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Total joint replacement infection control devices and methods

Abstract

An orthopedic system for delivery of a therapeutic agent to a bone includes an elongate stem adapted to be inserted into an intramedullary canal, an inlet configured to receive the therapeutic agent, and one or more outlets configured to deliver the therapeutic agent to the bone. The elongate stem may comprise one or more protrusions to engage the bone, and one or more channels extending longitudinally therein, fluidly coupled to the inlet. The therapeutic agent flows from the inlet through the one or more channels and exits into the intramedullary canal through the one or more outlets. The system may be configured to allow one or more dimensions of the system to be adjusted to accommodate the anatomy of a patient.

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References Cited**U.S. PATENT DOCUMENTS**

Patent No.	Issued Date	Patentee Name	U.S. Cl.	CPC
3648294	12/1971	Shahrestani	N/A	N/A
4274163	12/1980	Malcom et al.	N/A	N/A
4399814	12/1982	Pratt, Jr. et al.	N/A	N/A
4488549	12/1983	Lee et al.	N/A	N/A
4653487	12/1986	Maale	N/A	N/A
4711233	12/1986	Brown	N/A	N/A
4888024	12/1988	Powlan	N/A	N/A
4892550	12/1989	Huebsch	N/A	N/A
5116377	12/1991	Skripitz et al.	N/A	N/A
5133767	12/1991	Frey et al.	N/A	N/A
5133771	12/1991	Duncan et al.	N/A	N/A
5133772	12/1991	Hack et al.	N/A	N/A
5156606	12/1991	Chin	N/A	N/A
5290291	12/1993	Linden	N/A	N/A
5340362	12/1993	Carbone	N/A	N/A
5370698	12/1993	Heimke et al.	N/A	N/A
5376123	12/1993	Klaue et al.	N/A	N/A
5433718	12/1994	Brinker	N/A	N/A

5501687	12/1995	Willert et al.	N/A	N/A
5514137	12/1995	Coutts	N/A	N/A
5549702	12/1995	Ries et al.	N/A	N/A
5554111	12/1995	Morrey et al.	N/A	N/A
5562736	12/1995	Ray et al.	N/A	N/A
5571204	12/1995	Nies	N/A	N/A
5618286	12/1996	Brinker	N/A	N/A
5681289	12/1996	Wilcox et al.	N/A	N/A
5683472	12/1996	O'Neil et al.	N/A	N/A
5693099	12/1996	Harle	N/A	N/A
5702446	12/1996	Schenck et al.	N/A	N/A
5725596	12/1997	Burke	N/A	N/A
5741265	12/1997	Chan	N/A	N/A
5755811	12/1997	Tanamal et al.	N/A	N/A
5827289	12/1997	Reiley et al.	N/A	N/A
5871484	12/1998	Spievack et al.	N/A	N/A
5916269	12/1998	Serbousek et al.	N/A	N/A
5954771	12/1998	Richelsoph et al.	N/A	N/A
5980573	12/1998	Shaffner	N/A	N/A
6066154	12/1999	Reiley et al.	N/A	N/A
6106495	12/1999	Scott	N/A	N/A
6113639	12/1999	Ray et al.	N/A	N/A
6132674	12/1999	Compton et al.	N/A	N/A
6155812	12/1999	Smith et al.	N/A	N/A
6217619	12/2000	Keller	N/A	N/A
6235043	12/2000	Reiley et al.	N/A	N/A
6248110	12/2000	Reiley et al.	N/A	N/A
6336941	12/2001	Subba Rao et al.	N/A	N/A
6361731	12/2001	Smith et al.	N/A	N/A
6361780	12/2001	Ley et al.	N/A	N/A
6423083	12/2001	Reiley et al.	N/A	N/A
6447514	12/2001	Stalcup et al.	N/A	N/A
6544472	12/2002	Compton et al.	N/A	N/A
6589281	12/2002	Hyde, Jr.	N/A	N/A
6679890	12/2003	Margulies et al.	N/A	N/A
6692529	12/2003	Shah	N/A	N/A
6740090	12/2003	Cragg et al.	N/A	N/A
6740120	12/2003	Grimes	N/A	N/A
6783515	12/2003	Miller et al.	N/A	N/A
6899716	12/2004	Cragg	N/A	N/A
6921403	12/2004	Cragg et al.	N/A	N/A
6942475	12/2004	Ensign et al.	N/A	N/A
6942702	12/2004	Mitsugi et al.	N/A	N/A
6969404	12/2004	Ferree	N/A	N/A
6979336	12/2004	Durniak	N/A	N/A
6981981	12/2005	Reiley et al.	N/A	N/A
6989033	12/2005	Schmidt	N/A	N/A
7048743	12/2005	Miller et al.	N/A	N/A
7112205	12/2005	Carrison	N/A	N/A
7141053	12/2005	Rosa et al.	N/A	N/A

7141067	12/2005	Jones et al.	N/A	N/A
7211113	12/2006	Zelener et al.	N/A	N/A
7217260	12/2006	Molander et al.	N/A	N/A
7250055	12/2006	Vanderwalle	N/A	N/A
7255713	12/2006	Malek	N/A	N/A
7300282	12/2006	Sapian	N/A	N/A
7306629	12/2006	Saladino et al.	N/A	N/A
7427296	12/2007	Evans	N/A	N/A
7429346	12/2007	Ensign et al.	N/A	N/A
7534240	12/2008	Johnson	N/A	N/A
7572293	12/2008	Rhodes et al.	N/A	N/A
7601157	12/2008	Boyd et al.	N/A	N/A
7601176	12/2008	Soffiati et al.	N/A	N/A
7641698	12/2009	Gibbs et al.	N/A	N/A
7771428	12/2009	Siravo et al.	N/A	N/A
7842095	12/2009	Klein	N/A	N/A
7862619	12/2010	Clark	N/A	N/A
7914585	12/2010	Keller	N/A	N/A
8038682	12/2010	McGill et al.	N/A	N/A
8097039	12/2011	Evans	N/A	N/A
8135466	12/2011	Fuller et al.	N/A	N/A
8366782	12/2012	Wright	N/A	N/A
8388881	12/2012	Giori	N/A	N/A
8454706	12/2012	de Beaubien	N/A	N/A
8475505	12/2012	Nebosky et al.	N/A	N/A
8496711	12/2012	Anapliotis et al.	N/A	N/A
8500819	12/2012	Meridew et al.	N/A	N/A
8529532	12/2012	Pinto et al.	N/A	N/A
8579985	12/2012	Podolsky et al.	N/A	N/A
8608802	12/2012	Bagga et al.	N/A	N/A
8652216	12/2013	Chen et al.	N/A	N/A
8673018	12/2013	Walls	N/A	N/A
8685432	12/2013	Evans et al.	N/A	N/A
8721520	12/2013	Caira et al.	N/A	N/A
8900322	12/2013	de Beaubien	N/A	N/A
8900323	12/2013	de Beaubien	N/A	N/A
8974538	12/2014	Teeny et al.	N/A	N/A
9173742	12/2014	Faccioli et al.	N/A	N/A
9198759	12/2014	Faccioli	N/A	A61F 2/3609
RE46283	12/2016	de Beaubien	N/A	N/A
9707008	12/2016	Krebs et al.	N/A	N/A
9795486	12/2016	Faccioli et al.	N/A	N/A
RE46669	12/2017	de Beaubien	N/A	N/A
9925363	12/2017	Magagnoli	N/A	N/A
10433965	12/2018	de Beaubien et al.	N/A	N/A
RE48119	12/2019	de Beaubien	N/A	N/A
2001/0051831	12/2000	Subba Rao et al.	N/A	N/A
2002/0143402	12/2001	Steinberg	N/A	N/A

2002/0169507	12/2001	Malone	N/A	N/A
2003/0060891	12/2002	Shah	N/A	N/A
2003/0097184	12/2002	Mitsugi et al.	N/A	N/A
2003/0187513	12/2002	Durniak	N/A	N/A
2004/0036189	12/2003	Ensign et al.	N/A	N/A
2004/0111162	12/2003	Southworth	N/A	N/A
2004/0193268	12/2003	Hazebrouck	N/A	N/A
2004/0193281	12/2003	Grimes	N/A	N/A
2004/0225360	12/2003	Malone	N/A	N/A
2005/0004680	12/2004	Saladino et al.	N/A	N/A
2005/0021084	12/2004	Lu et al.	N/A	N/A
2005/0107794	12/2004	Hazebrouck	N/A	N/A
2005/0187555	12/2004	Biedermann et al.	N/A	N/A
2005/0277936	12/2004	Siravo et al.	N/A	N/A
2006/0004431	12/2005	Fuller et al.	N/A	N/A
2006/0014120	12/2005	Sapian	N/A	N/A
2006/0030945	12/2005	Wright	N/A	N/A
2006/0093646	12/2005	Cima et al.	N/A	N/A
2006/0121083	12/2005	Mor	N/A	N/A
2007/0005142	12/2006	Rhodes et al.	N/A	N/A
2007/0016163	12/2006	Santini et al.	N/A	N/A
2007/0088442	12/2006	Cima et al.	N/A	N/A
2007/0110804	12/2006	Royer	N/A	N/A
2007/0123835	12/2006	Molander et al.	N/A	N/A
2007/0179609	12/2006	Goble et al.	N/A	N/A
2009/0069899	12/2008	Klein	N/A	N/A
2009/0130167	12/2008	Shelton et al.	N/A	N/A
2010/0042167	12/2009	Nebosky et al.	N/A	N/A
2010/0042213	12/2009	Nebosky et al.	N/A	N/A
2010/0042214	12/2009	Nebosky et al.	N/A	N/A
2010/0042215	12/2009	Stalcup et al.	N/A	N/A
2010/0114324	12/2009	Gibbs et al.	N/A	N/A
2010/0217401	12/2009	de Beaubien	N/A	N/A
2010/0292803	12/2009	Giori	N/A	N/A
2011/0015754	12/2010	Leonard et al.	N/A	N/A
2011/0208315	12/2010	Anapliotis et al.	N/A	N/A
2011/0218644	12/2010	Meridew et al.	N/A	N/A
2011/0236501	12/2010	Guelcher et al.	N/A	N/A
2012/0109303	12/2011	Capote	N/A	N/A
2012/0209382	12/2011	Forsell	623/14.12	A61F 2/34
2013/0041472	12/2012	Rabiner et al.	N/A	N/A
2013/0158595	12/2012	Mavani et al.	N/A	N/A
2013/0209522	12/2012	Brooks et al.	N/A	N/A
2013/0211334	12/2012	de Beaubien	N/A	N/A
2013/0211369	12/2012	de Beaubien	N/A	N/A
2013/0218100	12/2012	Armbruster et al.	N/A	N/A
2013/0237908	12/2012	Clark	N/A	N/A
2013/0289621	12/2012	Fulmer et al.	N/A	N/A
2014/0194810	12/2013	Barsoum et al.	N/A	N/A
2014/0194811	12/2013	Barsoum et al.	N/A	N/A

2014/0277532	12/2013	Teeny et al.	N/A	N/A
2015/0038941	12/2014	Nebosky	604/285	A61B 17/866
2016/0199190	12/2015	Sharifi-Mehr et al.	N/A	N/A
2020/0330661	12/2019	Canner et al.	N/A	N/A
2020/0360578	12/2019	Loske et al.	N/A	N/A

FOREIGN PATENT DOCUMENTS

Patent No.	Application Date	Country	CPC
104168857	12/2013	CN	N/A
3704089	12/1987	DE	N/A
19722359	12/1997	DE	N/A
19722389	12/1997	DE	N/A
102010052914	12/2011	DE	N/A
0692226	12/1995	EP	N/A
2326287	12/2015	EP	N/A
2943164	12/2016	EP	N/A
2478425	12/2010	GB	N/A
VI 20000025	12/2000	IT	N/A
2005-028129	12/2004	JP	N/A
2012-500056	12/2011	JP	N/A
2012-501228	12/2011	JP	N/A
2014-176714	12/2013	JP	N/A
101377900	12/2013	KR	N/A
279442	12/1997	NZ	N/A
WO-03/037166	12/2002	WO	N/A
WO-2005/122932	12/2004	WO	N/A
WO-2007/047420	12/2006	WO	N/A
WO-2010/019781	12/2009	WO	N/A
WO-2010/080667	12/2009	WO	N/A
WO-2012/030331	12/2011	WO	N/A
WO-2013/041906	12/2012	WO	N/A
WO-2013/059609	12/2012	WO	N/A
WO-2014/110313	12/2013	WO	N/A
WO-2016/205077	12/2015	WO	N/A

OTHER PUBLICATIONS

Ekpo, T.E. et al. (Sep. 22, 2012). “Abbreviated Two-Stage Exchange Arthroplasty for Periprosthetic Joint Infection: 2 to 6 Year Results.” [Poster presentation]. 31st Annual meeting of the European Bone and Joint Infection Society, Montreux, Switzerland. 1 page. cited by applicant

Finsterbusch, A. et al. (1970). “Bone and joint perfusion with antibiotics in the treatment of experimental staphylococcal infection in rabbits.” J Bone Joint Surg Am, 52(7): p. 1424-1432. cited by applicant

Florschutz, A.V. et al. (2015). “Infection after primary anatomic versus primary reverse total shoulder arthroplasty.” J Shoulder Elbow Surg, 24(8): p. 1296-1301. cited by applicant

Lescun, T.B. et al. (2000). “Continuous infusion of gentamicin into the tarsocrural joint of horses.” Am J Vet Res, 61(4): p. 407-412. cited by applicant

Lescun, T.B. et al. (2006). “Treatment with continuous intrasynovial antimicrobial infusion for

septic synovitis in horses: 31 cases (2000-2003).” J Am Vet Med Assoc, 228(12): p. 1922-1929. cited by applicant

Lloyd, K.C. et al. (1988). “Effect of gentamicin sulfate and sodium bicarbonate on the synovium of clinically normal equine antebrachio-carpal joints.” Am J Vet Res, 49(5): p. 650-657. cited by applicant

Lloyd, K.C., et al. (1988). “Plasma and synovial fluid concentrations of gentamicin in horses after intra-articular administration of buffered and unbuffered gentamicin.” Am J Vet Res, 49(5): p. 644-649. cited by applicant

Schneider, R.K. et al. (1992). “Open drainage, intra-articular and systemic antibiotics in the treatment of septic arthritis/tenosynovitis in horses.” Equine Vet J, 24(6): p. 443-9. [Abstract: 2 pages]. cited by applicant

