ABSTRACT

"IMPLANTS AND BIODEGRADABLE FIDUCIAL MARKERS"

Implantable materials may be used in an iatrogenic site. Applications include radioopaque materials for fiducial marking.

CLAIMS

1. A pharmaceutically acceptable implant system comprising:

a collection of pharmaceutically acceptable, covalently-crosslinked hydrogel particles having a radioopaque agent covalently attached to a plurality of the particles in the collection, with the radioopaque agent being present in the collection at a concentration of at least about 0.1% w/w.

2. The system of claim 1 with the particle collection further comprising particles free of a covalently-bound radioopaque agent.

3. The system of claim 1 with the collection further comprising a non-covalently bound radioopaque agent.

4. The system of claim 1 wherein the collection particles are spheroidal with a maximum diameter of between about 20 to about 200 microns.

5. The system of claim 1, with the particles being biodegradable to produce only degradation products that are absorbed into the circulatory system and cleared from the body via renal filtration.

6. The system of claim 5 with the particles being hydrolytically biodegradable.

7. The system of claim 6 wherein the particles, before hydrolysis, have a total swellability in physiological solution of no more than about 30% by volume.

8. The system of claim 6 wherein the degradation products comprise a polyethylene glycol covalently bound to the radioopaque agent, with the radioopaque agent comprising iodine.

9. The system of claim 8 wherein the polyethylene glycol is a branched polyethylene glycol with at least four arms.

10. The system of claim 9 wherein between 25% and 90% of the arms comprise the radioopaque agent.

11. The system of claim 1 with the collection having a lubricity and maximum diameter for manual passage out of a syringe through a 30 gauge needle.

12. The system of claim 11 further comprising an osmotic agent that comprises a linear hydrophilic polymer, with the agent present in a mixture with the collection.

13. The system of claim 1 wherein the collection of particles is completely biodegradable at a time between about 30 and about 365 days.

14. The system of claim 13 wherein the collection comprises a plurality of sets of the particles, with the sets having different rates of biodegradation.

15. The system of claim 14 wherein a first set of the particles is biodegradable within about 8 to about 12 days and a second set of the particles is degradable within about 45 to about 55 days.

16. The system of claim 1 wherein the particles are hydrolytically degradable.

17. The system of claim 1 wherein a plurality of the particles are not biodegradable.

18. The system of claim 1 further comprising an applicator, with the particles being disposed in the applicator.

19. The system of claim 18 wherein the particles are dehydrated.

20. The system of claim 19 further comprising a container of physiological saline fluidly connectable to the applicator to mix the saline and particles in the applicator.

21. The system of claim 1 further comprising a therapeutic agent.

22. The system of claim 1 further comprising a radiation source.

23. A process for making an implantable system comprising preparing a hydrogel matrix comprising covalently attached radioopaque agents and breaking the matrix into a collection of pharmaceutically acceptable, covalently-crosslinked hydrogel particles.

24. The process of claim 23 wherein the matrix has a porosity of at least about 30% by volume and the radioopaque agent is present at a concentration of at least about 0.1% w/w, with the particles being biodegradable to produce only water soluble degradation products absorbable into a circulatory system and essentially cleared via renal filtration.

25. The process of claim 23 wherein the matrix is passed through a mesh at least twice to form the particles.

26. The process of claim 25 wherein the matrix is passed through a first mesh having about 50 microns between mesh strands and is then passed through a second mesh having about 20 microns between mesh strands.

27. The process of claim 23 wherein the matrix is formed from a first precursor comprising a plurality of first functional groups and a second precursor comprising a plurality of second functional groups, with the first functional groups forming covalent bonds with the second functional groups to thereby form the matrix.

28. The process of claim 27 wherein the first precursor further comprises the radioopaque agent.

29. The process of claim 23 wherein the particles are prepared by grinding, milling, chopping, micellar polymerization, or emulsion polymerization.

30. A pharmaceutically acceptable implant system comprising:

a collection of pharmaceutically acceptable, covalently-crosslinked hydrogel particles that comprises a plurality of sets of the particles, with the sets having different rates of biodegradation.

31. The system of claim 30 wherein a first set of the particles is biodegradable within about 8 to about 12 days and a second set of the particles is degradable within about 45 to about 55 days.

32. The system of claim 30 further comprising a set of particles that is biodegradable within about 60 to about 90 days.

33 The system of claim 30 wherein the particles are hydrolytically degradable.

34. The system of claim 30 comprising a plurality of the particles having a covalently attached radioopaque agent, with the radioopaque agent being present in the collection at a concentration of at least about 0.1% w/w.

35. The system of claim 34 wherein the particles are formed from a first precursor comprising a plurality of first functional groups and a second precursor comprising a plurality of second functional groups, with the first functional groups forming covalent bonds with the second functional groups to thereby form the matrix, with at least one of the precursors comprising polyethylene glycol.

36. The system of claim 35 wherein at least one of the precursors comprises a polyethylene glycol having a plurality of branches terminated with triiodobenzoate.

37. A method of treating a patient with a pharmaceutically acceptable implant system comprising implanting a collection of pharmaceutically acceptable, covalently-crosslinked hydrogel particles.

38. The method of claim 37 wherein the collection comprises a plurality of sets of the particles, with the sets having different rates of biodegradation.

39. The method of claim 37 comprising a plurality of the particles having a covalently attached radioopaque agent, with the radioopaque agent being present in the collection at a concentration of at least about 0.1% w/w.

40. The method of claim 37 comprising placing the collection between two tissues and preparing a radiation treatment plan that comprises a therapeutic dose of radiation to treat a cancer in one of the tissues.

41. The method of claim 37 comprising placing the collection in a tissue for augmentation.

42. A method for treating a tissue comprising placing a hydrogel in a iatrogenic site, wherein the hydrogel conforms to margins of the site and has a Hounsfield number of more than about 50.

43. The method of claim 42 with the hydrogel further comprising a radioopaque agent.

44. The method of claim 42 further comprising introducing a liquid comprising a hydrogel precursor into the site that flows into the site and reacts in the site to form the hydrogel as a covalently crosslinked continuous phase that adheres to the margins.

45. The method of claim 44 further comprising a second precursor that reacts with the first precursor to form covalent bonds to form the hydrogel.

46. The method of claim 44 wherein the precursor comprises a covalently bound radioopaque agent.

47 The method of claim 46 wherein the radioopaque agent comprises iodine.

48. The method of claim 46 wherein the precursor comprises a branched polyethylene glycol, with the radioopaque agent being disposed on at least one of the branches.

49. The method of claim 44 further comprising substantially filling the site with the hydrogel.

50. The method of claim 44 wherein the hydrogel is biodegradable.

51. The method of claim 50 wherein the hydrogel comprises a radioopaque agent.

52. The method of claim 44 further comprising forming a radiation plan based on the hydrogel as a fiducial marker.

53. The method of claim 44 wherein the plan sets forth margins of less than about 20 mm.

54. The method of claim 44 wherein the hydrogel comprises a collection of covalently-crosslinked hydrogel particles.

55. The method of claim 54 wherein the a collection of hydrogel particles comprises a radioopaque agent covalently attached to a plurality of the particles in the collection, with the radioopaque agent being present in the collection at a concentration of at least about 0.1% w/w.

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HRISHIKESH RAY CHAUDHURY
OF REMFRY & SAGAR
ATTORNEY FOR THE APPLICANTS