

DELIVERY CATHETER

TECHNICAL FIELD

[0001] The present disclosure generally relates to catheters. In particular, some embodiments of the present disclosure relate to delivery catheters configured to deliver a composition such as a cell composition or gene therapy to a target site.

BACKGROUND

[0002] Catheters may be used to deliver therapeutic or diagnostic agents to a patient. Targeted delivery of therapeutic or diagnostic agents to a patient may improve patient outcomes.

[0003] To safely and accurately deliver the therapeutic or diagnostic agents to a patient, mapping of the target site is typically performed. This may involve using a map or model of part of the patient's body, such as the heart, to help in identifying the area(s) for treatment.

[0004] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present disclosure as it existed before the priority date of each of the appended claims.

[0005] Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

SUMMARY

[0006] Some embodiments relate to a delivery catheter configured to deliver a composition to a target site, the catheter comprising:
a catheter tube, defining:

a first lumen extending between a proximal end and a distal end of the catheter tube, wherein the catheter tube comprises a flexible portion configured to enable deflection of the distal end relative to the proximal end;

a first passage in a wall of the tube, the first passage containing a first pull wire configured to effect, in a first direction, the deflection of the distal end;

a second passage in the wall of the tube, the second passage containing a second pull wire configured to effect, in a second direction, the deflection of the distal end;

a tip assembly connected to the distal end of the catheter tube, the tip assembly comprising a tip electrode and an electrode band, wherein the tip electrode defines a delivery lumen connected to the first lumen of the catheter tube;

a control handle for controlling the deflection of the distal end of the catheter tube, the control handle connected to the proximal end of the catheter tube;

an injection handle for controlling delivery of the composition, the injection handle connected to the control handle and comprising:

a barrel defining a bore extending between a first end and a second end of the barrel;

a piston configured to slide within the bore;

a spring disposed in the bore and configured to resist sliding of the piston towards the first end of the barrel;

a needle assembly comprising a flexible needle extending from a needle hub, the needle extending: (i) through the injection handle; (ii) through the control handle; (iii) through the first lumen of the catheter tube; and (iv) into the delivery lumen of the tip assembly;

wherein the needle hub is connected to the piston of the injection handle, such that the sliding of the piston towards the first end of the barrel causes the needle to extend through the tip assembly to deliver the composition; and

wherein the injection handle is configured to retract the flexible needle into the tip assembly after delivering the composition.

[0007] The control handle may comprise a first pulley assembly connected to the first pull wire, wherein rotation of the first pulley assembly applies tension to the first pull wire to effect the deflection of the distal end in the first direction; and a second pulley assembly connected to the second pull wire, wherein rotation of the second pulley

assembly applies tension to the second pull wire to effect the deflection of the distal end in the second direction.

- [0008] The first and second passages may be disposed at opposed radial locations along the wall of the tube.
- [0009] The wall of the tube may comprise: (i) a first ridge extending from the wall of the tube into the first lumen to define the first passage; and (ii) a second ridge extending from the wall of the tube into the first lumen to define the second passage.
- [0010] The first direction and the second direction may be opposed directions for the deflection of the distal end.
- [0011] The deflection of the distal end in the first direction may cause the flexible portion of the catheter tube to have a first radius of curvature. The deflection of the distal end in the second direction may cause the flexible portion of the catheter tube to have a second radius of curvature. The first and second radius of curvature may not be equal.
- [0012] The delivery lumen may be centrally disposed in the tip assembly.
- [0013] The first and second pulley assembly may comprise a moment arm arrangement configured to: (i) magnify; or (ii) reduce; the tension respectively applied to the first and second pull wire to effect the deflection of the distal end. The moment arm arrangement may comprise: (i) a linkage; or (ii) a gear system; or (iii) a linkage and a gear system. The first and second pulley assembly may be disposed on opposed lateral sides of the control handle.
- [0014] The first and second pull wire may be disposed on opposed sides of the needle in the control handle.
- [0015] The first and second pull wire may be disposed on opposed sides of the needle in the catheter tube.
- [0016] The injection handle may further comprise a rotatable needle actuator ring on the piston, wherein the rotatable needle actuator ring is configured to limit the sliding of the piston within the bore. The rotation of the rotatable needle actuator ring may be configured to cause the rotatable needle actuator ring to travel along the piston to shorten or lengthen a distance that the piston is able to slide within the bore.
- [0017] The injection handle may further comprise a groove and pin, the groove formed on the piston, and the pin configured to engage with the groove to: (i) limit the sliding of the piston within the bore; and/or (ii) limit rotation of the piston within the bore. The pin

may be configured to engage with the groove to resist a spring force exerted by the spring on the piston.

[0018] Some embodiments relate to a delivery catheter configured to deliver a composition to a target site, the catheter comprising:

a catheter tube, defining:

a first lumen extending between a proximal end and a distal end of the catheter tube, wherein the catheter tube comprises a flexible portion configured to enable deflection of the distal end relative to the proximal end;

a first passage in a wall of the tube, the first passage containing a first pull wire configured to effect, in a first direction, the deflection of the distal end;

a second passage in the wall of the tube, the second passage containing a second pull wire configured to effect, in a second direction, the deflection of the distal end;

a tip assembly connected to the distal end of the catheter tube, the tip assembly comprising a tip electrode and an electrode band, wherein the tip electrode defines a delivery lumen connected to the first lumen of the catheter tube;

a control handle for controlling the deflection of the distal end of the catheter tube, the control handle connected to the proximal end of the catheter tube;

an injection handle for controlling delivery of the composition;

a needle assembly connected to the injection handle and comprising a flexible needle extending from a needle hub, the needle extending: (i) through the injection handle; (ii) through the control handle; (iii) through the first lumen of the catheter tube; and (iv) into the delivery lumen of the tip assembly to deliver the composition;

wherein the injection handle is configured to retract the flexible needle into the tip assembly after delivering the composition.

[0019] Some embodiments relate to a delivery catheter configured to deliver a composition to a target site, the catheter comprising:

a catheter tube, defining:

a first lumen extending between a proximal end and a distal end of the catheter tube, wherein the catheter tube comprises a flexible portion configured to enable deflection of the distal end relative to the proximal end;

a first pull wire configured to effect, in a first direction, the deflection of the distal end;

a second pull wire configured to effect, in a second direction, the deflection of the distal end;

a tip assembly connected to the distal end of the catheter tube, the tip assembly comprising a tip electrode and an electrode band, wherein the tip electrode defines a delivery lumen connected to the first lumen of the catheter tube;

a control handle for controlling the deflection of the distal end of the catheter tube, the control handle connected to the proximal end of the catheter tube and comprising:

a first pulley assembly connected to the first pull wire, wherein rotation of the first pulley assembly applies tension to the first pull wire to effect the deflection of the distal end in the first direction; and

a second pulley assembly connected to the second pull wire, wherein rotation of the second pulley assembly applies tension to the second pull wire to effect the deflection of the distal end in the second direction;

an injection handle for controlling delivery of the composition;

a needle assembly connected to the injection handle and comprising a flexible needle extending from a needle hub, the needle extending: (i) through the injection handle; (ii) through the control handle; (iii) through the first lumen of the catheter tube; and (iv) into the delivery lumen of the tip assembly to deliver the composition;

wherein the injection handle is configured to retract the flexible needle into the tip assembly after delivering the composition.

[0020] Some embodiments relate to a delivery catheter configured to deliver a composition to a target site, the catheter comprising:

a catheter tube defining a first lumen extending between a proximal end and a distal end of the catheter tube, wherein the catheter tube comprises a flexible portion configured to enable deflection of the distal end relative to the proximal end;

a tip assembly connected to the distal end of the catheter tube, the tip assembly comprising a tip electrode and an electrode band, wherein the tip electrode defines a delivery lumen connected to the first lumen of the catheter tube;

a control handle for controlling the deflection of the distal end of the catheter tube, the control handle connected to the proximal end of the catheter tube;

an injection handle for controlling delivery of the composition, the injection handle connected to the control handle and comprising:

a barrel defining a bore extending between a first end and a second end of the barrel;

a piston configured to slide within the bore;

a spring disposed in the bore and configured to resist sliding of the piston towards the first end of the barrel;

a needle assembly comprising a flexible needle extending from a needle hub, the needle extending: (i) through the injection handle; (ii) through the control handle; (iii) through the first lumen of the catheter tube; and (iv) into the delivery lumen of the tip assembly;

wherein the needle hub is connected to the piston of the injection handle, such that the sliding of the piston towards the first end of the barrel causes the needle to extend through the tip assembly to deliver the composition;

wherein the injection handle is configured to retract the flexible needle into the tip assembly after delivering the composition.