Shelly, M. et al. (2011). “Renal Toxicity Related to Antibiotic-Containing Orthopedic Cement.” Pharmacokinetics and Adverse Drug Reactions. 2 pages. cited by applicant

Thabe, H. et al. (2007). “Two-stage Reimplantation with An Application Spacer and Combined with Delivery of Antibiotics in the Management of Prosthetic Joint Infection” Oper. Orthop Traumatol, 1:78-100. [German language and English language]. cited by applicant

Ure, K.J. et al. (1998). “Direct-exchange arthroplasty for the treatment of infection after total hip replacement. An average ten-year follow-up.” J Bone Joint Surg Am, 80(7): p. 961-968. cited by applicant

Whitehair, K.J., et al. (1992). “Regional Limb Perfusion for Antibiotic Treatment of Experimentally Induced Septic Arthritis.” Vet Surg, 21(5): p. 367-73. [Abstract: 2 pages]. cited by applicant

Whiteside, L. et al. (2011). “Methicillin-resistant *Staphylococcus aureus* in TKA Treated With Revision and Direct Intraarticular Antibiotic Infusion.” Clin Orthop Relat Res, 469:26-33. cited by applicant

Wroblewski, B.M. (1986). “One-stage Revision of Infected Cemented Total Hip Arthroplasty.” Clin Orthop Relat Res, (211): p. 103-107. cited by applicant

Zavala, J.A. et al. (2012). “Management of deep infection after reverse total shoulder arthroplasty: a case series.” J Shoulder Elbow Surg, 21(10): p. 1310-1315. cited by applicant

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Background/Summary

CROSS-REFERENCE (1) This application is a continuation of U.S. Non-Provisional application Ser. No. 16/513,599, filed Jul. 16, 2019, which is a divisional application of U.S. Non-Provisional application Ser. No. 14/841,529, filed Aug. 31, 2015, now U.S. Pat. No. 10,433,965, which claims the benefit of U.S. Provisional Application No. 62/180,986, filed on Jun. 17, 2015, entitled “Total Joint Replacement Infection Control Devices and Methods”, the entire contents of which are incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

(1) A total joint replacement (TJR) is a medical procedure that involves the repair and replacement of joints, such as hips and knees. In these surgical procedures, the bones at the hip or knee joints receive orthopedic implants that mimic the structure of the joint that is replaced.

(2) In some cases, infection occurs and this is can be a devastating complication of TJR surgeries.

Unless an infection is properly diagnosed within the first two to four weeks following the original surgery (which is uncommon), the infected implant must be removed in combination with an extensive debridement of the surrounding joint tissue and bone.

(3) The current standard of care for treatment of an infected TJR in the United States typically involves a two-stage re-implantation process. In the first stage of this process, the infected components are surgically exposed by incision. Scar tissue is then de-bulked and other soft tissue may be released, and sometimes an osteotomy is performed. This stage also includes the removal of all prosthetic components and foreign material including, for example, acrylic bone cement. After extensive joint debridement of infected soft tissue and bone, a spacer block consisting of heavily dosed antibiotic bone cement is placed temporarily into the joint space. The purpose of the antibiotic bone cement is to sterilize the joint environment and to serve as an antibiotic delivery system. Additionally, the bone cement acts as a spacer to preserve joint space and maintains ligament length. However, the antibiotic released by the bone cement is uncontrolled and is quite costly to use. In addition, more operating room time is necessary to prepare this spacer material. This increases the cost of the operation

(4) Following the removal of the infected implant and the insertion of the antibiotic bone cement spacer, the patient must generally wait between six and twelve weeks before the second stage of the procedure can be performed. This period of time is necessary so that medical professionals can be confident that the infection has been successfully eradicated. Only after the infectious condition has been eliminated, may the second stage proceed. During the second stage, the new prosthesis is re-implanted.

(5) In other countries, such as throughout Europe, a one-stage re-implantation process has been popular. This involves the removal of the infected implant, as noted above, followed by aggressive debridement and then immediate re-implantation of a new implant. The success rate for this technique has typically been lower than the two-stage procedure. The one-stage implantation process is generally reserved for patients who are considered to be too feeble or sick to undergo the traditional two-stage re-implantation process.

(6) In certain situations, both one- and two-stage procedures can have disadvantages. For example, and as noted above, the two-stage re-implantation process requires six to twelve weeks between operations. This is a very difficult time for the patient as they do not have a functional joint in place and it is typically very painful to mobilize or ambulate with an antibiotic spacer. Articulating spacers are somewhat better than static spacers, but are also more expensive as well as more difficult and time-consuming to place during the original stage one procedure. From a health care standpoint, the two-stage procedure also requires two separate hospitalizations. Finally, from a surgeon's standpoint, a significant amount of scar tissue develops during the time span between the two procedures. This makes for a very difficult and time-consuming second stage operation. In addition, the two-stage re-implantation process involves not one, but two, very difficult and costly surgical procedures.

(7) On the other hand, a one-stage re-implantation surgical protocol requires absolute identification of the infecting organism in order to proceed. Unfortunately, it is very difficult to achieve this absolute identification in the current health care system. In addition, a one-stage re-implantation protocol requires the use of fully-cemented components. Fully-cemented components are typically not favored by U.S. surgeons for revision surgery because they require a high amount of antibiotic which may structurally weaken the cement.

(8) Moreover, and in both one-stage and two-stage re-implantation surgical protocols, the release of the antibiotic from the bone cement is completely uncontrolled. This is a significant disadvantage of both protocols and essentially acts to lengthen the time between the first and the second surgical procedures in the two-stage re-implantation process.

(9) Thus, there remains a need for a device that may be employed during re-implantation surgical procedures that may be used to deliver antibiotic or other therapeutic agents in a controlled and

titratable manner directly into the synovial joint cavity and adjoining medullary canals as a means of eliminating the infection following the removal of a previous orthopedic implant. In addition, there remains a need for such a device that can provide stability and maintain the physical dimensions of joint space and normal soft tissue envelope in any joint undergoing the re-implantation of an orthopedic implant. In addition, there remains a need for such a device that may be easily employed, facilitates the reduction in the time needed to conduct the stage one re-implantation surgery and that reduces the overall time between the first and second stages of a two-stage re-implantation surgical protocol. At least some of these will be addressed by the devices and methods described herein.

2. Description of the Background Art

(10) Other patents which disclose devices and methods for delivery of an antibiotic to an intramedullary canal include: U.S. Pat. Nos. 8,900,323; 8,900,322; and 8,454,706.

SUMMARY OF THE INVENTION

(11) The present invention generally relates to medical systems, devices and methods, and more particularly relates to orthopedic devices used to deliver a therapeutic agent to a joint or intramedullary canal in a bone.

(12) In one aspect of the present invention, a therapeutic agent delivery system comprises a first intramedullary stem configured to be disposed in a first medullary canal of a first bone, a second intramedullary stem configured to be disposed in a second medullary canal of a second bone, and a coupling member coupled to the first intramedullary stem and the second intramedullary stem. Each of the first intramedullary stem and the second intramedullary stem comprises an elongate body having a longitudinal axis, a first end, a second end opposite the first end, and a channel extending between the first end and the second end. Each of the first intramedullary stem and the second intramedullary stem further comprises a plurality of protrusions extending radially outward from the elongate body, wherein adjacent protrusions define or more fluted regions therebetween. The plurality of protrusions are configured to engage the first medullary canal in a stable fashion, and one or more outlet holes are disposed in the one or more fluted regions, wherein the one or more outlet holes are in fluid communication with the channel. The coupling member may be coupled to the first end of the first intramedullary stem and the first end of the second intramedullary stem, wherein the coupling member holds the first and second intramedullary stems together and at a fixed distance. The coupling member may further comprise an inlet in fluid communication with the channels in the first and second intramedullary stems.

(13) In some embodiments, the coupling member may comprise an adjustable height manifold configured to increase or decrease a distance between the first ends of the two intramedullary stems when the adjustable height manifold is actuated. The adjustable height manifold may comprise a housing with a central housing channel disposed therethrough, a rotating nut coupled to the housing, and an adjustable connector disposed in the housing channel. The adjustable connector may have an adjustable connector channel disposed therein. The inlet coupled to the housing may be fluidly connected to the adjustable connector channel, and the adjustable connector channel may be fluidly coupled with the channel in the first stem or the second stem. Rotation of the nut can extend or retract the adjustable connector relative to the housing. The rotating nut may be threadably engaged with the adjustable connector, and the adjustable connector may be slidably disposed in the housing channel, where rotation of the rotating nut moves the adjustable connector up or down in the housing channel without rotation of the adjustable connector.

(14) In some embodiments, the coupling member may comprise a wedge element, wherein disposition of the wedge element between the first end of the first intramedullary stem and the first end of the second medullary stem adjusts a distance between the first ends of the two intramedullary stems.

(15) The therapeutic agent delivery system may further comprise a source of the therapeutic agent for delivery to the medullary canals from the one or more outlet holes in the one or more fluted

regions of the first and second stems. The therapeutic agent may be an antibiotic, wherein the antibiotic may comprise vancomycin, tobramycin, or a combination thereof.

(16) In some embodiments, the first medullary canal may be in a femur and the first stem may be configured to be disposed therein. The second medullary canal may be in a tibia and the second stem may be configured to be disposed therein.

(17) In some embodiments, the coupling member may be releasably coupled to the first and second intramedullary stems.

(18) In some embodiments, the first stem may be identical to the second stem.

(19) In some embodiments, the first stem or the second stem may comprise four fins equally spaced around the elongate body and extending along the longitudinal axis thereof. The first stem or the second stem may further comprise a plurality of outlet holes extending axially along a line substantially parallel to the longitudinal axis thereof.

(20) In some embodiments, the coupling member may comprise a flanged region, wherein the first end of the first or second stem comprises a recessed region for receiving the flanged region, and wherein rotation of the flanged region relative to the recessed region can releasably lock the first end with the coupling member. One or more pins may be disposed in the first end of the first or second stem, and the one or more pins may protrude therefrom thereby engaging the flanged region and preventing further rotation of the first or second stem relative to the coupling member. In some embodiments, the coupling member may comprise a snap fit section or a dovetailed section for engaging a corresponding dovetailed section or a corresponding snap fit section on the first stem or the second stem.

(21) In some embodiments, the channel may extend from the first end to the second end of the first or second stem, and the channel may extend through both the first end and the second end. The system may further comprise a plug disposed in the channel at the second end of the first stem or the second stem. In some embodiments, the channel may be a blind channel in the first stem or the second stem, the blind channel having a closed second end.

(22) In some embodiments, the elongate body of the first stem or the second stem may be tapered.

(23) In some embodiments, the coupling member may comprise a housing, a first stem connector configured to engage the first end of the first intramedullary stem, and a second stem connector configured to engage the first end of the second intramedullary stem. The first and second stem connectors may be disposed on opposite sides of the housing. The first stem connector may have an orientation relative to the second stem connector, wherein the orientation may remain the same during actuation of the adjustable height manifold.

(24) In some embodiments, the coupling member may comprise a housing, wherein a concave groove is disposed circumferentially around at least a portion of the housing. The concave groove may be sized to receive a tubing.

(25) The therapeutic agent delivery system may further comprise a cover disposed over the first stem or the second stem, or a sponge disposed in at least some of the one or more fluted regions of the first stem or the second stem. The cover or the sponge can be configured to facilitate even distribution of the therapeutic agent therefrom to the first or the second intramedullary canal.

(26) The therapeutic agent delivery system may further comprise a pump configured to pump the therapeutic agent into the channel of the first or the second stem.

(27) The therapeutic agent delivery system may further comprise a vacuum pump, the vacuum pump configured to remove unwanted fluids from the first or the second medullary canal via the one or more outlet holes or the channel in the first stem or the second stem.

(28) In some embodiments, the plurality of protrusions in the first stem or the second stem may be spirally disposed therearound, or the one or more fluted regions in the first stem or the second stem may be spirally disposed therearound.

(29) In some embodiments, the first stem or the second stem may have a surface area, and 50% or less of the surface area may be configured to contact bone in the first medullary canal or the second

medullary canal.

(30) The therapeutic agent delivery system may further comprise an outlet fluidly coupled to the first stem, the second stem, or the coupling member.

(31) In another aspect of the present invention, a method for treating a joint comprises positioning a first intramedullary stem in a first medullary canal of a first bone, positioning a second intramedullary stem in a second medullary canal of a second bone, coupling the first intramedullary stem to the second intramedullary stem with a coupling member therebetween, and delivering a therapeutic agent to the first and second medullary canals.

(32) In some embodiments, the coupling member may comprise an adjustable height manifold, and the method may further comprise actuating the adjustable height manifold, thereby adjusting a distance between a first end of the first intramedullary stem and a first end of the second intramedullary stem. Actuating the adjustable height manifold may comprise rotating a nut coupled to a housing of the adjustable height manifold, and rotating the nut can move an adjustable connector of the adjustable height manifold relative to the housing.

(33) In some embodiments, the coupling member may comprise a wedge element having a fixed height, and the method may further comprise selecting a wedge element from a plurality of wedge elements having different fixed heights. Coupling the first stem to the second stem with the coupling member may comprise coupling the first intramedullary stem to the second intramedullary stem with the selected wedge element therebetween, thereby adjusting a distance between a first end of the first intramedullary stem and a first end of the second intramedullary stem.

(34) In some embodiments, positioning the first intramedullary stem in the first medullary canal or positioning the second intramedullary stem in the second medullary canal may comprise engaging a plurality of protrusions on the first or second stem with bone lining the respective first or second medullary canal.

(35) In some embodiments, delivering the therapeutic agent may comprise delivering an antibiotic, wherein the antibiotic may comprise vancomycin, tobramycin, or a combination thereof.

(36) In some embodiments, delivering the therapeutic agent may comprise delivering the therapeutic agent from one or more outlet holes disposed in a fluted region of the first stem or the second stem.

(37) In some embodiments, the first bone may be a femur and the second bone may be a tibia.

(38) In some embodiments, coupling may comprise engaging a flanged region in the adjustable height manifold with a recessed region in the first end of the first stem or the second stem.

(39) In some embodiments, delivering the therapeutic agent may comprise pumping the therapeutic agent from the first stem or the second stem to the respective first or second medullary canal.

(40) The method may further comprise suctioning unwanted fluids from the first or the second medullary canal, wherein the unwanted fluids pass through one or more holes in the first stem or the second stem.

(41) In some embodiments, positioning the first stem or the second stem may comprise positioning the first stem or the second stem in the respective medullary canal such that 50% or less of a surface area of the first stem or the second stem contacts bone in the respective first or second medullary canal.

