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(54) Title: APPARATUS AND METHOD FOR RAPID INTRAOSSEOUS FLUID INFUSION

(57) Abstract: A system allows for rapid intraosseous delivery of fluids from a fluid reservoir via an intraosseous port having a tip disposed within the bone marrow of a patient. The system includes a housing with a chamber and a plunger. An actuator is moveable between first and second positions to move the plunger between the distal and proximal positions. A valve housing includes a first one-way valve fluidly coupled to the fluid reservoir, and a second one-way valve fluidly coupled to the intraosseous port. The valves of the valve housing are oriented such that movement of the actuator from the first to the second position moves the plunger from the distal to the proximal position, drawing fluid from the fluid reservoir through the first valve and into the chamber. Movement of the actuator from the second to the first position moves the plunger from the proximal to the distal position, driving fluid from the chamber through the port and second valve and through the intraosseous port. A grip manipulated by a user effects movement of the actuator, which provides sufficient mechanical advantage for the user to easily overcome resistance to the flow of fluid into the bone marrow. The plunger may be biased in the proximal position such that it is automatically retracted to that position, causing re-filling of the chamber, when the user releases forces imparted to the grip. The tubing and valve mechanism are of sufficient caliber to allow rapid and low-resistance flow of fluid from the reservoir into the chamber. The combination of these components allows rapid infusion of large volumes into the bone marrow without user fatigue, and requiring only one hand to operate the mechanism.



APPARATUS AND METHOD FOR RAPID INTRAOSSEOUS FLUID INFUSION

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5 This application claims the benefit of US Provisional Application No. 61/800,400, filed March 15, 2013, which is incorporated herein by reference.

BACKGROUND

10 Rapid fluid administration is essential for patients suffering from a variety of life-threatening illness including septic shock, trauma with significant blood loss, severe dehydration, and anaphylaxis. The American Heart Association's PAL's (Pediatric Advanced Life Support) Guidelines recommend fluid resuscitation volumes of 20 ml per kilogram of body weight over a period of 5 minutes. Intravenous (IV) and intraosseous (IO) fluid administration are the two primary methods of rapid fluid resuscitation in these emergent situations. In certain patients dehydration, low blood pressure or other factors can make it difficult to establish venous access
15 for IV fluid administration. This is particularly true in children. In such patients, the IO route is preferred.

20 IO access is achieved by inserting a specialized needle into one of the long bones of the leg or arm. A fluid source is connected to the IO port, allowing fluids to be delivered into the bone marrow and to thus flow directly into the systemic circulation. Typical entry sites for the IO port include the anterior tibia, the distal femur, the humeral head, and in adults the manubrium of the sternum. Commercially available systems for placing IO needles include the Bone Injection Gun (B.I.G., Waismed, Houston, TX), the EZ-IO (VidaCare Corp., San Antonio, TX), and the FAST1 adult intraosseous infusion system (Pyng Medical Corp., Richmond, British Columbia, Canada).

25 The standard set of components used to deliver fluids through an IO port includes a fluid reservoir, a syringe, a three-way stopcock, and IV tubing linking these components with the IO port. The user withdraws the plunger to fill the syringe from the fluid reservoir, turns the stopcock, and then depresses the plunger to drive the fluid through the IO port and into the bone marrow. The process is repeated multiple times until the desired volume has been delivered.

Alternatively, one provider fills syringes from the IV fluid bag, while another connects the syringe, administers the fluid, disconnects the empty syringe, and repeats the process.

It is well documented that resistance to fluid flow in the bone marrow is high, often requiring the user to generate pressures of 300-450mmhg to achieve adequate flow rates. High resistance to fluid flow into the bone marrow represents a key barrier to the rapid administration of fluid via the IO route. The increased resistance requires emergency healthcare providers to either: 1) use great force with a large-volume syringe, often with two hands, and quickly resulting in user fatigue, or 2) to refill a small-bore syringe multiple times to achieve adequate volume, resulting in slow administration times and significant distraction for one or more workers. In either case two providers are often necessary, with one user infusing the fluid, and the other refilling syringes or operating the stopcock.