[0021] Some embodiments relate to a kit for a delivery catheter configured to deliver a composition to a target site, the kit comprising:

a catheter tube;

a tip assembly configured to be connected to a distal end of the catheter tube;

a control handle for controlling deflection of the distal end of the catheter tube, the control handle configured to be connected to a proximal end of the catheter tube;

an injection handle for controlling delivery of the composition, the injection handle configured to be connected to the control handle; and

a needle assembly for delivering the composition through a flexible needle extending from the tip assembly, the needle assembly configured to be connected to the injection handle;

wherein the catheter tube is the catheter tube as described herein.

[0022] Some embodiments relate to a kit for a delivery catheter configured to deliver a composition to a target site, the kit comprising:

a catheter tube;

a tip assembly configured to be connected to a distal end of the catheter tube;

a control handle for controlling deflection of the distal end of the catheter tube, the control handle configured to be connected to a proximal end of the catheter tube;

an injection handle for controlling delivery of the composition, the injection handle configured to be connected to the control handle; and

a needle assembly for delivering the composition through a flexible needle extending from the tip assembly, the needle assembly configured to be connected to the injection handle;

wherein the control handle is the control handle as described herein.

[0023] Some embodiments relate to a kit for a delivery catheter configured to deliver a composition to a target site, the kit comprising:

a catheter tube;

a tip assembly configured to be connected to a distal end of the catheter tube;

a control handle for controlling deflection of the distal end of the catheter tube, the control handle configured to be connected to a proximal end of the catheter tube;

an injection handle for controlling delivery of the composition, the injection handle configured to be connected to the control handle; and

a needle assembly for delivering the composition through a flexible needle extending from the tip assembly, the needle assembly configured to be connected to the injection handle;

wherein the injection handle is the injection handle as described herein; and

wherein the needle assembly the needle assembly as described herein.

[0024] The delivery catheter as described herein, or the kit for the delivery catheter as described herein, may be configured to deliver: (i) a cell composition; or (ii) gene therapy.

BRIEF DESCRIPTION OF DRAWINGS

[0025] Embodiments are described in further detail below, by way of example, with reference to the accompanying drawings, in which:

[0026] Fig. 1A is a top view of a catheter, according to some embodiments;

[0027] Fig. 1B is a side view of the catheter of Fig. 1A, according to some embodiments;

[0028] Fig. 1C is a section view of the catheter of Fig. 1B, according to some embodiments;

[0029] Fig. 2A is an end view of a catheter tube, according to some embodiments;

- [0030] Fig. 2B is a top view of the catheter tube of Fig. 2A, according to some embodiments;
- [0031] Fig. 2C is a longitudinal section view of the catheter tube of Fig. 2A, according to some embodiments;
- [0032] Fig. 2D is a radial section view of the catheter tube of Fig. 2B, according to some embodiments;
- [0033] Fig. 3 is a section view of a tip section of the catheter of Fig. 1A, according to some embodiments;
- [0034] Fig. 4A is a top section view of a catheter control handle, according to some embodiments;
- [0035] Fig. 4B is an exploded perspective view of the catheter control handle of Fig. 4A, according to some embodiments;
- [0036] Fig. 5A is an exploded perspective view of a catheter injection handle, according to some embodiments;
- [0037] Fig. 5B is a side view of the assembled catheter injection handle of Fig. 5A, according to some embodiments;
- [0038] Fig. 5C is a section view of the assembled catheter injection handle of Fig. 5B, according to some embodiments;
- [0039] Fig. 6A is an exploded perspective view of a catheter needle assembly, according to some embodiments;
- [0040] Fig. 6B is a side view of the assembled catheter needle assembly of Fig. 6A, according to some embodiments; and
- [0041] Fig. 6C is a section view of the assembled catheter needle assembly of Fig. 6B, according to some embodiments.

DETAILED DESCRIPTION

- [0042] The present disclosure generally relates to catheters. In particular, some embodiments of the present disclosure relate to delivery catheters configured to deliver a composition such as a cell composition or gene therapy to a target site. The delivery catheter may also be understood to comprise an injection catheter, although for ease of reference, the term “delivery catheter” will be used herein.

- [0043] Figs. 1A-1C show an embodiment of a delivery catheter 100 configured to deliver a composition to a target site. The catheter 100 may comprise a catheter tube 200, a tip assembly 300, a control handle 400, an injection handle 500, and a needle assembly 600. Fig. 1A is a top view of the catheter 100. Fig. 1B is a side view of the catheter 100. Fig. 1C is a section view of the catheter 100, taken along the line B-B marked on Fig. 1B.
- [0044] Turning to Figs. 2A-2D, the catheter tube 200 may comprise a tube wall 202 defining a first end 210 and a second end 220 of the catheter tube 200, wherein the first end 210 and the second end 220 are disposed at opposite ends of the catheter tube 200. Fig. 2A is an end view of the catheter tube 200. Fig. 2B is a top view of the catheter tube 200. Fig. 2C is a section view of a length of the catheter 100, taken along the line A-A marked on Fig. 2A. Fig. 2D is a section view of a diameter of the catheter 100, taken along the line B-B marked on Fig. 2B. The tube wall 202 may comprise multiple layers. In some embodiments, the layers of the tube wall 202 comprise a combination of different materials. The tube wall 202 may comprise a layer of braiding to strengthen the tube wall 202 against bending. The braiding may extend along a substantial length of the catheter tube 200. The braiding may be 16 gauge wire. The wire braid may have a "one under two, over two" configuration or pattern. The wire braid may have a braid density of 28-30 programmable picks per inch (PPI).
- [0045] The distance between a first extremity 212 disposed at the first end 210 and a second extremity 222 disposed at the second end 220 defines an overall length of the catheter tube 200. A longitudinal reference axis 230 is shown on Fig. 2C extending through the catheter tube 200 between the first end 210 and the second end 220. The overall length of the catheter tube 200 may be measured along the longitudinal reference axis 230.
- [0046] When the catheter 100 is in use, the first end 210 of the catheter tube 200 is closer to the target site (and further from the user) while the second end 220 is comparatively further from the target site (and closer to the user), as measured along the overall length of the catheter tube 200. Accordingly, the first end 210 may alternatively be referred to as the distal end 210, and the second end 220 may alternatively be referred to as the proximal end 220. The catheter tube 200 may define a first lumen 240 extending between the distal end 210 and the proximal end 220 of the catheter tube. At least part of the catheter tube 200 may be flexible. The catheter tube 200 may comprise at least one flexible portion (not shown) configured to enable deflection of the distal end relative to

the proximal end. The flexible portion may be a joint that connects separate subsections of the catheter tube. The separate subsections of the catheter tube 200 may be comparatively less flexible than the flexible portion. The whole catheter tube 200 may be flexible. In some embodiments, the whole catheter tube 200 is flexible, with some sections of the catheter tube 200 being more flexible than others.

[0047] Turning to Fig. 2D, in some embodiments, the catheter tube wall 202 defines a first passage 250. The first passage 250 may be configured to contain a first pull wire 260. The first pull wire 260 may be configured to effect deflection of the distal end 210 of the catheter tube 200 in a first direction.

[0048] In some embodiments, the catheter tube wall 202 defines a second passage 270. The second passage 270 may be configured to contain a second pull wire 280. The second pull wire 280 may be configured to effect deflection of the distal end 210 of the catheter tube 200 in a second direction. The passages 250, 270 may protect the respective pull wires 260, 280 from abrasion or damage. The passages 250, 270 may protect the respective pull wires 260, 280 from the needle (not shown) as it translates in and out of the catheter tube 200 (during injection and retraction).

[0049] The tube wall 202 may comprise a first ridge 204 extending from an inner surface of the tube 200 into the first lumen 240 to define the first passage 250. The tube wall 202 may comprise a second ridge 206 extending from the inner surface of the tube 200 into the first lumen 240 to define the second passage 270.

[0050] The ridges 204, 206 defining the passages 250, 270 may be present at the distal end 210. The ridges 204, 206 may extend from the distal end 210 and extend along the tube wall 202 towards the proximal end 220. The ridges 204, 206 may extend from the distal end 210 along the tube wall 202 until the proximal end 220. The ridges 204, 206 may extend from the distal end 210 along the tube wall 202 into the proximal end 220.

[0051] For clarity, Fig. 2D shows a sizable gap between the pull wires 260, 280 and the interiors of their respective passages 250, 270. However, in some embodiments, the gap may be smaller to reduce the amount of radial movement of the pull wires 260, 280 in their respective passages 250, 270. Fig. 2D further shows that the first and second passages 250, 270 are disposed at opposed radial locations along the tube wall 202. In some embodiments, the first and second passages 250, 270 are disposed at different radial locations along the tube wall 202, but are not opposite each other.