(42) In another aspect of the present invention, a therapeutic agent delivery system comprises a femoral head configured to be disposed in an acetabulum, and a femoral stem coupled to the femoral head, the femoral stem configured to be disposed in a femoral medullary canal. The system may further comprise an inlet coupled to the femoral stem, and a plurality of outlets in the femoral head or the femoral stem. The therapeutic agent may be introduced into the system from the inlet, and the therapeutic agent may be deliverable from the plurality of outlets into the acetabulum or the femoral medullary canal.

(43) In some embodiments, the femoral stem may comprise a threaded neck region, the threaded neck region configured to be threadably engaged with the femoral head thereby allowing

adjustment of a distance between the femoral head and the femoral stem.

(44) In some embodiments, the femoral stem may comprise a plurality of protrusions extending axially along a longitudinal axis of the femoral stem.

(45) In some embodiments, the femoral stem may comprise an elongate channel extending therethrough, the channel fluidly coupled with the inlet and the plurality of outlets. The elongate channel may be a through hole, wherein one end of the femoral stem comprises a plug.

(46) In some embodiments, the femoral stem may be tapered.

(47) In some embodiments, the plurality of outlets may be disposed in the femoral head. The femoral head may comprise a central channel, the central channel fluidly coupled with the plurality of outlets via a plurality of channels extending radially outward from the central channel.

(48) The therapeutic agent delivery system may further comprise an outlet for fluid removal from the femoral head or the femoral stem.

(49) The therapeutic agent delivery system may further comprise an acetabular cup coupled to the femoral head, wherein the therapeutic agent is delivered from the acetabular cup to the acetabulum.

(50) In some embodiments, the plurality of outlets may comprise a plurality of holes having varying diameters.

(51) In some embodiments, the femoral head may be at least partially hollow.

(52) The therapeutic agent delivery system may further comprise a locking mechanism for locking the femoral head with the femoral stem.

(53) In another aspect of the present invention, a method for treating a joint comprises positioning a femoral stem in a medullary canal of a femur, coupling a femoral head with the femoral stem, positioning the femoral head in an acetabulum, and delivering a therapeutic agent to the medullary canal and the acetabulum.

(54) In some embodiments, the coupling may comprise adjusting a distance between the femoral head and the femoral head. In some embodiments, the coupling may comprise threadably engaging the femoral head with the femoral stem.

(55) In some embodiments, positioning the femoral stem may comprise engaging a plurality of protrusions on the femoral stem with bone lining the medullary canal.

(56) In some embodiments, delivering the therapeutic agent may comprise delivering an antibiotic, wherein the antibiotic may comprise vancomycin, tobramycin, or a combination thereof.

(57) In some embodiments, delivering the therapeutic agent may comprise delivering the therapeutic agent from one or more outlet holes disposed in a fluted region of the femoral stem.

(58) In some embodiments, delivering the therapeutic agent may comprise pumping the therapeutic agent from the femoral stem to the medullary canal or from the femoral head to the acetabulum.

(59) The method may further comprise suctioning unwanted fluids from the medullary canal or the acetabulum.

(60) In some embodiments, positioning the femoral stem may comprise positioning the femoral stem into the medullary canal such that 50% or less of a surface area of the femoral stem contacts bone in the medullary canal.

(61) In another aspect of the present invention, a device for delivering a therapeutic agent to a joint in a patient comprises an implant having a plurality of outlets for delivering the therapeutic agent to the joint, wherein the joint is a shoulder joint, an ankle joint, or a spinal joint.

(62) These and other embodiments are described in further detail in the following description related to the appended drawing figures.

INCORPORATION BY REFERENCE

(63) All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

Description

BRIEF DESCRIPTION OF THE DRAWINGS

- (1) The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:
- (2) FIG. 1A is a perspective view of an exemplary therapeutic agent delivery system for a knee;
- (3) FIG. 1B is an exploded view of the therapeutic agent delivery system of FIG. 1A;
- (4) FIG. 2A is a perspective view of an exemplary intramedullary stem;
- (5) FIGS. 2B and 2C are side views of an exemplary intramedullary stem;
- (6) FIGS. 3A and 3B show alternative embodiments of the elongate body of an intramedullary stem;
- (7) FIG. 4A shows an exemplary embodiment of an adjustable height manifold in a collapsed configuration;
- (8) FIG. 4B shows the adjustable height manifold of FIG. 4A in an extended configuration;
- (9) FIG. 5 is an exploded view of the adjustable height manifold of FIG. 4A;
- (10) FIG. 6A is a perspective view of an exemplary embodiment of a housing of the adjustable height manifold of FIG. 4A;
- (11) FIG. 6B is a side view of the housing of FIG. 6A;
- (12) FIG. 6C is a top view of the housing of FIG. 6A;
- (13) FIG. 6D is a bottom view of the housing of FIG. 6A;
- (14) FIG. 6E is a vertical cross sectional view of the housing of FIG. 6A;
- (15) FIG. 7A is a perspective view of an exemplary embodiment of a rotating nut of the adjustable height manifold of FIGS. 4A-4B;
- (16) FIG. 7B is a top view of the rotating nut of FIG. 7A;
- (17) FIG. 7C is a vertical cross sectional view of the rotating nut of FIG. 7A;
- (18) FIG. 8A is a perspective view of an exemplary embodiment of an adjustable connector of the adjustable height manifold of FIGS. 4A-4B;
- (19) FIG. 8B is a bottom view of the adjustable connector of FIG. 8A;
- (20) FIGS. 8C and 8D are side views of the adjustable connector of FIG. 8A;
- (21) FIG. 9 shows an exemplary embodiment of a manifold pin of the adjustable height manifold of FIGS. 4A-4B;
- (22) FIG. 10A is a top view of the assembled adjustable height manifold in the collapsed configuration, as shown in FIG. 4A;
- (23) FIG. 10B is a vertical cross sectional view of the assembled adjustable height manifold of FIG. 10A;
- (24) FIG. 11A is a perspective view of an exemplary embodiment of a fixed height wedge;
- (25) FIGS. 11B and 11C are side views of the fixed height wedge of FIG. 11A;
- (26) FIGS. 12A-12H illustrate an exemplary mechanism for coupling an intramedullary stem to a coupling member;
- (27) FIGS. 13A-13C illustrate another exemplary mechanism for coupling an intramedullary stem to a coupling member;
- (28) FIGS. 14A-14D illustrate another exemplary mechanism for coupling an intramedullary stem to a coupling member;
- (29) FIG. 15 shows a method of treating a knee with a therapeutic agent delivery system;
- (30) FIG. 16 shows a method of treating a knee with a therapeutic agent delivery system;
- (31) FIG. 17A is a perspective view of an exemplary therapeutic agent delivery system for a hip;
- (32) FIG. 17B is an exploded view of the therapeutic agent delivery system of FIG. 17A;

- (33) FIG. 18A is a perspective view of an exemplary embodiment of a femoral stem;
- (34) FIG. 18B is a side view of the femoral stem of FIG. 18A;
- (35) FIG. 18C is a side cross-sectional view of the femoral stem of FIG. 18A;
- (36) FIG. 18D is a bottom view of the femoral stem of FIG. 18A;
- (37) FIG. 19 shows an exemplary embodiment of a stem plug;
- (38) FIG. 20A is a side view of an exemplary embodiment of a femoral head;
- (39) FIG. 20B is a side cross-sectional view of the femoral head of FIG. 20A;
- (40) FIGS. 21A and 21B are side cross-sectional views of another exemplary embodiment of a femoral head;
- (41) FIG. 22 is a side cross-sectional view of another exemplary embodiment of a femoral head;
- (42) FIGS. 23A and 23B show exemplary mechanisms for coupling a femoral head to a femoral stem;
- (43) FIGS. 24A and 24B show an exemplary mechanism for locking a set distance between a femoral head and a femoral stem;
- (44) FIGS. 24C-24F illustrate a method of assembling the locking mechanism of FIGS. 24A and 24B;
- (45) FIGS. 25A and 25B show an exemplary embodiment of a therapeutic agent delivery system having an acetabular cup;
- (46) FIG. 26 shows an exemplary embodiment of a therapeutic agent delivery system for a hip;
- (47) FIG. 27 shows a method of treating a hip using a therapeutic agent delivery system;
- (48) FIGS. 28A and 28B illustrate the use of negative pressure wound therapy with an intramedullary device;
- (49) FIG. 29 shows an optional cover for an intramedullary stem;
- (50) FIG. 30 shows an exemplary embodiment of a therapeutic agent delivery system;
- (51) FIGS. 31A and 31B show exemplary embodiments of therapeutic agent delivery systems with inlets and outlets;
- (52) FIGS. 32A and 32B illustrate an exemplary configuration for the internal channels of an intramedullary device;
- (53) FIGS. 33A-33C illustrate another exemplary configuration for the internal channels of an intramedullary device; and
- (54) FIGS. 34-36 show exemplary embodiments of therapeutic agent delivery systems.

DETAILED DESCRIPTION OF THE INVENTION

- (55) Specific embodiments of the disclosed device, delivery system, and method will now be described with reference to the drawings. Nothing in this detailed description is intended to imply that any particular component, feature, or step is essential to the invention.
- (56) Described herein are therapeutic agent delivery systems that may be used in a knee joint, a hip joint, or any other joint. For example, the therapeutic agent delivery system may be used to treat a shoulder or ankle joint, or a portion of the spine. One of skill in the art will appreciate that other joints may also be treated with the systems, devices, and methods disclosed herein. Optionally in any embodiment, the therapeutic agent delivery system may comprise one or more intramedullary stems, configured to be disposed stably in a medullary canal of a bone. The intramedullary stem may be configured to deliver the therapeutic agent to the medullary canal, the joint space, or a combination thereof. Optionally, in any embodiment, an intramedullary stem is coupled to another component, such as another intramedullary stem or a femoral head, in a way that allows the distance between the stem and the other component to be adjusted to fit a patient, or the distance therebetween may be fixed.
- (57) The therapeutic agent delivered by the delivery systems described herein may comprise any fluid. For example, the therapeutic agent may comprise an antibiotic fluid such as a vancomycin or tobramycin, combinations thereof, or other antibiotics commonly used to treat implant-associated infections. One of skill in the art will appreciate that any therapeutic agent may be also be delivered

alone, or in combination with an antibiotic or other therapeutic agent. Other exemplary therapeutic agents may include saline or other fluids used to irrigate the joint or medullary canals being treated.

(58) Therapeutic Agent Delivery System for Knee

(59) FIGS. 1A and 1B show an exemplary therapeutic agent delivery system **100** for a knee. FIG. 1A shows the components of the delivery system assembled together, while FIG. 1B shows the components of the delivery system disassembled and aligned for assembly. The delivery system **100** comprises a first intramedullary stem **110**, a second intramedullary stem **120**, and a coupling member **130**. Each of the two intramedullary stems **110** and **120** can be configured to be disposed in a medullary canal of a bone. For example, the first intramedullary stem **110** can be configured to be disposed in the medullary canal of a femur of a patient, while a second intramedullary stem **120** can be configured to be disposed in the medullary canal of a tibia of the patient. The coupling member **130**, configured to be disposed in the joint space, can couple the two stems in a stable configuration, while maintaining a desired distance **105** between the two stems throughout the length of use of the therapeutic agent delivery system in a patient.

(60) The first intramedullary stem **110** and the second intramedullary stem **120** may be any intramedullary stem as described herein. The two stems may be two identical stems, or they may be two different stems, configured to have one or more differences in dimensions, configurations, or features. For example, the delivery system may comprise a first intramedullary stem specifically configured to engage a femur, and a second intramedullary stem specifically configured to engage a tibia. The two stems may differ in one or more dimensions, such as length, diameter, or degree of taper. Alternatively or in combination, the two stems may differ in one or more configurations or features as described herein (e.g., configuration of the stem channel, number, shape, and size of the protrusions, the fluted regions, and/or the outlet holes, etc.).

(61) The coupling member **130** may comprise any coupling member as described herein, such as an adjustable height manifold or a fixed height wedge. In many embodiments of the delivery system **100**, the coupling member **130** can be configured to allow the distance **105** between the two stems to be adjusted, so as to accommodate the anatomy of the patient. The coupling member can be configured to fluidly couple to a source of a therapeutic agent and receive the therapeutic agent, and distribute the therapeutic agent to the intramedullary stems for delivery to the medullary canals.

(62) The first stem **110** and the second stem **120** may be releasably coupled to the coupling member **130**. Each of the first stem and the second stem may be configured to couple to a stem connector **132** of the coupling member. The first stem may couple to a first stem connector **132a**, and the second stem may couple to a second stem connector **132b**. Various mechanisms for the connection between the stem and the coupling member are described herein, any of which may be incorporated into the coupling member **130** for coupling with the first stem or the second stem. The first stem and the second stem may couple to the first stem connector and the second stem connector, respectively, via identical mechanisms or via different mechanisms. Accordingly, the first stem connector **132a** and the second stem connector **132b** of the coupling member may be identical or different. In preferred embodiments, the first stem and the second stem are identical, such that the coupling member accordingly comprises two identical stem connectors configured to couple to the first stem and the second stem via identical mechanisms.

(63) Intramedullary Stem

(64) FIGS. 2A-2C show an exemplary intramedullary stem **200**, suitable for incorporation with a therapeutic agent delivery system for a knee. FIG. 2A is a perspective view, and FIGS. 2B and 2C are side views of the intramedullary stem **200**. Each intramedullary stem **200** comprises an elongate body **205** having a longitudinal axis **210**, the elongate body having a first end **215** and a second end **220** opposite the first end. The first, or proximal, end may be configured to couple to a coupling member **130**, such as an adjustable height manifold or a fixed height wedge as described herein. The second, or distal, end may be disposed in the medullary canal of a bone. The elongate body

205 comprises a stem channel **225** extending between the first end **215** and the second end **220**, the stem channel configured to deliver the therapeutic agent through the stem and to the medullary canal. The first end **215** of the intramedullary stem **200** may be configured to couple the stem to a coupling member. The first end may comprise any mechanism for connecting the stem to the coupling member (e.g., flanged region, dovetail joints, snap buckle, winged nut, etc.), as described in further detail herein.

