[0038] Another object of the present invention is to provide an improved treatment and/or diagnostic strategy to those of the prior art. For example, it is desirable to provide a relatively non-invasive therapy which rejuvenates degenerated or partially-degenerated intervertebral discs, or the nucleus pulposus thereof, in a patient population which can benefit most from such therapy.

[0039] Another object of the invention is to revitalise cells and/or extra cellular matrices, suitably by altering or (at least partially) restoring a favourable local environmental for the cells and/or extra cellular matrices.

SUMMARY ~~OF THE INVENTION~~

[0040] The present ~~invention~~disclosure provides effective solutions to problems inherent in the prior art. Such solutions involve relatively non-invasive treatments, especially when compared to traditional surgical treatments. Such treatments generally involve introduction or injection of a treatment composition to a target site of a subject in need of such a treatment. Subjects (whether animal or human) who may benefit most from treatments of the ~~invention~~disclosure (e.g. subjects in need of such treatments) generally exhibit a defined degradation state in respect of one or more target sites (i.e. "partially-degraded target sites") and / or symptoms corresponding with such a degradation state. Such target sites, which are suitably specific regions of a human or animal body (e.g. an intervertebral disc or a component part thereof, such a nucleus pulposus), typically degrade to the defined degradation state as a consequence of biological degeneration at the target site, in particular cellular and/or extracellular degradation. Though, depending on the definition of the degradation state (i.e. window of degradation in question), such biological degeneration need not necessarily be accompanied by (substantial) structural degradation, in some cases a degree of structural degradation may also be exhibited, though most suitably such structural degradation will not have proceeded beyond a defined point.

[0041] Treatments of the ~~invention~~disclosure generally seek to rejuvenate these one or more partially-degraded target sites rather than replacing them. Such rejuvenation suitably involves introduction (typically *via* injection) to the target site(s) of materials which restore or mimic a degree of healthiness, which suitably in turn prompts an enthusiastic biochemical response that revitalises or further revitalises the target site(s).

[0042] In view of the foregoing, it may first be useful to identify subjects who may benefit most from treatments of the ~~invention~~disclosure (i.e. a specific patient population or sub-population), or subjects in need of such treatments. To this end, candidate subjects may be identified by reference to a degradation state of one or more target sites (e.g. partially-degraded target sites) thereof. Subjects identified as exhibiting a defined "degradation state" in respect of one or more target sites, i.e. patients exhibiting one or more partially-degraded target sites, may be considered "a subject in need of" a treatment according to the ~~invention~~disclosure.

[0042a] According to one aspect of the present disclosure, there is provided the use of a treatment composition in the manufacture of a medicament for treating a subject with a partially-degraded cartilaginous target site exhibiting early-stage degeneration, wherein the treatment composition comprises: an active precursor component; and an activator agent, which promotes physical and/or chemical transformation of the active precursor component into an active component; wherein the use comprises: providing an injection device comprising: an activatable reservoir containing an activatable composition comprising the active precursor component; an activator reservoir containing an activator composition comprising the activator agent, which promotes physical and/or chemical transformation of the active precursor component into an active component; and a mixing chamber with an outlet; wherein the activatable reservoir and the activator reservoir maintain separation between the activatable and activator compositions; operating the injection device: to deliver the activatable composition from the activatable reservoir and the activator composition from the activator reservoir into the mixing chamber to form the treatment composition, wherein the total volume of the treatment composition (i.e. the total combined volume of the activatable composition and the activator composition) is between 0.1 and 3 mL; and the treatment composition is to be injected, suitably *via* a needle or cannula, into the partially-degraded cartilaginous target site, or extracellular matrix thereof; wherein the active precursor component physically and/or chemically transforms into the active component to provide, within the target site or extracellular matrix thereof, a non-biodegradable post-treatment composition comprising the active component; wherein the treatment composition is fluidly mobile and the post-treatment composition is a gel; wherein target site is a nucleus pulposus of an intervertebral disc (IVD), and the intervertebral disc is characterised by early-stage degenerative disc disease (DDD), wherein early-stage degenerative disc disease is diagnosed where the IVD target site is designated Grade II on the Pfirrmann scale.