- [0052] The first pull wire 260 and the second pull wire 280 may cause deflection in the same plane of movement. The first pull wire 260 and the second pull wire 280 may cause deflection in the same plane of movement but in opposite directions to each other. For example, with reference to Fig. 2C, the first pull wire 260 may move the distal end 210 leftwards of the longitudinal reference axis 230, while the second pull wire 280 may move the distal end 210 back towards the longitudinal reference axis 230. Conversely, the second pull wire 280 may move the distal end 210 rightwards of the longitudinal reference axis 230, while the first pull wire 260 may move the distal end 210 back towards the longitudinal reference axis 230.
- [0053] The first pull wire 260 and the second pull wire 280 may cause deflection in a different plane of movement. For example, the first pull wire 260 may cause deflection in a first plane of movement. The second pull wire 280 may cause deflection in a second plane of movement that may not be parallel with the first plane of movement.
- [0054] The deflection of the distal end 210 in the first direction may cause the flexible portion of the catheter tube 200 to have a first radius of curvature. The deflection of the distal end 210 in the second direction may cause the flexible portion of the catheter tube 200 to have a second radius of curvature. In some embodiments, the first and second radius of curvature are not equal. For example, the catheter tube 200 may curve more (i.e. a smaller radius of curvature) in the first direction compared to the second direction.
- [0055] The first pull wire 260 and the second pull wire 280 may cause deflection of different parts of the catheter tube 200. Deflection of the catheter tube 200, such as the tip, may be effected by applying tension to at least one of the first pull wire 260 and the second pull wire 280. The control handle 400 may comprise a mechanism configured to apply tension to the first pull wire 260 and/or the second pull wire 280. Various mechanisms for applying tension to the first pull wire 260 and/or the second pull wire 280 are subsequently described by way of example herein.
- [0056] Fig. 3 shows an embodiment of the tip assembly 300. The tip assembly 300 is configured to be connected to the distal end 210 of the catheter tube 200. In some embodiments, the tip assembly comprises a tip electrode 310 and an electrode band 320, wherein the electrode band 320 may also be referred to as a ring electrode 320. The tip electrode 310 may be connected to a tip electrode lead wire 330. The electrode band 320 may be connected to a ring electrode lead wire 332. The tip electrode lead wire 330 and

the ring electrode lead wire 332 may be connected to their respective electrodes by welding.

[0057] In some embodiments, the tip electrode 310 defines a delivery lumen 312. The delivery lumen 312 may be connected to the first lumen 240 of the catheter tube 200. The delivery lumen 312 may be connected to a tube 340 which is disposed inside the first lumen 240 and extends towards the tip assembly 300. The tube 340 may contain the injection needle (not shown) and separate the injection needle from the lead wires 330, 332. The tube 340 may insulate the injection needle (not shown) and from at least one of the electrodes 310, 320. The tube 340 may be made from a polyamide material. The tube 340 may extend into the delivery lumen 312 and extend to the tip of the tip electrode 310. The delivery lumen 312 may be centrally disposed in the tip assembly 300.

[0058] The tip assembly 300 may further comprise a transition tube 350 disposed at the distal end 210 of the catheter tube 200. The transition tube 350 may be configured to connect the tip electrode 310 to the distal end 210 of the catheter tube 200. The transition tube 350 may define a distal end 352 and a proximal end 354. The distal end 210 of the catheter tube 200 may be slightly tapered or have a step to define a reduced diameter to fit within the lumen of the transition tube 350.

[0059] The first pull wire 260 and the second pull wire 280 may extend through the first lumen 240 of the catheter tube 200 to be connected to the distal end 210. The first pull wire 260 and the second pull wire 280 may be connected to the distal end 210 near to the tip assembly 300. In some embodiments, the first pull wire 260 and the second pull wire 280 terminate at the proximal end 354 of the transition tube 350.

[0060] The tip electrode 310 is configured to be inserted into the distal end 352 of the transition tube 350. The tip electrode 310 may be secured to the distal end 352 of the transition tube 350 using an adhesive such as Dymax 215. The tip electrode 310 may comprise an end portion 314 and a plug section 316, wherein the plug section 316 has a smaller diameter than the end portion 314. The tip electrode 310 may comprise a step transition between diameters of the end portion 314 and the plug section 316, thereby defining a shoulder 318. The tip electrode 310 may abut the distal end 352 of the transition tube 350. The electrode band 320 may fit around the distal end 352 of the transition tube 350, and may also be disposed around the plug section 316 of the tip electrode 310. The electrode band 320 may be spaced apart from the distal end 352 of the

transition tube 350. The electrode band 320 may be spaced apart from the shoulder 318 of the tip electrode 310.

[0061] The tip assembly 300 may be used to provide a location of the catheter tip assembly 300 within the patient's body. The tip assembly 300 may be used together with an external locating (GPS) and/or mapping system to locate the tip assembly 300 relative to the target site in the patient's body. For example, the catheter 100 may be used to deliver a composition to the patient's heart. The patient may use a cardiac mapping system such as the EnSite Precision system manufactured by Abbott, which may produce a real-time map/model of the patient's heart and identify the condition of the heart tissue. The cardiac mapping system may also track the location of the catheter 100 when it enters the patient's heart. The cardiac mapping system may produce a high resolution model that provides actual mapping of heart tissue condition, thereby reducing or avoiding the need to interpolate between nearby measurement points to obtain an estimate of heart tissue condition in an intermediate location.

[0062] At least one of the tip electrode 310 and the electrode band 320 is a mapping electrode which monitors the precise location of the tip assembly 300 in the heart. The mapping electrode may assist in producing a high resolution model that provides actual mapping of heart tissue condition as described above. At least one of the tip electrode 310 and the electrode band 320 may be used to monitor electrical signals at the target site. For example, healthy heart tissue may provide a strong electrical signal that can be detected by one of the tip electrode 310 and the electrode band 320. Dead or diseased heart tissue may provide a weak or non-existent electrical signal. Areas of tissue that are damaged or inflamed may provide an intermediate strength electrical signal. By measuring the strength of the electrical signal generated from the heart tissue, the tip assembly 300 can identify the areas of heart tissue that require treatment, such as by delivery of a therapeutic composition.

[0063] Electrical signals measured by the tip assembly 300 may be transmitted via the tip electrode lead wire 330 and the ring electrode lead wire 332 to a computer system (not shown) which processes the data and displays it to the catheter operator. The computer system may also be in communication with the external cardiac mapping system.

[0064] The electrical signals measured by the tip assembly 300 may also be used to correlate and/or verify the cardiac map produced by the external cardiac mapping system. For example, if the cardiac map indicates that a specific location of the heart should have

a strong electrical signal (indicating healthy tissue), and the tip assembly 300 indicates otherwise, the catheter operator can check that the catheter tip is in the correct location in combination with the location data generated by the tip assembly and/or the cardiac mapping system.

[0065] The catheter 100 provides the advantage of combining or integrating the mapping and treatment functions. Combining the mapping and treatment functions avoids the need to use separate mapping and treatment catheters. This simplifies the procedure for catheter operators, and may reduce the risk of mistakes. The use of a combined mapping and treatment catheter may reduce the amount of the time that the patient is undergoing the procedure, which may improve the patient's experience and wellbeing.

[0066] The tip assembly 300 may be modular. In some embodiments, the tip assembly 300 may be interchangeable to suit different applications. For example, in some embodiments the tip assembly 300 comprises a tip assembly suitable for monitoring and/or treating hypoxia. In some embodiments the tip assembly 300 is used to deliver electrical stimulation to a target site.

[0067] As shown in Fig. 1C, the control handle 400 is configured to be connected to the proximal end 220 of the catheter tube 200 and may be adapted to control the deflection of the distal end 210 of the catheter tube 200. In some embodiments, such as shown in Fig. 4A, the control handle 400 may comprise a head end 401A to which the proximal end 220 of the catheter tube 200 is connected. The control handle 400 may be configured to control the deflection of the distal end 210 of the catheter tube 200 by actuation of pull wires, such as the first pull wire 260 and the second pull wire 280. The actuation of the pull wires may occur through various mechanisms. For example, the actuation of the pull wires may be effected by means of a lever system or pulley system, wherein rotation of a lever or pulley about a fulcrum or pivot applies tension to one or more of the pull wires, thereby deflecting the distal end 210. In some embodiments, rotation or translation of a dial or knob may apply tension to one or more of the pull wires, thereby deflecting the distal end 210. The actuation mechanism used may depend on the configuration of the pull wires as they transition from being in the control handle 400 to the catheter tube. For example, in embodiments where the pull wires 260, 280 move within passages 250, 270 formed in the walls of the catheter tube, the tube wall and/or passages 250, 270 may end forward of the actuation mechanism, such as shown in Fig. 4A, allowing more space for movement of the wires 260, 280 and potentially reducing stresses on the wires 260, 280.

By way of example, an embodiment of the control handle 400 is subsequently described in more detail, wherein the deflection of the distal end 210 is actuated by tensioning of pull wires through a pulley system. However, it will be understood that control handles with other means of controlling deflection of a distal end of a catheter tube, such as described above, may alternatively be used.