(65) The intramedullary stem **200** may comprise a plurality of protrusions **230**, protruding radially outward from the elongate body **205**. The plurality of protrusions may comprise any number of protrusions having any appropriate shape, size, or configuration to engage the medullary canal in a stable fashion. For example, the protrusions may comprise elongate fins extending along the longitudinal length of the elongate body, as shown in FIGS. 2A-2C. In one exemplary embodiment, the plurality of protrusions may comprise four fins, spaced equally at about 90° about the longitudinal axis **210** of the elongate body. The plurality of protrusions **230** and the elongate body **205** may be formed separately and coupled together. Alternatively or in combination, the plurality of protrusions **230** may be formed by removing material from the elongate body **205**, such that the plurality of protrusions and the elongate body are formed as a single member. Adjacent protrusions **230** may define one or more fluted regions **235** therebetween, the fluted regions radially recessed compared to the protrusions. The fluted regions may form a concave recessed region between adjacent protrusions.

(66) The plurality of protrusions and fluted regions can be configured to minimize the surface area of the stem contacting the bone lining the medullary canal, such that the area of the bone flushed with the therapeutic agent may be maximized. For example, the plurality of protrusions and fluted regions can be configured such that less than 50% of the surface area of the stem is in contact with the bone lining the medullary canal. Of course this is not intended to be limiting and one of skill in the art will appreciate that any percentage of the surface area of the stem may contact the bone. The stem may comprise a plurality of identical fluted regions defined by a plurality of elongate fins, distributed symmetrically about the longitudinal axis **210** of the stem, as shown in FIGS. 2A-2C. Alternatively, a plurality of fluted regions may be distributed asymmetrically about the longitudinal axis of the stem, and/or may have different shapes or sizes as described in further detail herein.

(67) An intramedullary stem **200** may further comprise a plurality of outlet holes **240** in fluid communication with the stem channel **225**. The plurality of outlet holes **240** may be configured to deliver the therapeutic agent, distributed through the stem channel **225**, to the medullary canal, as well as adjacent tissue including the joint. The plurality of outlet holes may be disposed in a fluted region **235**, so as to deliver the therapeutic agent to the area of the bone not in contact with the intramedullary stem. The plurality of outlet holes may comprise any number of outlet holes having any appropriate size, shape, or distribution. For example, the plurality of outlet holes may include a plurality of equally sized and spaced holes that extend axially along a line substantially parallel to the longitudinal axis **210** of the stem, as shown in FIGS. 2A-2C. The plurality of outlet holes may be arranged in various configurations, as described in further detail herein. The plurality of outlet holes may comprise holes having an identical shape and/or size, or holes having various shapes and/or sizes. Varying the hole size may allow further fluid control of therapeutic agent as it exits different regions of the stem.

(68) The stem channel **225** may be a through hole that extends from the first end **215** to the second end **220** through both the first end and the second end, such that the elongate body comprises an open second or distal end. The system may further comprise a plug (not shown) configured to couple to the open second end of the stem, so as to close the second end and thereby create a blind channel. Alternatively, the stem channel **225** may be a blind channel, wherein the second end of the elongate body is closed. In configurations wherein the second end is open, the therapeutic agent may exit the stem channel into the medullary canal through the second end and/or through a plurality of outlet holes disposed along the elongate body **205** as described herein. If the stem

comprises only the stem channel **225** extending through the first and second ends, without the plurality of outlet holes, the therapeutic agent may exit the stem channel only through the second end. In configurations wherein the second end of the stem is closed, the therapeutic agent may exit the stem channel into the medullary canal only through the plurality of outlet holes.

(69) The intramedullary stem **200** may be tapered to fit the medullary canal. For example, the elongate body **205** and/or the plurality of protrusions **230** may be tapered from the first end **215** to the second end **220**, as shown, so as to have a smaller radial cross-sectional area at the second end than at the first end. For example, the taper may comprise a gradual taper, wherein the extent of the taper may be preferably in a range from about 0.1° to about 10° , more preferably about 0.5° to about 5° , and even more preferably about 1° to about 5° , or about 1° to about 4° , or about 2° or about 3° . The taper may be adjusted to accommodate a medullary canal of a specific type of bone.

(70) The exemplary embodiment of FIGS. 2A-2C may comprise one or both of two intramedullary stems of a therapeutic agent delivery system for a knee as shown in FIGS. 1A and 1B. Preferably, the therapeutic agent delivery system for a knee comprises two identical intramedullary stems, such as the exemplary embodiment of FIGS. 2A-2C.

(71) FIGS. 3A and 3B show alternative embodiments of the elongate body **205** of the intramedullary stem **200** of FIGS. 2A-2C. FIG. 3A shows an elongate body **205** comprising one or more protrusions **231** spirally disposed around the elongate body **205** along the longitudinal length of the body. Adjacent spiral or helical protrusions **231** define one or more fluted regions **236** therebetween, also spirally disposed around the elongate body. FIG. 3B shows an elongate body **205** comprising a plurality of protrusions **232** resulting from cutting away or otherwise removing portions of the spirally disposed protrusions **231** shown in FIG. 3A. For example, as shown, a plurality of radial cuts may be made to elongate body to define the plurality of protrusions **232**. A plurality of fluted regions **237** may be defined between remaining portions of adjacent helical protrusions. Cutting away or removing portions of the spiral protrusions **231** as shown in FIG. 3B can further decrease the contact area between the stem and the bone, thus allowing the therapeutic agent to flow more freely along the medullary canal.

(72) In the embodiment of FIG. 3A, a plurality of outlet holes (not shown) may extend along a helical or spiral line, such as along the helical or spiral fluted regions **236**. In the embodiment shown in FIG. 3B, the plurality of outlet holes **240** may be disposed in the fluted regions **237**, such that the holes extend about a plurality of rings around the circumference of the elongate body.

(73) Adjustable Height Manifold

(74) FIGS. 4A and 4B show an adjustable height manifold **300** suitable for incorporation with a therapeutic agent delivery system for a knee such as in FIGS. 1A-1B. The adjustable height manifold **300** is one example of a coupling member that can couple the two intramedullary stems in a stable configuration, while maintaining a desired distance between the two stems throughout the length of use of the therapeutic agent delivery system in a patient. The adjustable height manifold further enables the adjustment of the distance between the two stems, such that the delivery system may be configured to optimally accommodate the anatomy of the patient. The adjustable height manifold **300** may comprise a housing **315**, a rotating nut **320**, and an adjustable connector **325**. The rotating nut **320** and adjustable connector **325** may be coupled to the housing **315**, and configured so as to allow the manifold height **305** to be increased or decreased, based on the desired set distance between the two stems for a patient. Rotating the nut **320** in clockwise and counterclockwise directions can collapse or extend the manifold, by translating the adjustable connector along a longitudinal axis **310** of the manifold. FIG. 4A shows the adjustable height manifold **300** in a collapsed configuration, such that the manifold height **305** is relatively short and the manifold can thus fit a patient who requires a shorter set distance between the two knee stems. FIG. 4B shows the adjustable height manifold **300** in an extended configuration, such that the manifold height **305** is relatively long and the manifold can thus fit a patient who requires a longer set distance between the two knee stems.

(75) The adjustable height manifold **300** further comprises a first stem connector **342** and a second stem connector **344**, disposed on opposite sides of the housing. The first stem connector **342** may be configured to couple to a first end of a first intramedullary stem, and the second stem connector **344** may be configured to couple to a first end of a second intramedullary stem. The first stem connector **342** may be coupled to the adjustable connector **325**, while the second stem connector **344** may be coupled to the housing **315**. Each stem connector may comprise a connection mechanism to couple to a corresponding connection mechanism disposed on the first end of the intramedullary stem. The first and second stem connectors may comprise different connection mechanisms, or they may comprise identical connection mechanisms. In preferred embodiments, the first and second stem connectors comprise identical connection mechanisms, and have a fixed orientation relative to one another, such that the orientation remains the same during actuation of the adjustable height manifold to adjust the manifold height. The fixed orientation of the two stem connectors relative to one another can allow proper and simultaneous coupling of the manifold to each stem during the implantation of the delivery system in a patient using the same actuation motion for both stems.

(76) FIG. 5 is an exploded view of the adjustable height manifold **300** of FIGS. 4A-4B. The adjustable height manifold **300** comprises a housing **315**, a rotating nut **320** having a scalloped outer surface to provide gripping regions for an operator's fingers and internal threads, and an adjustable connector **325**, wherein the three components are axially aligned along a longitudinal axis **310** of the manifold. The manifold further comprises a manifold pin **330**, configured to secure the coupling of the adjustable connector the housing and control the range of motion of the adjustable connector. The adjustable connector comprises a first stem connector **342**, configured to couple to a first intramedullary stem. The housing comprises a second stem connector **344**, configured to couple to a second intramedullary stem. The housing further comprises an inlet **335** coupled thereto, the inlet configured to fluidly couple to a source of the therapeutic agent (not shown) to be delivered to the patient. The housing is configured to couple to the rotating nut and slidably receive the adjustable connector. The rotating nut is configured to threadably engage the adjustable connector, so as to cause the adjustable connector to extend outwards from housing along the longitudinal axis **310**, or retract inwards into the housing along the longitudinal axis when the nut is rotated.

(77) FIGS. 6A-6E show an exemplary embodiment of a housing **315** of the adjustable height manifold **300** of FIGS. 4A-4B. FIG. 6A is a perspective view, FIG. 6B is a side view, FIG. 6C is a top view, FIG. 6D is a bottom view, and FIG. 6E is a vertical cross sectional view (cross section A-A of FIG. 6B) of the housing **315**. The housing **315** comprises an inlet **335** to fluidly couple to a source of the therapeutic agent, and a housing channel **340** (best seen in FIG. 6E) extending along the longitudinal axis **310** through the housing. The housing channel **340** is in fluid communication with the inlet **335**, such that the therapeutic agent added to the therapeutic agent delivery system through the inlet can be distributed to other components of the delivery system through the housing channel. The inlet **335** may comprise a barbed outer surface, to securely engage the inner surface of a tube (best seen in FIG. 28A) supplying the therapeutic agent. The housing may further comprise a concave groove **345**, disposed at least partially or completely about the circumference of the housing thereby minimizing profile of the tubing/housing assembly. The groove can allow for placement of tubing supplying the therapeutic agent, coupled to the inlet **335**.

(78) The housing **315** further comprises a second stem connector **344**, configured to couple to an intramedullary stem such as any intramedullary stem described herein. The housing channel **340** can extend through the stem connector **344**, such that the housing channel can be fluidly coupled to a stem channel of a stem coupled to the stem connector. The stem connector **344** may comprise any mechanism for connecting the coupling member to the stem (e.g., flanged region, dovetail joints, snap buckle, winged nut, etc.), as described in further detail herein.

(79) The housing channel **340** may be configured to have a geometry that allows the adjustable

connector disposed in the channel to slide axially along the longitudinal axis **310**, while preventing the adjustable connector from rotating within the channel. For example, the channel **340** may comprise two flat inner surfaces **347** disposed opposite one another, configured to interface with two flat side surfaces of the adjustable connector. The channel may further comprise two rounded side inner surfaces **349**, configured to interface with two corresponding rounded surfaces of the adjustable connector. For example, the rounded inner surfaces **347** may comprise concave surfaces, while the rounded side surfaces of the adjustable connector may comprise convex surfaces. The interfacing of the flat inner surfaces of the housing channel with the flat side surfaces of the adjustable connector can prevent the adjustable connector from rotating therein, ensuring that the adjustable connector moves only slidably, not rotatably, within the housing channel. Preventing rotation of the adjustable connector, which comprises the first stem connector **342**, can ensure that the orientation of the second stem connector **344** remains fixed with respect to the orientation of the first stem connector, even when the rotating nut **320** is rotated. The fixed orientation of the first and second stem connectors with respect to one another can ensure that the manifold can easily couple to both the first stem and the second stem. For example, the manifold can be inserted into the space between the first and second stems and then rotated in one direction to couple to both stems. Such a configuration of the stem connectors can facilitate the implantation of the delivery system in a patient, by obviating the potential need to rotate one or more intramedullary stems after the stems have already been inserted into the patient's medullary cavities.

(80) The housing may further comprise one or more prongs **355**, disposed about the periphery of the housing channel **340** and projecting longitudinally from housing. The prongs may comprise four prongs as shown in FIGS. **6A-6E**, each internal surface of the prong configured to engage each of the four sides of the adjustable connector to be disposed in the housing channel. Two of the prongs, disposed opposite one another, can be configured to have the flat inner surfaces **347** of the housing channel, while two of the remaining prongs, also disposed opposite one another, can be configured to have the rounded inner surfaces **349** of the housing channel. One or more of the prongs may further comprise an outward facing lip **357** disposed at the edge of the prong. The lip **357** may be configured to engage a corresponding manifold groove in the rotating nut as described in further detail herein, so as to securely couple the rotating nut to the housing and prevent axial movement of the rotating nut along the longitudinal axis **310** during rotation of the nut. The lip **357** may further comprise chamfers **359**, configured to facilitate the coupling of the rotating nut to the housing by guiding the lip into the manifold groove of the nut.

(81) The housing may further comprise a housing pin hole **360**, configured to receive a portion of the manifold pin. The pin hole **360** may be disposed on a prong **355** configured to engage the rotating nut, such that the pin hole **360** can be aligned with a nut pin hole in the rotating nut also configured to receive the manifold pin. When fully assembled, the manifold pin can be disposed partially in the housing and partially in slot in the adjustable connector disposed within the housing channel, to create a hard stop to prevent the manifold assembly from coming apart, as described in further detail herein. The housing pin hole **360** may be dimensioned to ensure the retention of the manifold pin within the pin hole. For example, the housing pin hole can have a diameter that is substantially equal to the diameter of the portion of the manifold pin configured to be disposed in the housing, such that the pin can be press fit into the housing pin hole.

(82) FIGS. **7A-7C** show an exemplary embodiment of a rotating nut **320** of the adjustable height manifold **300** of FIGS. **4A-4B**. FIG. **7A** is a perspective view, FIG. **7B** is a top view, and FIG. **7C** is a vertical cross sectional view (cross section A-A of FIG. **7B**) of the rotating nut **320**. The rotating nut **320** comprises a plurality of threads **362** disposed on a portion of its inner surface. The threads **362** may be configured to engage corresponding threads on a portion of the adjustable connector, such that rotation of the nut **320** about the adjustable connector can cause axial movement of the adjustable connector along the longitudinal axis of the manifold. The nut **320** may further comprise a manifold groove **364** disposed circumferentially about the inner surface of the nut. The manifold

groove may be configured to receive one or more lips disposed on one or more prongs of the housing as described herein, so as to lock the nut onto the housing while still allowing rotation of the nut relative to the housing. The nut may further comprise chamfers **366** disposed below the manifold groove, extending circumferentially about the inner surface of the nut. The chamfers **366** can be configured to correspond to the chamfers of a housing lip, so as to guide the lip into the manifold groove. The nut may further comprise a nut pin hole **368** disposed on a portion of the nut below the threads **362**, the nut pin hole configured to receive the manifold pin therethrough. During assembly of the manifold, the manifold pin may be pushed into and completely through the body of the rotating nut, to dispose the pin partially within the housing and partially within the adjustable connector and thereby avoiding physical obstruction of the rotation of the nut by the pin.

