Abstract: The present invention relates to new reinforced biodegradable scaffolds for soft tissue regeneration, as well as methods for support and for augmentation and regeneration of living tissue, wherein a reinforced biodegradable scaffold is used for the treatment of indications, where increased strength and stability is required besides the need for regeneration of living tissue within a patient. The present invention further relates to the use of scaffolds together with cells or tissue explants for soft tissue regeneration, such as in the treatment of a medical prolapse, such as rectal or pelvic organ prolapse, or hernia.

Claims

1. A biodegradable surgical implant for support, augmentation and regeneration of living tissue in a subject, comprising

a) a synthetic biodegradable homogenous sheet of scaffold,

b) one or more biodegradable reinforcing members.

2. The biodegradable surgical implant according to claim 1, wherein said synthetic biodegradable homogenous sheet of scaffold is hydrophilic.

3. The biodegradable surgical implant according to any one of claims 1 or 2, wherein said synthetic biodegradable homogenous sheet of scaffold has the ability to, within 5 minutes, such as within 2 minutes at 30°C, absorb water in an amount of at least 10%, such as at least 20%, such as at least 30%, such as at least 50% of the scaffold volume.

4. The biodegradable surgical implant according to any one of claims 1-3, wherein the volume % of said reinforcing member is less than 40 % of the implant.

5. The biodegradable surgical implant according to any one of claims 1-4, wherein said synthetic biodegradable homogenous sheets of scaffold exhibit a percent elongation at break in the range of about 10-200 %, such as in the range of about 30-100 %, such as in the range of about 30-70 %, such as in the range of about 30-60 %.

6. The biodegradable surgical implant according to any one of claims 1-5, wherein said surgical implant exhibit a percent elongation at break in the range of about 20-1000 %, such as in the range of about 20-800 %, such as in the range of about 20-500 %, such as in the range of about 20-400 %, such as in the range of about 20-300 %.

7. The biodegradable surgical implant according to any one of claims 1-6, wherein said synthetic biodegradable homogenous sheet of scaffold exhibit a tensile strength in the range of about 5-40 psi, such as in the range of about 8-30 psi, such as in the range of about 8-20 psi, such as in the range of about 8-16 psi, such as in the range of about 8-14 psi.

8. The biodegradable surgical implant according to any one of claims 1-7, wherein said surgical implant exhibit a tensile strength in the range of about 300-50000 psi, such as in the range of about 500-30000 psi, such as in the range of about 1000-20000 psi, such as in the range of about 1000-10000 psi, such as in the range of about 5000-10000 psi, or in the range of about 1000-8000 psi.

9. The biodegradable surgical implant according to any one of claims 1-8, wherein said synthetic biodegradable homogenous sheet of scaffold exhibit flexibility when wetted to saturation with a liquid.

10. The biodegradable surgical implant according to any one of claims 1-9, wherein said synthetic biodegradable homogenous sheets of scaffold has an open pore structure with a size in the range of 30 – 200 µm.

11. The biodegradable surgical implant according to any one of claims 1-10, wherein said synthetic biodegradable homogenous sheets of scaffold mainly has vertical pore structure.

12. The biodegradable surgical implant according to any one of claims 1-11, wherein said synthetic biodegradable homogenous sheet of scaffold has an open pore structure with interconnected pores.

13. The biodegradable surgical implant according to any one of claims 1-12, wherein said synthetic biodegradable homogenous sheet of scaffold is prepared by freeze-drying.

14. The biodegradable surgical implant according to any one of claims 1-13, wherein said biodegradable reinforcing member is based on fibres and/or threads with a thickness of about 10 nm-1000 µm, such as in the range of about 10 nm – 800 µm, such as in the range of about 10 nm – 500 µm.

15. The biodegradable surgical implant according to any one of claims 1-14, wherein said biodegradable reinforcing member is a sheet made of a woven fabric, knitted fabric, mesh, non-woven felt, made of filaments or fibres.

16. The biodegradable surgical implant according to claim 15, wherein said sheet has a thickness of 30 µm – 5 mm, such a 3-5 mm, such as 1-4 mm.

17. The biodegradable surgical implant according to any one of claims 1-16, wherein said synthetic biodegradable homogenous sheet of scaffold is completely degradable within 1-48 months, such as 4-36, such as 6-24, or 1-12 months of *in situ* application.