[0068] Turning to Fig. 4A, the inside of the control handle 400 is shown. The control handle 400 may comprise a housing 402 that is ergonomically shaped to be comfortable for a user to hold and operate. The housing 402 may comprise a hollow portion. The housing 402 may define a control portion 404 and a handle portion 406. The control handle 400 may further comprise a rocker 408 configured to actuate the first pull wire 260 and the second pull wire 280. The rocker 408 may be rotatably connected to the control portion 404 to allow the rocker 408 to rock fore and aft relative to the handle portion 406, thereby moving the first pull wire 260 and the second pull wire 280.

[0069] The first pull wire 260 and the second pull wire 280 may extend through the first lumen 240 of the catheter tube 200 into the control handle 400. The housing 402 may be split into two parts 402A and 402B, such as shown in Fig. 4B, which is an exploded view of the control handle 400 shown in Fig. 4A. Opening the two housing parts 402A and 402B may facilitate maintenance such as adjusting the tensioning of the first pull wire 260 and the second pull wire 280. The two housing parts 402A and 402B may be secured by screws 403 or by alternative fastening systems such as a snap lock. Similarly, the control portion 404 and a handle portion 406 may also be split into two corresponding parts 404A, 404B and 406A, 406B.

[0070] Continuing to refer to Fig. 4A, in some embodiments, the control handle 400 comprises a first pulley assembly 410 connected to the first pull wire 260, wherein rotation of the first pulley assembly 410 applies tension to the first pull wire 260 to effect the deflection of the distal end 210. The deflection of the distal end 210 may be in the first direction. In some embodiments, the control handle 400 comprises a second pulley assembly 420 connected to the second pull wire 280, wherein rotation of the second pulley assembly 420 applies tension to the second pull wire 280 to effect the deflection of the distal end 210. The deflection of the distal end 210 may be in the second direction.

[0071] The first and second pulley assemblies 410, 420 may directly apply tension to the respective pull wires by pulling on the pull wires 260, 280. The first and second pulley assemblies 410, 420 may each comprise a moment arm arrangement 430. In some

embodiments, the first and second pulley assemblies 410, 420 indirectly apply tension to the respective pull wires 260, 280 via the moment arm arrangement 430 that may magnify the force applied by the user to the respective pull wires 260, 280. The mechanical advantage created by the moment arm arrangement 430 reduces the force required for the user to input. Conversely, the moment arm arrangement 430 may be arranged to create a mechanical disadvantage. This may, for example, mean that a large input at the pulley assembly 410, 420 causes a small deflection of the distal end 210 of the catheter tube 200. This may provide the user with finer control of the movement of the distal end 210 of the catheter tube 200, particularly where small movements of the distal end 210 are required to meet a small target. This may improve flexibility and control for the catheter operator. This may improve safety for the patient.

[0072] In some embodiments, the moment arm arrangement 430 comprises a linkage such as linkage 448 or linkage 450, wherein the linkage 448 or 450 comprises at least one member and at least one pivot about which the member can rotate to exert an output force in response to an input force.

[0073] In some embodiments, the moment arm arrangement 430 comprises a gear system 440. The gear system 440 comprises at least one gear defining a plurality of gear teeth. In some embodiments, the gear system 440 comprises a plurality of the gears. Each of the gears may have a different number of gear teeth, and/or a different gear diameter.

[0074] The gear system 440 provides a moment through the distance between each gear tooth and the gear axis or pivot about which the gear rotates. The linkage 448 or 450 and/or gear system 440 may be configured to proportionally adjust an input force or input movement provided by the user at the first and second pulley assemblies 410, 420. In some embodiments, the moment arm arrangement 430 comprises a linkage 448 or 450 and a gear system 440.

[0075] The rocker 408 may be configured to actuate the pull wires 260, 280 through the moment arm arrangement 430. For example, the rocker 408 may engage the gear system 440 and/or the linkage 448 or 450, which in turn are connected to the pull wires 260, 280.

[0076] The first and second pulley assemblies 410, 420 may be disposed on opposed sides of the control handle 400.

[0077] An example embodiment of the moment arm arrangement 430 will now be described in detail, with specific components of the gear system 440 and the linkage 448, 450 described in relation to their connection with each other.

[0078] Turning to Fig. 4B, in some embodiments, the rocker 408 comprises a disc-shaped body 408A defining a central aperture 408B. The rocker body 408A may comprise a first knob 408C and a second knob 408D. The first knob 408C and a second knob 408D may be disposed along the circumference of the disc-shaped body 408A to protrude therefrom. The rocker body 408A may further define a first arcuate groove 408E and a second arcuate groove 408F. In some embodiments, the first arcuate groove 408E and a second arcuate groove 408F are disposed away from the centre of the disc-shaped body 408A and the central aperture 408B. The first arcuate groove 408E and a second arcuate groove 408F may trace the same circular path. The grooves 408E, 408F may be disposed between the circumference of the disc-shaped body 408A and the central aperture 408B.

[0079] The first arcuate groove 408E receives a first pivot pin 436, while the second arcuate groove 408F receives a second pivot pin 438. The pivot pins 436, 438 are configured to stay in fixed relation with the control portion 404 and/or the handle portion 406. The rocker 408 is configured to rotate relative to the control portion 404 and/or the handle portion 406. The rocker 408 may rotate about a central reference axis 409 that passes through the central aperture 408B. When the rocker 408 rotates, the grooves 408E, 408F move relative to the pivot pins 436, 438. The rocker 408 may rotate in a first direction (for example, clockwise) until the pivot pins 436, 438 abut an extremity of their respective grooves 408E, 408F, thereby preventing further rotation in the first direction. The rocker 408 may rotate in a second direction (for example, anticlockwise) until the pivot pins 436, 438 abut an opposite extremity of their respective grooves 408E, 408F, thereby preventing further rotation in the second direction. Rotation of the rocker 408 may be considered to cause relative travel/translation of the pivot pins 436, 438 in their respective grooves 408E, 408F.

[0080] The rocker 408 engages a gear system 440. The gear system 440 comprises a lever gear 442, a first segment gear 444, and a second segment gear 446. The central aperture 408B of rocker 408 may be shaped to receive and engage the lever gear 442, so that rotation of the rocker 408 also rotates the lever gear 442 about axis 409.

[0081] The first and second segment gears 444, 446 have teeth which engage with teeth on the lever gear 442. Rotating the rocker 408 causes corresponding rotation of the lever gear 442, which thereby causes rotation of the first and second segment gears 444, 446. The first segment gear 444 rotates about the first pivot pin 436 and the second segment gear 446 rotates about the second pivot pin 438.

- [0082] The first segment gear 444 engages with a first pulley or linkage 448. The second segment gear 446 engages with a second pulley or linkage 450. The first and second linkages 448, 450 may be configured to rotate about or along with pivot pins 436, 438 respectively. Alternatively or in combination with pivot pins 436, 438, the segment gears 444, 446 may comprise features which engage with a corresponding feature on the linkages 448, 450 to transmit torque. For example, the segment gears 444, 446 may comprise a ridge that engages a corresponding groove on the linkages 448, 450, so that rotation of the gears 444, 446 causes a corresponding rotation of the linkages 448, 450.
- [0083] The first and second linkages 448, 450 may each rotate about the pivot pins 436, 438 respectively. The first and second linkages 448, 450 may each comprise a wedge or triangular shaped member. The first pull wire 260 may be connected to the linkage 448 distal to the pivot pin 436. The second pull wire 280 may be connected to the linkage 450 distal to the pivot pin 438. Rotation of the linkages 448, 450 may therefore move the first pull wire 260 and the second pull wire 280.
- [0084] The rocker knobs 408C, 408D may facilitate manipulation of the rocker 408 by a user. The rocker knobs 408C, 408D may comprise a textured surface to improve grip. For example, to rotate the rocker 408 clockwise, the rocker knob 408C may be pushed towards the second end 220 of the catheter tube 200 and the rocker knob 408D pulled away from the second end 220 of the catheter tube 200. The second end 220 of the catheter tube 200 may be connected to the control handle 400 by a strain relief 470. In some embodiments, the strain relief 470 is configured to reduce the bending strain on the catheter tube 200 where it meets the control handle 400. The strain relief 470 may be an elongate member that connects the control handle 400 to a length of the catheter tube 200 at the second end 220 to distribute forces over a larger surface area. Bending of the catheter tube 200 at the second end 220 may also bend the strain relief 470. The strain relief 470 may be resiliently deformable, and may comprise an elastic material such as rubber.
- [0085] If rocker 408 is rotated clockwise, the lever gear 442 also rotates clockwise. The clockwise rotation of the lever gear 442 causes an anticlockwise rotation of the segment gears 444, 446. The anticlockwise rotation of the segment gears 444, 446 causes an anticlockwise rotation of the linkages 448, 450. The anticlockwise rotation of the linkage 448 causes a reduction in tension of the first pull wire 260. The anticlockwise rotation of the linkage 450 causes an increase in tension of the second pull wire 280.