[0043] ~~According to a first aspect~~In one example of the present ~~invention~~disclosure there is provided a method of determining a degradation state of a target site, the method comprising:

i) providing degradability data in respect of the target site;

ii) on the basis of the degradability data, determining the degradation state of the target site;

wherein suitably the degradation state is a qualitative and/or quantitative value indicative of a degree of degradation of the target site, and suitably the value facilitates an assessment of likely success of a treatment of the ~~invention~~disclosure upon the target site.

[0044] According to a further ~~aspect~~ example of the present ~~invention~~disclosure there is provided a method of determining a degradation state of an intervertebral disc or one or more components thereof (suitably within a subject), the method comprising: performing the method of determining a degradation state of a target site; wherein the target site is an intervertebral disc or one or more components thereof (e.g. nucleus pulposus, annulus fibrosus, and/or vertebral endplate(s)). Suitably the degradability data comprises one or more images (e.g. MRI images) of the intervertebral disc or one or more components thereof.

[0045] In the context of the present ~~invention~~disclosure, where a degradation state of a given target site is or complies with a pre-defined degradation state, that target site may be termed a "partially-degraded target site".

[0046] According to a further ~~aspect~~ example of the present ~~invention~~disclosure there is provided a method of identifying a candidate subject, suitably one in need of (or who may benefit from) a treatment according to the ~~invention~~disclosure, the method comprising:

(i) performing in respect of a subject the method of determining a degradation state of a target site upon one or more target sites of the subject (e.g. to determine whether any of the one or more target sites exhibit a pre-defined degradation state);

(ii) on the basis of degradation state(s) of the one or more target site(s), suitably in comparison to a pre-defined candidate degradation state, determining whether or not the subject is a candidate subject;

(iii) optionally identifying one or more partially-degraded target site(s) by reference to which of the one or more target site(s) comply with a pre-defined degradation state;

wherein the degradation state is a qualitative and/or quantitative value indicative of a degree of degradation of the one or more target regions of the subject, and suitably the value facilitates an assessment of likely success of a treatment of the ~~invention~~disclosure upon the subject or upon the one or more target site(s) of the subject.

[0047] According to a further ~~aspect~~ example of the present ~~invention~~disclosure there is provided a method of identifying a candidate subject, the method comprising:

(i) performing in respect of a subject the method of determining a degradation state of a target site upon one or more target sites of the subject;

(ii) identifying the subject as a candidate subject if any degradation state(s) of the one or more target site(s) comply with a pre-defined degradation state criterion;

(iii) optionally identifying one or more partially-degraded target site(s) by reference to which of the one or more target site(s) comply with the pre-defined degradation state criterion.

[0048] According to a further example~~aspect~~ of the present ~~invention~~disclosure there is provided a method of treating a candidate subject (suitably as defined herein) exhibiting one or more partially-degraded target site(s), the method comprising introducing or injecting a treatment composition into one or more partially-degraded target site(s) of the candidate subject.

[0049] According to a further ~~aspect~~ example of the present ~~invention~~disclosure there is provided a treatment composition for use in treating a candidate subject (suitably as defined herein) exhibiting one or more partially-degraded target site(s). In this context, "treating" suitably comprises a method of treating a candidate subject as defined herein.

[0050] According to a further example~~aspect~~ of the present ~~invention~~disclosure there is provided a method of treating a candidate subject (suitably as defined herein) exhibiting one or more partially-degraded target site(s), the

method comprising introducing a hydrogel composition (or post-treatment composition) into one or more partially-degraded target site(s).

[0051] According to a further exampleaspect of the present inventiondisclosure there is provided a hydrogel composition (or post-treatment composition) for use in treating a candidate subject (suitably as defined herein) exhibiting one or more partially-degraded target site(s). In this context, "treating" suitably comprises a method of treating a candidate subject as defined herein.

[0052] In some embodimentexamples, the treatment composition is (substantially) the same as the hydrogel composition (or post-treatment composition), whilst in some other embodimentexamples the treatment composition transforms or is transformed into the hydrogel composition (or post-treatment composition). As such, a treatment composition may be introduced or injected into one or more partially degraded target site(s) (e.g. as part of a method of administering the treatment composition to a candidate subject) and the treatment composition may transform (suitably *via* a physical and/or chemical reaction, optionally initiated by an initiator) into the hydrogel composition (or post-treatment composition) (e.g. a part of a method of administering the hydrogel composition or post-treatment composition to a candidate subject). The hydrogel composition (or post-treatment composition) suitably physically and/or chemically mimics healthy non-degenerated target sites.

