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(54) **Title:** METHOD OF MAKING, MANUFACTURING OR PRODUCING ORTHOPEDIC SOFT TISSUE

Figure 1

Figure 1A

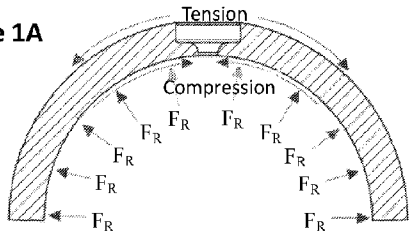


Figure 1B

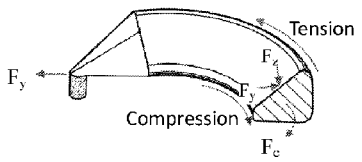


Figure 1C

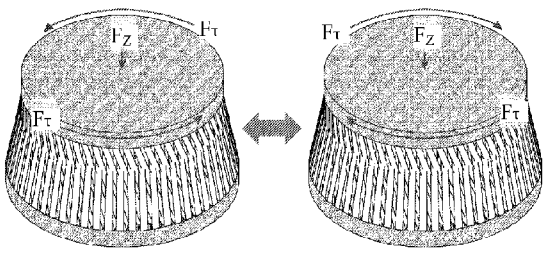
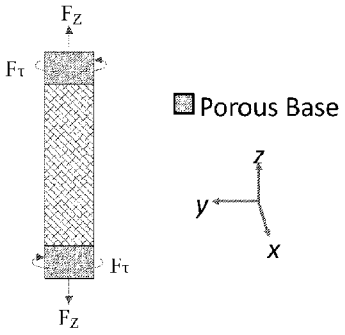


Figure 1D



(57) **Abstract:** An improved method of making, manufacturing and/or producing engineered orthopedic soft tissue including cartilage, meniscus, annulus fibrosus, and tendon/ligaments which results in engineered soft tissue in which the fibers are aligned the same or nearly the same as naturally occurring tissue. The present invention also includes molds and other apparatus for carrying out the methods of the invention and kits.

[Continued on next page]

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TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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— *with international search report (Art. 21(3))*
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INTERNATIONAL SEARCH REPORT

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PCT/US 18/56642

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61F 2/08 (2019.01)
CPC - A61F 2/08, A61F 2/30756, A61F 2/3094

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y -- A	US 2016/0228604 A1 (ORTHOX LIMITED) 11 August 2016 (11.08.2016) Entire document, especially Abstract, para[0002], [0031]-[0032], [0040]-[0046], [0131]-[0132].	1-3, 6-9, 11-12 ---------- 4-5 ---------- 10
Y	US 2005/0221703 A1 (STONE) 06 October 2005 (06.10.2005) Entire document, especially Abstract, para[0037], [0074]-[0081].	1, 4-5
Y	US 5,376,110 A (TU et al.) 27 December 1994 (27.12.1994) Entire document, especially Abstract, col 3, ln 37- col 4, ln 20, col 9, ln 20-24, col 14, ln 52- col 14, ln 10.	1
A	US 2010/0023130 A1 (HENRY et al.) 28 January 2010 (28.01.2010) Entire document, especially Abstract, para[0108].	10
A	US 2017/0224498 A1 (MCCULLEN et al.) 10 August 2017 (10.08.2017) Entire document.	1-12
A	US 2017/0224459 A1 (JULIUS-MAXIMILIANS-UNIVERSITAET WUERZBURG) 10 August 2017 (10.08.2017) Entire document.	1-12
A	US 4,880,429 A (STONE) 14 November 1989 (14.11.1989) Entire document.	1-12
A	US 2016/0213812 A1 (PATHAK HOLDINGS LLC) 28 July 2016 (28.07.2016) Entire document.	1-12

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
06 February 2019	03 MAY 2019
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/56642

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 33-34, 37-38
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, Claims 1-12: directed towards a method of manufacturing and/or producing engineered orthopedic soft tissue under conditions and for a time to allow the fiber orientation of the engineered orthopedic soft tissue to mimic or recapitulate the fiber orientation of naturally occurring orthopedic soft tissue.