- [0086] Conversely, if rocker 408 is rotated anticlockwise, the lever gear 442 also rotates anticlockwise. The anticlockwise rotation of the lever gear 442 causes an clockwise rotation of the segment gears 444, 446. The clockwise rotation of the segment gears 444, 446 causes an clockwise rotation of the linkages 448, 450. The clockwise rotation of the linkage 448 causes an increase in tension of the first pull wire 260. The clockwise rotation of the linkage 450 causes a reduction in tension of the second pull wire 280.
- [0087] The ease of rotation of the rocker 408 may, in some embodiments, be adjusted by a brake 452. The brake 452 is rotatably connected to first control portion 404A and is configured to frictionally engage the first control portion 404A. The frictional engagement may be adjusted by rotating the brake 452. The brake 452 may comprise a knob 454 connected to a plug 456. The knob 454 of the brake 452 may extend through the first housing portion 406A through an aperture 407 in first housing portion 406A. The user can turn the knob 454 to control the frictional engagement of the brake 452. The plug 456 may frictionally engage a surface of the first control portion 404A. The brake 452 may be aligned to rotate about axis 409.
- [0088] The brake 452 is connected to a nut plate 458 via a screw 460 that extends through the first control portion 404A, through the central aperture 408B of the rocker 408, and through a central hole formed in lever gear 442. The first control portion 404A, the rocker 408, and the lever gear 442 are sandwiched between the brake 452 and the nut plate 458. Rotating the brake knob 454 in a first direction tightens the screw 460, reducing the distance between the brake plug 456 and the nut plate 458 and causing increased frictional engagement between the brake plug 456 and the first control portion 404A. Conversely, rotating the brake knob 454 in an opposite second direction loosens the screw 460, increasing the distance between the brake plug 456 and the nut plate 458 and causing reduced frictional engagement between the brake plug 456 and the first control portion 404A. The screws 460 may cooperate with one or more washers 462 to distribute forces over a wider area and/or reduce friction by spacing apart adjoining surfaces.
- [0089] The control handle 400 may comprise a connector 480. The connector 480 is configured to connect to one or more of the electrodes 310, 320 via wire module 490. The wire module 490 may transmit and/or receive signals from the one or more of the electrodes 310, 320. The wire module 490 may supply electrical signals to one or more of the electrodes 310, 320. The wire module 490 may comprise a first wire connected to

the tip electrode 310, such as tip electrode lead wire 330. The wire module 490 may comprise a second wire connected to the electrode band 320, such as the ring electrode lead wire 332. The wire module 490 may be connected to the connector 480 via solder cup pins 482.

[0090] The connector 480 may comprise an adapter 484 configured to encase the connector 480 and the solder cup pins 482. The adapter 484 may engage with inside of the control handle 400. The adapter 484 may comprise a two-part configuration to facilitate access to the solder cup pins 482, such as a first adapter part 484A and a second adapter part 484B. In some embodiments, the adapter 484 defines a groove 486 configured to engage with retaining features 488 in the control handle 400. The connector 480 may be connected to the control handle 400 at a tail end 401B of the control handle 400, wherein the tail end 401B is distal to the head end 401A.

[0091] The control handle 400 and the injection handle 500 may be connected by a tether cable 492. The tether cable 492 may be connected to the tail end 401B. The control handle 400 may receive a needle 510 that extends from the injection handle 500. The needle 510 may enter the control handle 400 through the tether cable 492.

[0092] Fig. 5A shows an embodiment of the injection handle 500. The injection handle 500 is configured to control delivery of the composition through the needle 510. The injection handle 500 may be configured to control the delivery of the composition through translation of the needle 510 within the handle 500. Movement of the needle 510 may be governed by various means. For example, translation of the needle 510 may be effected by means of a lever system or pulley system, wherein rotation of a lever or pulley about a fulcrum or pivot applies an input force to a carriage to cause translation of the needle 510. In some embodiments, rotation or translation of a dial or knob applies an input force to a carriage to cause translation of the needle 510. The injection handle 500 may contain biasing means to provide resistance to the translation of the needle 510 towards the catheter tip. The biasing means may bias the needle away from the catheter tip when the input force is removed. By way of example, an embodiment of the injection handle 500 is subsequently described in more detail, wherein the translation of the needle 510 is effected by a sliding arrangement. However, it will be understood that injection handles with other means of controlling translation of the needle 510, such as described above, may alternatively be used. In some embodiments, such as shown in Fig. 5A, the injection handle 500 comprises a barrel 520 defining a bore 522 extending between a first

end 524 and a second end 526 of the barrel 520. The injection handle 500 may comprise a needle actuator hub 530 configured to receive the needle 510. The needle actuator hub 530 may be connected to the control handle 400 via the tether cable 492. The needle actuator hub 530 may be connected to the first end 524 of the barrel 520. The needle actuator hub 530 may comprise a threaded connection 531 that engages with a corresponding threaded connection 523 inside the bore 522 of the barrel 520 to prevent movement of the needle actuator hub 530 relative to the barrel 520.

[0093] The injection handle 500 may further comprise a piston 540 configured to slide within the bore 522. The injection handle 500 may further comprise a spring 550 configured to resist sliding of the piston 540 towards the first end 524 of the barrel 520. The spring 550 may be disposed in the bore 522. The spring 550 may contact the needle actuator hub 530. As the needle actuator hub 530 may be fixed relative to the barrel, sliding the piston 540 relative to the barrel 520 compresses the spring 550. The needle 510 may be encased within a tube 560 (such as Hypotube) to protect the needle 510 from compression and extension of the spring 550. The piston 540 may be received in the injection handle 500 at the second end 526 of the barrel 520.

[0094] The injection handle 500 is configured to safely retain the needle 510 in the catheter 100, for example during injection. The injection handle 500 may be configured to retract the needle 510 into the tip assembly 300 after delivering a composition. The spring 550 may cause the needle 510 to be retracted into the tip section 300, sheathing the needle 510 and covering the sharp point of the needle. The spring 550 may retract the needle 510 immediately upon release of the actuation force on the piston 540. This improves safety for the patient as the needle tip is not left exposed when the composition is not being delivered.

[0095] The needle assembly 600 is connected to the injection handle 500. In some embodiments, the needle assembly 600 is connected to the piston 540. In some embodiments, the needle assembly 600 is connected to a distal end 541B of the piston 540.

[0096] The needle assembly 600 is configured to deliver the composition to the target site. In some embodiments, the needle assembly 600 comprises a flexible needle 510 extending from a needle hub 610. The needle hub 610 is configured to be connected to the piston 540 of the injection handle 500. The needle 510 may extend through the injection handle 500. When the needle hub 610 is connected to the piston 540, the needle

510 may extend through the control handle 400, through the first lumen 240 of the catheter tube 200, and into the delivery lumen 312 of the tip assembly 300. Sliding of the piston 540 towards the first end of the barrel 520 may cause the needle 510 to extend through the tip assembly 300 to deliver the composition.

[0097] The needle hub 610 is subsequently described in more detail in Figs. 6A-6C.

[0098] Fig. 5B shows an assembled side view of the injection handle 500. Fig. 5C is a section view of the injection handle 500, taken along the line marked in Fig. 5B.

[0099] The needle actuator hub 530 may comprise a body 532 and a spigot 534. The spigot 534 may have a smaller diameter than the body 532 to define a shoulder 536. The spring 550 may abut and sit on the shoulder 536 so that the spigot 534 extends into the spring 550, which may stabilise the spring 550 and encourage it to compress along its longitudinal axis instead of bending or buckling. The spigot 534 defines a contact face 538 that may be abutted by a proximal end 541A of the piston 540, limiting its travel.

[0100] In some embodiments, the injection handle 500 further comprises a needle actuator ring 542 on the piston 540. The needle actuator ring 542 may be configured to provide a grip for the user to move the plunger 540 within the bore 522, for example to inject the composition. The needle actuator ring 542 may be configured to limit the sliding/translation of the piston 540 within the bore 522. This may accordingly limit the amount that the needle 510 may extend beyond the tip assembly 300, which may improve safety for the patient. In some embodiments, the needle actuator ring 542 has a larger diameter than the piston 540, so that as the piston 540 slides within the bore 522 towards the first end 524 of the barrel 520, the needle actuator ring 542 eventually abuts the second end 526 of the barrel 520, preventing further translation of the piston 540.

[0101] The needle actuator ring 542 may be configured to engage with the piston 540 to adjust the travel of the piston 540 within the bore 522. The needle actuator ring 542 may be slid along the piston 540 and locked at a specific point on the piston 540. In some embodiments, the needle actuator ring 542 comprises a threaded portion 544 that is configured to allow the needle actuator ring 542 to rotate along a corresponding thread 546 disposed on the outside of the piston 540. Rotating the needle actuator ring 542 to travel along the piston 540 may shorten or lengthen a distance that the piston 540 is able to slide within the bore 522. A pin 548 may lock the needle actuator ring 542 into a set position along the piston 540.