Medical providers are best able to deliver these pressures manually using a small bore (10 or 20ml) syringe to overcome bone marrow resistance. However, significant manual force, and repetitive filling and refilling of the syringe are therefore needed to achieve appropriate flow rates. Using the conventional set-up, users quickly become fatigued, and are consumed with the work of filling and refilling, distracting one (or two) providers from tending to other necessary assessment and care, and possibly limiting the effectiveness of resuscitation if the fluid is not delivered rapidly enough.

Consider the example of a 40 kg child with traumatic injury and massive blood loss. This child may require rapid infusion of 40-80 ml/kg of blood products, for a total of 1600-3200 ml. Repeated doses using a standard technique and 20 ml syringe would require 80-160 injections and the full attention of two healthcare workers, resulting in slow resuscitation and inefficient use of resources. The total infusion time could be 15-20 minutes, well outside the range of recommended rates, particularly in an actively bleeding child.

The present application describes a system that overcomes these limitations, allowing more rapid and efficient IO fluid delivery than could be achieved using existing equipment.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a side elevation view of a fluid injection system.

DETAILED DESCRIPTION

Disclosed herein is a system which provides higher infusion pressure than prior art systems with less hand fatigue, and which rapidly refills to allow rapid fluid resuscitation. The system allows for flow rates of at least 50 ml/min or higher (e.g. between 50 – 200 ml/min) into the bone marrow – rates which are not achievable using the prior art IO fluid delivery systems.

System

Referring to Fig. 1, fluid injection system 100 includes a housing 10 and a fluid chamber 12 supported by the housing. In the illustrated embodiment, the fluid chamber 12 comprises the barrel of a syringe such as a 20 ml syringe. The housing 10 may be configured to be reusable and designed such that a fresh, sterile, syringe may be removably coupled to the housing 10 prior to each use. In other embodiments, the housing 10 has an integrated chamber 12 and is disposable or sterilized between uses.

A valve housing 16 is fluidly coupled to the fluid chamber 12. In the Fig. 1 embodiment, the valve housing includes a proximal port/opening in communication with or coupled to a tubular port 14. Tubular port 14 is fluidly coupled to a distal portion of the chamber 12. A pressure measurement device 42 such as a manometer is positioned to measure pressure within the tubular port 14.

Valve housing 16 includes first and second one-way valves 18, 20. It should be noted, however, that in alternate embodiments the first and second one-way valves 18, 20 are not within a common housing.

A first conduit 22, which may be a length and caliber of tubing suitable for facilitating fluid passage at high flow rates, is coupled between the first valve 18 and a fluid reservoir 24 (e.g. saline or blood, and/or medication). A second conduit 26 is coupled between second valve 20 and an intraosseous port/needle 28 positioned with its distal end within bone marrow as described above. First valve 18 is oriented to allow one-way flow of fluid from reservoir 24 and

conduit 22 into the tubular port 14 and chamber 12. The tubing 22, valve 18, tubular port 14, and distal tip of chamber 12 are of sufficiently large caliber and sufficiently short length to allow free and rapid flow of fluid into chamber 12 as spring mechanism 40 acts to retract plunger 30. Second valve 20 is oriented to allow one-way flow of fluid from chamber and tubular port 14 to conduit 26 and intraosseous port 28.

A plunger 30 includes a distal end 30a moveable within the chamber 12 between proximal and distal positions. Movement of the plunger in a distal direction expels fluid from the chamber 12 through the tubular port 14. The system includes an actuator that provides a mechanical advantage necessary to drive the plunger 30 and overcome the expected resistance to flow into the bone marrow. One example of an actuator, which drives the plunger using manual force, will be described with reference to Fig. 1. It should be understood, however, that various alternative actuators (including those using motors, pneumatics, or other sources of force to drive the plunger) might instead be used. The actuator is configured to generate fluid pressures adequate to overcome the resistance to flow into the bone marrow, and preferably to generate pressures (e.g. 300-450mm/hg or higher) that will to achieve adequate flow rates into the IO space. While the optimal flow rate for a patient will depend on the size of the patient, the disclosed actuator allows average flow rates of at least 50ml/min, and preferably 50 – 200 ml/min, to be achieved, far exceeding flow rates that can be achieved using conventional systems.