Accordingly, when the manifold is completely assembled, the manifold pin does not traverse any portion of the rotating nut, such that the rotating nut can rotate freely. The nut pin hole **368** may be dimensioned to facilitate the insertion of the manifold pin into and through the pin hole. For example, the nut pin hole can have a diameter that is greater than the diameter of the largest portion of the manifold pin, such that the pin can easily pass through the nut pin hole.

(83) FIGS. **8A-8D** show an exemplary embodiment of an adjustable connector **325** of the adjustable height manifold **300** of FIGS. **4A-4B**. FIG. **8A** is a perspective view, FIG. **8B** is a bottom view, and FIGS. **8C** and **8D** are side views. The adjustable connector **325** comprises an adjustable connector channel **370** extending axially along the longitudinal axis **310**. The channel **370** extends through the length of the adjustable connector, and is configured to be in fluid communication with the housing channel **340** and hence with the inlet **335** fluidly coupled to the housing channel. The adjustable connector further comprises a first stem connector **342**, configured to couple to an intramedullary stem such as any intramedullary stem described herein. The connector channel **370** extends axially through the stem connector **342**, such that the channel **370** is in fluid communication with the stem channel of the stem coupled to the first stem connector **342**. The stem connector **342** may comprise any mechanism for connecting the coupling member to the stem (e.g., flanged region, dovetail joints, snap buckle, winged nut, etc.), as described in further detail herein.

(84) The adjustable connector may further comprise threads **372** configured to engage corresponding threads of the rotating nut, such that rotation of the nut can cause vertical movement of the adjustable connector into or out of the housing. The adjustable connector may comprise two flat side surfaces **327** and the two rounded side surfaces **329**, wherein the flat side surfaces may be configured to interface with the flat inner surfaces of the housing channel, and wherein the rounded side surfaces may be configured to interface with the rounded inner surfaces of the housing channel. As described herein, such a configuration can prevent the adjustable connector from rotating when the rotating nut is rotated, ensuring that the orientation of the adjustable connector and hence the first stem connector **342** remains constant with respect to the orientation of the second stem connector. Moreover, this translates the rotational actuation of the nut into linear motion of the adjustable connector.

(85) FIG. **8C** shows the proximal flat side surface **327a** of the adjustable connector, configured to be oriented proximally with respect to the inlet of the housing. The proximal flat side surface can be configured to have an open slot **374** that extends through the bottom of the adjustable connector. The open slot **374** may be fluidly coupled to the adjustable connector channel **370**, as best seen in FIG. **8B** showing the bottom view of the adjustable connector. The open slot **374** may be configured such that when the assembled manifold is in the collapsed configuration as shown in FIG. **4A**, the open slot is aligned with the inlet so as to fluidly couple the inlet to the adjustable connector channel **370**. When the assembled manifold is in the extended position as shown in FIG. **4B**, the open bottom of the open slot **374** can ensure that the inlet remains in fluid communication with the housing channel, and thereby with the adjustable connector channel.

(86) FIG. **8D** shows the distal flat side surface **327b** of the adjustable connector, configured to be

oriented distally with respect to the inlet of the housing. The distal flat side surface comprises a closed slot **376**, configured to engage a portion of the manifold pin retained in the housing. As described herein, the manifold pin may be coupled to the manifold assembly after the housing, rotating nut, and adjustable connector are assembled together. After full assembly, the manifold pin may be partially disposed in the housing, and partially disposed in the closed slot **376** of the adjustable connector. The manifold pin can be configured to remain engaged in the closed slot **376** during retraction or extension of the adjustable connector. The closed slot may be configured to have a width that is greater than the diameter of the portion of the manifold pin disposed in the slot, so as to facilitate the movement of the adjustable connector. When the assembled manifold is in the collapsed configuration as shown in FIG. **4A**, the manifold pin may be aligned with the top of the closed slot **376**. When the assembled manifold is in the extended configuration as shown in FIG. **4B**, the manifold pin may be aligned with the bottom of the closed slot **376**. The bottom of the closed slot **376** provides a hard stop to the extension of the adjustable connector from the housing, preventing the adjustable connector from extending any further. Thus, the closed slot **376** and the manifold pin can prevent the manifold assembly from coming apart.

(87) FIG. **9** shows an exemplary embodiment of a manifold pin **330** of the adjustable height manifold **300** of FIGS. **4A-4B**. The manifold pin **330** may comprise a small diameter portion **332** and a large diameter portion **334**. The small diameter portion **332** may be configured to engage the closed slot in the adjustable connector, while the large diameter portion **334** may be configured to be disposed in the manifold pin hole in the housing. As described herein, the manifold pin may be coupled to the manifold assembly by inserting the pin through the nut pin hole in the rotating nut. To facilitate the insertion of the manifold pin through the rotating nut, the large diameter portion **334** may have a diameter smaller than the diameter of the nut pin hole. To ensure the retention of the manifold pin within the housing, the large diameter portion **334** may have a diameter that is substantially equal to the diameter of the housing pin hole, such that the large diameter portion press fits into the housing pin hole. To facilitate translational motion of the adjustable connector within the housing channel, the small diameter portion **322** may have a diameter that is smaller than the width of the closed slot of the adjustable connector.

(88) FIG. **10A** is a top view and FIG. **10B** is a vertical cross sectional view (cross section A-A of FIG. **10A**) of the assembled adjustable height manifold **300** in the collapsed configuration, as shown in FIG. **4A**. The housing **315** is coupled to the rotating nut **320** via engagement of a lip **357** with a manifold groove **364** of the nut. The adjustable connector **325** is slidably disposed in the housing channel **340**, and threadably engaged with the rotating nut **320**. The large diameter portion **334** of the manifold pin **330** is disposed in the housing pin hole **360**, while the small diameter portion **332** is disposed within the closed slot **376** of the adjustable connector. When the rotating nut is rotated clockwise or counterclockwise, the adjustable connector can slide up or down within the housing channel without rotating. The manifold pin can control the extent to which the adjustable connector may be extended, by providing a hard stop when the pin hits the bottom of the closed slot **376**. The inlet **335** of the housing can be coupled to a source of a therapeutic agent to be delivered to the patient. The inlet can be fluidly connected to the housing channel **340** either directly or indirectly through the open slot **374** of the adjustable connector. When the manifold is in a collapsed configuration, the inlet can be fluidly coupled to the housing channel indirectly, through the open slot **374** of the adjustable connector. When the manifold is in an extended configuration, the inlet may be fluidly coupled directly to the housing channel. The housing channel can be fluidly connected to the adjustable connector channel **370**, so as to fluidly connect to the stem channel of the first stem, coupled to the first stem connector of the adjustable connector. The housing channel can also be fluidly connected to the stem channel of the second stem, coupled to the second stem connector of the housing. Thus, the therapeutic agent provided via the inlet **335** can be distributed to the first and second intramedullary stems coupled to the manifold.

(89) Fixed Height Wedge

(90) FIGS. 11A-11C show a fixed height wedge **400** suitable for incorporation with a therapeutic agent delivery system for a knee. FIG. 11A shows a perspective view, and FIGS. 11B and 11C show side views of the wedge **400**. The fixed height wedge **400** is one example of a coupling member **130** that can couple the two intramedullary stems in a stable configuration, while maintaining a desired distance between the two stems throughout the length of use of the therapeutic agent delivery system in a patient. The wedge provides a relatively simpler connection between two intramedullary stems, wherein the wedge comprises a single, monolithic component rather than an assembly of a plurality of components. While the wedge height **405** of a wedge is fixed, the wedge may be provided in multiple sizes having various wedge heights, and the most appropriate size may be selected for each patient according to the patient's anatomy.

(91) The fixed height wedge **400** comprises a first stem connector **442** configured to couple to a first intramedullary stem, and a second stem connector **444** configured to couple to a second intramedullary stem. The first and second stem connectors may comprise any mechanism for connecting the stem to the coupling member (e.g., flanged region, dovetail joints, snap buckle, winged nut, etc.), as described in further detail herein. The wedge further comprises an inlet **435**, configured to be coupled to a source of a therapeutic agent to be delivered to the patient. The inlet **435** can be fluidly connected to a wedge channel **440** extending along the longitudinal axis **410** of the wedge, through both the first stem connector and the second stem connector. Thus, the therapeutic agent provided through the inlet can be distributed via the wedge channel to the intramedullary stems coupled to the wedge.

(92) The fixed height wedge **400** may additionally comprise one or more of any applicable structures and features described in relation to the adjustable height manifold **300**. For example, the wedge may comprise a concave groove **445**, analogous to the concave groove **345** described in relation to the housing of the adjustable height manifold. Similarly to the concave groove **345**, concave groove **445** may be disposed partially about the circumference of the wedge, so as to provide for placement of tubing coupled to the inlet.

(93) Coupling Mechanisms

(94) FIGS. 12A-12H illustrate an exemplary mechanism for coupling an intramedullary stem **200** to a coupling member **130**. The stem **200** may comprise any embodiment of an intramedullary stem as described herein, and the coupling member **130** may comprise any embodiment of a coupling member as described herein. The stem **200** comprises a first end **215** configured to engage the coupling member, and the coupling member **130** comprises a stem connector **132** configured to engage the first end of the stem. The stem connector **132** may be any stem connector coupled to any coupling member as described (e.g., stem connector **342**, **344**, **442**, **444**, etc.). FIG. 12A is a perspective view of the first end **215** of the intramedullary stem **200**. FIG. 12B is a perspective view of the stem connector **132** of the coupling member **130**. FIGS. 12C and 12D are side views of a therapeutic agent delivery system **100** before assembly. FIG. 12E is a side view of an assembled delivery system **100** comprising two stems **200** and a coupling member **130** coupled together. FIG. 12F is an enlarged vertical cross sectional view of the portion of the assembled system **100** as indicated in FIG. 12C. FIGS. 12G and 12H are radial cross sections of the assembled system **100** along line A-A as indicated in FIG. 12E, at different steps of the assembly.

(95) As shown in FIG. 12A, the first end **215** comprises a raised portion **250** disposed about a portion of the periphery of the first end. The raised portion **250** defines a rounded cavity **251** therein, configured to receive a flanged region **150** of the coupling member **130** as shown in FIG. 12B. The raised portion **250** has a circumferential opening **252** configured to receive the flanged region **150** of the coupling member therethrough. The raised portion **250** further comprises a recessed lip **253** defining a recessed region **254**, as best seen in FIG. 12F. The recessed region **254** can receive and retain the flanged region **150**, so as to limit axial movement of the coupling member along the longitudinal axis **210** of the stem. As shown in FIGS. 12E and 12F, the flanged region **150** can have a length **154** that is longer than the width **152**. The flanged region can further

comprise two flat edges **157** extending along the length **154** of the flanged region, and two rounded edges **159** extending about the width **152** of the flanged region. The circumferential opening **252** may have a width that is greater than or equal to the width **152** of the flanged region **150**, but less than the length **154** of the flanged region, such that the flanged region can only enter the circumferential opening in the vertical orientation **151** with respect to the circumferential opening **252**, as shown in FIG. **12G**.

(96) FIGS. **12C** and **12D** show the delivery system **100** before assembly, wherein the coupling member **130** is aligned for insertion into the space between two intramedullary stems **200**. The flanged regions **150** of the first stem connector **132a** and second stem connector **132b** are in the vertical orientation with respect to the circumferential openings **252** of the raised portions of the intramedullary stems. While aligned in this orientation, the coupling member may be pushed into the space between the two intramedullary stems such that the flanged regions are inserted through the circumferential openings of each stem, and captured into the recessed regions of the raised portions as shown in FIGS. **12E**, **12F**, and **12G**.

(97) Once the flanged region **150** is placed within the rounded cavity **251**, the flanged region may be rotated in the direction shown by arrow **155**, as shown in FIG. **12G**. The flanged region may be rotated until the flanged region is disposed in the horizontal orientation **153** with respect to the circumferential opening **252**, as shown in FIG. **12H**. In the horizontal orientation, the flanged region can be prevented from sliding out of the rounded cavity through the circumferential opening, since the length **154** of the flanged region is greater than the size of the opening **252**. The first end **215** may further comprise one or more pins **255** disposed therein, configured to further secure the coupling between the stem and the stem connection. For example, the first end **215** may comprise two pins **255**, each pin angularly spaced at about 90° from the center of the circumferential opening **252**. Each rounded edge **159** of the flanged region **150** may comprise a smaller diameter edge **159a** and a larger diameter edge **159b**, such that a notch **156** is created at the intersection of edges **159a** and **159b**. As described, the flanged region **150** may be inserted through the opening **252** in the vertical orientation **151** as shown in FIG. **12G**, and subsequently rotated in the direction shown by arrow **155**, within the recessed region **254** of the first end **215**. As the flanged region rotates, the pin **255** can slide against the smaller diameter edge **159a**, until the pin hits the notch **156** created by the larger diameter edge **159b**. The pins may be configured, for example, to allow the flanged region to rotate by about 90° or a quarter turn before hitting the pins. The engagement of the notch **156** with the pin **255** can prevent further rotation of the stem relative to the coupling member. The pins **255** can thus provide a hard stop to the rotation of the flanged region, ensuring that the final orientation of the flanged region is the horizontal orientation **153**, which can prevent the flanged region from sliding out of the rounded cavity as described herein.

(98) FIGS. **13A-13C** illustrate another exemplary mechanism for coupling an intramedullary stem to a coupling member **130**. FIG. **13A** shows a perspective view and FIG. **13B** shows a top view of the coupling member **130** comprising the exemplary connection mechanism. FIG. **13C** shows a side view of a portion of an assembled delivery system **100**, comprising two stems **200** and a coupling member **130** coupled together. The stem **200** may comprise any embodiment of an intramedullary stem as described herein, and the coupling member **130** may comprise any embodiment of a coupling member as described herein. The stem **200** comprises a first end **215** configured to engage the coupling member, and the coupling member **130** comprises a stem connector **132** configured to engage the first end of the stem. The stem connector **132** may be any stem connector coupled to any coupling member as described (e.g., stem connector **342**, **344**, **442**, **444**, etc.). Each stem connector **132** may comprise one or more dovetailed regions **160**, configured to engage one or more corresponding dovetailed regions **260** of the first end **215** of the stem **200**. Each stem connector **132** may further comprise a snap buckle **162**, configured to engage a corresponding snap buckle (not shown) disposed on the first end **215** of the stem. The snap buckle **162** can comprise flexible stems **164** that can tension centrally when the coupling member **130** is

inserted slidably into the stems **200**. The coupling member can snap into place when the coupling member is pushed past the notch **166** within the stems.