- [0102] The injection handle 500 may further comprise a groove 570 and pin 572. The groove 570 may be formed on the piston 540. The groove 570 may extend along a length of the piston 540. The pin 572 may be configured to engage with the groove 570 to limit the sliding of the piston 540 within the bore 522 to the length of the groove 570. The pin 572 may be configured to engage with the groove 570 to limit rotation of the piston 540 within the bore 522. The pin 572 may be configured to engage with the groove 570 to resist a spring force exerted by the spring 550 on the piston 540. For example, the pin 572 may abut an extremity of the groove 570, preventing further travel of the piston 540. The groove 570 and the pin 572 may limit the amount that the piston 540 can travel, thereby limiting the amount that the needle 510 may extend beyond the tip assembly 300, which may improve safety for the patient.
- [0103] Fig. 6A is an exploded view of the needle assembly 600. Fig. 6B is a side view of the assembled needle assembly 600. Fig. 6C is a section view of Fig. 6B as taken along the line marked on Fig. 6B.
- [0104] The needle assembly 600 comprises the needle hub 610. The needle assembly 600 may further comprise a first tube 620 extending from the needle hub 610. The needle assembly 600 may further comprise a second tube 630. The second tube 630 is connected to the first tube 620. The second tube 630 may fit within the first tube 620. The needle 510 extends from the hub 610, through the first and second tubes 620, 630. The first and second tubes 620, 630 may reduce in diameter as they extend over the needle 510 to distribute the forces over a greater length the needle 510, in a similar manner to strain relief 470 and its interaction with the catheter tube 200.
- [0105] The needle 510 may extend from the needle hub 610, through the injection handle 500, through the control handle 400, through the catheter tube 200, and into the tip assembly 300. The first pull wire 260 and the second pull wire 280 may be disposed on opposed sides of the needle 510 in the control handle 400. The first and second pull wire 260, 280 may be disposed on opposed sides of the needle 510 in the catheter tube 200.
- [0106] The needle hub 610 may comprise a flange 612 for connecting to a syringe or other fluid source which contains the composition to be delivered using the catheter 100. The needle hub 610 may define a lumen 614 for receiving the composition. The lumen 614 is in fluid communication with the needle 510 for delivery to the target site. The needle hub 610 may comprise a threaded connection 616 to enable secure connection with a corresponding threaded connection of the piston 540. The piston 540 may be

hollow. The threaded connection 616 may be securely connected with the distal end 541B of the piston 540. The needle hub 610 may comprise a shoulder 618 that abuts the distal end 541B of the piston 540 to denote engagement along the full length of the threaded connection 616.

[0107] A needle insert 640 may be provided to facilitate attachment of the syringe to the lumen 614. An outer surface 642 of the needle insert 640 may engage with the inside of the lumen 614 to assist in locating the needle insert 640 relative to the lumen 614.

[0108] Embodiments of the catheter 100 may be provided in assembled or unassembled form. Some embodiments may relate to a kit for a delivery catheter 100 configured to deliver a composition to a target site. The kit may comprise the catheter tube 200, the tip assembly 300, the control handle 400, the injection handle 500, and the needle assembly 600.

Compositions

[0109] Various compositions can be administered using the catheter of the present disclosure. In an example, the composition is a biologic composition. For example, the composition may comprise a population of cells such as a population of mesenchymal precursor lineage cells or soluble factors derived therefrom, and/or extracellular vesicles isolated therefrom under culture conditions.

[0110] As used herein, the term “mesenchymal lineage precursor or stem cell (MLPSC)” refers to undifferentiated multipotent cells that have the capacity to self-renew while maintaining multipotency and the capacity to differentiate into a number of cell types either of mesenchymal origin, for example, osteoblasts, chondrocytes, adipocytes, stromal cells, fibroblasts and tendons, or non-mesodermal origin, for example, hepatocytes, neural cells and epithelial cells. For the avoidance of doubt, a “mesenchymal lineage precursor cell” refers to a cell which can differentiate into a mesenchymal cell such as bone, cartilage, muscle and fat cells, and fibrous connective tissue.

[0111] The term “mesenchymal lineage precursor or stem cells” includes both parent cells and their undifferentiated progeny. The term also includes mesenchymal precursor cells (MPCs), multipotent stromal cells, mesenchymal stem cells (MSCs), perivascular mesenchymal precursor cells, and their undifferentiated progeny.

[0112] MLPSCs can be autologous, allogeneic, xenogenic, syngenic or isogenic. Autologous cells are isolated from the same individual to which they will be reimplanted.

Allogeneic cells are isolated from a donor of the same species. Xenogenic cells are isolated from a donor of another species. Syngenic or isogenic cells are isolated from genetically identical organisms, such as twins, clones, or highly inbred research animal models.

- [0113] In an example, the MLPSCs are allogeneic. In an example, the allogeneic MLPSCs are culture expanded and cryopreserved.
- [0114] MLPSCs reside primarily in the bone marrow, but have also shown to be present in diverse host tissues including, for example, cord blood and umbilical cord, adult peripheral blood, adipose tissue, trabecular bone and dental pulp. They are also found in skin, spleen, pancreas, brain, kidney, liver, heart, retina, brain, hair follicles, intestine, lung, lymph node, thymus, ligament, tendon, skeletal muscle, dermis, and periosteum; and are capable of differentiating into germ lines such as mesoderm and/or endoderm and/or ectoderm. Thus, MLPSCs are capable of differentiating into a large number of cell types including, but not limited to, adipose, osseous, cartilaginous, elastic, muscular, and fibrous connective tissues. The specific lineage-commitment and differentiation pathway which these cells enter depends upon various influences from mechanical influences and/or endogenous bioactive factors, such as growth factors, cytokines, and/or local microenvironmental conditions established by host tissues.
- [0115] The terms “enriched”, “enrichment” or variations thereof are used herein to describe a population of cells in which the proportion of one particular cell type or the proportion of a number of particular cell types is increased when compared with an untreated population of the cells (e.g., cells in their native environment). In one example, a population enriched for MLPSCs comprises at least about 0.1% or 0.5% or 1% or 2% or 5% or 10% or 15% or 20% or 25% or 30% or 50% or 75% MLPSCs. In this regard, the term “population of cells enriched for MLPSCs” will be taken to provide explicit support for the term “population of cells comprising X% MLPSCs”, wherein X% is a percentage as recited herein. The MLPSCs can, in some examples, form clonogenic colonies, e.g. CFU-F (fibroblasts) or a subset thereof (e.g., 50% or 60% or 70% or 70% or 90% or 95%) can have this activity.
- [0116] In an example, MLPSCs of the disclosure are culture expanded from a population of MLPSCs that are STRO-1+. In an example, the MLPSCs are culture expanded from a population of MLPSCs which comprise about 0.1% to 75% STRO-1+ cells. In another example, the MLPSCs are culture expanded from a population of MLPSCs which

comprise about 0.5% to 75% STRO-1+ cells. In another example, the MLPSCs are culture expanded from a population of MLPSCs which comprise about 0.1% to 75% STRO-1+ cells. In another example, the MLPSCs are culture expanded from a population of MLPSCs which comprise about 0.1% to 75% STRO-1+ cells. In another example, the MLPSCs are culture expanded from a population of MLPSCs which comprise about 1% to 75% STRO-1+ cells. In another example, the MLPSCs are culture expanded from a population of MLPSCs which comprise about 0.1% to 75% STRO-1+ cells. In another example, the MLPSCs are culture expanded from a population of MLPSCs which comprise about 10% to 75% STRO-1+ cells.

[0117] In an example of the present disclosure, the MLPSCs are mesenchymal stem cells (MSCs). The MSCs may be a homogeneous composition or may be a mixed cell population enriched in MSCs. Homogeneous MSC compositions may be obtained by culturing adherent marrow or periosteal cells, and the MSCs may be identified by specific cell surface markers which are identified with unique monoclonal antibodies. A method for obtaining a cell population enriched in MSCs is described, for example, in U.S. Patent No. 5,486,359. Alternative sources for MSCs include, but are not limited to, blood, skin, cord blood, muscle, fat, bone, and perichondrium. In an example, the MSCs are allogeneic. In an example, the MSCs are cryopreserved. In an example, the MSCs are culture expanded and cryopreserved.

[0118] In another example, the MLPSCs are CD29+, CD54+, CD73+, CD90+, CD102+, CD105+, CD106+, CD166+, MHC1+ MSCs.

[0119] Isolated or enriched MLPSCs can be expanded *in vitro* by culture. Isolated or enriched MLPSCs can be cryopreserved, thawed and subsequently expanded *in vitro* by culture.

[0120] In one example, isolated or enriched MLPSCs are seeded at 50,000 viable cells/cm² in culture medium (serum free or serum-supplemented), for example, alpha minimum essential media (α MEM) supplemented with 5% fetal bovine serum (FBS) and glutamine, and allowed to adhere to the culture vessel overnight at 37°C, 20% O₂. The culture medium is subsequently replaced and/or altered as required and the cells cultured for a further 68 to 72 hours at 37°C, 5% O₂.