Referring again to Fig. 1, a handle on the housing 10 is engageable by a user to drive the plunger 30 distally. Handle includes a grip 32 pivotally coupled to the housing 10 at pivot 34. A pinion mechanism 36 on grip 32 is rotatable about pivot 34 when grip 32 is pivoted relative to the housing 10. A rack mechanism 38 includes gear teeth engaged with corresponding teeth on the pinion mechanism 36, and is slidable between proximal and distal positions. Movement of the rack mechanism 38 is mechanically coupled to the proximal end 30b of the plunger, such as through a direct or indirect connection between the rack 38 and proximal end 30b. Movement of the grip 32 in direction indicated by arrow A rotates pinion mechanism 36, which causes rack mechanism 38 to slide distally relative to the housing 10 as indicated by arrow B and to thus drive the plunger 30 distally.

The fluid injection system 100 preferably includes a mechanism for retracting the plunger 30 in a proximal direction upon release of the grip. In the Fig. 1 embodiment, a spring 40 biases the grip 32 such that when manual pressure against the grip 32 is released, the grip 32 pivots opposite to direction A, thus causing rack mechanism 38 to withdraw the plunger 30 proximally. In other embodiments, alternative mechanisms may be used to bias the plunger 30 in a proximal position.

Method

Use of the fluid injection system 100 will next be described. First, a syringe is mounted to the housing 10 and positioned with its outflow port in fluid communication with tubular port 14 and with the proximal portion 30b of plunger 30 coupled to the actuator (e.g. the rack mechanism 38). Prior to coupling a fluid reservoir 24 to the system, the user squeezes the grip 32 in direction A, driving the rack mechanism 38 and thus the plunger 30 distally. With the plunger 30 maintained in the distal position (a latch may be provided to engage the plunger in this position when needed), fluid reservoir 24 is fluidly coupled to first valve 18 via tubing 22. The user releases the grip 32, allowing the spring 40 to pivot the grip 32 to its resting position and to thus cause rack mechanism 38 to withdraw the plunger 30 to a proximal position. Retraction of the plunger 30 draws fluid from the fluid reservoir 24 through tubing 22 and valve 18 and into chamber 12 through tubular port 14. Each of these components is of sufficiently large bore (i.e. larger than more standard 3 mm diameter tubing and valves used in IO systems) to allow rapid and low-resistance flow into chamber 12 so that the user may rapidly administer the subsequent dose of fluid.

An intraosseous port 28 is fluidly coupled to tubing 26 and second valve 20. The port 28 is positioned with its distal tip within bone marrow as described above. The user squeezes the grip 32 in direction A, driving the rack mechanism 38 and thus the plunger 30 distally. Distal movement of the plunger 30 drives fluid from the chamber 12 through valve 20, and tubing 26, and into the bone marrow through the intraosseous port 28. Once the chamber 12 has been emptied, the user releases the grip 32, allowing the chamber 12 to be rapidly refilled from the fluid reservoir 24 as described in the preceding paragraph. The process is repeated, with the user repeatedly squeezing and releasing the grip to alternatingly deliver fluid and refill the chamber 12, until the appropriate volume of fluid has been administered.

The pressure measurement device 42 allows the user to monitor infusion pressures throughout fluid delivery, so as to avoid infusion pressures that can disrupt intraosseous needle placement. In some embodiments, the pressure measurement device 42 may include a visual or auditory indicator to alert the user when pressures exceed a threshold level so that the user may
5 release the grip or maintain its position until such time as additional fluid can be safely delivered.

While certain embodiments have been described above, it should be understood that these embodiments are presented by way of example, and not limitation. It will be apparent to persons skilled in the relevant art that various changes in form and detail may be made therein without departing from the spirit and scope of the invention. This is especially true in light of technology
10 and terms within the relevant art(s) that may be later developed.