(99) FIGS. **14A** and **14B** illustrate another exemplary mechanism for coupling an intramedullary stem **200** to a coupling member **130**. FIG. **14A** shows the first step of assembly of the stems and the coupling member using the exemplary mechanism, and FIG. **14B** shows the second step of the assembly. The stem **200** may comprise any embodiment of an intramedullary stem as described herein, and the coupling member **130** may comprise any embodiment of a coupling member as described herein. The stem **200** comprises a first end **215** configured to engage the coupling member, and the coupling member **130** comprises a stem connector **132** configured to engage the first end of the stem. The stem connector **132** may be any stem connector coupled to any coupling member as described (e.g., stem connector **342**, **344**, **442**, **444**, etc.). Each stem connector **132** may comprise one or more dovetailed regions **160**, configured to engage one or more corresponding dovetailed regions **260** of the first end **215** of the stem **200**. FIG. **14A** shows the coupling member **130** aligned for insertion into the space between two intramedullary stems **200**, wherein the dovetailed regions **160** of the coupling member are aligned with the corresponding dovetailed regions **260** of the stems. The coupling member may be pushed into the space between the two stems such that the dovetailed regions **160** are engaged within the dovetailed regions **260** of the stems. Optionally, the first end **215** of each stem may comprise a raised portion with a circumferential opening similarly as in the embodiment of FIGS. **12A-12H**, wherein the dovetailed region **260** is disposed within the rounded cavity defined within the raised portion. In such a configuration, the coupling member may be pushed into the space between the two stems until the dovetailed regions **160** hit a hard stop against the raised portions of the stems. The coupling member **130** or the intramedullary stem **200** may further comprise one or more turn stops **176**, configured to hold the coupling member in place once the coupling member is coupled to the stem. FIG. **14B** shows the assembled delivery system **100**, wherein each stem **200** comprises a turn stop **176** configured to hold the coupling member **130**. Each turn stop can be rotatable, such that the position of the turn stop with respect to the stem and the coupling member can be adjusted. During the step of assembly as shown in FIG. **14A**, each turn stop may be rotated such that the turn stop does not extend beyond the first end **215** of each stem, thereby allowing the dovetailed region **160** of the coupling member slidably engage the dovetailed region **260** of the stem without any physical obstruction from the turn stop. Once the coupling member is coupled to the stem, the turn stop may be rotated into the position shown in FIG. **14B**, such that the length of the turn stop extends over the junction between the stem and the coupling member. The turn stop can thus prevent the coupling member from sliding out of engagement with the intramedullary stem.

(100) FIGS. **14C** and **14D** show a variation of the embodiment shown in FIGS. **14A** and **14B**. Instead of turn stops, the coupling member **130** may comprise a winged nut **170**, rotatably fixed onto an anterior portion of the coupling member. The winged nut **170** can be configured to have a length **174** that is greater than the width **172**. The length **174** of the nut can be greater than the height **135** of the coupling member. During assembly, the coupling member **130** may be slidably inserted into the stems **200** with the winged nut **170** in the horizontal orientation **173** as shown in FIG. **14A**. Subsequently, the winged nut **170** may be rotated to so as to be in the vertical orientation **171** as shown in FIG. **14B**, such that the length **174** of the nut extends over the junction between the dovetailed regions **160** and **260**. In the vertical orientation, the winged nut can prevent the coupling member **130** from sliding out of the stems **200**.

(101) Method of Use of Therapeutic Agent Delivery System for Knee

(102) FIG. **15** illustrates a method **1500** of treating a patient's knee using the therapeutic agent delivery system for a knee as described herein. In step **1505**, a first intramedullary stem is positioned in the medullary canal of the femur of the patient. In step **1510**, a second intramedullary stem is positioned in the medullary canal of the tibia of the patient. In step **1515**, the height of an adjustable height manifold is adjusted to fit the joint space between the first stem and the second

stem. In step **1520**, the adjustable height manifold is coupled to the first stem and the second stem. The adjustable height manifold may be inserted in the joint space between the first stem and the second stem in a specific orientation appropriate for the connection mechanism used. For example, if the adjustable height manifold comprises stem connections with flanged regions as described herein, configured to engage corresponding rounded cavities of the stems, the adjustable height manifold may be inserted by leading with the two rounded edges of the flanged region. In step **1525**, the coupling between the adjustable height manifold and the first and second stems is further secured, via appropriate steps for the connection mechanism used. For example, if the adjustable height manifold comprises the flanged region as described herein, the manifold may be rotated to securely engage the flanged region into the corresponding cavity of the stems. If the adjustable height manifold and the stems comprise dovetailed regions with turn stops as described herein, the turn stops may be rotated to extend over the junction between the stem and the manifold, so as to prevent de-coupling of the manifold from the stems. In step **1530**, the therapeutic agent is delivered to the medullary canals of the femur and the tibia and the joint space.

(103) FIG. **16** illustrates a method **1600** of treating a patient's knee using the therapeutic agent delivery system for a knee as described herein. In step **1605**, a first intramedullary stem is positioned in the medullary canal of the femur of the patient. In step **1610**, a second intramedullary stem is positioned in the medullary canal of the tibia of the patient. In step **1615**, a fixed height wedge with an appropriate height to fit the joint space between the first stem and the second stem is selected. In step **1620**, the fixed height wedge is coupled to the first stem and the second stem, wherein the fixed height wedge may be inserted into the joint space between the first and second stems in a specific orientation appropriate for the connection mechanism used. For example, if the fixed height wedge comprises stem connections with flanged regions as described herein, configured to engage corresponding rounded cavities of the stems, the fixed height wedge may be inserted by leading with the two rounded edges of the flanged region. In step **1625**, the coupling between the fixed height wedge and the first and second stems is further secured, via appropriate steps for the connection mechanism used. For example, if the fixed height wedge comprises the flanged region as described herein, the fixed height wedge may be rotated to securely engage the flanged region into the corresponding cavity of the stems. If the fixed height wedge and the stems comprise dovetailed regions with turn stops as described herein, the turn stops may be rotated to extend over the junction between the stem and the fixed height wedge, so as to prevent de-coupling of the fixed height wedge from the stems. In step **1630**, the therapeutic agent is delivered to the medullary canals of the femur and the tibia and the joint space.

(104) The steps of methods **1500** and **1600** are provided as examples of methods of using a therapeutic agent delivery system in accordance with embodiments. A person of ordinary skill in the art will recognize many variations and modifications of methods **1500** and **1600** based on the disclosure provided herein. For example, some steps may be added or removed. One or more steps may be performed in a different order than as illustrated in FIGS. **15** and **16**. Some of the steps may comprise sub-steps. Many of the steps may be repeated as many times as appropriate or necessary.

(105) Therapeutic Agent Delivery System for Hip

(106) FIGS. **17A** and **17B** show an exemplary therapeutic agent delivery system **500** for a hip. FIG. **17A** is a perspective view of the assembled delivery system, while FIG. **17B** is an exploded perspective view of the system. The delivery system **500** comprises a femoral stem **510** and a femoral head **520**. The femoral stem **510** can be configured to be disposed in a femoral medullary canal of a patient. The femoral head **520** can be configured to be disposed in an acetabulum of the patient. The femoral stem may comprise an inlet **535** configured to couple to a source of a therapeutic agent to be delivered to the patient. The inlet can be fluidly coupled to a channel in the femoral stem, so as to allow the therapeutic agent to be distributed in the femoral medullary canal. The femoral stem and the femoral head may be configured to removably couple together so as to fluidly connect the femoral stem channel to one or more channels in the femoral head, such that the

therapeutic agent can also be distributed in the acetabular joint space. The femoral stem and the femoral head may be configured to couple in a stable configuration, so as to maintain a desired distance between the femoral stem and the femoral head through the length of use of the therapeutic agent delivery system in the patient. Optionally, the femoral stem and the femoral head may be connected in a fashion that allows the distance between the stem and the head to be adjusted to fit the anatomy of the patient. The system **500** may further comprise a stem plug **530**, configured to couple to an end of the femoral stem.

(107) Femoral Stem

(108) FIGS. **18A-18D** show an exemplary femoral stem **600** suitable for incorporation with a therapeutic agent delivery system for a hip. FIG. **18A** is a perspective view, FIG. **18B** is a side view, FIG. **18C** is a bottom view, and FIG. **18D** is a side cross-sectional view of the femoral stem **600**. The femoral stem **600** comprises an elongate body **605** having a longitudinal axis **610**, the elongate body having a first end **615** and a second end **620** opposite the first end. The elongate body comprises a neck region **650** disposed near the first end **615**, wherein the neck region may be configured to couple to the femoral head. The second end **620** may be configured be disposed in the femoral medullary canal. The femoral stem **600** further comprises an inlet **535**, configured to be coupled to a source of the therapeutic agent. The inlet **535** is in fluid communication with a stem channel **625** extending between the first end **615** and the second end **620**, as best seen in FIG. **18D**. The stem channel can be configured to deliver the therapeutic agent through the stem and to the medullary canal. Further, the stem channel can be configured to fluidly couple to one or more channels in the femoral head.

(109) The elongate body **605** may have one or more structures or features that are similar to the intramedullary stem **200** described previously. For example, the femoral stem **600** may comprise a plurality of protrusions **630**, protruding radially outward from the elongate body **605**. The plurality of protrusions may comprise any number of protrusions having any appropriate shape, size, or configuration to engage the medullary canal in a stable fashion. For example, the protrusions may comprise elongate fins extending along the longitudinal length of the elongate body, as shown in FIGS. **18A-18D**. In one exemplary embodiment, the plurality of protrusions may comprise four fins, spaced equally at about 90° about the longitudinal axis **610** of the elongate body. Of course this is not intended to be limiting, and the number of fins may be any number, such as three fins spaced approximately 120 degrees apart, five fins spaced approximately 72 degrees apart, etc. The plurality of protrusions **630** and the elongate body **605** may be formed separately and coupled together. Alternatively or in combination, the plurality of protrusions **630** may be formed by removing material from the elongate body **605**, such that the plurality of protrusions and the elongate body are formed as a single member. Adjacent protrusions **630** may define one or more fluted regions **635** therebetween, the fluted regions radially recessed compared to the protrusions.

(110) The plurality of protrusions and fluted regions can be configured to minimize the surface area of the stem contacting the bone lining the medullary canal, such that the area of the bone flushed with the therapeutic agent may be maximized. For example, the plurality of protrusions and fluted regions can be configured such that less than 50% of the surface area of the stem is in contact with the bone lining the medullary canal. Of course this is not intended to be limiting and one of skill in the art will appreciate that any percentage of surface area of the stem may contact the bone. The stem may comprise a plurality of identical fluted regions defined by a plurality of elongate fins, distributed symmetrically about the longitudinal axis **610** of the stem, as shown in FIGS. **18A-18D**. Alternatively, a plurality of fluted regions may be distributed asymmetrically about the longitudinal axis of the stem, and/or may have different shapes or sizes. For example, the elongate body **605** may comprise protrusions and fluted regions as described in relation to FIGS. **3A** and **3B**.

(111) The femoral stem **600** may further comprise a plurality of outlet holes **640** in fluid communication with the stem channel **625**. The plurality of outlet holes **640** may be configured to deliver the therapeutic agent, distributed through the stem channel **625**, to the femoral medullary

canal, as well as adjacent tissue including the joint. The plurality of outlet holes may be disposed in a fluted region **635**, so as to deliver the therapeutic agent to the area of the bone not in contact with the femoral stem. The plurality of outlet holes may comprise any number of outlet holes having any appropriate size, shape, or distribution. For example, the plurality of outlet holes may include a plurality of equally sized and spaced holes that extend axially along a line substantially parallel to the longitudinal axis **610** of the stem, as shown in FIGS. **18A-18D**. Alternatively, the plurality of outlet holes may extend along a helical or spiral line as shown in FIG. **3A**, or the holes may extend about a plurality of rings around the circumference of the elongate body, as shown in FIG. **3B**. The plurality of outlet holes may comprise holes having an identical shape and/or size, or holes having various shapes and/or sizes. Varying the hole size may allow further fluid control of therapeutic agent as it exits different regions of the stem.

(112) The stem channel **625** may be a through hole that extends from the first end **615** to the second end **620** through both the first end and the second end, such that the elongate body comprises an open second or distal end. The system may further comprise a plug, shown in FIG. **19**, configured to couple to the open second end of the stem, so as to close the second end and thereby create a blind channel. Alternatively, the stem channel **625** may be a blind channel, wherein the second end of the elongate body is closed. In configurations wherein the second end is open, the therapeutic agent may exit the stem channel into the medullary canal through the second end and/or through a plurality of outlet holes disposed along the elongate body **605** as described herein. If the stem comprises only the stem channel **625** extending through the first and second ends, without the plurality of outlet holes, the therapeutic agent may exit the stem channel only through the second end. In configurations wherein the second end of the stem is closed, the therapeutic agent may exit the stem channel into the medullary canal only through the plurality of outlet holes.

(113) The neck region **650** extends along a neck axis **655**, disposed at an angle **660** with respect to the longitudinal axis **610** of the elongate body **605**. The angle **660** may be in a range from about 120° to about 160°, about 130° to about 150°, about 140° to about 150°, or about 145°. The neck region may comprise one or more connection mechanisms or features to couple to the femoral head. For example, as shown, the neck region may comprise a plurality of threads **670**, configured to threadably engage complementary threads on the femoral head.

(114) The femoral stem **600** may be tapered to fit the medullary canal. For example, the elongate body **605** and/or the plurality of protrusions **630** may be tapered from the first end **615** to the second end **620**, as shown, so as to have a smaller radial cross-sectional area at the second end than at the first end. For example, the taper may comprise a gradual taper, wherein the extent of the taper may be in a range from about 0.1° to about 10°, about 0.5° to about 5°, about 1° to about 5°, about 1° to about 4°, or about 2° or about 3°. The taper may be adjusted to accommodate a medullary canal of a specific type of bone.

(115) FIG. **19** shows a stem plug **530** suitable for incorporation with any therapeutic agent delivery system as described herein. The stem plug **530** may comprise a smaller diameter region **535** and a larger diameter region **540**. The smaller diameter region may be configured to be press-fit into an open second end of an elongate body of any intramedullary stem or hip stem as described herein.

