted for non-traumatic contact to mammal viscera.

The method of repairing a tissue aperture is in the scope of the current invention; The repairing method comprises the steps of (a) providing an implantable mesh of a laminar extra-cellular-matrix-like structure comprising the layer 20 characterized by a predetermined porosity and the substantially non-porous layer 30; (b) inserting the mesh into a human cavity; and (c) tightly attaching the mesh to a mammal cavity wall.

The step of attaching the mesh further comprises a step of attaching the layer 20 to a human cavity wall such that wall tissues are able to infiltrate thereinto and the layer 30 is in non-traumatic contact to mammal viscera.

CLAIMS:

1. A fibrous mesh surgically implantable into mammal internal cavity; said mesh has a laminar extra-cellular-matrix-like structure; said mesh comprises a first layer characterized by a porosity effective for mammal tissue infiltration into said first layer and a substantially non-porous second layer; wherein said first layer is adapted to be surgically (tightly) adhered to said mammal abdominal wall such that wall tissues infiltrate thereinto while said second layer characterized by non-adhesion and adapted for non-traumatic contact to mammal viscera.
2. The mesh according to claim 1, wherein said mesh is effectively elastic for non-interfering with a repaired mammal cavity wall.
3. The mesh according to claim 1, wherein said mammal is a human.
4. The mesh according to claim 1, wherein said mesh comprises electrospun fibres.
5. The mesh according to claim 1, wherein said electrospun fibers are of nanometric size.
6. The mesh according to claim 1, wherein said first layer is made of polyurethane.
7. The mesh according to claim 1, wherein said first layer is made of collagen.
8. The mesh according to claim 1, wherein said first layer is made of fibrin.
9. The mesh according to claim 1, wherein said first layer is made of fibronectin,
10. The mesh according to claim 1, wherein said first layer is made of vitronectin.
11. The mesh according to claim 1, wherein said first layer is made of laminin.
12. The mesh according to claim 1, wherein said first layer is made of protein comprising cellular adhesion peptides.
13. The mesh according to claim 1, wherein said protein comprises arginine-glycine-aspartic acid-rich sequences.
14. The mesh according to claim 1, wherein said protein comprises RGDS (arf-gly-asp-ser)-rich sequences.
15. The mesh according to claim 1, wherein said protein comprises YIGSR (Tyr-Ile-Gly-Ser-Arg)-rich sequences.

16. The mesh according to claim 1, wherein said protein comprises CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg)-rich sequences.

17. The mesh according to claim 1, wherein said first layer comprising arginine-glycine-aspartic acid peptide linked polymer.

18. The mesh according to claim 1, wherein said first layer comprising RGDS (arf-gly-asp-ser) peptide linked polymer.

19. The mesh according to claim 1, wherein said first layer comprising YIGSR (Tyr-Ile-Gly-Ser-Arg) peptide linked polymer.

20. The mesh according to claim 1, wherein said first layer made of protein comprising CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg) peptide linked polymer.

21. The mesh according to claim 1, wherein said second layer is made of polytetrafluorethylene.

22. The mesh according to claim 1, wherein said second layer is made of fluor based polymer.

23. The mesh according to claim 1, wherein said second layer is made of polyvinylidene fluoride.

24. The mesh according to claim 1, wherein said second layer is made of a hydrophobic material.

25. The mesh according to claim 1, wherein said second layer is made of polyester..

26. The mesh according to claim 1, wherein said second layer is made of polypropylene.

27. The mesh according to claim 1, wherein said second layer is made of polyformaldehyde.

28. The mesh according to claim 1, wherein said second layer is made of silicone rubber.

29. The mesh according to claim 1, wherein said second layer is made of poly (ethylene glycol).

30. The mesh according to claim 1, wherein said second layer is made of acrylic acid.

31. The mesh according to claim 1, wherein said second layer is made of acrylate polymer.

32. The mesh according to claim 1, wherein said mesh comprises a plurality of open pores; said open pores are of sized selected from the group consisting of 10-20 μm, 20-30μm, 30-40μm, 40-50μm, 50-60μm, 60-70μm, 70-80μm, 80-90μm, 90-100μm, and any combination thereof,