What is claimed is:

1. A system for intraosseous delivery of fluids, the system comprising:

a housing configured to receive a chamber having a plunger moveable between distal and proximal positions within the chamber, the housing including an actuator moveable between first and second positions to move the plunger between the distal and proximal positions;

a first one-way valve fluidly couplable to a fluid reservoir, and

a second one-way valve fluidly couplable to an intraosseous port;

a tubular port fluidly couplable to the chamber,

wherein the valves are oriented such that

movement of the actuator from the first to the second position moves the plunger from the distal to the proximal position, drawing fluid from the fluid reservoir through the first valve and port and into the chamber; and

movement of the actuator from the second to the first position moves the plunger from the proximal to the distal position, driving fluid from the chamber through the port and second valve and through the intraosseous port.

2. The system of claim 1, further including a valve housing including the first and second one-way valves, wherein the tubular port extends from the valve housing.

3. The system of claim 1, further including a pressure measurement device positioned to measure pressure indicative of the pressure of fluid flowing from the intraosseous port.

4. The system of claim 2, wherein the pressure measurement device measures pressure within the tubular port.

5. The system of claim 1, wherein the actuator is biased in the second position.

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6. The system of claim 1, wherein the actuator includes a grip pivotable relative to the housing and a member linearly moveable in response to pivoting of the grip.

7. The system of claim 6, wherein the grip includes a pinion mechanism and the member comprises a rack mechanism engaged with the pinion mechanism.

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8. The system of claim 1, wherein movement of the actuator from the second to the first position causes the plunger to drive fluid into bone marrow at a pressure of at least 250mmhg.

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9. The system of claim 1, wherein movement of the actuator from the second to the first position cause the plunger to drive fluid into bone marrow at a pressure of at least 300 mmhg.

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10. The system of claim 5, further including a spring biasing the actuator in the second position.

11. A system for intraosseous delivery of fluids, the system comprising:

a housing including a chamber and a plunger moveable between distal and proximal positions within the chamber, the housing including an actuator moveable between first and second positions to move the plunger between the distal and proximal positions;

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a first one-way valve fluidly couplable to a fluid reservoir, and

a second one-way valve fluidly couplable to an intraosseous port;

a tubular port fluidly couplable to the chamber,

wherein the valves of the valve housing are oriented such that

movement of the actuator from the first to the second position
moves the plunger from the distal to the proximal position, drawing fluid
from the fluid reservoir through the first valve and port and into the
chamber; and

movement of the actuator from the second to the first position
moves the plunger from the proximal to the distal position, driving fluid
from the chamber through the port and second valve and through the
intraosseous port.

12. A system for intraosseous delivery of fluids, the system comprising:

a housing;

a chamber engageable with the housing and a plunger moveable between distal
and proximal positions within the chamber, the housing including an actuator
moveable between first and second positions to move the plunger between the distal
and proximal positions;

a fluid reservoir;

an intraosseous port;

a first one-way valve fluidly coupled to the fluid reservoir, and

a second one-way valve fluidly coupled to the intraosseous port;

a tubular port fluidly coupled to the chamber,

wherein the valves of the valve housing are oriented such that

movement of the actuator from the first to the second position
moves the plunger from the distal to the proximal position, drawing fluid

from the fluid reservoir through the first valve and port and into the chamber; and

movement of the actuator from the second to the first position moves the plunger from the proximal to the distal position, driving fluid from the chamber through the port and second valve and through the intraosseous port.

13. A method for intraosseous delivery of fluids, comprising:

providing a first valve and a second valve;

fluidly coupling a fluid reservoir to the first valve;

fluidly coupling the first and second valves to a chamber having a plunger;

moving the plunger from a distal position to a proximal position within the chamber, thereby drawing fluid from the reservoir through the first valve into the chamber;

positioning a tip of an intraosseous port within bone marrow of a patient and fluidly coupling the intraosseous port to the second valve ;

operating an actuator to move the plunger from the proximal position to the distal position, thereby driving fluid from the chamber through the second valve and out the intraosseous port into the bone marrow.

14. The method of claim 13, wherein the method provides a valve housing having the first and second valves, wherein the valve housing is fluidly coupled to the chamber.