[0053] According to a further exampleaspect of the present inventiondisclosure there is provided a method of revitalising one or more partially-degraded target site(s), the method comprising introducing a treatment composition or a hydrogel composition (or post-treatment composition) into one or more of the partially-degraded target site(s).

[0054] According to a further exampleaspect of the present inventiondisclosure there is provided a treatment composition or a hydrogel composition (or post-treatment composition) for use in a method of revitalising one or more partially-degraded target site(s) (suitably as defined herein).

[0055] According to a further example aspect of the present inventiondisclosure there is provided a method of revitalising cells or cellular function at one or more partially-degraded target site(s), the method comprising introducing a treatment composition or a hydrogel composition (or post-treatment composition) into one or more of the partially-degraded target site(s).

[0056] According to a further exampleaspect of the present inventiondisclosure there is provided a treatment composition or a hydrogel composition (or post-treatment composition) for use in a method of revitalising cells or cellular function (suitably as defined herein).

[0057] According to a further exampleaspect of the present inventiondisclosure there is provided a method of revitalising an extracellular matrix (ECM) (and optionally also cells associated therewith) at one or more partially-degraded target site(s), the method comprising introducing a treatment composition or a hydrogel composition (or post-treatment composition) into one or more of the partially-degraded target site(s).

[0058] According to a further exampleaspect of the present inventiondisclosure there is provided a treatment composition or a hydrogel composition (or post-treatment composition) for use in a method of revitalising an extracellular matrix (ECM) (and optionally also cells associated therewith) (suitably as defined herein).

[0059] According to a further exampleaspect of the present inventiondisclosure there is provided a method of retarding degradation (particularly the rate of degradation) of a partially-degraded target site, the method comprising introducing a treatment composition or a hydrogel composition (or post-treatment composition) into one or more of the partially-degraded target site(s). Such degradation may, for example, refer to any one or more of physical/structural degradation, biochemical degradation, cellular degradation, degradation of an extracellular

matrix. The degradation may extend beyond the target site, for example, to neighbouring sites or neighbouring tissues. The degradation may be or relate to degenerative disk disease (DDD). In an ~~embodiment~~example, retarding degradation comprises inhibiting progress of degenerative disc disease and/or cartilage degradation.

[0060] According to a further example~~aspect~~ of the present ~~invention~~disclosure there is provided a treatment composition or a hydrogel composition for use in a method of retarding degradation of a partially-degraded target site (suitably as defined herein).

[0061] According to a further example~~aspect~~ of the present ~~invention~~disclosure there is provided a method of treating or alleviating pain at or derived from one or more partially-degraded target site(s), the method comprising introducing a treatment composition or a hydrogel composition into one or more of the partially-degraded target site(s). The pain may, for instance, be discogenic pain and the target site(s) may be intervertebral discs (or the nucleus pulposus thereof).

[0062] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a treatment composition or a hydrogel composition for use in a method of treating or alleviating pain at one or more partially-degraded target site(s) (suitably as defined herein).

[0063] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a method of hydrating or rehydrating (or increasing water content of) an extracellular matrix (ECM) at one or more partially-degraded target site(s) (suitably of a candidate subject), the method comprising introducing (suitably *via* injection) a treatment composition or hydrogel composition to, into, around, and/or in the proximity of the extracellular matrix.

[0064] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a treatment composition or a hydrogel composition for use in a method of hydrating or rehydrating (or increasing water content of) an extracellular matrix (ECM) at one or more partially-degraded target site(s) (suitably as defined herein).

[0065] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a method of inhibiting the production, secretion, or accumulation of one or more inflammatory cytokines (e.g. IL-1, particularly IL-1β) at one or more partially-degraded target site(s), the method comprising introducing a treatment composition or a hydrogel composition into one or more of the partially-degraded target site(s).

[0066] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a treatment composition or a hydrogel composition for use in a method of inhibiting the production, secretion, or accumulation of one or more inflammatory cytokines (e.g. IL-1, particularly IL-1β) at one or more partially-degraded target site(s) (suitably as defined herein).

[0067] Suitably, in the above methods and compositions for use, the one or more partially-degraded target site(s) are part of or within a candidate subject, and suitably the method is performed *in vivo*. However, the method may be performed *in vitro*.