Group II, Clams 13-20, 30-32: directed towards a method of making, manufacturing and/or producing cartilage cartilage, comprising the steps of: a. placing a mold into a hemispherical container, wherein the mold comprises at least four leaflets which when held together by a leaflet collar around a central post, comprise a hemisphere; b. pouring a liquid polymer into the container, wherein the container surrounds the mold; e. placing the mold and the polymer onto an expander, wherein the expander contains a central threaded channel in which the central post of the mold is threaded; f. advancing the mold with the polymer on the expander.
------ see extra sheet ----------

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-12

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/56642

---------- Continuation of Box III: Observations where unity of invention is lacking (Continuation of item 3 of first sheet) ----------

Group III, Claims 21-29, 35-36: directed towards a method for making, manufacturing and/or producing meniscus, comprising the steps of: a. injecting a liquid polymer into an inlet port of a mold until the liquid polymer starts to flow from an outlet port, the mold being in the desired shape of the polymer and having an inlet port, an outlet port, an area for the polymer and an area for at least one rigid porous base and containing at least one rigid porous base; d. placing the partially crosslinked polymer and the at least one rigid porous base into a loading frame comprising at least one screw, a crank, and a post; e. fixing the rigid porous base to the screw on the loading frame; f. turning the crank of the loading frame clockwise to cause the rigid porous base to move toward the crank which in turn forces the polymer against the post.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding technical features for the following reasons:

Special Technical Features
Group I, includes the special technical features, of a method of manufacturing and/or producing engineered orthopedic soft tissue under conditions and for a time to allow the fiber orientation of the engineered orthopedic soft tissue to mimic or recapitulate the fiber orientation of naturally occurring orthopedic soft tissue, not required in any other group.

Group II, includes the special technical features of a method for making, manufacturing and/or producing cartilage cartilage, comprising the steps of: a. placing a mold into a hemispherical container, wherein the mold comprises at least four leaflets which when held together by a leaflet collar around a central post, comprise a hemisphere; b. pouring a liquid polymer into the container, wherein the container surrounds the mold; e. placing the mold and the polymer onto an expander, wherein the expander contains a central threaded channel in which the central post of the mold is threaded; f. advancing the mold with the polymer on the expander, not required in any other group.

Group III, includes the special technical features of a method for making, manufacturing and/or producing meniscus, comprising the steps of: a. injecting a liquid polymer into an inlet port of a mold until the liquid polymer starts to flow from an outlet port, the mold being in the desired shape of the polymer and having an inlet port, an outlet port, an area for the polymer and an area for at least one rigid porous base and containing at least one rigid porous base; d. placing the partially crosslinked polymer and the at least one rigid porous base into a loading frame comprising at least one screw, a crank, and a post; e. fixing the rigid porous base to the screw on the loading frame; f. turning the crank of the loading frame clockwise to cause the rigid porous base to move toward the crank which in turn forces the polymer against the post, not required in any other group.

Common Technical Features

Group I share with groups I-II the technical features of manufacturing an engineered tissue by cross-linking a polymer while forces are applied. However, these common technical features are anticipated by US 2016/0228604 A1 to ORTHOX LIMITED (hereinafter: Orthox). Orthox describes manufacturing an engineered tissue (Abstract, para[0046]) by cross-linking a polymer while forces are applied (para[0132]: "subjecting the fiber lay ... to hydrostatic pressure or compressive load ... during the cross-linking reaction"). Group I shares no further features with any other group.

Groups II-III further share the technical features of inserting liquid polymer into a mold, partially cross-linking the polymer, removing the polymer, cross-linking and applying forces to the polymer, and removing the polymer. However, these common technical features are anticipated by Orthox. Orthox describes inserting liquid polymer into a mold (para[0098]), partially cross-linking the polymer (para[0101]-[0102]), removing the polymer (para[0099]), cross-linking and applying forces to the polymer (para[0132]), and removing the polymer (final product, para[0102]-[0103]; e.g. see FIGS. 1-2, para[0057]-[0059]).

Accordingly, Groups I-III lack unity under PCT Rule 13.
Note: Claims 33-34, 37-38 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).