15. The method of claim 13, further including, after driving fluid into the bone marrow, re-filling the chamber by moving the plunger from the distal position to the proximal position to draw fluid from the reservoir through the first valve into the chamber.

16. The method of claim 15 wherein the actuator is biased to position the plunger in the proximal position, wherein operating the actuator to move the plunger to the distal position

includes applying manual force to the actuator against the bias, and wherein re-filling the chamber includes releasing the manual force from the actuator to allow the plunger to return to the proximal position.

5 17. The method of claim 13, wherein the chamber is carried by a device housing, and wherein operating the actuator includes pivoting a grip relative to the device housing.

10 18. The method of claim 17 wherein the grip is biased to position the plunger in the proximal position, wherein operating the actuator to move the plunger to the distal position includes applying manual force to the grip against the bias, and wherein re-filling the chamber includes releasing the manual force from the grip actuator to allow the plunger to return to the proximal position.

15 19. The method of claim 17, further including the step of coupling the chamber to the device housing and operatively engaging the plunger and actuator.

20 20. The method of claim 13, further including monitoring pressure of fluid flowing to the bone marrow.

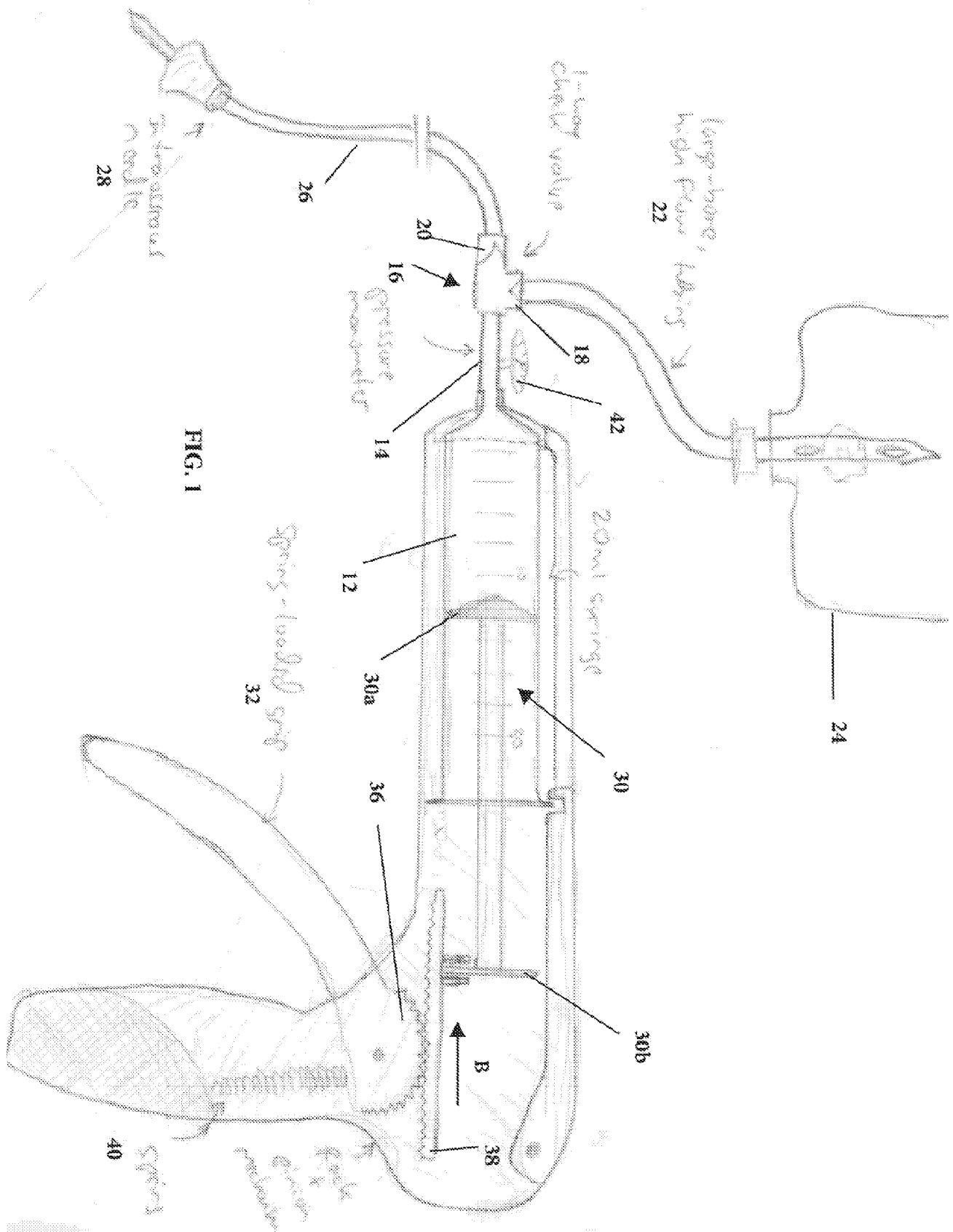
25 21. The method of claim 16, further including within the actuator sufficient mechanical advantage necessary to overcome expected resistance to fluid flow during plunger movement to the distal position