[0068] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a method of treating a candidate subject (suitably as defined herein) exhibiting one or more partially-degraded target site(s), the method comprising:

(i) identifying a candidate subject (suitably *via* a method as defined herein)

(ii) identifying one or more partially-degraded target site(s) of the candidate subject;

(iii) introducing or injecting a treatment composition or a hydrogel composition into one or more partially-degraded target site(s) of the candidate subject;

(iv) optionally thereafter examining the one or more target site(s) into which the treatment composition or hydrogel composition was introduced (e.g. *via* a method of determining a degradation state of a target site as defined herein) to assess treatment outcomes.

[0069] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a method of introducing a hydrogel composition into a partially-degraded target site (suitably of a candidate subject), the method comprising injecting a treatment composition (or an injectable form of the hydrogel composition) into the partially-degraded target site; and thereafter transforming the treatment composition (or an injectable form of the hydrogel composition) or allowing the same to transform into the hydrogel composition (or a non-injectable form thereof) within the target site (suitably of a candidate subject).

[0070] In further ~~aspect~~examples of the present ~~invention~~disclosure there is provided a treatment composition or hydrogel composition for use in the manufacture of an active medical device for performing any of the aforementioned methods which involve either or both the treatment composition and/or hydrogel composition.

[0071] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a post-treatment composition.

[0072] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a treatment composition. The treatment composition may be formed by mixing together an activatable composition and an activator composition.

[0073] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided a kit comprising an activatable composition and an activator composition.

[0074] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided an activatable composition.

[0075] According to a further ~~aspect~~example of the present ~~invention~~disclosure there is provided an activator composition.

[0076] Any features, including optional, suitable, and preferred features, described in relation to any particular aspect of the ~~invention~~disclosure may also be features, including optional, suitable and preferred features, of any other aspect of the present ~~invention~~disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[0077] For a better understanding of the invention, and to show how embodiments of the same are put into effect, reference is now made, by way of example, to the following diagrammatic drawings, in which:

[0078] FIG. 1 shows a sheep, and labels the specific vertebrae that were investigated / treated.

[0079] FIG. 2 shows a photograph of an excised sheep lumbar spine.

[0080] FIG. 3 shows microscopic images of an IVD displaying evidence of degeneration by way of: a) cell clusters; b) slits; and c) end-plate lesions.

[0081] FIG. 4 show microscopic images of histological disc tissue (left) incorporating viable cells (tiny dark nuclei) and fragmented post-treatment composition (i.e. after curing *in vivo*) on the right.

[0082] FIG. 5 shows microscopic images of viable cells (dark round nuclei) next to spaces left by the post-treatment composition.

CLAIMS:

1. Use of a~~A~~ treatment composition ~~for use~~ in the manufacture of a medicament for~~a method of~~ treating a subject with a partially-degraded cartilaginous target site exhibiting early-stage degeneration, wherein the treatment composition comprises~~comprising~~:

an active precursor component; and

an activator agent, which promotes physical and/or chemical transformation of the active precursor component into an active component;

wherein the use ~~method of treating~~ comprises:

providing an injection device comprising:

an activatable reservoir containing an activatable~~injecting the treatment~~ composition comprising~~into the partially-degraded cartilaginous target site, or extracellular matrix thereof;~~

~~wherein~~ the active precursor component~~; physically and/or chemically transforms into the active component to provide, within the target site or extracellular matrix thereof, a non-biodegradable post-treatment composition comprising the active component;~~

~~wherein the post-treatment composition is relatively less fluidly mobile than the treatment composition.~~

~~2. A kit for use in a method of treating a subject with a partially-degraded cartilaginous target site exhibiting early-stage degeneration, the kit comprising:~~

~~an activatable composition comprising an active precursor component; and~~

an activator reservoir containing~~composition comprising~~ an activator composition comprising the activator agent, which promotes physical and/or chemical transformation of the active precursor component into an active component; and

a mixing chamber with an outlet;

wherein the activatable reservoir and the activator reservoir maintain separation between the activatable and activator compositions;

operating the injection device:

to deliver~~wherein the method of treating comprises:~~

~~mixing together~~ the activatable composition from the activatable reservoir and the ~~and~~ activator composition from the activator reservoir into the mixing chamber to form the~~a~~ treatment composition, wherein the total volume of ~~; and~~

~~injecting~~ the treatment composition (i.e. the total combined volume of the activatable composition and the activator composition) is between 0.1 and 3 mL; and the treatment composition is to be injected, suitably *via* a needle or cannula, into the partially-degraded cartilaginous target site, or extracellular matrix thereof;

wherein the active precursor component physically and/or chemically transforms into the active component to provide, within the target site or extracellular matrix thereof, a non-biodegradable post-treatment composition comprising the active component;

wherein the post-treatment composition is relatively less fluidly mobile than the treatment composition.