33. A method of repairing a tissue aperture; said method comprises the steps of

    (a) providing an implantable mesh of a laminar extra-cellular-matrix-like structure comprising a first layer characterized by a predetermined porosity and a substantially non-porous second layer;

    (b) inserting said mesh into a mammal cavity; and

    (c) tightly attaching said mesh to a mammal cavity wall;

    wherein said step of attaching said mesh further comprises a step of attaching said first layer to a mammal cavity wall such that wall tissues are able to infiltrate into said first layer and said second layer is in non-traumatic contact to mammal viscera.

34. The method according to claim 33, wherein said mesh is effectively elastic for non-interfering with to a repaired mammal cavity wall.

35. The method according to claim 33, wherein said aperture is a hernia.

36. The method according to claim 33, wherein said hernia is selected from the group consisting of an inguinal hernia, a femoral hernia, an umbilical hernia, a diaphragmatic hernia and an incisional hernia.

37. The method according to claim 33, wherein said mammal is a human.

38. The method according to claim 33, wherein said mesh comprises electrospun fibres.

39. The method according to claim 33, wherein said electrospun fibers are of nanometric size.

40. The method according to claim 32, wherein said first layer is made of polyurethane.

41. The method according to claim 33, wherein said first layer is made of collagen.

42. The method according to claim 33, wherein said first layer is made of fibrin.

43. The mesh according to claim 33, wherein said first layer is made of fibronectin,

44. The method according to claim 33, wherein said first layer is made of vitronectin.

45. The method according to claim 33, wherein said first layer is made of laminin.

46. The method according to claim 33, wherein said first layer is made of protein comprising cellular adhesion peptides.

47. The method according to claim 33, wherein said protein comprises arginine-glycine-aspartic acid-rich sequences.

48. The method according to claim 33, wherein said protein comprises RGDS (arf-gly-asp-ser)-rich sequences.

49. The method according to claim 33, wherein said protein comprises YIGSR (Tyr-Ile-Gly-Ser-Arg)-rich sequences.

50. The method according to claim 33, wherein said protein comprises CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg)-rich sequences.

51. The method according to claim 33, wherein said first layer comprising arginine-glycine-aspartic acid peptide linked polymer.

52. The method according to claim 33, wherein said first layer comprising RGDS (arf-gly-asp-ser) peptide linked polymer.

53. The method according to claim 33, wherein said first layer comprising YIGSR (Tyr-Ile-Gly-Ser-Arg) peptide linked polymer.

54. The method according to claim 33, wherein said first layer made of protein comprising CDPGYIGSR (Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg) peptide linked polymer.