 22. The method of claim 16, further including large bore tubing and valve housing of sufficient caliber to allow low-resistance and rapid flow of fluid into the chamber during movement of plunger to proximal position

23. The method of claim 13, wherein the plunger drives the fluid at a pressure of at least 250mmhg to overcome resistance to flow of fluid into the bone marrow.

24. The method of claim 13 wherein the plunger drives the fluid into the bone marrow
5 at a rate of 40 ml/min or higher.

25. The method of claim 13 wherein the plunger drives the fluid into the bone marrow at a rate of 50 ml/min or higher.



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/030097**A. CLASSIFICATION OF SUBJECT MATTER****A61M 5/145(2006.01)i, A61B 17/56(2006.01)i, A61B 17/34(2006.01)i, A61M 39/22(2006.01)i**

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61M 5/145; A61M 31/00; A61J 1/18; A61M 5/00; A61M 5/14; A61B 6/00; A61M 5/178; A61B 17/32; A61B 17/56; A61B 17/34; A61M 39/22

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: intraosseous fluid infusion, chamber, plunger, valve

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5807340 A (POKRAS, N. M.) 15 September 1998 See abstract; column 4, lines 8-23; column 7, lines 42-45; column 8, lines 32-36; claims 1 and 4-5; figures 1, 3 and 7.	1-12
A	US 2011-0282197 A1 (MARTZ, K. R.) 17 November 2011 See abstract; paragraphs [0032]-[0035]; claims 1, 9 and 18-20; figures 1-2C.	1-12
A	US 5389070 A (MORELL, R. C.) 14 February 1995 See abstract; claims 1 and 18; figure 1.	1-12
A	US 2002-0116021 A1 (GORDON, E) 22 August 2002 See abstract; claim 1; figure 1.	1-12
A	US 6989000 B2 (SCHREIJAG, K. et al.) 24 January 2006 See abstract; claim 1; figure 1.	1-12
A	US 2010-0204649 A1 (MILLER, L. J. et al.) 12 August 2010 See abstract; claim 1.	1-12



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/030097

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

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

1. ☒ Claims Nos.: 13-25
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 13-25 pertain to a method for treatment of the human by surgery, and thus relate to a subject matter which this International Searching Authority is not required, under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv), to search.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2014/030097

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 05807340 A	15/09/1998	None	
US 2011-0282197 A1	17/11/2011	CA 2751252 A1 CN 102307608 A EP 2401008 A1 JP 2012-516756 A WO 2010-091132 A1	12/08/2010 04/01/2012 04/01/2012 26/07/2012 12/08/2010
US 05389070 A	14/02/1995	US 05929289 A	27/07/1999
US 2002-0116021 A1	22/08/2002	US 2002-0007143 A1 US 6616677 B2	17/01/2002 09/09/2003
US 6989000 B2	24/01/2006	DE 10326306 A1 DE 10326306 B4 US 2005-0020983 A1	30/12/2004 23/09/2010 27/01/2005
US 2010-0204649 A1	12/08/2010	WO 2008-134355 A2 WO 2008-134355 A3	06/11/2008 29/01/2009