[0121] As will be appreciated by those of skill in the art, cultured MLPSCs are phenotypically different to cells *in vivo*. For example, in one embodiment they express one or more of the following markers, CD44, NG2, DC146 and CD140b. Cultured

MLPSCs are also biologically different to cells *in vivo*, having a higher rate of proliferation compared to the largely non-cycling (quiescent) cells *in vivo*.

[0122] In one example, the population of cells is enriched from a cell preparation comprising STRO-1+ cells in a selectable form. In this regard, the term “selectable form” will be understood to mean that the cells express a marker (e.g., a cell surface marker) permitting selection of the STRO-1+ cells. The marker can be STRO-1, but need not be. For example, as described and/or exemplified herein, cells (e.g., mesenchymal precursor cells (MPCs)) expressing STRO-2 and/or STRO-3 (TNAP) and/or STRO-4 and/or VCAM-1 and/or CD146 and/or 3G5 also express STRO-1 (and can be STRO-1bright). Accordingly, an indication that cells are STRO-1+ does not mean that the cells are selected solely by STRO-1 expression. In one example, the cells are selected based on at least STRO-3 expression, e.g., they are STRO-3+ (TNAP+). For example, the MPCs can be isolated from bone mononuclear cells with an anti-STRO-3 antibody.

[0123] Reference to selection of a cell or population thereof does not necessarily require selection from a specific tissue source. As described herein STRO-1+ cells can be selected from or isolated from or enriched from a large variety of sources. That said, in some examples, these terms provide support for selection from any tissue comprising STRO-1+ cells (e.g., mesenchymal precursor cells) or vascularized tissue or tissue comprising pericytes (e.g., STRO-1+ pericytes) or any one or more of the tissues recited herein.

[0124] In one example, the cells used in the present disclosure express one or more markers individually or collectively selected from the group consisting of TNAP+, VCAM-1+, THY-1+, STRO-2+, STRO-4+ (HSP-90β), CD45+, CD146+, 3G5+ or any combination thereof.

[0125] By "individually" is meant that the disclosure encompasses the recited markers or groups of markers separately, and that, notwithstanding that individual markers or groups of markers may not be separately listed herein the accompanying claims may define such marker or groups of markers separately and divisibly from each other.

[0126] By "collectively" is meant that the disclosure encompasses any number or combination of the recited markers or groups of markers, and that, notwithstanding that such numbers or combinations of markers or groups of markers may not be specifically listed herein the accompanying claims may define such combinations or sub-

combinations separately and divisibly from any other combination of markers or groups of markers.

[0127] As used herein the term "TNAP" is intended to encompass all isoforms of tissue non-specific alkaline phosphatase. For example, the term encompasses the liver isoform (LAP), the bone isoform (BAP) and the kidney isoform (KAP). In one example, the TNAP is BAP. In one example, TNAP as used herein refers to a molecule which can bind the STRO-3 antibody produced by the hybridoma cell line deposited with ATCC on 19 December 2005 under the provisions of the Budapest Treaty under deposit accession number PTA-7282.

[0128] Furthermore, in one example, the STRO-1+ cells are capable of giving rise to clonogenic CFU-F.

[0129] In one example, a significant proportion of the STRO-1+ cells are capable of differentiation into at least two different germ lines. Non-limiting examples of the lineages to which the STRO-1+ cells may be committed include bone precursor cells; hepatocyte progenitors, which are multipotent for bile duct epithelial cells and hepatocytes; neural restricted cells, which can generate glial cell precursors that progress to oligodendrocytes and astrocytes; neuronal precursors that progress to neurons; precursors for cardiac muscle and cardiomyocytes, glucose-responsive insulin secreting pancreatic beta cell lines. Other lineages include, but are not limited to, odontoblasts, dentin-producing cells and chondrocytes, and precursor cells of the following: retinal pigment epithelial cells, fibroblasts, skin cells such as keratinocytes, dendritic cells, hair follicle cells, renal duct epithelial cells, smooth and skeletal muscle cells, testicular progenitors, vascular endothelial cells, tendon, ligament, cartilage, adipocyte, fibroblast, marrow stroma, cardiac muscle, smooth muscle, skeletal muscle, pericyte, vascular, epithelial, glial, neuronal, astrocyte and oligodendrocyte cells.

[0130] In an example, MLPSCs are obtained from a single donor, or multiple donors where the donor samples or MLPSCs are subsequently pooled and then culture expanded.

[0131] MLPSCs encompassed by the present disclosure may also be cryopreserved prior to administration to a subject. In an example, MLPSCs are culture expanded and cryopreserved prior to administration to a subject.

[0132] In an example, the present disclosure encompasses MLPSCs as well as progeny thereof, soluble factors derived therefrom, and/or extracellular vesicles isolated therefrom. In another example, the present disclosure encompasses MLPSCs as well as

extracellular vesicles isolated therefrom. For example, it is possible to culture expand MLPSCs of the disclosure for a period of time and under conditions suitable for secretion of extracellular vesicles into the cell culture medium. Secreted extracellular vesicles can subsequently be obtained from the culture medium for use in therapy.

[0133] The term “extracellular vesicles” as used herein, refers to lipid particles naturally released from cells and ranging in size from about 30 nm to as large as 10 microns, although typically they are less than 200 nm in size. They can contain proteins, nucleic acids, lipids, metabolites, or organelles from the releasing cells (e.g., mesenchymal stem cells; STRO-1⁺ cells).

[0134] The term “exosomes” as used herein, refers to a type of extracellular vesicle generally ranging in size from about 30 nm to about 150 nm and originating in the endosomal compartment of mammalian cells from which they are trafficked to the cell membrane and released. They may contain nucleic acids (e.g., RNA; microRNAs), proteins, lipids, and metabolites and function in intercellular communication by being secreted from one cell and taken up by other cells to deliver their cargo.

[0135] The term “culture conditions” is used to refer to cells growing in culture. In an example, culture conditions refers to an actively dividing population of cells. Such cells may, in an example, be in exponential growth phase. In an example, the cells may be in a stationary phase. In an example, soluble factors and/or extracellular vesicles obtained from cells growing under culture conditions are obtained after at least two or three days in culture. In another example, the soluble factors and/or extracellular vesicles are obtained after about 30 to 84 hours of co-culture.

[0136] Other examples of biologic compositions include gene therapy products. In the context of the present disclosure, such products function by transfer of genetic materials into cells, for example cells in the heart of a subject to be treated. It will be appreciated by those of skill in the art that such products may be provided in their own delivery system such as a cell population, liposome or the like.

[0137] It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the above-described embodiments, without departing from the broad general scope of the present disclosure. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

[0138] The present application claims priority from US63/587,583 filed 3 October 2023, the disclosures of which are incorporated herein by reference.

- [0139]** All publications discussed and/or referenced herein are incorporated herein in their entirety.
- [0140]** Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present disclosure. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present disclosure as it existed before the priority date of each claim of this application.

CLAIMS:

1. A delivery catheter configured to deliver a composition to a target site, the catheter comprising:
 - a catheter tube, defining:
 - a first lumen extending between a proximal end and a distal end of the catheter tube, wherein the catheter tube comprises a flexible portion configured to enable deflection of the distal end relative to the proximal end;
 - a first passage in a wall of the tube, the first passage containing a first pull wire configured to effect, in a first direction, the deflection of the distal end;
 - a second passage in the wall of the tube, the second passage containing a second pull wire configured to effect, in a second direction, the deflection of the distal end;
 - a tip assembly connected to the distal end of the catheter tube, the tip assembly comprising a tip electrode and an electrode band, wherein the tip electrode defines a delivery lumen connected to the first lumen of the catheter tube;
 - a control handle for controlling the deflection of the distal end of the catheter tube, the control handle connected to the proximal end of the catheter tube;
 - an injection handle for controlling delivery of the composition, the injection handle connected to the control handle and comprising:
 - a barrel defining a bore extending between a first end and a second end of the barrel;
 - a piston configured to slide within the bore;
 - a spring disposed in the bore and configured to resist sliding of the piston towards the first end of the barrel;
 - a needle assembly comprising a flexible needle extending from a needle hub, the needle extending: (i) through the injection handle; (ii) through the control handle; (iii) through the first lumen of the catheter tube; and (iv) into the delivery lumen of the tip assembly;
- wherein the needle hub is connected to the piston of the injection handle, such that the sliding of the piston towards the first end of the barrel causes the needle to extend through the tip assembly to deliver the composition; and

wherein the injection handle is configured to retract the flexible needle into the tip assembly after delivering the composition.