55. The method according to claim 33, wherein said second layer is made of polytetrafluorethylene.

56. The method according to claim 33, wherein said second layer is made of fluor based polymer.

57. The method according to claim 33, wherein said second layer is made of polyvinylidene fluoride.

58. The method according to claim 33, wherein said second layer is made of a hydrophobic material.

59. The method according to claim 33, wherein said second layer is made of polyester.

60. The method according to claim 33, wherein said second layer is made of polypropylene.

61. The method according to claim 33, wherein said second layer is made of polyformaldehyde.

62. The method according to claim 33, wherein said second layer is made of silicone rubber.

63. The method according to claim 33, wherein said second layer is made of poly (ethylene glycol).

64. The method according to claim 33, wherein said second layer is made of acrylic acid.

65. The method according to claim 33, wherein said second layer is made of acrylate polymer.

66. The method according to claim 33, wherein said electrospun fibers are of nanometric size.

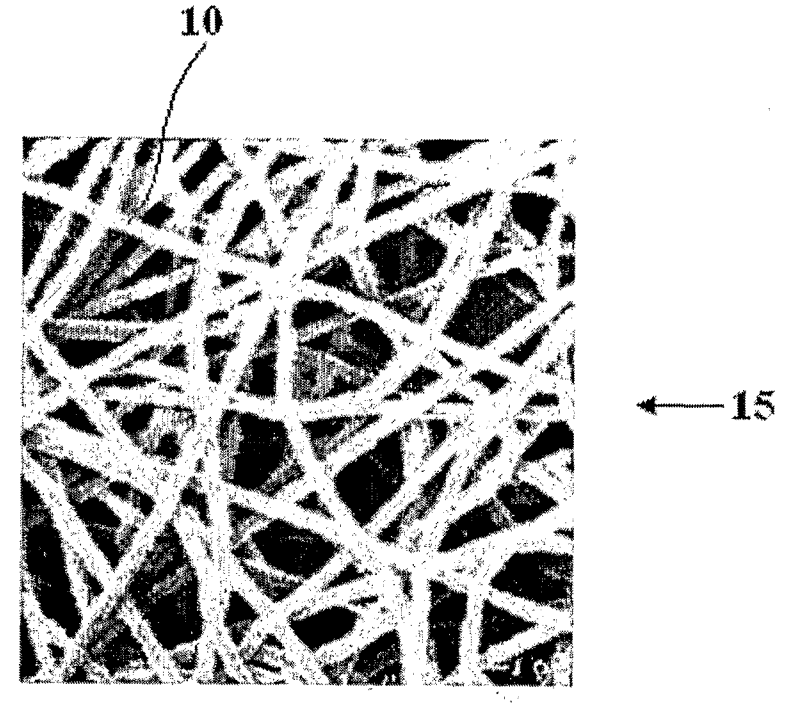

Fig. 1

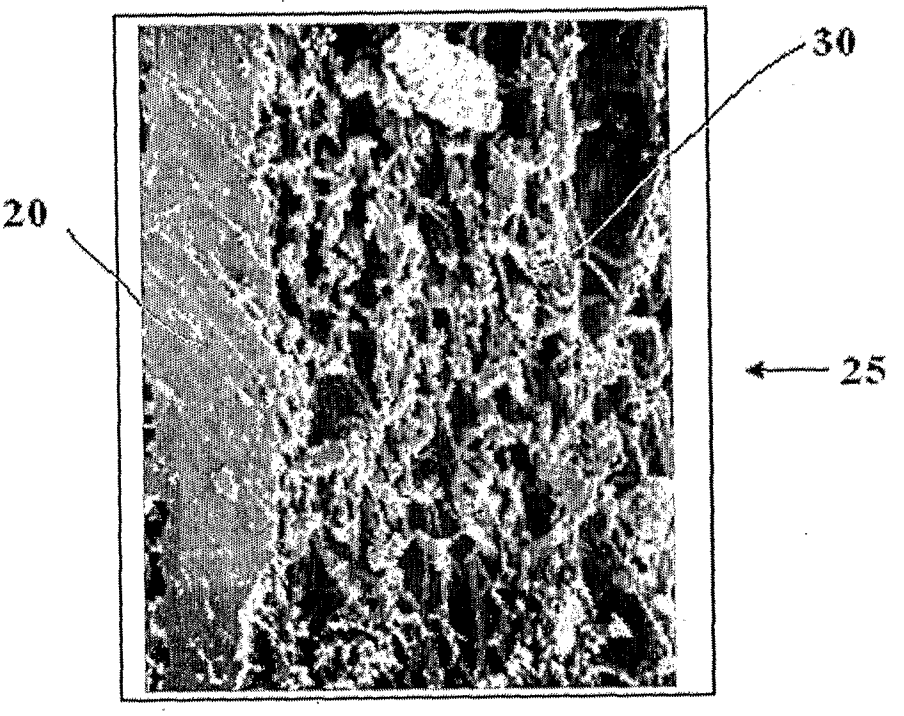

Fig. 2