18. The biodegradable surgical implant according to any one of claims 1-17, wherein said biodegradable reinforcing member promotes cell attachment and in-growth of cells derived from the living tissue in said subject or from the application of cell or tissue explants.

19. The biodegradable surgical implant according to any one of claims 1-18, wherein said reinforcing biodegradable member is completely degradable within 1-12 months of *in situ* application.

20. The biodegradable surgical implant according to any one of claims 1-19, wherein said reinforced biodegradable member is made from a polymer of poly(lactide-co-glycolide) PLGA, such as a polymer wherein the molar ratio of (i) lactide units and (ii) glycolide units in the poly(lactide-co-glycolide) residue is in the range of 90:10 to 10:90, such as in the range of 80:20 to 10:90, such as about 10:90.

21. The biodegradable surgical implant according to any one of claims 1-20, wherein said synthetic biodegradable homogenous sheet of scaffold is a polymer of the general formula:

$A\text{-}O\text{-}(CHR^1CHR^2O)_n\text{-}B$
wherein;
A is a poly(lactide-co-glycolide) residue of a molecular weight of at least 4000 g/mol, the molar ratio of (i) lactide units and (ii) glycolide units in the poly(lactide-co-glycolide) residue being in the range of 80:20 to 10:90;

B is either a poly(lactide-co-glycolide) residue as defined for A or is selected from the group consisting of hydrogen, C_{1-6}-alkyl and hydroxy protecting groups,
one of R^1 and R^2 within each $-(CHR^1CHR^2O)-$ unit is selected from hydrogen and methyl, and the other of R^1 and R^2 within the same $-(CHR^1CHR^2O)-$ unit is hydrogen;

n represents the average number of $-(CHR^1CHR^2O)-$ units within a polymer chain and is an integer in the range of 10-1000; and wherein

the molar ratio of (iii) polyalkylene glycol units $-(CHR^1CHR^2O)-$ to the combined amount of (i) lactide units and (ii) glycolide units in the poly(lactide-co-glycolide) residue(s) is at the most 20:80;
and wherein the molecular weight of the copolymer is at least 10,000 g/mol, preferably at least 15,000 g/mol.

22. The biodegradable surgical implant according to claim 21, wherein both of R1 and R2 within each unit are hydrogen.

23. The biodegradable surgical implant according to claim 21 or 22, wherein B is a poly(lactide-co-glycolide) residue as defined for A.

24. The biodegradable surgical implant according to any one of claims 21-23, wherein B is C1-6-alkyl.

25. The biodegradable surgical implant according to any one of claims 21-24, wherein B is a hydroxy protecting group.

26. The biodegradable surgical implant according to any one of claims 21-25, wherein B is a hydroxy group.

27. The biodegradable surgical implant according to any one of claims 21-26, wherein the weight percentage of (iii) polyalkylene glycol units -(CHR^1CHR^2O)- to the combined amount of (i) lactide units and (ii) glycolide units in the poly(lactide-co-glycolide) residue(s) is in the range of 4% - 10% w/w.

28. The biodegradable surgical implant according to any one of claims 1-27, wherein said synthetic biodegradable homogenous sheet of scaffold is prepared by freeze-drying a solution comprising the biodegradable polymer in solution.

29. The biodegradable surgical implant according to any one of claims 1-28, wherein said reinforcing member is made of biodegradable sutures and/or threads.

30. The biodegradable surgical implant according to claim 29, wherein said reinforcing member is in a pattern selected from the group consisting of: triangles, circles, connecting waves, non-connecting waves, and overlapping waves.

31. The biodegradable surgical implant according to any one of claims 1-30, wherein said reinforcing member is made from welding seams of the synthetic biodegradable homogenous sheets of scaffold, such as welding seams provided in square- and hexagonal pattern or along the edge of the implant.

32. The biodegradable surgical implant according to any one of claims 1-31, wherein said synthetic biodegradable homogenous sheet of scaffold is a polymer of molecular weight greater than about 1 kDa, such as between about 1 kDa and about 1.000.000 kDa, such as between 25 kDa and 100 kDa.

33. The biodegradable surgical implant according to any one of claims 1-32, which implant further comprises, within said scaffold, one or more components which facilitate the cell adhesion and/or in-growth for regeneration of tissue, such as a component selected from the group consisting of: estrogen, estrogen derivatives, thrombin, ECM powder, chondroitin sulfate, hyaluronan, hyaluronic acid (HA), heparin sulfate, heparan sulfate, dermatan sulfate, growth factors, fibrin, fibronectin, elastin, collagen, such as collagen type I and/or type II, gelatin, and aggrecan, or any other suitable extracellular matrix component.