3. An activatable composition for use in a method of treating a subject with a partially-degraded cartilaginous target site exhibiting early-stage degeneration, the activatable composition comprising:

an active precursor component;

wherein the method of treating comprises:

mixing the activatable composition with an activator composition to form a treatment composition; and

injecting the treatment composition into the partially-degraded cartilaginous target site, or extracellular matrix thereof;

wherein the active precursor component physically and/or chemically transforms into the active component to provide, within the target site or extracellular matrix thereof, a non-biodegradable post-treatment composition comprising the active component;

wherein the post-treatment composition is a gel; relatively less fluidly mobile than the treatment composition;

wherein the activator composition comprises an activator agent which promotes physical and/or chemical transformation of the active precursor component into an active component.

4. The treatment composition for use as claimed in claim 1, the kit for use as claimed in claim 2, or the activatable composition for use as claimed in claim 3, wherein the subject with a partially-degraded cartilaginous target site exhibiting early-stage degeneration is identified by reference to qualitative and / or quantitative pre-defined degradation state criteria in relation to the target site, wherein optionally said pre-defined degradation state criteria comprises inclusion criteria and/or exclusion criteria.

5. The treatment composition for use, the kit for use, or the activatable composition for use, as claimed in claim 4, wherein target site is a nucleus pulposus of an intervertebral disc (IVD), and the intervertebral disc is characterised by early-stage degenerative disc disease (DDD),).

6. The treatment composition for use, the kit for use, or the activatable composition for use, as claimed in claim 5, wherein early-stage degenerative disc disease is diagnosed by reference to images and / or data obtained by magnetic resonance imaging (MRI) of the nucleus pulposus, wherein optionally at least some of the data relates to the hydration state of the nucleus pulposus.

7. The treatment composition for use, the kit for use, or the activatable composition for use, as claimed in claim 6, wherein early-stage degenerative disc disease is diagnosed where the IVD target site is designated Grade II or III on the Pfirrmann scale.

2. The use as claimed in claim 1, wherein the injection device is or comprises a double-barrelled syringe with a mixing chamber, wherein one barrel of the syringe contains the activatable composition and another

barrel of the syringe contains the activator composition, and the syringe is operable to mix the activatable composition and activator composition within the mixing chamber.

3. The use as claimed in claim 1 or 2, wherein the volumetric ratio of the activatable composition to activator composition is between 4-15 : 1.

4. The use as claimed in any one of claims 1-3, wherein the injection device comprises a needle, through which the treatment composition is dispensable, whose largest inner dimension (or inner diameter) is between 0.2 and 2 mm.

~~8. The treatment composition for use, the kit for use, or the activatable composition for use, as claimed in any claims~~ 5. The use as claimed in any one of claims 1-4~~5 to 7~~, wherein upon injection the treatment composition diffuses into crevices, cracks, tears, or fissures present within the nucleus pulposus, and thereafter cures therein to form the post-treatment composition as a non-bolus hydrogel.

~~9. The treatment composition for use, the kit for use, or the activatable composition for use, as claimed in any claims 5 to 8, wherein injecting the treatment composition comprises injecting between 0.5 mL and 4 mL of treatment composition.~~

6. The use as claimed in any one of claims 1-5~~10. The treatment composition for use, the kit for use, or the activatable composition for use, as claimed in any preceding claim~~, wherein the treatment composition comprises:

1-30 wt% active precursor component (e.g. active precursor polymer); and

sufficient quantities of a physical activator agent (e.g. pH-modifier, e.g. a base, e.g. NaOH) to furnish a pH above pH 5.

7~~11~~. The ~~treatment composition for~~ use~~, the kit for use, or the activatable composition for use,~~ as claimed in any one of claims 1-6~~preceding claim~~, wherein the treatment composition comprises:

1-30 wt% active precursor component (e.g. active precursor polymer); and

0.001-6 wt% chemical activator agent(s) (e.g. an initiator and/or accelerator).