(116) Femoral Head

(117) FIGS. **20A** and **20B** show an exemplary embodiment of a femoral head **700**, suitable for incorporation with a therapeutic agent delivery system for a hip. FIG. **20A** is a side view, and FIG. **20B** is a side cross-sectional view of the femoral head **700**, along line A-A as shown in FIG. **20A**. The femoral head **700** can comprise the shape of a truncated sphere, wherein the truncated base **715** of the head is configured to couple to the femoral stem. The femoral head **700** comprises a head central channel **725**, extending axially along a central axis **710** of the femoral head. The central channel **725** is configured couple to the neck of the femoral stem, and thereby be in fluid communication with the hip stem channel when the femoral head is connected to the femoral stem. The femoral head further comprises a plurality of outlet holes **740**, fluidly coupled to the central

channel **725**. The outlet holes may be configured to extend radially outwards from the central channel. Thus, a therapeutic agent may be supplied to the delivery system via an inlet of the femoral stem, move through the stem channel into the central channel **725** of the femoral head, and exit into the acetabular joint space through the outlet holes **740**.

(118) The base **715** may comprise one or more mechanisms for coupling the femoral head to the neck region of the femoral stem. For example, as shown, a portion of the central channel **725** near the base **715** may comprise a plurality of threads **770**, configured to threadably engage a plurality of complementary threads of the femoral stem neck. A threaded connection between the femoral head and the femoral stem neck can allow the distance between the femoral head and the femoral stem to be adjusted to fit the patient's anatomy. Optionally, the femoral head may be further configured to receive one or more set screws near the base, wherein the set screws can fix the distance between the femoral head and the femoral stem once the distance is appropriately set. For example, as shown in FIG. **20B**, the base may comprise two set screw receiving regions **780**, wherein each set screw receiving region comprises a plurality of threads **785** to engage a set screw having complementary threads. The set screw receiving regions can extend radially outwards from the central channel, such that the ends of the set screws can be directly or indirectly coupled to the neck of the femoral stem disposed within the central channel. While FIG. **20B** shows two set screw receiving regions radially offset from one another by about 180°, the femoral head may comprise any number of set screws distributed in any appropriate configuration. For example, the femoral head may comprise three set screw receiving regions radially offset from one another by about 120°, or four set screw receiving regions radially offset from one another by about 90°.

(119) FIGS. **21A** and **21B** show another exemplary embodiment of a femoral head **800**, suitable for incorporation with a therapeutic agent delivery system **500** for a hip. The femoral head **800** is partially hollowed, so as to reduce the material mass and weight of the femoral head. The femoral head **800** comprises a central channel **825**, configured to be in fluid communication with the stem channel of the femoral stem as described herein. The femoral head further comprises an inner shell **830** and an outer shell **835**, wherein the inner and outer shells are thin, truncated spherical shells disposed about the periphery of the femoral head. The inner shell **830** is connected to the material disposed about and defining the central channel **825**. The outer shell **835** is connected to the inner shell **830** via a plurality of support struts **845** extending between the inner shell and the outer shell. The inner shell defines an inner cavity **855** between the inner shell and the material defining the central channel. The inner cavity **855** is hollow, and configured to be sealed against the central channel and the inner shell, such that no fluid can enter the inner cavity during use of the delivery system. The inner shell and the outer shell define an outer cavity **850** therebetween, wherein the outer cavity **850** is fluidly coupled to the central channel **825**. The outer shell comprises a plurality of outlet holes **840**, such that fluid in the outer cavity **850** can exit the femoral head through the outlet holes. Thus, the therapeutic agent supplied through an inlet of a femoral stem can move through the stem channel into the central channel **825** of the femoral head **800**, into the outer cavity **850**, and through the outlet holes **840** into the acetabular joint space. Components of the femoral head **800** may be formed via 3D printing or laser sintering.

(120) FIG. **22** shows another exemplary embodiment of a femoral head **900**, suitable for incorporation with a therapeutic agent delivery system for a hip. The femoral head **900** comprises a central channel **925**, configured to be in fluid communication with the stem channel of the femoral stem as described herein. The femoral head further comprises a plurality of hollow tubes **940** extending radially outwards from the central channel **925** and fluidly coupled to the central channel. The femoral head further comprises an outer shell **935**, a thin, truncated spherical shell disposed about the periphery of the femoral head. The outer shell **935** is coupled to the plurality of hollow tubes **940**, such that the hollow tubes **940** extend through the thickness of the outer shell. The hollow tubes, the outer shell, and the material disposed about defining the central channel together define a plurality of inner cavities **855**, which are hollow and configured to be fluidly

sealed, such that no fluid can enter the inner cavities during use of the delivery system. Thus, the therapeutic agent supplied through an inlet of a femoral stem can move through the stem channel into the central channel **925** of the femoral head **900**, into the plurality of hollow tubes **940**, and into the acetabular joint space. The internal diameter of the hollow tubes and/or the thickness of the hollow tubes may be varied to control the flow of fluid within the femoral head, and to adjust the amount of support provided by the hollow tubes to the outer shell to protect the integrity of the outer shell.

(121) Coupling Mechanisms

(122) FIGS. **23A** and **23B** show exemplary mechanisms for coupling a femoral head **520** to a femoral stem **510**. The femoral head **520** may comprise any femoral head as described herein, such as femoral heads **700**, **800**, and **900** described in relation to FIGS. **20A-22**. The femoral stem **510** may comprise any femoral stem as described herein, such as any embodiment of the femoral stem **600** described herein. FIG. **23A** is a side cross sectional view of a femoral head **520** coupled fixedly to a femoral stem **510**. The neck region **650** of the stem is fixedly coupled to a portion of the central channel **725** of the femoral head, such that the length **540** of the neck that engages the femoral head is fixed. For example, the neck **650** may be press-fitted into the central channel **725**, such that the neck advances into the central channel by a pre-determined length. The neck **650** may comprise regions having different diameters so as to create a notch between the regions, wherein the notch can provide a stop against the femoral head surface when the neck **650** has been advanced into the central channel by the pre-determined length. In a delivery system incorporating such a connection mechanism, the distance between the femoral head and the femoral stem is fixed. FIG. **23B** is a side cross sectional view of a femoral head **520** coupled adjustably to a femoral stem **510**. The neck region **650** of the stem is adjustably coupled to a portion of the central channel **725**, for example via engagement of threads **670** disposed on the neck **650** of the stem with complementary threads **770** disposed on a portion of the central channel **725**. The length **540** of the neck that engages the central channel can thereby be increased or decreased by threadably rotating the femoral head about the femoral stem. As the femoral head is rotated to axially translate the head farther away from the femoral stem, the length **540** decreases, and the distance between the femoral head and the femoral stem increases such that the delivery system can be suitable for patients requiring a longer set distance between the femur and the acetabulum. As the femoral head is rotated to axially translate the head closer to the femoral stem, the length **540** increases, and the distance between the femoral head and the femoral stem decreases such that the delivery system can be suitable for patients requiring a shorter set distance between the femur and the acetabulum. In a delivery system incorporating such a connection mechanism, the distance between the femoral head and the femoral stem can be thus adjusted to accommodate the anatomy of a patient.

(123) FIGS. **24A** and **24B** show an exemplary mechanism for locking a set distance between a femoral head **520** and a femoral stem **510** of a therapeutic agent delivery system for a hip. The femoral head **520** may comprise any femoral head as described herein, such as femoral heads **700**, **800**, and **900** described in relation to FIGS. **20A-22**. The femoral stem **510** may comprise any femoral stem as described herein, such as any embodiment of the femoral stem **600** described herein. FIG. **24A** is a perspective view and FIG. **24B** is a bottom view of a femoral head **520** comprising the exemplary mechanism. As described herein, a femoral head **520** may comprise a pair of set screw receiving regions **780** near the base **715** of the head, which can receive a pair of set screws configured to engage the femoral stem neck disposed in the central channel **725** of the femoral head, so as to fix the position of the stem neck therein. The femoral head may further comprise a pair of blocks **550** disposed within the set screw receiving regions **780**, adjacent to the central channel **725**. Each block can be coupled with a set screw **554**, wherein the block may comprise a rounded cavity to receive the end of the set screw, and wherein the end of the set screw may be free to rotate within the rounded cavity. Two dowel pins **552** may be coupled to the block-set screw assembly so as to limit the translational motion of the set screw relative to the block.

Rotation of the set screw within the set screw receiving region can cause the block coupled thereto to translate radially inwards or outwards. The block may be translated radially inwards until the block engages and pushes against the neck region of the stem disposed within the central channel, thereby preventing further rotation of the femoral head about the femoral stem. The block can distribute the forces between the neck and the set screw across a broader surface, to more effectively lock the position of the neck. While FIGS. **24A-24F** show a pair of set screw receiving regions radially offset from one another by about 180° , the locking mechanism may comprise any number of set screws distributed in any appropriate configuration. For example, the femoral head may comprise three set screw receiving regions radially offset from one another by about 120° , or four set screw receiving regions radially offset from one another by about 90° .

(124) FIGS. **24C-24F** illustrate a method of assembling the locking mechanism of FIGS. **24A** and **24B**. FIG. **24C** shows the femoral head **520** and components of the locking mechanism before assembly. As described previously, the femoral head may comprise one or more set screw receiving regions **780** extending radially outwards from the central channel **725**. Each set screw receiving region can be configured to receive a set screw **554**, a block **550**, and a pair of dowel pins **552**. FIG. **24D** shows the first step of assembly of the locking mechanism, wherein the block **550** is coupled to the femoral head **520**. The femoral head may comprise a block receiving region **556** adjacent the central channel **725**, and the block may be inserted into block receiving region from the base **715** of the femoral head. As best seen in FIG. **24B**, the block **550** may have a concave surface **551** on a first end and a round indent **553** on a second end opposite the first end. As shown in FIG. **24C**, the block may be inserted into the femoral head with the concave surface directed radially inwards, facing the central channel, and the round indent directed radially outwards. FIG. **24E** shows the second step of assembly of the locking mechanism, wherein the set screw **554** is coupled to the femoral head **520**. As best seen in FIG. **24B**, the set screw receiving region **780** comprises set screw threads **785**, configured to engage the thread region of the set screw. The set screw may be threadably engaged with the set screw threads within the set screw receiving region, to translate the set screw radially inwards within the set screw receiving region. As best seen in FIG. **24D**, the set screw can comprise a set screw head **555**, an unthreaded region of the set screw having a smaller diameter than the threaded region of the set screw. During the step shown in FIG. **24E**, the set screw can be translated radially inwards until the set screw head is disposed within the round indent **553** of the block **550** (as best seen in FIG. **24B**). FIG. **24F** shows the final step of assembly of the locking mechanism, wherein the dowel pins **552** are coupled to the femoral head. The two dowel pins may be pressed into the block **550** with an interference fit. When the dowel pins are pressed completely into the block, the leading ends of pins can engage the set screw head **555**, such that the pins prevent the set screw from separating from the block. For example, the screw head may comprise a concave groove **557** (as best seen in FIGS. **24B** and **24D**) extending about the circumference of the set screw head **555**. The leading ends of the dowel pins may be configured to engage the concave groove when the pins are pressed completely into the block (as best seen in FIG. **24B**) such that the set screw cannot separate from the block.

(125) Optional Features

(126) FIGS. **25A** and **25B** show an exemplary embodiment of a therapeutic agent delivery system **500** for a hip, further comprising an acetabular cup **560**. FIG. **25A** is a perspective view and FIG. **25B** is a side cross sectional view of the system **500**. The delivery system **500** may further comprise a separate acetabular cup **560**, configured to be inserted into the acetabular space of the hip joint. The femoral head **520** thus interfaces with the acetabular cup, rather than interfacing directly with the acetabulum of the patient. The acetabular cup may comprise a plurality of fluted external structures **565**, through which fluid may flow to reach the acetabulum.

(127) FIG. **26** shows an exemplary embodiment of a therapeutic agent delivery system **500** for a hip. The therapeutic agent delivery system **500** as described herein may be configured to function as the final implant, rather than as a temporary implant intended for the first stage of a two-stage

re-implantation procedure. The system **500** may comprise a femoral stem **510** such as any femoral stem described herein, a femoral head **520** such as any femoral head described herein, and a stem plug **530**. In addition, the system **500** may further comprise a liner **570** and an acetabular cup **560** configured to be implanted between the femoral head **520** and the acetabulum of the patient. Fluid may flow through the femoral head and out the liner and acetabular cup, into the joint space and the acetabulum. Optionally, alternatively to or in combination with the inlet **535** of the femoral stem **510**, the acetabular cup **560** may comprise a separate inlet, through which the therapeutic agent may be supplied.

(128) Method of Use of Therapeutic Agent Delivery System for Hip

(129) FIG. **27** illustrates a method **1700** of treating a patient's hip using a therapeutic agent delivery system for a hip as described herein. In step **1705**, a femoral stem is positioned in the medullary canal of the patient's femur. In step **1710**, a femoral head is coupled to the femoral stem. In step **1715**, which is optional, the distance between the femoral stem and the femoral head is adjusted such that the delivery system best fits the patient's anatomy. For example, if the femoral head is coupled to the femoral stem via a threaded connection mechanism as described herein, the distance between the femoral stem and head may be adjusted by threadably rotating the femoral head about the stem. Step **1715** may further comprise locking the distance between the femoral head and the femoral stem, for example via the set screw mechanism described in relation to FIGS. **24A-24F**. In step **1720**, the femoral head is positioned in the patient's acetabulum. In step **1725**, the therapeutic agent is delivered to the medullary canal and the acetabulum via the delivery system.

(130) The steps of method **1700** are provided as examples of a method of using a therapeutic agent delivery system in accordance with embodiments. A person of ordinary skill in the art will recognize many variations and modifications of the method **1700** based on the disclosure provided herein. For example, some steps may be added or removed. Some of the steps may comprise sub-steps. Many of the steps may be repeated as many times as appropriate or necessary. One or more steps may be performed in a different order than as illustrated in FIG. **27**. For example, the femoral head and the femoral stem may be coupled together and, if necessary, the distance between the head and stem adjusted, before the assembled device is positioned in the patient's femur and acetabulum.

(131) Additional Features of Therapeutic Agent Delivery Systems

(132) In any of the therapeutic agent delivery systems described herein, the flow of fluid within the system may be adjusted by modifying one or more dimensions or configurations of the channels and/or outlet holes. For example, the diameter of the channels and/or outlet holes may be increased or decreased, or channels may be configured to have varying diameters along the length of the assembly, to bias the flow of fluid in a particular direction. Angles at junctures between the channels may also be varied to bias fluid flow within the system.