34. The biodegradable surgical implant according to any one of claims 1-33, which implant further comprises, within said scaffold, one or more components selected from the group consisting of growth factors, such as Insulin-like growth factors (IGFs), such as IGF-1 or IGF-2, or Transforming growth factors (TGFs), such as TGF-alpha or TGF-beta, or

Fibroblast growth factors (FGFs), such as FGF-1 or FGF-2, or Platelet-derived growth factors (PDGFs), such as PDGF-AA, PDGF-BB or PDGF-AB, or Nerve growth factor (NGF), or Human growth hormone (hGH), and Mechano Growth Factor (MGF).

35. The biodegradable surgical implant according to any one of claims 1-34, which implant further comprises, within said scaffold, a sample of cells or tissue explants.

36. The biodegradable surgical implant according to any one of claims 1-35, which implant is formed as a tube and/or comprises a flap and/or a pocket suitable for application of a suspension of a sample of cells or tissue explants to said implant.

37. The biodegradable surgical implant according to any one of claims 1-36, which implant comprises two or more separated pieces of synthetic biodegradable homogenous sheets of scaffold, such as 3, 4, 5 or 6 pieces of synthetic biodegradable homogenous sheets of scaffold attached to a reinforcing member, such as a mesh of a different polymer.

38. The biodegradable surgical implant according to any one of claims 1-37, which implant comprises two or more, such as 4 or 6 arms or extensions for attachment to structures in the site of implantation, such as in the pelvic region.

39. A method for the preparation of a biodegradable surgical implant comprising a synthetic biodegradable scaffold and autologous cells or tissue explants of a subject, suitable for support augmentation and regeneration of living tissue within said subject, said method comprising ex vivo application of a sample of said autologous cells or tissue explants on or within said biodegradable surgical implant comprising a synthetic biodegradable scaffold prior to implantation within said subject at the site wherein support, augmentation and regeneration of living tissue is required.

40. A biodegradable surgical implant comprising a synthetic biodegradable scaffold for use in a method for support, augmentation and regeneration of living tissue within a subject, said method comprising implantation of said biodegradable surgical implant comprising a synthetic biodegradable scaffold together with a sample of autologous cells or tissue explants

within said subject at the site wherein support, augmentation and regeneration of living tissue is required.

41. A biodegradable surgical implant comprising a synthetic biodegradable scaffold; for use in a method for support, augmentation and regeneration of living tissue within a subject, said method comprising the steps of (i) extracting a tissue sample from the subject; (ii) disintegration or disruption of the tissue sample; (iii) implanting the scaffold and the crushed tissue sample into the subject.

42. The biodegradable surgical implant according to claim 41., wherein said disintegration or disruption is done by crushing the tissue sample in a device comprising holes or a mesh for crushing a tissue sample by the application of pressure by which the tissue sample is forced through said mesh or holes.

43. A kit comprising

a) a biodegradable surgical implant comprising a synthetic biodegradable scaffold;
b) a sample of autologous cells or tissue explants; and
c) optionally instructions for use in a method for support, augmentation and regeneration of living tissue within a subject, such as in a subject with a medical prolapse, such as rectal or pelvic organ prolapse, or hernia, said method comprising implantation of said biodegradable surgical implant together with an autologous sample of cells or tissue explants within said subject at the site wherein support, augmentation and/or regeneration of living tissue is required.

44. A kit comprising

a) a synthetic biodegradable scaffold; and

b) a device suitable for disintegration or disruption of a tissue sample.

45. The kit according to claim 44, wherein said device suitable for disintegration or disruption comprises holes or a mesh for crushing said tissue sample by the application of pressure by which the tissue sample is forced through said mesh or holes.

46. The kit according to claim 44, wherein said device suitable for disintegration or disruption is based on a mill, ultra sonic treatment, homogenizer, high pressure, or physical force from knives or other instruments.

~~64~~ 65

~~47~~. The kit according to any one of claims ~~43~~-46, wherein said synthetic biodegradable scaffold is as defined in any one of claims 1-38.

Dated this 13/1/2012

[HRISHIKESH RAY CHAUDHURY]
OF REMFRY & SAGAR
ATTORNEY FOR THE APPLICANTS