8~~12~~. The ~~treatment composition for~~ use~~, the kit for use, or the activatable composition for use,~~ as claimed in any one of claims 1-7~~preceding claim~~, wherein the treatment composition comprises:

1-30 wt% active precursor component (e.g. active precursor polymer);

sufficient quantities of a physical activator agent (e.g. pH-modifier, e.g. a base, e.g. NaOH) to furnish a pH above pH 5;

0.001-5 wt% initiator(s) (e.g. ammonium persulphate); and

0.0001-2 wt% accelerator(s) (e.g. ascorbic acid).

9~~13~~. The ~~treatment composition for use, the kit for use, or the activatable composition for~~ use, as claimed in any one of claims 6~~10~~ to 8~~12~~, wherein the treatment composition comprises a contrast agent and/or visualisation agent (e.g. $BaSO_4$).

10~~14~~. The ~~treatment composition for~~ use~~, the kit for use, or the activatable composition for use,~~ as claimed in any one of claims 1-9~~preceding claim~~, wherein the active precursor component comprises microgel particles bearing vinyl-containing moieties grafted onto their respective surfaces, and the activator agent comprises a free-radical initiator (e.g. ammonium persulphate) which promotes, optionally in the presence of an additional accelerator (e.g. ascorbic acid), direct inter-microgel particle crosslinking *via* free-radical coupling of the vinyl-containing moieties grafted to the surfaces of adjacent microgel particles.

11~~15~~. The ~~treatment composition for~~ use~~, the kit for use, or the activatable composition for use,~~ as claimed in any one of claims 1-10~~preceding claim~~, wherein the ~~method of~~ treating of the subject comprises one or more of:

i) Revitalising one or more partially-degraded target site(s);

ii) Revitalising cells or cellular function associated or within one or more partially-degraded target site(s);

iii) Revitalising the extracellular matrices (ECMs) at one or more partially-degraded target sites;

iv) Revitalising cells surrounding or in close proximity to crevices, cracks, or slits within a target site and filled with the treatment and/or the post treatment composition;

v) Improving cellular nutrient diffusion at one or more partially-degraded target site(s);

vi) Retarding or inhibiting degradation at one or more partially-degraded target site(s);

vii) Retarding or inhibiting degradation of cells or cellular function associated or within one or more partially-degraded target site(s);

viii) Retarding or inhibiting degradation of the extracellular matrices (ECMs) at one or more partially-degraded target sites;

ix) Retarding or inhibiting degradation of cells surrounding or in close proximity to crevices, cracks, or slits within a target site;

x) Retarding or inhibiting degradation of cellular nutrient diffusion at one or more partially-degraded target site(s);

xi) Retarding or inhibiting biochemical degradation at one or more partially-degraded target site(s);

xii) Retarding or inhibiting structural or mechanical degradation at one or more partially-degraded target site(s);

xiii) Retarding or inhibiting progression of DDD at one or more partially-degraded target site(s), or retarding or inhibiting progression of DDD to the next stage on the Pfirrmann scale;

xiv) Treating or alleviating pain at one or more partially-degraded target site(s);

xv) Treating or alleviating discogenic pain at one or more partially-degraded IVD(s);

xvi) Reducing the risk or likelihood of future pain at one or more partially-degraded target site(s);

xvii) Reducing the risk or likelihood of a future requirement for surgery at one or more partially-degraded target site(s);

xviii) Increasing or facilitating maintenance of hydration at one or more partially-degraded target site(s);

xix) Treating or reducing inflammation or inflammatory responses at one or more partially-degraded target site(s);

xx) Inhibiting production of one or more inflammatory cytokines at one or more partially-degraded target site(s); and

xxi) Restoring a positive balance of cytokine mediated anabolic/catabolic reaction in partially degraded target sites.

~~16. A treatment composition comprising: 10-20 wt% crosslinkable microgel particles comprising poly(MMA/MAA/EGDMA) cores surface-functionalised with GMA, wherein the cores comprise about 60-70% MMA, about 30-40% MAA and 0.1 to 1% EGDMA based on the total monomer mass, and wherein 2-8 mol.% of all monomers of the cores are functionalised with GMA; 0.01-0.2 wt% ascorbic acid (or a salt thereof); 0.05-0.5 wt% ammonium persulfate; and a pH modifier; wherein the composition is characterised by a pH between 7 and 7.8.~~

~~17. A post-treatment composition comprising formed by crosslinking the crosslinked microgel particles of the treatment composition as claimed in claim 16.~~