(133) Any therapeutic agent delivery system as described herein may further comprise a pump, operatively coupled to the inlet. The pump may be configured to pump the therapeutic agent into one or more channels of the system.

(134) Any therapeutic agent delivery system as described herein may optionally comprise a vacuum pump that may be coupled to an inlet or an outlet of the system. The vacuum pump may be configured to remove any unwanted or excess fluids from the body of the patient, before introducing the therapeutic agent to the body using the delivery system.

(135) Any therapeutic agent delivery system as described herein may optionally comprise a port under the skin that is coupled to an inlet or outlet of the delivery system. The port may be accessed via a needle or syringe as necessary.

(136) FIGS. **28A** and **28B** illustrate the use of negative pressure wound therapy with a therapeutic agent delivery system for a knee. Negative pressure wound therapy may optionally be used in tandem with the therapeutic agent delivery system, in order to further improve the prognosis of the treatment. The wound of the patient can be packed with sponges **90** and optionally covered with a

wound dressing **85** coupled to a vacuum pump **80**. Actuation of the vacuum pump can then draw blood and nutrients to infected areas. As shown in FIG. **28B**, optional sponges for negative pressure wound therapy may also be provided as strips **95** of sponges configured to be disposed along the intramedullary stems **200** of the delivery system **100**. The strips of sponges may be trimmed to fit the space along the fluted regions **235** of any intramedullary stem **200**. Negative pressure wound therapy can pull material through the sponge and into the plurality of outlet holes of the stem, into the stem channel, and out of the body through the inlet or outlet of the system. While a delivery system for a knee is shown in FIGS. **28A** and **28B**, negative pressure wound therapy may be used with any therapeutic agent delivery system as described herein, including delivery systems for joints other than the knee.

(137) FIG. **29** shows an optional cover **75** for an intramedullary stem **200**, suitable for incorporation with any therapeutic agent delivery system described herein. The cover **75** may comprise a thin, cone-shaped sponge, configured to fit inside the medullary canal as an interface between the bone and the intramedullary stem **200**. The cover can be configured to cover the substantially all of the elongate body **205** of the stem, and thus evenly interface with the intramedullary bone. When covered with the cover **75**, the therapeutic agent can disperse within the cover and reach the corresponding surface of the medullary canal, regardless of the shape of the intramedullary stem (e.g., shape, size, number, or configuration of protrusions and fluted regions). This exemplary configuration may also be used in conjunction with the negative pressure wound therapy previously described.

(138) FIG. **30** shows an exemplary embodiment of a therapeutic agent delivery system **1000**. The delivery system **1000** may comprise an intramedullary stem **1010** which may be any intramedullary stem as described herein, such as intramedullary stems **110**, **120**, or **200**, or femoral stems **510** or **600**. The stem **1010** may comprise a stem channel **1025** that extends through both the first end **1015** and the second end **1020** of the stem. Instead of receiving the therapeutic agent from a coupling member coupled to the stem, the stem **1010** may be configured to receive a catheter **1030** supplying the therapeutic agent through the first end **1015**. The therapeutic agent may be delivered to the medullary canal through the second end **1020**.

(139) FIGS. **31A** and **31B** show exemplary embodiments of therapeutic agent delivery systems with inlets and outlets. FIG. **31A** shows an exemplary embodiment of a therapeutic agent delivery system **100** for a knee, as described herein. The delivery system **100** may comprise an inlet **140**, configured to couple to a source of the therapeutic agent. The inlet **140** may be fluidly coupled to one or more channels of a coupling member **130**, and the one or more channels of the coupling member may be fluidly coupled to the stem channels in the stems **200**. Optionally, the system may further comprise an outlet **145**, configured to remove the therapeutic agent and/or any other fluid from the body. The stems and the coupling member may comprise internal channels configured to direct fluid between the inlet and the stem channel, and between the stem channel and the outlet. Other aspects of the system may generally take the same form as previously described. FIG. **31B** shows an exemplary embodiment of a therapeutic agent delivery system **500** for a hip, as described herein. The delivery system **500** may comprise an inlet **535**, configured to couple to a source of the therapeutic agent. The inlet **535** may be fluidly coupled to a channel of the femoral stem **510**, and the stem channel may be fluidly coupled to a central channel of the femoral head **520** coupled to the femoral stem. Optionally, the system may further comprise an outlet **545**, configured to remove the therapeutic agent and/or any other fluid from the body. The femoral stem and the femoral head may comprise internal channels configured to direct fluid between the inlet and the channels of the stem and the head, and between the outlet and the channels of the stem and the head. Other aspects of the system may generally take the same form as previously described.

(140) FIGS. **32A** and **32B** illustrate an exemplary configuration for the internal channels of an intramedullary stem. FIG. **32A** is a sectional view and FIG. **32B** is a cross sectional view of an intramedullary stem **1100** comprising a plurality of separate internal fluid paths. Stem **1100** may

comprise any intramedullary stem as described herein, such as intramedullary stems **110**, **120**, or **200**, or femoral stems **510** or **600**. Stem **1100** may comprise a first internal channel **1110** centrally disposed along the longitudinal axis of the stem, and a second internal channel **1120** disposed about the periphery of the first internal channel (the second internal channel can form the shape of a cylindrical shell surrounding the first internal channel). The first internal channel may be fluidly coupled to a first plurality of outlet holes **1115**, each of the first plurality of outlet holes extending from the first internal channel, through the second internal channel, to an outer wall of the stem (such as a fluted region **1135** of the stem). The second internal channel may be fluidly coupled to a second plurality of outlet holes **1125**, each of the second plurality of outlet holes extending from the second internal channel directly to an outer wall of the stem. The first internal channel and the second internal channel may be fluidly sealed against one another, and each of the first plurality of outlet holes **1115** may cross over the second internal channel **1120** through a side channel that is fluidly sealed against the second internal channel. Therefore, the first internal channel and the second internal channel can form two separate internal fluid paths, each of which can be used to deliver fluid to the tissue or remove fluid from the tissue. As shown in FIG. **32B**, the first plurality of outlet holes **1115** and the second plurality of outlet holes **1125** may be linearly arranged along the length of the stem in an alternating manner, such that every other hole is in fluid communication with a different internal fluid path.

(141) FIGS. **33A-33C** illustrate another exemplary configuration for the internal channels of an intramedullary stem. FIG. **33A** is a perspective view, FIG. **33B** is a vertical cross sectional view, and FIG. **33C** is a horizontal cross sectional view of an intramedullary stem **1200** comprising a plurality of separate internal fluid paths. Stem **1200** may comprise any intramedullary stem as described herein, such as intramedullary stems **110**, **120**, or **200**, or femoral stems **510** or **600**. Stem **1200** may comprise a first internal channel **1210** running along the length of the stem, and a second internal channel **1220** adjacent the first internal channel, also running along the length of the stem. The first and second internal channels may be fluidly sealed against one another, such that each channel forms a separate internal fluid path. The first internal channel may be fluidly coupled to a first plurality of outlet holes **1215**, each of the first plurality of outlet holes extending from the first internal channel to an outer wall of the stem (such as a fluid region **1235** of the stem), without cutting through the second internal channel. The second internal channel may be fluidly coupled to a second plurality of outlet holes **1225**, each of the second plurality of outlet holes extending from the second internal channel to an outer wall of the stem, without cutting through the first internal channel. Therefore, the first internal channel and the second internal channel can form two separate internal fluid paths, each of which can be used to deliver fluid to the tissue or remove fluid from the tissue. As shown in FIG. **33A**, the first plurality of outlet holes **1215** and the second plurality of outlet holes **1225** may be arranged along the length of the stem in an alternating manner, such that every other hole is in fluid communication with a different internal fluid path.

(142) An intramedullary stem comprising two or more separate internal fluid paths as shown in FIGS. **32A-33C** may be used to simultaneously deliver fluid to and remove fluid from the tissue, without cross-contaminating the fluid to be delivered with the fluid to be removed. For example, a first internal channel may be fluidly coupled to an inlet (such as inlet **140** of FIG. **31A** or inlet **535** of FIG. **31B**) configured to receive a therapeutic agent from a source, while the second internal channel may be fluidly coupled to an outlet (such as outlet **145** of FIG. **31A** or outlet **545** of FIG. **31B**) configured to remove fluid from the tissue. In this configuration, the first plurality of outlet holes can deliver the therapeutic agent to the tissue, while the second plurality of outlet holes can remove fluid from the tissue, thereby allowing simultaneous delivery of therapeutic agent and removal of fluid from the tissue without cross-contamination between the therapeutic agent and the fluid to be removed. In another exemplary configuration, the first internal channel may be fluidly coupled to a first inlet configured to receive a first therapeutic agent, while the second internal channel may be fluidly coupled to a second inlet configured to receive a second therapeutic agent

different from the first therapeutic agent. In this configuration, simultaneous delivery of two different therapeutic agents can be achieved, without cross-contamination between the two agents before the agents reach the tissue.

(143) FIGS. **34-36** show exemplary embodiments of therapeutic agent delivery systems adapted for use in various joints. While descriptions of the therapeutic agent delivery systems are primarily directed to systems to be used in the knee or in the hip, systems comprising similar components and features may be used to treat any other joint. FIG. **34** shows an exemplary embodiment of a delivery system **1200** for a shoulder, FIG. **35** shows an exemplary embodiment of a delivery system **1300** for an ankle, and FIG. **36** shows an exemplary embodiment of a delivery system **1400** for a spine. In the embodiments shown, the delivery systems **1200**, **1300**, and **1400** comprise an inlet **140** through which the therapeutic agent may be supplied, and a plurality of outlet holes **240** through which the therapeutic agent may be delivered to the respective location of the body. Any of the delivery systems **1200**, **1300**, and **1400** may incorporate any other structures or features disclosed herein in relation to delivery systems for the knee and the hip.

(144) Components of the therapeutic agent delivery systems as described herein may be formed from one or more of many materials commonly used in orthopedic implants, including but not limited to titanium alloy Ti 6Al-4V, polyether ether ketone (PEEK), polymethyl methacrylate (PMMA), and ultra high molecular weight polyethylene (UHMWPE). The materials may incorporate an antibiotic-impregnated outer layer, such as an antibiotic-impregnated PMMA outer layer. The surface of the components may be polished to prevent bone growth and formation of biofilms. Alternatively, the surface of the components may be grit-blasted or plasma-sprayed, incorporate one or more of an hyaluronic acid (HA) coating, silver coating, or antibiotic carrier coating, or be passivated and irradiated to form a hydrophilic nanostructure. The delivery systems as described herein may comprise one or more of machined parts or sintered parts.

(145) While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

Claims

1. A fluid delivery system for disinfecting a joint after removal of a prosthesis from said joint, said system comprising: a femoral head configured to be disposed in an acetabulum, the femoral head comprising: a partially spherical, outer shell forming an external surface of the femoral head, the outer shell comprising a plurality of outlets and a first radius of curvature; a partially spherical, inner shell located internal to the outer shell, the inner shell comprising a second radius of curvature smaller than the first radius of curvature; a central shaft projecting through the interior of the femoral head, the central shaft coupled to a region of the inner shell and defining a central channel; an outer cavity disposed near a periphery of the femoral head, the outer cavity bound by an inner surface of the outer shell and an outer surface of the inner shell, wherein the outer cavity is in fluid communication with the central channel and the plurality of outlets; and an inner cavity located inside the femoral head internal to the outer cavity, wherein the inner cavity is defined, in part, by an inner surface of the inner shell, wherein the inner cavity is not in fluid communication with any of the central channel, the outer cavity, or the plurality of outlets; a femoral stem coupled to the femoral head so as to be in fluid communication with the central channel, the femoral stem configured to be disposed in a femoral medullary canal, wherein the femoral stem comprises a threaded neck region, the threaded neck region configured to be threadably engaged with the

femoral head thereby allowing adjustment of a distance between the femoral head and the femoral stem; and an inlet coupled to the femoral stem, wherein, when the system receives a fluid from the inlet, the fluid is deliverable from the plurality of outlets into the acetabulum.

2. The system of claim 1, wherein the femoral stem comprises a plurality of protrusions extending axially along a longitudinal axis of the femoral stem.

3. The system of claim 1, wherein the femoral stem comprises an elongate channel extending therethrough, the elongate channel fluidly coupled with the inlet and the plurality of outlets.

4. The system of claim 3, wherein the elongate channel is a through-hole, and wherein one end of the femoral stem comprises a plug.

5. The system of claim 1, wherein the femoral stem is tapered.

6. The system of claim 1, wherein the central channel is fluidly coupled with the plurality of outlets via a plurality of channels extending radially outward from the central channel.

7. The system of claim 1, further comprising an outlet for fluid removal from the femoral head or the femoral stem.

8. The system of claim 1, further comprising an acetabular cup coupled to the femoral head, and wherein the fluid is delivered from the acetabular cup to the acetabulum.

9. The system of claim 1, wherein the plurality of outlets comprise a plurality of holes having varying diameters.

10. The system of claim 1, further comprising a locking mechanism for locking the femoral head with the femoral stem.

11. The system of claim 1, further comprising a plurality of outlets in the femoral stem that are in fluid communication with the inlet.

12. The system of claim 1, wherein the femoral head is configured to be removably disposed in the acetabulum for use in a two-stage re-implantation procedure.

13. The system of claim 1, wherein the inner shell is connected to the outer shell via a plurality of support struts.

14. A method for treating a joint using the system of claim 1, said method comprising: positioning the femoral stem in the femoral medullary canal of a femur; coupling the femoral head with the femoral stem; positioning the femoral head in the acetabulum; and delivering the fluid to the medullary canal and the acetabulum.

15. The method of claim 14, wherein coupling comprises adjusting a distance between the femoral head and the femoral stem.

16. The method of claim 14, wherein delivering the fluid comprises delivering an antibiotic, saline, or irrigation fluid.

17. The method of claim 14, wherein delivering the fluid comprises delivering an antibiotic, the antibiotic comprising vancomycin, tobramycin, or a combination thereof.

18. The method of claim 14, wherein delivering the fluid comprises delivering the fluid from one or more outlet holes disposed in a fluted region of the femoral stem.

19. The method of claim 14, wherein delivering the fluid comprises pumping the fluid from the femoral stem to the medullary canal or from the femoral head to the acetabulum.

20. The method of claim 14, further comprising suctioning unwanted fluids from the medullary canal or the acetabulum.