2. The catheter of claim 1, wherein the control handle comprises:
 - a first pulley assembly connected to the first pull wire, wherein rotation of the first pulley assembly applies tension to the first pull wire to effect the deflection of the distal end in the first direction; and
 - a second pulley assembly connected to the second pull wire, wherein rotation of the second pulley assembly applies tension to the second pull wire to effect the deflection of the distal end in the second direction;
3. The catheter of claim 1 or claim 2, wherein the first and second passages are disposed at opposed radial locations along the wall of the tube.
4. The catheter of any one of claims 1 to 3, wherein the wall of the tube comprises: (i) a first ridge extending from the wall of the tube into the first lumen to define the first passage; and (ii) a second ridge extending from the wall of the tube into the first lumen to define the second passage.
5. The catheter of any one of claims 1 to 4, wherein the first direction and the second direction are opposed directions for the deflection of the distal end.
6. The catheter of any one of claims 1 to 5, wherein:
 - the deflection of the distal end in the first direction causes the flexible portion of the catheter tube to have a first radius of curvature;
 - the deflection of the distal end in the second direction causes the flexible portion of the catheter tube to have a second radius of curvature;
 - wherein the first and second radius of curvature are not equal.
7. The catheter of any one of claims 1 to 6, wherein the delivery lumen is centrally disposed in the tip assembly.

8. The catheter of claim 2, or of any one of claims 3 to 7 when dependent on claim 2, wherein the first and second pulley assembly comprises a moment arm arrangement configured to: (i) magnify; or (ii) reduce; the tension respectively applied to the first and second pull wire to effect the deflection of the distal end.
9. The catheter of claim 8, wherein the moment arm arrangement comprises: (i) a linkage; or (ii) a gear system; or (iii) a linkage and a gear system.
10. The catheter of claim 2, or of any one of claims 3 to 9 when dependent on claim 2, wherein the first and second pulley assembly are disposed on opposed lateral sides of the control handle.
11. The catheter of any one of claims 1 to 10, wherein the first and second pull wire are disposed on opposed sides of the needle in the control handle.
12. The catheter of any one of claims 1 to 11, wherein the first and second pull wire are disposed on opposed sides of the needle in the catheter tube.
13. The catheter of any one of claims 1 to 12, wherein the injection handle further comprises a rotatable needle actuator ring on the piston, wherein the rotatable needle actuator ring is configured to limit the sliding of the piston within the bore.
14. The catheter of claim 13, wherein rotation of the rotatable needle actuator ring is configured to cause the rotatable needle actuator ring to travel along the piston to shorten or lengthen a distance that the piston is able to slide within the bore.
15. The catheter of claim 13 or claim 14, wherein the injection handle further comprises a groove and pin, the groove formed on the piston, and the pin configured to engage with the groove to: (i) limit the sliding of the piston within the bore; and/or (ii) limit rotation of the piston within the bore.

16. The catheter of claim 15, wherein the pin is configured to engage with the groove to resist a spring force exerted by the spring on the piston.
17. A delivery catheter configured to deliver a composition to a target site, the catheter comprising:
- a catheter tube, defining:
 - a first lumen extending between a proximal end and a distal end of the catheter tube, wherein the catheter tube comprises a flexible portion configured to enable deflection of the distal end relative to the proximal end;
 - a first passage in a wall of the tube, the first passage containing a first pull wire configured to effect, in a first direction, the deflection of the distal end;
 - a second passage in the wall of the tube, the second passage containing a second pull wire configured to effect, in a second direction, the deflection of the distal end;
 - a tip assembly connected to the distal end of the catheter tube, the tip assembly comprising a tip electrode and an electrode band, wherein the tip electrode defines a delivery lumen connected to the first lumen of the catheter tube;
 - a control handle for controlling the deflection of the distal end of the catheter tube, the control handle connected to the proximal end of the catheter tube;
 - an injection handle for controlling delivery of the composition;
 - a needle assembly connected to the injection handle and comprising a flexible needle extending from a needle hub, the needle extending: (i) through the injection handle; (ii) through the control handle; (iii) through the first lumen of the catheter tube; and (iv) into the delivery lumen of the tip assembly to deliver the composition;
 - wherein the injection handle is configured to retract the flexible needle into the tip assembly after delivering the composition.
18. A delivery catheter configured to deliver a composition to a target site, the catheter comprising:
- a catheter tube, defining:

a first lumen extending between a proximal end and a distal end of the catheter tube, wherein the catheter tube comprises a flexible portion configured to enable deflection of the distal end relative to the proximal end;

a first pull wire configured to effect, in a first direction, the deflection of the distal end;

a second pull wire configured to effect, in a second direction, the deflection of the distal end;

a tip assembly connected to the distal end of the catheter tube, the tip assembly comprising a tip electrode and an electrode band, wherein the tip electrode defines a delivery lumen connected to the first lumen of the catheter tube;

a control handle for controlling the deflection of the distal end of the catheter tube, the control handle connected to the proximal end of the catheter tube and comprising:

a first pulley assembly connected to the first pull wire, wherein rotation of the first pulley assembly applies tension to the first pull wire to effect the deflection of the distal end in the first direction; and

a second pulley assembly connected to the second pull wire, wherein rotation of the second pulley assembly applies tension to the second pull wire to effect the deflection of the distal end in the second direction;

an injection handle for controlling delivery of the composition;

a needle assembly connected to the injection handle and comprising a flexible needle extending from a needle hub, the needle extending: (i) through the injection handle; (ii) through the control handle; (iii) through the first lumen of the catheter tube; and (iv) into the delivery lumen of the tip assembly to deliver the composition;

wherein the injection handle is configured to retract the flexible needle into the tip assembly after delivering the composition.

19. A delivery catheter configured to deliver a composition to a target site, the catheter comprising:

a catheter tube defining a first lumen extending between a proximal end and a distal end of the catheter tube, wherein the catheter tube comprises a flexible portion configured to enable deflection of the distal end relative to the proximal end;

a tip assembly connected to the distal end of the catheter tube, the tip assembly comprising a tip electrode and an electrode band, wherein the tip electrode defines a delivery lumen connected to the first lumen of the catheter tube;

a control handle for controlling the deflection of the distal end of the catheter tube, the control handle connected to the proximal end of the catheter tube;

an injection handle for controlling delivery of the composition, the injection handle connected to the control handle and comprising:

a barrel defining a bore extending between a first end and a second end of the barrel;

a piston configured to slide within the bore;

a spring disposed in the bore and configured to resist sliding of the piston towards the first end of the barrel;

a needle assembly comprising a flexible needle extending from a needle hub, the needle extending: (i) through the injection handle; (ii) through the control handle; (iii) through the first lumen of the catheter tube; and (iv) into the delivery lumen of the tip assembly;

wherein the needle hub is connected to the piston of the injection handle, such that the sliding of the piston towards the first end of the barrel causes the needle to extend through the tip assembly to deliver the composition; and

wherein the injection handle is configured to retract the flexible needle into the tip assembly after delivering the composition.

20. A kit for a delivery catheter configured to deliver a composition to a target site, the kit comprising:

a catheter tube;

a tip assembly configured to be connected to a distal end of the catheter tube;

a control handle for controlling deflection of the distal end of the catheter tube, the control handle configured to be connected to a proximal end of the catheter tube;

an injection handle for controlling delivery of the composition, the injection handle configured to be connected to the control handle; and

a needle assembly for delivering the composition through a flexible needle extending from the tip assembly, the needle assembly configured to be connected to the injection handle;

wherein the catheter tube is the catheter tube of claim 1.

21. A kit for a delivery catheter configured to deliver a composition to a target site, the kit comprising:
- a catheter tube;
 - a tip assembly configured to be connected to a distal end of the catheter tube;
 - a control handle for controlling deflection of the distal end of the catheter tube, the control handle configured to be connected to a proximal end of the catheter tube;
 - an injection handle for controlling delivery of the composition, the injection handle configured to be connected to the control handle; and
 - a needle assembly for delivering the composition through a flexible needle extending from the tip assembly, the needle assembly configured to be connected to the injection handle;
- wherein the control handle is the control handle of claim 1.
22. A kit for a delivery catheter configured to deliver a composition to a target site, the kit comprising:
- a catheter tube;
 - a tip assembly configured to be connected to a distal end of the catheter tube;
 - a control handle for controlling deflection of the distal end of the catheter tube, the control handle configured to be connected to a proximal end of the catheter tube;
 - an injection handle for controlling delivery of the composition, the injection handle configured to be connected to the control handle; and
 - a needle assembly for delivering the composition through a flexible needle extending from the tip assembly, the needle assembly configured to be connected to the injection handle;
- wherein the injection handle is the injection handle of claim 1; and
- wherein the needle assembly the needle assembly of claim 1.

23. The delivery catheter of any one of claims 1 to 19, or the kit for a delivery catheter of any one of claims 20 to 22, wherein the delivery catheter is configured to deliver: (i) a cell composition; or (ii) gene therapy.
24. The steps, features, integers, compositions and/or compounds disclosed herein or indicated in the specification of this application individually or collectively, and any and all combinations of two or more of said steps or features.